THE TREATMENT OF SYPHILIS WITH SALVARSAN.

A Thesis for the Degree of M.D.

by

VICTOR F. USHER,

M.B., Ch.B., F.R.C.S., Edin.

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Most of the material for this thesis was collected while I was house surgeon at the Seamen's Hospital, Greenwich; and all the cases described were treated by myself and were under my own personal observation.

I am greatly indebted to Mr. McGavin (London) for giving me entire charge of all cases in the venereal wards of the Seamen's Hospital and to Mr. Davies, pathologist (London), for his valuable assistance with the Wassermann test performed upon most of the cases. Also to Mr. Dowden (Edinburgh) for allowing me to follow up all cases treated by him and for the excellent opportunities he afforded me for continuing my investigations at the Royal Infirmary Edinburgh.
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<td></td>
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SECTION I

INTRODUCTION.
INTRODUCTION.

In the therapeutics of organismal diseases, the trend of research during recent years has been devoted almost entirely to the study of vaccine and serum therapy, but the latest discovery in therapeutic science comes from another direction. Ehrlich has shown us that chemistry has its place in the treatment of these affections and the rôle that chemico-therapy is likely to play, opens up a still wider field for research and may even rival the discoveries in serum therapy. The results of the researches made by Ehrlich are by no means chance ones. For twenty five years he endeavoured to put into practice a principle that he alone held, namely that, to get a therapeutic effect a drug can have influence only upon the tissues of the body with which it forms a chemical combination.

As some drugs could act very injuriously upon the living cells of the body, he strove to find those which act similarly upon the organisms which are the causes of the various diseases. He conceived the theory of chemico-septors and worked with substances which according to their chemical characteristics formed combinations with the tissues upon which he desired to produce an effects.

For years he conducted his experiments entirely at
his own expense, and it was not until the "Speyerhaus" was built by a private donation with ample resources, that Ehrlich was enabled to obtain, all the means and opportunities, for his investigations.

Working now hand in hand with some dozen co-experimenters - biologists and chemists - he endeavoured to discover the specific chemico-septors of certain drugs and put into practice his principles of chemico-therapy. His first point was to discover those substances which act upon parasites, that is, which are parasitotrophic, and from these to select those which, though parasitotrophic, were not organotrophic, having therefore no action upon the cells of the host.

He divided the drugs which have a parasiticidal action into three groups.

1. Arsenic and Antimony.
2. The Azo dyes e.g. trypan red, and trypan blue.
3. The basic triphenylmethane dyes e.g. parafuchsin, methyl violet, and pyrcomin.

The action of these drugs was tried upon trypanosomes and the spirilla of relapsing fever and as these organisms live and multiply in the blood, investigations were easily made both in vivo and in vitro, and by these means specific chemico-septors were established between any one preparation of the above named groups and the organism/
organism in question.

The products of the two dye groups he found, though actively parasito-tropic, were also organo-tropic and thereby produced severe toxic effects upon the host.

Arsenic, though usually pentavalent and toxic to the cells of the host, if used in its trivalent form was found by Ehrlich to establish arseno-septors with the trypanosomes and the spirilla of relapsing fever and to be innocuous to the cells of the host. Consequently attention was directed to the arsenic group. He sought for a preparation that was trivalent and readily soluble and could produce "by the one fell swoop and in twenty four hours a therapia magna sterilizans" with perfect safety to the host.

Beginning with the synthetic arsenical compound, Atoxyl - which had already been introduced as a treatment for trypanosomiasis - the ultimate product of his researches is the substance now known as "Salvarsan or 606" with which he hoped to revolutionise the treatment in protozoal diseases.

At first his object was to confine his investigations to trypanosomes and the spirilla of relapsing fever but they were extended later on to syphilis as well.

The starting point in the discovery of salvarsan was the finding of the correct constitution of atoxyl. This/
This drug was discovered in 1863 by a French Chemist named Bechamp, who considered the substance to be a very loose combination of analin and arsenic acid.

\[
\text{Bechamp's Formula.}
\]

Ehrlich working with Bertheim however, discovered atoxyl to be the sodium salt of para-amidophenylarsenic acid, a stable and active chemical substance capable of forming numerous compounds.

\[
\text{Ehrlich's Correct Formula.}
\]

Atoxyl was first brought into clinical importance by Thomas of Liverpool - in treating trypanosomiasis - but was soon abandoned on account of its extremely toxic effects, especially upon the kidneys and the optic nerves. The reason for this was shown by Ehrlich when he reconstituted its chemical formula. He proved that the arsenic was present in the pentavalent form, as shown/
shown by his formula, and that in the body atoxyl was split up into two arsenic components, in one of which the arsenic was trivalent, and in the other probably pentavalent. The former was capable of fixation with the parasites, but the latter being incapable of fixation at all, accumulated in the body as the result of continual medication and caused toxic effects in persons with a natural sensitiveness to arsenic.

Starting then with atoxyl, Ehrlich found that the reduction products he made from it outside the body were more active in the body, proportionally to the amount of their reduction. Arsacetin was the next step along the line but clinically it unfortunately possessed the same dangerous sequelae to its use. By further reduction arsenophenylglycin - designated as 418 - was the next trivalent arsenical compound discovered, but biologically, though acting strongly upon trypanosomiasis, it was shown to have very little action upon the spirilla of recurrent fever and therefore not an ideal preparation. Experimenting further, greater success was obtained with arsenophenel which killed the spirilla of relapsing fever after two injections. Later, greater success still was obtained with dichlorphenalamensic acid which would do the same after one injection.

With this drug the goal had been reached, the therapia/
"therapia magna sterilisans" which Ehrlich had been searching for; but the substance could never be used clinically on account of the extremely toxic effects which it produced upon animals. With one single injection mice suffered for two weeks with progressive nervous symptoms, beginning with shaking of the head and travelling over the body until the mice became dancing mice.

Further investigation revealed the drug called dioxydiamido-arsenobenzol or 592, but as this salt was insoluble its dihydrochloride was searched for. The action of both however is identical.

The dihydrochloride of the dioxydiamido-arsenobenzol therefore is the substance "606" or "salvarsan" now upon the market as Ehrlich's preparation for the treatment of spirillary diseases.

"606" then is the 606th derivative of atoxyl, which is an amido derivative of phenylarsenic acid and though it can be prepared from atoxyl by a complicated process, it bears no direct relationship to it.

The formula of dioxydiamido-arsenobenzol is \( \text{C}_{12} \text{H}_{12} \text{N}_2 \text{O}_2 \text{As}_2 \) and is represented graphically as follows:

![Chemical structure of dioxydiamido-arsenobenzol](image)
and the dihydrochloride (606) as

\[
\begin{array}{c}
\text{\textit{O}} \\
\text{\textit{H}} \\
\text{\textit{O}} \\
\text{\textit{H}}
\end{array}
\]

The dioxydiamido-arsenobenzol is a yellow powder, readily oxidized, insoluble in water, but dissolves easily on the addition of sodium hydrate. The dihydrochloride is also a yellow powder, easily oxidized, into poisonous compounds and accordingly preserved in sealed tubes in vacuo or containing inert gases. It is soluble in water and readily soluble in warm normal saline; this solution is strongly acid in reaction. If the acidity of this solution is neutralized by the addition gradually of sodium hydrate the free base, dioxydiamido-arsenobenzol, is liberated and thrown down as a precipitate.

Thus:

\[
\begin{align*}
(HCl \cdot HN)(OH) C_6H_5 \overset{\text{As}}{\text{O}} & : \overset{\text{O}}{\text{As}} \underset{\text{C}_6\text{H}_5}{\text{O}} (\overset{\text{O}}{\text{OH}})(\text{NH}_2\text{HCl}) + 2 \text{NaOH} \\
= (H_2N)(OH) C_6H_5 \overset{\text{As}}{\text{O}} & : \overset{\text{O}}{\text{As}} \underset{\text{C}_6\text{H}_5}{\text{O}} (\text{OH})(\text{NH}_2) + 2 \text{NaCl} - 2 \text{H}_2\text{O}
\end{align*}
\]

Then if further sodium hydrate is added to the precipitate, the hydrogen atoms of the phenol hydroxyls become replaced by soda to form the soluble sodium salt (the phenolate of the base) and the compound goes into salt solution as the disodium of dioxydiamido-arsenobenzol. Thus/
Thus:

\[
\begin{align*}
(NH_3)(OH)C_6H_5O_2 & : C_6H_5OH(NH_3) + 2NaOH \\
& = (NH_3)O(NaC_6H_5O_2) : C_6H_5OH(NH_3) + 2H_2O
\end{align*}
\]

Graphically, the result of the above reaction may also be shown as follows:

DiOxyDiAmidoArsenoBenzol Disodium salt: (alkaline solution)

Ehrlich emphasises in the constitution of salvarsan two important facts. Firstly, that it is trivalent - seen by the formula, and secondly, the para-position of the hydroxyl groups. This position is correlated with marked spirillicidal properties. With this second compound of arsenic then, we have radicals introduced which (a) reduce the toxicity of the compound, (b) increase spirillicidal properties, (c) render the compound more stable. Working on the chemical properties of salvarsan Buchner and Hilpert estimated the amount of arsenic in that compound. Taking an ordinary market specimen they found, after careful weighing, the tube to be .6510 grm, the extra weight of .0510 grm, being due to inert gases or vapour.

Then/
Then calculating the arsenic content on the assumption that the tube contained 0.6grm. of real salvarsan, 35.16% of arsenic was indicated by titration with tenth-normal iodine.
SECTION II

HATA'S BIOLOGICAL EXPERIMENTS.
Before the new remedy could be used clinically its toxicity and dosage had to be ascertained, and for this purpose Ehrlich requested Hata to undertake a series of experiments upon animals infected with all three forms of spirochaetes. Regarding the results of his experiments Hata writes:

"Of this substance mice will tolerate one c.c. of a \(\frac{1}{300}\) dilution for every twenty grms. of body weight. One c.c. of a \(\frac{1}{800}\) dilution is still capable of sterilizing an infected mouse weighing twenty grms.; the effect of still weaker dilutions e.g. \(1:1000\) is uncertain. The dosis tolerata of this substance for rats is 0.2 grm. per kilo, the dosis curativa being 0.06 grm per kilo.

<table>
<thead>
<tr>
<th>Dosis Tolerata</th>
<th>Dosis Curativa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse 1/300 grm per 20 grm.</td>
<td>1/800 grm per 20 grm.</td>
</tr>
<tr>
<td>2.7</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rat 0.2 grm per kilo.</th>
<th>0.06 grm per kilo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Curative effects may be produced even with smaller doses but only when repeatedly administered.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Permanently cured after one application</th>
<th>Permanently cured after two applications</th>
<th>Permanently cured after three applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: 600</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1: 700</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1: 800</td>
<td>100%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>1: 1000</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1: 1500</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1: 2000</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1: 3000</td>
<td>50%</td>
<td>33%</td>
<td>33%</td>
</tr>
</tbody>
</table>

It/
"It is not advisable to give the injection more than three times; nor is the effect of more than three injections any greater than that of two or three. This remedy also possesses a prophylactic effect against recurrent fever in mice and particularly in rats, although the protection is of but brief duration.

"The disagreeable by-effects in the nervous system i.e. tremor, dancing and especially amaurosis, which are so readily produced by atoxyl, arsacetin etc., have never been observed in animals treated with salvarsan. The alkaline solution, however, when subcutaneously injected produces a more or less distinct infiltration at the site of injection, apparently causing considerable pain and possibly necrosis if the amount injected is too great.

"As compared with recurrent fever in mice and rats, the cure of chicken spirillosis is effected far more easily. Uhlenhuth succeeded in curing the disease by administering atoxyl and atoxylate of mercury. Chicken spirillosis can also be cured without any difficulty with arsacetin and arsenophenylglycin, both of which, like atoxyl and atoxylate of mercury are also entirely ineffective in recurrent fever in mice. The facility with which chicken spirillosis can thus be cured makes it a suitable medium for testing a remedy as to its effect/
effect on spirilla in general, and especially to compare it with the effectiveness of various other remedies. I submit the following table to show the comparative efficiency of the various remedies and their toxic properties.

Results of treatment for chicken spirilosis.

<table>
<thead>
<tr>
<th>Injection Intramuscular</th>
<th>Treatment 2 days after injection. Also intramuscular.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remedy</td>
<td>Dosis Tolerata per kilo.</td>
</tr>
<tr>
<td>Atoxyl</td>
<td>0.06 grm.</td>
</tr>
<tr>
<td>Arsacatin</td>
<td>0.1 &quot;</td>
</tr>
<tr>
<td>arsenophenyglycin</td>
<td>0.4 &quot;</td>
</tr>
<tr>
<td>arsenilate of mercury</td>
<td>0.1 &quot;</td>
</tr>
<tr>
<td>Salvarsan</td>
<td>0.2 &quot;</td>
</tr>
</tbody>
</table>

This comparison clearly shows that the results with the first four remedies are far less satisfactory than that with the SOS, in which the ratio \(\frac{C}{T}\) is actually ideal.

In the prophylactic experiments with salvarsan, a very interesting fact was revealed, which I would briefly mention in this connection. I injected 0.07 grm. per kilo intramuscularly into chickens and found that the animals after thirty days still remained completely immune to infection. However thirty five days after the treatment, the infection appeared; but it was very slight and only after fifty days could a prophylactic effect be no longer determined.

"On the other hand, if the remedy is administered intravenously/
intravenously the protective effect barely lasts four days; and six days after the injection, the animals react quite normally towards the infection.

"The reason of the extremely long duration of the protective effect in the case of the intramuscular injection was clearly demonstrated at once by the fact that at the site of the injection, a large deposit of the remedy was discovered. The remedy causes coagulation of the muscle and remains firmly combined with it for a long time. Gradually the substance is absorbed from the coagulated mass and transferred to the blood; but even fifty days after the injection the presence of the deposit in the muscle can still be distinctly determined.

"As we have already seen, the parasites are destroyed by a minimum amount of the substance; the small quantities absorbed from the deposit are evidently sufficient to stop their growth. Although the explanation of this fact is quite simple it is undoubtedly of great importance in the practical application of the remedy. The intramuscular application is to be preferred to the intravenous in the prophylaxis of chicken spirillosis because the protective effect of the former method is far more certain and lasting than that of the latter.

"It is still uncertain whether deposits of this kind unexpected injury may not follow, or sudden intoxication may occur, or the pain may be of long duration. For/
For this reason I am of the opinion that in human therapy, the intravenous application where the remedy is completely eliminated from within the body in a few days, is to be preferred to the intramuscular injection.

"Finally experiments were made upon syphilis. We used rabbits in which three forms of syphilis may be artificially produced, viz: syphilitic keratitis; syphilitic chancre of the scrotum; (studied by Truffi); and syphilitic orchitis recently described by Uhlenhuth. Keratitis in rabbits is a very unreliable medium for experimental work, in as much as the clinical symptoms sometimes spontaneously disappear, only to reappear later. Therefore this disease is not suitable for therapeutic experiments. Syphilitic orchitis is quite suitable for maintaining the strain, because it offers a pure culture - but chemo therapeutic studies cannot be very well pursued in this regard, because the swelling of the testicle alternately increases and decreases of its own accord. These two forms of syphilis in rabbits are especially unsuitable for repeated examinations for the spirochaetes, and this is of great importance in chemo-therapeutic experiments. In the case of chancre however, this is simply and readily affected by pricking the edge of the infiltration with a needle and making pressure. A fresh specimen is taken from the drops of sero-sanguineous/
"aero-sanguineous liquid then appearing, and this is studied under the microscope with the dark field illumination.

"The method of inoculating the scrotum is as follows:- At some point of the scrotum of a full grown rabbit a small incision is made in the skin and a pocket is formed into which some of the inoculating material is inserted as deeply as possible. After some ten to fourteen days a small white or slightly reddish infiltration appears at the point of inoculation growing slowly until it attains the size of a bean approximately. After four or five weeks, the skin at this point gradually becomes necrotic and a crust forms. The margin of the ulcer thus developed is of cartilaginous consistence and projects above the surrounding healthy skin. When the moist crust is removed slight bleeding sets in from the foul necrotic base, the latter being sometimes so much depressed as to cause a distinct elevation of the marginal infiltration. Thus the puncture presented, greatly resembles the primary chancre in man. The entire induration gradually increases in size and thickness, occasionally measuring an inch in diameter and three fourths of an inch in thickness. This condition lasts for several months. Only such animals were selected for the experiments in which the pathological condition/
condition was unmistakable and stationary.

