

14 Braid Hills Road.

Edinburgh.
March 22nd 1913.

The Dean.
Faculty of Medicine
University of Edinburgh.

Sir,

I have the honour to submit herewith my thesis
for the degree of "M. D. or" "The action & uses of
Salvarsan".

I have inserted a reprint of a paper, from the Journal
of the Royal Army Medical Corps for March 1913, on
"Some Observations on the Pathology of Dimerate
Snake and Ant." This is an epitome of some work
done by me in 1910.

I have the honour to be

Sir

Your obedient servant
J. J. Harper Nelson.

M. B., Ch. B.

Captain. I. M. S.

Decl. in
thesis
1910. J. H. S.

DECLARATION

I hereby declare that the whole of the work
of this Thesis was per-
formed by myself and by no one else in the
University of Edinburgh.

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THESIS for M.D. DEGREE 1913

on

The ACTION and USES of SALVARSAN

by

JOHN JOSEPH HARPER NELSON

M.B., Ch.B. (1907, with First Class Honours)

Captain, Indian Medical Service.

L.B.
John Joseph Harper Nelson
Captain, Indian Medical Service



DECLARATION

I hereby declare that the whole of the work forming the subject matter of this Thesis was performed by myself, unassisted by anyone either in the making of observations or in recording them, during the interval between May 1911 and December 1912 whilst holding the appointment of Officer in Charge Brigade Laboratory, Bangalore, India.

Action on the Skin	23
Do. on the Mucous Membranes	24
Do. on Gust	
Do. on Circ	
Do. on Perf	
Do. on Prog	
Do. on the	
Do. on the	
Bangalore, India,	40
December 1912.	53
Do. on the Specific Index	67
Do. on the Red Blood Corpuscles	70
Do. on Coagulation time of Blood	76
Do. on the Nervous System	80
Do. on Urinary System	92
Do. on Metabolism	98
Elimination	

I N D E X

	<u>Page</u>
Introduction - - -	1
Chemistry of Salvarsan - - -	4
Preparation of Solution for Injection	6
Apparatus used - - -	7
Dosage - - -	11
Diagnosis of Cases - - -	13
Preparation of Patient for Injection	18
Effects following the Injection -	19
Action on the Skin - - -	23
Do. on the Mucous Membranes -	24
Do. on Gastro-intestinal Track -	24
Do. on Circulation - - -	28
Do. on Perfusion of Vessels -	28
Do. on Frog's Heart - - -	32
Do. on the Pulse - - -	36
Do. on the Blood Pressure -	42
Do. on the Blood - - -	46
Do. on the Leucocytes - - -	53
Do. on the Opsonic Index -	67
Do. on the Red Blood Corpuscles	70
Do. on Coagulation time of Blood	75
Do. on the Nervous System -	80
Do. on Urinary System - - -	92
Do. on Metabolism - - -	95
Elimination /	

	<u>Page</u>
Elimination of Salvarsan -	97
Therapeutic Effects -	99
Do. do. in Syphilis -	101
Primary -	102
Secondary -	107
Tertiary -	116
Do. do. in Lupus Vulgaris	124
Do. do. in Malaria -	128
Do. do. in Piroplasma Canis	131
Summary of Thesis - -	140
Bibliography - -	145
Appendix - Extracts from Case Sheets.	

INTRODUCTION

During the past twenty months I have had the opportunity of making a close study with regard to the actions and uses of Salvarsan in the treatment of 34 Syphilitic and 2 non-syphilitic cases. In addition I have used the drug in the treatment of four wire-haired Irish terriers suffering from Piroplasma Canis.

It is my purpose to attempt, as the result of personal observation, to explain the effect of Salvarsan with reference to its pharmacological action on the body, and also to consider its uses as a therapeutic agent.

I have been considerably handicapped in many ways in making my observations and deducing the true nature of their meaning.

In the first place one has had to work single-handed, with no skilled person to advise or criticise one's work. Secondly; one has been very much hampered for want of literature to refer to for corroboration of one's results or for guidance in relation to what has or has not been done with reference to the pharmacological action and uses of the drug. Thirdly; the laboratory in which all my work has been carried out /

out is small and poorly equipped, with the result that graphic records have been impossible to make.

On the other hand I have had certain advantages in that all my cases have been soldiers who are well disciplined, well fed, and live under good conditions. Further; they are always at one's disposal for purposes of observation and in consequence it has been possible to watch very closely the action of Salvarsan both in relation to its toxic effects and therapeutic uses.

My Thesis, therefore, falls naturally into two main parts. The first is the pharmacological study of its action. The second is a study of its therapeutic uses as observed by myself; that is to say, I have only entered into a consideration of its uses in conditions treated by me, so that all deductions made are the result of personal observation and experience.

As an Appendix I have inserted epitomised Case Sheets for reference. Each Case Sheet has attached a Chart which I had printed for readily recording certain facts and for easy reference to them afterwards without having to wade through copious notes to obtain one's facts. The 86 Cases studied have all been treated by the intravenous method of administering the drug, which /

which I began to use in May 1911. Prior to this, from October 1910, I had been treating cases by intramuscular injections but with not too satisfactory results. None of these cases have been included in my present series unless subsequently treated by an intravenous injection.

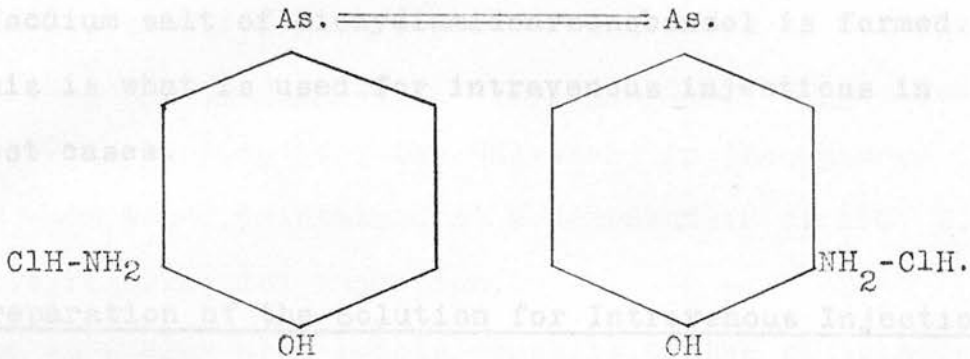
Chemistry of Salvarsan

The foundation on which Salvarsan has been built up was laid when Ehrlich and Bertheim recognised the constitution of atoxyl. Atoxyl was previously thought to be an anilido derivative of arsenic acid, but these investigators proved that it was the sodium salt of Para-amido-phenylarsenic acid. This is a very active substance and is capable of forming numerous synthetic compounds. By diazotosing, para-amido-phenylarsenic acid becomes converted into para-oxyphenylarsenic acid and the latter by nitration and reduction gives rise to meta-amido-para-oxyphenylarseneous oxide. The condensation of two molecules of this gives dioxydiamido-arsenobenzol the dihydrochloride of which is Salvarsan.

Ehrlich thus points out that though the two substances, atoxyl and Salvarsan, are related, their relationship is a distant one. He points out the 'parasitotrophic' importance of the unsaturated trivalent arsenic, such as we have in the formula for "606", as compared with the pentavalent compounds, such as we have in the formula for atoxyl and also the para-position of the hydroxyl group in Salvarsan. This position of the OH is co-related with a high spirillicidal action. The placing of the amido group /

group in the ortho position to the OH group was found to increase the therapeutic efficiency to a maximum.

Salvarsan is the dihydrochloride of dioxydiamidoarsenobenzol. It is a pale yellow powder readily soluble in hot normal saline solution or hot water. It has the following formula :



It is a very easily oxidised substance and is issued in hermetically sealed glass capsules in vacuo or containing some inert gas. When oxidised it forms poisonous compounds. It contains 34.15 per cent of arsenic. The base, dioxydiamidoarsenobenzol, is a yellow powder insoluble in water but dissolves on the addition of an alkali. It is said to contain 40.96 per cent of arsenic.

When the dihydrochloride, Salvarsan, is dissolved in water it forms a pale yellow strongly acid solution. On the addition of sufficient $\frac{N}{1}$ caustic soda solution to neutralise the acidity, the insoluble base is precipitated as a flocculent deposit. If only half /

half the amount of NaOH to do this be added to the solution, the mono-hydrochloride of dioxydiamido-arsenobenzol is formed.

If, however, sufficient NaOH is added to redissolve the precipitated base the hydrogen atoms of the phenol hydroxyls become replaced by sodium and the disodium salt of dioxydiamidoarsenobenzol is formed. This is what is used for intravenous injections in most cases.

Preparation of the Solution for Intravenous Injection

In all my cases the following method of preparing the Salvarsan has been adopted.

Freshly distilled water is prepared on the morning of the injection and with it .85% normal saline solution is made and sterilised. The normal saline to be used is therefore perfectly fresh.

Into a sterile glass beaker 100 c.c's of warm freshly distilled sterile water is measured. The Salvarsan capsule is then opened and the salt dissolved by gradually adding ^{it to the} distilled water, stirring vigorously all the time with a glass rod. I have found that by adding the powder in this way solution is more rapidly effected than by adding the whole of the powder to the water at the one time. When the whole /

whole of the salt has been dissolved 140 c.c's of warm .85% normal saline solution is added, the bulk thus being made up to 240 c.c's. From a burette normal caustic soda is run into this solution until the precipitated base is redissolved. The amount of NaOH required is about 4.2 c.c's. Each 40 c.c's of this solution then contains .1 grammes of Salvarsan so that the dose to be given can readily be measured. The vessel containing the Salvarsan is then placed in warm water, maintained at a temperature of 110° F., till required for injection.

The Apparatus used : This consists of two containers of a capacity of 250 c.c's. each and graduated in 10 c.c's. One of these containers is used for normal saline solution and the other for Salvarsan. These receptacles are suspended from an adjustable stand which can be raised or lowered as required and the pressure in the containers thus altered at will. From the bottom of each container a piece of rubber tubing 9 inches long is led to a glass Y-piece. The rubber leading from the Salvarsan container is divided and a piece of glass tubing, to act as a window, is used to unite the cut ends. On both of these tubes clips are placed near the Y-piece. From the lower end of the Y-piece four feet of rubber tubing is /

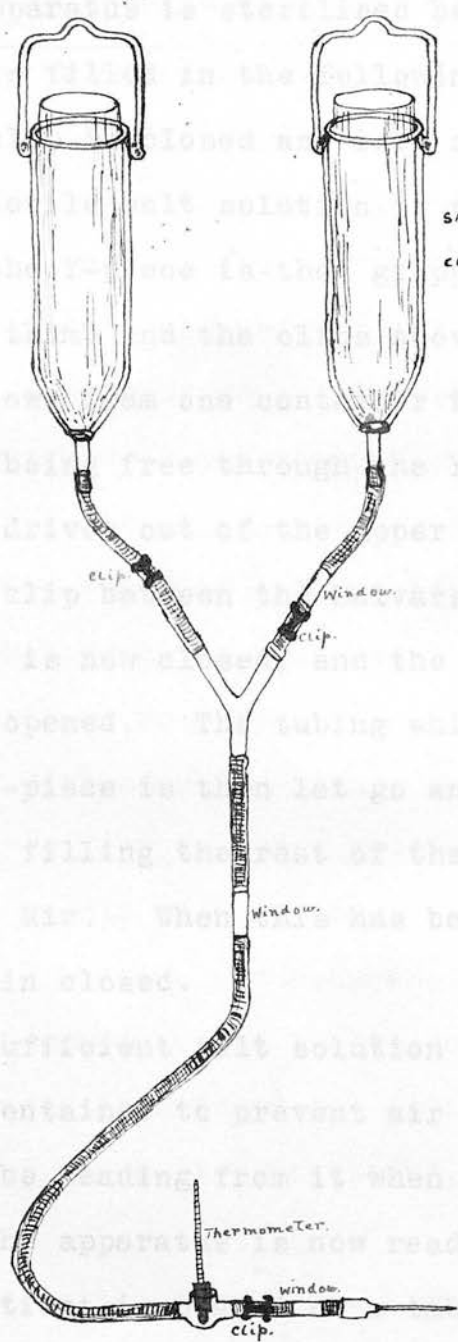
is attached, to the distal end of which a needle can be fixed. This tubing has a short glass window about half way down. Six inches from the needle a glass expansion is let in into which the bulb of a mercurial thermometer is passed. This thermometer indicates the temperature of the solution just before it enters the vein selected for the injection. By coiling the four feet of tubing in a basin of hot water it is an easy matter to maintain a temperature of 100° F., as indicated by the thermometer. If the temperature is rising above this limit some of the tubing is removed from the basin, if it is falling more tubing is added to the basin.

Between the thermometer and base of the hypodermic needle used for entering the vein another small glass window is let in. The object of this is to enable one to tell at once if the vein has been entered. As soon as the needle passes into the lumen of the selected vein blood passes up into the tubing and can be seen through this window. If the needle misses the vein and enters the surrounding tissues no blood regurgitates. A spring clip is placed between the thermometer and this bottom window. I find a coarse hypodermic needle with a sharp point the best kind to use for entering the vein.

The apparatus is sterilized before use by boiling. It is filled in the following manner. The lowermost portion of each of the containers are held up to the level of the normal saline container. The tub-

NORMAL SALINE CONTAINER.

SALVARSAN. CONTAINER.



finger and the thumb and the clips have opened. Salt solution flows from one container to the other, communication being free through the Y-piece. In this way air is driven out of the upper part of the apparatus. The clip between the saline container and the Y-piece is now closed and the bottom clip near the needle opened. The tubing which was gripped below the Y-piece is then let go and salt solution passes down filling the rest of the apparatus and expelling all air. When this has been done the lower clip is again closed.

Only sufficient salt solution is left in the salvarsan container to prevent air bubbles passing into the tube leading from it when the container is filled. The apparatus is now ready for use.

The patient is placed in the recumbent position, and a vein in one of his arms selected for the injection. I usually make use of one of the superficial veins, about an inch or two out of the elbow joint. If none large enough can be found the median basilic or median cephalic can usually be felt through the skin and entered.

Sketch of Apparatus.

daying /

The apparatus is sterilised before use by boiling. It is filled in the following manner. The lowermost clip is closed and into one of the containers warm sterile salt solution is poured. The tubing below the Y-piece is then gripped between the finger and thumb and the clips above opened. Salt solution flows from one container to the other, communication being free through the Y-piece. In this way air is driven out of the upper part of the apparatus. The clip between the Salvarsan container and the Y-piece is now closed, and the bottom clip near the needle opened. The tubing which was gripped below the Y-piece is then let go and salt solution passes down filling the rest of the apparatus and expelling all air. When this has been done the lower clip is again closed. One can generally feel the

Only sufficient salt solution is left in the Salvarsan container to prevent air bubbles passing into the tube leading from it when the container is filled. The apparatus is now ready for use.

The patient is placed on a table, in the recumbent position, and a vein in one of his arms selected for the injection. I usually make use of one of the superficial veins below and in front of the elbow joint. If none large enough can be found the median basilic or median cephalic can usually be felt through the skin and entered.

Having /

Having selected a vein the skin is painted with tincture of iodine. An assistant then applies pressure by gripping the upper arm firmly with his two hands and the patient is made to open and close his hand several times. The contraction of the muscles forces blood out into the veins which then become prominent. A tourniquet or elastic band may be used to apply pressure to the upper arm but I have always found the hands of an assistant satisfactory for this purpose. The veins of natives of India are much more difficult to enter than are those of Europeans as they cannot be so easily seen.

Having distended the vein a few drops of saline are allowed to flow from the needle to displace any air and the needle is then thrust sharply through the skin into the vein. One can generally feel the needle enter the lumen of the vessel and doubt is soon removed as to whether one is in or not by the appearance of blood, if successful, in the lower window.

As soon as the vessel has been entered pressure above is relaxed and about 10 c.c's. of normal saline run in. If the vessel has been perforated or missed a swelling begins to form at the site of injection under the skin.

Having /
 this amount in the course of a fortnight or three weeks. In only very few cases have more than two injections been required.

Having been assured that the vein has been entered the Salvarsan is poured into its container and the clip on the tubing leading from it to the Y-piece opened, the clip on the saline side being at the same time closed.

The Salvarsan then runs into the vein and the rate of flow can be regulated by raising or lowering the height of the container. The Salvarsan is allowed to flow down until it comes to the window in the tubing between its container and the Y-piece, when it is shut off and saline turned on. Sufficient saline is then run through to wash out the Salvarsan from the tubing below - usually about 20 c.c.'s is required to do this. The lowermost clip is then closed and the needle withdrawn, a dressing being applied if necessary. The injection usually takes about 11 minutes to complete.

Dosage

In nearly every case I have used .5 grammes for intravenous injection. In one or two cases I have given the full dose of .6 grammes, but the reaction following has been sufficiently severe to make one somewhat afraid of so great a dose.

The present position adopted by me is to give .5 grammes and repeat this amount in the course of a fortnight or three weeks. In only very few cases have more than two injections been required.

The /

The question of repeating a dose has been always determined by, (a) noting the effect on the clinical signs of the disease, and (b) by noting the results of the Wassermann reaction. No Mercury has been given in most of my cases.

lesions present, and

(2) The Wassermann reaction, as modified by Hecht-Flewing.

(1) With regard to the finding of the *Tropomana Pallidum*, the Indian ink method suggested by Hellere in 1909, and first utilized by Beak and Volenko⁴⁸, has been used. Serum is obtained from primary sores, mucous patches, and papular eruptions, by first cleaning the surface then scraping with a scalpel and when bleeding has ceased swabbing with ethylated spirit. Clear serum is in this way obtained in sufficient quantity to draw up in a capillary tube. Grunther and Wagner's Indian ink was used by me, and is mixed with the serum in equal parts. A drop of the mixture is then deposited on a slide and a film made in the usual way, by spreading with another slide held at an angle. This method of determining the presence of the *tropomana pallida* I found to be easier and more reliable than by using Geimess or Leishman's methods.

Diagnosis of Cases.

In selecting cases of venereal infection for treatment one has relied almost wholly on two diagnostic tests :

- (1) The finding of the Treponema Pallidum in the lesions present, and
- (2) The Wassermann reaction, as modified by Hecht-Fleming.

(1) With regard to the finding of the Treponema

Pallidum, the Indian Ink method suggested by Hellers in 1909, and first utilised by Hecht and Welenko³⁴, has been used. Serum is obtained from primary sores, mucous patches, and papular eruptions, by first cleaning the surface then scraping with a scalpel and when bleeding has ceased swabbing with methylated spirit. Clear serum is in this way obtained in sufficient quantity to draw up in a capillary tube. Grunther and Wagner's Indian ink was used by me, and is mixed with the serum in equal parts. A drop of the mixture is then deposited on a slide and a film made in the usual way, by spreading with another slide held at an angle. This method of determining the presence of the trepomena pallida I found to be easier and more reliable than by using Geimsas or Leishmann's methods /

methods of staining. It is also very much more rapid as the film can be examined as soon as it has dried.

(2) The Wassermann reaction : All the cases of syphilis treated by me have had the Wassermann test applied before receiving an injection of Salvarsan, except the cases of very early infection, with only a typical Hunterian chancre as evidence of infection, and from which the *Treponema Pallidum* had been isolated. The results of treatment with Salvarsan have also been controlled by the Wassermann reaction repeated at regular intervals after the injection of the drug. One has in this way, as far as possible, made certain that only genuine cases of syphilis have been treated. Again, by regularly inspecting the cases for considerable periods after treatment, and making frequent Wassermann tests, one has been enabled to form very definite opinions as to the value of the drug in the treatment of specific disease. In the Army the following of cases has been a comparatively easy matter. The test as applied : The Hecht-Fleming²⁷ method has been adopted with slight modifications. Basset-Smith⁹ examined 500 cases by this method, and controlled his results by simultaneous examinations with the original Wassermann test. He concluded a positive result with /

with Fleming's method was reliable.

Fleming's modification depends on two factors, (1) the complement employed is that present in the serum to be tested, and (2) the natural amboceptor for sheep or goats corpuscles present in human sera is taken advantage of.

A most important point is that the serum to be tested should be fresh. I therefore make a practice of drawing off 5 c.c.'s. of blood from the patient the evening before the test is to be done, with a Roux's syringe, and the serum is separated from the clot the next morning by gently pouring it into a clean test tube.

The goat's corpuscles must also be fresh. I have obtained fresh supplies by keeping a goat and drawing off from the jugular vein 3 c.c.'s of blood with a Roux's syringe containing 2 c.c.'s of 1.5 per cent citrate of soda in .85 per cent saline solution. This prevents clotting of the blood. The 5 c.c.'s are then centrifuged and the supernatant fluid pipetted off. Normal saline is then added and the corpuscles gently shaken and the suspension again centrifuged. This washing is repeated three times to get rid of the goat's plasma, and I then dilute the red corpuscles 1 in 10 with .85 per cent normal saline for use.

The /

The antigen used is made by grinding rat's heart muscle in absolute alcohol - 5 c.c.'s of absolute alcohol are used for each gramme of heart muscle. Browning and Mackenzie's¹⁵ method of diluting the antigen is used. The alcoholic extract is floated on the top of the salt solution, a ring forming at the point of junction, and diffusion is effected by slowly rotating the test tube in which dilution is being made between the palms of the hands.

I have employed three strengths of antigen 10%, 5%, and $2\frac{1}{2}\%$. By doing this the degree of deviation of complement can be estimated. It is well known that non-syphilitic sera will deviate complement in the presence of a suitable antigen provided sufficiently strong extracts are used. Strengths of over 10% do this. But a case of severe syphilis will show deviation of complement with $2\frac{1}{2}\%$ or even 1% of alcoholic extract. As treatment progresses deviation is only got with higher dilutions, so that the progress of the case can be followed, improvement being marked by a reduction of the degree of complement deviation.

It is not my purpose to enter into a detailed examination regarding the Wassermann test in the diagnosis and treatment of syphilis. McDonagh⁵¹ states that it is not present in 40% of cases until the disease has become a systemic one, but as the *Treponema Pallidum* /

Pallidum can be found in serum from the primary sore the test is not required then. He states that a positive reaction can be obtained in 97% of early and late cases. Boas of Copenhagen has obtained similar results. Browning and Mackenzie¹⁵ state that it is present in 97% of cases in the secondary stage and 75% in the tertiary.

The effect of treatment on the Wassermann test is of importance. If energetic mercurialisation is begun early and continued long enough the serum reacts negatively. I have found, however, that the serum of large numbers of men who had been under treatment by mercurial injection with Grey oil for considerable periods of time still give a positive reaction. The presence of a positive reaction in these cases was then considered sufficient reason for administering Salvarsan even in the absence of any clinical signs of disease. (Success result followed the administration of the drug.)

The temperature, pulse, and respiratory rate, of each patient is taken before beginning the injection and immediately after its completion. These are then recorded at definite intervals afterwards.

Effects of

Preparation of the Patient for injection : Cases for treatment are taken into hospital the previous evening and given a mild purgative. They have only a very light meal in the early morning. The urine is always carefully examined for the presence of albumin but a small amount is not considered of sufficient importance to postpone treatment. The circulatory and nervous systems are examined, and the condition of the digestive system enquired into.

As all my cases have been soldiers, British or Indian, and are therefore young men and selected lives, I have not come across any with sufficiently marked contra-indications to postpone treatment.

In all cases the organs of special sense, particularly the eyes and ears, have been examined carefully both before, and for a considerable period after, treatment. I shall refer to this later on, as in no case has any untoward result followed the administration of the drug.

The temperature, pulse, and respiratory rate, of each patient is taken before beginning the injection and immediately after its completion. These are then recorded at definite intervals afterwards.

Effects /

Effects following an intravenous injection of Salvarsan

The dose administered in nearly all my cases has been 0.5 grammes, and as each 0.1 grammes is dissolved in 40 c.c.'s of normal saline, it means that each man receives altogether a little over 200 c.c.'s of solution. (This includes the saline run into the vein before the Salvarsan is turned on, to insure that the vessel has been entered, and that run in on completion of the injection to wash out the apparatus and thus ensure that the whole dose has been given.)

The average time occupied is about 11 minutes. In no case, during the injection, have any untoward symptoms appeared. The patients feel no pain and complain of nothing.

After the injection the patient is at once put to bed. In most cases, about an hour later, the effects of the injection begin to manifest themselves. A feeling of chilliness is complained of and this often develops into an actual rigor, the temperature running up three or four degrees, and in one of my cases reaching as high as 105° F.

On examination the skin of the face, neck, and upper part of chest, is found to be flushed, and the conjunctivae are markedly congested. Headache begins, felt mainly over the frontal regions. The pulse increases /

increases in rate and becomes soft and easily compressed. There may be some irregularity (see cases 30 and 83). The respiration is hurried and dull aching in the back and lower limbs is complained of. The clinical picture presented is remarkably similar to that of a person suffering from a malarial paroxysm. A feeling of nausea comes on and is in most cases followed by severe vomiting. In some cases the bowels are opened freely and griping pains in the abdomen experienced. These effects last as a rule for four or five hours and then subside, and by bedtime the men again feel fairly fit. The temperature drops to the normal, the headache goes, the vomiting ceases and the pulse becomes slowed in rate. But headache, purging, temperature, disinclination for food, and general malaise, may continue for a day or more longer.

The vomitted matter is often very copious being fluid in consistence and green in colour, in one or two cases being even blood tinged.

The stools are watery, but contain no disintegrated mucous membrane on examination.

Where vomiting is severe the urine becomes diminished in quantity, but this is probably owing to the loss of fluid by emesis and not due to any specific action on the kidneys.

There /

There is considerable difference of opinion as to the cause of the reaction after Salvarsan.

Werchselmann⁷⁰ has asserted that a high temperature is due to the formation of febrile bodies in the distilled water used for making the solutions for injection. I cannot agree with him in regard to this as in all my cases the water has been distilled on the morning of the injection, and the normal saline solution then made and sterilised in an autoclave. There is therefore no time for the development of these febrile bodies.

Schrieber⁶¹ asserts that the reaction is due to the liberation and rapid absorption of endo-toxins and Ehrlich agrees with him in this assertion.

I am of the personal opinion that the cause of the reaction is twofold. It is the reaction, in the first place, of the body to the salt injected. This is evidenced by the fact that the same train of symptoms occurs in non-syphilitics treated in this way by intravenous injection of the drug. Two cases, Nos. 85 and 86, in my series support me in this matter, and Litterer⁴⁴ of Nashville, Tenn, U.S.A., confirms me in that he too has observed the same thing.

But Schrieber's theory is undoubtedly true in that the reaction in syphilitics is generally more severe /

severe^{than} in non-syphilitics. That is to say, the reaction is more marked in the case of men with severe recent syphilitic lesions than in others, the more intense reaction being due to the liberated endotoxins accentuating the drug action.

When injected under the skin Salvarsan gives rise to a good deal of pain and irritation. The salt is deposited at the site of the injection and the irritation may be followed by abscess formation. Subcutaneous and intramuscular injections were first used by me in October 1910 in the treatment of Syphilis, but as several men developed abscesses at the seat of injection I soon abandoned this method of using the drug.

Following the intravenous injection of the drug a variety of cutaneous affections may arise. The commonest one in my experience is Herpes. This begins as small red papules which develop into vesicles. There is no accompanying pain. The commonest site for appearance of the herpes has been round the lips, but it may even occur on the mucous membrane of the mouth and palate.

Other observers report erythematous rashes of various kinds and pigmentary changes, but in none of my

PHARMACOLOGICAL ACTION

On the Skin : Applied to the unbroken skin neutral, and faintly alkaline, solutions of Salvarsan have no effect. If there is an abrasion present, slight irritation is set up, and a mild degree of hyperaemia induced.

When injected under the skin Salvarsan gives rise to a good deal of pain and irritation. The salt is deposited at the site of the injection and the irritation may be followed by abscess formation. Subcutaneous and intramuscular injections were first used by me in October 1910 in the treatment of Syphilis, but as several men developed abscesses at the seat of injection I soon abandoned this method of using the drug.

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Other observers report erythematous rashes of various kinds and pigmentary changes, but in none of
my /

my cases have any of these conditions appeared.

Sensation to touch, heat and cold, and pain, is unaffected by Salvarsan.

Action on Mucous Membranes : The alkaline solution when applied to the mucous membrane of the mouth or prepuce gave rise to no sensations or visible changes unless some lesion were present when slight irritation was produced.

Action on the gastro-intestinal track : One of the commonest effects after an intravenous injection of Salvarsan is a feeling of nausea and vomiting, and not infrequently diarrhoea follows. These effects are due to the action of Salvarsan on the mucous membrane lining the stomach and intestine.

In support of this assertion is the fact that Stopford-Taylor and MacKenna have found arsenic in the vomited matter, and it is eliminated in the foeces. The effect is therefore probably due to the excretion of arsenic by the mucous membrane of the stomach and intestine.

Boehm states that arsenic causes the capillaries and vessels of the intestinal track to dilate and this is followed by a partial destruction of the epithelium and transudation of fluid.

It /

It is extremely hard to obtain reliable information with reference to a similar effect following the administration of Salvarsan, but the vomiting, griping, and diarrhoea which occurs after its use resembles a mild degree of poisoning with arsenic, and it is a feasible assumption that in both cases the local effects are similar.

Reference to post mortem records of death following the administration of Salvarsan gives little direct evidence in support of this irritant action but certain indirect evidence is afforded which is of value.

Thus Prof. Anton⁵ of Halle reporting on a man who died $3\frac{1}{2}$ hours after the intravenous injection of 0.4 grammes of Salvarsan, states that the post mortem revealed "hyperaemia with oedema of the lungs, a flabby atrophic heart with fatty infiltration of the right side, hypoplasia of the left kidney, enlarged spleen and hyperaemia of the liver". The presence of hyperaemia of the liver suggests a vascular change similar to that produced by arsenic.

Again, Ehrlich,¹⁰ reporting on a case of a young man of 23 who died in November 1910, states that the post mortem revealed "fatty degeneration of the liver". He suffered from acute jaundice before death. Ehlers¹¹ reporting /

reporting on another case states that the post mortem revealed "acute parenchymatous degeneration of the internal organs".

(2) These changes are very similar to those produced by an inorganic arsenical salt, and as the clinical effects of Salvarsan so closely resemble those following poisoning by arsenic, one has good grounds for suspecting that the action of both substances is similar in nature.

But one has other direct evidence in favour of my theory that Salvarsan is a gastro-intestinal irritant. Kolmer and Schamberg⁴² administered Salvarsan by the mouth to seven persons suffering from Syphilis. Three of these complained of no unpleasant symptoms. Three suffered from vomiting and diarrhoea and one from diarrhoea only. Here then, we have Salvarsan administered by the mouth producing the same effects as arsenic - vomiting and diarrhoea.

Further, Auer⁷, has found the vessels of the intestines dilated in animals autopsied after an intravenous injection of Salvarsan, an effect resembling that described by Boehm with regard to arsenic.

One has, therefore, the following facts in support of the theory that Salvarsan is, like arsenic, a gastro-intestinal irritant.

(1) /

- (1) It causes vomiting and diarrhoea administered either by the mouth or intravenously, just as arsenic does.
- (2) It causes dilatation of the vessels of the intestinal track.
- (3) It causes degenerative changes in the liver similar to the changes produced by arsenic.

I have therefore made some investigations proceeding along the following lines.

(1) The effect of perfusing the vessels of a frog with Salvarsan in dilutions of from 1 in 50 in 0.55% normal saline solution up to 1 in 200, in alkaline solution, as used for intravenous injections.

(2) Observing the effects of similar strengths dropped on to the exposed heart of the frog.

(3) Taking careful note of patients at definite intervals after the injection of the drug, and by recording changes in the blood pressure and taking pulse tracings endeavouring to formulate some definite opinion as to the effect of Salvarsan on the heart and vessels.

(1) Perfusion of the vessels of frogs : The procedure adopted was as follows. After the frog had been pinned its thorax was opened and aorta exposed. Into the

Action of Salvarsan on the circulation :

A question of supreme importance is whether Salvarsan has any effect on the circulatory system, and if so, as to what the nature of the action is.

I have been unable to find much literature regarding experimental work on animals with regard to this question, and owing to lack of apparatus it has not been possible for me to obtain any graphic records of personal observations.

I have therefore made some investigations proceeding along the following lines.

- (1) The effect of perfusing the vessels of a frog with Salvarsan in dilutions of from 1 in 50 in 0.85% normal saline solution up to 1 in 200, in alkaline solution, as used for intravenous injections.
- (2) Observing the effects of similar strengths dropped on to the exposed heart of the frog.
- (3) Taking careful note of patients at definite intervals after the injection of the drug, and by recording changes in the blood pressure and taking pulse tracings endeavouring to formulate some definite opinion as to the effect of Salvarsan on the heart and vessels.

(1) Perfusion of the vessels of frogs : The procedure adopted was as follows. After the frog had been pithed its thorax was opened and aorta exposed. Into the /

the aorta a canula was passed and the sinus venosus opened. The frog was suspended and Salvarsan run through the vessels, the number of c.c.'s per minute being measured and noted. Sufficient 0.85% sodium chloride was first run through until a steady flow had been established. The Salvarsan was then turned on.

In all cases the same effect was got, the flow through the vessels increased steadily in quantity. The accompanying records of two of these experiments well illustrates this, and the effect of charting makes it easy to follow the changes.

In experiment I the Salvarsan was in a strength of 1 in 50. The rate of flow when the drug was turned was 1.2 c.c.'s per minute. Forty minutes later the rate had gone up to 2.5 c.c.'s per minute.

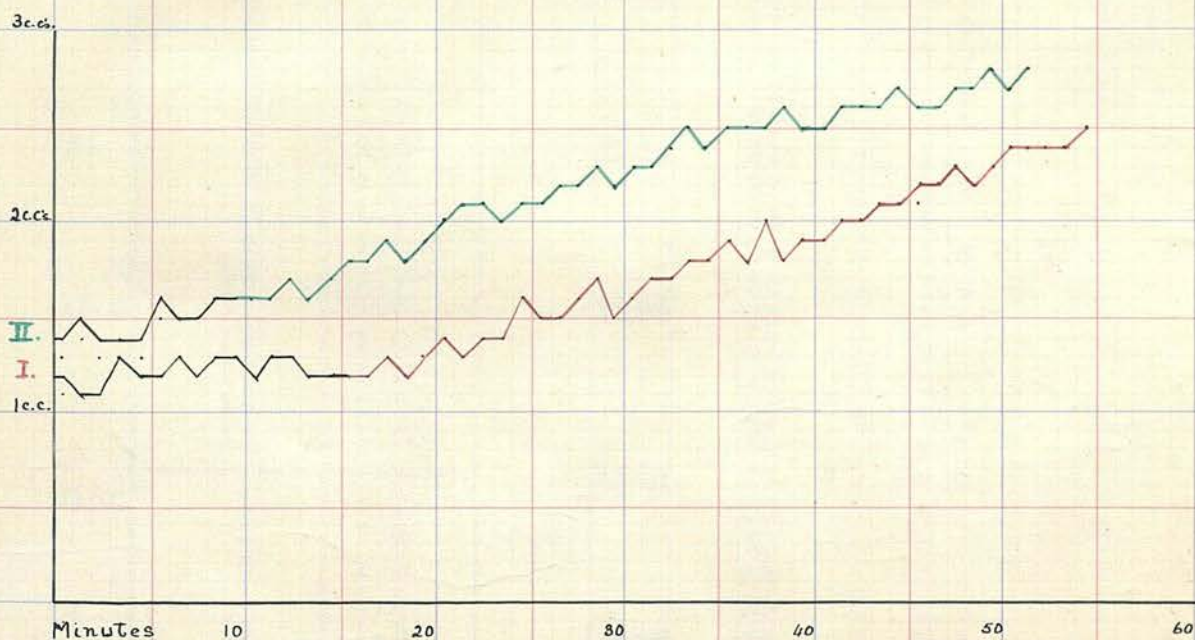
Experiment II was with a strength of 1 in 200. The rate of flow was 1.6 c.c.'s per minutes when the Salvarsan was turned on, and it then rose steadily so that 42 minutes later it had increased to 2.8 c.c.'s per minute. These results indicate that the vessels dilate as the result of the action of Salvarsan. In none of my experiments was there any sign of a preliminary contraction. There was therefore in the frog a definite vaso-dilator action following the perfusion of the vessels with Salvarsan.

Perfusion of Vessels of Frog.

Black = Normal Saline.

I. Red = Salvarsan 1 in 50.

II. Green = Salvarsan 1 in 200.



Perfusion of Vessels

Expt. I. Date 11.8.11. Temp. of Room 75° F.

Frog pithed at 10.20 a.m. Weight 50 grms.

Strength of Solution 1 in 50. in .85% NaCl.

Height of fluid above canula 6".

Perfusion begun 10.45 a.m.