The rabbit comfortably tolerates an intravenous injection of 0.1 grm. of salvarsan per 1000 grms of body weight. When the chancre is fairly well developed on the scrotum, showing innumerable spirochaetes, one injection of a sufficient dose of the remedy is administered intravenously. On the very next day the spirilla have completely disappeared from the chancre, and a few days later the crust has become dry and the induration is very soft, disappearing completely after seven to ten days, at which time the crust falls off entirely. Within two to three weeks the large chancre has been reduced to a small scar. Of course rapidity of the complete destruction of the spirochaetes depends upon the size of the dose administered, but also upon the size and especially the thickness of the induration and the number of the spirochaetes. If the dose is too small or the chancre extremely thick, the spirilla will take two or three days to disappear. For complete healing two to three weeks are generally required; this naturally depends upon the size of the chancre and the presence or absence of suppuration, that is mixed infection. Should any other complication arise, for example pneumonia, the process of healing may be considerably retarded. For this reason therefore, the disappearance of the spirochaetes is a
far more certain criterion of the effect of a remedy than the time required for the complete healing of the chancre.

In my therapeutic experiments with salvarsan I obtained the following results:

Results of Treating Syphilitic Rabbits with salvarsan

One Intravenous Injection.

<table>
<thead>
<tr>
<th>Dose per kilo</th>
<th>Relation to Dosis Tolerata</th>
<th>Spirochaetes disappeared within</th>
<th>Complete cure if no complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.04</td>
<td>1/2.5</td>
<td>24 hrs</td>
<td>2 to 3 weeks</td>
</tr>
<tr>
<td>0.03</td>
<td>1/3</td>
<td>24 &quot;</td>
<td>2 to 3 &quot;</td>
</tr>
<tr>
<td>0.02</td>
<td>1/5</td>
<td>24 &quot;</td>
<td>2 to 3 &quot;</td>
</tr>
<tr>
<td>0.015</td>
<td>1/7</td>
<td>24 &quot;</td>
<td>2 to 3 &quot;</td>
</tr>
<tr>
<td>0.01</td>
<td>1/10</td>
<td>2 days</td>
<td>2 to 3 &quot;</td>
</tr>
<tr>
<td>0.0075</td>
<td>1/14</td>
<td>2 to 3 &quot;</td>
<td>2 to 3 &quot;</td>
</tr>
<tr>
<td>0.005</td>
<td>1/20</td>
<td>2 to 3 &quot;</td>
<td>3 to 4 &quot;</td>
</tr>
<tr>
<td>0.004</td>
<td>1/25</td>
<td>still present</td>
<td>one exception</td>
</tr>
<tr>
<td>0.003</td>
<td>1/30</td>
<td>after 30 days</td>
<td>not cured</td>
</tr>
</tbody>
</table>

"According to those figures, a dose 0.015 to 0.01grm. per kilo is required for immediate sterilization. This is one-seventh to one-tenth of the dose tolerata. But rabbits may be ultimately cured with smaller doses even with 0.005grm. per kilo, or one twentieth of the dosis tolerata. The dose of 0.3grm. thus far administered to man, actually corresponds to this small dose, given to rabbits. Further observation will determine whether or not it is sufficient to prevent subsequent recurrence in man, or whether larger doses must eventually be administered."

Thus, we see that here we have a remedy by which the three types of spirochaetes are absolutely destroyed without/
without injury to the organism of the host i.e. a remedy capable of readily curing animals infected by spirochaetes.
SECTION III.

THE DIFFERENT SOLUTIONS USED FOR INJECTION.

AND THE DIFFERENT WAYS OF INJECTING THEM.
Methods of preparing the drug for injection.

After Hata had submitted the results of his biological experiments to Behring, the latter supplied many well-known syphilologists with the drug to have its properties tested clinically, before allowing it to be placed upon the market.

Many painful and unpleasant phenomena were encountered after an injection in the human subject, with the result that quite a number of different solutions and methods of injecting them were devised by the various observers to obviate as far as possible these undesired sequelae. Most of these methods however, have passed into history, and only the most important will be given here.

Seeing that salvarsan is an arsenical compound containing that metal in a low state of oxidation and decomposed by bodies which are oxidizers it is very important to examine the glass capsule containing the drug to see that it is not cracked and no air has gained access to the contents. Also the preparation for injection should be made immediately before use.

The acid solution (the di-hydrochloride):-

Dissolve the drug in ten to twenty c.c. of warm sterile water or warm physiological saline solution. The preparation of salvarsan now upon the market needs no alcohol to dissolve it as formerly required. This solution/
solution as previously shown is strongly acid, and is in its most irritating and most toxic form.

The mono acid solution: Dissolve the drug to form the strongly acid solution as explained above. When an alkali is added to neutralise completely this solution the alkaline base is formed, which precipitates out. If half the amount of alkali to produce complete neutralization is added to the original solution, a solution of the mono acid compound is formed. This preparation is also extremely irritating.

The alkaline solution (the disodium salt). This is the solution recommended by Ehrlich and used by Hata in his experiments on animals. It was later used clinically by Professor Alt at Uchtpringe and is now generally known as Alt's alkaline solution.

Mix six c.c. of sterile water with the powder in a sterile glass vessel, introduce twenty to thirty small glass beads and shake the mixture thoroughly. When in solution add, drop by drop, a fifteen per cent caustic soda solution until the resulting precipitate is again just dissolved and the solution clear. The beads are washed with sterile water to prevent losing any of the mixture. This is the most efficacious of the solutions used for subcutaneous and intramuscular injections although/
although it may cause considerable pain in persons with a hypersensitiveness to arsenic.

The suspension of the base (the dioxydiamidoarsenobenzol): Wechselmann devised what is called the neutral suspension method, and from the fact that the preparation is neutral in reaction, claims the distinction of being the least painful of all the small injections. The method of preparation he recommended is as follows. Place the drug in a mortar and dissolve in one or two c.c. of commercial caustic soda, then glacial acetic acid is added, drop by drop, until a fine yellow slimy sediment is precipitated, to which one or two c.c. of distilled water are added. Now, according to the reaction shown by litmus paper the liquid is neutralised by the addition of one-tenth normal caustic soda or one percent acetic acid.

Another preparation, and one which has been used in Great Britain to a considerable extent is as follows. Put the powder into a mortar and add 1 c.c. of a saturated solution of sodium hydrate. Mix and then dissolve in four c.c. of very hot distilled water. For an indicator, add three drops of the standard alcoholic solution of phenolphthalein which colours the solution a bright red. Then add just so many drops of glacial acetic acid till a yellow emulsion is produced and finally one or two drops/
drops of sodium hydrate are put in until the emulsion assumes a rose pink tint.

The neutral suspension is the preparation most frequently used for intramuscular injections in the treatment of pernicious anaemia, leprosy etc, where a slow absorption and continuance of arsenic in the body is required.

Other suspensions: - Kramayer, Wolf, and Volk, advocate an emulsion in paraffin oil. The advantages claimed for this preparation are, reduced pain, permanency of the preparation, and the practicability of treating outdoor patients. Rub up salvarsan with ten per cent paraffin oil, then add a sufficient quantity of water so that one c.c. of the emulsion will contain 0.1 gram of the remedy. This should be protected from the light, and before use shaken thoroughly. But with this preparation absorption is too slow to get a good therapeutic effect in syphilis.

Citron and Kulzer recommended an emulsion in calcium carbonate. In a syringe containing salvarsan pour hot sterile water to the five c.c. mark, and shake until the mixture is in solution. To this add forty drops of a ten percent calcium carbonate solution (normal salt). The thick creamy emulsion which ensues is/
is shaken thoroughly and from 5 to 6.5 c.c. injected. Almond oil and olive oil suspensions have also been used.

The alkaline solution (the disodium salt) in great dilution for intravenous injection.

This method was first introduced by Schreiber of Magdeburg who adapted it in preference to any of the other methods. The preparation here described is the one used by myself; and all the cases described in this work, were treated by it.

Procure a long graduated 300 c.c. glass flask of the same calibre throughout (it is of advantage to have a closely fitting stopper to this flask) and into this pour ten to fifteen c.c. of hot distilled water. After examining the capsule containing the salvarsan and breaking through its neck, slowly empty the contents into the ten to fifteen c.c. of water. This is best done by tapping the capsule on the mouth of the flask, thereby knocking in a few grains at a time. After a few grains have been deposited in the water, shake thoroughly until all are dissolved. Continue this until all is in solution; at first only add a few grains at a time, but towards the end much more can be added as the substance then more readily dissolves. The solution is of a clear yellow colour. Now add, drop by drop, a solution of fifteen per cent caustic hydrate (NaOH), and/
and at once a yellow slimy precipitate is formed.

Go on adding drops, shaking the yellow solution between each, until all the insoluble base (the dioxydiamidoarsenobenzol) is precipitated. This takes from eighteen to twenty drops. One or two drops more will cause the precipitate to redissolve, and one or two more drops further are added, to keep the substance in solution. This is now the same solution that Alt originally used and could be well injected intramuscularly. For the intravenous injection, however, fill the flask up to the 300 c.c. mark with warm normal physiological salt solution, and the preparation is now ready for use. Seeing that 0.6 grm. is dissolved in 300 c.c. it is an easy matter to regulate the dose. Fifty c.c. of the solution equal 0.1 grm. of salvarsan.

Methods of Injection.

Three methods of injecting the drug have been devised namely, the subcutaneous, the intramuscular, and the intravenous; the two former ones were the first methods to be employed and it was not until a year's experience with them had been attained, that the intravenous method was resorted to.

The subcutaneous method : All the preparations excepting/
(excepting the one in 500c.c. solution) that have been described, have been injected subcutaneously. The parts of the body best suited for this method are, either just below the angle of the scapula, or in the region of the breast. The needle must be placed between the skin and subcutaneous tissue, otherwise very unpleasant sequelae are apt to occur, and the amount injected should be as small as possible consistent with the dose. After the injection has been made, the part must be massaged in order that the fluid may be dispersed over as wide an area as possible. Wechselmann's neutral suspension is the best preparation for this method of injection.

The intramuscular injection: The same preparations are employed here as in the subcutaneous method. The position of the body best suited for the intramuscular method is the gluteal region. A line is taken from the middle of the body behind, to the tip of the Great Trochanter and the injection is made deeply into the gluteal muscles at the junction of the outer and middle thirds of this line, thus evading the important structures coming through the Great Sacro-Sciatic Foramen. The needle employed should be about one and three quarters to two inches in length.

The best method to make the injection is to drive the needle in full length, and discharge a small amount of/
of the contents, then with drawing the needle a little it is pushed home in a slightly different direction and more of the substance deposited. Continuing in this method until the syringe is emptied, the injection should take from three to five minutes to make, and the pain and discomfort due to the sudden distension of the tissues is thereby greatly alleviated. After the injection is finished, massage the part as in the subcutaneous method to reduce the swelling. A half injection may be made into each Glutei if thought advisable.

After this injection, it is safer to keep the patient in bed a few days to prevent any tendency of the drug to gravitate down the leg and come into contact with the sciatic nerve, as it is apt to do if he is allowed to walk about. One has seen sciatica caused in this way lasting for four weeks.

The intramuscular method of injection is more advantageous than the subcutaneous and Alt's alkaline solution is the preparation of choice.

The intravenous method: - As already explained the solution is in a 300 c.c. flask ready for use, and kept at a temperature of about 100 F to 110 F by being stood in a basin of hot water. Besides this a litre of warm normal saline is also at hand. For injecting, a very simple apparatus is required and one that can be/
be easily sterilized by boiling before hand. A funnel flask with a tapering bottom (the same as that used for ordinary intravenous transfusion) to which is attached about three feet of rubber tubing. To the other end of this tube is attached the needle which is to be passed into the vein. About two to three inches from the needle an inch of glass tubing is placed to act as a window through which the fluid can be seen, on its passage to the vein. The needle used matters but little, as long as it is of a decent sized calibre and the fluid can flow quickly. A convenient shape is a slightly curved one, enabling the point to enter the vein almost parallel to its lumen, thus slightly obviating the risk of going through the opposite wall as well. Some observers prefer to cut down upon a selected vein in every case and in the event of this, the ordinary transfusion cannula is the instrument required in the place of a sharp needle.

A clip is placed between the needle and the glass window in the tube, and the funnel and tubing down to the clip are filled with the warm normal saline. With the patient lying on his back one of the large veins at the bend of the elbow is selected. In preference the Median Vein just before it reaches the antecubital space or the Median Basilic just beyond it. Asking the patient/
patient to open and close his hand vigorously, the surgeon places an elastic bandage tightly around the middle of the upper arm, and if the veins are of normal size they now stand out prominently.

Sterilize the skin by smearing the part with iodine. With the saline flowing, the needle is placed with the convex surface along the vein, the point being in the direction of the blood stream. In this position it is easy to drive the point through the skin and into the lumen of the vein. One can easily tell if the needle is in the vein and not in the loose surrounding tissues, by the smooth feeling the needle has as it passes along the vein walls, and also on loosening the clip seeing the blood quickly appear at the glass window. All now is ready; remove the elastic bandage from the arm and the clip from the rubber tube, and allow the saline to flow into the vein. Before the funnel is quite empty pour in the salvarsan solution, (which has been maintained at a temperature of 100 F to 110 F), and just before all of this has passed from the funnel into the tubing fill up the funnel again with more saline, thereby washing the remains of the former solution from the tubing into the blood stream, and with the saline still flowing withdraw the needle. Apply a strip of gauze and a bandage to the part, and the bleeding (if any) quickly stops.
stops. In some instances, especially in very fat persons or those whose superficial veins are very small, it is often very difficult to find a vein suitable for direct injection. In such a case a vein must be exposed by operation. A transverse incision is made over one of the superficial veins as the Median or Median Basilic, or the Internal Saphenus and the vein dissected free from the surrounding tissues. An opening in the vein is made and the fluid allowed to run in through a canula in exactly the same manner as already described.

One has seen a case in which the operator had to make incisions in both arms and in both legs before a suitable vein could be found, in order to administer the remedy. If a vein is quickly got into, either by direct injection or by dissection, the operation of administering the drug should take about seven minutes. Care must be taken never to allow any of the salvarsan to escape from the needle or canula, otherwise an indurated lump or a sloughing ulcer may follow, but if the directions given are closely attended to there is very little likelihood of an escape taking place. On the other hand if the accident did occur, douche the wound well with normal saline before putting on the bandage.
SECTION IV.

The preparation of the patient for an injection and the subsequent clinical course.

The advantages and disadvantages of each method of injection.
The Preparation of the Patient for Injection.

In most hospitals and especially where the patient can be put to bed before the injection, it is customary to prepare him somewhat for the ordeal. If this is done the after-effects are not so severe as a rule. A purge at night to clear out the stomach and intestines and a light breakfast next day (if the injection be given in the morning) are of advantage in reducing the intestinal effects which might ensue. If vomiting follows, it is not so severe; if diarrhoea, it is reduced; or if constipation, it is of advantage to have had the bowels cleared out before hand.

The part into which the injection is made must be thoroughly well sterilised, otherwise in the case of subcutaneous or intramuscular injections an abscess might form, or in the case of intravenous injections organisms are introduced into the blood stream. It is usually enough to smear the part with iodine, but some operators prefer to rub the skin with ether until quite red.

Clinical course following injections:— With subcutaneous and intramuscular injections, the clinical course following, is much the same.

Pain:— Pain is almost always a constant symptom especially with the acid or alkaline solutions and is usually/
usually more marked in subcutaneous injections, especially if the injection be made into the skin, instead of beneath it. Immediately after the injection, the pain is usually very acute in both methods, lasting ten to fifteen minutes; it is due to distension of the tissues. This is followed by a dull ache varying in duration in different subjects from one to three weeks. With the neutral suspension preparation, the pain is greatly diminished, if not absent; one has often seen intramuscular injections made with this preparation with practically no pain at all.

Swelling: A swelling usually forms immediately due to the extra fluid injected; but on the third day it may be increased by a toxic oedema. This swelling is best relieved by hot or cold applications or the alternation of both. When the swelling gets smaller and harder, Ichthyol or a belladonna plaster, aid absorption most. If the pain is very severe morphia must be given. After the pain and oedema have subsided, the material injected usually remains in the tissues as an inert mass or swelling for weeks or even months, causing no inconvenience to the patient and only painful when pressed upon.

Temperature: There is usually a rise of temperature either the first night or delayed for a day or two, and the/
the rise may be anything up to 103° F, but 99 to 100° F is the rule. With the neutral suspension there is often no rise at all. The rise of temperature cannot be taken as an indication that the drug is acting well.

**Clinical Course Following Intravenous Injection.**

The phenomena following this method vary almost with each person injected. No one can tell how the patient is going to receive the drug; on the one hand he may suffer from severe constitutional effects, while on the other he may remain absolutely undisturbed. It is however far more usual to have definite constitutional disturbances than not, and it is therefore imperative to keep the patient in bed for a few hours to see what follows.

Some or all of the following phenomena may be expected to occur.

**Temperature:** A rise of temperature is one of the most constant sequelae to this method of injection. By the cases shown, it will be seen that the temperature may rise from normal to 103° or 104° F in a few hours. The most common rise however, is from 99.4° to 101.2°. It is practically impossible to tell in what kind of case the temperature is likely to rise highest; some observers thought the highest temperatures were got in secondary/
secondary syphilis, that is when the disease becomes constitutional, but one frequently found secondary cases, where the rise was no more than to 99.8° or 100°F, and on the other hand tertiary cases were met with where the rise was as high as to 103°F or higher. The temperature usually starts to rise within the first hour after the injection, and reaches its highest point in from three to five hours; it remains at this for an hour or two and then falls to normal, either by crisis or by lysis, the former being the more common. Sometimes there is another rise on the second day after injection (as a rule not so high as the first), or the first rise may be delayed until the second day, a phenomenon seen mostly in nervous cases.

Rigor:—When the temperature reaches its highest point, and especially if it rises over 100°F, there is usually a definite rigor followed by prolonged shivering for half an hour to two or three hours, which ceases as the temperature falls. If the temperature rises for a second time it may be accompanied also by a rigor, though to a much less degree than the first rise.

Vomiting:—There may be simply nausea or it may extend to actual vomiting. If vomiting does occur it is usually easy and without pain, and is over in a few minutes.

Diarrhoea:—/
Diarrhoea: Though real diarrhoea may occur for a day or so after injection, this intestinal disturbance is usually more of the nature of one or two violent watery motions than actual diarrhoea, and may or may not be accompanied by abdominal pain in varying degrees of severity.

Headache and other phenomena: A headache or a dull heavy feeling is very common after an injection. If there is a headache present due to the disease, this is usually made much worse for a few hours and then clears up entirely.

Various aches and pains in different parts of the body, especially the long bones, are quite a common sequelae. Also the various syphilitic lesions present such as sore throats, skin ulcerations, and gummata are often made much more painful and sore for the few days before they begin to heal up.

Thirst is often complained of as in other febrile conditions and in some cases there is a slight suppression of urine. This latter however, is never of severe degree, and one has never seen a case where artificial means were required to relieve the patient in this respect. Most patients pass urine within the first six hours after an injection, though every now and then one is met with, who goes from fifteen to twenty hours before micturating.

Though/
Though these are very definite phenomena not all need necessarily occur; it greatly depends upon the individual injected. A rise of temperature is the commonest and nothing else may accompany it. Again there may be vomiting and diarrhoea and abdominal pain, and yet the temperature may not rise above 99°F. A rigor too need not necessarily occur, though this depends greatly upon the height to which the temperature rises.

When the injection is being given, the patient should either be in bed or lying upon a couch, and go to bed immediately afterwards, until all constitutional disturbances have passed off. If the patient though infected with syphilis, be otherwise healthy, the drug may be administered the same day that he is admitted to hospital or nursing home. And if the temperature does not rise above 99.6° or 100° and the vomiting or other phenomena do not make him feel too ill, he may be permitted to leave the same day. However on the other hand if there has been a rigor with vomiting and a rise of temperature above 100° which is coming down but slowly, it is better the patient should stay in bed for two or three days until he feels quite himself again. In healthy persons, there is no need that they should be away from work more than three days after an intravenous injection.
injection of salvarsan.

Variations of the blood pressure:—In every case that one has examined after an intravenous injection, there are changes in the blood pressure. While the injection is being given there is a rise of from five to ten m.m. of mercury, and after the patient has gone back to bed there is a further rise. Within the first quarter of an hour after an injection however, this rise begins to recede, and the pressure gradually gets lower as the constitutional disturbances come on.

Taking 120 m.m. of mercury as the average blood pressure of a young and healthy man, it quickly rises to 130 m.m. or even 140 m.m. while the injection is being given, and for the first few minutes following it. Then within fifteen minutes it begins to fall again gradually, and after two or three hours it may even fall as low as 110 m.m. At this it remains until the constitutional effects of the injection have passed off, when it gradually rises again to its usual position.

(2) McDonagh also found similar variations in the blood pressure and reports cases where the after-fall was excessive needing very active stimulation to keep the patient conscious. I have never seen however anything approaching this severity, in fact in all the cases I have examined, the patients were in no way embarrassed by the variations.
Advantages and Disadvantages

of the various methods of injection.

It has been seen by the foregoing description that the clinical pictures following the intramuscular and subcutaneous methods differ very greatly to that following the intravenous method. We shall now consider the advantages and the disadvantages of each.

The Intramuscular Method:— The advantage of this method over the others and the intravenous especially, is that it can be performed in certain cases where the latter is rather inconvenient or dangerous. Seeing that with the method in question, the general constitutional disturbances are but slight, and that a large quantity of extra fluid is not injected into the body, it is often of advantage (1) in very feeble patients where shock is to be avoided; (2) in patients with a weak and diseased circulatory system where a rise in the blood pressure is certainly dangerous; and (3) in case of syphilitics such as tabes and general paralysis where, as shown by Professor Alt cyanosis and respiratory complications are much more likely to follow the intravenous than the intramuscular method, probably on account of increased intracranial pressure.

(4) It is in infants however, where the intramuscular method/
method is of the greatest advantage, because in these little patients, it is practically impossible to inject the drug intravenously.

On the other hand the disadvantages are extremely obvious. The pain, the swelling, and the toxic oedema to say nothing of the resultant masses and perhaps abscess formation and necroses are quite sufficient for the method to be replaced by the intravenous method.

With intramuscular injections there is always a certain amount of definite combination between the tissues and the arsenical compound injected. In the most successful cases after the acute swelling and oedema have subsided, there remains a resultant mass often easily palpable for weeks. In other cases quite a visible tumour remains, which on being incised reveals quite a quantity of arsenic. The mass is brown or brownish yellow, with a hard dark centre containing for the most part pure arsenic. A definite inflammatory wall with an infiltration of leucocytes is formed around the mass due to the irritation set up by the compound. Outside the harder and darker centre the swelling consists mostly of necrosed tissues, thrombosed vessels, and degenerated nerve fibres, all in combination with arsenic. It is thus seen that absorption of the remedy from this necrotic mass is essentially very slow. Of course the amount of swelling and/
and necrosis depends greatly upon the individual treated and the kind of preparation injected; the neutral suspension forming larger and more persistent swellings from which absorption of the drug is much slower than is the case with Alt's alkaline solution. Nevertheless with any kind of preparation of the drug used intramuscularly (especially in persons with a hyper-sensitivity to arsenic) a necrotic mass is always apt to form and requires a certain amount of treatment.

These masses must never be incised as healing of the incision wound is greatly retarded, absorption is slower, and septic material is almost certain to gain access to the already irritated tissues.

In some cases the mass resolves into fluid with indefinite fluctuation and in such cases the treatment is either to leave it alone or else aspirate it, and allow the yellowish debris to escape. These necrotic masses are always sterile and the greatest care must be undertaken to keep them so, for if they became infected the resultant abscess formation is extremely painful.

Whenever the drug is used intramuscularly or subcutaneously great care must be taken with the sterilization of the skin, because salvarsan although a powerful irritant, is in no way an antiseptic and organisms introduced at the time of the injection find a splendid nidus for growth.
Abscess formation then is always a possible complication of this method and should be kept in mind when one is about to use the drug.

The Subcutaneous Injection: The advantages of this method apply to certain cases in somewhat similar ways as the intramuscular do, but its disadvantages are even more pronounced. It is extremely difficult to inject the drug exactly between the skin and the underlying tissues. If injected into the dermis there is immediate excruciating pain, and necrosis of the skin is almost certain to follow, taking the form either, of a dark brown parchment-like area, or a deeply sloughing ulcer. Then if the compound is discharged into the subcutaneous fat the latter is immediately acted upon by the irritating arsenic and a necrotic ulcer is almost certain to result. The needle then should be placed between the skin and the subcutaneous tissue, and when all the material is discharged from the syringe the part should be thoroughly massaged to disperse the fluid over as wide an area as possible. The operation, however, is at all times difficult, and since we have now a later way of administration the method should be entirely given up.

The Intravenous Method: This method is the one now usually adopted by most syphilologists in Great Britain, though/
though some of the Continental workers still adhere to the intramuscular and subcutaneous routes. In the early days of clinical work with salvarsan, Ehrlich recommended the intramuscular injection of the alkaline preparation of Professor Alt of Uchtpringe, and injected deeply into the gluteal muscles. About twelve months later, however, after studying the records of Schreiber and others, he recommended the intravenous method instead, and requested Dr. Wechselmann to try the method on his patients instead of the neutral suspension he had hitherto used. After a thorough trial the advantages of the intravenous method are very evident.

1. The drug is brought more directly into contact with the spirochaetes and is therefore in its most potent form.

2. There is no continual absorption of arsenic.

3. There is rapid elimination rendering a second injection much safer.

4. One is better able to regulate the dosage.

5. The whole of the dose injected is brought into action.

6. There is no inconvenience of a coagulated mass in the tissues from which the amount of arsenic absorbed is slow and uncertain.

7. It is painless when compared with the other methods.

8. The by-effects of the injection (seen in the first few hours) are soon over and never return.
9. The patient is out of the doctor's hands sooner as there is no risk of necrosis etc.

After studying the above facts there can be no doubt as to the advantages of this method, and still more evident do they become when we look at the disadvantages.

1. The idea that a sort of surgical operation is required - the passage of a needle into a vein or the cutting down upon a vein if the former is impossible. This disadvantage is more apparent than real. If the proper precautions are taken and sufficient care is exercised, the required dexterity is very quickly attained.

2. The constitutional effects of the injection. Though rigors, vomiting and diarrhoea, are apt to occur with any patient injected, there is in reality (in most cases) very little disturbance. The vomiting is painless though the diarrhoea may be accompanied with slight abdominal pains, which pass off without needing treatment. The rigors do not seem to upset the patient much and though the pulse may rise to 120° or so, one has had no occasion to inject cardiac stimulants. In fact the patient looks wonderfully well all the time, and in twenty four hours generally declares he feels better than he has done for a long time.

3. Thrombosis of veins. The vein is most likely to thrombose/
thrombose when the needle is being passed directly into it, as here one is apt to injure the vessel walls or bury the needle point in the adventitious coats of the vein. Extravasation of blood occurs and a haematoma forms; the salvarsan refuses to flow and on withdrawing the needle and cutting down upon the vein, the vessel is found to be thrombosed. In such a case as this another vein must be tried or cut down upon; but the accident does not happen often, however, and usually the solution flows freely especially if normal saline be used instead of distilled water, and the needle be bright and clean, and free from rust.

Also if the fluid injected be too alkaline it aids the tendency to thrombosis (McDonagh)

With infants of course it is impossible to inject the drug intravenously, and as before stated a small dose of the alkaline solution should be used when it is thought necessary to inject salvarsan in these cases.
SECTION V

Including the dosage, the appearance of toxic rashes, the Jarisch-Herxheimer Reaction and contra indications. Also the elimination of arsenic and the effect of salvarsan upon the Wassermann Reaction.
The Dose.

Salvarsan is done up in tubes containing .6 grm. or nine grains, this being considered the full dose. Some of the observers, especially the earlier ones, considered .3 grm. for women and .45 grm. for men, sufficient but it is now usual to give .6 grm. for a dose to both men and women alike. It is a great point in treating syphilis by salvarsan to give with safety the largest dose possible, for it has been shown by experience that larger doses are much more potent than smaller ones, thereby reducing the necessity of another injection. Calculating from animal experimentation, including monkeys, it is considered a dose of five or six grms. could be given to a human being at one injection without fatal results, but the test has never been carried out.

Some observers as Iversen (St. Petersburg) consider 0.9 grm. (in combined intravenous and intramuscular injections) the correct dose, and Duhot has given one grm. and over without evil effects, but the tendency is to approximate .6 grm. in the one dose for adults. In children the dose is considered to be from .02 to .03 grm. according to their age and nutrition.

Toxic Rashes

Rashes considered to be due to the toxic action of the drug may make their appearance about the first week after injection. They cannot be said to occur often;
of the two hundred odd cases of which one has had ex-
perience only once has such a rash developed. The
commonest is an erythema which usually occurs on parts
of the body and not completely over it. In the case
referred to, this rash appeared on both arms and slightly
on the trunk, and only lasted a few days.

Other rashes such as an exanthema resembling measles
or scarlet fever, and also a true urticaria have been
described. A herpes of the face and genitals have been
known to occur.

The Jarisch - Herxheimer Reaction.

In the treatment of syphilitic rashes with mercury
for the first time (especially after the first or second
inunction) the rash is often, in certain cases, intensified;
this reaction is called the Jarisch Herxheimer reaction,
and is supposed to be due to the temporary stimulation
of the spirochaetes. The same reaction has since been
observed, and often in a more intensified form, after the
treatment with salvarsan, but was considered for a long
time to occur only when given in too small a dose.

Loeb, has noticed it two hours after injection while
Truffi, by the administration of very small doses .025
to .05 grm., observed the reaction in a very distinct
form in many subjects.

Ehrlich/
Ehrlich considered the reaction to be due to the stimulation of the spirochaetes and showed that the drug was not affecting a sterilization.

Later however, Gennerich, Wechselmann, and Herxheimer himself observed the reaction even with quite large doses (.8grm.) and considered the phenomenon due to the liberation of endotoxines brought about by the death of the spirochaetes.

The development of a rash, the intensification of a rash, or the aggravation of any syphilitic lesions present, such as intensified sore throat, or increased discharge of an ulcer, is considered by some observers as the Jarisch-Herxheimer reaction.

If the reaction occurs it does not mean that a good therapeutic effect is not produced as the phenomenon quickly passes off and the lesions heal up without further treatment. One has noticed the reaction occur several times after doses of .6grm. and the rash in these cases cleared up just as quickly as in those in which the reaction was absent.

Contra-indications to the use of Salvarsan.

Since salvarsan has come into such common use, the contra-indications against its employment have become less and less. One has never met with a case - in the ordinary routine practice of a lock ward - where the patient/
patient could not stand the administration of the drug in some form. If it is considered the patient cannot stand a full dose, a much reduced one, often repeated, is usually well tolerated and produces the same beneficial effect. The greatest contra-indications are, disease of the heart and blood vessels, advanced diseases of the brain and spinal cord, and diabetes. Optic atrophy, retinal affections and nephritis, when of non syphilitic origin, are regarded by most observers as contra-indications also; but if the affection of any of these parts be a syphilitic one, then an injection should be given. Even with chronic (non syphilitic) nephritis the patient can usually stand a modified dose.

In some cases, haemorrhage has been produced in previously damaged kidneys by too large a dose, but this usually passes off and the kidneys settle down to their previous condition. One has seen albumen in the urine due to syphilitic infection of the kidneys clear up wonderfully well after an intravenous injection.(see case - Tertiary Syphilis - F. W.)

Patients suffering from pulmonary tuberculosis stand the new remedy extremely well - except in advanced and emaciated cases, and especially where a haemorrhage may be expected. Salvarsan seems to exert a toxic effect upon the small blood vessels, hence in patients where/
where an haemoptosis has recently occurred the drug should not be used. Likewise in patients recently operated upon, its use should be withheld, as both McDonagh, Wechselmann have reported cases where severe haemorrhage has occurred at the site of operation.

Jaundice occurring in the secondary stage of syphilis is usually of syphilitic origin and the patient should be given an injection. Hoppe reports such a case to clear up entirely in nine days; but for jaundice in advanced cases of syphilis, where there is probably a good deal of destruction to the liver tissue salvarsan should not be given, as further degeneration of the liver is likely to ensue.

Lastly, old and emaciated patients should not be given an injection; there is practically nothing to be gained by it and in all probability their systems are too weak to stand the shock of an administration.

The Elimination of Arsenic.

After an injection of salvarsan the arsenic of the compound is excreted from the body, mainly by the urine but also by the faeces, while traces of inorganic arsenic have been found in the milk of mothers. Fischer and Hoppe did some experimental work in determining the rate of excretion of arsenic in the urine and/
and faeces of paralytics, who were injected subcutaneously with .3grm. of salvarsan. They found that arsenic ceased to be demonstrated in the urine in from twelve to fourteen days after the injection, but the amount secured was something like .02 to .07grm. of arsenic. With healthy syphilitics or with patients with healthy kidneys the excretion was a little faster, usually ending about the tenth day. Also elimination from the intestine ceased about the tenth day.

After an intravenous injection the elimination was faster both from the urine and from the faeces, ceasing in the former, on an average, in three days, and in the latter in six days.

Disappearance from the blood is at about the same rate as from the urine and faeces.

As an easy clinical test for arsenic in the urine Aberlin gives the following method.

To about five c.c. of urine acidulated with hydrochloric acid, add a few drops of a .5 per cent solution of silver nitrite. To this add about three c.c. of a ten per cent solution of resorcin made alkaline with a few drops of sodium bicarbonate solution. If arsenic be present a clear, bright red colour forms. With this method, one has got arsenic in about three hours after an intravenous injection, and as a rule the lower the temperature, sooner was a positive result obtained.