Time	Minutes after flow begun	Number of c.c.'s per minute	Re- marks	Time	Minutes after flow begun	Number of c.c.'s per minute	Re- marks
10.55	1	1.2		11.25	16	1.6	
	2	1.1			17	1.7	
	3	1.1			18	1.7	
	4	1.3			19	1.8	
	5	1.2			20	1.8	
11	6	1.2		11.30	21	1.9	
	7	1.3			22	1.8	
	8	1.2			23	2.	
	9	1.3			24	1.8	
	10	1.3			25	1.9	
11.5	11	1.2		11.35	26	1.9	
	12	1.3			27	2.	
	13	1.3			28	2.	
	14	1.2			29	2.1	
	15	1.2			30	2.1	
11.10	1	1.2		11.40	31	2.2	
	2	1.2	"606"		32	2.2	
	3	1.3			33	2.3	
	4	1.2			34	2.2	
	5	1.3			35	2.3	
11.15	6	1.4		11.45	36	2.4	
	7	1.3			37	2.4	
	8	1.4			38	2.4	
	9	1.4			39	2.4	
	10	1.6			40	2.5	
11.20	11	1.5					
	12	1.5					
	13	1.6					
	14	1.7					
	15	1.5					

Perfusion of Vessels

Expt. II. Date 17.8.11. Temp. of Room 72° F.

Frog pithed at 10.15 a.m. Weight 68 grms.

Strength of Solution 1 in 200 in .85% NaCl.

Height of fluid above canula 7½"

Perfusion begun 10.56 a.m.

Time	Minutes after flow begun	Number of c.c's per minute	Re- marks	Time	Minutes after flow begun	Number of c.c's per minute	Re- marks
11.1	1	1.4	"606"	11.30	20	2.2	
	2	1.5			21	2.3	
	3	1.4			22	2.3	
	4	1.4			23	2.4	
11.5	5	1.4		11.35	24	2.5	
	6	1.6			25	2.4	
	7	1.5			26	2.5	
	8	1.5			27	2.5	
11.10	9	1.6		11.40	28	2.5	
	10	1.6			29	2.6	
	1	1.6			30	2.5	
	2	1.6			31	2.5	
11.15	3	1.7		11.45	32	2.6	
	4	1.6			33	2.6	
	5	1.7			34	2.6	
	6	1.8			35	2.7	
11.20	7	1.8		11.50	36	2.6	
	8	1.9			37	2.6	
	9	1.8			38	2.7	
	10	1.9			39	2.7	
11.25	11	2.			40	2.8	
	12	2.1			41	2.7	
	13	2.1			42	2.8	
	14	2.					
	15	2.1					
	16	2.1					
	17	2.2					
	18	2.2					
	19	2.3					

(10) Effect on the rate of the heart: No marked changes were observed with regard to the rate of contraction. With solutions of 1 in 50 and 1 in 75, there was a preliminary

(2) Effect of Salvarsan when dropped on to the exposed heart of a frog : The frog having been pithed was pinned out on its back and its heart exposed in the usual way, care being taken that no injury was inflicted when opening the pericardium.

I then placed vertically over the exposed heart a burette containing my solution of Salvarsan, opening the stopcock so that 10 to 15 small drops fell on the heart regularly per minute. The lower end of the burette was about $1\frac{1}{2}$ inches above the heart so as to diminish any possible irritation from the falling of the drops of the drug.

Experiments were carried out with dilutions varying from 1 in 50 to 1 in 200 in strength.

The following points were noted :

- (a) Effect on the rate of the cardiac contractions per minute.
 - (b) Effect on the completeness of the systolic contractions and on the co-ordinate action of ventricle and auricles.
 - (c) Effect of substituting a solution of Strophanthin, 1 in 40000 in .85% normal saline, when the heart was ceasing to contract and becoming arrhythmic.
- (a) Effect on the rate of the heart : No marked changes were observed with regard to the rate of contraction. With solutions of 1 in 50 and 1 in 75, there was a preliminary /

preliminary acceleration of rate which soon became slowed again.

(b) Effect on the completeness of systole and co-ordination of ventricle and auricles : In all dilutions changes regarding these features became evident.

The first change was a lessening of the completeness of the ventricular systole. The ventricle became less small and white on contracting. Later on it was noticed that the ventricle became larger during diastole than at the beginning of the experiment, in addition to its diminished completeness of contraction. If the Salvarsan was not stopped the ventricle gradually became less and less active until it would finally contract only once to every two contractions of the auricles, and eventually it ceased in marked diastole, the auricles still continuing to beat regularly.

This points to a definite action on the cardiac muscle, the ventricle being mainly affected.

(c) Effect of substituting a solution of Strophanthin : If Strophanthin, 1 in 40,000, was substituted for the Salvarsan, before complete cessation of the ventricular contractions, a wonderful change followed. In a very short time the ventricular systole began to increase in power and soon it was beating regularly and more /

more completely than before the Salvarsan had been applied. This observation is, to my mind, of great importance. Sir Thomas R. Fraser has proved conclusively that the action of Strophanthus on the heart is a direct one on the cells and causes an enhanced degree of contraction. The fact that a dilute solution of Strophanthin soon restores the heart after Salvarsan points to the latter drug being a muscle poison, and further, one gets a decided proof that, in the event of any heart failure following the use of Salvarsan, the treatment to adopt is to use a cardiac tonic such as Strophanthus.

I have been unable to find any references in literature to the action of Salvarsan on the frog's heart, but Auer⁷ of New York has published his observations with regard to the action of the drug on the hearts of dogs and rabbits, and I propose to quote him fully. He concludes "That alkaline and acid solutions in 0.5% strength may affect the heart. "With the alkaline solution this action is not so obvious as with the acid solution, nor is it so constant. Neither the blood pressure nor the volume changes of the heart form a safe guide with the alkaline solution, for it was shewn above that both these indicators may be but moderately affected and "yet /

"yet a comparatively slight extra strain put upon
 "the heart was sufficient to throw it into a fatal
 "fibrillation. This failure is probably due to an
 "inherent weakness of the cardiac muscle which is
 "brought out by the injection of Salvarsan, and the
 "contention of Ehrlich and many clinicians that
 "myocarditis be regarded as a contra-indication for
 "the intravenous injection of Salvarsan has thus
 "experimental support".

With reference to 0.5% acid solution he states
 that there is "a profound weakening of the heart con-
 "tractions preceded by a marked drop in the blood pres-
 "sure. But this drop in pressure cannot be attribu-
 "ted entirely to vaso-motor disturbance, as is done
 "by Hoke and Rihl, for the volume record demonstrates
 "that the ventricles are full of blood but are prac-
 "tically unable to expel their contents, at least as
 "far as the left ventricle is concerned. These
 "facts clearly indicate that an effect upon the heart
 "muscle is produced by acid Salvarsan".

The effect of Salvarsan on the heart and vessels
 of man is difficult to gauge. I have endeavoured to
 determine the nature of the action by paying careful
 attention to the following points :

(a) /

(a) The effect on the pulse.

(b) The effect on the blood pressure as measured by Martin's modification of the Riva-Rocci sphygmomanometer

(a) The effect on the pulse : The rate of beat is invariably increased after an injection of Salvarsan, the rate may go up to .150 beats per minute. The accompanying table gives the results of the average of 20 cases (Nos.1 to 20). From it it is seen that the maximum rate is at the 4th hour.

Effect of Salvarsan on Pulse Rate

Before Salvarsan	After Salvarsan							
	1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
75	85	98	112	106	83	75	74	73

As a rule the rythm is not altered - it continues to be regular in time and the character of succeeding beats remains the same. But a marked change soon reveals itself with regard to the systolic and diastolic pressure. In a radial pulse in which the maximum pressure, or force, was good and the minimum pressure, or tension, well maintained, changes soon become manifest. One finds the rise instead of being gradual becomes abrupt and the fingers on the vessel feel as though tapped from the inside. The sudden rise is followed by just as sudden a fall of the pulse. The impression conveyed is very similar to what one gets in aortic incompetence. A pulse tracing, using a Dudgeons sphygmograph, brings out these points clearly. The case of Pte.F. (Case No. /

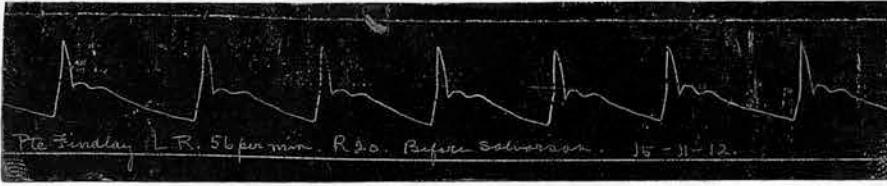
No.83) well illustrates the changes. Tracing I was taken immediately before getting Salvarsan. His blood pressure registered 120 m.m. of mercury. The pulse is that of an ordinary healthy man. Tracing II was taken one hour later. The blood pressure had fallen to 104 m.m. of mercury. Two points stand out clearly (1) The tracing showing a sudden abrupt rise and fall with a sharp apex, and (2) an irregularity in rate. The beat is prolonged and gradually returns to normal. This irregularity was irregular in respect of time. It did not exist before the drug was given and, on examination of his heart, a faint murmur could be detected over the mitral area propagated into the axilla and the apex had become displaced from 3 inches to $3\frac{1}{2}$ inches from the mid sternal line in the fifth intercostal space, thus indicating a slight dilatation of the viscus. Tracing III was taken eight hours later. The systolic blood pressure stood at 108 m.m. of mercury. Well marked diastole is present. Tracing IV was taken 24 hours later. The systolic pressure stood then at only 100 m.m. of mercury and a slight irregularity is still discernible though the apex had returned to its normal place and no murmur could be heard. This case is of considerable importance from the point of view of the action of Salvarsan on the circulatory system. /

system. From a study of it one concludes that there is a definite toxic action on the heart muscle causing an irregularity in rate with some weakness and dilatation. Coincident with these central effects one gets a marked fall in blood pressure. The tracings of Pte. R. (Case No.80), illustrate in a minor degree the same thing. Tracing I was taken before the intravenous injection of 0.5 grammes of Salvarsan. The systolic blood pressure was high, standing at 130 m.m. of mercury. Tracing II was taken one hour later when the blood pressure had fallen to 124 m.m. Tracing III, taken eight hours later, shows a further change with a blood pressure of only 112 m.m. Tracing IV, taken twenty-four hours shows a partial recovery.

The Tracings of Pte.C. (Case No.79), resemble those of Pte. R. except that the blood pressure had continued to fall, and twenty four hours after his injection was still showing no signs of recovering its normal.

Pulse Tracing I. Pte.F. Blood pressure 120 m.m.of Hg.

Before Salvarsan



Pulse Tracing II. Pte.F. Blood pressure 104 m.m.of Hg.

1 hour after Salvarsan



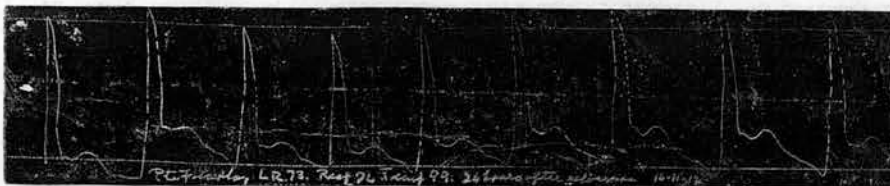
Pulse Tracing III. Pte.F. Blood pressure 108 m.m.of Hg.

8 hours after Salvarsan



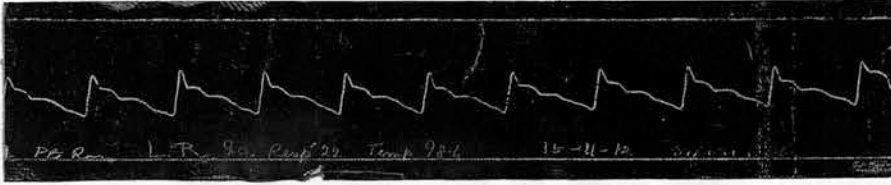
Pulse Tracing IV. Pte.F. Blood pressure 100 m.m.of Hg.

24 hours after Salvarsan



Pulse Tracing I. Pte.R. Blood pressure 130 m.m.of Hg.

Before Salvarsan.



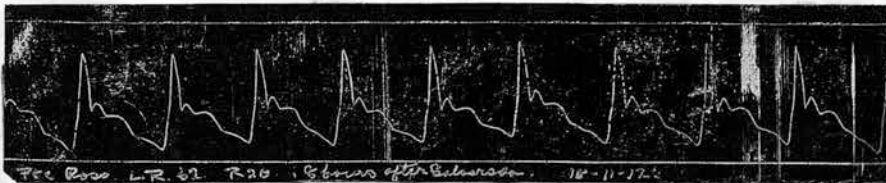
Pulse Tracing II. Pte.R. Blood pressure 124 m.m.of Hg.

1 hour after Salvarsan.



Pulse Tracing III. Pte.R. Blood pressure 112 m.m.of Hg.

8 hours after Salvarsan



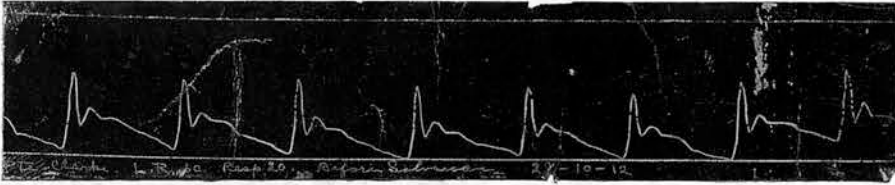
Pulse Tracing IV. Pte.R. Blood pressure 120 m.m.of Hg.

24 hours after Salvarsan.



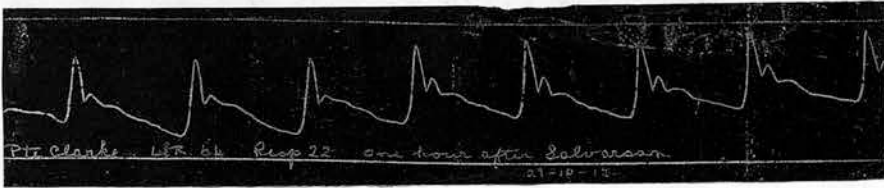
Pulse Tracing I. Pte.C. Blood pressure 122 m.m.of Hg.

Before Salvarsan



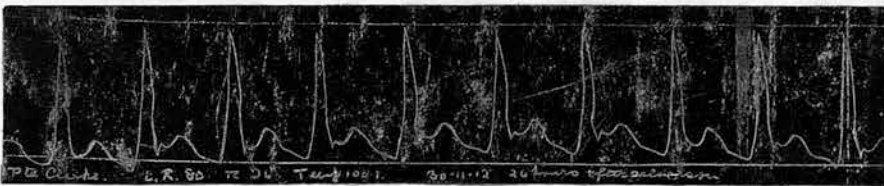
Pulse Tracing II. Pte.C. Blood pressure 114 m.m.of Hg.

1 hour after Salvarsan.



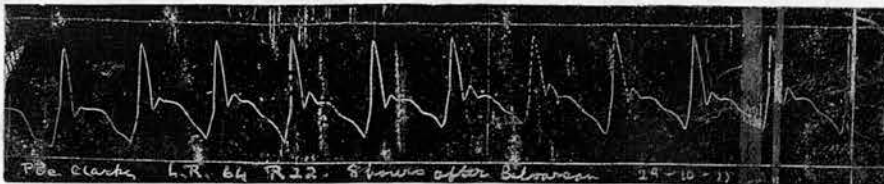
Pulse Tracing III. Pte.C. Blood pressure 108 m.m.of Hg.

8 hours after Salvarsan



Pulse Tracing IV. Pte.C. Blood pressure 116 m.m.of Hg.

24 hours after Salvarsan



(b) Effect of Salvarsan on the blood pressure : In order to obtain accurate information on this subject I made observations of the systolic pressure on 20 men the day before being given Salvarsan intravenously and then at intervals of 1 hour, 2, 4, 8, 24 and 48 hours after the injection. The accompanying table gives the figures obtained and by taking the average of the readings fairly reliable data is at one's disposal

Record of Blood Pressures

Case No.	Before Salvarsan	After Salvarsan					
		1 hr	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs
22	120	118	110	100	110	118	120
26	116	114	94	96	112	118	120
27	130	120	108	108	114	112	122
33	122	110	100	106	112	110	120
34	120	110	98	98	96	100	116
43	126	124	115	109	112	115	122
44	132	122	108	112	110	122	128
64	128	116	112	114	110	122	126
65	124	114	106	104	108	116	122
66	118	122	112	104	110	108	116
67	128	124	120	112	118	122	130
68	134	130	126	126	128	130	124
69	126	124	106	108	104	110	124
70	128	124	115	118	114	120	125
71	118	112	110	108	112	110	112
73	130	126	114	114	118	126	128
77	126	112	104	106	110	116	126
82	120	112	100	98	104	110	118
81	124	120	120	116	115	126	123
84	128	122	95	94	100	115	120
Total	2,498	2,376	2,173	2,151	2,317	2,326	2,442
Average	124.9	118.8	108.6	107.5	115.8	116.3	122.1

From this Table it will be seen that the average pressure /

pressure before the injection of Salvarsan is 124.9 m.m. of Mercury. One hour after the injection it has fallen to 118.8 m.m.. Two hours later it is down to 108.6 m.m. Four hours later it is 107.5 m.m. Eight hours later it has begun to rise and stands at 115.2 m.m., and at the end of twenty four hours it is up to 116.3 m.m. Forty eight hours after the injection it has reached 122.1 m.m. - practically normal again.

As a result of these observations one has obtained the following information.

- (a) The rate of the heart's beats is considerably increased.
- (b) There is some irregularity of the heart with slight dilatation.
- (c) There is a rapid fall of blood pressure.

The question arises as to the significance of these facts. Nicolai⁵⁴ has stated, on the basis of electro-cardiograms, that Salvarsan does not affect the heart. But from close observation of my cases I am not disposed to accept this assertion. I have shewn with regard to the frog that there is a definite action on the myocardium. Auer's work has proved a weakening effect on the heart's of dogs and rabbits. The observations above recorded seem to me to prove a similar action on the human heart.

The /

The fall of blood pressure is probably accentuated by another factor, namely vomiting. In practically every case nausea and vomiting have been present from the first to the fourth hours after the administration of the drug. The attendant symptoms of emesis are a rapid feeble pulse, lowered blood pressure and cold perspiration. But when vomiting ceases these effects pass off. In my series of cases I have shewn that it takes over forty eight hours for the blood pressure to regain its normal level. There must therefore be the prolonged action of some substance to keep the pressure low. Undoubtedly this substance is Salvarsan. Beveridge and Dunbar Walker¹² have shewn that Salvarsan is excreted most rapidly during the first three or four days after the intravenous injection of the drug. It is probable therefore that as the arsenic circulating in the body becomes diminished in quantity the blood pressure rises.

I have shewn in the frog that perfusion with Salvarsan dilates the blood vessels. In the human being, following the injection of the drug and coinciding with the fall of blood pressure, the vessels of the skin, especially of the face and chest, become visibly dilated and the conjunctivae are congested. This may be merely due to the flush accompanying the rise of temperature that follows the administration of /

of the drug. But I am inclined to think it is due to a vaso-dilator effect of Salvarsan. Auer has found the vessels of the mesentery "moderately distended with blood" when doing autopsies of rabbits who died after the injection of the drug. This may indicate that the vessels in the splanchnic area are dilated, but there is no definite evidence of this.

The fall in blood pressure is therefore mainly due to the weakening of the heart's action and the fall is augmented by a slight vaso-dilator action of the vessels of the head and neck and possibly of the splanchnic area as well.

3. The effect on the coagulation time of blood.

1. The effect on the white cells: Literature and references have been almost beyond one's reach, so that first of all a large series of observations on the blood contents of individuals in India who were in a good state of health, had to be made to establish a normal, or control, for further observations.

Twenty five men were selected, and by reference to their medical history sheets, which are regularly kept for each soldier, assurance was made that none of them had suffered from Malaria, Venereal disease, or any other severe illness since arriving in this country. In each case an actual leucocytic count with the Thoma-Zsiss Haemocytometer and differential counts /

Action of Salvarsan on the blood :

I have now made a large number of observations to determine the effect of Salvarsan on the blood. I propose to deal with these effects in the following order :

1. Effect on the white cells :
 - (a) With reference to their numbers (leucocytosis)
 - (b) With reference to the differential count.
 - (c) With reference to the opsonic index.
2. The effect on the red blood corpuscles :
 - (a) With reference to their numbers.
 - (b) With reference to their haemoglobin content.
3. The effect on the coagulation time of blood.

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counts with reference to four varieties of cells - polymorphonuclears, lymphocytes, large mononuclears, and eosinophiles were made. The red blood corpuscles were also enumerated and haemoglobin estimated by means of Gowers haemoglobinometer. The Table below gives details, in brief, regarding these cases. I may add that Bangalore, where this work has all been done, is a very healthy station. It is nearly 4,000 feet above sea level. The climate is very equable, the maximum temperature in the shade during the hot months only touching 98.1° F., on one occasion during the last summer. My observations, therefore, with reference to normal counts, do not by any means stand good for the whole of India.

5411	P.	3	2900000	82%	7200	88	22	1	3
5205	G.	3	5100000	91%	8900	73	20	4	3
5567	F.	3	4500000	88%	7200	74	21	5	0
<u>Average</u>			4300000	91.5%	7120	71	25	5	1

From a study of these figures one notes that the blood of Europeans in India is slightly different from the dweller in Europe. There is a slight diminution in red blood corpuscles and haemoglobin, but the white cells remain practically unchanged.

Having in this way established a control count, for the class of men with whom I am dealing, I proceeded to examine the bloods of fifty soldiers suffering from Syphilis so as to determine any changes that might follow infection with the *Treponema Pallidum*.

Blood Counts - Normal

Regt. No.	Rank, Name and Regt.	Service in India	R.b.c.	Hb.	Leuco-cytes	P.	L.	L.M.	E.
7742	Pte.B., C.H.	3 yrs	4900000	96%	7500	69	22	6	3
7178	" C., "	3 "	5200000	93%	6900	73	23	4	0
7266	" H., "	7 "	4600000	92%	7900	70	24	5	1
7936	" F., "	3 "	4900000	96%	7100	68	26	4	2
8879	" F., "	1 "	5500000	98%	6200	72	26	2	0
6070	" K., "	3 "	4800000	91%	7200	65	27	7	1
7981	" K., "	3 "	4800000	86%	7500	70	25	4	1
-	J.J.H.N.	4 "	5000000	96%	7000	74	20	6	0
7599	Pte.K., C.H.	7 "	4400000	88%	6600	69	28	3	0
7118	" M., "	4 "	4600000	93%	5600	71	23	5	1
7606	" S., "	5 "	4900000	95%	7700	70	24	5	1
7891	" S., "	6 "	4700000	89%	6200	75	22	3	0
7287	" C., "	7 "	4700000	94%	5900	64	30	4	2
8883	" L., "	2 "	4900000	80%	7500	68	22	8	2
8669	" C., "	2 "	5100000	94%	7200	73	23	4	0
3883	Sgt.G., "	8 "	4500000	91%	5300	70	27	3	0
7292	Pte.W., "	3 "	5300000	97%	7000	67	26	6	1
8312	" M., "	2 "	4800000	90%	6000	74	21	5	0
8605	" M., "	2 "	4600000	93%	7800	76	19	5	0
7392	" S., "	5 "	4900000	87%	6300	73	22	4	1
8672	" A., "	3 "	5400000	96%	7500	78	18	4	0
8674	" A., "	2 "	4800000	85%	5600	71	22	5	2
8411	" B., "	3 "	4900000	88%	7200	68	22	7	3
8205	" C., "	3 "	5100000	91%	6900	73	20	4	3
8567	" F., "	3 "	4600000	88%	7200	74	21	5	0
<u>Average</u>			4800000	91.5	7120	71	23	5	1

From a study of these figures one notes that the blood of Europeans in India is slightly different from the dweller in Europe. There is a slight diminution in red blood corpuscles and haemoglobin, but the white cells remain practically unchanged.

Having in this way established a control count, for the class of men with whom I am dealing, I proceeded to examine the bloods of fifty soldiers suffering from Syphilis so as to determine any changes that might follow infection with the Treponema

Pallidum /

Pallidum. By doing this I obtain information which, when placed alongside my normal counts, allow^{ed} me readily to make a note of the changes due to Syphilis. These figures cannot be taken as accurately representing the blood changes in Syphilis however. A large percentage of the men on whom observations were made had been under mercurial treatment for varying periods. This will have considerably modified the original blood condition.

Again, as concealment of the venereal disease is a serious crime in the Army, it means that the remainder of my observations were made on men recently infected and before gross changes had become manifest, thus modifying the results as compared with what other observers have found.

I have been unable to find any recent work on this subject with which to compare my results. But in spite of the factors recorded as probably modifying the changes in the blood of Syphilitics my results closely resemble those obtained by Newmann and Konreid⁵³ in 1893.

The following table gives full details of my observations.

Blood Counts of Syphilitics before Salvarsan

Case Number	Date of Infection	Previous Treatment	R.b.c.	Hb.	Leuco-cytes	P.	L.	L.M.	E
5	Apl. 1911	Hg. 4 injections	4,570,000	75%	7,812	68	30	2	0
6	Dec. 1911	Hg. 2 courses	4,100,000	65%	9,062	60	34	5	1
6	Dec. 1910	Hg. 2 courses and "606" .5 grammes	4,900,000	92%	7,187	75	18	5	2
7	May 1910	Hg. 4 injections	4,800,000	78%	8,437	70	24	5	1
9	Jne. 1910	Hg. 3 injections	4,000,000	60%	9,687	64	28	8	0
10	Sep. 1909	Hg. 5 courses	3,500,000	46%	11,370	52	36	7	5
10	Sep. 1909	Hg. 5 courses and "606" 3 doses.	4,700,000	94%	6,250	67	27	4	2
11	May 1911	Nil	4,200,000	68%	8,437	62	28	10	0
12	Jly. 1911	Nil	4,600,000	68%	9,375	47	43	8	2
13	May 1910	Hg. 4 courses	3,100,000	50%	5,625	61	33	5	1
15	Jan. 1911	Hg. 2 courses	4,000,000	70%	10,937	70	26	4	0
16	Dec. 1910	Hg. 2 courses and "606" .6 grammes	4,300,000	62%	9,375	62	35	3	0
17	? 1910	Hg. 4 courses	4,900,000	90%	8,750	65	30	5	0
19	Jan. 1911	Hg. 3 courses	4,200,000	80%	8,437	64	31	5	0
22	Mch. 1911	Hg. 2 courses and "606" .6 grammes	4,000,000	66%	9,687	64	32	4	0
23	Feb. 1911	Hg. 2 courses	4,600,000	75%	8,750	65	30	4	1
24	? 1910	Hg. 4 courses	4,800,000	88%	8,125	64	29	7	0
25	Sep. 1911	Nil	3,800,000	70%	9,062	61	33	3	1
28	May 1911	Hg. 8 injections	4,200,000	65%	9,687	68	29	2	1
29	Oct. 1911	Hg. 1 injection	3,550,000	60%	10,312	59	34	6	1
31	Sep. 1911	Nil	4,500,000	86%	13,125	60	35	3	2
32	Jne. 1910	Hg. 3 courses	4,800,000	92%	6,562	60	32	8	0
36	Oct. 1911	Nil	4,300,000	70%	10,370	60	36	3	1
38	Oct. 1911	Nil	4,700,000	86%	9,525	64	30	6	0
39	Dec. 1910	Hg. 3 courses and "606" .6 grammes	4,900,000	90%	6,250	66	27	6	1
40	Oct. 1911	Nil	4,900,000	94%	8,437	60	35	5	0
41	Oct. 1911	Nil	4,700,000	85%	10,937	60	31	7	2
42	Oct. 1909	Hg. 4 courses	4,300,000	75%	7,500	62	34	3	1
43	Dec. 1910	Hg. 3 courses	4,600,000	88%	9,062	60	34	5	1
44	? 1902	Hg. 4 courses	4,700,000	70%	8,125	62	33	5	0
45	? 1901	Hg. 5 courses	4,800,000	90%	8,437	56	36	8	0
46	Nov. 1911	Nil	3,200,000	66%	10,837	64	31	5	0
48	Nov. 1911	Nil	3,900,000	60%	10,525	65	31	4	0
55	Feb. 1912	Nil	3,600,000	72%	10,312	66	27	6	1
56	Apl. 1912	Nil	4,500,000	80%	9,375	57	40	2	1
57	Mch. 1912	"606" .5 grammes	5,000,000	96%	7,812	72	22	5	1
58	Feb. 1912	"606" .5 grammes	4,300,000	75%	7,937	63	33	3	1
60	Jne. 1911	Hg. 1 course	4,000,000	70%	7,925	69	23	8	0
63	Jne. 1912	"606" .5 grammes	4,600,000	78%	6,562	60	32	8	0
70	Aug. 1912	Nil	4,800,000	90%	12,185	69	27	4	0
71	Jly. 1912	Nil	4,400,000	84%	8,437	65	30	3	2
72	Sep. 1912	Nil	4,000,000	65%	9,062	67	26	7	0
73	Jne. 1910	Hg. 4 courses	4,500,000	90%	8,437	62	33	5	0
74	Aug. 1912	Nil	4,200,000	70%	11,370	76	22	2	0
75	Aug. 1912	Nil	4,500,000	80%	13,125	59	36	3	2
76	Jly. 1912	Nil	4,500,000	65%	10,312	63	33	3	1
78	Sep. 1912	Nil	4,500,000	90%	9,375	68	29	2	1
79	Oct. 1912	Nil	4,800,000	90%	9,375	62	35	3	0
80	Oct. 1912	Nil	4,800,000	92%	6,625	71	24	5	0
81	Nov. 1910	Hg. 3 courses	4,500,000	70%	8,750	60	32	6	2
		<u>Average</u>	4,360,000	77%	9,160	65	29	5	1

The occurrence of eosinophilia has been reported but I could find no evidence of it. The excess of lymphocytes is in accordance with the changes as observed by Cabat.

The results of my observations are well brought out by placing them side by side as follows :

	Normal Blood (average of 25 cases)	Syphilitic Blood (average of 50 cases)
R.b.c.	4,810,000	4,360,000
Hb.	91.5%	77.4%
Blood Index	.9	.89
Leucocytes	7,120	9,160
Polymorphs	71%	65%
Lymphocytes	23%	29%
Large Monos	5%	5%
Eosinophiles	1%	1%

From this table it is evident that in men suffering from Syphilis the following changes have occurred :

- (a) The red blood corpuscles are diminished by 450,000 per c.m.
- (b) The Haemoglobin is diminished by 14%
- (c) The total leucocytes are increased by 2,000 per c.m.
- (d) The differential count shows
 - (1) The polymorphonuclears are diminished by 6%
 - (2) The lymphocytes are increased by 6%
 - (3) The large mononuclears and eosinophiles are unchanged.

My object in analysing these results is not so much to draw attention to the changes induced by Syphilis as to enable me to compare them with the changes that follow the intravenous injection of Salvarsan.

At present I only propose to study the immediate effects of the injection of the drug on the white cells. Its action on the red cells and haemoglobin content I propose to consider later.

In order to do this careful blood studies have been made in 30 cases at intervals of 1 hour, 2, 4, 8, 24, 48, 72 and 96 hours after the injection of the drug, paying attention to the same factors as already studied in controls and syphilitics before being treated by Salvarsan.

The changes effected are constant. They have no doubt been reported on by other observers, but I have been unable to find any records of published results. The full details regarding figures and calculations in my series of cases will be found on pages 62 to 66. I only place here a table of results obtained for easy reference.

However, differs from me in that he states there is a "transitory increase in lymphocytes at the expense of polymorphonuclear cells". There is, therefore, undoubtedly

Effect of Salvarsan on Leucocytes

(Average of 30 cases)

	Before	After Salvarsan							
	Salvarsan	1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
Leuco- cytosis	8,763	8,426	11225	13510	12424	9290	7175	6364	6469
Polynu- clears	65%	67%	81%	87%	83%	77%	72%	72%	71%
Lympho- cytes	29%	28%	16%	11%	13%	18%	23%	23%	23%
Large Monos.	5%	5%	3%	2%	3%	4%	5%	4%	5%
Eosino- philes	1%	0%	0%	0%	1%	1%	1%	0%	1%

(a) The effect of Salvarsan on the number of Leucocytes per c.m. : The intravenous injection of Salvarsan is followed always by a well marked Leucocytosis reaching its highest point about the fourth hour after the administration of the drug. Reference to the table on page 62, which contains the results of the actual counts of my 30 cases, shews the constancy with which this increase occurs. The average of these 30 cases gives an increase of over 50% of white cells at the fourth hour.

Halberstaedter³³ and McDonagh⁴¹ confirm this observation, both noting a hyper-leucocytosis. Ferrannini²⁴ however, differs from me in that he states there is a "transitory increase in lymphocytes at the expense of polymorphonuclear cells" There is, therefore, undoubtedly /

undoubtedly a leucocytosis following the injection intravenously of Salvarsan.

The question has then to be decided as to whether the increase in leucocytes is due to the chemiotactic action of arsenic, or to the possible destruction of large numbers of treponemata which have to be removed.

The settlement of this question is not easy but there are good grounds for assuming that the marked leucocytosis is largely due to a definite pharmacological action of the arsenical salt. In favour of this is the fact that a marked increase occurs where the drug has been used in non-syphilitic conditions.

I am fortunate enough to have had two such cases on whom observations were made.

One, Pte. B., 2nd Q.O. Cameron Highlanders, developed typical Lupus Vulgaris on the bridge of his nose in November 1911. There was no history of previous Syphilitic disease. On four occasions his blood gave a negative Wassermann reaction. Von Pirquets cutaneous tuberculin test was positive. The diagnosis was agreed to by several medical officers independently.

The condition resisted all forms of treatment and in February 1912 he was sent to Secunderabad to undergo the X-Ray treatment for lupus. After five months, with /

with the necessary intervals, he was sent back to Bangalore with the remark "the condition much improved by treatment". In less than a month's time the disease had again begun with deep ulceration spreading dangerously near the inner canthi of both eyes. The eyes were congested and lids oedematous. The condition being very serious, and grave danger of losing his eyes being present, with the patient's consent I administered 0.5 grammes of Salvarsan intravenously on October 9th 1912. The ulceration was treated locally with hydrogen-peroxide. The effect on the disease was remarkable, the eyes soon ceasing to be congested and the oedema of the lids subsiding in a few days. I shall refer to the therapeutic effects later, but at present have digressed to refer to the blood count which was as follows :

	Before	After Salvarsan							
	Salvarsan	1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
Leucocytosis	7,182	7500	8750	11875	9687	8437	7812	7500	6925
Polynuclears	78%	78%	82%	88%	85%	76%	68%	70%	73%
Lymphocytes	16%	17%	14%	10%	12%	20%	25%	24%	21%
Large Monos.	5%	4%	4%	2%	3%	3%	5%	5%	4%
Eosinophiles	1%	1%	0%	0%	0%	1%	2%	1%	2%

One is well aware that a negative Wassermann reaction does not mean no Syphilis. This case may be one /

one of those called by Hutchison "Syphilitic Lupus". But the history of the case and clinical picture was so like that of Lupus Vulgaris that one is forced to conclude that that is a correct diagnosis.

This being granted the blood count after Salvarsan in this non-syphilitic condition resembles so closely that which follows an injection of the drug in a syphilitic person that one concludes there must be a common stimulatory action causing the leucocytosis.

A second injection of 0.5 grammes on October 25th 1912, gave a very similar blood count which I omit as it is unnecessary.

My second case favouring the theory of a definite chemical stimulus, is that of Sapper Doraswamy, 2nd Q.V.O. Sappers and Miners. This man was in hospital suffering from severe malignant malaria, with enlarged spleen, and numerous crescents in his peripheral blood. Quinine in large doses by the mouth seemed to have little effect on the parasites. When giving Salvarsan to a syphilitic on October 14th 1912 I also administered 0.4 grammes to the malarial case. No differential estimations were made, but prior to the injection he had a leucocytosis of 12,000 white cells c.m. Four hours later this number had increased up to

to 22,000 per c.m. Twenty four hours later it was still 15,000.

Stockmann and Greig⁶⁷ have shewn that in normal animals the effect of an inorganic arsenical salt on the bone marrow is to excite a condition of unusual activity as evidenced by increased vascularity, an increase of red corpuscles, and lessened fat cells. Bettmann⁶⁸ asserts that arsenic acts on the blood and blood forming organs. Charteris⁶⁹ has recently shown that Salvarsan has a stimulating effect on the bone marrow of rabbits.

I am of the opinion that in man a similar effect is produced and on studying my cases I find a good deal of evidence in support of this assertion.

In the first place one has the clinical symptoms of a dull aching pain in the lower limbs, often complained of after the intravenous injection of Salvarsan, to account for. This aching is probably caused by hyperaemia and active changes occurring in the bone marrow.