If the temperature rose high the reaction/
reaction, though delayed, could be got for a much longer period than if it rose but slightly; therefore, greater the constitutional disturbances, slower the secretion of arsenic. There are however, great individual differences regarding the secretion of arsenic even with patients injected on the same day and the drug prepared in the same manner; so one found it extremely difficult to make comparisons. Heuser declares he has found arsenic three months in the urine after an intravenous injection and nine months after an intramuscular one.

Retention of arsenic in the body:—Ehrlich said that salvarsan is not organo-tropic, and in support of this Wechselfmann reports two cases from the Magdeburg Altstardt Hospital, where death occurred due to intercurrent diseases on the fourteenth and thirty sixth day respectively after an intramuscular injection. In both cases, in the organs that were examined, no arsenic could be found, but at the site of the injection was the brown mass already described.

Bornstein however, experimenting upon animals found that a large quantity of the salvarsan injected intravenously, did not remain in the blood, but was deposited in the liver, spleen, and kidneys, with small quantities in other organs. He later confirmed these findings in a man/
The effect upon the Wassermann reaction.

If a positive Wassermann reaction is to be looked upon as a sign of active syphilis, it is without a doubt the hardest of all the symptoms of that disease to treat. Under the influence of mercury, it usually takes months or even years to get the reaction changed to negative, and sometimes when the change has taken place, serious syphilitic lesions may still be found on the patient. Since the introduction of salvarsan however, a great deal of further study and research has been done. And although there are a few syphilologists who consider the test to be of very little practical value, the great majority of them consider that a positive Wassermann reaction, means that living spirochaetes are present in the body, causing an alteration in the blood of the host and that a "therapeia magna sterilisans" has not been accomplished until the blood has returned to its normal reaction.

What influence salvarsan has upon this blood reaction and the question whether it is superior to mercury or not/
not has caused the publication of a great many conflicting views, but there seems little doubt that these differences of opinion are due to the great variety of methods employed in carrying out the test. It is the experience of the most competent observers that Wassermann's original method is the best and that such modifications as Fleming's, Stern's or Bauer's cannot be relied upon for accuracy to the same degree as the former method. Under salvarsan the Wassermann reaction may be influenced in the following directions. Firstly, changed from positive to negative; secondly, positive to negative then to positive again; thirdly, no effect; fourthly, negative turned to positive.

The time required to change a positive to a negative reaction, depends not upon the severity of the clinical manifestations present, but upon (1) the strength of the positive reaction at the time the test is made (provided the affection is no longer merely local) and (2) to a certain extent the length of time the patient has been infected. When a patient is first infected his blood may give a negative result to the test, but this is not to say that the disease is not syphilis, for in a few days or weeks a positive result may be got and this denotes that the disease has spread from the local source and become general.
In a primary case with no secondary manifestations, if an injection be administered early enough, one may never get a positive Wassermann reaction. This denotes that the disease has been prevented from becoming constitutional. A recently developed positive reaction, if only weakly so, may be changed to negative in a week or two, but if strongly developed the time required is longer and is in direct relationship to the strength of the reaction. The presence of a positive result of long standing however, such as is got in the tertiary stages of the disease or in para-syphilitics, is much more slowly influenced and therefore needs much more vigorous treatment; while in Congenital syphilitics the reaction may remain absolutely uninfluenced, in spite of all efforts made to bring about a change.

In some cases especially those of long standing, an injection may turn a positive into a negative result, but before long the reaction again returns to the positive. This occurs most frequently in old tertiary cases. Lastly it may happen, especially in malignant types and in those who have taken mercury for a long time, who give a negative Wassermann reaction, that an injection will turn this negative result into a positive one for a week or two, but it usually slowly returns to the negative again, getting weaker and weaker until the normal/
normal condition is reached.

Wechselmann, McDonagh, Zeissl and Ivy McKenzie consider that a positive reaction can be changed into a negative one in all cases of acquired syphilis, if the treatment be vigorous enough, and that if there is any sign of a positive result no matter how indefinitely, another injection should be given. Lange, after closely watching 256 cases brought about a negative result in almost all of them by re-injection, and says that he saw cases strongly positive (total inhibition) gradually became less and less so until a negative reaction was obtained (complete haemolysis), and that just before the change was complete the reaction was neither definitely positive nor negative.

Wechselmann and Lange consider the average time for the change to take place is from one to seven weeks. McDonagh, four to six weeks; Schreiber and Hoppe fifty days, while Iversen brought about the desired result in the majority of his cases in from twenty to forty days. Other observers making no note of the time occupied, published only their percentages; Kramayer and Stern got a negative reaction in 50% of their cases. Neisser got it in 44% and Jeronme in 60%. On the other hand Fleming, Schwartz, and others declare that salvarsan in no way influences the chemistry of the Wassermann reaction, whatsoever.
whatsoever, that it is indifferent, neither hastening nor retarding, nor otherwise affecting haemolysis.

The intravenous method of injection has a much more permanent effect upon the blood reaction, than the intramuscular. James McIntosh and Paul Fildes injected thirty patients intramuscularly with doses increasing from .3 to 1.1 grms. as the initial course, and after observing the Wassermann reaction weekly for nine months they found that eighteen out of the thirty either did not become negative or that after becoming negative returned to the positive again. They then injected twenty patients intravenously with doses increasing from .8 to 1.5 grms. and on examining the blood in the same way every week, they found that all gave a negative reaction within ten weeks after the initial course, and that there were no relapses to the positive after a period of ten months. These observers consider that the intramuscular method has about the same amount of influence upon the blood serum as mercury has, but that the intravenous method is much more potent than either, and is admirably adopted for the treatment of all active syphilis.

Ivy McKenzie also points out the superiority of the intravenous method over the intramuscular in regard to its influence upon the Wassermann reaction.
With my own cases very little study could be done upon the Wassermann reaction, because most of the patients being seamen, refused to stay in hospital after the clinical manifestations had healed. However while in hospital their blood was examined by Fleming's method nearly every week, and in the majority of cases it was found distinctly that the reaction became progressively weaker, until about the time when the patient was discharged (in four to six weeks), the reaction was only indefinitely positive. A re-injection or the addition of mercury always seemed to hasten the change. One malignant case that gave a negative reaction on admission remained negative after the injection all the time he was in hospital; and one case negative to start with changed to positive about a week after the injection; he was however gradually becoming negative again when discharged. Five cases changed from positive to negative while in hospital, within six weeks.

Most observers now consider that an intravenous injection of salvarsan has a much more lasting influence upon the Wassermann reaction than mercury, but if the reaction does not change to negative within six weeks or at any time returns to positive, after being negative, treatment has not been sufficient and another injection is indicated.
SECTION VI

Alleged neuro-tropic action of salvarsan and the cause of the general toxic symptoms.

Deaths.
The Alleged Neuro-tropic Action of Salvarsan.

When salvarsan was first given to the Medical pro-

fession and its constitution announced as a synthetic
arsenical compound very grave fears were expressed
regarding the result of its wholesale use.

Arsenic has long been looked upon as having a select-
ive action upon nerve tissue. Therapeutists have used
it as a nerve tonic for centuries, but at the same time
have dreaded the deleterious result of its action upon
nerve structure, should accumulation in the body occur
from too prolonged a use. Dentists use it constantly
for killing nerves prior to stopping teeth. The metal
arsenic accordingly can be looked upon as having a
distinct neurotropic action. And when some five or six
years ago two of its synthetic compounds, atoxyl and
arsacetin, and a little later arsenophenylglycin came
to be used in the treatment of protozoal diseases and
amaurosis occurred there is little wonder that the
compound salvarsan (more powerful than all the rest)
thought by the majority of the profession to be too
dangerous for universal use. Ehrlich had conscientious-
ly experimented with all the compounds leading up to
salvarsan; he discovered his chemico-septors and putting
aside all substances with a pentavalent molecule and
working with only those of the trivalent group he
thoroughly/
thoroughly established the fact that the new remedy (dioxydiamido-arsenobenzol) had absolutely no arganotropic action whatsoever. Great alarm was produced however, when the reports of two cases of optic atrophy following upon the treatment by salvarsan were published, and Professor Ehrlich sent round notices to those to whom the drug had been entrusted asking how many cases of optic atrophy had been produced by the new remedy, and after 40,000 doses had been used not another single case beyond the two already reported, could be discovered.

The reports of these two cases came from Finger and Hallopeau. Finger's case is very interesting; a young woman was treated by salvarsan (.4grm.) for malignant syphilis of long duration, and three months after the injection double optic atrophy set in which progressed to total blindness. It was afterwards ascertained that during the previous year she had been treated with nearly one hundred injections of atoxyl and enesal both synthethic compounds of arsenic. This as far as one can ascertain is the only authentic case of optic atrophy produced by or at any rate following upon, the use of salvarsan for, the case of Hallopeau reported by him second hand, "probably never existed" (McDonagh). The new remedy should never be employed when atoxyl, arsacetin, or arsenophenylglycin, have been used previously for/
for the latter have an accumulative action and salvarsan administered on the top of them, though harmless in itself may precipitate a condition that these other compounds have a tendency to produce. On the 25th October, 1910 Professor Ehrlich issued a circular stating that he considered the reliability of his remedy thoroughly established, and that its only contra-indications were advanced disease of the brain and nervous system, and optic atrophy other than of syphilitic origin.

Since this announcement, many observers have treated syphilitic affection of the eye with marked success; Von Grosz, Sieskind, Sielegsohn, Wechselmann, and McDonagh have all treated syphilis of this organ with salvarsan, and have thereby established the rule that optic atrophy unless of non-syphilitic origin, is not a contra-indication to its use. Wechselmann treated six cases of early syphilitic optic atrophy and not one of them became worse, whereas on the other hand, optic neuritis especially if not far advanced, nearly always entirely cleared up. In one's own cases, one has noticed congestion of veins, oedema of the retina and blurring of the disc, clear up quite satisfactorily. Of course if atrophy is already established the damage cannot be repaired, but if salvarsan is indicated for other syphilitic lesions present, it can be given with tolerable certainty.
that the eye condition, if it be due to syphilis too, will not be made worse by its use. Beside the optic nerve, other nerves have become affected after the use of arsenobenzol namely the sixth nerve, (as in the case A. F.), causing paralysis of the left external rectus in this patient, and the acoustic or eighth nerve giving rise to deafness, or giddiness and vomiting, according to which branch of the nerve is affected. Hallopeau and Urbantschitsch believe these lesions to be the result of a truly toxic action of salvarsan upon the nerves in question, but most observers as Wechselmann, Benario Mcdonagh, and Ehrlich himself, regard them either as neuro-recurrences of the syphilitic disease, or else lesions that have not been reached by the circulating drug. These nerves run in firm canals and it may be as Schreiber suggests that — following the rule of most lesions when acted upon by salvarsan — there is a hyperaemia and infiltration of leucocytes which may give rise to symptoms of compression if there be syphilitic disease of any of these nerves. Ehrmann and Hoffman have demonstrated the presence of spirochaetes in the lymph spaces of nerves, and it is quite possible that syphilis of the nerves existed before salvarsan was given in such cases. Some have asserted that lesions of cranial nerves are more frequent now salvarsan has been brought into/
into practice, but in all probability this is not so. It is more likely that these lesions have been more directly brought under our notice than previously. Besides most of these neuro-recurrences - as the majority of authors now call them - occur in the secondary stages of the disease; Dr. Benario reports from Ehrlich's institute, that out of 14,000 cases only 126 showed complications of the above named nerves, and that 86% of these occurred in the secondary stage. Some of the symptoms are only transitory, but those that are not disappear with further treatment of salvarsan or mercury and iodides. Hirschfelder gives the following reasons why they should be considered as syphilitic and not toxic:

1. The long period elapsing between the injection and the amaurotic or other nervous manifestations.
2. The nature of the pathological process which, as is best shown in the optic nerve, is an irritation and inflammation, and not a degeneration such as is seen with other arsenic preparations.
3. The fact that they occur almost exclusively in the early stages of syphilis;
4. They have never been known to occur in non-syphilitic patients, treated with salvarsan.
5. Their curability with salvarsan or other anti syphilitic remedies.
6. The fact that they occur almost only after small doses of salvarsan.

7. The fact that precisely the same symptoms occur after mercurial treatment.

Out of nearly three hundred injections with which one has been associated one has seen only the one cranial nerve complication (the case already mentioned) and this case though improving was not observed long enough for one to see the ultimate result. One or two observers have had unfortunate experiences in this way, with only a few injections, while others in the same country or even in the same town have had none, out of a large number of cases.

Other Toxic Symptoms.

The general constitutional disturbances which usually follow an injection of salvarsan, especially the intravenous method, are also looked upon by most observers, as being due to the result of the toxic action of the compound. As already pointed out no one can tell in what kind of patients these effects are going to be the most marked. Wechselmann with his neutral suspension preparation - injecting intramuscularly or subcutaneously - rarely got any after disturbances whatsoever, except perhaps/
perhaps a little pain. If he did get a discolouration of the skin at the site of the injection, or a slight rise of temperature with nausea, or on the other hand an erythematous rash, he would call this a local, or a general hypersensitiveness, as the case may be, to the drug. With the alkaline or non acid solution however there was more often a rise of temperature, even up to 103°F, followed by constitutional disturbances which were looked upon by Alt always as toxic in origin. Then Schreiber introduced his intravenous method after which there were severer disturbances than ever, and the temperature rose still higher. As these phenomena do not occur in every case, some patients were said to have a greater susceptibility than others towards the drug. Schreiber however endeavoured to treat psoriasis patients with salvarsan and in these he got no response whatsoever. The same was noticed by other observers when treating non-syphilitics as lupus with salvarsan. Schreiber therefore concluded and Ehrlich now agrees with him, that all the phenomena observed after an injection of salvarsan are due to the absorption of endotoxines liberated at the death of the spirochaetes. The same observer in support of his own theory also pointed out, that the temperature rose highest and the rigors were severest in cases of secondary syphilis, and this/
this was due to the fact that at this stage the organisms were more numerous and more virulent than in the primary or tertiary stages, and at their death more endotoxines are thrown into the circulation. Further, Ehrlich had feared that if several injections had to be given the toxic symptoms would become worse after each injection due to an accumulation of arsenic in the body, but Schreiber declares, and many agree with him, that this does not take place, but rather the reverse, the patient showing less and less symptoms after each injection due to the absorption of less and less endotoxine. 

Wechselmann also considered that the infants who died during his early investigations were overwhelmed by excessive absorption of endotoxines.

Using the same dose and method of preparation and injection as Schreiber, one's own personal experience however seems to indicate but little doubt that the majority of symptoms following an injection, are due to the salvarsan. Endotoxines may play a part, but one has found that in no kind of patient and in no stage of the disease could it be determined how severe the effects following an injection would be. In tertiary cases the disturbances were quite as severe as in secondary cases. Also in malignant types, with a negative Wassermann reaction due to long administration of mercury,
and in primary cases, before the disease has become
general, one has seen quite severe constitutional dis-
turbances. With re-injection too, one cannot say how
the second injection is going to be received; some-
times it produces less symptoms but several times one
has observed much severer effects than after the first.
Taken on the whole, the manifestations following an
intravenous injection are much about the same in most
patients, no matter in which stage of the disease they
may be, or how severely infected, but every now and again
one meets with a patient who shows distinct susceptibility
towards the drug.

One great argument in favour of the toxic theory
as the cause of the rise of temperature and other
phenomena, is that when testing for arsenic in the urine
one found that in those who exhibited but a very slight
rise say to 99° or to 99.6° arsenic could be got in a few
hours, while with those in whom the temperature rose
much higher, say to 102.5° or to 103° no arsenic could be got
for the first twelve and sometimes twenty four hours
after an injection. And further, instead of being
excreted quickly in two or three days, it remained much
longer in the system. The amount of the dose, too,
makes a difference for with small doses the following
effects are always notably less.

On/
On the other hand contrary to Schreiber's experience (57), William Littler of Nashville Tenn., U.S.A. got constitutional disturbances in cases other than syphilitic when treated with salvarsan. This observer treated five pellagra cases with the new remedy, and three of the five gave a marked reaction, in one case the temperature rising to 104° F and in the other two it rose to 102° F. All five denied syphilis, showed no clinical manifestations and all gave a negative Wassermann reaction. He also describes two cases where patients with sarcoma were injected with salvarsan. One of them exhibited next day a rise of temperature to 100° F and vomited twice.

To any one who uses salvarsan freely in both hospital and in private practice, and who sees how extremely well nearly every patient stands the dose prescribed, it is wonderful how little toxic the substance really is.

(58) Dr. Gennerich shows how well some patients stand re-injections. He often gave many re-injections to abstinate cases, especially malignant types. To one patient he gave four intravenous injections and one subcutaneous, in all 2.5 grms in 75 days, while to another he gave two intramuscular, two subcutaneous and two intravenous, in all 3.0 grms in 60 days.

Deaths/
Deaths.

It is impossible to give accurately at the present stage, the mortality following the use of salvarsan, but as far as one can gather some forty two deaths have been recorded. The opponents of the drug declare that many deaths have resulted which have never been published, while those advocating its use assert that the majority of deaths have occurred in spite of, and not on account of, the new remedy; while faults in technique and inattention to definite contra-indications have been accountable for many of the fatal cases that have been notified. McDonagh gives the case mortality at one in five thousand, while Wansey Bayley last July published it at .2 per cent.

Deaths have been reported by many observers, (McDonagh, Oltramare, Hoffmann and others), but the great majority were in old syphilitics, suffering from advanced nervous or visceral disease, and it was the second injection that proved fatal, death following within the first week after its administration. The common symptoms seemed to be breathlessness, cyanosis, convulsions quickly followed by coma and hyperpyrexia, and because post mortem, encephalitis and chronic leptomeningitis were found, Altramare suggested that salvarsan "acted upon the brain in a subject with leptomeningitis in evolution". Gaucher and Caraven however had deaths in cases where meningitis was absent, and Gaucher considers that the symptoms above given are uraemic and due/
due to acute arsenical nephritis. Ehrlich attributed
the earliest cases of death after salvarsan reported
to him to be due in every case to the advanced stage
of the disease in vital organs (as found at autosies),
or to shock in the case of a delicate and emaciated
woman in whom no direct cause could be found.

In the three hundred cases with which I have been
associated no deaths have occurred, nor have any of the
alarming symptoms—recorded by Hallopeau and others—
indicating increased intracranial pressure or uraemia
been found; in fact in no case has there been any
need for the slightest anxiety.
SECTION VII

Clinical experiences with Salvarsan and its effect upon the various syphilitic lesions.
In the history of the cases described in this work, endeavour has been made to show both the rate of healing and the method of healing of the various syphilitic lesions present. Nearly all the cases treated were in seamen, strong young men, and presenting no contraindications.

The majority of them stayed in hospital until all clinical evidence of the disease had disappeared and were satisfactorily passed by the Shipping Federation as being fit for sea. Others however, being of an irritable and more neurotic temperament and tired of confinement which all sailors hate, refused to stay long enough for continued observation of their symptoms, or refused a second injection when their respective lesions lagged in healing or became stationary. All those discharged "healed" were immediately passed by the Federation doctors as being fully capable of discharging their duties as seamen, a privilege, which many had been refused while suffering from chronic clinical manifestations before they came to hospital for treatment. Several of them had been treated with mercury and iodides before, for similar lesions and most of them voluntarily declared that they had never returned to work so quickly, and feeling so well after previous/
previous relapses.

Excepting acute cases or any which had not received previous treatment, all of them thought the effect of the new drug marvellous, as they saw their lesions healing rapidly in comparison with the long and retarded progress which they had previously made under the chronic treatment with mercury and potassium iodide. In nearly every case after an injection the patient felt himself instantly improved, and healing immediately began, thus rescuing his hopes from despair as he left hospital feeling a new man.

Primary Syphilis.

Primary Sore :- The length of time occupied by a chancre in healing depends for the most part on the amount of infiltration or sclerosis present; in fact the greater the induration, the longer is the time required. Chancres situated in different positions present different appearances, varying in their shape, the amount of infiltration, and the presence or absence of necrosed epithelium over them forming a shallow ulcer from which there exudes a sero-purulent discharge. The hardest chancre to heal is one often seen at the end of the prepuce, apparently of deep infection forming a large mass of induration as hard/
Hard Primary Syphilitic Sore - five days old.
Showing the general characters of the granulation tissue at centre of lesion, with marked cellular infiltration. (100 diam.)

Same - Showing the condition of the vessels in the fibro-cellular tissue, their walls are seen to be thickened and becoming fibrosed. This condition increases as time goes on. (300 diam.)
hard as cartilage, and with smooth intact epithelium covering it. In such a chancre, it is hard for the salvarsan to reach the spirochaetes, due to the large practically amount of non-vascular sclerosis in which they are buried. One has seen a chancre of this description, take as long as even six weeks to resolve after a single injection of salvarsan. On the other hand, there is the sore of mixed infection, forming a large shallow ulcer with but a small amount of infiltration around its margins or beneath the granulations on its base. This is the chancre which heals in the shortest time, the small amount of induration quickly disappearing and new epithelium rapidly growing over its floor. Such will probably heal in from five to ten days.

Between these two types there are chancres varying in all degrees of sclerosis and necrosis, and the length of time taken in healing, simply depends upon the ability of the salvarsan to penetrate the infiltrated area and destroy the infecting organism.

The first action of the injected compound is to kill all the spirochaetes with which it comes in contact and then to stimulate the growth of young epithelium. On the death of the spirochaetes the hard indurated area immediately begins to soften, and this is easily demonstrated by palpation in about forty eight hours; and if there is necrosis/
necrosis and a discharge as well the latter quickly dries up and the healthy ulcer formed is covered over with new epithelium in a few days. Thus the three phenomena — the resolving of the induration, the drying up of the discharge, the commencement of epithelial growth — are often seen proceeding hand in hand, until the whole chancre has entirely disappeared.

If there is a large purulent discharge from the necrosed area, or the sore be of a mixed infection i.e. Spirochaeta Pallida plus Ducrey's Bacillus, local treatment with antiseptics should always be administered in addition to the injection of salvarsan, because although discharging surfaces seem to dry up under the latter's influence, such ulcerations heal quicker if the surface organisms are attacked locally. A primary infection leading on to phagedaenic ulceration or gangrene of the penis, "due to a mixed infection of spirochaetes and Rona's Bacillus" (Wechselmann), also does excellently under salvarsan. The spreading ulceration ceases and the gangrenous sloughs drop off, and with the aid of local treatment the whole area is turned into a clean healing ulcer which is rapidly epidermized.

Out of eighteen chancres that were closely watched after a single injection of salvarsan, fifteen of them healed in from five to seventeen days, but the average rate/
rate of healing of most of them was from twelve to fourteen days. Of the other three, one healed in thirty-four days, another in forty-two days, and the third but slightly improved in twenty-four days, after which time the patient left hospital.

Lymphatic Glands:—The first lymphatic glands to become enlarged are the inguinal glands, and these usually show signs of infection after the primary sore has become well established and just before the infection becomes a constitutional disease. They vary in size and usually feel like a chain of beans hard and firm, along Poupart's ligament. On other occasions however one or two glands may swell as large as a two shilling piece, and may be hard, or soft and tender, according as to whether the primary lesion be a case of mixed infection or not.

Other glands in different parts of the body such as at the elbow, in the posterior triangles of the neck, or under the chin, become enlarged later, as the disease travels to them by the blood stream and the lymphatic trunks. The effect of salvarsan upon the different lymphatic glands varies considerably in different patients and in different situations of the same patient. Sometimes/
Sometimes if very large, they will rapidly become much smaller say to a half or a quarter of their original size, but remain in this state for months afterwards. Othertimes, after remaining in the same state as at the time of the injection for a week or two, as though the drug had had no influence upon them, they would slowly and smaller begin to get smaller, until they were just palpable. One found that lymphatic glands rarely went back to their natural size after syphilitic enlargement, but usually remained as little hard lumps just palpable under the skin. Sometimes they would be quickly influenced by salvarsan, but sometimes would remain as the last of all the syphilitic manifestations for which the drug was given, and be visible as the sole surviving lesion for weeks.

The glands most readily influenced by an injection are the submaxillary, the submental, and the sternomastoid glands. These sets even if greatly enlarged will often rapidly recede so as to become just palpable. It should be noted that these are the glands enlarged in constitutional syphilis.

On the other hand those least influenced by salvarsan are those sets first enlarged after the primary infection has been established, namely the inguinal glands. As shown in the cases described, these glands are much more slowly.
slowly influenced by the salvarsan, and remain long after the primary sore and rash have entirely disappeared. In the case of mixed infection, salvarsan has absolutely no influence in preventing any glands becoming inflamed and breaking down with abscess formation.

Lymphatic infection of the penis, whereby the main dorsal lymphatic trunk is made to stand out like whip cord under the skin, is evidently readily influenced by salvarsan, for in the one patient injected, who exhibited this phenomenon, the latter cleared up in one week.

**Secondary Syphilis.**

**Skin Rashes:** Among the many manifestations of secondary syphilis, skin rashes are probably the most constant. They begin to appear on an average six to eight weeks after the primary infection and develop in various forms all of which are more or less readily influenced by salvarsan.

**The Roseola Rash:** This rash is of course evanescent, but if left untreated often takes a long time to fade away, leaving brown pigmented spots. Under salvarsan, however, this rash usually disappears within a week, leaving the skin absolutely clean, and if an injection be given before the later rashes put in an appearance they almost/
almost always never develops. In any of the cases described a papular rash never appeared after an injection.

The Papular Rash:—This rash presents itself in various forms. Sometimes the spots are very small, other times in blotches almost as large as a sixpenny piece, but what concerns us mostly is that the rash is always an infiltration of the skin. Of all the manifestations of the secondary stage of syphilis, this lesion is probably the one least influenced by salvarsan. The time occupied in the disappearance of its different types entirely depend upon the amount of infiltration, and is therefore comparable to the sclerosis of the primary sore. It is often difficult to tell how much the skin is infiltrated, but by running the hand over it and feeling to what extent the spots are raised above the skin, and also by taking up a spot between the thumb and fore-finger and feeling the induration, a fair idea can be got. The largest spots are not always the most infiltrated; one has seen spots the size of a threepenny piece entirely disappear in a fortnight to three weeks; whereas on the other hand small spots closely aggregated forming a lichenoid syphilide, may be almost entirely uninfluenced by a single injection, (as in the case described W.S.). But this type too as a rule clears up in quite a satisfactory manner. (McDonagh)
In some cases a papular rash will fade rapidly after an injection to a certain point, and then take much longer for the remainder to entirely disappear; in other cases it remains uninfluenced for nearly a week and then disappears altogether in a miraculous fashion. But as a rule however — and as in the cases described — it gradually disappears as the infiltration is removed, the dull red spots changing to brown pigmented areas which slowly fade.

Sixteen typical papular rashes were closely watched after one injection of salvarsan; some of them were extremely indurated others only slightly so. The rates of healing were from eight to twenty nine days, but the majority took sixteen days, even including the disappearance of the resulting brown pigmentation. In the case of the one which took twenty nine days to disappear there was another accompanying rash, this healed in fourteen days leaving only the papular rash. The lichenoid rash had only improved - the induration becoming a little less - in twenty four days. Another case that of psoriasis syphilide where the whole of the anterior surfaces of both legs from the knee downwards were intensely infiltrated and raised above the skin and covered with thick scales, only improved after twenty eight days by the infiltration becoming slightly/
slightly less, the masses less raised, and the scales dropping off.

In a third case, that of a deeply infiltrated papular rash accompanied by condylomata, the rash disappeared in twenty-eight days but left very darkly stained areas the same colour as the rash had been, but the infiltration had entirely gone. All the condylomata completely disappeared in eight days.

Squamous Rashes:— All squamous syphilides rapidly disappear under treatment with salvarsan. If there be no infiltration under the scales, the body is usually quite clean in a week; but if there be accompanying infiltration, the latter is left behind taking much longer to subside. It is quite typical in the treatment of syphilis with salvarsan where several rashes are present, say a macular, squamous, and papular, for the two former to entirely disappear in a week or so, leaving the papular as though it were the only rash that had developed.

Pustular Rashes:— Pustular rashes are also very favourably influenced by salvarsan. It is astonishing to see how quickly the pustular heads dry up and the surrounding bases turned into brown non-indurated areas.

Rupia:— It is interesting to see how rupia heals under salvarsan. If the patches be typical and the conical crusts intact, healing takes place between the skin and the /
the crusts, and when this is complete the latter drop off en mass. The process is painless and is therefore in contrast to the painful method of knocking off the crusts and treating the resultant open sores. When the crusts have dropped off in the natural way, there is always a non-adherent darkly pigmented glossy scar, which is also absolutely painless. In one case treated sixteen large rupial patches,situated on the trunk, fell off in nine days.

Echthyma :- Superficial ulcers; usually seen accompanying pustular rashes, should be treated locally with antisepsics in addition to an injection, and the rate of healing simply depends upon the rate in which the ulcerated surfaces epidermize, - it is usually very rapid.

Onychia :- Superficial ulceration under the finger nails does well with salvarsan. There is usually a good deal of inflammation accompanying this syphilide and local treatment in addition is advisable. If there has been considerable destruction and disfiguration, this cannot be repaired, but the painful and inflamed fingers will usually completely heal with one injection. In the only one case treated four very badly ulcerated finger tips completely healed in twenty eight days, enabling the patient to return to his work from which he had been absent many months.

Other/
Other manifestations of the secondary syphilis in connection with the skin, such as condylomata, falling out of the hair, and pustular rashes found in the beard and hair, are no exception to the rule when treated with salvarsan. Condylomata rapidly dry and shrivel up, pustular eruptions in the head and beard rapidly dry up and the scabs drop off, while the hair ceases to drop out almost immediately after an injection.

Mouth and Throat Lesions:—

Rarely is the treatment for any disease seen to better advantage than is the treatment of syphilitic lesions in the mouth, by salvarsan. Mucous patches and superficial ulcers of the lips and buccal surfaces of the cheeks, cracks and fissures of the tongue, all heal with remarkable rapidity.

Secondary lesions as well as tertiary ulcerations of the mouth and throat are often extremely resistant to mercury. It is very common to see patients after a long course of mercury come to hospital, with teeth loose, gums swollen and spongy, mucous patches on the cheeks, red and inflamed throat and very foul breath, complaining that though they have taken their medicine regularly, they have been able to take nothing but fluids or the softest of foods for weeks. It is in these kind of cases that one so often finds the patient emaciated/
emaciated and anaemic. He may be even suffering from
mercurial poisoning and yet these painful lesions
refuse to heal. In such cases it is useless to go on
with mercury. A full dose of salvarsan will do all
that is required in a week. One has often seen such
patients who have taken practically nothing for weeks,
eat a full meal with relish in four or five days after
an injection. The gums go down and the teeth tighten
up; the inflamed throat disappears and the ulcers as
quickly epidermize, and the patient will tell you he
has never had his mouth so comfortable for months.
For the first day, never longer, after an injection the
throat may appear to be worse, i.e. feels hot and burning,
or may feel as though it would crack, but this rapidly
passes off and usually on the third day all is quite
natural again.

Bones:—
Another common accompaniment of secondary syphilis
is pains in the head over the frontal bones, and pains
in the arms and legs especially along the ulnar and
tibia. These symptoms often assume the features of an
evanescent periostitis, occurring at night - but sometimes
in the day time as well - causing the patients to have
a great deal of discomforture, if not weeks of sleepless
nights. Under salvarsan these pains will disappear
in a night. In one particular patient who had had severe pains in his head for days and at times, (especially at night) becoming almost maniacal, got an injection at 4 p.m., by midnight the slight constitutional response had passed off and falling asleep he slept till wakened at eight the next morning. This was the first sleep the patient had had since he came to hospital. Every night after this was peaceful; he required no more hypnotics or Analgesics, and in a few days returned to sea.

Another patient complained of great weakness and stiffness in the muscles of his legs and arms, accompanied with aching pains. He had taken mercury for some months but still the pains continued. In one night after an injection the pains had disappeared and in two days the stiffness had gone.

Joints :-

Among other manifestations, one patient - who came to hospital for treatment - suffered from a synovial hydrops of the right knee as well. This latter condition entirely subsided and the knee returned to its natural condition in one week after an injection.
Affection of The Eyes.

Iritis: - The commonest affection of the eyes in secondary syphilis is iritis, which usually comes on sometime within the first twelve months after the primary affection. One has had the disadvantage of being associated with only two cases of syphilitic iritis treated with salvarsan. One is described in the series of cases in this work. A seaman who developed intense iritis of the right eye with marked photophobia and lachrymation three months after the primary infection. On May 15th he was given .3grm. of salvarsan intravenously. In a few days the photophobia and lachrymation had disappeared and by May 23rd (i.e. in eight days), he could read as well with the right eye as he could with the left. By May 30th all the oedema and exudation of the iris had completely disappeared, the pupil dilated quite equally and looking at both eyes one could scarcely tell which one had been affected. In a few days he was given another injection of .15 grm. to clear up the remains of a rash, and after this there was a slight reaction in the right eye, (a little injection of the circum-corneal blood vessels) but this passed off in two or three days, and when last seen in July 10th the patient was perfectly well (clinically) in every respect.

The/
The other case was that of a colleague who had been suffering with double irido cyclitis for some months, at first considered to be of a rheumatic nature. Later - another diagnosis having been made - he was put on to mercury, but in no way improved. He was advised to try salvarsan, and so accordingly an intravenous injection was given (the dose unknown). When seen two months later he was perfectly well, and spoke in the highest terms of the action of the drug.