Again, on two occasions (Cases 41 and 58) when doing differential blood counts after the administration of Salvarsan, I have found nucleated red blood corpuscles present, none having been found prior to the injection. And in one case (No. 72) I found several /

several typical myelocytes in the film when doing a count after treatment with Salvarsan. Where did these cells come from and why did they appear? The only reason I am able to advance to explain their presence is that they have been passed into the general circulation prematurely owing to the bone marrow having been stimulated to excessive activity by the Salvarsan. A further point in favour of my assertion is the marked increase in polymorphonuclear cells present after Salvarsan as compared with the other varieties of white corpuscles. As polymorphs have their genesis in the bone marrow the large numbers of them present must be due to the stimulatory effect of the drug on the marrow. The small numbers of other cells present will then indicate a very slight activity of their source of supply. I have been unable to find any reference to these points in the literature on Salvarsan to confirm my observation, but that is no reason for my not referring to what one has observed and advancing facts to confirm my findings.

(b) With reference to the differential counts : As already mentioned the outstanding feature with reference to differential counts after the administration of Salvarsan intravenously is the marked increase of the

and Schreiber have shown that the organisms in primary

the polymorph cells. The average numbers of these present in 30 cases under review before Salvarsan was 64%. Eight hours after the injection they form 87% of the white corpuscles, an increase of 23%. The increase is still present at the end of 96 hours when they form 70 per cent of the leucocytes.

These figures are of considerable interest on comparing them with the results obtained by Beattie¹⁰ when studying phagocytosis in animals inoculated with active cultures of organisms. Beattie has shewn that after inoculation the polymorphs become numerous after three hours. They continue to increase for twelve hours and finally diminish in from thirty six to forty eight hours.

It is therefore evident that after an injection of Salvarsan a similar reaction occurs due to a chemical stimulus. The marked increase serves a useful purpose, however, in that large numbers of treponemata will have been destroyed by the Salvarsan and the increase in polymorph cells provides scavengers for their removal. During the period of a high leucocytosis, with the polymorph preponderance, which lasts in a marked degree for forty eight hours and continues in a lesser degree for a further period of forty eight hours, is the time when the syphilitic organisms disappear from the lesions. Thus Sieskind and Schreiber⁶⁵ have shewn that the organisms in primary and /

and secondary lesions usually cannot be found after forty eight hours. Spiethoff got similar results on examining serum expressed from primary sores. Scholtz,⁶⁰ on examining 32 cases, found the same thing. Iversen,³¹ in 10 cases of secondary syphilitic lymphadenitis on puncturing the glands, found that the organisms had disappeared in three to five days. Lastly, Herxheimer³⁵ on examining the internal organs of a congenital syphilitic, who died four days after an injection of Salvarsan, could find no organisms except a few degenerate forms in the lungs.

In five cases examined by me (Nos. 74, 75, 76, 78 and 79) prolonged search, three days after Salvarsan, failed to reveal any organisms though easily found before the drug was injected.

It is clear therefore that there is a close connection between the time of disappearance of the syphilis organisms and the high degree of leucocytosis. It may therefore be asserted that the increase in white cells is not due to a chemiotactic action of Salvarsan but occurs in response to an organismal stimulus owing to the destruction of large numbers of treponemata by the drug. Against this, however, is the fact recorded by Charteris, that blood changes occur in animals after Salvarsan and there are my two cases of non-syphilitics /

syphilitics in both of whom a well marked leucocytosis was present, after the injection of the drug. On the strength of this I am inclined to adhere to the view that Salvarsan, when injected intravenously, causes an increase in total leucocytes, and especially polymorphs, on account of its stimulating the bone marrow to great activity. The increase in leucocytes serving a useful purpose however by acting as scavengers of dead organisms.

The mononuclear cells, both lymphocytes and large mononuclears, shew practically no changes. At no time do they exceed the normal in percentage present even up to 96 hours. In this respect the reaction after Salvarsan differs from that obtained by Beattie.

41	10,800	8437	11370	10837	9687	9687	7812	6250	5337	7812
42	7,800	8437	11370	10837	9687	9687	7812	6250	5337	6525
43	7,812	8125	9375	9687	8437	7187	6250	518	5337	6525
44	7,937	7500	10625	13850	12187	8375	5925	5337	5337	5316
45	8,538	5625	9687	11370	11370	8125	6250	5337	5337	6562
46	8,437	8437	12500	12500	17500	12317	7500	7500	7500	5316
47	11,370	10812	11837	20687	21875	20600	9375	5925	5925	7187
48	13,125	9687	15125	19375	10538	8437	5316	6250	6250	6562
49	10,312	9687	14062	29325	18125	10000	7187	5625	5625	6562
50	9,375	10512	12187	13000	15250	8750	5925	7500	7500	7187
51	8,062	8437	10625	14062	12500	7812	6562	5625	5625	6525
52	8,585	7500	9375	8125	6750	8125	6250	5437	5437	6562
53	8,750	8125	15312	20625	16250	11370	7500	5625	5625	6250
Average	8763	6425	11225	13510	12425	9290	7170	6364	6364	6469

Analyses of Leucocytic Counts

(30 Cases)

I. Leucocytosis

Case Number	Before	After Salvarsan							
	Salvarsan	1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
5	7,812	7500	10312	12185	9375	8750	6562	6250	6562
6	9,062	10312	16250	19375	12500	9687	6925	5460	6250
6	7,187	7812	11370	11370	9687	9375	6250	6562	5937
7	8,437	7812	10937	12500	11370	8750	7187	6250	5625
9	9,687	11567	16512	18125	17500	16875	12817	6562	5937
10	11,370	10312	14062	16512	12500	8125	5625	6250	6925
10	6,250	6562	8125	7812	8437	7187	6925	6562	6562
11	8,437	8750	9375	12500	12980	10612	7812	6925	6250
12	9,375	9687	12185	15912	16250	10312	8437	6250	5937
13	5,625	5937	5937	8125	9687	9375	6562	6250	6250
15	10,937	6925	5700	8125	7187	6250	6562	5937	6925
16	9,375	9687	11370	10937	12185	8750	7500	6562	6925
19	8,437	7812	8750	10060	9375	7500	7500	6250	6562
23	8,750	9062	13856	14062	8125	5316	5937	5000	7887
28	9,681	8437	10312	11370	9375	6925	6925	6250	6562
39	6,250	6562	7187	7812	7500	5937	5937	6925	5625
40	8,437	7500	8437	10060	9375	8125	7187	6562	6925
41	10,937	9687	10312	10528	9062	8437	8750	8437	7812
42	7,500	8437	11370	10937	9687	9062	7812	6250	6525
57	7,812	8125	9375	9062	8437	7187	6250	5316	6562
58	7,937	7500	10525	13856	12187	9375	6925	5625	5316
63	6,562	5625	9062	11370	11370	8125	6250	6562	6562
72	8,437	8437	12500	15000	17500	12817	7500	7500	5316
74	11,370	10312	11567	20600	21875	20600	9375	6925	7187
75	13,125	9062	18125	19375	10525	8437	5316	6250	6562
76	10,312	9062	14062	29362	18125	10060	7187	5625	6562
78	9,375	10312	12185	15000	13850	8750	6925	7500	7187
79	9,062	8437	10525	14625	12500	7812	6562	6562	6925
80	6,525	7500	9375	8125	8750	8125	6250	5937	6562
81	8,750	8125	15312	20625	16250	11370	7500	5625	6250
<u>Average</u>	8763	8425	11225	13510	12423	9290	7175	6364	6469

II. Polymorphonuclear Leucocytes

Case Number	Before Salvarsan	After Salvarsan							
		1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
5	68%	72%	88%	92%	82%	78%	70%	72%	69%
6	60%	68%	80%	94%	86%	80%	70%	72%	70%
6	75%	78%	82%	85%	84%	79%	71%	70%	69%
7	70%	68%	88%	94%	90%	82%	76%	70%	72%
9	64%	70%	89%	95%	94%	88%	81%	76%	70%
10	52%	62%	68%	82%	80%	74%	68%	70%	72%
10	67%	69%	74%	78%	82%	76%	70%	70%	68%
11	62%	63%	76%	88%	88%	80%	72%	70%	72%
12	47%	52%	68%	80%	88%	82%	76%	70%	71%
13	61%	64%	62%	72%	84%	80%	70%	71%	71%
15	70%	68%	71%	86%	82%	77%	70%	71%	70%
16	62%	75%	83%	86%	85%	78%	73%	70%	69%
19	64%	65%	69%	78%	74%	68%	72%	70%	69%
23	65%	71%	85%	81%	74%	71%	75%	72%	73%
28	68%	64%	77%	90%	84%	72%	68%	72%	71%
39	66%	68%	72%	77%	74%	69%	70%	71%	74%
40	60%	62%	78%	90%	84%	76%	70%	74%	71%
41	60%	64%	88%	91%	82%	76%	74%	70%	74%
42	62%	68%	88%	91%	84%	80%	72%	74%	70%
57	72%	78%	88%	86%	80%	74%	70%	68%	71%
58	63%	75%	91%	93%	90%	80%	76%	71%	70%
63	62%	77%	84%	90%	83%	76%	66%	68%	72%
72	62%	56%	86%	92%	93%	85%	79%	72%	70%
74	76%	74%	95%	92%	86%	85%	62%	77%	65%
75	59%	71%	86%	82%	75%	74%	68%	70%	76%
76	63%	61%	81%	80%	78%	76%	70%	71%	73%
78	68%	64%	78%	90%	86%	75%	70%	72%	71%
79	62%	62%	86%	88%	82%	77%	72%	70%	69%
80	71%	66%	70%	82%	76%	74%	69%	70%	71%
81	60%	56%	92%	94%	90%	84%	75%	70%	71%
Average	64%	67%	81%	87%	83%	77%	72%	71%	70%

III. Lymphocytes

Case Number	Before Salvarsan	After Salvarsan							
		1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
5	30%	24%	10%	7%	14%	20%	24%	20%	24%
6	34%	24%	16%	6%	10%	15%	24%	21%	23%
6	18%	19%	14%	10%	14%	15%	23%	24%	23%
7	24%	26%	10%	5%	8%	16%	20%	20%	22%
9	28%	24%	9%	5%	5%	10%	16%	20%	22%
10	36%	30%	26%	16%	12%	21%	25%	22%	22%
10	22%	25%	20%	16%	12%	18%	23%	24%	26%
11	28%	33%	20%	10%	9%	14%	24%	24%	23%
12	43%	38%	24%	17%	10%	16%	19%	23%	23%
13	33%	28%	32%	23%	13%	15%	18%	24%	23%
15	26%	28%	23%	12%	14%	20%	22%	24%	23%
16	35%	20%	14%	11%	11%	15%	24%	23%	22%
19	31%	27%	23%	18%	21%	25%	22%	24%	25%
23	30%	26%	14%	16%	18%	26%	20%	23%	21%
28	29%	32%	21%	7%	12%	23%	26%	22%	23%
39	27%	25%	22%	20%	19%	23%	23%	23%	21%
40	35%	32%	18%	8%	13%	20%	23%	21%	22%
41	31%	30%	10%	8%	16%	20%	20%	23%	21%
42	34%	28%	10%	8%	14%	14%	22%	21%	22%
57	22%	18%	10%	10%	16%	23%	24%	25%	23%
58	33%	23%	6%	6%	8%	16%	20%	23%	22%
63	32%	21%	12%	8%	14%	21%	26%	25%	19%
72	33%	36%	12%	8%	6%	13%	16%	18%	22%
74	22%	20%	5%	7%	9%	10%	35%	21%	28%
75	36%	26%	13%	15%	15%	18%	30%	27%	19%
76	33%	33%	17%	14%	15%	18%	22%	23%	21%
78	29%	34%	20%	8%	10%	20%	23%	22%	23%
79	35%	33%	11%	10%	14%	18%	22%	25%	24%
80	24%	30%	24%	16%	20%	20%	23%	23%	24%
81	32%	36%	8%	5%	9%	14%	22%	24%	18%
Average	30%	28%	16%	11%	13%	18%	23%	23%	22%

IV. Large Mononuclears

Case Number	Before Salvarsan	After Salvarsan							
		1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
5	2%	3%	2%	1%	3%	2%	5%	7%	6%
6	5%	7%	4%	0%	4%	4%	5%	6%	6%
6	5%	3%	4%	4%	2%	5%	5%	4%	7%
7	5%	5%	2%	4%	2%	2%	3%	7%	5%
9	8%	5%	2%	0%	1%	2%	3%	4%	6%
10	7%	6%	5%	2%	7%	5%	6%	6%	5%
10	4%	4%	5%	5%	4%	6%	6%	5%	5%
11	10%	3%	4%	2%	3%	5%	4%	5%	4%
12	8%	8%	7%	3%	2%	2%	4%	6%	5%
13	5%	7%	6%	5%	3%	4%	4%	5%	5%
15	4%	4%	5%	2%	4%	3%	6%	4%	5%
16	3%	5%	3%	3%	4%	6%	3%	6%	8%
19	5%	7%	6%	4%	4%	6%	7%	5%	8%
23	4%	3%	1%	3%	7%	2%	4%	5%	4%
28	2%	4%	0%	2%	4%	4%	4%	5%	5%
39	6%	6%	7%	3%	5%	7%	6%	4%	4%
40	5%	5%	4%	2%	3%	4%	5%	4%	6%
41	7%	6%	2%	1%	2%	3%	5%	5%	4%
42	3%	4%	2%	1%	2%	5%	6%	5%	6%
57	5%	4%	2%	3%	3%	3%	5%	5%	5%
58	3%	2%	2%	1%	2%	3%	4%	6%	4%
63	8%	2%	3%	1%	2%	3%	6%	6%	5%
72	5%	8%	2%	0%	1%	2%	1%	7%	7%
74	2%	5%	0%	0%	5%	4%	3%	2%	5%
75	3%	3%	1%	3%	8%	6%	2%	2%	4%
76	3%	5%	2%	5%	6%	6%	5%	4%	6%
78	2%	4%	2%	2%	3%	4%	6%	5%	4%
79	3%	5%	2%	2%	3%	4%	5%	4%	5%
80	5%	3%	5%	2%	4%	5%	6%	6%	5%
81	6%	8%	0%	1%	1%	2%	2%	5%	4%
<u>Average</u>	5%	5%	3%	2%	3%	4%	5%	5%	5%

V. Eosinophiles

Case Number	Before Salvarsan	After Salvarsan							
		1 hr.	2 hrs	4 hrs	8 hrs	24 hrs	48 hrs	72 hrs	96 hrs
5	0%	1%	0%	0%	1%	0%	1%	1%	1%
6	1%	1%	0%	0%	0%	1%	1%	1%	1%
6	2%	0%	0%	1%	0%	1%	1%	2%	1%
7	1%	1%	0%	1%	0%	0%	1%	3%	1%
9	0%	1%	0%	0%	0%	0%	0%	0%	2%
10	5%	2%	1%	0%	3%	0%	1%	2%	1%
10	2%	2%	1%	1%	2%	0%	1%	1%	1%
11	0%	1%	0%	0%	0%	1%	0%	1%	1%
12	2%	2%	1%	0%	0%	0%	1%	1%	1%
13	1%	1%	0%	0%	0%	1%	1%	0%	1%
15	0%	0%	1%	0%	0%	0%	2%	1%	2%
16	0%	0%	0%	0%	0%	1%	0%	1%	1%
19	0%	1%	2%	0%	1%	1%	0%	1%	2%
23	1%	0%	0%	0%	1%	1%	1%	0%	2%
28	1%	0%	2%	1%	0%	1%	2%	1%	1%
39	1%	1%	0%	0%	2%	1%	1%	2%	1%
40	0%	1%	0%	0%	0%	0%	2%	1%	1%
41	2%	1%	0%	0%	0%	1%	1%	2%	1%
42	1%	0%	0%	0%	0%	1%	0%	0%	2%
57	1%	0%	0%	1%	1%	0%	1%	2%	1%
58	1%	1%	1%	0%	0%	1%	0%	0%	4%
63	0%	0%	1%	0%	1%	0%	2%	1%	3%
72	0%	0%	0%	0%	0%	0%	4%	3%	2%
74	0%	1%	0%	1%	0%	1%	0%	0%	2%
75	2%	0%	0%	0%	2%	2%	0%	1%	1%
76	1%	1%	0%	1%	1%	0%	3%	2%	0%
78	1%	0%	0%	0%	1%	1%	1%	1%	2%
79	0%	0%	1%	0%	1%	1%	1%	1%	2%
80	0%	1%	1%	0%	0%	1%	2%	1%	1%
81	2%	0%	0%	0%	0%	0%	1%	1%	2%
<u>Average</u>	1%	0%	0%	0%	1%	1%	1%	0%	1%

The effect of Salvarsan on the Opsonic Index : Having

obtained evidence regarding the marked increase in leucocytes, and especially the polymorph variety, after an injection of Salvarsan, an endeavour was made to find out whether the increase in numbers was accompanied by any increase in the opsonic powers. For this purpose I selected ten cases, taking the Index before the administration of the drug, to establish a normal, and again four, eight, and twenty four hours after. I used a culture of staphylococcus aureus for purposes of my investigation, using the same organism in all experiments. An emulsion was made in .85% normal saline and standardised by the gravi-metric method to contain 50 million cocci in each cubic centimetre of solution.

The technique of the opsonic index used was as advocated by Wright. The men examined were only too willing to allow me to trouble them for blood and took a keen interest in the results obtained.

In all my cases a hundred polymorphonuclear cells were counted. The tubes were stationary during incubation. Rosenow has recently stated that more accurate results are obtained when the tubes are shaken during incubation, but if ones controls and experiments are all conducted on similar /

similar lines the error is constant in both and reliable deductions can be made on comparing them.

The following table gives the results obtained by me :

Opsonic Indices

Case Number	Before Salvarsan		After Salvarsan					
	Total cocci	Average per cell	4 hours after		8 hours after		24 hours after	
			Total cocci	Average per cell	Total cocci	Average per cell	Total cocci	Average per cell
45	366	3.66	340	3.4	318	3.18	405	4.05
46	311	3.11	356	2.56	379	3.79	326	3.26
47	389	3.89	392	3.92	343	3.43	361	3.61
48	395	3.95	357	3.57	364	3.64	312	3.12
49	316	3.16	349	3.49	360	3.6	339	3.39
50	356	3.56	333	3.33	372	3.72	368	3.68
51	332	3.32	387	3.87	329	3.29	322	3.22
52	378	3.78	348	3.48	387	3.87	390	3.9
53	349	3.49	367	3.67	351	3.51	312	3.12
54	301	3.01	376	3.76	358	3.58	340	3.4
	3493	3.493	3605	3.605	3561	3.561	3475	3.475

Average 3.493 3.605 3.561 3.475

Index 1 1.03 ± 1.02 ± 1.

From these results it is evident that Salvarsan has little effect on the Opsonic Index with reference to the staphylococcus aureus. It would be interesting to compare the results of using a pure culture of the Treponema Pallidum in reference to this question. At the end of the fourth hour there is a very slight increase, but not sufficiently marked to be taken note of. A point of importance, however, is, that though the phagocytic activity of the cells remains unchanged there is, as already pointed out, at the fourth and eighth hours a marked leucocytosis, which means a high total phagocytic action.

In making the observations with regard to the Opsonic Indices I used my own white cells. These were obtained by pricking one's fingers and allowing blood to flow into a solution of citrate of soda in order to prevent coagulation. The mixture was then centrifuged and the supernatant clear serum carefully pipetted off, The white corpuscles were then carefully "creamed off" and diluted with normal saline. They were then centrifuged once more, the clear fluid being removed for a second time. This was done in order to wash the white cells free from my own plasma.

No control observations were made on non-syphilitic persons, as the object of the investigation was to determine whether, coincident with the increase in leucocytes, there was a corresponding increase of opsonins in the plasma of men treated with Salvarsan. As already noted no increase could be demonstrated.

and a loss of 23% of haemoglobin as compared with normal individuals.

In the ten cases now under consideration the changes in the red elements have been still more marked than those recorded above. The red blood corpuscles were only 3,875,000 per c.m. or only 77.5% of normal, and the haemoglobin was reduced to 55%. This shows a reduction of 1,125,000 red cells per c.m. and 38% of haemoglobin. The following table shows the changes produced by treatment with salvarsan :

Action of Salvarsan on the Red Blood Corpuscles andHaemoglobin : A careful study of the effect of

Salvarsan on the red blood corpuscles with reference to the total number and haemoglobin content has been made in ten cases, and as a result one can make certain deductions. It may be asserted that ten cases are too few to give reliable data, but those selected for study were men showing marked changes in the red cells of secondary anaemia, and as in all of them the results were of a similar nature my conclusions can be claimed to be of some value.

I have shewn that the result of the examination of the blood of fifty cases of syphilitics before treatment with Salvarsan, is to give an average red count of 4,360,000 cells per c.m. or only 80% of the normal, and the haemoglobin content was only 77%. There was a reduction therefore of 640,000 red corpuscles per c.m. and a loss of 23% of haemoglobin as compared with normal individuals.

In the ten cases now under consideration the changes in the red elements have been still more marked than those recorded above. The red blood corpuscles were only 3,878,000 per c.m., or only 77.5% of normal, and the haemoglobin was reduced to 63%. This shews a reduction of 1,122,000 red cells per c.m. and 38% of haemoglobin. The following table shews the changes produced by treatment with Salvarsan :

	Before Salvarsan	After Salvarsan					
		4 days	10 days	20 days	30 days	40 days	50 days
Red Blood Corpuscles	3878000 (77.5%)	4140000 (82.8%)	4521800 (90.4%)	4721000 (94.4%)	4760000 (95.2%)	4958000 (99.1%)	4805000 (96.1%)
Haemo- globin	63%	75.2%	86.4%	91%	92%	94%	93.2%
Colour Index	.813	.908	.955	.964	.962	.948	.98

The comparative study of these figures is of considerable interest and importance. It will be seen at once that the immediate effect of Salvarsan is more marked on the haemoglobin than on the red cells. Thus, four days after the injection of the drug, the red cells have increased by only 5.3% as against an increase of no less than 12.2% in haemoglobin. Ten days later the red cells have increased 12.9% as against 22.3% of haemoglobin. Twenty days later the red cells have increased 16.9% as against 27.6% of haemoglobin. After this the red cells increase in greater proportion than does the haemoglobin, thus between the twentieth and thirtieth days after the injection of the drug, the red corpuscles increased by .8% as against 1% of haemoglobin, and between the thirtieth and fortieth days the reds increased 3.9% as compared with 2% of haemoglobin. This remarkable and rapid improvement in the condition of the red cells is worthy of further study. The anaemia of syphilis is included under /

under the heading of secondary anaemias. That is to say the poor condition of the blood is due to the presence and action of some toxic substance. This substance is now known to be the *Treponema Pallidum*. The rapid regeneration of the red cells can therefore be justly ascribed to the destructive effect of Salvarsan on the *Treponemata* and the removal of their toxins. This fact is supported by comparing the action of Salvarsan with that of Mercury in Syphilis. Thus Gaillard has shewn that under Mercury the red cells increased for the first fourteen days and the haemoglobin for twenty four days. If Mercury is continued beyond this time, the haemoglobin and later the red cells begin to diminish. The usual effect of Mercury is to destroy the red cells and haemoglobin. Its beneficial effect on these constituents in syphilis must therefore be due to its action on the causative organism.

Salvarsan causes improvement on account of its parasitotrophic powers. But in addition there is the undoubtedly beneficial effect of the arsenic it contains on the blood forming centres, particularly the bone marrow. In this connection it is interesting to note the excellent results obtained by Bramwell in treating cases of pernicious anaemia. The red cells /

cells and haemoglobin were both affected in his series of cases, but the red corpuscles were the most benefited.

One is therefore justified in stating that Salvarsan has a very definite regenerating effect on the red cells and haemoglobin in syphilis, due to its action in destroying the organism but also augmented by its action on the sources in which the red constituents arise.

II. Haemoglobin

Case No.	Before	After Salvarsan					
	Salvarsan	4 days	10 days	20 days	30 days	40 days	50 days
8	75%	87%	90%	94%		96%	
6	55%	71%	80%	92%	90%	94%	
9	60%	75%	84%		95%	96%	
10	48%	64%	75%	84%	88%		90%
11	68%	74%	80%	94%	95%		97%
13	50%	70%	82%		90%		92%
19	70%	75%	80%	92%			94%
22	65%	78%	90%	92%	94%		96%
25	78%	80%	90%		94%	95%	
29	80%	80%	85%	90%	92%	93%	
Average	68%	75.25	80.45	91%	92%	94%	95%

Effect of Salvarsan on Red Blood Corpuscles and HaemoglobinI. Red Blood Corpuscles.

Case No.	Before	After Salvarsan					
	Salvarsan	4 days	10 days	20 days	30 days	40 days	50 days
5	4,510,000	4,445,000	4,890,000	4,900,000		5,000,000	
6	4,120,000	4,360,000	4,670,000	4,780,000	4,850,000	4,910,000	
9	4,000,000	4,400,000	4,620,000		4,970,000	5,220,000	
10	3,500,000	3,850,000	4,220,000	4,335,000	4,480,000		4,500,000
11	4,200,000	4,220,000	4,540,000	4,720,000	4,750,000		4,830,000
13	3,100,000	3,720,000	4,310,000		4,560,000		4,632,000
15	4,000,000	4,175,000	4,480,000	4,790,000			4,965,000
22	4,000,000	4,125,000	4,628,000	4,840,000	5,000,000		5,100,000
25	3,800,000	4,200,000	4,500,000		4,900,000	4,880,000	
29	3,550,000	3,900,000	4,360,000	4,682,000	4,760,000	4,780,000	
<u>Average</u>	3,878,000	4,140,000	4,521,800	4,721,000	4,760,000	4,958,000	4,805,000

II. Haemoglobin

Case No.	Before	After Salvarsan					
	Salvarsan	4 days	10 days	20 days	30 days	40 days	50 days
5	75%	82%	90%	94%		96%	
6	65%	74%	88%	92%	90%	94%	
9	60%	75%	84%		95%	96%	
10	46%	64%	78%	84%	88%		90%
11	68%	74%	88%	94%	95%		94%
13	50%	70%	82%		90%		92%
15	70%	75%	86%	92%			94%
22	66%	78%	90%	92%	94%		96%
25	70%	80%	90%		94%	92%	
29	60%	80%	86%	90%	92%	92%	
<u>Average</u>	63%	75.2%	86.4%	91%	92%	94%	93½%

Effect of Salvarsan on the Coagulation time of blood :

The investigation of the action of Salvarsan on the coagulation time of blood is important owing to the fact that if on administration intravenously it increases, in any marked degree, the rate of coagulation there is a risk of the rapid formation of small thrombi and consequent blocking of small vessels.

Silbermann states that arsenic increases the coagulability of the blood leading to widespread rapid intravascular coagulation. Heinz supports this assertion and states that the coagulation caused is due to thrombi formed by agglutination of blood plates. It is interesting to note in this connection that Don R. Joseph⁴⁴ has shewn recently that acid solutions of Salvarsan injected intravenously into dogs and rabbits, even in the concentration used in man, produce a precipitate in the blood stream. Alkaline solutions of Salvarsan, even in strong concentration, never produce a precipitate when injected intravenously. Macdonagh⁴⁵ states that if the fluid is too alkaline thrombosis is aided. It is therefore important to determine whether Salvarsan has any effect in increasing the coagulation rate of the blood, and if so, what precautions must be taken to prevent this happening.

I have carefully studied the effect on the coagulation time of the intravenous injection of Salvarsan /

Salvarsan in six cases at definite intervals after administration of the drug. The method used was that advocated by McGowan.²² Time was taken with a stop-watch by my laboratory assistant. In all cases two readings were taken each time, a fresh prick being made and the first drop appearing being drawn up into the capillary tubes.

I first of all made a series of observations on normal non-syphilitic persons, taken two readings daily from each of them on three successive days. This gave me a normal or control for this station with which to compare the results obtained from observations on the syphilitics. The temperature in my laboratory was carefully noted each day to ascertain whether slight variations had any effect on the coagulation time. The readings were taken between 10 a.m. and 12 noon. The laboratory temperature did not vary much on these occasions, ranging from 23.3°C. to 27.8°C. McGowan neglects the influence of temperature. Sabrazes and Addis²³ endeavour to maintain a temperature of 18°C. Dale and Laidlaw have recently shewn that the temperature is an important consideration and that though there is very little variation between 35°C and 40°C. the temperature coefficient becomes very large when it falls below 22°C.

The temperature in the wards, where the observations on the bloods of patients after the injection of /

of Salvarsan were made ranged from 21.1° to 25.6° C.

The following table gives the results of my controls :

Coagulation Time of Blood
(Controls).

Date	Temperature of Room.	J.J.H.N.	J.V.B.	S. A-S.	W.B.	Daily Average
20.3.11	24.4° C.	4'15" 3'45"	4'10" 3'50"	3'29" 3'35"	3'46" 3'31"	3'42"
21.3.11	23.3° C.	4'5" 4'20"	3'30" 3'52"	3'41" 4'2"	4'15" 3'56"	3'57"
22.3.11	27.8° C.	3'28" 3'35"	3'48" 3'35"	3'15" 3'25"	4' 3'40"	3'36"
<u>Average</u>	25.1° C.	3'54"	3'48"	3'34"	3'51"	<u>3'45"</u>

This table shews that at a temperature of 25.1° C. the coagulation time in normal non-syphilitic persons is 3'45", obtained from an average of twenty-four observations.

Having thus obtained a control time from healthy men I made observations on six cases of syphilis taking the readings the day before getting an injection of Salvarsan and again at intervals of four, eight, twenty four, forty eight and seventy two hours after the administration of the drug. The results obtained can be readily seen on reference to the following table :

Coagulation Time of Blood

(Syphilitics).

Case No.	Day before Salvarsan			After Salvarsan									
	Date	Temp.	Coagulation time.	4 hours		8 hours		24 hours		48 hours		72 hours	
				Temp.	Coagulation time	Temp.	Coagulation time	Temp.	Coagulation time	Temp.	Coagulation time	Temp.	Coagulation time
55	9.4.12	26.7°C	3'41" 3'10"	27.2°C	3'33" 3'41"	23.3°C	3'42" 4'	26.7°C	3'29" 3'36"	25.6°C	3'39" 3'56"	28°C	3'40" 3'28"
56	20.5.12	28°C	4'10" 3'50"	27.6°C	3'46" 3'57"	26.5°C	4'12" 4'7"	27°C	3'51" 3'41"	24.4°C	3'31" 3'46"	25.2°C	3'55" 3'48"
59	30.5.12	23.3°C	4'20" 4'11"	25°C	4'1" 4'10"	22.2°C	3'46" 3'54"	25.8°C	4'6" 3'53"	26.8°C	4'10" 4'1"	23.2°C	3'59" 4'14"
60	21.6.12	22.4°C	3'29" 3'47"	23.6°C	3'39" 3'43"	20.1°C	3'56" 3'51"	23.4°C	3'29" 3'47"	24.6°C	3'37" 3'33"	24.4°C	3'51" 3'47"
61	1.7.12	20°C	3'48" 3'41"	20.8°C	3'29" 3'53"	18.4°C	4'3" 3'40"	22.2°C	3'46" 3'35"	20.1°C	3'44" 3'53"	19.8°C	3'56" 3'43"
62	15.7.12	18.6°C	4'18" 4'3"	18°C	4'14" 4'1"	17.1°C	3'58" 3'56"	20°C	4'5" 3'49"	18.6°C	3'50" 4'12"	22.2°C	3'57" 3'40"
<u>Average</u>		23.2°C	<u>3'57"</u>	23.8°C	<u>3'50"</u>	21.3°C	<u>3'55"</u>	24.3°C	<u>3'45"</u>	23.3°C	<u>3'49"</u>	23.6°C	<u>3'49"</u>

It will be at once seen that there is no marked change in the coagulation time after an injection of Salvarsan. The average of twelve observations before treatment gives 3'57" as the coagulation time of Syphilitics, which is slightly slower than my normal (3'45"). The variation after Salvarsan is very small the time increasing by only a few seconds. The increase is most marked twenty four hours after treatment where there is a difference of twelve seconds between the rate before and after the drug. As the temperatures of the rooms were not the same, being 1.1° C. higher after the drug was given, the increased rapidity of coagulation may be ascribed to this factor which is in accordance with Dale and Laidlaw's findings.

As a result of these observations I conclude that Salvarsan has no effect on the coagulation time of the blood. Joseph's observation that acid solutions of Salvarsan causes precipitates to form in the blood is of interest in that it tallies with the observations of Silbermann regarding arsenic. My own work points to the close pharmacological resemblance in action between Salvarsan and arsenic, which is again borne out in this connection and emphasises the powerful effects of the arsenic radicle in Salvarsan.

Action of Salvarsan on the Nervous System :

In all my cases very special attention has been paid to a study of the effect of Salvarsan on the Central Nervous System, Peripheral Nerves, and Organs of Special Sense.

Firstly, with regard to the Central Nervous System. In forming an opinion as to the effect of Salvarsan I have relied on

(1) Subjective symptoms complained of by the patient

(2) Physical signs observed by myself.

(1) Subjective symptoms : The one constant symptom present is headache. This may be very mild in nature or of a considerable degree of severity. It is almost always frontal in situation, and is described as being of a beating character with a feeling of tightness across the head. It may come on within ten or fifteen minutes after the injection of the drug, or its onset may be delayed for an hour or more. It is usually of short duration and is quite gone the morning after the injection of the drug. In a few cases it has persisted for a day or two longer.

The question at once arises as to the cause of the headache. Schrieber and Wechselman⁶² state that the headache is due to the liberation of large quantities of endo-toxins and their subsequent absorption. Ehrlich agrees with these authors. But from a careful study of my cases I am of the opinion that Salvarsan /

Salvarsan may give rise to a severe headache on account of a definite action on the cells of the cortex. In favour of this view is the fact that in the two cases of non-syphilitics (Nos. 85 and 86) to whom I administered the drug, severe headache was a well marked feature. Litterer⁴⁶ of Nashville, Tenn., U.S.A., got similar results when administering the drug to cases other than those of Syphilis.

But I am quite prepared to admit that the headache may be accentuated by the liberation of endotoxins from the large numbers of destroyed Treponemata. This view is supported by the fact that in the very great majority of the cases the headache after a first injection, when the patient has well marked obvious signs of disease, has been more severe than after a second injection, when only a positive Wassermann has justified a repetition of the cure. The headache seems to have a definite relationship in its intensity with the severity of the infective condition at the time of the injection. This, however, is not invariably the case, as I have found, on occasion, that the reaction after the second injection has been much severe than after the first. This is well borne out on reference to Case 5 in the Appendix. Private H. had a first injection of .5 grammes Salvarsan on June 9th 1911. The maximum pulse rate reached /

reached was 96 per minute, temperature 101.6° F. Headache severe from the second to the eighth hour after treatment, and was quite gone the next morning. On July 28th, he was given a second injection of .5 grammes Salvarsan. There were no clinical signs of disease to justify this, but only a positive Wassermann reaction. Yet his pulse reached 108 per minute, respiration 30, temperature 103.8 , and he suffered from a severe headache all the following day.

The case of Pte.W. (No.28) is another example of this. He received an injection of .5 grammes Salvarsan on November 25th 1911, and though showing active signs of disease, with a strongly positive Wassermann, he had a mild reaction with only a slight headache for a few hours. On January 3rd 1912, he received a second injection of .5 grammes, because of a persistent positive Wassermann reaction. He had no signs of disease. Yet his reaction was very severe. The temperature ran up to 103° F. and he suffered from a very bad headache for twenty four hours.

Further cases illustrating this point could easily be quoted, but I have merely instanced these two to prove that one cannot rely on getting a mild reaction in any case. What the factor is that gives rise to such severe reactions in the absence of clinical signs of the disease is hard to say. In both /

both the cases referred to the Wassermann reaction was less intense than when they received their first dose.

The case of Lupus Vulgaris (Pte.B. No.85) reacted fairly severely after both his injections of Salvarsan, suffering from severe headache on each occasion. He had no syphilitic endo-toxins to liberate so that they could not be the cause of the discomfort. The case of Malaria (Sapper D. No.86) also suffered from a bad head after treatment. These two cases seem to me to justify my first assertion that Salvarsan may give rise to headache on account of a definite pharmacological action on the cells of the cortex.

A well marked effect of the drug is its action on the mental state of patients. This was early impressed on my mind by the effect produced on my first cases. Nos. 1, 3 and 6 were men who had had various treatments, but with very little benefit. They had lost heart and were almost in a state of melancholy. Within twenty four hours after the injection of the drug they brightened up and never looked back again. The same effect was noted in Case 72. This man was a Sapper, a native of India, and came to hospital with a hard sore on his prepuce giving rise to marked phimosis. I have not seen a native /

native look more doleful. The mental change following an injection of Salvarsan was nothing short of marvellous as he brightened up and appeared a different man. *These pains were nervous in origin.*

(R) Hoppe and Schreiber³⁸ have noted the same thing, and they ascribe it to the stimulating effect of Salvarsan on the lecithin-metabolism. I am unable to express any opinion as to the cause of the change, but one would like to have a case of ordinary melancholia, with no superadded syphilis, and to inject such a case with .5 grammes Salvarsan and note the result. In syphilitics there is the possibility that the mental change may be induced by "faith" in a new remedy. In the case of the Sapper this would not apply however as he had never heard of the drug. *In a needle, heat*

300 In only one of my cases were any sensations referred to Peripheral Nerves. This was Pte.M. (No.75) who complained of severe neuralgic pain in the teeth of the lower jaw after .5 grammes of Salvarsan. His teeth were remarkably good and he had never previously suffered from neuralgia. The pain began one hour after the injection and persisted for six hours, and then ceased. The cause of this I cannot explain. He had no tender points along any of his cranial or peripheral nerves and no visible changes could be found. *It was tested and no change was ever found after*

found in his lower jaw.