McDonagh reports the case of a man who developed severe iritis of the right eye in spite of vigorous mercurial treatment. He was given 45gms. of salvarsan and on the next day he could dispense with his eye-shield. In four days only a slight conjunctivitis remained, while on the tenth day there were practically no symptoms left whatever. When seen nine months later no one could tell that the eye had ever been infected.

Wechselmann also reports a case of irido-cyclitis successfully treated by salvarsan. A young woman developed severe irido cyclitis, marked circum-corneal injection and a large papule growing from the ciliary portion of the iris. Very vigorous mercurial treatment failed to produce any improvement whatsoever. On July 15th she was injected with salvarsan and improvement immediately began; the papule disappeared, and the iritis and/
and cyclitis gradually subsided so that she could be discharged from hospital on August 13th with a vision of one half.

**Choroido-retinitis** :- Syphilitic choroido-retinitis has also been successfully treated by Salvarsan. Fehr and Seeligsohn observed considerable improvement in several cases, "the turbidity of the vitreous body disappearing and the choroidal foci being absorbed one after another."

**Optic Neuritis** :- Sieskind, in his record of cases, reports prompt regression in syphilitic optic neuritis and Anscherlik reports a case where a gumma of the retina cleared up in ten days, after an injection of salvarsan.

One has never had the advantage of treating an advanced syphilitic neuritis with salvarsan. But several times one has seen a blurring of the margins of the disc, oedema of the retina, and congestion of blood vessels, in cases of cerebral syphilis, entirely disappear - after an injection of salvarsan - instead of advancing on to optic atrophy as reported by some authorities as Hallopeau and Professor Finger.
Tertiary Syphilis.

Syphilis is considered to have advanced into its third or tertiary stage after about two years from the time of the primary infection, and at a time when the spirochaeta pallida shows a preference for the tissues derived from the mesoblastic layer of the embryo such as the subcutaneous cellular tissues, bones, muscles and the visera.

The chief characteristic of the disease at this stage is the formation of granulation tissue. And in this, it is in contrast to the primary infection and to many of the manifestations of the secondary stage, both of which are for the most part a definite sclerosis or dense infiltrations. Owing to this fact as we shall see, the tertiary symptoms are influenced much more quickly under treatment by salvarsan than are the manifestations of the other stages.

Gummata: In the cases described, one unbroken subcutaneous gumma almost the size of a two shilling piece and very tender when pressed upon, melted away entirely in twelve days after a single injection. A more interesting case however, is that of a woman (case E.W.) who had had syphilis for four years and resisted all mercurial treatment. Among other lesions of the mouth and nose she/
she had a large fungating mass, growing from the soft tissues of the nasal septum, and big enough to completely hide from view both nostrils. She was given .45 grm. of salvarsan and in less than twenty four hours it began to dry; in fourteen days more the whole growth had entirely shrivelled up, leaving nothing of its existence except a tiny healing ulcer marking the place from which it had sprung.

But the healing power of salvarsan and its stimulation of epithelial growth is seen to greatest advantage in all gummatous ulcerations, whether of the skin and subcutaneous tissues, or of the mouth, pharynx or larynx.

Gummatous Ulcerations of the skin:–

In nearly every case where salvarsan is administered these lesions heal with the greatest rapidity. Immediately after an injection the ulcer may show signs of irritation for a few hours, i.e. it may become a little reddened, or the discharge may be increased, or as is often the case the limb upon which it is situated may ache for three or four hours. These however, quickly pass off and before twenty four hours are over the healing process has commenced. The discharge dries up, and the sloughs - if any - separate from the base, healthy granulations spring up which are quickly covered by new epithelium growing in from the margins of the ulcer.
In the cases described no such ulcer has failed to heal. If the discharge is profuse and there are sloughs to separate, it is best to treat the lesion locally with hot fomentations of some mild antiseptic, to cleanse the ulcer, and this enables the granulations and epithelium to grow faster. Only one example will be given under this heading, but it is typical of all the others mentioned in the cases described.

A man came in suffering from two typical ulcerations, one on the leg, the other on the arm, and both were deep and discharging. He was given a full dose of salvarsan and at the same time both ulcers treated locally. There was no after irritation of the lesions and healing set in at once. When the injection was given each ulcer was nearly the size of a five shilling piece. The leg ulcer healed first; in six days it was covered by a thin layer of glossy epithelium and in another week this epithelium was hard and firm. The ulcer on the arm took a little longer; the granulations had grown up on a level with the surrounding skin in six or seven days, but local treatment having been stopped, a scab formed and this took another fourteen days to drop off, but when it did, firm healthy epithelium covered the place where the ulcer had been.

Gummatus ulcerations of the mouth and pharynx:
Gummatous ulcerations of the mouth and pharynx:

Tertiary syphilitic lesions of the mouth, are not so common as secondary, but among these that do occur, ulceration of the uvula and perforation of the palate are perhaps the most obstinate to treat. One has treated perforations of the palate for months with both iodides and mercury without the slightest improvement resulting.

Under salvarsan however these lesions do extremely well. In the cases described only two had perforated palates and both healed in the most satisfactory manner. The one was the case of the woman already referred to. Her soft palate was absolutely gone — only an ulcerated margin remaining — and there was a hole in the hard palate the size of a pea. After the injection the discharge quickly stopped, and the ulcerating margin — the remains of the soft palate — healed in ten days. But the hole in the hard palate took a little longer; the margins were clean and epithelium was growing over them, but at this date healing was not complete. She left hospital and returned in another twelve days to report and by this time everything had healed. On examining her mouth, excepting for the loss of tissue all parts looked quite natural. The mucous membrane was of a normal colour, and completely covered all places where/
where ulcerations had been. Thus in about three weeks the mouth condition had completely healed.

The other case was that of a man with a hole in his palate the size of a sixpence with foul ulcerating margins. In his case the margins were absolutely healed in thirty seven days after a single injection.

A woman, whom I saw but did not treat, had suffered from the same lesions. On being asked to examine her mouth one saw three holes, one behind the other, in her hard palate. These looked absolutely healthy as though she had been born with them, and her doctor said he had given her salvarsan some three months previously.

Ulcerations of the pharynx:

In the same way gummatous disease of the pharynx heals in an astounding fashion. A seaman who had been taking mercury for some months came to hospital with the following lesions. Deep ulceration and excavation of both tonsils, with large white sloughs and a filthy discharge. Ulceration of both anterior and posterior pillars of the fauces and ulceration of the soft palate with entire loss of the uvula. He coughed and expectorated continually and could only take food with the greatest difficulty. Salvarsan - full dose - was injected intravenously and for the first two days his throat was worse - it was redder and the discharge increased.
increased; but on third day this exacerbation settled down, and healing commenced. On the seventh day the discharge had stopped and the sloughs separated leaving deep clean cavities where the tonsils had previously been. He gained much more rest now the expectoration had stopped. In fifteen days the throat had completely healed, all the ulcerated surfaces being completely covered by epithelium.

Larynx:—To cases of syphilitic disease of the larynx will show that the disease in this region is also no exception to the rule when treated with salvarsan. A Portuguese was admitted to hospital suffering from various ulcerative lesions about his mouth, and also considerable ulceration of the right ventricular band. He was suffering from a good deal of pain and refused to take anything but fluids. No improvement followed four weeks treatment with mercury. He was injected with salvarsan and immediately his pain was relieved. All the small ulcers in his mouth healed, and on the thirteenth day after the injection when he was examined with the laryngoscope it was found that the ventricular band had absolutely healed. His voice too, equally improved. Before the injection no one could understand what he said, but before long he could speak quite distinctly.

The other case also a seaman, came to hospital complaining of/
of sore throat and unable to speak above a whisper. By laryngoscopic examination it was seen that the epiglottis was swollen to twice its natural size with ulceration of its upper rounded margin. He was treated with mercury and large doses of potassium iodide for five weeks without the slightest effect. He was injected with only .4grm. of salvarsan and a good result quickly followed after a slight exacerbation. He was soon able to eat with much comfort and his voice daily improved. When he was discharged twenty nine days after admission, his voice seemed to be almost natural and he could make himself heard from end to end of a fairly large ward. On re-examining the throat the epiglottis was seen to have returned to its normal size (except for a small piece at its attachment where it was still a little swollen), and all the ulcerations had healed.

Superficial Glossitis:— According to McDonagh and others this syphilide does equally well under salvarsan. It is well known to be particularly resistant to mercury and iodides, and in fact it is even said to be made worse by them—especially by mercury when taken internally. There are no cases of chronic superficial glossitis in the cases described in this work, but McDonagh gives the reports on three, and all did extremely well after one injection. These patients had all taken mercury for a long/
long time and the condition was of long standing. Their tongues were greatly swollen, the papillae atrophied, the mucous membrane smooth and glossy, and studded with fissures. None of them could eat with any degree of comfort and all perfectly miserable. Each received a single injection. In one week afterwards one was absolutely cured and the other two almost so, and all three able to eat with perfect comfort.

Lymphatic enlargement in late syphilis:—

Enlargement of the lymphatic glands has been dealt with to a certain extent under the heading of Secondary Syphilis, but as one or two interesting tertiary cases are described, it will be of advantage to relate them here. These glands are much more readily influenced by salvarsan than the early inguinal enlargements. A man suffering from malignant syphilis showed considerably enlarged lymphatic glands in the neck on one side, and the skin over them was very red. He was injected with salvarsan and the glands quickly began to recede, and the skin over them returned to its natural colour. In four weeks after the injection they had entirely disappeared.

Another man was admitted with enlarged glands in several parts of the body namely, in both submental regions, on both sides of the neck, in both submaxillary regions/
regions, and in the left inguinal region. In nearly all the areas the glands were enlarged to the size of a two shilling piece. In three weeks after the injection of .6grm. of salvarsan, the sterno mastoid glands, the submaxillary glands, and the submental glands, were only just palpable in both sides of the neck. The inguinal glands however remained practically the same size as they were at the time of the injection.

Debility:— It is very common to meet with cachexia, general debility, unfitness for work and greatly depressed spirits in cases of late syphilis. The administration of mercury and iodides seems to depress them more and more (especially if they have any persistant lesion which refuses to heal) and they entirely loose confidence in their medicine. An injection of salvarsan, especially if given intravenously seems to act as a huge tonic. They feel better immediately, the high temperature falls to normal, the lost appetite returns and they begin to put on flesh rapidly. New hope is installed and the patient returns to work as he often tells you "feeling a new man."
Malignant Syphilis.

Although it is very difficult to determine the essential factor underlying malignant syphilis, it is usual to designate by that name all syphilitic infections (of more or less long standing) that absolutely refuse to respond to treatment with mercury and potassium iodide. Whether the disease is due to a strain of spirochaetes, a form of infection upon which these drugs have no parasiticidal action, or whether it is due to an idiosyncrasy on the part of the patient towards mercury and iodides is not known. But the fact remains that in certain cases, one lesion after another appears (or as one heals another develops) no matter to what extent mercury and iodides are pushed. In fact it seems often to be the case, the more these drugs are administered, the worse the syphilitic manifestations become.

Among the cases described there are three that can be considered to come fairly well under the heading of "Malignant Syphilis."

Judging by the experience gained in treating these three cases (and also by the reports on similar cases by the many continental exponents of the drug) salvarsan, is the only remedy worth considering when patients suffering from this form of the disease apply for treatment. They are usually in a shocking state of weakness, emaciation/
emaciation, and anaemia, and their mouths only too truly bear testimony to the futility in persevering with the chronic treatment with mercury and iodides. These patients will tell you they have lost two or three stones in as many years, that they are too weak to work, and that when their medicine is pushed to any extent they suffer from violent gastric disturbances or an intractable diarrhoea. And yet, when examined, one usually finds the remnants of previous rashes, a gumma, a recurrent ulcer, or as in the majority of cases a foul smelling ulcerated throat.

The description of the case of a seaman, W. J. M., is of extreme interest. He became infected with syphilis and was soon admitted to hospital where mercurial treatment was started at once. In spite of treatment by oral administration, by injections and inunctions, three distinct rashes appeared each of a different nature. His temperature fluctuated daily between 99°F and 102.6°F, his gums became swollen and his teeth loose, and violent diarrhoea having set in, he left hospital in disgust, after being an inpatient for three and a half months. In a month's time he was readmitted and although he had persevered with his treatment all the time he seemed even in a worse state than when he left hospital. A brilliant papular rash covered his whole body; an ulcer had reappeared.
reappeared on the site of the old scar on the penis, and
enlarged glands could be felt down both sides of his
neck. His mouth was in such a shocking state that for
months he could take practically no solid food at all,
and had lost nearly 3 stones in less than twelve months.
On readmission he was given a full dose of salvarsan
intravenously, and all mercurial treatment stopped.
In exactly four weeks time, a stranger looking at the man
could never have imagined he had been so ill. His mouth
had so improved that he could eat a full meal of any
kind of food with relish. His temperature had remained
normal since the date of the injection, and the ulcer on
his penis had absolutely healed. Every vestige of in-
tiltration of the papular rash had completely disappeared,
and he had gained exactly fifteen and a half pounds in
weight. The man's whole outlook in life had changed;
instead of being miserable and despondent, he was now
bright and hopeful. In three or four more days he was
put upon the working gang of the hospital and after gain-
ing another two or three pounds in the following week,
he left hospital. On August 5th he secured another ship
and went back to sea.

The second case is of not quite so serious a type
but it too, is interesting. A seaman, A. R., got in-
fected with a hard chancre and at once attended hospital
for/
for treatment and was put on to mercury as usual. Even after two months continual treatment a rash developed, and later sores broke out on his body, head and legs. He was then taken into hospital and only after six months vigorous treatment with large quantities of mercury, did these manifestations slowly disappear. He continued taking mercury, but in eight months time his throat became extremely sore and an ulceration appeared at the junction of the hard and soft portions of the palate, which quickly perforated, leaving a hole the size of a sixpenny piece. Soon after this, huge gummatous ulcerations broke out on both sides of his neck and spread upwards on to both cheeks. He also developed very bad stomatitis, a synovial hydrops of the right knee joint, and a remittant temperature rising to 100.4 F. He was given a full dose of salvarsan and as in the case with the other patient, improvement immediately followed. Of course there was a great deal to heal, but in thirty-eight days there was an immense improvement. The huge ulcerations of the neck had healed - excepting a little soft scar tissue on his cheeks, from which a serous discharge exuded. The hole in the palate had completely healed and its margins covered by firm healthy epithelium. The stomatitis had disappeared in a few days as usual, and the knee joint returned to its natural size almost as/
as quickly. As the serous exudate from the small areas of soft scar tissue on both cheeks remained obdurate, he was given another but smaller dose of salvarsan. And although further improvement followed the discharge appeared intermittently for two months, after which time it ceased altogether. The patient was greatly benefited both physically and mentally and when he left hospital was determined to return to sea.

The third case is that of a clerk who was infected with syphilis twelve years ago. The usual rash and secondary oral manifestations developed, but disappeared under treatment. About two and a half years afterwards however, a foul discharge kept coming from his nose, and he felt as though he had a chronic cold in the head. After some months he started mercurial treatment again, but the condition did not improve until a large piece of bone came away. At this time he was abroad and returned to England for further treatment. After a time as the condition did not heal up and the discharge still continued he was sent to Germany, and there received a three months course of mercurial injections. After this course he was much better, and again went abroad. After some time however, the discharge reappeared and more necrosed bone came away and he was treated with mercury pills and calomel blown up his nostrils. This treatment/
treatment seemed to aggravate the condition, so after some months he returned to England a second time and underwent a course of inunctions. He was again recommended to go to Germany and there treated by similar methods (inunctions and injections). But his nose steadily got worse and the whole of the nasal septum, bone, cartilage, and soft tissues came away leaving a big hole in the centre of his face. The bridge of his nose fell right in, his left eye became greatly inflamed and external strabismus developed due to the loss of origin of the internal rectus muscle. He could take mercury no longer. At first he could tolerate it fairly well but now it made him ill every time he underwent treatment. By the time he had returned to England again, salvarsan was placed upon the market and he was recommended to have an injection. He consented to this and an injection was given intramuscularly into the muscles of the back. A certain amount of improvement certainly followed, the filthy discharge stopped and the nose became dry. After about six months however, the discharge began to reappear and ulceration began to creep around the remaining soft parts of his nose on to the face. This time he came to hospital for treatment. When examined the bridge of the nose had gone, and a large hole represented the nostrils. There was/
was a purulent discharge with a foul smell and ulceration creeping outwards on to the upper lip.

An intravenous injection of .6grm. of salvarsan was given and the discharge quickly began to dry up. In twelve days the discharge had practically dried up, and the ulceration stopped spreading. In four weeks after the injection, the patient declared his nose to be drier, and healthier, than it had been for many years; in fact so comfortable did it feel that paraffin injections were given to raise the bridge. When last seen two months after the injection, the bridge had been raised to a respectable height and as no discharge came from the cavity this was kept closed by plaster, and the patient breathed continually through his mouth.

McDonagh, Wechselmann, and Schreiber, have reported excellent results in malignant cases where mercury or mercury in combination with iodides failed to bring about an improvement in the patients' condition.
SECTION VIII

Syphilis of the Central Nervous System.

Treatment with Serum.
Alt was the first to use salvarsan in syphilitic conditions of the central nervous system. He had been treating paralytics with arsenophenylglycin with fairly good results, but later substituted salvarsan in place of the more poisonous drug. Having determined that 3grm. was quite a safe dose, he injected eighteen paralytics deeply into the gluteal muscles. The results were very good; the majority of the patients improved and in the rest the disease was rendered stationary. Several other continental observers followed Alt's example with more or less success, but Ehrlich warned them against the use of the drug in those with advanced degenerated conditions of the nervous system, and in a private communication to Dr. Bernard Sachs stated that already two patients, suffering from advanced disease of the nervous system, had died after being treated with salvarsan. Theoretically, salvarsan is not supposed to have any effect upon parasyphilitic conditions, but in the early stages of tabes and general paralysis a certain amount of improvement may be expected. In cerebral syphilis on the other hand, where the lesion is due to the presence of the spirochaete itself, quite a good result should follow if the disease has not advanced too far.

Michaelis/
Michaelis treated fifteen cases of tabes, eight of paralysis and four of cerebral syphilis. Of the latter (i.e. cerebral syphilis) three cases cleared up splendidly and the fourth - when the report was written - had not been under treatment long enough. Of the other cases he found that general improvement followed in tabetics in ataxia, but he does not hold out much hope in advanced degenerative conditions.

Meyer treated twelve paralytics without any permanent improvement.

Glück and Favento both treated paralytics without effect, but in three tabetics the pains disappeared.

Sießkind, published a case of typical tabes with symmetrical atrophic ulcers of the big toe, in which the ulcers healed quickly, and the lancinating pains and the ataxic symptoms disappeared.

Wechselmann, who had a large experience noticed improvement in cerebral syphilis with tumour formation, in luetic apoplexy, in tabes and in early progressive paralysis. This author considers the use of the new remedy quite justifiable in all syphilitic nervous conditions. He has observed the rapid disappearance of serious intercostal neuralgia that required the constant employment of narcotics, and the disappearance of lancinating pains almost without exception. He has also observed/
observed gastric crises to cease or become less severe, and lost sexual power to return to a remarkable degree. Wechelmann does not know however, if these improvements are constant, but they are certainly not due to suggestion as improvement does not commence sometimes for two or three days.

McDonagh gives some interesting results of his observations. He treated nineteen cases of tabes and in two of these the pains were made worse, in five however the pains vanished and so far have not returned, while the other twelve remained in statu quo. He noticed the knee jerks return in one case, while in another a perforating ulcer slowly healed.

McDonagh considers the patient should be well examined and if the disease has not advanced too far an injection should be given. But as the constitutional disturbances after an injection in nervous cases are sometimes very severe, only half a dose (.3grm.) at the most should be given, and if improvement follows, this dose can be repeated. The patient however, should always be told the risks he is undertaking.

In the cases described in this work there are three of active syphilis of the central nervous system, but none of tabes or of General Paralysis. The former consist of (1) a cerebral tumour causing a facial paralysis, (2)
(2) epileptiform seizures, and (3) syphilitic affection of the spinal cord.

The cerebral tumour was in a negro, who was admitted complaining of constant headache and weakness on walking. On examination he was seen to have complete left sided facial paralysis and his tongue when protruded deviated to the left side. Though left handed the left grip was weaker than the right. His eyes showed nystagmus on extreme lateral rotation, and ophthalmoscopically showed blurring of both discs especially the left, suggesting an early optic neuritis.

He was given a full dose of salvarsan and all the above manifestations slowly subsided. He refused to stay in hospital more than eleven days, but even in this short time the constant headache had gone, he improved greatly in walking, and the facial paralysis was hardly evident even on laughing.

The second case mentioned was that of a seaman who was thought to be developing general paralysis, and who was constantly troubled with epileptiform seizures. He was injected with salvarsan and he became much brighter and more confident in himself immediately. He only stayed in hospital however, sixteen days after the injection, but he was again seen 103 days after the injection and no more fits had occurred during that period.
period. The constitutional disturbances in this case were certainly severer than are seen usually in ordinary syphilis.

The third man injected presents a very interesting case. He had been suffering from severe spastic paraplegia of both legs with numbness and tingling. There were several areas of anaesthesia about his body and legs and at times he was quite unable to hold his urine and faeces. He received two injections of salvarsan intravencously, .3grm. and .6grm. respectively, with an interval of four weeks between them. Before the first injection he could only walk with the aid of crutches as he was quite unable to lift his toes off the ground. Improvement set in immediately the salvarsan was administered, and when it was seen how well he progressed after the first small injection, he was given another larger one to complete the cure as far as possible. He left hospital after forty six days, and when discharged he could walk about the ground freely and easily without the aid of a crutch or a stick. All the tingling sensations and areas of anaesthesia had disappeared; the knee jerks had practically returned to their normal condition and the organic reflexes had almost regained their natural strength.
Treatment with Serum.

As there is undoubtedly an element of risk in giving salvarsan to advanced para-syphilitics, a method of treatment has been devised which is considered to obviate the danger in some degree. It has been shown by a French physician that dioxydiamido-arsenobenzol is secreted into the Cerebro-Spinal fluid. Working upon this fact the physicians of West House and Craig Edinburgh House Asylums introduced the idea of treating patients - i.e. general paralytics - by injecting a salvarsan serum directly into the spinal canal. The serum is obtained from an actively syphilitic patient, forty-eight hours after an intravenous injection. At this time it is presumed, the patient will have circulating in his blood, firstly, a certain amount of arsenical compound; secondly, endotoxines liberated at the death of the spirochaetes; and thirdly, antitoxines produced by the absorption of the endotoxines.

The technique is to place a bandage around the patient's upper arm, and a needle with a good calibre is driven into the most prominent vein. The escaping blood is collected in sterile test tubes and allowed to stand for twelve hours. After this time, the serum and the clot have separated, and after pouring the former from the latter, the serum is now centrifuged to deposit any/
any blood cells that it may contain; - decant and the serum is now ready for use.

The injection into the spinal canal of the para-
syphilitic is made in exactly the same way as for spinal anaesthesia. A lumbar puncture needle is driven into the spinal canal between the third and fourth lumbar vertebrae, and five or six c.c. of cerebro spinal fluid allowed to escape. About eight to ten c.c. of the salvarsan serum is now taken up in a syringe, and injected through the lumbar puncture needle into the spinal canal.

If the injection is made in the afternoon there is usually a rise of temperature either the same night or the next day.

The temperature of general paralytics, especially in the secondary stage, is usually subnormal, about 97°F, and if after an injection the temperature rises to say 99°F it is practically equivalent to a temperature rising from 36.4°F to 100°F, or even higher, as regards the constitutional disturbances of the patient. After a serum injection in a general paralytic the temperature has been seen to rise from 97°F to 102°F. There are always accompanying effects similar to those after an intravenous injection of salvarsan namely, headache, nausea, or vomiting, and even rigors.

There/
There is always a leucocytosis up to 10,000 and it has once been seen up to 15,000.

It is the custom of these experimenters to inject their patients once a week, until four doses have been given, and usually the constitutional effects are less after each dose.

As general paralytics often become stationary, or spontaneously recede, under generally improved conditions, it is very difficult to say how much improvement has been derived from this form of treatment. However, four out of the twenty patients already injected have certainly improved by it. They are less talkative, better workers, and understand their surroundings and conditions much more intelligently. With the other sixteen, on the other hand very little improvement, if any, can be noticed.
SECTION IX

Salvarsan, in the treatment of Congenital Syphilis in adults and infants.
Administration during pregnancy.
Congenital Syphilis.

In the cases described only two patients were treated with salvarsan, for congenital manifestations, and these were cases of interstitial keratitis.

Congenital interstitial keratitis, in marked contrast to the secondary syphilitic affections of the eyes, is very little influenced by an injection of salvarsan. McDonagh injected seven cases without improvement following, and Sieskind experienced the same unfavourable result with his cases. Seeligsohn injected two cases; one slightly improved, but in the second case the injection did not prevent the other eye from becoming affected.

This experience was also encountered in the following case.

A seaman aged eighteen was admitted to hospital suffering with severe pain, lachrymation and photophobia of the left eye. On forcing the eyelids apart, intense circum-corneal injection, iritis, and interstitial flakes over the cornea, were seen. He was put on to the usual local treatment (atropine etc.) accompanied with mercurial inunctions; but after four weeks perseverance very little improvement was seen. It was therefore thought advisable to try salvarsan, and a full dose was injected intravenously. Immediately an/
an exacerbation set in - the lachrymation and photophobia, the circum-corneal injection, and the pain, all being intensified - and this took three or four days to subside. After eighteen days the circum-corneal injection of vessels, though still present, was considerably less than on admission, but the keratitis remained just the same and the patient could only just see a hand held before him against the light at ten inches. On exactly the twenty fourth day after the injection of salvarsan, the right eye became affected, and showed exactly the same symptoms as the left had done; and these increased so rapidly and the eye became so painful that a second full injection had to be administered.

The reaction of the right eye to the drug was similar to that of the left, taking some days to settle down. The keratitis, however, went on increasing, while the opacity in the left eye remained in statu quo. In four weeks after the second injection the opacity of the left eye began to clear up a little and the patient could count fingers at twelve inches; but the right eye remained unimproved and salmon coloured patches covered the whole cornea. During the next four weeks the cornea of the left eye certainly cleared a little and the vision improved, but the opacity of the right eye remained much the same, the only improvement being a clearing/
clearing of its margins and the centre changing from salmon colour to white. Thus over a period of one hundred and three days, during which time two full injections of salvarsan had been given, the patient made very little progress towards a good recovery.

The second case is that also of a young seaman, aged nineteen, who was admitted for double interstitial keratitis. At the time of the injection of salvarsan both corneas were fairly opaque, but there was no injection of the circum-corneal blood vessels, as both eyes had had a considerable amount of local treatment. With the right eye the patient could read distinctly fingers at three feet, but at only half that distance, with the left eye. In five days after the injection, marked improvement could be noticed in the left eye, and with it he could see to read fingers at three feet also. From this time onwards the opacity in both eyes slowly decreased, until after nearly a hundred days he could read the large print of a book fairly well, but only with great difficulty the small print of a newspaper. There was, however, a good deal of opacity still to clear up, especially in the left eye, for although it was the first to be influenced by the salvarsan, it ultimately proved to be the more obstinate of the two.

It/
It is very difficult to understand, compared to other congenital syphilitic lesions, why interstitial keratitis should be so unfavourably influenced by salvarsan. In the first case it is clearly demonstrated that, when one eye is affected an injection of even a full dose will not prevent the other eye from becoming affected also. In this respect then, salvarsan is no better than mercury, while in the second case an injection after the acute stages had passed off, had very little influence in clearing up the resultant opacities in the corneae. On the other hand, syphilitic keratitis in rabbits produced by inoculation, yields to salvarsan with the greatest rapidity.

Seeing that the spirochaetes of congenital keratitis are, in all probability, present in the cornea at birth, and live for some years in a non-vascular medium, McDonagh considers that these organisms have undergone some biological and chemical change, and therefore behave differently towards the drug when compared with the organisms that produce a vascularization soon after inoculation, - as in the case with keratitis of the rabbit.
The treatment of infants suffering from Congenital Syphilis.

Wechselmann was the first to inject infants born with advanced syphilitic disease. When asked first (among others) to ascertain the clinical value of salvarsan, this author chose these little patients who were destined to almost certain death. He injected five infants suffering with syphilitic pemphigus with his neutral suspension preparation, commencing with a dose of .03grm. and later reducing it to .015grm. Of the five infants treated, four died and one recovered, the former had had doses of .03grm. and the latter .015 grm. repeated twice. At the autopsy, no changes either macroscopically or microscopically, could be discovered suggesting arsenical poisoning, and Wechselmann therefore concluded that death was due to the overwhelming quantities of endotoxines brought about by the death of vast numbers of spirochaetes, in such delicate little patients. He then reduced his dose by one half and repeating this when necessary he achieved much better results. Then, in March 1911, Döblin published his results of treating infants with salvarsan. He injected subcutaneously and intramuscularly six congenital syphilitics, one to three months old, with doses varying from .025grm. to .06grm. Their general condition before/
before injection was good in three cases, moderate in one case, and bad in two cases. Out of the six, two improved, but four died within the first four days after the injection; and at the Autopsy on these fatal cases, one case (that of a well nourished child who had received .05grm.) showed oedema of the subcutaneous tissue and mesenteric glands suggesting, as Döblin considered, acute arsenical poisoning. Of the two cases that survived, the skin eruptions cleared up, but there was no improvement in the glandular swellings nor in the rhinitis which were present at the time of the injection.

(88)
Taege, hit upon another plan. A young woman came to his clinique in the last months of pregnancy, exhibiting a distinct syphilitic rash, large condylomata on the genitals, and a positive Wassermann reaction. He waited until the child was born to see to what degree it was infected with syphilis; and for the first fourteen days after the delivery - which was at full term - the child looked colourless, wilted, and senile, and refused to take the breast. Then five pemphigus vesicles appeared which grew rapidly larger, and paronychia developed upon three fingers of the right hand. The mother herself was then injected with .3grm. of salvarsan and after the ordinary constitutional disturbances had passed off she became wonderfully improved.
improved. The child was induced to take the breast immediately after the injection, and for the first two days the existing symptoms became much worse, but then suddenly, a marked recession of all manifestations took place. By the fifth day after the mother's treatment, the grey fawn colour of the infant had changed to a normal red; the paronychia was absent and the pemphigus had gone; and instead of wailing he now cried vigorously and easily emptied the breast at each feeding. A few months later Duhot (independently of Taegge's observations) injected a young woman who had just been delivered of her baby, and who was suffering from severe syphilitic ulceration of her face. He found much to his surprise that the child (which was markedly syphilitic as well as the mother) after being allowed to suckle, improved wonderfully. The infant, at the time of the mother's injection showed nasal catarrh, papular efflorescences all over the body, and isolated pemphigus vesicles; it cried faintly and fed very sparingly. On the third day these manifestations suddenly began to disappear; the nasal catarrh vanished, the efflorescences and vesicles disappeared, and within the first week the dark red colour of its skin had assumed its normal rosy hue. In this case, as in the last, the whole condition of the child changed completely; it soon took the breast eagerly, the senile appearance/
appearance was replaced by a natural expression, and the skin tightening up, the child began to put on weight rapidly—forty ounces in three weeks.

Besides Taege and Duhot, Dobrowitsch and Reubischik confirm the good influence upon the suckling child by injecting the mother with salvarsan. But two observers, Jeanselme, and Jesionek, cannot agree with Taege and Duhot, as to the certainty of a good result to a syphilitic child by treating the mother.

Jeanselme injected sixteen mothers and allowed the child to suckle its mother in every case. He found that in some instances a good result was no doubt brought about, but he often got recurrences, and in some cases mercury had to be given to finish clearing up the syphilitic manifestations left in the child. Out of the sixteen cases, Jeanselme considers six were successes but ten were failures, and in four cases mercury had to be given to clear up the lesions that refused to heal.

Jesionek got very bad results in two infants fed upon an injected mother's milk. In both cases there was a violent eruption of fresh syphilides and the children seemed to be overwhelmed by the disease. He advocates giving salvarsan to goats and feeding syphilitic children upon the milk of goats thus treated.

Taken upon the whole however, most workers upon the subject, consider that to a more or less degree, a favourable/
favourable result can certainly be gained by injecting the mother, for congenital syphilis in young infants.

To what then can this result be due? Professor lhrlich after seeing the observations of Taege and Duhot, considered the therapeutic effect to be produced by antitoxines excreted in the mother's milk. Neither Taege nor Duhot found any arsenic in 100c.c. of milk taken from injected mothers, and Scholtz and Wechselmann found only traces of inorganic arsenic when the milk was treated with HCl and KClo3.

The antitoxines are formed by the absorption of endotoxines liberated by the decomposition of spirochaetes, and in all probability there are endotoxines, antitoxines and traces of inorganic arsenic in the milk of these mothers, but the inorganic arsenic being in such minute quantities can have no possible therapeutic effect. Therefore, we are forced to believe that the influence upon the disease in the child is brought about by the formation of the above named antibodies.

It is now recognised however, that a "cure" cannot be expected from these antitoxines alone, and in the case of syphilitic infants a small dose (.004 to .005 grm. per pound weight of the child) of the drug itself should be injected, after the good influence of the mother's milk has ceased to exist.
Pregnancy.