A large number of men suffered from aching pains in the loins and legs, but in none of them could one say that these pains were nervous in origin.

(2) Nervous system effects judged by Physical Signs :

In all cases treated careful note has been taken with regard to the following points :

- (a) Sensory functions.
- (b) Motor functions.
- (c) Reflexes.
- (d) Effect on cranial nerves, with special reference to those of the eyes and ears.

(a) Sensory functions : No abnormal sensations were complained of except in case No.75 as noted above. The senses of touch, pain tested with a needle, heat and cold, and muscular sense, were not in any affected by Salvarsan.

(b) Motor functions : These were not in any way affected. Muscles remained well nourished. No tremors were detected. Co-ordination was not interfered with. No electrical reactions were done as no apparatus was at hand.

(c) Reflexes : The superficial reflexes tested were the conjunctival and plantar. In no case was any change noted in these. Of the deep reflexes only the patellar was tested and no change was ever found after /

after giving the drug.

Deglutition, defaecation, and micturition were unaffected in all my cases.

(d) Effect on cranial nerves : Special attention was paid to an investigation of the effects of Salvarsan on the cranial nerves, especially those of the eye and ear, owing to the alleged dangers of the drug in causing various degenerations of these nerves.

The only nerve commonly affected was the fifth. In a large proportion of my cases a herpes developed two to four days after the injection of the drug. With persistent regularity it involved the region round the mouth and in two cases even appeared on the palate. The eruption was very much like any other common herpes. It was not painful. It began as small red raised points which soon developed into vesicles. These vesicles lasted about a day and then dried forming scabs which fell off a couple of days later without leaving any scars. The main features of the herpes are its painlessness, rapid course, and absence of scarring. In these three things it differed markedly from Herpes Zoster or Herpes Frontalis. No treatment was called for.

Others have recorded similar observations regarding the development of a herpes. Fisichella²⁶ reports two /

two cases in which a Herpes Zoster of the fifth and sixth intercostal space occurred, and he comments on the mildness of the attack. He does not state whether the herpes was symmetrical. In all my cases a marked feature has been the fact that both sides of the mouth have been equally affected.

The cause of the herpes is difficult to ascertain but I am inclined to think it is due to the effect of the arsenic radicle of Salvarsan. It is well known that inorganic arsenic, as again pointed out by Sir Jonathan Hutchinson in the British Medical Journal of April 29th 1911, will give rise to a herpes.

It has been suggested that the herpes is due to excessive alkalinity of the Salvarsan when being injected, but I do not agree with this view, as all my solutions for injection were carefully prepared by myself and, on many occasions, I made use of litmus solution to determine when the first degree of alkalinity was attained, instead of relying merely on the disappearance of the precipitated base to tell that the solution was alkaline. I am therefore certain that no men received an excessively alkaline solution of salvarsan, and when a herpes appeared it must have been due to some other cause.

On /

On several occasions I inoculated media with fluid from the vesicles, but never succeeded in obtaining any growth of organisms. The media used were gelatine slopes and stab, agar-agar slopes and stab, broth, and MacConkeys bile salt glucose agar. I also inoculated blood agar slope media with negative results.

Treponemata were not searched for as one would not expect to find them in lesions appearing two or three days after an injection of the drug.

I therefore conclude that the herpes is non-organismal and is due to some action of the arsenic present.

With regard to the optic nerve. All my cases had their eyes carefully examined before the administration of Salvarsan. The examination consisted in testing the acuity of vision by Snellins types, colour by wools, and the field of vision by the hand. In addition an ophthalmoscopic examination of the fundus oculi was made. Similar tests were carried out after the treatment had been given at varying intervals. In not a single instance did any untoward result follow the injection of the drug. All my cases being soldiers any interference with vision would soon /

(Case 10) received five intravenous injections

soon be noted as their shooting would become less accurate.

Finger of Vienna, stated at the Fifth German Congress of Neurologists held in Frankfort in October 1911, that no less than 9 per cent of the cases treated by him developed nerve complications amongst which optic neuritis formed a considerable proportion. Gaucher³⁹ has reported a case of optic neuritis following an injection of Salvarsan. It is now generally accepted that cases shewing any affection of the optic nerve after Salvarsan should be given a second injection of the drug as the neuritis is said to be due to the action of the liberated toxins from destroyed Treponemata. Wechselmann⁷⁰, Grass, Schanz,⁵⁷ and Hirsch,³⁷ have shewn how useful the drug is in neuroretinitis. Ehrlich has given warning against using the drug where gross eye lesions are present. Browning and Mackenzie⁶⁶ have shewn that Finger's main case had undergone various other arsenical cures before being given Salvarsan, and they ascribe the resulting blindness to this fact.

What concerns me in my thesis is not so much what others have found, but to record what my experience has been. As above noted, not one of my cases have suffered from any ill effects. One man Pte.M., (Case 10) received five intravenous injections of /

of Salvarsan in six months, giving a total of 2.3 grammes of the drug with no bad effects. Another case, Pte.S. (No.3), was suffering from severe syphilitic iritis which cleared up after one injection in a marvellous manner to recur slightly and finally be cured with a second injection.

I am, therefore, of the opinion that there is little danger to be feared from Salvarsan giving rise to optic neuritis.

The auditory nerve was tested with my watch which I could hear at 30 inches distant from both ears. None of my cases had any involvement in the auditory apparatus.

Of interest in this connection is the work of Don R. Joseph⁴¹ on the action of Salvarsan upon the irritability of nerve and muscle. As a result of his investigations he concludes "that Salvarsan is a "comparatively inactive drug when applied to the "muscle and nerve of the frog. In perfusion experiments no detrimental action is to be seen either "upon the direct or the indirect irritability. In "bathing experiments, in which the concentration of "the Salvarsan in the various solutions was much "higher than that in which it reaches the peripheral "tissues in the human subject through the circulation, "the /

"the loss of irritability occurred only after a long
 "period of exposure to the drug".

The cases I have had have been good test ones
 in regard to this question, as they are not lost
 sight of, and I have no fear of any untoward results
 following the use of the drug.

In all my cases the urine has been carefully
 tested for the presence of albumin before and after
 the injection and specific gravity noted. In none
 of them has albumin ever been found after the intra-
 venous injection of the drug. One case, Pts. S.
 (No. 53) had well marked albuminuria before the injec-
 tion was given him, and I at first felt somewhat
 chary of risking the treatment. But as the albumin
 was small in amount I decided to proceed with the in-
 jection. The results fully justified this action as
 no albumin could be found the following day, and none
 was ever found again. Traudel and Lind report simi-
 lar cases, and Browning and Mackenzie also confirm
 this observation.

Other observers have, however, reported contrary
 results. Thus Weller reports two cases out of a
 series of five hundred in which acute nephritis fol-
 lowed the subcutaneous injection of the drug. Again
 Heller in a series of 366 cases refers to two cases
 of latent nephritis which became active after the
 subcutaneous

Action of Salvarsan on the Urinary System :

I do not intend to devote much time to a critical survey of the action of Salvarsan on the kidneys and bladder, as my own series of cases have furnished me with very little evidence of any kind in relation to this subject.

In all my cases the urine has been carefully tested for the presence of albumin before and after the injection and specific gravity noted. In none of them has albumin ever been found after the intravenous injection of the drug. One case, Pte.S. (No.63) had well marked albuminuria before the injection was given him, and I at first felt somewhat chary of risking the treatment. But as the albumin was small in amount I decided to proceed with the injection. The results fully justified this action as no albumin could be found the following day, and none was ever found again. Truepel and Lini⁶⁹ report similar cases, and Browning and Mackenzie¹⁵ also confirm this observation.

Other observers have, however, reported contrary results. Thus Weiler⁷⁰ reports two cases, out of a series of five hundred, in which acute nephritis followed the subcutaneous injection of the drug. Again Sellei⁶⁴ in a series of 350 cases refers to two cases of latent nephritis which became active after the subcutaneous /

subcutaneous administration of Salvarsan. It must be noted that in these cases the intravenous method was not employed. As a result of the subcutaneous method Salvarsan may have been deposited in the tissues, as so often occurs, and the effect on the kidneys may have been due to the action of decomposition products of the Salvarsan.

Wechselmann,⁷⁰ in a series of 1,200 cases, and Schreiber,⁶³ in a series of 1,000 cases, both using the intravenous method of medication, make no reference to the presence of albuminuria as a sequence of the injection.

One therefore need not fear the action of the drug on the kidneys, as it seems to have very little effect in causing albumin to appear in the urine. Where albumin is present, due to syphilitic disease of the kidneys, the drug undoubtedly does good.

A constant effect is produced on the specific gravity which is raised, but this is an effect following any febrile condition and cannot be attributed to a specific action of Salvarsan.

A complication, said to follow treatment by Salvarsan, is retention of urine. Bohac and Sabotka⁷³ report three cases of this, and in all three the knee jerks were absent. These authors attribute the /

the symptoms to a toxic influence of the drug on the spinal chord. Eitner,¹³ Malinowski,⁴⁶ Herxheimer,³⁵ and others report similar cases, but it is impossible to find evidence of a common cause of the symptoms.

My personal opinion, as a result of my own observations, is that Salvarsan has very little effect on the urinary system.

to a stimulating effect on the lecithin-metabolism. Whatever be the explanation a marked improvement in general condition rapidly follows the administration of the drug. I have shown that the anæmia of syphilis rapidly improves, the condition of the red cells returning to normal in a few weeks. Coinciding with this the body weight rapidly increases. The following table shows the improvement in the ten cases whose red cells and hæmoglobin have already been studied, (see page 79).

Effect of Salvarsan on Body Weight

(Recorded in pounds)

Case Number	Before	After Salvarsan					
	Salvarsan	4 days	10 days	20 days	30 days	40 days	50 days
5	132.5	135	135	136	138	139	
6	114	116	116	119	118	122	
9	140.5	142	144		145	148.5	
10	121	122	125	127	129	129	131
11	134	134	135	138	140		141.5
13	124	126	127	129	130		130
15	130.5	132	134	137	138	140	140
22	135	137	138.5	139	141.5		143
25	170	174	176	176	175	178	180
29	140	143	144	144	147	147	
Average	134.15	136.1	137.6	138.4	140.5	142.2	145.5

Effect on Metabolism :

In all my cases careful note has been taken of the weight of patients before and after treatment with Salvarsan. Reference has already been made to the wonderful feeling of well being that quickly follows the injection of the drug, and ascribed by Hoppe and Schreiber³⁸ to a stimulating effect on the lecithin-metabolism. Whatever be the explanation a marked improvement in general condition rapidly follows the administration of the drug. I have shewn that the anaemia of syphilis rapidly improves, the condition of the red cells returning to normal in a few weeks. Coinciding with this the body weight rapidly increases. The following table shews the improvement in the ten cases whose red cells and haemoglobin have already been studied, (see page 70).

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		4 days	10 days	20 days	30 days	40 days	50 days
5	132.5	135	136	136	136	137	
6	114	116	118	119	118	122	
9	140.5	142	144		145	145.5	
10	121	122	125	127	129	129	131
11	134	134	136	138	140		141.5
13	124	126	127	129	130		136
15	130.5	132	134	137	138	140	140
22	135	137	138.5	139	141.5		145
25	170	174	176	176	175	178	180
29	140	143	144	144	147	147	
<u>Average</u>	134.15	136.1	137.8	138.4	140.5	142.2	145.6

It will be noted that the increase in weight, the average of ten cases, is no less than 11.5 lbs. in fifty days. These ten cases have not been specially selected by me to illustrate my point, much better ones being available. They were just picked out because the blood changes had been studied in connection with them, that is to say they are random selections. The case of Pte.C. (No.30), is a much more striking example of the rate of increase in weight. On November 25th 1911, he weighed 142 lbs. On February 2nd 1912, only sixty nine days later, he weighed 160 lbs, giving an increase of 18 lbs, and this was well maintained, for a year later he scaled 159 lbs.

Again take the case of Driver W., (No.37), On December 12th 1911 he only weighed 112 lbs. He was given an intravenous injection of .5 grammes Salvarsan on December 18th. On January 15th 1912, only thirty days after treatment, he weighed 124 lbs, having put on twelve pounds in this time.

It is useless multiplying cases in illustration of my point. One never met anything to approach these beneficial effects when using Mercury in the treatment of Syphilis, either in respect of rapidity or magnitude of the increase in weight and improvement in the general condition of the patient.

Elimination of Salvarsan :

I have not carried out any observations with reference to the elimination of Salvarsan, but in order to complete this part of my thesis I wish briefly to refer to this question. As all my work has been carried out by the intravenous injection of the drug I only intend to consider elimination after the use of Salvarsan by this method.

Beveridge and Walker¹² found "that in the case of "an intravenous injection the urine is not free until "the ninth, tenth, or eleventh day. The excretion is "irregular, but the highest amount is excreted on the "first, second, third and fourth days. It is also "excreted by the intestines, so the examination of "the urine alone cannot be the final proof of elimina- "tion. In the case of intravenous injection, arsenic "persists longer in the stools than in the urine". These observers also state that the excretion after a second dose shews no marked difference in rate from the excretion after the first.

Fischer and Hoppe¹⁵ obtained very similar results. Loeb¹⁶ found arsenic present in traces up to the eighth week after injection. Whether the drug is potent over this long period is very doubtful.

After the injection of Salvarsan the urine soon contains /

contains arsenic. Stopford-Taylor and MacKenna found it in the urine first voided after the injection. Browning and Mackenzie¹⁵ state that it can be found in the urine two hours after administration either by intravenous or subcutaneous injection.

Stopford-Taylor and MacKenna also report that they have found arsenic present in the vomited matter. This points to its being excreted into the stomach.

I have been unable to find any reference to its presence in other secretions such as the milk and saliva.

The drug is therefore mainly excreted by the kidneys but it is also present in vomited matter and foeces. The excretion begins soon after the administration and the drug is completely got rid of in eleven or twelve days as a rule, though it may be present for eight weeks.

In dealing with the therapeutic uses of Salvarsan I propose to limit myself to those conditions in which I have personally used the drug. This reduces the discussion of the problem to four diseases.

The foremost of these is the therapeutic efficacy of Salvarsan in Syphilis. Next I propose to discuss its value in three non-specific conditions - Lupus Vulgaris,

THERAPEUTIC USES of SALVARSAN

Lupus vulgaris, Malaria, and Piroplasma Canis.

- I. Syphilis.
- II. Lupus Vulgaris.
- III. Malaria.
- IV. Piroplasma Canis.

One is well aware of the fact that Salvarsan has been used with more or less success in numerous other conditions, such as, Fracobiosis, Leprosy, Perniosis, Anaemia, Scarlet Fever, etc. But following the same lines as in the first part of my thesis I wish to limit myself to those conditions in which I have had personal experience of the use of the drug. ANY deductions one may make have the virtue of personal experience behind them and are of much more value than the mere splicing of other people's results.

In dealing with the therapeutic uses of Salvarsan I propose to limit myself to those conditions in which I have personally used the drug. This reduces the discussion of the problem to four diseases. The foremost of these is the therapeutic effects of Salvarsan in Syphilis. Next I propose to discuss its value in three non-specific conditions - Lupus Vulgaris, Malaria and Piroplasma Canis. The last topic concerns more the Veterinary Surgeon, but as I have had four dogs under my charge suffering from Piroplasmosis, and have therefore had an opportunity of observing the effects of the drug on this condition, I intend to refer to the subject fairly fully.

One is well aware of the fact that Salvarsan has been used with more or less success in numerous other conditions, such as, Framboesia, Leprosy, Pernicious Anaemia, Scarlet Fever, etc. But following the same lines as in the first part of my thesis I wish to limit myself to those conditions in which I have had personal experience of the use of the drug. Any deductions one may make have the virtue of personal experience behind them and are of much more value than the mere epitomising of other people's results.

From heart or kidney disease not of specific origin, every case of Syphilis should be treated by Salvarsan.

One /

I. Therapeutic uses of Salvarsan in Syphilis :

At the annual meeting of the British Medical Association held in Birmingham in 1911, a discussion was inaugurated by Mr E.J. Lane on "Recent developments in the recognition and treatment of Syphilis". In the course of his remarks he stated "I do not think that the general use of the intravenous injection of Salvarsan is to be commended, and I remain of the opinion that there are many objections to its being employed as a routine treatment".

Gaucher considers that "Salvarsan is a dangerous drug which should only be used with extreme prudence, and should be reserved for cases in which Mercury fails or is not tolerated, but such cases are extremely rare".

The alleged dangers following the use of Salvarsan have been so constantly and persistently preached that it is not to be wondered at that the general use of the drug has been somewhat tardily taken up.

But the extraordinary success that has followed its use in the hands of trained observers has largely broken down prejudice and one's own personal opinion is, that provided no contra indications are present from heart or kidney disease not of specific origin, every case of Syphilis should be treated by Salvarsan.

One /

One asserts this notwithstanding the above quoted warnings from two men of standing and with no intention of being dogmatic, but because personal experience of the use of the drug has forced one to the conclusion that the curative effects of Salvarsan in Syphilis are much more rapid, and no less permanent, than what is ever accomplished by Mercury alone.

Having made so decided a statement it is necessary to adduce facts that will justify it on careful examination. I therefore propose to devote some little time to a critical analysis of my own series of cases with reference to the immediate effects of Salvarsan on the clinical signs of the disease and with reference to the permanence of cure, as controlled by the Wassermann reaction.

Primary Syphilis.

In this class I have placed only those cases in which a typical hard chancre was the sole manifestation of the disease, and in the serum of which the *Treponema Pallidum* had been found. A few of the cases had a positive Wassermann reaction, shewing that though the lesion present was a localised one, the infection had become general. But none of them had developed any rash or other visible sign of disease usually described as indicating the secondary state /

stage of syphilis.

In this class I have nine cases (Nos. 72, 75, 77, 78, 79, 80, 82, 83 and 84). These men received an intravenous injection of Salvarsan but no other treatment, either local, in the form of dressings, or general, by Mercury. That is to say I put the drug I was using to a severe test to see whether it alone could cause a disappearance of the primary lesion. In none of these cases did I fail to get a rapid and complete eradication of all signs of disease, and in all but three this was accomplished by one injection of .5 grammes of Salvarsan. Of the three cases who received the second injection in only one (No. 77) was it given because the primary sore did not heal. The other two received injections because in one (No. 79) a faintly positive Wassermann reaction was got eighteen days after the first injection, and in the other (No. 80) there was a slight recurrence in the form of a sore throat.

Not only did Salvarsan cause a disappearance of the sores but it accomplished this in incredibly short periods of time. In three cases (Nos. 75, 82 and 84) no sign of a chancre could be found six days after the injection of the drug. In one case (No. 78) the sore had completely disappeared on the seventh day. In another case (No. 83) the lesion had disappeared in nine /

nine days and in another (No.72) it could not be found on the eleventh day. In only one case (No.77) was a second dose given on account of the persistence of the hard sore, which was still present eighteen days after the first injection but healed six days after the second.

Comparing these excellent results with what one obtained under the old mercurial method of treating similar cases, one cannot recall anything to approach the curative effects either in rapidity of occurrence or in the completeness of the cure effected. In fact one of these nine cases illustrates the point. Pte.M. (No.75) had been diagnosed and treated for a soft sore with the usual Black Wash dressing and Iodiform dusting. This had gone on for twelve days with no improvement and I was then asked to see the patient. He had a small hard sore on the front of his prepuce, shotty to the feel, and I managed to isolate the *Treponema Pallidum* from it on September 9th 1912. Two days later he was given .5 grammes Salvarsan intravenously, and six days later he was discharged hospital to duty with no active signs of disease. He never returned with any further signs of disease, and his Wassermann reaction was negative on the two occasions when it was done afterwards at intervals of one and two months after treatment.

But /

But further evidence of the powerful destructive action of Salvarsan on the *Treponema Pallidum* is got from a study of these cases. In six of the cases, in which the organism was carefully searched for, no trace of the infective germ could be found three days after treatment. In the remaining three cases no search for it was made. I am not aware of any observations in regard to this matter having been made when energetic mercurial treatment has been carried out, and I doubt very much whether such rapid destruction of the organism would follow its use as I have shewn occurs when treatment with Salvarsan is adopted.

My observations regarding the disappearance of the organisms after the intravenous injection of Salvarsan, are in line with those of other investigators. Sieskind and Schreiber⁶⁵ found the *Treponema* absent from primary and secondary lesions two days after treatment. Scholtz⁶⁶ examined thirty two cases and found in fifteen of these *Treponemata* could not be found after twenty hours. In twelve they disappeared in two to three days and in only five cases could they be found after the fourth day. Iversen⁶⁷ punctured glands in ten cases of secondary syphilis and could find no organisms after the third to the fifth days.

It is therefore obvious that Salvarsan has a very powerful spirillicidal action causing a rapid and complete disappearance of the effective agent in Syphilis.

The next question that arises is whether a complete sterilisation of the body is effected or no. Is a permanent cure obtained by one or two injections of the drug ?

I am not able to make definite statements regarding this question from an examination of these nine cases as they were not long enough observed by me. Cases 72, 75 and 77 had no return of symptoms and a constantly negative Wassermann reaction for four months. Cases 78 and 79 had no recurrence and a constantly negative Wassermann reaction for over two months. Case 80 had recurrence, in the form of a slight sore throat, thirteen days after the first injection, but this cleared up at once on receiving a second injection.

(1) The fact that the primary sores all healed and no secondary manifestations had appeared, in three cases up to four months, is a great point in favour of the use of Salvarsan, and I do not expect these cases to shew any further signs of disease. A sterilans magna has been probably obtained.

(2) Fourth course of nine injections - 9 weeks.

(3) Interval of 24 weeks - 24 weeks

Secondary Syphilis /

Period under observation and treatment 102 weeks.

The treatment consists of weekly injections with grey oil and intervals as shown above. Each injection consists /

consists of 12 Secondary Syphilis.

Out of my series of cases no less than fifty three have been men suffering from Syphilis which had reached the secondary stage.

Of this number no less than twenty-five had had previous treatment by mercurial injection for long or short periods. In the Army a uniform system of treatment is adopted. When a man reports sick with Syphilis he is taken into hospital and kept there till all active signs of the disease have disappeared. He is at once put on a Syphilis Register and remains on it for at least two years, during the whole of this period he is under treatment and observation. The treatment consists of courses of mercurial injections with intervals as follows :

- (1) First course of nine injections = 9 weeks.
- (2) Interval of 6 weeks = 6 weeks
- (3) Second course of nine injections = 9 weeks.
- (4) Interval of 12 weeks = 12 weeks.
- (5) Third course of nine injections = 9 weeks.
- (6) Interval of 24 weeks = 24 weeks.
- (7) Fourth course of nine injections = 9 weeks.
- (8) Interval of 24 weeks = 24 weeks

Period under observation and treatment 102 weeks.

The treatment consists of weekly injections with grey oil and intervals as shewn above. Each injection consists /

consists of 10 minims of Grey Oil containing 1 grain of Metallic Mercury. The injection is given into the buttock. If at the end of two years the patient shews no further signs of disease he is struck off the Syphilis Register. If necessary an extra course of Mercury may be given. During the whole of the period during which the soldier is under treatment and observation he suffers severely financially as he is considered "unfit for active service" and loses 6d. a day "service pay". This is a decided hardship in many ways, but this is not the place to discuss this point. Suffice to say that since using Salvarsan, and controlling one's cases by the Wassermann reaction, it has been possible to greatly lessen the period of inefficiency.

Out of my twenty-five cases who have had previous treatment, one had had five complete courses of Mercury. Six had had four courses, eight had had three courses, eight had had two courses, and two had had one course.

A very interesting point in this connection is to note the effect of mercurial treatment on the progress of the disease. Take Case No.21 for example. This man contracted Syphilis at the end of 1906. He had had no less than five courses of Mercury and had been /

been struck off the Syphilis Register for over a year. When seen by me in October 1910 his Wassermann reaction was strongly positive, but the interesting point is that the active signs of disease from which he was suffering were a very typical secondary Syphilitic throat with ulceration of his fauces. The disease had merely been held in check by treatment, and when it recurred it began as an early manifestation.

Again, of the six cases who had had four courses of Mercury every one shewed early secondary symptoms when seen by me.

In instance these cases merely to bring out this point that mercurial treatment, thoroughly carried out, in a very large percentage of cases, apparently only holds the disease in abeyance. This is further emphasised when one notes that all my tertiary cases, twelve in number, had had prolonged treatment with Mercury, and in addition ten more of my cases, who had no active signs of disease, had a positive Wassermann reaction of a considerable degree of intensity.

Varieties of cases treated by the intravenous injection of Salvarsan and effects of the treatment.:

It is almost impossible to group men according to the lesions present. Roughly they may be classified as follows :

(1) / take solid food without discomfort and in

consequence /

(1) Throat lesions	25 cases
(2) Rashes	22 "
(3) Condylomata	3 "
(4) Rupia	1 "
(5) Cutaneous ulcers	1 "
(6) Rash and Rheumatism	1 "
	<u>Total</u> 53 "

(1) Throat lesions : Included in this group are all cases in which the mouth, palate, tonsils, and pharynx, were in any way diseased. The lesions present varied from simple congestion to well marked severe ulceration. Where congestion has alone been present a single injection of Salvarsan causes it rapidly to subside in twenty four hours. Mucous patches may be completely healed in forty eight hours and seldom persist after the fifth day. Ulcers of the tongue, pharynx, or tonsils, vary in the rate of healing, but six to nine days is seldom exceeded in effecting a cure.

A marked feature of the drug is its effect in banishing pain. Case 6 well illustrates this point. This man had such severe pain accompanying the ulcerated condition of his tonsil that he could barely swallow even fluids. In twenty four hours he was able to take solid food without discomfort and in consequence /

consequence his general condition rapidly improved. Ehrlich and other observers have also noted this effect of Salvarsan in mitigating pain.

(2) Rashes : Of my series of cases twenty two had well marked widely spread macular rashes when first treated. The effect of Salvarsan was not so rapid in causing these lesions to clear up. In some cases (example Case 11) the rash did not completely fade until a second injection of the drug had been administered. But in the majority of my cases after a single dose of .5 grammes no rash could be found in from ten to fourteen days, being longest discernible on the sides of the abdomen and the back.

(3) Condylomata : In my series of cases I had three men with extensive condylomata round the anus. The very rapid cure effected by Salvarsan in these cases was almost incredible. In none of them (Nos. 29, 31 and 38) was any local treatment used. In all three the lesions had completely disappeared in eight days after a single injection of .5 grammes of Salvarsan. I can recall nothing to equal in rapidity and efficiency the action of Salvarsan in these cases.

(4) Rupia : I had only one case who developed rupia. He was a Bombadier in the Royal Horse Artillery and was admitted on June 27th 1912, having contracted Syphilis at the end of the previous March. When admitted /

admitted his condition was bad. Two phagadenic sores were present on his glans penis. His lymphatic glands were all enlarged and shotty. A papular rash was scattered all over his chest, abdomen, back and limbs. His forehead, face, back, scrotum, and thighs had numerous rupeal ulcers on them. He had a severe infection of malignant Syphilis. On July 2nd 1912, he was given .5 grammes Salvarsan intravenously. Five days later (on July 7th) the rupeal scabs had begun to fall off and his rash had almost faded. Twelve days later (July 14th) his rash had faded, primary sores had disappeared, and practically every rupeal ulcer had healed.

On July 16th, he was given a second dose of Salvarsan, and on July 25th, only twenty three days after being first treated, he was discharged hospital and returned to duty.

He received no Mercury afterwards, and for five months has had no recurrence of symptoms and a persistently negative Wassermann reaction.

Senior Officers, who saw this case before treatment, assured me that a few years ago such cases were quite common in the Army, and invariably they ended in being invalided home to Netley in a condition beyond description. In three weeks this man was completely cured. It is impossible to describe the case as it was. /

was. It is equally impossible to forget the transformation effected by so simple a means. It requires only one such case to convert the most sceptical person into an ardent supporter of the use of Salvarsan in Syphilis.

(5) Cutaneous Ulcers : I only encountered one such case amongst my patients (No.15). This man had had two courses of Mercury when I saw him first. He then had a secondary ulcer on the calf of his left leg and one on his right instep. Both these ulcers had completely healed ten days after receiving an injection of .5 grammes of Salvarsan.

(6) Rheumatism : One case (No.41) suffered from severe syphilitic rheumatism on admission. Three days after receiving .5 grammes of Salvarsan intravenously he was quite well and free from all pain.

As a result of one's observations in secondary Syphilitic conditions one is forced to the conclusion that the most rapid and effective treatment is by the use of the intravenous injection of Salvarsan.

But not only is the cure rapid, it is also, in a very large percentage of cases, permanent. All my cases have been carefully controlled by the Wassermann reaction. Out of the fifty three cases of secondary Syphilis treated by me, I have had twenty under observation for twelve months and over.

Fourteen /

Fourteen of these had received other treatment in the form of Mercurial injections before being given Salvarsan. None of them had any other treatment after the injection of Salvarsan. That is to say I deliberately put the drug to a test to determine its potency as regards permanency as well as rapidity of cure.

The six cases who had had no previous treatment all received two intravenous injections of .5 grammes each. Seven cases who had had previous treatment received only one injection of Salvarsan. The remaining seven cases who had had previous treatment each received two injections of Salvarsan.

Of these twenty cases not a single one relapsed. All the men were frequently inspected and blood tests made as nearly as possible every two months. They were all able to do their full military duties, which included hard Battalion and Brigade training. Their physical powers were thus put to a severe test and with no failures to record.

Of the remaining thirty three secondary cases twelve were under observation for from six to twelve months after treatment. One of these cases (No.40) had a relapse in the form of a positive Wassermann six months after his first injection of the drug. The others had no further signs of disease.

The /

The remaining twenty-one cases of this class were under observation for less than six months, which is too short a period of time to enable one to make any definite statements regarding the permanency of cure.

Tertiary Syphilis.

As a result of these observations one concludes (1) that in every case of secondary Syphilis the lesions can be completely eradicated in ten to twenty days by a single injection of .5 grammes of Salvarsan. (2) In every case a positive Wassermann can be converted into a negative reaction. (3) The negative Wassermann reaction is permanent in the majority of cases who are given two injections of Salvarsan at intervals of fourteen to twenty one days.

These effects obtained by me are in accord with those which other observers have got. McDonagh,⁴⁹ Zeissl⁷³ and Pick⁵⁸ record the conversion of a positive into a negative Wassermann reaction in all their cases. Gennérich³¹ thinks this conversion is accelerated by the second injection, and my cases support this observation. A single injection of the drug lessens the degree of complement deviation in all cases, but does not make it necessarily complete. Where the deviation has been reduced so that it can be got with 10% dilutions of antigen after a single injection

injection a second one given then will make the reaction complete. Cases 5, 25, 26, 28, 29, 30, 36, and 46 in my series well illustrate this point.

June 23rd. The discharge ceased completely on July 17th, thirty nine Tertiary Syphilis.

Included in this group are twelve cases. Of these eight were typical cases of punched out tertiary ulcers with wash leather bases. There were two cases of necrosis of the bones of the nose and one each of a gumma and perforation of the palate.

The effect of Salvarsan on tertiary ulcers was not so rapid as in the ulcers of secondary Syphilis, but still the curative powers of the drug were well marked. The first process of healing was the separation of the wash leather sloughs giving healthy bases to the ulcers. The most refractory of these cases was Gunner G. (No.14) who had severe tertiary ulcers on both legs. These did not completely heal until he had been given three injections of Salvarsan. Thirty eight days elapsed between his getting his first dose of .5 grammes and the complete healing of the last ulcer. The remaining cases of ulcers healed in fourteen to twenty one days.

The two cases with necrosis of bones were very refractory. Pte.S. (No.3) had an offensive mucopurulent discharge from his nose, the septum of which had /

had necrosed and bridge fallen in. Small pieces of necrosed bone were coming away. He received .5 grammes Salvarsan on June 8th 1911 and another on June 23rd. The discharge ceased completely on July 17th, thirty nine days after treatment was begun, and it did not trouble him again. His Wassermann was negative on August 15th, and remained negative whilst he was under observation for a further period of two months. He had had no less than five courses of Mercurial injections and two .6 grammes intramuscular injections of Salvarsan before getting the drug intravenously. Yet though he had resisted this treatment he was rapidly cured by the intravenous administration of the drug. Used and a fortnight later his Wassermann

Pte.M. (No.10) was of great interest and resembles one described by Browning and Mackenzie on page 210 of their recent book. He contracted the disease in China in 1909. He had had four complete courses of Mercury. When seen by me he was much emaciated and was suffering from necrosis of the nasal bones with a very offensive discharge from the nose. So offensive was the discharge that he could not mix with his companions in his Regiment. He received .5 grammes Salvarsan intravenously on July 7th 1911. This reduced the amount of the discharge and rendered it less offensive, but did not completely stop it. On August /

August 4th he was given another injection of .5 grammes Salvarsan but the discharge continued. On September 5th he was given a third injection of .3 grammes. This made the discharge very scanty, but as his Wassermann remained positive he was given a fourth injection of .5 grammes Salvarsan on November 14th. His general condition was excellent by this time, but his Wassermann continued to remain positive and a slight discharge was still present from his nose. On December 20th 1911 he was given a fifth injection of .5 grammes Salvarsan. On January 20th 1912 a large piece of necrosed bone was removed from his nose under chloroform. Ten days later the nasal discharge had completely ceased and a fortnight later his Wassermann reaction was found to be negative. He had no after treatment of Mercury and there was no recurrence of the disease, either clinically or by the Wassermann reaction, though observed for eleven months longer. This man received five injections of Salvarsan and a total of 2.3 grammes of the drug in five months. He suffered no untoward results.

One realises now a mistake being made in not searching for and removing the dead bone by operation sooner in this case. Had this been done the disease would probably have been cured much sooner. The Salvarsan will stop further advances of the disease and /

and cure lesions present, but dead bone will not be absorbed by it and should therefore be sought for and removed.

The gumma of the foot (Case No.2) responded splendidly to treatment with Salvarsan. Eighteen days after an injection of .5 grammes of the drug it had completely healed and the patient was sent back to duty. He had no further trouble with his gumma.

The perforated palate (No.1) healed completely thirteen days after his second injection of Salvarsan and had no recurrence of the condition.

With regard to the permanency of cure in these cases one has every reason to be satisfied. Three of them (Nos.10,13 and 42) were under observation for twelve months and longer and in none of them did the disease recur and in all the Wassermann reaction remained negative. Six of the cases were under observation for six months or longer and again with no recurrence. The remaining cases were not long enough under me to enable one to express an opinion as to the permanency of the cure obtained.

In tertiary Syphilis, as exemplified in these cases, Salvarsan was no less effective in accomplishing the disappearance of the lesions than in the primary and secondary stages of the disease. That its action is far more powerful and efficient than is that /

that Mercury is shewn by the fact that all my cases had been under treatment with injections of Grey Oil for almost two years and yet without a cure being wrought. Two or three intravenous injections of Salvarsan however, caused in all, except Case 10, a complete disappearance of symptoms and the establishment of a permanently negative Wassermann reaction in less than two months.

Such excellent results fully justify the widespread claims of expert observers to place Salvarsan in the forefront of one's therapeutic agents in the treatment of specific disease. Where the patient cannot be kept constantly under observation, or where one has not sufficient faith in the potency of Salvarsan alone, then this treatment may be supplemented by the use of Mercury. But in all cases Salvarsan should first be used.

Quiescent Cases.

The last of my series of cases were ten men who had no active signs of disease, but whose blood gave a positive Wassermann reaction. In all of them a single injection of Salvarsan was sufficient to convert the reaction into a negative one. This change took place with great rapidity in some cases. Thus

in /

in Case 62 it was found to have become negative nine days after the injection of .5 grammes of Salvarsan and remained permanently negative for the succeeding five months during which he was under observation.

In case 54, the Wassermann was converted from a positive to a negative in sixteen days. In Cases 65 and 66 the transformation was complete in nineteen days. In three other cases, Nos. 73, 64 and 39 it had become negative in less than four weeks after treatment. It is probable that in most of these cases the reaction had changed much earlier had it been looked for sooner.

In only one, Case 51, was the reaction slow in changing its character as it was still faintly positive fifty-two days after the injection but had become negative when next tested for.

Of these ten men, whose positive reaction was the sole indication for treatment, the Wassermann remained permanently negative for four months and longer in eight. The remaining two were not observed sufficiently long to enable any opinion as to the permanent character of the change being formed.

To sum up regarding the efficiency of Salvarsan in the treatment of Syphilis, one is justified in stating, as a result of the study of one's cases, that in all stages of the disease the active manifestations rapidly disappear as a result of the use of the /

the drug.

The earlier treatment is begun the more efficacious it appears to be. Thus, primary sores heal with great rapidity after a single injection of the drug. Secondary lesions are more quickly got rid of than tertiary, but all manifestations of the disease are eventually completely eradicated.

Of still more importance, as indicating the curative powers of the drug, is the transformation of a positive Wassermann reaction into a negative one. Two or more injections of Salvarsan may be required to accomplish this, but in all cases it can be eventually brought about. Not only so but the changed reaction is generally of a permanent character.

As already pointed out practically none of my cases received any other treatment after the injection of Salvarsan. All went back to duty and carried out severe military training, with hard work, without shewing any signs of a recurrence of the disease for which they had been treated. This fact, coupled with the permanently negative Wassermann reaction, substantiates my expressed opinion "that every case of Syphilis should be treated with Salvarsan".

Browning and Mackenzie¹⁵ state that "the criteria by which the results of treatment can be judged are (1) the continued absence of symptoms and (2) the permanent /

"permanent negative reaction of the blood". Judged by these two factors my cases afford strong evidence in favour of placing Salvarsan in the position of being probably the most rapid and effective anti-syphilitic remedy at present known. Neo-Salvarsan, which closely resembles it, is said however to be even more efficient, but as I was unable to obtain a supply of this drug I cannot express any opinion on the comparative value of these two arsenical preparations.

For the lesion present and its appearance was typically that of Lupus Vulgaris. In favour of this diagnosis are the following facts. The disease began as a brownish pink nodule on the nose near the tip. It was painless and caused no discomfort. The patient disregarded it at first but as the nodule broke down and the margins began to enlarge, he reported sick. Extension was slow and as one part apparently healed another part was found to be progressing. Various applications were tried to arrest the disease but without success. He was then sent to Secunderabad to undergo a course of X-Ray treatment. This did more good than any other remedy and after five months treatment he returned to Bangalore with his nose practically healed except for two small areas on each side of the bridge half way up. A few weeks after his

Salvarsan in Lupus Vulgaris.

Reference has been made, earlier in my thesis, to a case of Lupus Vulgaris in which rapid and complete cure followed the intravenous injection of Salvarsan.

The question of accurate diagnosis in this case is the one factor regarding which objections may be raised. But from a very careful observation and inquiry one could not discover any other cause to account for the lesion present and its appearance was typically that of Lupus Vulgaris. In favour of this diagnosis are the following facts. The disease began as a brownish pink nodule on the nose near the tip. It was painless and caused no discomfort. The patient disregarded it at first but as the nodule broke down and the margins began to enlarge, he reported sick. Extension was slow and as one part apparently healed another part was found to be spreading. Various applications were tried to arrest the disease but without success. He was then sent to Secunderabad to undergo a course of X-Ray treatment. This did more good than any other remedy and after five months' treatment he returned to Bangalore with his nose practically healed except for two small areas on each side of the bridge half way up. A few weeks after his

followed the treatment. His nose became less congested.

his return these two areas again broke down and the disease began to spread upwards on each side of the nose. Two ulcers, the size of a shilling, were thus formed, and the deeper tissues were now invaded with the process.

In order to exclude Syphilis, a Wassermann reaction was performed on several occasions but always with a negative result. This proof against the disease being Syphilitic was further supported by the fact that no other signs of specific disease could be found anywhere, either in the form of a scar from a healed primary sore, from enlarged glands, from pigmented patches of healed ulcers, or from any bone lesions. In addition the patient gave a strongly positive Von-Pirquet reaction. The only weak point about confirming the diagnosis was that no scrapings were examined for giant cells or tubercle bacilli.

As the lupus ulcers were steadily spreading upwards towards the eyes, and there appeared to be grave danger of their being involved, I suggested to him that an intravenous injection of Salvarsan be tried. The patient readily consented to this proposition. On October 12th 1912 he was given .5 grammes Salvarsan intravenously. He had a moderately severe reaction after the injection but was quite well the next day. A rapid improvement in his condition followed the treatment. His eyes became less congested /

congested and the ulcers on the nose began to heal rapidly. A Wassermann reaction was done six days after the administration of the drug to see whether, as a result of the injection, a positive result might not have been set up. In Syphilis a provocative injection of Salvarsan is said to often give rise to a positive Wassermann. No positive result was got in this case. He developed a well marked leucocytosis after the injection.

On October 25th, a second injection of .5 grammes Salvarsan was given and on October 31st he was discharged hospital.

Seen frequently afterwards the nose continued to do well. The skin was red and slightly puckered from the contraction of the tissues after healing, but was otherwise healthy and no further signs of disease could be found.

This case is extremely interesting as I have not seen or heard of Salvarsan having been used in the treatment of Lupus Vulgaris. One swallow does not make a summer, and my one case does not mean that Salvarsan is a specific in Lupus. But it is undoubtedly very curious that such great benefit should follow the use of the drug. The modus operandi of the drug I cannot explain, unless the well marked leucocytosis set up in any way aided the tissues to overcome the invasion of the tubercle bacillus. Success is said to have been obtained in the treatment of

of /

of Leprosy with Salvarsan. The organisms at work in both these conditions resemble each other closely in their characters and in the type of lesions they produce. Possibly in both conditions therefore any benefit which follows the use of Salvarsan is due to the stimulating power of the drug on the leucocyte producing centres causing such an increase of white cells that phagocytosis destroys the invading organisms. Beyond this one can offer no explanation to account for the benefit that follows the use of the drug.

I have only used the intravenous injection of Salvarsan in one case and can only express a very uncertain opinion as to its value in this condition. Other observers have, however, used it fairly extensively and apparently with a considerable amount of success.

Iversen first used the drug in the treatment of this disease in five cases of Benign Tertian Malaria and with excellent results. Encouraged by his success in these cases he then used it in sixty others including twenty-seven Simple Tertian, four quartan, and twenty-seven Malignant conditions. He obtained very encouraging results in his benign cases, obtaining 70% of cures after the intravenous injection of .5 gramme of Salvarsan. Parasites disappeared from the blood

Salvarsan in Malaria

It is a well known fact that many cases of Malaria that do not yield completely to treatment with quinine in large doses by the mouth often respond to a substitution of arsenic for the quinine. One has seen a goodly number of such cases.

It is not to be wondered at that Salvarsan has therefore been used in the treatment of Malaria on account of the large percentage of arsenic present in this substance.

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in twelve to twenty-four hours. In 30% of his cases paroxysms ceased, but parasites did not disappear.

Schreiber⁶¹ reports having used the intravenous injection of Salvarsan in Malaria and Relapsing Fever. Ehrlich recommends the intravenous injection of the drug one day followed by an intramuscular injection the next. In eleven cases of Simple Malaria the parasites disappeared promptly. In eleven cases of Malignant Malaria the parasites disappeared in five cases, but in the other six it was impossible to completely get rid of them.

My solitary case was certainly benefited by using the drug. He had been in hospital for two months. His pyrexia was controlled by quinine in ten grain doses thrice daily, but his spleen remained large and crescents were always readily found in his peripheral blood on examination. On October 14th 1912, I gave him .4 grammes of Salvarsan intravenously. No search for parasites was made until a week after the injection when none could be found on prolonged search. His spleen receded considerably and ten days later I discharged him from hospital. Twice a week he attended for ten grain doses of quinine by the mouth. On several occasions his blood was examined but no parasites were found and six weeks after his discharge from /

from hospital his spleen was barely palpable.

The case is interesting in this connection. Quinine by the mouth apparently held the disease in check but did not destroy the parasites. Arsenic, in the form of Salvarsan, caused the crescents to rapidly disappear from the peripheral blood and further treatment with quinine then completed the cure. The patient was able to return to duty and two months later had no relapse and no parasites could be found in his blood.

The urine contains albumin and haemoglobinuria is frequently present.

The blood is pale and watery and the red cells may diminish from 7 million down to 2 million per c.c. The haemoglobin is lessened also.

The white cells are increased in number and may amount to 40 thousand per c.c. instead of the normal 7 thousand in the dog.

(2) The chronic form: Fever is only present for a few days. There is intense anæmia and debility with anorexia and weakness and a stuffy nose.

The appetite slowly returns and the patient gradually regains weight.

Salvarsan in Piroplasma Canis.

The last topic I propose to consider in my thesis is the effect of Salvarsan in Piroplasma Canis. This is a disease due to infection with a parasite which attacks the red blood corpuscles of dogs.

Symptomatology : There are two varieties of the disease (1) an acute and (2) a chronic form.

(1) The acute form : There is a loss of appetite with a high temperature. The mucous membranes are intensely pale, from destruction of red blood corpuscles, and jaundice is a well marked feature. Weakness is very noticeable and actual paresis of the hind legs may develop. Towards the end the animal becomes comatose.

The urine contains albumin and haemoglobinuria is frequently present.

The blood is pale and watery and the red cells may diminish from 7 million down to 2 million per c.m. The haemoglobin is lessened also.

The white cells are increased in number and may amount to 40 thousand per c.m. instead of the normal 7 thousand in the dog.

(2) The chronic form : Fever is only present for a few days. There is intense anaemia and emaciation with anorexia and weakness and a scurfy skin.

The appetite slowly returns and mucous membranes regain /

* regain their colour, convalescence taking six weeks to three months.

Very young dogs are said to never recover from the initial attack. Older dogs, which do not die from the severity of the infection in four or five days, may die with progressive anaemia or emaciation. Robertson⁵⁵ states that many dogs which appear to have recovered succumb eventually.

Mode of Infection : Ticks normally are the channel of transmission of the Piroplasmata. Smith and Kilbourne have conclusively proved this in reference to the closely allied Texas Fever in cattle. Lounsbury has shewn that in South Africa Piroplasmosis in dogs is conveyed by the tick *Haemaphysalis Leachi*. In India infection is spread by *R. Sanguineus* which is the common tick found on dogs. This has been conclusively proved by Christophers.

Infection can also occur by inoculation of an unaffected animal with blood from an infected animal of the same species.

The period of incubation is stated by Nocard and Motas⁵⁵ to be three to five days after intravenous, and five to six days after subcutaneous, inoculation.

Susceptibility : *Piroplasma Canis* is endemic amongst pariah dogs in Madras which may shew ~~but~~ few symptoms /

symptoms even when harbouring numerous parasites. If dogs from Europe are brought in contact with these pariahs they are readily infected.

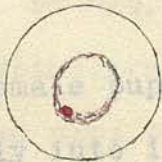
This is well illustrated by reference to the four dogs observed by me. The mother was a pure bred wire-haired Irish terrier. She was crossed in Ireland and brought to India where she threw a litter of three pups - one dog and two bitches. The owner was posted to Bellary and took the four dogs with him. Shortly after arrival there all four took ill, suffering from fever and anaemia. Owing to their value they were at once sent to Bangalore to a Veterinary Surgeon for treatment. I had been doing a certain amount of blood work on horses for him when the dogs arrived, and I was asked to examine these dogs to see whether I could throw any light on the condition from which they were suffering. Piroplasma Canis was not suspected as it was not known to exist in Bellary. The dogs arrived on September 5th 1911. I began observations by taking blood films from each of the dogs. By staining by Romanowski's method pear-shaped intracorpuseular parasites were found in all the films, which one at once recognised to be the Piroplasma Canis. In order to make quite sure of one's diagnosis I took fresh films and sent them to Captain W.S. Patton Indian Medical Service, in Madras, for confirmation.

This /

This Officer I knew had been working at the subject in Madras and he kindly confirmed my findings.

The Parasite : Various forms have been described by different observers. Nocard and Motas⁵² found an amoeboid form with protrusion of pseudopodia and active movements. They also describe early infective forms and a round refractile type. Luhe has described ring forms, and free forms with centrally situated chromatin have been observed.

All the films examined by me contained the very characteristic pear-shaped forms. The majority of the parasites are said to come under this heading. As a rule two, or multiples of two, parasites occur in each cell. The narrow ends of the "pear" are toward each other. The chromatin tends to lie near the periphery. These forms are developed by fission. They stain readily with Romanowski's stain or its modifications.



Pathological changes : The spleen is markedly enlarged and is dark purple in colour and more tumid than normally. The liver is enlarged and congested, and shews well marked fatty changes. The kidneys are often

often enlarged and pale. Haemorrhages are not present as in Texas Fever. Other organs show no characteristic changes except those following intense anaemia.

I have very briefly sketched the main features of the disease and now wish to refer to the cases treated by me.

As already noted I had the mother and three pups of about four months. All showed symptoms of the acute form of the disease.

On September 9th 1911 I began treatment as follows.

- (a) The mother. - Given .3 grammes Salvarsan in alkaline solution into the muscles of its back.
- (b) One female pup. - No treatment. This pup was kept as a control.
- (c) One male pup. - Given .2 grammes Salvarsan in alkaline solution intravenously into its external jugular vein.
- (d) One female pup. - Given .2 grammes Salvarsan intravenously into its external jugular vein.

September 13th 1911. The untreated female pup died, and on post mortem the changes above noted were found to be present. Smears of the spleen shewed numerous parasites.

The mother was apparently somewhat better and was /

was taking a little food.

Pups (c) and (d) were very much better. Blood smears from them showed no parasites. They were lively and much more ready for food than before treatment.

September 16th. Mother died. Post mortem appearances characteristic but no parasites were found in smears from the spleen.

Pups (c) and (d) making rapid progress. Blood smears showed no parasites. They were running about and already beginning to put on flesh.

September 20th. Pups (c) and (d) making rapid progress to recovery. Both were bright and eating well. The anaemia was much lessened. Blood smears negative.

September 23rd. Two black and white country born fox terrier pups three months old were taken by me and into the external jugular vein of each I injected 3 c.c.'s. of blood from pups (c) and (d). The blood was withdrawn from the external jugular veins of the infected pups with separate Roux's syringes containing 2 c.c.'s. of 1.5% citrate of soda solution in normal saline to prevent coagulation. The fox terrier pups were injected with the withdrawn blood immediately. This was done to see whether the disease could be conveyed to them. At the age of three months they were /

were extremely susceptible.

Schroeder⁶³ has shewn that the blood of recovered animals may be infective for years after recovery from an attack of Piroplasmosis. Robertson⁵⁸ has confirmed this fact, and has shewn that the blood of infected dogs many months after recovery, when no parasites could be found microscopically, is still able to give rise to a fatal infection.

It was therefore with considerable interest that I noted the effects of injecting susceptible uninfected pups with the blood of these recently infected ones. Had Salvarsan effected a complete cure? Had all the parasites been destroyed by its use? Or had the two pups recovered, as a certain percentage do, without treatment? If they had got over the disease they would still be able to infect fresh dogs.

Nocard and Motas⁶⁵ have shewn that the incubation period is three to five days after intravenous inoculation. I kept the two fox terrier pups inoculated by me under observation for four weeks without either of them developing any signs of the disease. Frequent blood examinations gave negative results, and spleen puncture, in each of them, ten days after the attempted infection, was also negative.

The two pups (c) and (d) made an uninterrupted recovery and I lost sight of them two months later.

An /

An interesting experiment would have been to try to reinfect the two cured pups by feeding ticks from infected dogs on them and by direct intravenous inoculation. This observation was denied me however.

To summarise the results of one's observations :

- (1) The untreated pup died three days after the others had been treated, shewing characteristic post mortem appearances and parasites in smears from its spleen.
- (2) The mother died seven days after being given .3 grammes Salvarsan intramuscularly, shewing characteristic post mortem signs of the disease but with no parasites in spleen smears.
- (3) Pups (c) and (d) both recovered after .2 grammes Salvarsan intravenously and the injection of uninfected fox terrier pups with 3 c.c's. of their blood fourteen days after treatment failed to reproduce the disease in them either clinically, on blood examinations, or on spleen puncture.

Conclusions regarding these observations : As a result of these observations and experiments, I conclude that Salvarsan is a powerful and efficient remedy if administered intravenously in *Piroplasma Canis*. Its action is rapid and the cure effected is the result of the complete destruction of the invading parasites.

I know of no other observer having tried the remedy in this and allied conditions, such as Texas Fever in cattle and Bilary Colic in horses, but the results of treatment obtained by me afford strong evidence in support of its use in these conditions.

can was used for intravenous injection. It is dissolved in .50% normal saline, and is injected at intervals every 40 c.c.'s of the solution. The amount of Salvarsan.

Dosage : In practically every case 1.0 gram of Salvarsan was injected each time. As a rule not more than two injections were given at intervals of twenty to twenty-one days. If necessary a further injection was administered, the injections being controlled by the Wassermann reaction.

Apparatus used : The apparatus used was the one devised by Gibbard.

Diagnosis of Cases : All cases treated had the diagnosis confirmed by either Wassermann or the Indirect Pallidum in serum from the patient or by the performance of a Wassermann reaction. After treatment and progress of cases were controlled by the Wassermann reaction.

Preparation of Patient for the Injection : Patients were taken into hospital the previous day before the injection was to be given. They were given a mild purge

A brief Summary of Observations recorded.

Chemistry : Salvarsan is the di-hydrochloride of dioxy-diamido-arseno-benzol. It is a pentavalent arsenical compound.

Solution for Injection : The di-sodium salt of Salvarsan was used for intravenous injections. It is dissolved in .85% normal saline, and is diluted so that every 40 c.c's of the solution contains .1 grammes of Salvarsan.

Dosage : In practically every case .5 grammes Salvarsan was injected each time. As a rule not less than two injections were given at intervals of fourteen to twenty-one days. If necessary a further injection was administered, the indications being controlled by the Wassermann reaction.

Apparatus used : The apparatus used was the one devised by Gibbard.

Diagnosis of Cases : All cases treated had the diagnosis confirmed by either demonstrating the Treponema Pallidum in serum from the lesions, or by the performance of a Wassermann reaction. After treatment and progress of cases were controlled by the Wassermann reaction.

Preparation of Patient for the Injection : Patients were taken into hospital the evening before the injection was to be given. They were given a mild purge /

purge and only a light meal was allowed on the morning of the injection. Before treatment all were carefully examined, special attention being paid to the circulatory, nervous, digestive, and urinary systems.

Effects following the injection of Salvarsan : Rigors, a rise of temperature, headache, nausea and vomiting, and occasionally diarrhoea, follow the administration of the drug. The face and eyes become congested and the pulse and respiration accelerated. Cyanosis was noted in a few cases. All these effects have generally passed over by the following day.

Action on Skin and Mucous Membranes : Applied, in alkaline solution, to the unbroken skin or mucous membranes produced no effects. If abrasions were present slight irritation with hyperaemia was noted.

Action on the gastro-intestinal track : Salvarsan is an irritant causing vomiting, and not infrequently diarrhoea with colicky pains.

Action on the circulation : The cutaneous vessels of the face and chest are dilated by the injection of Salvarsan, and probably the vessels of the splanchnic area are similarly affected. On perfusing the vessels of a frog with the drug it causes them to dilate.

The heart is accelerated in rate and may become slightly /

slightly irregular and even dilate. In the frog the heart ceases in diastole, the ventricles being first to cease contracting. In the dog a similar effect is produced, the organ becoming engorged with blood.

As a result of the weakening on the heart's action, and the dilatation of vessels, the blood pressure falls.

Action on the white blood corpuscles : A well marked leucocytosis is set up, due to the increase of the polymorphonuclear cells. The opsonic index is not affected.

Action on the red cells and haemoglobin : Salvarsan causes a rapid increase in the red cells and haemoglobin where these are deficient, the increase being more marked at first in the haemoglobin.

The coagulation time of the blood is not affected.

Action on the nervous system : Well marked headache follows the injection of the drug, due probably to its toxic action on the cells of the cortex. The sensory and motor nerves are not affected by the drug.

Action on the urinary system : No bad effects were observed. In one case albumin in the urine disappeared after the injection of Salvarsan.

Action on metabolism : Rapid increase in weight and a great improvement in general condition, with a sense /

sense of well-being follows the injection of Salvarsan.

Elimination : Salvarsan is mainly excreted in the urine, but it is also present in vomited matter and foeces.

Therapeutic effects : (1) In Syphilis.- Salvarsan causes a rapid disappearance of the lesions in all stages of the disease and accomplishes this in extremely short periods of time. The Wassermann reaction can, in all cases, be changed from a positive to a negative.

A permanent cure is probably effected by the use of Salvarsan alone with^{out} supplementing it with Mercury.

(2) In Lupus Vulgaris : Great benefit follows the administration of the drug in this condition

(3) Malaria : Good results follow its use in Malaria, especially the Benign Tertian form of the disease.

It may succeed in accomplishing a cure where quinine has failed, this being especially marked in Malignant Malaria.

(4) Piroplasma Canis : The administration of Salvarsan to dogs suffering from this condition gave rise to extremely satisfactory results. Complete cure followed the intravenous injection of the drug in the case of two Irish terrier pups treated in this way. A great field /

field of usefulness in the treatment of this and the allied conditions of Texas Fever, and Biliary Colic in horses, is apparently open to the use of the drug.

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Name : Pte. M. 14th Kings Hussars. Case No. 1

Admitted : February 6th, 1911.

Condition on Admission : Extensive ulceration of tonsils and fauces with marked oedema. Small perforation of soft palate (about size of a pea). Inguinal, cervical and supra trochlear glands abnormally and enlarged.

Previous Syphilitic History : Disease contracted in Bangalore in beginning of 1909; underwent four complete courses of Mercury and was struck off Syphilis register in April 1910; admitted to Station Hospital in January 1911 suffering from tonsillitis which was found to be specific in origin, transferred to Section Hospital on 6th February 1911.

7.2.11 : Wassermann reaction ++, weight 126 lbs.

Vision normal, Hearing normal.

9.2.11 : Salvarsan .6 grammes intramuscularly into right buttock.

10.2.11 : Pain at sight of injection troublesome.

11.2.11 : Slough round margins of perforation of palate separated.

12.2.11 : Ulcers spreading, edges touched with chromic acid. Given Pot Iodide grains X t.i.d.

15.2.11 : Ulcers spreading, very unhealthy looking. weight 125 lbs.

2.6.11 /

Name : Pte. M. 14th Kings Hussars. Case No.1

Admitted : February 6th, 1911.

Condition on Admission : Extensive ulceration of tonsils and fauces with marked oedema. Small perforation of soft palate (about size of a pea). Inguinal, cervical and supra trochlear glands shotty and enlarged;

Previous Syphilitic History : Disease contracted in Bangalore in beginning of 1908; underwent four complete course of Mercury and was struck off Syphilis register in April 1910; admitted to Station Hospital in January 1911 suffering from tonsillitis which was found to be specific in origin, transferred to Section Hospital on 6th February 1911.

7.2.11 : Wassermann reaction +++ weight 128 lbs.

Vision normal, Hearing normal.

9.2.11 : Salvarsan .6 grammes intramuscularly into right buttock.

10.2.11 : Pain at sight of injection troublesome.

11.2.11 : Slough round margins of perforation of palate separated.

13.2.11 : Ulcers spreading, edges touched with chromic acid. Given Pot Iodide grains X t.i.d..

10.3.11 : Ulcers spreading, very unhealthy looking; weight 125 lbs.

8.6.11 / Left Bangalore for home with his Regiment.

No signs of disease.

- 8.6.11 : Ulcer indolent. Patient much depressed;
weight 124½ lbs. Wassermann reaction +++.
- 12.6.11 : Salvarsan .5 grammes intravenously; reac-
tion moderate.
- 13.6.11 : Patient slept well; headache ceased,
slight diarrhoea
- 15.6.11 : Well marked herpes about lips; ulcer look-
ing better. Congestion of throat completely gone.
- 18.6.11 : Throat and tonsils normal; discharged
hospital to attend; weight 127 lbs.
- 16.7.11 : Patient doing well, no active signs.
Weight 127½ lbs. Wassermann reaction ++.
20. 8.11 : Tonsils enlarged. Small ulcer on palate.
Feels well. Wassermann reaction ++.
- 25.9.11 : Readmitted into hospital. Salvarsan .4
grammes intravenously. Maximum temperature 101.
Pulse 100. Slight vomiting and diarrhoea.
- 26.9.11 : Feels quite well. Temperature and pulse
normal; vision normal.
- 27.9.11 : Ulceration and erosion of throat much im-
proved.
- 30.9.11 : Throat, tonsils and fauces normal, ulcer on
palate healing rapidly, discharged hospital to attend
Wassermann reaction. +.
- 20.10.11 : No signs of disease. Weight 132½ lbs.
Wassermann reaction.—.
- 25.10.11 : Left Bangalore for Mhow with his Regiment.
No signs of disease.

Name : Pte J. No.3155. 14th Kings Hussars. Case 2

Admitted : May 3rd 1911.

Condition on Admission : Well marked secondary rash all over face, shoulders, chest abdomen and lower limbs; Has a swelling over the outer side of dorsum of his right foot, elastic to the touch, giving a feeling of pus under tension. States this began after being trod on by his horse. Well marked enlarged shotty glands in both groins.

Previous Syphilitic History : Contracted Syphilis in Bangalore a year ago. Has had three complete courses of mercury and two intramuscular injections of .5 grammes each of Salvarsan.

5.5.11 : Swelling on dorsum of foot opened revealing a typical gumma with discolouration of skin for some distance round and well marked infiltration of surrounding tissues.

25.5.11 : Gumma shewing no signs of improvement.

Wassermann reaction +++ Weight 142 lbs.

12.6.11 : Salvarsan .5 grammes intravenously. Reaction severe; maximum temperature 102.6; pulse 152; very severe headache and slight vomiting.

13.6.11 : Patient feels quite well. Headache better vomiting ceased.

15.6.11 : Slight Herpes round lips. Has a slight attack of diarrhoea accompanied by griping pains.

17.6.11 : /

17.6.11 : Diarrhoea ceased. Rash almost faded from face and thighs.

21.6.11 : Rash completely disappeared. Gumma healing rapidly. Weight $144\frac{1}{2}$ lbs.

30.6.11 : Gumma quite healed. Weight 145 lbs.

4.7.11 : No active signs; patient discharged hospital to attend.

5.8.11 : No active signs. Wassermann reaction —, Weight 145 lbs.

15.10.11 : Patient quite well; no recurrence of symptoms, looks and feels well. Wassermann reaction —. Weight $145\frac{1}{2}$ lbs. Vision normal. Hearing normal.

25.10.11 : Left Bangalore for Mhow with his Regiment; no further signs of disease.

	1924				1920	1918	1922	1925
Wassermann	Nil				Nil	Nil	Nil	Nil
Diarrhoea	Nil	Slight	Severe	Very Severe	Nil	Nil	Nil	Nil
Weight	Nil	Nil	Slight	Slight	Nil	Nil	Nil	Nil
Diarrhoea	Nil	Nil	Nil	Nil	Nil	Slight	Nil	Nil

Name : Pte. S. No.5501. 14th Kings Hussars. Case 3

Admitted : May 25th 1911. *... he feels quite well.*

Condition on Admission : Necrosis of nasal septum with a mucu-purulent discharge from nose. Pieces of necrosed bone coming away. Complains of severe pain over right supra orbital ridge. Has well marked iritis with pain, photophobia, lachyramation and congestion of both eyes. Nose is much deformed owing to the bridge having completely collapsed. Inguinal and supra trochlear glands enlarged. Patient is very hopeless and depressed. *... normal.*

Previous Syphilitic History : Contracted Syphilis in Bangalore in December 1908. Has had five complete courses of Mercury and two injections of .5 grammes Salvarsan intramuscularly. (The injection of Salvarsan was given with every precaution in January and February 1911 in the intra-scapular region. In both cases induration occurred at the sight of injection and eventually suppuration. The two areas had to be excised and in the indurated tissues a greyish powder was found giving the reactions of an arsenic salt). *... another man. Has an*

27.5.11 : Wassermann reaction+++ . Weight 128 lbs.

8.6.11 : Salvarsan .5 grammes intravenously. Reaction severe. Maximum temperature 103.6; pulse 126. Suffered from very severe headache all day with a tendency to delirium.

9.6.11 /

9.6.11 : Morning temperature 99, evening normal.

Headache continues otherwise he feels quite well.

10.6.11 : Feels quite well. Nasal discharge lessened.

13.6.11 : Herpes on upper lip. Eyes much better, pain gone, congestion lessened, photophobia gone.

16.6.11 : Improvement maintained but nasal discharge still continues. Weight 130 lbs. He is much more cheerful and bright.

21.6.11 : Complains of black spots before his eyes. Some congestion of conjunctivae. Discs normal. Wassermann reaction ++.

23.6.11 Salvarsan .5 grammes intravenously. Reaction moderate. Maximum temperature 102.8, pulse 112, slight vomiting and headache.

26.6.11 : Doing very well. Eyes quite normal, discharge from nose almost ceased, weight 131 lbs.

15.7.11 : No active signs of disease, discharged hospital to attend.

15.8.11 : Weight 135 lbs. Wasserman reaction —.

15.9.11 : No active signs of disease. Patient states that he feels quite another man. Has an excellent appetite and steadily puts on weight. Now scales 136 lbs. Wassermann reaction —.

23.9.11 : Patient quite well, left Bangalore for Mhow with his regiment.

Name : L/c B. No.7677. 2nd Dorset Regiment. Case 4

Admitted : May 10th 1911.

Condition on Admission : Severe ulceration of both fauces. Mucous patches on inside of cheeks.

Enlarged glands in groin and neck. ~~discharged~~

Previous Syphilitic History : Contracted the disease in Bangalore in December 1910. Has had two courses of Mercury and in March 1911 an intramuscular injection of .6 grammes Salvarsan.

11.5.11 : Wassermann reaction + + +. Weight $142\frac{1}{2}$ lbs. Treponema pallida demonstrated in serum from cheeks by Indian Ink method.

12.6.11 : Salvarsan .5 grammes intravenously. Reaction severe. Suffered from severe headache, vomiting and diarrhoea. Maximum temperature 102.8, Pulse 128.

15.6.11 : Slight herpes on lips, otherwise well.

17.6.11 : Herpes dried. Complains of pain in right tonsil which is much inflamed.

19.6.11 : Mucous patches all disappeared. Slight ulceration of fauces still present. Weight 140 lbs.

10.7.11 : Small ulcers still present on fauces.

Weight $141\frac{1}{2}$ lbs. Wassermann reaction + +.

15.7.11 : Salvarsan .5 grammes intravenously. Reaction slight. Maximum 102.2; pulse 110.

18.7.11 : /

18.7.11 : Patient feels quite well. Ulcers on fauces healing rapidly.

24.7.11 : Throat quite normal, no active signs of disease. Weight 143 lbs.

29.7.11 : No active signs of disease, discharged hospital to attend. Wassermann reaction—.

2.9.11 : Patient quite well, no signs of disease. Wassermann reaction—, Vision normal. Hearing normal.

(a) Polymorphs								
(b) Lymphocytes								
(c) Large monon.								
(d) Eosinophiles								
(e) Corporules								
Haemoglobin								
Urine (at 11 p.m.)	1024				1020	1020	1018	1018
(a) Albumin	Nil				Nil	Nil	Nil	Nil
Reaction	Nil	Nil	Severe	Severe	Severe	Slight	Nil	Nil
Yeasting	Nil	Nil	Severe	Severe	Nil	Nil	Nil	Nil
Diastase	Nil	Nil	Nil	Slight	Slight	Slight	Nil	Nil

Name : Pte. H. No.5687. 14th King's Hussars. Case 5.

Admitted : 18th May 1911

Condition on admission : Well marked secondary rash on face, arms and thighs. Fauces congested.

Shotty glands in inguinal region. Chancre on back of glans penis healed.

Previous Syphilitic History : Contracted the disease in Bangalore in April 1911. Has had 4 intramuscular injections of Mercury (4 grains Hg). No other treatment.

21.5.11 : Wassermann reaction +++ . Vision normal,

Hearing normal. Weight 132 lbs.

9.6.11 : Salvarsan .5 grammes intravenously. Reaction severe. Maximum temperature 101.6. Pulse 96. Respiration 26. Suffered from severe headache, slight vomiting, and feeling of cold extremities. Eyes much congested and face flushed.

Red blood corpuscles 4,510,000. Haemoglobin 75%.

10.6.11 : Morning temperature 99.4. Evening temperature 98.8. Pulse 80. Complains of a sense of heaviness in the head and limbs.

12.6.11 : Well marked herpes round lips and on hard palate and inner sides of cheeks. Feels fairly well. R.b.c. 4,450,000. Hb. 82%.

15.6.11 : Herpes drying. Rash fading. Throat normal

23.6.11 : /

23.6.11 : Patient has no active signs. Wassermann reaction ++. R.b.c. 4,890,000. Hb. 90%.

28.7.11 : Readmitted on account of a positive Wassermann and given .5 grammes Salvarsan intravenously. Maximum temperature 102.8. Pulse 108. Respiration 30. Severe vomiting and headache. Weight 132½ lbs. R.B.c. 4,900,000. Hb.94%.

1.8.11 : Feels quite well. No active signs. Weight 135 lbs.

8.8.11 : No active signs. Discharged hospital to attend. R.b.c. 5,000,000. Hb.96%.

27 8.11 : No active signs. Weight 136 lbs.

15.9.11 : Patient is in excellent health. No signs of Syphilis. Wassermann reaction —. Weight 137 lbs.

20.10.11 : No active signs of disease. Feels quite well. Left Bangalore for Mhow with his Regiment.

Name : Driver W. "O" Battery R.H.A. Case 6.

Admitted : 8th May 1911.

Condition on admission : A large semicircular ulcer on right tonsil with wash leather base. Much oedema of throat with pain and difficulty in swallowing. Is not able to tolerate Mercury and has had a good deal of stomatitis. Has lost weight considerably and is anaemic and emaciated. Very depressed and appears to have lost all interest in himself.

Previous Syphilitic History : Contracted the disease in Bangalore in December 1910. Has had two courses of Mercury which he took badly, suffering from mild mercurialism.

8.6.11 : Wassermann reaction+++ Vision normal; hearing normal. Weight 114 lbs. R.b.c.4,120,000. Hb. 64%.

9.6.11 : Salvarsan .5 grammes intravenously. Reaction severe. Rigors. Severe headache and vomiting. Maximum temperature 103.2 Pulse 130. Respiration 36.

10.6.11 : Morning temperature 99.2. Evening temperature 99. Pulse 82. Had a restless night but is feeling much better. Headache still present.

11.6.11 : Complains of a feeling of heaviness about the head, otherwise well.

13.6.11 : /

- 13.6.11 : Slough separated from right tonsil leaving a ragged base . Weight 116 lbs. R.b.c.4,360,000 Hb. 74%.
- 18.6.11 : Condition improving rapidly. Ulcer healing oedema of throat quite gone, no pain or difficulty on swallowing. Weight 118 lbs. R.b.c.4,670,000. Hb. 88%.
- 28.6.11 : Only active sign of disease is a small ulcer on the right tonsil. Looks and feels well. Mental condition very bright. Weight 119 lbs. R.b.c. 4,780,000. Hb. 92%.
- 12.7.11 : Complains of pain round left tonsil which is enlarged Wassermann reaction ++. Weight 118 lbs. R.b.c. 4,850,000. Hb. 90%.
- 20.7.11 : Readmitted on account of positive Wassermann and given .4 grammes Salvarsan intravenously. Reaction mild. Slight headache and vomiting. Maximum temperature 102. Pulse 100. R.b.c.4,910,000 Hb. 94%.
- 24.7.11 : Tonsils quite healthy and throat normal. No active signs of disease. Discharged hospital to attend.
- 14.9.11 : No active signs of disease. Weight 126 lbs.
- 15.11.11 : No active signs of disease. Wassermann reaction -. Weight 136½ lbs. R.b.c.5,120,000. Hb. 96%.
- 20.12.11 /

Name : Pte. J. No.5047. 14th Kings Hussars. Case 7

Admitted : 6th June 1911.

Disease contracted : Bangalore in May 1910

Previous treatment : 4 complete courses of Mercury.

Condition on admission : Marked ulceration of both tonsils with oedema of fauces. Inguinal glands enlarged. Vision normal. Hearing normal.

Weight 144 lbs. Wassermann reaction + + +.

12.6.11 : Salvarsan .45 grammes intravenously. Reaction moderate. Severe headache. Slight vomiting. Face flushed and conjunctivæ congested.

13.6.11 : Patient feels quite well.

15.6.11 : Herpes on lips. Ulcers rapidly healing. Oedema of fauces gone.

20.6.11 : Throat normal. Herpes healed. No active signs of disease. Discharged hospital to attend. Weight 145 lbs.

10.8.11 : No active signs of disease. Weight 144½ lbs. Wassermann reaction —.

10.12.11 : No active signs of disease. Wassermann reaction —.

24.12.11 : Patient in excellent condition. Left Bangalore with his Regiment for Mhow.

Six months under observation and no recurrence.

Name : Pte. M. No.7645. Cameron Highlanders. Case 8

Admitted : 10th June 1911.

Disease contracted : In Bangalore September 1910.

Previous treatment : 4 complete courses of Mercury.

Condition on admission : Severe ulceration of both tonsils. Mucous patches on tongue and inner side of cheeks. Has had frequent admissions for throat trouble. Vision normal. Hearing normal.

Weight 129 lbs. Wassermann reaction + + +.

12.6.11 : Salvarsan .4 grammes intravenously.

Reaction mild. Slight headache and vomiting.

14.6.11 : Feels quite well. Well marked herpes on lips.

18.6.11 : Ulcers healed leaving scars on tonsils.

Mucous patches on tongue and cheeks disappeared.

Herpes gone. No active signs. Discharged hospital to attend.

15.7.11 : Wassermann reaction -, Weight 130½ lbs.

No active signs.

20.12.11 : Patient in excellent health. No active

signs of disease. Wassermann reaction -,.

Weight 133½ lbs.

8.1.12 : No active signs of disease. Struck off

Syphilis Register.

15.6.12 : No signs of disease. Wassermann reaction -,.

8.12.12 : No active signs. Wassermann reaction -,.

Under observation for eighteen months. No recurrence.

Name : Pte. C. No.7771. Cameron Highlanders. Case 9

Admitted : 22nd June 1911.

Disease contracted : In Bangalore June 1910

Previous treatment : 3 complete courses of Mercury

Condition on admission : Severe ulceration of both

tonsils, with marked oedema and congestion of

throat. Vision normal. Hearing normal.

Weight 140½ lbs. Wassermann reaction +++.

23.6.11 : Salvarsan .5 grammes intravenously. Reac-

tion very severe. Bad headache and severe vomit-

ing. R.b.c. 4,000,000. Hb. 60%

24.6.11 : Feels much better, but still suffers from

a slight headache. Morning temperature 100, even-

ing 99.2. Pulse 94.

25.6.11 : Feels quite well. Herpes on lips.

30.6.11 : Oedema and congestion of throat subsided.

Ulcers healed. No active signs of disease. Dis-

charged hospital to attend. Weight 144 lbs.

R.b.c. 4,620,000. Hb. 84%

19.7.11 : No active signs of disease. Wassermann

reaction -. Weight 145 lbs. R.b.c. 4,970,000.

Hb. 95%

10.8.11 : Patient in excellent condition. Weight

145½ lbs. R.b.c. 5,220,000. Hb. 96%

20.12.11 : No active signs of disease. Weight 147

lbs. Wassermann reaction -.

3.12.12 :

Name : Pte. M. No.6045. Cameron Highlanders. Case 10

Admitted : 6th July 1911

Disease Contracted : In China in 1909.

Previous treatment : 4 complete courses of Mercury

Condition on admission : Necrosis of nasal bones and septum, with a very offensive discharge from nostrils preventing him associating with his companions. Much debilitated and anaemic. Vision normal. Hearing normal. Weight 121 lbs. R.b.c. 3,500,000.

Hb. 46% Wassermann reaction +++

7.7.11 : Salvarsan .6 grammes intravenously. Reaction moderate. Slight headache, no vomiting.

8.7.11 : Feels quite well.

10.7.11 : No improvement in nasal condition. Herpes on lips. Weight 122 lbs. R.b.c. 3,850,000.

Hb. 64%

20.7.11 : Nasal discharge less copious and offensive, but progressing slowly. Weight 125½ lbs.

R.b.c. 4,220,000. Hb. 78%

1.8.11 : Discharge still continues. Wassermann re-

action ++. Weight 127 lbs. R.b.c. 4,335,000.

Hb. 84%. Weight 133 lbs.

4.8.11 : Salvarsan .3 grammes intravenously. Practically no reaction. Maximum temperature 99.

Pulse 90. Reaction mild

5.8.11 /

5.8.11 : Discharge still continues, but is much less offensive. General condition of patient much improved. Weight 129 lbs. R.b.c. 4,480,000. Hb. 88%.

5.9.11 : Salvarsan .3 grammes intravenously, (third injection). Reaction mild. Maximum temperature 99.2. Pulse 90.

6.9.11 : Patient feels quite well. Weight 131 lbs. R.b.c. 4,500,000. Hb. 90%.

20.9.11 : Discharge still present, but scanty and inoffensive. Weight 131 lbs. R.b.c. 4,630,000. Hb. 92%.

4.11.11 : Wassermann reaction +.

14.11.11 : Salvarsan .5 grammes intravenously, (fourth injection). Reaction severe. Vomiting and diarrhoea severe. Headache troublesome. Aching pains in legs. Maximum temperature 101.4 Pulse 112.

15.11.11 : Morning temperature 99, evening 98. Feels much better.

18.11.11 : General condition excellent, but discharge still present. Weight 133 lbs.

20.12.11 : Wassermann reaction +. Weight 134½ lbs.

3.1.12 : Salvarsan .5 grammes intravenously (fifth injection). Reaction mild .

8.1.12 /

- 8.1.12 : Slight discharge from nose still present.
- 20.1.12 : A large piece of necrosed bone removed from nose under chloroform.
- 25.1.12 : Since removal of piece of necrosed bone the nasal discharge has almost ceased.
- 5.2.12 : No active signs of disease. Weight $136\frac{1}{2}$ lbs
Wassermann reaction —.
- 23.6.12 : Patient in excellent health. Wassermann reaction —.
- 29.8.12 : No signs of disease. Struck off Syphilis Register.
- 10.12.12 : No active signs of disease. Eyes carefully examined and found to be perfectly normal. Hearing normal. Feels and looks well. Wassermann reaction —.
- Patient has received five intravenous injections of Salvarsan, totalling 2.2 grammes. Period under observation eighteen months, and no recurrence.

Name : Pte.D. No.5578. 14th Kings Hussars. Case 11

Admitted : 6th July 1911. Temperature 99.8. Pulse 90.

Disease contracted : In Bangalore in May 1911 134 lbs.

Previous treatment : Nil.

Condition on admission : Diffuse macular rash over face, body and limbs. Severe ulceration of right tonsil. Large phagadenic chancre on glans penis. Running slight temperature. Vision normal. Hearing normal. Weight 134 lbs. Wassermann reaction + + +.

17.7.11 : R.b.c. 4,200,000. Hb..68%

20.7.11 : Salvarsan .4 grammes intravenously.

Reaction severe.

21.7.11 : Morning temperature 99. Evening normal.

Slight headache, otherwise well. reaction negative.

24.7.11 : Ulcer on tonsil almost healed. Rash rapidly fading. Chancre healing rapidly. Herpes on lips. Weight 134 lbs. R.b.c. 4,220,000.

Hb. 74%

27.7.11 : Throat quite normal. Rash still faintly present on chest and back. Sore on penis healing.

3.8.11 : Rash still visible on chest and back.

Throat quite normal. Chancre healed. Wassermann reaction + +. Weight 132 lbs. R.b.c. 4,540,000.

Hb. 88%

4.8.11 : /

4.8.11 : Salvarsan .4 grammes intravenously. Reaction mild Maximum temperature 99.8. Pulse 90.

5.8.11 : Patient feels quite well. Weight 138½ lbs.
R.b.c. 4,600,000. Hb. 90%

10.8.11 : Rash completely gone. Throat normal.
Sore on penis healed. No active signs of disease.
Discharged hospital to attend. Weight 138 lbs.
R.b.c. 4,720,000. Hb. 94%.

20.8.11 : No active signs of disease. Weight 140 lbs. R.b.c. 4,750,000. Hb. 95%.

15.9.11 : No active signs of disease. Weight 141½ lbs. Wassermann reaction —. R.b.c. 4,830,000. Hb. 94%.

15.10.11 : No active signs of disease. Patient in excellent health. Wassermann reaction negative. Left Bangalore for Mhow with his Regiment.

Four months under observation; no recurrence.

Name : Gunner P. No.48028. 2nd Battery R.S.O. Case 12

Admitted : 15th August 1911

Disease contracted : In Bangalore in July 1911.

Previous treatment : Nil

Condition on admission : Chancre on glans penis healed.

Well marked macular rash on chest and limbs. Inguinal and cervical glands enlarged and shotty.

Well marked disordered action of heart. Pulse irregular. Complains of praecordial discomfort.

Faint systolic mitral bruit propagated towards axilla. Patient is a heavy cigarette smoker.

Vision normal. Hearing normal. Weight 156 lbs.

Wassermann reaction + + +. R.b.c. 4,600,000. Hb.68%

17.8.11 : Salvarsan .5 grammes intravenously. Reaction very severe. Well marked cyanosis of face and chest. Pulse rapid, slightly irregular, easily compressible. Feeling much better by evening.

18.8.11 : Patient feels quite well. Pulse still rapid, 92 per minute, and slightly irregular.

19.8.11 : Feels quite well. Herpes round lips.

21.8.11 : Rash fading rapidly. Glands slightly smaller. Weight 154 lbs.

1.9.11 : Rash completely faded. Glands normal. No active signs of disease. Discharged hospital to attend.

4.10.11 /

4.10.11 : No active signs of disease. Weight 157 lbs.

Wassermann reaction —.

11.11.11 : No active signs Wassermann reaction ++.

4.12.11 : Salvarsan .5 grammes (second dose).

Reaction slight. Maximum temperature 100. Pulse 80.

5.12.11 : Patient feels quite well. No active signs.

Weight 157 lbs.

15.1.12 : No active signs. Wassermann reaction —.

23.6.12 : No active signs. Wassermann reaction —.

10.12.12 : No active signs. Wassermann reaction —.

Period under observation sixteen months, and no recurrence.

Name : Pte. R. No.7336. Cameron Highlanders. Case 13

Admitted : 18th August 1911.

Disease contracted : In Bangalore in May 1910.

Previous treatment : 3 complete courses of Mercury

Condition on admission : Severe erosion and ulceration

of both tonsils. Slight conjunctivitis. Vision normal. Hearing normal. Weight 124 lbs. Very anaemic. R.b.c. 3,100,000. Hb. 60% Wassermann reaction +++.

20.8.11,: Salvarsan .5 grammes intravenously.

21.8.11 : Reaction moderately severe. Slight headache and vomiting.

26.8.11 : Slough separated from left tonsil leaving an ulcer with a healthy base. Right tonsil almost healed. Herpes on lips. Weight 126 lbs. R.b.c. 3,720,000. Hb. 70%.

28.8.11 : Tonsils normal. No signs of disease. Discharged hospital to attend.

30.8.11 : No active signs of disease. Weight 127 lbs. R.b.c. 4,310,000. Hb. 82%.

15.9.11 : No active signs of disease. Weight 130 lbs. R.b.c. 4,560,000. Hb. 90%.

20.10.11 : Patient in excellent condition. Weight 136 lbs. R.b.c. 4,632,000. Hb. 92% Wassermann reaction —.

8.2.12 /

Name : Gunner G. No.34954. "O" Battery R.H.A. Case 14.

Admitted : 28th August 1911.

Disease contracted : In Bangalore in 1908

Previous treatment : 4 complete courses of Mercury.

Condition on admission : Has been off Syphilis Register since December 1910. as cured. Tertiary ulcers on legs and feet, five on outer side of right calf and three on outer side of left calf. Three on right instep. Vision normal. Hearing normal. Weight $155\frac{1}{2}$ lbs. Wassermann reaction +++.

23.8.11 : Salvarsan .5 grammes intravenously. Reaction severe. Maximum temperature 103.2 and pulse 112, 4 hours after the injection. Frequent vomiting and severe headache.

24.8.11 : Feels quite well.

25.8.11 : Sloughs separating from all the ulcers which are looking healthy and shew signs of healing. Herpes on lips.

27.8.11 ; Ulcers healing. Punched out appearance gone.

1.9.11 : Ulcers on left leg all healed. Those on the right stationary.

5.9.11 : Salvarsan .3 grammes intravenously. Reaction mild. Maximum temperature 101.8. Pulse 100. Slight headache and vomiting.

9.9.11 /

9.9.11 : Ulcers healing rapidly. Herpes on lips.

25.9.11 : One indolent ulcer left on right instep.

Others all healed. Wassermann reaction ++.

Salvarsan .4 grammes intravenously, (third injection). Reaction mild. Slight headache; no vomiting. Maximum temperature 101.2. Pulse 100.

30.9.11 : Indolent ulcer on right instep has healed.

No active signs of disease. Discharged hospital to attend.

20.10.11 : No active signs of disease. Wassermann reaction -.

15.1.12 : No active signs of disease. Wassermann reaction -.

Left for England time expired. Period under observation, five months and no recurrence. Total Salvarsan = 1.2 grammes.

9.9.11 : Ulcer on left leg completely healed. The one on the right instep almost gone. Weight 134 lbs. R.B.C. 4,480,000. Hb. 85%.

10.9.11 : Ulcers all healed. Discharged hospital to attend.

13.9.11 : No active signs of disease. Weight 137 lbs. R.B.C. 4,790,000. Hb. 92%. Wassermann reaction +.

20.10.11 : No active signs of disease. Weight 140 lbs. R.B.C. 4,965,000. Hb. 94%. Wassermann

reactions-. Left Bangalore for Khaw with his Regiment.

Under observation 2 months and no recurrence.

Name : Pte. D. No.5630. 14th Kings Hussars. Case 15

Admitted : 20th August 1911.

Disease contracted : In Bangalore in January 1911.

Previous treatment : 2 courses of Mercury.

Condition on admission : Typical secondary ulcer on calf of left leg, size of a shilling, another size of a threepenny piece on right instep. Vision normal. Hearing normal. Weight 130½ lbs.

R.b.c. 4,000,000. Hb. 70%. Wassermann reaction + + +.

28.8.11 : Salvarsan .5 grammes intravenously. Reaction moderate. Severe headache. Slight vomiting.

30.8.11 : Patient feels quite well.

1.9.11 : Ulcer on left leg healing rapidly. That on right instep indolent. Weight 132 lbs.

R.b.c. 4,175,000. Hb. 75%.

7.9.11 : Ulcer on left leg completely healed. The one on the right instep almost gone. Weight 134 lbs. R.b.c. 4,480,000. Hb. 88%.

10.9.11 : Ulcers all healed. Discharged hospital to attend.

18.9.11 : No active signs of disease. Weight 137 lbs. R.b.c. 4,790,000. Hb. 92%. Wassermann reaction +.

20.10.11 : No active signs of disease. Weight 140 lbs. R.b.c. 4,965,000. Hb. 94%. Wassermann reaction -. Left Bangalore for Mhow with his Regiment. Under observation 2 months and no recurrence.

Name : Pte.B. No.5817. Cameron Highlanders. Case 16

Admitted : 26th August 1911.

Disease contracted : In Bangalore in December 1910.

Previous treatment : Two courses of Mercury, and .6 grammes Salvarsan intramuscularly.

Condition on admission : Large ulcers on both tonsils with tenacious sloughs. Vision normal. Hearing normal. Weight $136\frac{1}{2}$ lbs. Wassermann reaction + + +.

28.8.11 : Salvarsan .5 grammes intravenously. Reaction severe. Headache and vomiting.

29.8.11 : Patient had a restless night. Morning temperature 99.4. Evening normal. Pulse 80.

30.8.11 : Feels quite well. Wonderful improvement in throat. Sloughs have all come away and ulcers are looking healthy.

2.9.11 : Patient feels very fit. Ulcers healed. Discharged hospital to attend.

7.9.11 : Throat quite normal. Weight 138 lbs. Wassermann reaction +.

11.11.11 : No active signs of disease. Wassermann reaction -.

15.1.12 : No signs of disease. Weight 147 lbs. Wassermann reaction -.

23.6.12 : /

Name : Pte.G. No.1689. 14th Kings Hussars. Case 17

Admitted : 3rd September 1911.

Disease contracted ; In Bangalore in January 1910.

Previous treatment : 4 courses of Mercury

Condition on admission : Ulceration and congestion of fauces with oedema. Vision normal. Hearing normal. Weight 134 lbs. Wassermann reaction +++.

5.9.11 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache and vomiting.

15.9.11 : Oedema all gone, and ulcers healing.

20.9.11 : Ulcers all healed. Slight congestion of throat continues.

30.9.11 : Salvarsan .4 grammes intravenously. Reaction mild. Maximum temperature 102. Pulse 108. Slight headache; no vomiting.

1.10.11 : Patient feels quite well. Weight 138 lbs.

15.10.11 : Throat normal. No active signs of disease.

Discharged hospital to attend.

25.10.11 : No active signs of disease. Wassermann reaction -. Left Bangalore for Mhow with his regiment.

Under observation two months, and no recurrence.

Name : Pte.E. No.3075 14th Kings Hussars. Case 18.

Admitted : 3rd September 1911.

Disease contracted : In Bangalore in 1909

Previous treatment : 4 courses of Mercury

Condition on admission : Ulceration of fauces and pharynx. Vision normal. Hearing normal.

Weight 156 lbs. Wassermann reaction + + +.

5.9.11 : Salvarsan .5 grammes intravenously.

Reaction mild. Severe headache. Slight vomiting.

10.9.11 : Ulcers on fauces healed. Ulcer on pharynx almost gone. Discharged hospital to attend.

Weight 160½ lbs.

15.9.11 : Throat quite normal. No active signs of disease.

15.10.11 : No active signs of disease. Wassermann reaction —.

20.10.11 : No signs of disease. Left Bangalore for Mhow with his Regiment.

Under observation, six weeks.

Name : Pte.D. No.7999. Cameron Highlanders. Case 19

Admitted : 20th September 1911.

Disease contracted : In Bangalore in January 1911

Previous treatment : 3 courses of Mercury

Condition on admission : Ulcers on both tonsils.

Vision normal. Hearing normal. Weight 155 lbs.

Wassermann reaction + + +.

25.9.11 : Salvarsan .5 grammes intravenously. Reaction moderate. Slight headache and vomiting.

29.9.11 : Ulcers on tonsils healed. Throat normal.

Discharged hospital to attend.

25.10.11 : No active signs of disease. Wassermann reaction +.

20.11.11 : No active signs of disease. Wassermann reaction -.

8.2.12 : No active signs of disease. Vision normal.

Hearing normal. Weight 162½ lbs. Wassermann

reaction - . Left Bangalore for Madras.

Under observation, five months, and no recurrence.

Name : Pte. M. No.6878. Cameron Highlanders. Case 20

Admitted : 5th October 1911.

Disease Contracted : In China in 1909

Previous treatment : 4 courses of Mercury and .6
grammes Salvarsan intramuscularly.

Condition on admission : Tertiary ulcers with wash
leather bases on both tonsils. Hearing normal.

Vision normal. Weight 130 lbs. Wassermann
reaction + + +.

10.10.11 : Salvarsan .5 grammes intravenously.

Reaction slight. Severe headache. No vomiting.

14.10.11 : Ulcers on throat healed. Discharged hos-
pital to attend. Weight 132 lbs.

20.11.11 : No active signs of disease. Wassermann
reaction —.

20.12.11 : Throat normal. No signs of disease.

Wassermann reaction —.

Patient left for England, time expired.

Under observation, two months.

Name : Pte.B. No.5296. 8th Battery R.F.A. Case 22.

Admitted : 15th October 1911.

Disease contracted : In England in March 1911

Previous treatment 2 courses of Mercury and .6 grammes
Salvarsan intramuscularly.

Condition on admission : Severe ulceration of tonsils,
with marked oedema and congestion of pharynx.

Vision normal. Hearing normal. Weight 136 lbs.

R.b.c. 4,000,000. Hb.66%. Wassermann reac-
tion + + +.

18.10.11 : Salvarsan .5 grammes intravenously. Re-
action severe. Bad headache and vomiting.

19.10.11 : Morning temperature 99.4, evening 99.
Slight headache, otherwise feels well.

20.10.11 : Slight headache still continues.

22.10.11 : Patient quite well again. Sloughs separ-
ated from tonsils leaving healthy bases. Weight
137 lbs. R.b.c. 4,125,000. Hb.78%.

27.10.11 : Ulcers healing rapidly. Weight 138 lbs.
R.b.c. 4,628,000. Hb.90%. Wassermann reaction +.

30.10.11 : Ulcers healed. Throat normal. Discharged
hospital to attend.

11.11.11 : No active signs of disease. Weight 139
lbs. R.b.c. 4,840,000. Hb. 92% . Wassermann
reaction +.

14.11.11 : Salvarsan .4 grammes intravenously. Reac-
tion mild. Maximum temperature 100.8. Pulse 100.

20.11.11 /

20.11.11 : No active signs of disease. R.b.c
5,000,000. Hb. 94%

20.12.11 : No active signs of disease. Wassermann
reaction —. Weight 141 lbs.

28.3.12 : Patient in excellent health. Weight 144
lbs. R.b.c. 5,100,000. Hb. 96%

14.4.12 : No signs of disease. Wassermann reac-
tion —.

17.5.12 : No signs of disease. Struck off Syphilis
Register.

23.6.12 : No active signs of disease. Wassermann
reaction —.

10.12.12 : No signs of disease. Wassermann reac-
tion —.

Under observation, fourteen months and no recurrence.

Name : Driver H. No.52803. "O" Battery R.H.A. Case 23

Admitted : 15th October 1911.

Disease contracted : In England in February 1911

Previous treatment : 2 courses of Mercury.

Condition on admission : Secondary ulcers on both tonsils. Vision normal. Hearing normal.

Weight 144 lbs. Wassermann reaction + + +.

18.10.11 : Salvarsan .5 grammes intravenously.

Reaction mild. Severe headache, slight vomiting.

Congestion of face and chest.

25.10.11 : Ulcers healing. Well marked rash on face, which was not present on admission.

30.10.11 : No active signs. Discharged hospital to attend.

11.11.11 : No active signs of disease. Wassermann reaction + +.

14.11.11 : Salvarsan .4 grammes intravenously.

Maximum temperature 101.4. Pulse 104. Severe headache, slight vomiting, accompanied by diarrhoea.

15.11.11 : Patient feels quite well. Slight diarrhoea still continues.

20.11.11 : Patient quite well. Discharged hospital to attend.

10.12.11 : No active signs. Wassermann reaction —.

24.12.11 : No active signs. Patient in excellent health. Left for Amballa with his Battery.

Name : Pte.H. No.5721. 14th Kings Hussars. Case 24.

Admitted : 15th October 1911.

Disease contracted : In Bangalore in June 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : Marked congestion of throat,
with deep ulcers on pharynx. Vision normal.

Hearing normal. Weight 144½ lbs. Wassermann
reaction + + +.

18.10.11,: Salvarsan .5 grammes. Reaction mild.

Slight headache and vomiting.

21.10.11 : Congestion of throat gone. Ulcers heal-
ing rapidly.

24.10.11 : Ulcers healed. No signs of disease.

Discharged to attend.

11.11.11 : No active signs of disease. Wassermann
reaction +.

20.11.11 : No signs of disease.

Left Bangalore for Mhow with his regiment.

Name : Pte. M. No.7587. Cameron Highlanders. Case 25

Admitted : 10th November 1911. Weight 175 lbs.

Disease contracted : In Bangalore in September 1911.

Previous treatment : Nil. Weight 180 lbs.

Condition on admission : Well marked secondary rash on chest, back and limbs. A hard sore on dorsum of penis, practically healed. Inguinal and cervical glands enlarged. Vision normal. Hearing normal. Weight 170 lbs. Wassermann reaction +++.

R.b.c. 3,800,000. Hb. 70%. Weight 167 lbs.

14.11.11 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache and vomiting. Pulse rapid and easily compressed. Face, chest and conjunctivae congested.
 14 days and no recurrence.

18.11.11 : Glands getting smaller. Chancre healed.

Rash almost disappeared. Weight 174 lbs.

R.b.c. 4,200,000. Hb. 80%.

24.11.11 : Glands small but shotty. Rash quite gone.

Weight 176 lbs. Wassermann reaction ++.

R.b.c. 4,500,000. Hb. 90%.

10.12.11 : Slight congestion of throat and oedema of

fauces. R.b.c. 4,900,000. Hb. 94%. Weight

175 lbs.

18.12.11 : Salvarsan .5 grammes intravenously. Reaction

slight. Maximum temperature 100.8. Pulse

104. Slight headache and vomiting.

21.12.11 /

21.12.11 : Throat normal. Glands just palpable.

R.b.c. 4,880,000. Hb. 92%. Weight 178 lbs.

Discharged hospital to attend.

15.1.12 : No signs of disease. Weight 180 lbs.

Wassermann reaction —.

23.6.12 : No signs of disease. Wassermann reac-

tion —.

22.8.12 : No signs of disease. Wassermann reac-

tion —. Struck off Syphilis Register.

25.10.12 : No signs of disease. Weight 181 lbs.

Wassermann reaction —.

12.12.12 : No signs of disease. Wassermann reac-

tion —.

Under observation fourteen months and no recurrence.

Name : Pte.M. No.7523. Cameron Highlanders. Case 26.

Admitted : 10th November 1911.

Disease contracted : In Bangalore in June 1910.

Previous treatment : 3 courses of Mercury.

Condition on admission : Well marked congestion and oedema of throat. Vision normal. Hearing normal. Weight 144 lbs. Wassermann reaction + + +.

25.11.11 : Salvarsan .5 grammes intravenously. Reaction slight. Severe headache and slight vomiting.

30.11.11 : Throat normal. No active signs of disease
Discharged hospital to attend.

20.12.11 : No signs of disease. Wassermann reaction + +.

3.1.12 : Salvarsan .5 grammes intravenously. Reaction mild as regards headache and vomiting and temperature, which only reached 100°, but pulse very rapid, 140 in four hours, weak and easily compressible. Well marked cyanosis.

5.1.12 : No signs of disease. Discharged hospital to attend.

15.1.12 : No signs of disease. Weight 148 lbs.
Wassermann reaction +.

15.2.12 : No signs of disease. Wassermann reaction —.

22.7.12 : No signs of disease. Wassermann reaction —. Struck off Syphilis Register.

12.12.12 /

Name : Pte. R. No.7276. Cameron Highlanders. Case 27

Admitted : 10th November 1911.

Disease contracted : In Scotland in December 1910.

Previous treatment : 3 courses of Mercury.

Condition on admission : Secondary ulcers on fauces.

Vision normal. Hearing normal. Weight 140 lbs.

Wassermann reaction + + +.

25.11.11 : Salvarsan .5 grammes. Reaction mild.

Severe headache. Vomitted four times between
second and fourth hours.

1.12.11 : Ulcers almost healed.

10.12.11 : Throat normal. No active signs. Dis-
charged hospital to attend.

20.12.11 : No active signs. Weight 143 lbs.

Wassermann reaction -.

14.4.12 : No active signs. Wassermann reaction -.

17.5.12 : No active signs. Struck off Syphilis

Register.

23.6.12 : No active signs. Wassermann reaction -.

12.12.12 : No active signs. Wassermann reaction -.

Under observation thirteen months and no recurrence.

Name : Pte.W. No.7229. 7th Q.O.Hussars. Case 28.

Admitted : 10th November 1911.

Disease contracted : In England in May 1911.

Previous treatment : 8 injections of Mercury.

Condition on admission : Mucous patches on inner sides of cheeks, and on tongue and palate. Several small ulcers on fauces. Vision normal. Hearing normal. Weight 146 lbs. Wassermann reaction+++.

25.11.11 : Salvarsan .5 grammes intravenously.

Reaction very mild. Slight headache for six hours and a little vomiting. Face, eyes, and chest congested.

30.11.11 : Mucous patches all gone, and ulcers almost healed.

2.12.11 : No signs of disease. Discharged hospital to attend.

28.12.11 : No signs of disease. Wassermann reaction ++.

3.1.12 : Salvarsan .5 grammes intravenously. Reaction severe. Bad headache from second hour until evening. Pulse 100. Maximum temperature 103.2.

Given Caffiene Cit grs. 1, Phenacetin grs. 5.

4.1.12 : Temperature normal. Pulse 90. Slight headache.

6.1.12 : Patient quite well. Discharged hospital to attend.

15.2.12 /

Name : Pte.F. No.3562. 7th Q.O.Hussars. Case 29

Admitted : 10th November 1911.

Disease contracted : In England in October 1911

Previous treatment : Nil

Condition on admission : Secondary ulcers on both tonsils. Extensive condylomata round anus.

Vision normal. Hearing normal. Weight 140 lbs.

Wassermann reaction + + +.

25.11.11 : Salvarsan .5 grammes intravenously. Reaction moderate. Severe headache and vomiting.

29.11.11 : Ulcers on tonsils healed. Condylomata almost gone. A very rapid and extraordinary improvement. Weight 143 lbs. R.b.c.3,900,000. Hb.80%

2.12.11 : Throat normal. Condylomata disappeared.

4.12.11 : No active signs. R.b.c. 4,360,000.

Hb. 86%. Discharged hospital to attend.

15.12.11 : No active signs. Weight 145 lbs.

R.b.c. 4,683,000. Hb. 90%. Wassermann reaction + +.

23.12.11 : No active signs. Weight 147 lbs.

R.b.c. 4,760,000. Hb. 92%.

2.1.12 : No active signs. R.b.c. 4,780,000. Hb. 92%

15.1.12 : No active signs. Wassermann reaction + +.

24.1.12 : Salvarsan .5 grammes intravenously. Reaction very mild. Maximum temperature 99.8. Pulse 90. Slight headache, no vomiting.

26.1.12 /

Name : Pte.C. No.3946. 7th Q.O.Hussars. Case 30.

Admitted : 24th November 1911.

Disease contracted : In England in July 1911.

Previous treatment : 2 courses of Mercury

Condition on admission : Large secondary ulcers on both tonsils. Mucous patches on tongue and cheeks. Vision normal. Hearing normal. Weight 142 lbs. Wassermann reaction +++.

25.11.11 : Salvarsan .5 grammes intravenously. Reaction moderately severe. Very bad headache and slight vomiting. Pulse soft and markedly irregular. Some cyanosis.

26.11.11 : Temperature 99. Pulse 82, no irregularity discernible. Patient feels himself again.

30.11.11 : Mucous patches all disappeared. Ulcers healing rapidly.

2.12.11 : Throat normal. No active signs of disease. Discharged hospital to attend. Weight 160 lbs.

9.12.11 : No active signs. Wassermann reaction ++.

15.12.11 : Salvarsan .5 grammes intravenously. Reaction slight. Maximum temperature 99.8. Pulse 86. No irregularity. Headache severe. Vomiting severe.

16.12.11 : Temperature 98.6. Pulse 86. Patient feels quite well. Discharged hospital to attend. Weight 159 lbs.

2.2.12 /

2.2.12 : No active signs. Weight 160 lbs.

4.4.12 : No active signs. Weight 160 lbs. Wassermann reaction—.

23.6.12 : No active signs. Weight 160 lbs. Wassermann reaction—.

18.10.12 : No active signs. Wassermann reaction—.

8.12.12 : No active signs. Wassermann reaction—.

Under observation thirteen months and no recurrence.

Name : Pte.M. No.6127. 7th Q.O. Hussars. Case.31.

Admitted : 18th November 1911. Weight 147 lbs. Wassermann

Disease contracted : In England in September 1911.

Previous treatment : Nil. Wassermann reaction

Condition on admission : Secondary ulcer on pharynx.

Large condyloma round anus. Vision normal.

Hearing normal. Weight 140 lbs. Wassermann
reaction + + +.

25.11.11 : Salvarsan .5 grammes intravenously.

Reaction severe. Headache and vomiting troublesome. Pulse rapid but regular.

26.11.11 : Morning temperature 99.2, evening normal.

Pulse 80. Slight headache still present.

28.11.11 : Feels quite well. Ulcer on pharynx

healing. Condyloma very much improved.

4.12.11 : Throat normal. Condyloma disappeared,

the rapidity with which it has healed is almost incredible.

9.12.11 : No active signs. Weight 144 lbs.

Wassermann reaction + +.

16.12.11 : Salvarsan .5 grammes intravenously. Reaction

fairly severe. Maximum temperature 102.4.

Pulse 98. Severe headache and vomiting.

17.12.11 : Feels quite well. No active signs.

Discharged hospital to attend.

15.2.12 /

Name : L/c K. Cameron Highlanders. Case 32

Admitted : 30th November 1911.

Disease contracted : In Bangalore in June 1910.

Previous treatment : 3 courses of Mercury.

Condition on admission : Enlarged tonsils with marked congestion of throat. Has had frequent admissions for throat trouble. Hearing normal. Vision normal. Weight 145 lbs. Wassermann reaction + + +.

1.12.11 : Salvarsan .5 grammes intravenously. Reaction moderate. Headache and vomiting severe. Slight diarrhoea with cramps in abdomen. Pulse soft but regular.

2.12.11 : Morning temperature 99, evening normal. Slight diarrhoea continuing. No pains.

3.12.11 : Feels quite well. Diarrhoea ceased. Herpes round lips.

6.12.11 : Throat normal. Discharged hospital to attend.

10.1.12 : No active signs. Weight 147½ lbs. Wassermann reaction -.

12.2.12 : No active signs. Wassermann reaction -.

1. 7.12 : No active signs. Weight 148 lbs. Wassermann reaction - , Struck off Syphilis Register.

25.10.12 : No active signs. Wassermann reaction -.

5.12.12 : No active signs. Wassermann reaction -.

Under observation thirteen months and no recurrence.

Name : L/c.C. No.7825. Cameron Highlanders. Case 33

Admitted : 25th November 1911.

Disease contracted : In Bangalore in March 1911.

Previous treatment : 2 courses of Mercury and Salvarsan
.6 grammes intramuscularly.

Condition on admission : Congestion of throat and
several ulcers on tonsils. Has had frequent ad-
missions for throat trouble. Hearing normal.
Vision normal. Weight 148 lbs. Wassermann
reaction + + +.

1.12.11 : Salvarsan .5 grammes intravenously. Reac-
tion moderate. Severe headache, slight vomiting.
Face and eyes congested.

2.12.11 : Morning temperature 99.6, evening normal.

4.12.11 : Ulcers on tonsils healing. Herpes round
lips.

6.12.11 : Ulcers healed. Throat normal. Discharged
hospital to attend.

9.12.11 : No active signs. Wassermann reaction + +.

18.12.11 : Salvarsan .5 grammes intravenously. Reac-
tion severe. Temperature before injection 97.6.
Pulse 70. Immediately after injection temperature
99.8, pulse 76. Two hours later temperature 98,
pulse 68. Complains of severe frontal headache.
Four hours later temperature 100.8, pulse 110.
Severe headache continues, accompanied by vomiting.
Face and conjunctivae congested. Slight diarrhoea.
Complains of severe pain below left costal margin.

19.12.11 /

19.12.11 : Temperature normal. Pulse 84. Feels quite well. Discharged hospital to attend.

3.1.12 : No active signs. Weight 149 lbs. Wassermann reaction +.

15.2.12 : No active signs. Wassermann reaction -.

8.7.12 : No active signs. Wassermann reaction -.

16.7.12 : Salvarsan .5 grammes intravenously.

This injection was given for provocative purposes to see whether the negative Wassermann reaction would remain negative or become positive again.

Reaction moderately severe. Maximum temperature 101. Pulse 112. Severe headache and slight vomiting.

20.7.12 : No active signs. Wassermann reaction -.

25.8.12 : No active signs. Wassermann reaction -.

Struck off Syphilis Register.

18.10.12 : No active signs. Wassermann reaction -.

10.12.12 : No active signs. Wassermann reaction -.

Under observation thirteen months and no recurrence.

Name : Pte.M. No.8088. Cameron Highlanders. Case 34.

Admitted : 28th November 1911.

Disease contracted : In Lucknow in July 1910.

Previous treatment : 3 courses of Mercury .

Condition on admission : Large ulcer on left tonsil
with a sloughy base. Congestion of throat.

Swelling and oedema of fauces. Vision normal.

Hearing normal. Weight 144 lbs. Wassermann
reaction + + +.

1.12.11 : Salvarsan .5 grammes intravenously. Reac-
tion mild. Marked congestion of face, eyes and
chest.

4.12.11 : Herpes round lips.

6.12.11 : Slough separated from ulcer on tonsil
which is looking healthy. Herpes on lips drying.

8.12.11 : Throat normal. Ulcer healed. Discharged
hospital to attend.

10.12.11 : No active signs. Wassermann reaction +.

5.1.12 : No active signs. Wassermann reaction -.

15.2.12 : No active signs. Wassermann reaction -.

18.10.12 : No active signs. Struck off Syphilis
Register. Wassermann reaction -.

10.12.12 : No active signs. Wassermann reaction -.

Under observation twelve months and no recurrence.

Name : Pte.J. Cameron Highlanders. Case 35.

Admitted : 25th November 1911.

Disease contracted : In Bangalore in May 1910.

Previous treatment : 3 courses of Mercury and .6 grammes Salvarsan intramuscularly.

Condition on admission : Throat congested and ulcers on fauces. Vision normal. Hearing normal.

Weight 149 lbs. Wassermann reaction + + +.

1.12.11 : Salvarsan .5 grammes intravenously. Reaction mild. Slight frontal headache and vomiting. Congestion of face and eyes.

4.12.11 : Throat very much improved. Congestion gone. Ulcers on fauces healing.

6.12.11 : Throat normal. No active signs. Discharged hospital to attend.

10.12.11 : No active signs. Wassermann reaction +.

20.12.11 : No active signs. Wassermann reaction -.

15.2.12 : No active signs. Weight 151 lbs. Wassermann reaction -.

23.6.12 : No active signs. Wassermann reaction -.

26.7.12 : No active signs. Salvarsan .5 grammes intravenously - a provocative injection. Reaction very mild. Slight headache one hour after injection when temperature was 98.4 and pulse 80. Vomitted once. Complains of colicky pains in abdomen but had no motion. Four hours later temperature /

Name : Pte.W. No.7147. 7th Q.C. Hussars. Case 36.

Admitted : 26th November 1911.

Disease contracted : In England in October 1911.

Previous treatment : Nil

Condition on admission : Typical Hunterian chancre on glans penis. Faint secondary papular rash on chest, flanks and legs. Vision normal. Hearing normal. Weight 144 lbs. Wassermann reaction+++.

1.12.11 : Salvarsan .5 grammes intravenously. Reaction severe. Marked frontal headache and vomiting and later diarrhoea accompanied by colicky pains and cramps in lower limbs.

2.12.11 : Feels better to-day, but still complains of headache and diarrhoea. Tongue furred, no appetite. Morning temperature 99 8, evening normal. Pulse 94.

3.12.11 : Feels quite fit. Herpes round lips.

6.12.11 : Rash quite faded. Chancre almost healed.

8.12.11 : Chancre healed. Discharged hospital to attend.

20.12.11 : No active signs. Wassermann reaction++.

3.1.12 : Slight congestion of throat. Salvarsan .5 grammes intravenously. Reaction not severe but cardiac effects marked. Pulse 120 per minute, regular in rate and rhythm, but soft and easily compressible. Marked cyanosis of face and congestion of /

Name : Driver W. 2nd Battery R.F.A. Case 37.

Admitted : 12th December 1911

Disease contracted : In England in November 1910.

Previous treatment : 3 courses of Mercury and .6
grammes Salvarsan intramuscularly.

Condition on admission : Slight congestion of throat.

No other active signs. Vision normal. Hearing
normal. Weight 112 lbs. Wassermann reaction + + +.

18.12.11 : Salvarsan .5 grammes intravenously.

Reaction very mild. Slight headache and vomiting.

20.12.11 : No active signs. Discharged hospital to
attend.

28.12.11 : No active signs. Weight 122 lbs.

Wassermann reaction —.

15.1.12 : No active signs. Weight 124 lbs.

Wassermann reaction —.

14.4.12 : No active signs. Wassermann reaction —.

22.7.12 : No active signs. Wassermann reaction —.

25.8.12 : No active signs. Wassermann reaction —.

18.10.12 : No active signs. Wassermann reaction —.

10.12.12 : No active signs. Wassermann reaction —.

Under observation twelve months and no recurrence.

Name : Pte.M. No.8090. 14th Kings Hussars. Case 38

Admitted : 10th December 1911.

Disease contracted : In Madras in October 1911.

Previous treatment : Nil Wassermann reaction -

Condition on admission : Typical hard chancre on glans penis near fraenum. Mucous on inner side of cheeks. Ulcer on tip of tongue. Large condyloma round anus. Vision normal. Hearing normal. Weight 118 lbs. Wassermann reaction +++.

18.12.11 : Salvarsan .5 grammes intravenously. Reaction moderately severe. Rigors. Severe headache. Slight vomiting. Face flushed, eyes congested.

20.12.11 : Ulcer on tongue almost healed. Mucous patches on cheeks gone. Condyloma rapidly healing. Chancre much improved.

22.12.11 : Condyloma practically gone. Chancre almost healed.

25.12.11 : Condyloma healed. Chancre disappeared. No signs of disease. Discharged hospital to attend.

27.12.11 : No active signs. Wassermann reaction ++.

3.1.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 100.8. Pulse 104. Severe headache. Slight vomiting. No diarrhoea.

5.1.12 /

Name : Pte.M. No.8094. Cameron Highlanders. Case 39.

Admitted : 18th December 1911.

Disease contracted : In Bangalore in December 0910.

Previous treatment : 4 courses of Mercury.

Condition on admission : No active signs of disease.

Wassermann reaction + + +. Vision normal. Hearing normal.

18.12.11 : Salvarsan .5 grammes intravenously. Reaction very mild. Slight frontal headache and vomiting.

19.12.11 : Feels quite well. Discharged hospital to attend.

28.12.11 : No active signs. Wassermann reaction +.

15.1.12 : No active signs. Wassermann reaction -.

22.7.12 : No active signs. Wassermann reaction -.

Struck off Syphilis Register.

25.10.12 : No active signs. Wassermann reaction -.

11.12.12 : No active signs. Wassermann reaction -.

Under observation twelve months and no recurrence.

Name : Pte.D. No.7391. 7th Q.C. Hussars. Case 40.

Admitted : 12th December 1911.

Disease contracted : In October 1911.

Previous treatment : Nil.

Condition on admission : Hard chancre on glans penis.

Secondary macular rash on chest and limbs. Inguinal and cervical glands enlarged and shotty. Vision normal. Hearing normal. Weight 143 lbs. Wassermann reaction + + +.

18.12.11 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache and vomiting. Rapid pulse. Eyes congested, face cyanosed. Respiration hurried.

19.12.11 : Feels better to-day. Tongue furred, no appetite.

22.12.11 : Rash almost gone. Chancre healing rapidly.

28.12.11 : No active signs. Weight 145 lbs.

Wassermann reaction —.

14.1.12 : No active signs. Discharged hospital to attend.

14.4.12 : No active signs. Weight 154 lbs. Wassermann reaction —.

15.6.12 : Recurrence of disease in that the negative Wassermann reaction has become positive again.

21.6.12 /

Name : Pte.B. No.7596. Cameron Highlanders. Case 41

Admitted : 28th December 1911.

Disease contracted : In Bangalore in October 1911.

Previous treatment : Nil

Condition on admission : Small primary sore on corona, practically healed. Faint rash on chest and flanks. Rheumatic pains in knees and ankles. Vision normal. Hearing normal. Weight 144 lbs. Wassermann reaction +++.

3.1.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Slight headache and vomiting.

6.1.12 : Complains of slight frontal headache, otherwise feels well. Rheumatic pains in joints gone. Rash on chest fading. Neucleated red blood corpuscles were found in the films taken at the fourth and eighth hours after the injection of the drug, none having previously been found, whilst doing the differential counts.

10.1.12 : Sore on penis healed. Rash almost disappeared.

14.1.12 : No active signs. Weight 145 lbs. Wassermann reaction ++.

16.1.12 : Salvarsan .5 grammes intravenously. Reaction moderately severe. Severe headache and slight vomiting. No diarrhoea. Maximum temperature 102. Pulse 84.

19.1.12 /

Name : Pte.L. No.5428. 7th Q.O. Hussars. Case 42.

Admitted : 30th December 1911.

Disease contracted : In England in September 1909.

Previous treatment : 4 courses of Mercury.

Condition on admission : Two large tertiary ulcers on front of right forearm. Two similar ulcers on back of left forearm. Inguinal glands enlarged. Large ulcer on outer side of calf of left leg. Vision normal. Hearing normal. Weight 146 lbs. Wassermann reaction + + +.

3.1.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache and vomiting. Rigors. Complains of severe pain over lumbar region of spine.

4.1.12 : Morning temperature 99, evening normal.

6.1.12 : Feels fairly fit. All the ulcers are beginning to look healthy. The only dressing used has been dry sterile gauze.

11.1.12 : All the ulcers healed except the one on his right forearm, which is looking very healthy however.

13.1.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Maximum temperature 100.2. Pulse 100. Complains of frontal headache. A little vomiting, no diarrhoea.

16.1.12 /

Name : L/c S. 7th Q.O. Hussars. Case 43.

Admitted : 28th December 1911.

Disease contracted : In England in December 1910.

Previous treatment : 3 courses of Mercury.

Condition on admission : Mucous patches on inner side of both cheeks. Tonsils enlarged and throat congested. Vision normal. Hearing normal.

Weight 147 lbs. Wassermann reaction + + +.

5.1.12. : Salvarsan .5 grammes intravenously. Reaction moderate. Slight headache and vomiting.

Complains of dull aching pains in loins and lower part of legs. Face and eyes congested.

8.1.12 : Tonsils normal. Mucous patches healing.

10.1.12 : Throat normal. Mucous patches gone.

No active signs. Discharged hospital to attend.

12.2.12 : No active signs. Wassermann reaction -.

28.3.12 : No active signs. Weight 149 lbs. Wassermann reaction -.

8.7.12 : No active signs. Weight 151 lbs. Wassermann reaction -.

15.12.12 : No active signs. Wassermann reaction -.

Under observation twelve months and no recurrence.

Date. 5.1.12

SALVARSAN.

.5 Grammes. Case number. 43

Date.	Before Salvarsan.	After Salvarsan.							
		1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	80	76	88	100	96	72	74	70	70
Respiration.	24	26	26	26	24	22	20	18	20
Temperature.	98.	98.	100.	102.6	102.	99.	98.4	98.4	98.4
Blood-pressure.	126	124	115	109	112	115	122		
Leucocytosis.	9062								
(a) Polymorphs.	60%								
(b) Lymphocytes.	34%								
(c) Large monos.	5%								
(d) Eosinophiles.	1%								
Red corpuscles.	4600000								
Haemoglobin.	88%								
Urine. (a) Sp. gr.	1020					1024	1020	1020	1018
(b) Albumin.	Nil					Nil	Nil	Nil	Nil
Headache.	Nil	Nil	Slight	Slight	Slight	Nil	Nil	Nil	Nil
Vomiting.	Nil	Nil	Slight	Slight	Slight	Nil	Nil	Nil	Nil
Diarrhoea.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

The ulcers are practically healed.

Name : Pte.B. No.7678. 2nd Leicester Regt. Case 44.

Admitted : 28th December 1911.

Disease contracted : In Gibraltar in 1902.

Previous treatment : 4 complete courses of Mercury.

Has been off Syphilis Register since 1907.

Condition on admission : A large typical tertiary ulcer on right forearm, another one on left forearm, and a third one on the outer side of the right thigh above the knee. Vision normal. Hearing normal. Weight 146 lbs. Wassermann reaction +++.

5.1.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Slight headache, no vomiting, no diarrhoea.

8.1.12 : All the ulcers beginning to look healthy and shew signs of healing.

12.1.12 : Ulcer on right arm almost healed. The ulcers on left arm and thigh look healthy but are not progressing very rapidly.

15.1.12 : Salvarsan .5 grammes intravenously. Reaction slight. Maximum temperature 99. Pulse 100. Slight headache, no vomiting, no diarrhoea.

18.1.12 : Ulcers healing rapidly. Patient feels very fit.

22.1.12 : All the ulcers are practically healed.

3.2.12 /

Name : Pte.H. No.4639. Cameron Highlanders. Case 45.

Admitted : 23rd January 1912.

Disease contracted : In Gibraltar in 1901.

Previous treatment : 4 courses of Mercury. Has been off Syphilis Register since 1906.

Condition on admission : Two punched out ulcers on left hip with wash leather bases and several old pigmented scars of old ulcers round them. Vision normal. Hearing normal. Weight 158 lbs. Wassermann reaction +++.

24.1.12 : Salvarsan .6 grammes intravenously. Reaction moderate. Severe headache and vomiting.

25.1.12 : Ulcers looking healthier. Sloughs separated from their bases

3.2.12 : Ulcers healing rapidly.

7.2.12 : Salvarsan .6 grammes intravenously. Reaction slight. Maximum temperature 99.8. Pulse 100. Slight headache and vomiting. No diarrhoea.

12.2.12 : Ulcers healed. Discharged hospital to attend.

8.3.12 : No active signs. Wassermann reaction +.

1.7.12 : No active signs. Weight 160 lbs. Wassermann reaction -.

15.12.12 : No active signs. Wassermann reaction -.

Under observation eleven months and no recurrence.

Name : Pte.C. No.8420. Cameron Highlanders. Case 46

Admitted : 23rd January 1912.

Disease contracted : In Bangalore in 1911.

Previous treatment : Nil

Condition on admission : Congested throat. Secondary macular rash on chest and limbs. Vision normal. Hearing normal. Weight 146 lbs.

Wassermann reaction +++.

24.1.12 : Salvarsan .6 grammes intravenously.

Reaction severe. Severe headache and vomiting.

25.1.12 : Feels well except for slight frontal headache.

28.1.12 : Throat normal. Herpes round lips.

3.2.12 : Rash almost gone. Herpes disappeared.

8.2.12 : No active signs. Discharged hospital to attend.

26.2.12 : No active signs. Wassermann reaction ++.

6.6.12 : No active signs. Wassermann reaction +.

22.6.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 101. Pulse 88. Slight headache and vomiting. No diarrhoea. Severe pain in loins and lower extremities.

23.6.12 : Slight headache still present, otherwise well.

24.6.12 : Complains of constantly feeling inclined to be sick. Tongue furred, no appetite. Slight herpes round lips. Urine normal.

26.6.12 /

26.6.12 : No active signs. Discharged hospital to attend.

SALVARSAN.
(First dose)

9.7.12 : No active signs. Wassermann reaction —.

12.12.12 : No active signs. Wassermann reaction —.

Under observation eleven months and no recurrence.

	78	80	100	112	104	80	70	70	66
Respiration.	22	20	25	26	24	15	20	20	18
Temperature.	98.2	99.	101.	103.	100.	98.6	98.4	98.4	98.4
Haemoglobin.									
Leucocytes.	10937								
(a) Polymorphs.	64%								
(b) Lymphocytes.	31%								
(c) Large monon.	5%								
(d) Eosinophils.	0%								
Red corpuscles.	3200000								
Hæmoglobin.	66%								
Urea (a) Sp. gr.	1020					1026	1018	1016	1016
(b) Albumin.	Nil					Nil	Nil	Nil	Nil
Headache.	Nil	Slight	Severe	Severe	Severe	Slight	Nil	Nil	Nil
Vomiting.	Nil	Nil	Severe	Severe	Nil	Nil	Nil	Nil	Nil
Diarrhoea.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Opsonic index	See table on page 68								

Date. 24.1.12

SALVARSAN.

.6 Grammes. Case number. 46

(First dose)

	Before Salvarsan.	After Salvarsan.							
Date.	23.1.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	78	80	100	112	104	80	70	70	66
Respiration.	22	20	23	26	24	18	20	20	18
Temperature.	98.2	99.	101.	102.	100.	98.6	98.4	98.4	98.4
Blood-pressure.									
Leucocytosis.	10937								
(a) Polymorphs.	64%								
(b) Lymphocytes.	31%								
(c) Large monos.	5%								
(d) Eosinophiles.	0%								
Red corpuseles.	3200000								
Haemoglobin.	66%								
Urine. (a) Sp. gr.	1020					1026	1018	1016	1018
(b) Albumin.	Nil					Nil	Nil	Nil	Nil
Headache.	Nil	Slight	Severe	Severe	Severe	Slight	Nil	Nil	Nil
Vomiting.	Nil	Nil	Severe	Severe	Nil	Nil	Nil	Nil	Nil
Diarrhoea.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Opsonic Index	See	table on page 68							

Name : Pte.C. No.7563. Cameron Highlanders. Case 47.

Admitted : 23rd January 1912. Wassermann reaction -

Disease contracted : In Bangalore in November 1911.

Previous treatment : Nil.

Condition on admission : Throat congested. Macular rash on face and limbs. Inguinal glands enlarged and shotty. Mucous patches on inner side of cheeks. Vision normal. Hearing normal. Wassermann reaction +++.

24.1.12 : Salvarsan .6 grammes intravenously. Reaction moderate. Severe headache. Very slight vomiting. No diarrhoea.

27.1.12 : Throat normal. Mucous patches gone. Rash fading. Glands stationary.

31.1.12 : Rash almost faded. Glands subsiding.

3.2.12 : Rash still faintly visible.

10.2.12 : Salvarsan .5 grammes intravenously. Reaction slight. Maximum temperature 99. Pulse 106. Slight headache and vomiting. No diarrhoea.

15.2.12 : Rash disappeared. No active signs. Discharged hospital to attend.

26.2.12 : No active signs. Wassermann reaction +.

18.4.12 : No active signs. Wassermann reaction -.

9.7.12 : No active signs. Wassermann reaction -.

9.10.12 /

Name : Pte.D. No.6698. Cameron Highlanders. Case 48

Admitted : 24th January 1912.

Disease contracted : In Bangalore in December 1911.

Previous treatment : Nil

Condition on admission : Throat congested. Tonsils enlarged. Inguinal glands shotty. Macular rash on chest and limbs. Vision normal. Hearing normal. Wassermann reaction

28.1.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Slight headache. Nausea but no vomiting. No diarrhoea.

6.2.12 : Throat normal. Tonsils normal. Rash fading rapidly.

10.2.12 : Rash almost gone. Glands just palpable.

12.2.12 : No active signs. Wassermann reaction ++.

Discharged hospital to attend.

25.4.12 : No active signs. Wassermann reaction -.

8.7.12 : No active signs. Wassermann reaction -.

9.10.12 : No active signs. Wassermann reaction -.

8.12.12. : No active signs. Wassermann reaction -.

Under observation eleven months and no recurrence.

Date. 28.1.12

SALVARSAN.

.5 Grammes. Case number. 48

	Before Salvarsan.	After Salvarsan.							
Date.	27.1.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	78	80	100	110	80	72	70	72	70
Respiration.	24	24	26	26	24	20	18	20	18
Temperature.	98.4	98.	99.2	101.8	99.2	98.4	98.4	98.4	98.4
Blood-pressure.									
Leucocytosis.	10525								
(a) Polymorphs.	65%								
(b) Lymphocytes.	31%								
(c) Large monos.	4%								
(d) Eosinophiles.	0%								
Red corpuseles.	3900000								
Haemoglobin.	60%								
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.									
Vomiting.									
Diarrhoea.									
Opsonic Index	See	table on page 68							

Name : Pte. B. No.8826. 2nd Leicester Regt. Case 49.

Admitted : 21st January 1912.

Disease contracted : In Bellary in December 1911.

Previous treatment : Nil

Condition on admission : Hard chancre on penis.

Enlarged inguinal glands. Macular rash on chest
and limbs. Vision normal. Hearing normal.

Weight 132 lbs. Wassermann reaction + + +.

28.1.12 : Salvarsan .6 grammes intravenously. Reac-
tion moderate. Severe headache, slight vomiting,
no diarrhoea.

1.2.12 : Rash fading rapidly. Chancre healing.

6.2.12 : Rash almost disappeared. Chancre healed.

16.2.12 : Rash gone. Glands normal. No active
signs. Wassermann reaction + +.

22.2.12 : Salvarsan .5 grammes intravenously. Reac-
tion mild. Maximum temperature 100. Pulse 102.
Slight headache and vomiting. No diarrhoea.

29.2.12 : No active signs. Discharged hospital to
attend.

25.4.12 : No active signs. Weight 140 lbs. Wasser-
mann reaction + +.

10.5.12 : Salvarsan .5 grammes intravenously. Reac-
tion mild. Maximum temperature 99. Pulse 100.
Slight headache, no vomiting or diarrhoea.

17.5.12 : No active signs. Wassermann reaction -.

16.6.12 : No active signs. Wassermann reaction -.

Transferred to Bellary.

Name : Pte.R. Cameron Highlanders. Case 50.

Admitted : 26th January 1912.

Disease contracted : In Scotland in October 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : Small ulcer on tip of tongue.

Another on right cheek. Vision normal. Hearing normal. Wassermann reaction + + +.

28.1.12 : Salvarsan .6 grammes intravenously. Reaction moderate. Slight headache and vomiting. No diarrhoea.

4.2.12 : Ulcer on tongue healed. The one on cheek almost gone.

6.2.12 : Ulcers healed. No active signs. Discharged hospital to attend.

26.2.12 : No active signs. Wassermann reaction -.

8.7.12 : No active signs. Wassermann reaction -.

Struck off Syphilis Register.

1.12.12 : No active signs. Wassermann reaction -.

Under observation eleven months and no recurrence.

Name : Pte.H. No.7179. Cameron Highlanders. Case 51

Admitted : 29th January 1912.

Disease contracted : In China in 1909.

Previous treatment : 4 courses of Mercury

Condition on admission : No active signs but as his Wassermann reaction was strongly positive and he soon leaves the service an injection of Salvarsan was given at his own request. Vision normal. Hearing normal.

2.2.12 : Salvarsan .6 grammes intravenously. Reaction mild. Slight headache, no vomiting, no diarrhoea. Complains of pain in loins and lower extremities.

4.2.12 : No active signs. Discharged hospital to attend.

26.3.12 : No active signs. Wassermann reaction +.

20.5.12 : No active signs. Wassermann reaction -.

8.9.12 : No active signs. Wassermann reaction -.

17.10.12 : No active signs. Wassermann reaction -.

Patient left for England, time expired.

Under observation eight months and no recurrence.

Date. 2.2.12.

SALVARSAN.

.6 Grammes. Case number. 51

	Before Salvarsan.	After Salvarsan.							
Date.	1.2.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	64	72	84	98	90	78	70	66	68
Respiration.	18	18	22	22	20	18	18	20	18
Temperature.	97.8	98.6	99.	100.	98.8	98.4	98.2	98.	98.2
Blood-pressure.									
Leucocytosis.									
(a) Polymorphs.									
(b) Lymphocytes.									
(c) Large monos.									
(d) Eosinophiles.									
Red corpuseles.									
Haemoglobin.									
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.									
Vomiting.									
Diarrhoea.									
Opsonic Index	See	table on page 68.							

Name : Pte.B. No.7077. 7th Q.O.Hussars. Case 52.

Admitted : 21st January 1912. NO active signs.

Disease contracted : In England in November 1911

Previous treatment : Nil. Weight 107 lbs. Wassermann-

Condition on admission : Severe congestion of throat.

Secondary macular rash on chest, back and limbs. of

Vision normal. Hearing normal. Weight 114 lbs.

Wassermann reaction + + +. Wassermann reaction -

2.2.12 : Salvarsan .5 grammes intravenously. Reaction severe. Suffered from severe frontal headache all day with very little vomiting. No diarrhoea. Pains in lumbar region and lower extremities. Face flushed. Pulse rapid.

3.2.12 : Morning temperature 100.8, evening 99.

Morning pulse 110, evening 82. Slight headache continues. Tongue furred. No appetite.

4.2.12 : Feels quite well. Temperature and pulse normal. No headache.

5.2.12 : Throat normal. Rash fading rapidly.

14.2.12 : No active signs. Discharged hospital to attend.

28.3.12 : No active signs. Weight 126 lbs.

Wassermann reaction +

9.5.12 : No active signs. Wassermann reaction + +.

21.5.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 99.8. Pulse 84.

No /

No headache, no vomiting, no diarrhoea.

23.5.12 : Feels quite well. No active signs.

Discharged hospital to attend.

23.6.12 : No active signs. Weight 127 lbs. Wassermann reaction —.

4.7.12 : No active signs. Commenced first course of Mercury.

9.10.12 : No active signs. Wassermann reaction —.
Struck off Syphilis Register.

3.12.12 : No active signs. Wassermann reaction —.

Under observation seven months, and no recurrence.

Ophthalmic
Index

See table on page 140

Name : Pte.H. No.6828. 2nd Leicester Regt. Case 53.

Admitted : 22nd January 1912.

Disease contracted : In Bellary in November 1911.

Previous treatment : Nil

Condition on admission : Large hard chancre on glans penis. Inguinal glands enlarged. Throat congested and tonsils enlarged. Macular rash on chest and limbs. Vision normal. Hearing normal. Weight 134 lbs. Wassermann reaction + + +.

2.2.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache, slight vomiting, rapid feeble pulse, congested eyes and flushed face, respirations hurried, pains in small of back.

3.2.12 : Morning temperature 99.6. Evening normal. Morning pulse 100. Evening 80.

6.2.12 : Throat normal. Chancre healing. Rash fading.

14.2.12 : Rash faded. Chancre almost gone.

20.2.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Highest temperature 102. Pulse 100. Slight headache, no vomiting or diarrhoea.

28.2.12 : No active signs. Weight 147 lbs. Discharged hospital to attend. Commenced first course of Mercury.

4.4.12 : No active signs. Weight 152 lbs. Wassermann reaction -.

11.5.12 : No active signs. Wassermann reaction -.
Sent back to Bellary.

Date. 2.2.12.

SALVARSAN.

.5 Grammes. Case number. 53

	Before Salvarsan.	After Salvarsan.							
Date.	1.2.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	64	68	94	116	110	100	88	72	66
Respiration.	18	20	28	30	28	22	20	18	18
Temperature.	99.	99.8	101.4	103.6	102.2	99.6	98.4	98.	98.2
Blood-pressure.									
Leucocytosis.									
(a) Polymorphs.									
(b) Lymphocytes.									
(c) Large monos.									
(d) Eosinophiles.									
Red corpuseles.									
Haemoglobin.									
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.									
Vomiting.									
Diarrhoea.									
Opsonic Index	See	table on page 68.							

Name : Pte. J. No. 8832. 2nd Leicester Regt. Case 54.

Admitted : 1st February 1912.

Disease contracted : July 1911.

Previous treatment : 3 courses of Mercury.

Condition on admission : No active signs. Wassermann reaction + + +. Vision normal. Hearing normal.

2.2.12 : Salvarsan .6 grammes intravenously. Reaction moderate. Severe headache and vomiting.

6.2.12. : Feels quite well. Discharged to attend.

26.2.12 : No active signs. Weight 136 lbs. Wassermann reaction —.

7.5.12 : No active signs. Wassermann reaction —.

Sent back to Bellary.

Wassermann	Nil	Slight	Severe	Severe	Severe	Slight	Nil	Nil	Nil
Vision	Nil	Severe	Severe	Nil	Nil	Nil	Nil	Nil	Nil
Hearing	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Cytologic Index	See table on page 68.								

Name : Pte.G. No.7386. Cameron Highlanders. Case 55

Admitted : 9th April 1912.

Disease contracted : In Bangalore in February 1912.

Previous treatment : Nil

Condition on admission : Large hard chancre on prepuce. Inguinal glands enlarged and hard, especially on left side. Throat and tonsils congested. Macular rash on chest, back and limbs. Vision normal. Hearing normal. Weight 118 lbs.

Wassermann reaction + + +.

10.4.12 : Salvarsan .5 grammes intravenously. Reaction severe. Bad headache ten minutes after injection, which lasted for four hours. Very little vomiting. No diarrhoea.

12.4.12 : Rash fading rapidly, almost gone from back. Throat normal. Inguinal glands much smaller. Herpes on lips.

14.4.12 : Rash barely visible. Glands just palpable. Chancre healing rapidly.

18.4.12 : Rash faded. Glands normal. Chancre practically healed.

25.4.12 : No active signs. Discharged hospital to attend.

26.6.12 : No active signs. Wassermann reaction —.

25.8.12 : No active signs. Wassermann reaction —.

18.10.12 : No active signs. Wassermann reaction —.

16.12.12 /

16.12.12 : No active signs. Weight 128 lbs.

Wassermann reaction $-$.

Eight months under observation and no recurrence.

Temp.	98.4, 100
Pulse rate.	76
Respiration.	24
Temperature.	88.2
Blood pressure.	
Leucocytes.	10310
(a) Polymorphs.	45%
(b) Lymphocytes.	27%
(c) Large monon.	6%
(d) Mononuclears.	1%
Red corpuscles.	3400000
Hemoglobin.	78%
Urea, (a) Sp. gr.	
(b) Amount.	
Starche.	NII
Yeasting.	NII
Diarrhoea.	NII
Coagulation.	5.41"
Time.	3.10"

Date. 10.4.12.

SALVARSAN.

.5 Grammes. Case number. 55

	Before Salvarsan.	After Salvarsan.							
Date.	9.4.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	96	130	130	120	90	76	70	64	68
Respiration.	26	38	36	34	26	22	18	20	20
Temperature.	98.8	99.6	101.2	100.4	99.2	98.4	98.	98.	98.2
Blood-pressure.									
Leucocytosis.	10312								
(a) Polymorphs.	66%								
(b) Lymphocytes.	27%								
(c) Large monos.	6%								
(d) Eosinophiles.	1%								
Red corpuseles.	3600000								
Haemoglobin.	72%								
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.	Nil	Severe	Severe	Slight	Nil	Nil	Nil	Nil	Nil
Vomiting.	Nil	Slight	Slight	Nil	Nil	Nil	Nil	Nil	Nil
Diarrhoea.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Coagulation time	3'41" 3'10"		3'33" 3'41"		3'42" 4'	3'29" 3'36"	3'39" 3'56"	3'40" 3'28"	

Name : Pte.H. No.7781. Cameron Highlanders. Case 56.

Admitted : 20th May 1912.

Disease contracted : In Bangalore in April 1910.

Previous treatment : Nil.

Condition on admission : Well marked macular rash over chest, back and limbs. A few pustules on back legs and chest. Lymphatic glands enlarged and shotty, especially in inguinal and cervical regions. Congested fauces. Paraphimosis due to large chancre on prepuce. Circumcised on day of admission. Vision normal. Hearing normal. Wassermann reaction + + +.

22.5.12 : Salvarsan .5 grammes intravenously. Reaction severe. Pulse very rapid and soft. Temperature 104 at the fourth hour. Severe headache, no vomiting.

24.5.12 : Has had diarrhoea during the last twenty-four hours, otherwise feels well.

26.5.12 : Rash all disappeared, except on abdomen on back where it is faintly visible. Herpes on lips.

30.5.12 : No active signs. Wound caused by circumcision healed. Discharged hospital to attend.

27.6.12 : No active signs. Weight 160 lbs.

18.7.12 : No active signs. Wassermann reaction —.

21.10.12 : No active signs. Wassermann reaction —.

15.12.12 : No active signs. Wassermann reaction —.

Seven months under observation and no recurrence.

Name : Pte.M. No.7781. Cameron Highlanders. on Case 57

Admitted : 28th May 1912. Left Bangalore on fer-

Disease contracted : In Bangalore in March 1912.

Previous treatment : Nil. *though. No active signs.*

Condition on admission : Primary sore on glans penis
healed, but scar present. Throat congested.

Inguinal and cervical glands enlarged and shotty.

Macular rash on chest, abdomen, back and limbs.

Weight 153 lbs. Wassermann reaction + + +.

29.5.12 : Salvarsan .5 grammes intravenously. Reac-
tion moderate. Severe headache and slight vomit-
ing.

6.6.12 : Rash disappeared from chest and limbs.

Faintly visible on abdomen. Throat normal.

Glands much smaller.

17.6.12 : Sore reappeared on glans penis. Faint
rash visible on chest.

22.6.12 : Salvarsan .5 grammes intravenously. Reac-
tion mild. Maximum temperature 100.4. Pulse 77.
Severe headache, slight vomiting. Complains of
pains all over body.

24.6.12 : Sore on penis healed without any local
treatment.

28.6.12 : No active signs. Discharged hospital to
attend.

4.7.12 /

Name : Pte.M. No.7432. Cameron Highlanders. Case 58.

Admitted : 28th May 1912.

Disease contracted : In Bangalore in March 1912.

Previous treatment : Nil

Condition on admission : Throat congested and tonsils enlarged. Cervical glands enlarged and shotty.

Macular rash over body and limbs. Hearing normal.

Vision normal. Weight 157 lbs. Wassermann reaction + + +.

29.5.12 : Salvarsan .5 grammes intravenously. Reaction severe. Rigors fifteen minutes after the injection. Severe headache and vomiting.

30.5.12 : Nucleated red blood corpuscles were present in the films at the eighth hour when doing differential counts.

2.6.12 : Throat normal. Rash disappeared. Discharged hospital to attend.

18.6.12 : No active signs. Weight 164 lbs. Wassermann reaction —.

9.8.12 : Patient readmitted with a fresh chancre on glans penis near fraenum. The original sore was on the dorsum of the glans near corona. This sore is probably the results of reinfection, the patient admitting having run the risk. Wassermann reaction + + +.

13.8.12 /

Name : Pte.W. No.8563. Cameron Highlanders. Case 59.

Admitted : 28th May 1912.

Disease contracted : In Bangalore in April 1912.

Previous treatment : Nil.

Condition on admission : Typical hard chancre on prepuce. Macular rash on chest, back and limbs. Throat congested and tonsils enlarged with a mucous patch on the left one. Inguinal and cervical glands enlarged and shotty. Vision normal. Hearing normal. Wassermann reaction +++.

31.5.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Severe rigors during first hour after injection. Slight headache and vomiting.

3.6.12 : Throat normal. Chancre healing. Rash rapidly fading on chest and back. Left inguinal glands still enlarged.

6.6.12 : Sore on penis healed. Rash faded except on chest where it is very faintly visible.

10.6.12 : Glands normal. Rash faintly visible.

12.6.12 : No active signs. Discharged to attend.

18.7.12 : No active signs. Wassermann reaction —.

25.8.12 : No active signs. Wassermann reaction —.

15.12.12 : No active signs. Wassermann reaction —.

Under observation seven months and no recurrence.

Date. 31.5.12 **SALVARSAN.** .5 Grammes. Case number. 59

	Before Salvarsan.	After Salvarsan.							
Date.	30.5.12	1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	100	88	106	110	84	78	76	70	74
Respiration.	24	22	26	24	22	22	22	20	20
Temperature.	98.4	98.4	102.6	102.	98.4	98.4	98.4	98.4	98.4
Blood-pressure.									
Leucocytosis.									
(a) Polymorphs.									
(b) Lymphocytes.									
(c) Large monos.									
(d) Eosinophiles.									
Red corpuseles.									
Haemoglobin.									
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.									
Vomiting.									
Diarrhoea.									
Coagulation time	4'20" 4'11"			4' 1" 4'10"	3'46" 3'54"	4'6" 3'53"	4'10" 4'1"	3'59" 4'14"	

Name : L/c H. No.8650. Cameron Highlanders. Case 60.

Admitted : 20th June 1912.

Disease contracted : In Aldershot in June 1911.

Previous treatment : 2 courses of Mercury

Condition on admission : Tonsils enlarged with ulcer on right one. Vision normal. Hearing normal.

Wassermann reaction + + +.

22.6.12 : Salvarsan .5 grammes. Reaction moderate.

Severe headache and vomiting. Pains over whole body. Face and eyes congested.

24.6.12 : Tonsils less congested. Ulcer looking healthy.

27.6.12 : Tonsils healthy. Ulcer almost healed.

Herpes round mouth, on tip of tongue and palate, and also on upper left eyelid.

30.6.12 : No active signs. Discharged to attend.

18.7.12 : Began first course of Mercury and transferred to Wellington.

3.10.12 : Returned from Wellington. No active signs.

17.10.12 : No active signs. Wassermann reaction -.

14.12.12 : No active signs. Wassermann reaction -.

Six months under observation and no recurrence.

Name : Bomb.J. No.53181."S" Battery R.H.A. Case 61

Admitted : 27th June 1912.

Disease contracted : In Bangalore in March 1912.

Previous treatment : Nil.

Condition on admission : Indurated sore on corona and another behind meatus. Paraphimosis. Glands over body enlarged and shotty, especially in right inguinal region. Throat congested. Papular syphilides on back, chest and knees. Well marked rupia on forehead, face, back, scrotum and inner sides of thighs. Complaining of severe headache, running a temperature between 99.2 and 100.4.

Vision normal. Hearing normal. Weight 130 lbs.

Wassermann reaction + + +.

28.6.12 : Circumcised.

2.7.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache, slight vomiting, slight diarrhoea.

3.7.12 : Morning temperature 99.2, evening normal.

Morning pulse 120, evening 104. Feels fairly well however.

7.7.12 : Rash fading. Sores on penis healing.

Rupial scabs coming off - those on inner sides of thighs have come off, probably due to the rubbing of his legs together when walking. Raw surfaces dusted with boric powder and calomel. Sore on penis practically healed. Circumcision healed and sutures removed.

11.7.12 /

11.7.12 : Rash barely visible. Several rupial scabs have fallen off leaving a healed depressed scar. Those on inner sides of thighs healed. Sores on penis almost gone. Glands much improved. Looks bright and feels well. Weight 132 lbs.

14.7.12 : Looks remarkably well. Rash completely gone. Rupia on forehead, face, chest and scrotum healed, leaving depressed scars. Few left on back of legs, and those on inner sides of thighs are healing. Sores on penis healed, the right inguinal gland now normal in size but still shotty. Weight 134 lbs.

16.7.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight rigors, no headache or vomiting. No diarrhoea. Four hours after temperature 100.2, pulse 112. Eight hours later temperature normal, pulse 80.

18.7.12 : All rupial scabs have separated. Glands all normal.

25.7.12 : No active signs, except the depressed scars where rupial scabs have fallen from. Looks and feels well. Discharged hospital to attend. Weight 136 lbs.

17.9.12 : No active signs. Weight 146 lbs. Wassermann reaction —.

16.11.12 /

16.11.12 : No active signs. Weight 146 lbs.

Wassermann reaction -.

15.12.12 : No active signs. Wassermann reaction -.

Five months under observation and no recurrence.

Weight	108	130	112	125	120	130	85	97	75
Respiration	22	22	24	24	24	22	17	22	24
Temperature	99.6	100.0	101.0	101.5	102.0	99.3	98.4	98.4	98.4
Blood pressure									
Leucocytes									
(a) Polymorphs									
(b) Lymphocytes									
(c) Large monos									
(d) Eosinophils									
Red corpuscles									
Hæmoglobin									
Urine. (a) Sp. gr.									
(b) Albumin									
Resinche	Slight	Slight	Slight	Slight	Slight	Slight	Nil	Nil	Nil
Scumming	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Hardness	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Coagulation time	3'48"					3'48"	3'48"	3'48"	3'48"

Date. 16.7.12

SALVARSAN.

.5 Grammes. Case number. 62

Date.	Before Salvarsan.	After Salvarsan.							
		1 hour.	2 hours.	4 hours.	8 hours.	24 hours.	48 hours.	72 hours.	96 hours.
Pulse rate.	80	76	88	108	108	62	68	72	70
Respiration.	22	20	24	24	24	20	20	18	20
Temperature.	98.	99.	99.2	101.8	101.	97.6	98.4	98.4	98.4
Blood-pressure.									
Leucocytosis.									
(a) Polymorphs.									
(b) Lymphocytes.									
(c) Large monos.									
(d) Eosinophiles.									
Red corpuseles.									
Haemoglobin.									
Urine. (a) Sp. gr.									
(b) Albumin.									
Headache.									
Vomiting.									
Diarrhoea.									
Coagulation time	4'18" 4'3"			4'14" 4'1"	3'58" 3'56"	4'5" 3'49"	3'50" 4'12"	3'57" 3'40"	

Name : Pte.S. No.7921. Cameron Highlanders. Case 63.

Admitted : 20th July 1912.

Disease contracted : In Bangalore in June 1912.

Previous treatment : Nil

Condition on admission : Large indurated chancre in front of base of glans penis. Macular rash on chest, back and limbs. Congestion of fauces. Inguinal glands enlarged and shotty, especially on left side. Temperature 99.4. Vision normal. Hearing normal. Wassermann reaction + + +

26.7.12 : Salvarsan .5 grammes intravenously. Reaction severe. Two hours after injection temperature was 103.8 and pulse 120. Suffered from severe rigors with severe headache but no vomiting. Felt quite well by evening.

29.7.12 : Feels quite well. Herpes round sides of nose. Throat normal. Rash fading rapidly. Chancre healing and inguinal glands improving.

2.8.12 : No active signs. Discharged hospital to attend.

10.8.12 : Salvarsan .5 grammes intravenously. Reaction mild.

12.8.12 : Feels quite well. Discharged hospital to attend.

17.9.12 : No active signs. Wassermann reaction —,

12.11.12 : No active signs. Wassermann reaction —,

14.12.12 : No active signs. Wassermann reaction —,

Name : Pte.M. No.7856. Cameron Highlanders. Case 64

Admitted : 25th July 1912.

Disease contracted : In China in March 1910.

Previous treatment : 4 courses of Mercury

Condition on admission : No active signs, but strongly positive Wassermann reaction. Vision normal.

Hearing normal.

26.7.12 : Reaction mild. Slight headache, vomiting and diarrhoea.

27.7.12 : Feels well, except for slight dulness about the front of the head.

28.7.12 : No active signs. Discharged hospital to attend.

21.8.12 : No active signs. Wassermann reaction —.

18.10.12 : No active signs. Wassermann reaction —.

12.12.12 : No active signs. Wassermann reaction —.

Name : Pte.C. No.7123. Cameron Highlanders. Case 65.

Admitted : 28th July 1912.

Disease contracted : In Bangalore in July 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : No active signs, but positive Wassermann reaction. Hearing normal. Vision normal.

30.7.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting or diarrhoea.

1.8.12 : Patient feels quite well. Discharged hospital to attend.

18.10.12 : No active signs. Wassermann reaction —.

15.11.12 : No active signs. Wassermann reaction —.

17.12.12 : No active signs. Wassermann reaction —.

Under observation five months and no recurrence.

Name : Pte.F. No.8289. Cameron Highlanders. Case 66.

Admitted : 29th July 1912.

Disease contracted : In Aldershot in May 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : No active signs, but positive Wassermann reaction.

30.7.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting, no diarrhoea.

1.8.12 : Discharged hospital to attend.

18.10.12 : No active signs. Wassermann reaction—.

29.11.12 : No active signs. Wassermann reaction—.

Four months under observation and no recurrence.

Name : Pte.R. No.7424. Cameron Highlanders. Case 67.

Admitted : 29th July 1912.

Disease contracted : In Bangalore in June 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : No active signs, but positive Wassermann reaction.

30.7.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting. Severe pains in small of back and lower extremities.

1.8.12 : No active signs. Discharged hospital to attend.

15.9.12 : No active signs. Wassermann reaction—.

30.11.12 : No active signs. Wassermann reaction—.

Under observation four months and no recurrence.

Name : Pte.C. No.8594. Cameron Highlanders. Case 68.

Admitted : 7th September 1912.

Disease contracted : In Bangalore in August 1912.

Previous treatment : Nil.

Condition on admission : Large hard sore on fraenum.

Inguinal glands enlarged. A faint macular rash on chest, abdomen, back and limbs. Vision normal.

Hearing normal. Wassermann reaction.+++.

10.9.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight rigor and headache one hour after the injection. No vomiting or diarrhoea.

Herxheimer's reaction well marked - the very faint rash before the injection became very well marked two to four hours later and continued so all day.

11.9.12 : Feels quite well. Rash still well marked.

12.9.12 : Chancre healing. Rash beginning to fade.

16.9.12 : Chancre almost healed. Rash almost gone, only a faint mottling about loins. Left inguinal glands still hard but much smaller.

19.9.12 : Chancre healed. Rash disappeared. Discharged hospital to attend.

25.9.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 100, pulse 98.

Slight headache, no vomiting.

26.9.12 : No active signs. Discharged hospital to attend.

25.11.12 No active signs. Wassermann reaction—.

Name : Piper D. No.8479. Cameron Highlanders. Case 69.

Admitted : 7th September 1912.

Disease contracted : In Bangalore in July 1912.

Previous treatment : Nil.

Condition on admission : Large hard chancre on glans penis near meatus. Inguinal glands enlarged and hard. Macular rash on chest, back and limbs. Vision normal. Hearing normal. Wassermann reaction + + +

10.9.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting. Slight diarrhoea with colicky pains in abdomen. Herxheimers reaction well marked four hours after the injection.

12.9.12 : Rash fading. Sore looking healthier.

19.9.12 : Sore healed. Rash disappeared. Glands normal. Discharged hospital to attend.

25.9.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 100.4, pulse 102. No vomiting, no diarrhoea. Slight headache.

27.9.12 : Discharged hospital to attend.

18.10.12 : No active signs. Wassermann reaction —.

12.12.12 : No active signs. Wassermann reaction —.

Name : Pte.G. No.8301. Cameron Highlanders. Case 70.

Admitted : 5th September 1912.

Disease contracted : In Bangalore in August 1912.

Previous treatment : Nil.

Condition on admission : Hard sore on prepuce. Inguinal glands enlarged. Faint rash on chest, back and limbs. Vision normal. Hearing normal.

Wassermann reaction + + +.

10.9.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight rigors and headache. No vomiting, no diarrhoea.

12.9.12 : Chancre beginning to heal. Glands subsiding.

17.9.12 : Rash almost gone. Glands normal. Chancre practically healed.

21.9.12 : No active signs. Discharged hospital to attend.

21.10.12 : No active signs. Wassermann reaction—.

29.11.12 : No active signs. Wassermann reaction—.

Name : Pte.G. No.8111. Cameron Highlanders. Case 71.

Admitted : 10th September 1912.

Disease contracted : In Bangalore in July 1912.

Previous treatment : Nil.

Condition on admission : A hard indurated sore on right side of fraenum. Inguinal glands shotty. Faint rash on chest, back and limbs. Fauces congested. Tonsils enlarged with mucous patch on right one. Vision normal. Hearing normal. Wassermann reaction + + +.

13.9.12 : Salvarsan .5 grammes intravenously. Reaction severe. Rigors half an hour after injection. Pulse rapid and feeble. Patient fainted three hours after injection. Given Brandy and strophanthus, then hot water bottles applied to feet.

14.9.12 : Patient feels quite well again.

16.9.12 : Congestion of fauces disappeared. Tonsils subsiding. Rash almost gone. Chancre healing rapidly.

19.9.12 : Rash completely disappeared. Chancre healed. Throat normal. Discharged hospital to attend.

15.10.12 : No active signs. Wassermann reaction —.

12.12.12 : No active signs. Wassermann reaction —.

Name : Sapper N. 2nd "Q.V.O" S. & Miners. Case 72.

Admitted : 7th August 1912.

Disease contracted : In Bangalore in July 1912.

Previous treatment : Nil.

Condition on admission : Typical hard chancre on prepuce giving rise to marked phimosis. Inguinal glands enlarged and shotty. Treponema Pallidum demonstrated in serum from the chancre. No other signs of disease. Vision normal. Hearing normal.

14.8.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache with cramps in abdomen but no diarrhoea. No vomiting.

15.8.12 : Feels quite well. Myelocytes found in blood film at eighth hour when doing differential blood count.

17.8.12 : Chancre healing. No Treponema Pallidum found in serum from chancre on prolonged search though abundant when previously looked for.

22.8.12 : Chancre almost healed. Patient has brightened up considerably.

25.8.12 : No active signs. Phimosis has become reducible. Discharged hospital to attend.

29.9.12 : No active signs. Wassermann reaction —.

16.12.12 : No active signs. Wassermann reaction —.

Under observation four months and no recurrence.

Name : Gunner J. No.44988. 8th Battery R F.A. Case 73.

Admitted : August 10th 1912.

Disease contracted : In Kirkee in June 1910.

Previous treatment : 4 courses of Mercury.

Condition on admission : No active signs, but positive Wassermann reaction.

13.8.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting.

16.8.12 : No active signs. Discharged hospital to attend.

7.9.12 : No active signs. Wassermann reaction -.

18.10.12 : No active signs. Wassermann reaction -.

29.11.12 : No active signs. Wassermann reaction -.

Med. requests 400000

Temperature 68°

Time (9.30.12)

(4) Admin.

Headache Nil Nil Severe Severe Slight Nil Nil

Vomiting Nil Nil Nil Nil Nil Nil Nil

Diarrhoea Nil Nil Nil Nil Nil Nil Nil

Name : Pte.H. No.7731. Cameron Highlanders. Case 74.

Admitted : 7th October 1912.

Disease contracted : In Bangalore in September 1912.

Previous treatment : Nil.

Condition on admission : Two small hard sores in front of base of glans penis in the serum of which the Treponema Pallidum was demonstrated. Left inguinal glands enlarged and hard. Macular rash on chest, back, abdomen and limbs. Vision normal. Hearing normal. Wassermann reaction + + +.

8.10.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Severe headache, slight vomiting. Pains in loins. Felt giddy four hours after injection.

9.10.12 : Feels well except for pain in loins.

12.10.12 : Rash fading rapidly. Sores healing.

Treponema Pallidum searched for in serum from sores but not found.

18.10.12 : Rash faded, sores healed, glands normal.

Discharged hospital to attend.

16.12.12 : No active signs. Wassermann reaction —.

Name : Pte.M. No.6435. 7th "Q.O"Hussars. Case 75.

Admitted : 25th August 1912.

Disease contracted : In Bangalore in July 1912.

Previous treatment : Patient was not seen by me until September 6th 1912. He had been diagnosed on admission as suffering from soft chancre, which was treated by dusting with iodiform and applying black wash dressings.

Condition on 6.9.12 when seen by me : Patient had a small hard sore on end of prepuce, in the serum of which Treponema Pallidum was demonstrated. Vision normal. Hearing normal. Wassermann reaction +.

8.9.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache, markedly congested face, severe pain in lower limbs. Complained of neuralgic pains in the teeth of the lower jaw which were in very good condition.

10.9.12 : Sore healing rapidly. Treponema Pallidum searched for but not found.

14.9.12 : No active signs. Discharged hospital to attend.

16.11.12 : No active signs. Wassermann reaction -.

10.12.12 : No active signs. Wassermann reaction -.

Under observation three months and no recurrence.

Name : Sapper K. No.6464. 2nd "Q.V.O" S.& Miners. Case 77

Admitted : 9th August 1912.

Disease contracted : In, Bangalore in July 1912.

Previous treatment : Nil.

Condition on admission : Large hard chancre on glans penis in the serum of which Treponema Pallidum was abundant. Inguinal glands enlarged and shotty. Throat congested.

12.8.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache with vomiting and diarrhoea. Pains in lower limbs and back.

13.8.12 : Slight headache, otherwise patient feels quite well.

15.8.12 : Throat normal. Chancre healing. Glands still enlarged.

26.8.12 : Chancre almost healed. Glands still palpable.

30.8.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting, no diarrhoea.

6.9.12 : No active signs. Discharged hospital to attend.

27.10.12 : No active signs. Wassermann reaction —.

15.11.12 : No active signs. Wassermann reaction —.

14.12.12 : No active signs. Wassermann reaction —.

Four months under observation and no recurrence.

Name : Pte.C. No.8524. Cameron Highlanders. Case 78.

Admitted : 14th October 1912.

Disease contracted : In Madras in September 1912.

Previous treatment : Nil.

Condition on admission : Hard indurated sore on glans penis in the serum of which the Treponema Pallidum was demonstrated. No other signs of disease.

16.10.12 : Salvarsan .5 grammes intravenously. Reaction mild. Slight headache, no vomiting, no diarrhoea.

19.10.12 : Chancre healing. Prolonged searched failed to reveal Treponema Pallidum in serum from chancre.

23.10.12 : Chancre healed. Discharged hospital to attend.

28.11.12 : No active signs. Wassermann reaction —.

16.12.12 : No active signs. Wassermann reaction —.

Name : Pte.C. No.8131. Cameron Highlanders. Case 79.

Admitted : 23rd October 1912.

Disease contracted : In Bangalore in September 1912.

Previous treatment : Nil.

Condition on admission : Hard sore on prepuce in the serum of which the Treponema Pallidum was found. Inguinal glands enlarged. Throat slightly congested.

25.10.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache and vomiting. Colicky pains in abdomen, but no diarrhoea.

28.10.12 : Throat normal. Chancre healing. Failed to find the Treponema Pallidum on prolonged search in serum from chancre.

8.11.12 : Chancre healed. Glands normal. Discharged hospital to attend.

12.11.12 : No active signs. Wassermann reaction +.

15.11.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 100, pulse 96. Slight headache, no vomiting, no diarrhoea.

17.11.12 : Discharged hospital to attend.

29.11.12 : No active signs. Wassermann reaction —.

Name : Pte.R. No.8888. Cameron Highlanders. Case 80.

Admitted : 24th October 1912.

Disease contracted : In Bangalore in beginning of October 1912.

Previous treatment : Nil.

Condition on admission : Two typical hard sores, one near fraenum and one in front of glans near corona. The Treponema Pallidum demonstrated in expressed serum. Inguinal glands enlarged. Throat slightly congested. Wassermann reaction negative.

30.10.12 : Salvarsan .5 grammes intravenously. Reaction moderately severe. Rigors one hour after injection. Severe headache. Slight vomiting. Pains in back and lower limbs.

1.11.12 : Throat normal. Chancres healing, herpes on lips.

8.11.12 : Chancres healed. No active signs. Discharged hospital to attend.

12.11.12 : Throat congested. Potassium chlorate gargle given.

14.11.12 : Small ulcer on right tonsil.

15.11.12 : Salvarsan .5 grammes intravenously. Reaction mild. Maximum temperature 99. Pulse 82. Slight headache, no vomiting.

24.11.12 : No active signs. Discharged hospital

16.12.12 : No active signs. Wassermann reaction —

Name : Pte.M. No.4435. 7th Q.O. Hussars. Case 81.

Admitted : 10th September 1912.

Disease contracted : In Hounslow in July 1910.

Previous treatment : 3 courses of Mercury.

Condition on admission : No active signs. Wassermann reaction +++.

13.9.12 : Salvarsan .5 grammes intravenously. Reaction very slight. Slight headache. No vomiting. No diarrhoea.

16.9.12 : No active signs. Discharged hospital to attend.

23.10.12 : No active signs. Wassermann reaction -.

27.10.12 : No active signs. Wassermann reaction -.

Name : Pte.F. No.8753. Cameron Highlanders. Case 83.

Admitted : 13th November 1912.

Disease contracted : In Bangalore in October 1912.

Previous treatment : Nil

Condition on admission : Hard chancre on prepuce in the serum of which Treponema Pallidum was demonstrated.

15.11.12 : Salvarsan .5 grammes intravenously. Reaction severe. Severe headache and vomiting, with pains in the back. Face very congested. Pulse irregular, (see tracings)

16.11.12 : Feels quite well.

18.11.12 : Chancre healing. Failed to demonstrate Treponema Pallidum in serum on prolonged search.

24.11.12 : No active signs. Discharged hospital to attend.

14.12.12 : No active signs. Wassermann reaction.—.

Name : Pte.B. No.8475. Cameron Highlanders. Case 85.

Readmitted : 10th August 1912.

Disease : Lupus vulgaris. Began in December 1911

with an apple jelly nodule on left side of nose near tip. This broke down forming an ulcer with a rough base, resistant of all treatment. No history of Syphilis nor any visible signs of it. The Wassermann reaction on several occasions negative. Von Pirquet cutaneous tuberculin reaction positive. Ulcer spreading in spite of everything, involving both sides and tip of nose, and in February he was sent to Secunderabad for X-Ray treatment. Returned in July to Bangalore with two small ulcers, one each side of bridge of nose half way up. On his Medical History sheet it was noted that the condition had much improved as the result of X-Ray treatment which he had undergone for four months with the necessary intervals. These ulcers rapidly increased in size, and he was readmitted into hospital on August 10th. The ulcers continued to spread, approaching dangerously near the inner canthia of both eyes and threatening to involve both of them. The eyes were much congested, the conjunctivae puffy and the lids much swollen. As all treatment had no effect in arresting the disease and there was considerable danger /

danger of the patient losing his eyesight it was suggested to him that it might be advisable to try the effect of an injection of Salvarsan on the disease. He readily consented to this proposition and on October 12th 1912 he was given .5 grammes Salvarsan intravenously. Reaction was moderately severe. Suffered from severe headache, no vomiting. Severe colicky pains in abdomen with slight diarrhoea. Felt faint for several hours after injection.

13.10.12 : Reaction passed off and patient feels well. Condition of eyes unchanged, but the disease has not progressed.

15.10.12 : There is a wonderful improvement in condition of patient's eyes. The lids are less puffy the conjunctivae less swollen and the congestion has subsided very considerably. The ulcers on nose are looking much more healthy. Hydrogen Peroxide sprayed on surface of ulcers.

17.10.12 : Congestion of eyes quite gone. Lids normal and ulcers beginning to heal rapidly. The margins are bluish and healthy and the bases covered with fresh healthy granulations. Patient is feeling better than he has done for many months.

18.10.12 /

18.10.12 : Wassermann reaction repeated with a negative result. This was done in order to again make sure, if possible, that there was no Syphilitic taint as it had been stated that an injection of Salvarsan might stimulate a negative reaction to become a positive one.

24.10.12 : Ulcers healing rapidly. Eyes normal.

25.10.12 : Salvarsan .5 grammes intravenously. Reaction moderate. Maximum pulse 98, temperature 102. Severe headache. Slight vomiting. Abdominal pains but no diarrhoea.

26.10.12 : Patient feels quite well.

31.10.12 : Ulcers completely healed. Patient discharged hospital.

15.11.12 : Nose looking very well. The ulcers are completely covered with a new thin epithelium, but there are no signs of any breaks in it.

15.12.12 : Nose quite healthy, but a little red. Patient's weight is now 120 lbs., having put on 12 lbs. in the last two months.

This case may possibly have been a case of "Syphilitic Lupus" as described by Hutchinson, but I am not inclined to think that it was. The appearances were typically those of severe Lupus Vulgaris, and I am supported in this opinion by several other Medical Officers who saw the patient. Further support is given /

given by the fact that on all occasions on which a Wassermann reaction was performed a negative result was obtained. Again a positive Von Pirquet favours the diagnosis of Lupus Vulgaris. I have not found any records of Lupus being treated in this way, but the success attending its use in this case would seem to justify it being used for this purpose.

	129	112	104	105	110	116	120		
Temperature	97.6	99	101.4	100.3	100	99.9	99.6	98.4	98.4
Wassermann	129	112	104	105	110	116	120		
Leucocytes	7500	8700	13800	14600	10800	8500	7000	3100	7500
(a) Polymorphs	74%	78%	64%	52%	63%	61%	70%	71%	70%
(b) Lymphocytes	20%	18%	13%	38%	18%	18%	20%	28%	21%
(c) Large monon.	6%	4%	3%	2%	4%	3%	4%	3%	4%
(d) Eosinophiles	1%	0%	0%	0%	1%	0%	1%	2%	2%
Haemoglobin	70%								
Haematocrit	22%								
Time of up & down	10:30					10:30	10:30	10:30	10:30
in clinic	Nil					Nil	Nil	Nil	Nil
Headache	Nil	Slight	Severe	Severe	Severe	Nil	Nil	Nil	Nil
Fatigue	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Diarrhoea	Nil	Nil	Slight	Slight	Nil	Nil	Nil	Nil	Nil

Name : Sapper Doraswamy. 2nd Q.V.O. S.& Miners. Case 86

Patient was admitted to hospital in August 1912, suffering from Malignant Malaria with enlarged spleen which extended three inches below the left costal margin. Large numbers of Malignant Tertian Malarial parasites were found in his peripheral blood. He was placed on Quinine Bisulph grains 10 three times a day. He ceased to run a temperature but the Malarial parasites continued to be present in his blood. When giving Salvarsan to a Syphilitic on October 14th 1912, I administered .5 grammes intravenously to this patient. On examining his blood on October 20th, I was not able to find any Malarial Parasites though searched for for over an hour. Quinine by the mouth had been continued during this time, but I am inclined to think that the disappearance of the Parasites is undoubtedly due to the action of the Salvarsan. He was discharged from hospital on October 30th and though his blood was again examined on two occasions no parasites could be found.

No. 3.

March, 1913.

Vol. XX.

Journal

OF THE

Royal Army Medical Corps

EDITED BY

COLONEL W. H. HORROCKS,

ROYAL ARMY MEDICAL CORPS

ASSISTED BY

MAJOR C. E. POLLOCK,

ROYAL ARMY MEDICAL CORPS

ISSUED MONTHLY



Printed and Published by

JOHN BALE, SONS & DANIELSSON, LTD.

OXFORD HOUSE,

88-91, GREAT TITCHFIELD STREET, OXFORD STREET, W.

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ENTERIC FEVER.

Professor C. A. EWALD, reporting from the Kaiserin Augusta Hospital, Berlin, says:—"Sanatogen, on account of its being very easily absorbed and of a perfectly non-irritating character, may be used with great advantage for the purpose of increasing the nutritive value of a given diet, in all cases of physical weakness, especially in those maladies which are accompanied by high rise of temperature, and particularly in Enteric Fever."

TYPHOID.

Sanatogen was used during the Lincoln Typhoid outbreak, and "The condition (of the patients) improved rapidly."—*The Lancet*, 1st July, 1905.

MALARIA.

Cape Town Physician writes:—"The experience I have had of Sanatogen has been extremely satisfactory, notably in cases of severe Malarial Cachexia from the East Coast, in which it acted wonderfully."

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times both in this country (Sierra Leone) and in India. Beyond a little temporary local pain and stiffness sometimes following an injection, I have not seen any unfavourable local or general results occur from it.

I cannot agree with his statement that "subcutaneous and intramuscular injections in solutions of the usual strength (1—2 to 1—8) are inferior to quinine by the mouth in 'rapidity of action and thoroughness of absorption.'" I have repeatedly seen cases of malignant tertian infection which have resisted quinine given by the mouth, no vomiting being present, and have yielded to the same dosage by injection. I have known cases which have had more than one attack of malaria ask to have injections administered in preference to mouth treatment, as they had received better and quicker results from it in former attacks. Further, the class of case which has early vomiting, and it is fairly often seen, is certainly in my experience more advantageously treated by injections. With regard to the results recorded above, it will be seen that marked differences exist between the monkey and the guinea-pig. The monkey more nearly resembles man in the amount of the dose which is fatal. Taking the acknowledged fatal dose for an adult as about 4 dr., and also taking the minimum lethal dose of a 1—8 or 1—5 dilution to be about 0·25 gm. per kilo of monkey, it will be noticed that the doses closely approximate. A 10-stone man receiving quinine in the proportion of 0·25 gm. per kilo will get about 4·08 dr., whereas if he were given the minimum lethal dose for a guinea-pig (1—8 dilution) he would get over 9·8 dr. I think it may be accepted, therefore, that the monkey more closely resembles man in his reaction to quinine than the guinea-pig does.

In conclusion, it will be seen from the above tables that the mode of administration giving the quickest action and the best absorption of quinine in monkeys is as follows, commencing with the most efficacious:—

- (1) Injections of 1—8 dilution.
- (2) " 1—5 "
- (3) " 1—3 "
- (4) " 1—2 "
- (5) Oral administration with or without fasting.

The actual minimum lethal dose for the oral administration methods and that for the low dilutions by injections, have not been established, because, as stated at the beginning of these notes, the object of these experiments was to throw further light on the much debated question as to which method gives the quickest and most thorough result, oral administration or injection.

SOME OBSERVATIONS ON THE BACTERIOLOGY
OF INCINERATOR SMOKE AND ASH.¹BY CAPTAIN J. J. H. NELSON.
Indian Medical Service.

THE steady development of incineration in Indian cantonments as an economical and efficient method of night-soil disposal has, as might be expected, aroused a certain amount of opposition. Some of the objections raised have an undoubted justification, while others are mainly loose statements based on uncertain facts, and directed to arouse hostility on the plea that incineration, as carried out, transgresses the principles which animate scientific preventive medicine. Among these statements is one which has gained much credence and which, if true, would go very far to weaken the case in favour of incineration. This statement is to the effect that incineration is so imperfectly carried out that the smoke and ash from the incinerators contain faecal micro-organisms, and that consequently the procedure is an unsafe method of night-soil disposal. To test the accuracy of this allegation, I have carried out certain experimental observations; their publication seems to me desirable. The experiments were made in Bangalore, using an incinerator of simple construction, which may be best described as a modified "Sialkot." It was made with mud walls and roof, surmounted by a short chimney, and provided with two layers of grate bars. This incinerator represented quite a crude type and far more primitive than most of those with which incineration is usually carried out. The results which I have obtained with so primitive a design should go far to allay fears which have been aroused as to the survival of faecal and pathogenic micro-organisms in materials and products subjected to and derived from ordinary incinerators.

(I) *Experiments with Petri Dishes containing Conradi-Drigalski Medium.*—For the purpose of obtaining good results the following plan was decided upon. Petri dishes $4\frac{1}{2}$ in. in diameter, containing Drigalski-Conradi medium were exposed for varying intervals at different distances from the incinerator. The plates were exposed by removing their lids and allowing the smoke to blow on to the surface of the medium. At the same time control plates were exposed, well away from the incinerator, in the station hospital

¹ Received for publication October 14, 1912.

compound for the same length of time as the plate exposed in the incinerator smoke. In this way one was enabled to judge to what greater extent *Bacillus coli* was present in the vicinity of the incinerator than in the open fields. I have tabulated the results as follows:—

No. of experiment	Date	Distance from incinerator	Duration of exposure	Control plate. Number of colonies of <i>B. coli</i> present	Incinerator plate. Number of colonies of <i>B. coli</i> present	Comments
1	20.8.10	3 yards	5 minutes	2	1	August 20, 1910.—Dry day. Moderate breeze from the N.E. Fair amount of dust flying. Control plates were about 400 yards from incinerator.
2	20.8.10	3 "	10 "	1	3	
3	20.8.10	3 "	15 "	4	4	
4	20.8.10	10 "	5 "	1	1	August 21, 1910.—Dry day. Less dust flying. Slight breeze. Control plates as before.
5	20.8.10	10 "	10 "	1	2	
6	20.8.10	10 "	15 "	3	2	
7	21.8.10	20 "	5 "	0	2	
8	21.8.10	20 "	10 "	3	1	
9	21.8.10	20 "	15 "	3	4	
				Total, 18	Total, 20	

From this table it will be seen that three plates 3 yd. from the incinerator contained a total of 8 colonies of *B. coli* as against 7 colonies on the three control plates exposed in the open. This gives only an excess of 1 colony, and considering the large amount of litter, &c., near the incinerator plates the excess is very little. At 10 yd. distance from the incinerator the three plates contained a total of 5 colonies as against 5 on the controls—no excess. At 20 yd. the incinerator plates contained a total of 7 colonies as against 6 in the controls—an excess of 1. On the whole series of experiments the incinerator plates contained a total of 20 colonies of *B. coli* as against 18 on the controls—only a difference of 2 colonies. The following reactions show that the *B. coli* of Escherich was present:—

Lactose	Saccharose	Dulcitol	Adonitol	Inulin	Proskauer	Motility	Gram	Litmus milk
+	-	+	-	+	-	+	-	+

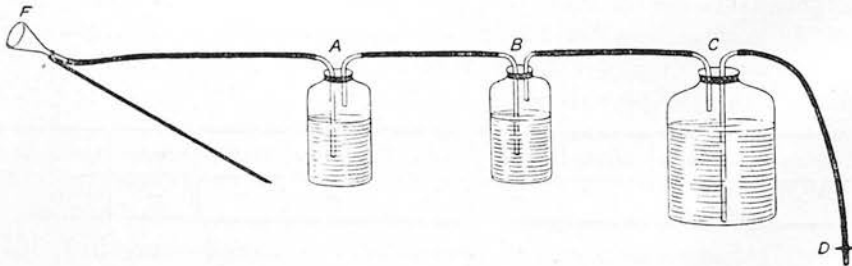
(II) *The second series of experiments* was carried out as in I, but was much more interesting. The *B. coli communis* is so commonly present in dust, &c., that I determined to attempt the isolation of *B. typhosus* from the incinerator smoke. For this purpose I noted four typhoid patients from whose stools I had isolated *B. typhosus*

on August 22, four days previously. On August 26 the stools from the same patients were brought to the incinerator in closed receptacles, no disinfectant having been added. Four specimens were taken from these stools and *B. typhosus* was found on examination to be still present. There was, therefore, no doubt that *B. typhosus* was present when these four stools were placed in the incinerator. The following is a tabular statement of results:—

No. of experiment	Date	Distance from incinerator	Time elapsed since placing stool on fire	Duration of exposure of plate	Number of <i>B. typhosus</i> colonies isolated	Comments
1	26.8.10	5 yards	5 minutes	5 minutes	Nil	August 26, 1910.— Dry day. Slight wind from S.W.
2	26.8.10	5 "	10 "	10 "	"	
3	26.8.10	10 "	15 "	15 "	"	
4	26 8.10	10 "	20 "	15 "	"	
5	26.8.10	20 "	25 "	20 "	"	

Control plates were set up as before, but, as was to be expected, no *B. typhosus* colonies grew on any of them.

(III) *Experiments to isolate B. coli communis from Smoke by Washing the Smoke in Sterile Tap-water.*—My next series of experiments was directed towards an attempt to isolate the *B. coli communis* from incinerator smoke by aspirating the smoke through bottles containing sterile tap-water and thus washing it. The diagram below will render the description easy to follow. A glass funnel F was attached to bottle A by 6 ft. of rubber tubing. Bottle A was similarly attached to bottle B and B to C. Bottles A, B, and C each contained sterile tap-water, the capacity of A and B being 2 litres and of C 4 litres. Bottle C was for syphoning purposes.



The whole apparatus was sterilized and carefully carried to the incinerator. A piece of iron was attached to the glass funnel as a handle and the funnel passed inside the incinerator door. I was afraid the heat might melt the rubber tubing, but it did not do so.

A clip at D was then opened and 4 litres of water in bottle C were syphoned out. This took seven minutes to complete. As a vacuum was created in bottle C suction was exerted on B and then on A. Smoke was thus drawn through the funnel F into bottle A. It then passed through the sterile tap water in A to B and thence through the sterile water in B to C, being twice washed in transit. Smoke could be seen in the bottles, so there was no doubt as to its passage through them. Of course, it does not follow that 4 litres of smoke passed through each bottle A and B. The amount passing is not of great importance so far as the object of the experiment is concerned, which was to trap *B. coli* in the water in bottles A and B. When syphonage was completed bottles A and B were at once taken to the Brigade Laboratory and samples of water examined for *B. coli*. The results were as follows:—

	Date	Total colonies in 1 c.c. on agar	Lactose fractors	<i>B. coli</i> of Escherich	Comments
Bottle A ..	27.8.10	5	Present in 20 c.c.	Present ..	None of the 5 colonies on agar were <i>B. coli</i> .
Bottle B ..	27.8.10	0	Not present in 40 c.c.	None found..	

From this table it is seen: (1) That by washing smoke as many as five colonies per cubic centimetre were added to sterile tap-water in bottle A, but none reached bottle B.

(2) Lactose fractors were present in 20 c.c. of bottle A water, but none in up to 40 c.c. of bottle B water.

(3) These lactose fractors were found on further examination to belong to the *B. coli* group.

(IV) *An attempt to isolate B. typhosus*, using the apparatus as in Experiment III. Stools from which the *B. typhosus* had been isolated were put into the incinerator and five minutes after placing them there smoke was aspirated as before through bottles A and B. The results were as follows:—

	Date	Total colonies in 1 c.c. on agar	Lactose fractors	<i>B. typhosus</i>	Comments
Bottle A ..	29.8.10	4	Present in 30 c.c.	Not found ..	None of the 4 colonies on agar were <i>B. typhosus</i> .
Bottle B ..	29.8.10	0	Not present in 40 c.c.	Not found ..	

(V) *Examination of Fresh Ash from Incinerators.*—The last series of experiments was carried out with fresh ash from under the incinerator bars. The following plan was adopted. On August 27 five tubes of MacConkey's neutral red bile salt lactose broth were taken to the incinerator and each one inoculated with a loopful of fresh ash by thrusting a sterile platinum loop into the undisturbed ash. No change occurred in any of the tubes. Subcultures on agar and Drigalski-Conradi media gave no growth.

On August 30 this experiment was repeated. In order to ensure the adhesion of ash to my platinum loop I first sterilized it, then wet it by thrusting it into sterile tap-water and then put it into undisturbed ash. Each tube was inoculated in turn in this way, but all five remained sterile. This pointed to the fact that so high a temperature had been attained during incineration that all organisms were killed.

This ended my series of observations, and as a result of them I made the following conclusions :—

(1) That smoke from an incinerator is not a source of danger to persons in its vicinity.

(2) That a properly managed incinerator is a sure and safe method of rapidly disposing of night-soil.

(3) That the ash from an incinerator is not a source of danger if blown about, but merely a nuisance.

(4) That incineration is well suited for disposing of infected stools and deleterious matter and when properly supervised can destroy all night-soil and refuse with a minimum of labour and maximum of safety.



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CONTENTS.

ORIGINAL COMMUNICATIONS.	PAGE
Archibald Arnott, Surgeon, 20th Foot. By Major E. B. STEEL, R.A.M.C.	239
The Physique of the Indian Army: An Appreciation. By Colonel R. H. FIRTH	242
Travelling Kitchens. By Captain N. DUNBAR WALKER, R.A.M.C.	248
On the Results of Cultures made with Material obtained from the Joints in Twenty-eight Cases of Rheumatic Fever. By Major W. S. HARRISON, R.A.M.C.	275
Notes of Some Experiments made to determine the Rate of Absorbability and Intensity of Action of Quinine given Hypodermically and by the Mouth, as shown by the Minimum-Lethal-Dose Method. By Major A. L. A. WEBB, R.A.M.C.	280
Some Observations on the Bacteriology of Incinerator Smoke and Ash. By Captain J. J. H. NELSON, I.M.S.	286
CLINICAL AND OTHER NOTES.	
Leprosy and the Bed-Bug. By Captain D. S. SKELTON, R.A.M.C., and J. G. PARHAM, Government Bacteriologist, Zanzibar	291
Poisoning by Prussic Acid. By Major E. A. BOURKE, R.A.M.C.	293
Observations on the Value of Certain Chemicals for the Sterilization of Water, made under the supervision of Captain W. R. Gallwey in the 9th (Secunderabad) Division Laboratory. By Private F. C. BOULTON, Sherwood Foresters	294
A Case of Infective Granuloma necessitating Cæsarean Section. By Captain A. G. WELLS, R.A.M.C.	298
Note on the "Carrier" in Paratyphoid Fever. By Captain J. L. WOOD, R.A.M.C.	299
REPORTS.	
Extract from the Report, by Lieutenant-Colonel M. T. YARR, R.A.M.C., Medical Inspector of Recruits, Scottish Command, for the Year 1911	300
Sanitary Report of Manœuvres, Burma Division, 1912. By Major B. TILBURY BROWN, R.A.M.C.	311
ECHOES FROM THE PAST.	
The "Death March" through the Khyber Pass in the Afghan Campaign, 1878-79. By Surgeon-Major G. J. H. EVATT, M.D.	333
REVIEWS	365
CURRENT LITERATURE	369