All pregnant women bear an injection of salvarsan well; and in reviewing the literature, one can find no case (beyond the one reported by Glück) in which an abortion was produced, no matter in what month of pregnancy, the injection was administered.

McDonagh injected one woman in the sixth month of pregnancy for primary syphilis, and at full term she was delivered of (as far as could be judged) an absolutely healthy child. Wechselmann, on the other hand, injected three pregnant women suffering from advanced syphilis and only one gave birth to a healthy child; the other two infants showed slight signs of syphilis.

Erwin Langes investigated this form of treatment for syphilis in pregnant women with some care; he injected eight pregnant women and twelve puerperal women suffering from syphilis, and in none of the pregnant women were labour pains produced by the injection of the puerperal women, six had given birth to syphilitic children, but in no case was a woman delivered of a syphilitic child when the injection was administered during pregnancy. Langes therefore considers that salvarsan cannot be given too early in pregnant syphilitic women.
SECTION X.

The need for re-injection. The administration of mercury and salvarsan.
It is now generally recognised by those who use the new remedy, that in the majority of cases one injection alone is not sufficient to bring about a cure. That it does in a few cases is undoubted (at least as far as can be judged at present) especially in the primary or early secondary stages when the system is not so saturated with the disease as in the later stages. But all observers have had relapses and the numbers vary according to the method of injection and to the length of time under which the patients are kept under observation. Broadly speaking there are two occasions when a reinjection may be needed. Firstly, to clear up retarding lesions; secondly, for a return of the disease.

It is the rule that after the first injection the symptoms rapidly recede, either to complete recovery, or else stop at a point just before recovery is reached. It is easily noticed when the lesions cease to heal and become stationary, and this is the time for another injection; the response is immediate and if there is any risk at all, it is less at this juncture than when given within the first 8 to 14 days as advised by some observers. It was suggested by Wechselmann and others that it was due to what they called "resistant strains" of the infective organism, that occasionally a patient was found whose lesions did/
did not regress rapidly under the influence of Salvarsan. But Margaret Marguiles, working upon this point with rabbits infected with syphilis, found that no symptoms were resistant. Very small injections were given and often repeated, and every time the lesions slowly healed and the spirochaetes, at no time, became resistant to salvarsan - in the case of rabbits at any rate. The reason why in a few cases, lesions are but slightly influenced by one injection, is, in all probability because, they are not reached in sufficient quantities by the circulating drug, and another injection should be given to bring about a sterilization of the foci that refuse to heal.

Then, regarding the second occasion, either the return of a syphilitic lesion or the return of a positive Wassermann reaction should be equally considered as an indication for another injection of Salvarsan. It is impossible to give a percentage of relapses at this early stage because experiences are so varied, and with my own cases none have been kept under observation long enough to gain an accurate idea. So far only one man has returned with fresh manifestations after those for which an injection was given had cleared up, and this was about 3 months afterwards with mucous patches on his lips.

Most pathologists now think that if patients are closely/
closely watched and their blood continually tested every few months, the first indication of a return of the disease is the return of a positive Wassermann reaction. Of course, the reaction may never have been rendered negative after the first course, and in such a case further treatment should have been persevered with. But, after having once become negative even for several months, it may again become positive due to some focus hidden in the internal organs, which has again (after a latent period) become active, and supplies the blood with the necessary material for a positive reaction, and as time goes on another fresh outbreak of serious lesions may be expected. For such a return of a positive reaction another injection is indicated.

**Salvarsan and Mercury.**

Mercury, or mercury and potassium iodine, can always be given along with salvarsan, and there is no doubt that a greater beneficial effect can be got, along with a more comfortable course of treatment, than with either alone. Mercury has undoubtedly (though to not such a degree as salvarsan) a specific action upon the Spirochaeta Pallida, but besides this action it helps to absorb infiltrated lesions, so that when/
when an injection of the new arsenic preparation is
given after a course of mercury, the symptoms often
clear up much more rapidly than when the former is
given alone. It is often therefore advantageous to
give a fortnight's or three weeks' course of vigorous
mercurial treatment, before an injection of salvarsan
is given in secondary syphilis with an intensely
infiltrated rash, or greatly enlarged inguinal glands.
Both drugs act upon the spirochaete at the same time,
but neither causes the organism to become immune to
the other so the two drugs go well hand in hand. In
malignant and in old tertiary cases however, where a
great deal of mercury has in all probability been
taken, this drug should be stopped altogether when
salvarsan is given because in these cases the patient
is usually suffering greatly from mercurial poisoning
as well as from syphilis.

On the other hand, the administration of mercury
along with salvarsan often aids in bringing about
a negative Wassermann's reaction especially in the
eyear stages of the disease. In one or two instances
in the cases described, the Wassermann reaction under
the combined administration became negative quicker
than under salvarsan alone.

Greven says that the elimination of arsenic from
the system after an injection of salvarsan is retarded
when the patient takes mercury as well.
SECTION XI.

The Demonstration of the Spirochaeta Pallida as an aid to diagnosis.

Personal opinion of Salvarsan, and its advantages and disadvantages in comparison with Mercury.
The Demonstration of the Spirochaeta Pallida as an aid to diagnosis.

Before the year 1905 the medical profession possessed no knowledge as to the real cause of syphilis; the disease was simply a clinical entity, and a diagnosis had to be made upon certain definite manifestations as they appeared at, or some time after the date of infection. In 1905 however, Schaudinn and Hoffmann discovered the Spirochaeta Pallida, and since then it has been definitely established as the cause of syphilis. Firstly, because it is found in almost every syphilitic lesion, especially in the primary and secondary lesions though less frequently in the tertiary; secondly, it is found in the organs of fetuses and infants inheriting syphilis; thirdly, its transference from human beings to monkeys, rabbits, and dogs causes the disease in these animals; and fourthly, it can be cultivated upon artificially prepared media.

Before this date a patient with a lesion suspicious of syphilitic infection was put to a great disadvantage, especially in the primary stages. On the one hand, he either had to start a prolonged and uncomfortable treatment with mercury to prevent secondary symptoms developing, or on the other, he was obliged/
obliged to wait (until the development of secondary symptoms) for a definite diagnosis to be established, by which time his chance of a cure was very much reduced.

At the present day however, besides our clinical knowledge of a syphilitic infection, we have a valuable acquisition in a rapid method of demonstrating the infective organism by which we can clinch the diagnosis when the clinical manifestations are as yet indefinite. Only two of the latest methods will be described as they are the most simple and at the same time the most certain, namely, (1) "The Dark Ground Illumination"; and (2) the "Indian Ink Method".

For the first method a special apparatus is required- A Leitz condenser bull's-eye lens, and a Nerst lamp. With this method the organism is found almost at once and in its active state.

To procure the spirochaete a film is made. Wash the chancre carefully with soap and water to remove necrotic debris and surface organisms. Then, sometimes by merely rubbing with a piece of gauze, but better by scraping with a scalpel, at the junction of sound and necrotic tissue, serum exudes from the depths of the chancre, and it is in this serum that the spirochaetes are looked for. If there is bleeding it is promptly stopped by pressure with gauze or by the application of a little absolute alcohol. In a minute or two...
serum flows freely and washes the infective organism from the deeper parts of the sclerosed tissues. A large drop of serum is put on to a clean slide and a cover slip placed on top and rung with vaseline to prevent evaporation. By means of the special apparatus under the microscope the spirochaetes are seen to be moving about and can be studied in the living condition. If enough serum cannot be got a little sterile broth added to the former helps to keep the cover slip sufficiently raised above the slide to enable the organisms to move freely. They are seen to rotate on their long axis in either direction; their motion is very rapid but not necessarily accompanied by a change of position, and they progress from place to place but not so rapidly as other forms of spirochaetes.

The Indian ink method of Burri is the simpler of the two. It can be performed in any consulting room, without the need of a special apparatus, and by any person even though he be without a definite experience in the staining of microorganisms.

Serum is obtained from the chancre as in the previous method and a drop placed upon the slide. About an equal amount or perhaps a little more, of Gunther - Wagner's Indian Ink is added to the drop of serum and the mixture spread over the slide and allowed to dry without heating. When dry, it is immediately/
Scraping from a Syphilitic primary sore, treated by Burri's Indian ink method. Shows the characteristic appearance of the spirochaete pallida. (1000 diam.)

Film treated by the same method, showing the spirochaete refringens. (1000 diam.)
immediately placed (without a cover-slip) under the oil emersion lens of the microscope, and all spirochaetes are seen as clear thin wavy lines unstained by the Indian Ink.

By both methods, Red blood corpuscles and several forms of spirochaetes will be seen, but the spirochaeta Pallida must be definitely recognised. In size, it varies in length from about one to three times the diameter of a red blood corpuscle (7 to 21 microns) and has the shape of an extremely slender thread closely wound in a cork screw form, the windings being very acute and absolutely regular.

The Spirochaeta Refringens - the spirochaete which most often accompanies the Pallida in smears or scrapings from genital chancre - is very easily differentiated. Its thread is thicker, and it has but 4 to 6 convolutions (the Pallida possesses 10 to 14) which are much broader and much more wavy in form, than those of the organism of syphilis. Under the Dark Ground Illuminator it is seen to be much more motile than the Pallida; rapidly rotating about its long axis, and actively shooting backwards and forwards.

With the Indian Ink method one has obtained spirochaeta Pallida in suspicious sores on the genitals in five minutes after first seeing the patient, and/
and an injection of salvarsan given the same day.

With this easy method of diagnosis, the patient who has contracted syphilis, has a very much better chance of a cure than he had when it was often necessary to wait for the appearance of secondary symptoms or the development of a Wassermann reaction, both of which denoting that the disease has become general and that very much more vigorous and prolonged treatment is necessary than would be the case if the diagnosis were made at the outset.

The effect of Salvarsan upon the Spirochaeta Pallida:

Sieskind made extensive microscopical examinations of spirochaetes after an injection of salvarsan. He found that their screw like and oscillating motion is considerably decreased and frequently only slight movements are seen which gradually cease altogether. They become bulky and swollen, and attain a much greater refracting power but nevertheless, they retain their spiral form even in this condition of immobility. Taken on the whole he considers that the new arsenic preparation exerts a distinct specific effect upon the organism of syphilis.
Personal opinion of Salvarsan, and its advantages and disadvantages in comparison with mercury.

In advocating a new remedy for a disease, the question, can it be given universally, and in all cases, immediately presents itself. In my own personal experience salvarsan can, and should be given, in every case of syphilis that does not present the contra-indications already described. Of the cases of syphilis that present themselves for treatment I have met with none - beyond advanced parasyphilics - who were not in a fit state to receive the drug, and a great many other observers are also in the same position, thus showing how seldom these contra-indications are met with. Again, if a full dose cannot be administered on account of the patient's condition, a modified one nearly always can and that is certainly better than none at all. Then this smaller dose can always be repeated at different intervals and the desired effect (as far as possible) attained in the same way as with a much larger single administration.

Of course, Ehrlich's original idea of a "therapia magna sterilisans in one fell swoop and within twenty-four hours", is but rarely attained, and that salvarsan will not entirely replace our well tried remedy mercury, is also thoroughly well established.
But at the same time, only a very few of those who have conscientiously worked with the new drug, will not admit that salvarsan is the most potent remedy at our disposal, and that if it will not absolutely cure syphilis it will certainly rob the disease of most of its terrors.

The contention that it is too expensive; or too difficult to administer, and produces too severe constitutional disturbances so that patients refuse a second injection, is but poor argument when treating a disease like syphilis. And taken on the whole, one has found (excepting for a few timid neurotics) that patients are only too willing to submit to almost any form of treatment in their desire to rid themselves of their disease.

**Primary syphilis:**— It is in primary syphilis that one has the best chance of bringing about a cure. If the infection is fairly recent, and no secondary symptoms are present it is always advisable to look for the Spirochaeta Pallida by one or the other of the methods described — especially in innocent looking lesions — and these got, there is no doubt about the diagnosis. The next procedure is to have the serum tested for the Wassermann reaction, and if this prove to be negative, then in all probability the disease has not become general. Most syphilologists now/
now recommend the destruction of the chancre, either by excision where possible, or by caustics etc. where the former is impossible; for, if the Wassermann reaction has not become positive, then there is much less chance of its doing so if the site of infection is got rid of when the disease is still local. Besides, supposing a few organisms have got into the blood or lymphatic streams, these few are much more easily eradicated by an injection of salvarsan than if they were allowed to traverse the circulatory system in swarms. On the other hand, Hoffmann has definitely established the Spirochaeta Pallida in the old scars of healed chancre which at any time could light up a new infection. One has often seen sores reform on the sites of old chancre that have healed for months or even years. McDonagh recently reports three cases of what he calls auto-infection. He had treated three men presenting symptoms of primary and early secondary syphilis with a single injection each of salvarsan. All the manifestations healed and the Wassermann reaction turned to negative in each case. But at varying intervals, each man got another indurated swelling on the site of his previous infection, and a little later a typical secondary rash developed.
developed. The Primary infection, though healed still contained organisms in its scar, and by injury or irritation lighted up a fresh infection, which spread through the system a second time after the first had been eradicated by the injection of salvarsan. This McDonagh asserts could not possibly occur if the original chancre had been destroyed.

The most advantageous time of all then, to give the new remedy, is before the Wassermann reaction has become positive either from the fact that no spirochaetes have succeeded in getting into the general circulation, or if they have, so few in numbers that the blood has not been turned from its normal into an abnormal state, and they are easily destroyed by the injection of a full dose of salvarsan. By these methods and at this stage of the disease Ehrlich and all those who advocate his remedy are convinced there is the best chance of a positive cure of syphilis.

In the case of a colleague who became infected with primary syphilis .6 grm. of salvarsan was administered intravenously and in about 5 weeks the chancre healed. It is now nearly twelve months since the date of infection and although no treatment beyond the one injection of Salvarsan, has been administered, no secondary symptoms have developed and the/
the Wassermann reaction has remained permanently negative.

Secondary Syphilis: With secondary syphilis the chance of a cure is less than with primary, but not so remote as with tertiary. The lesions of this stage - especially the skin lesions - are apt to be indurated and therefore resist for a longer period than those of the tertiary stage. But if a cure is judged by the blood reaction, then the earlier stage as a rule has the advantage, as the Wassermann test is more easily rendered negative, (most pathologists notice that it gradually becomes weaker and weaker in a regular manner and does not exhibit irregular fluctuations between positive and negative as is often seen under mercurial administration).

Tertiary Syphilis: Tertiary lesions heal the most quickly simply because the tissues attached do not become so indurated, and the drug can acquire access to the infective organism. But it is in this stage that relapses are most likely to occur on account of the greater amount of tissue to be sterilized, seeing that internal organs are very likely to be affected as well as the external, and the Wassermann test lingers on in a positive reaction showing that spirochaetal products continue/
continue to be poured into the blood.

In whatever stage of syphilis salvarsan is administered there are certain benefits which stand out most clearly and cannot be denied by its most vigorous opponents. These are, firstly, its tonic effect upon the patient; secondly, its reduction of the cachectic state; thirdly, its very active healing power especially in stimulating the growth of epithelium; fourthly, the rapid relief of pain; and fifthly, (as Wechselmann pointed out) the restoration of sexual power where it has been lost in those suffering from nervous syphilis.

It is really wonderful to see how a feeble patient will begin to improve almost immediately after an injection. His appetite and strength return in such a way that the patient seems to think he has taken a new lease of life.

A fluctuating temperature is invariably brought to the normal within a few hours, and the cachectic look of the patient is changed to quite a normal expression.

The healing power in stimulating the growth of epithelium is phenomenal, and speaks for itself as a good testimony for the new remedy.

The almost immediate relief of pain, in which mercury is practically powerless, is extremely gratifying. Though in some cases pain is made worse for a few/
few hours, it matters but little when compared with
the intense relief that follows after the reaction has
passed off; while in other cases relief ensues al­
most immediately following an administration.

Ehrlich considers that pain in syphilis is due to the
action of the products of the spirochaetes upon the
tissues, and not to the anatomical damage, and that
the rapid relief of pain after an injection is due to
the neutralisation of these products by the salvarsan.

Wechselmann reports several cases where sexual
power was restored after being lost for several
years, and so vigorously indulged in that severe repressive
measures had to be adopted.

In comparison with mercury salvarsan has many
advantages. One injection is more potent than a
moderately long course of mercury, and frequently,
cases are met with where mercury is intolerable, but
salvarsan is well borne, and results are attained that
mercury would fail entirely to bring about.

Relapses are less severe after salvarsan than
after a course of mercury. If symptoms return after
treatment with mercury, it is simply surmised that
treatment has not been sufficient and a further
course is administered. Just so with salvarsan,
when symptoms cease to improve or if they return,
another/
another injection is indicated, and the result is quicker and in most cases more far-reaching than when mercury alone is relied upon. The digestive disturbances, and toxic effects arising out of the uncertainty of the dosage in the oral administration of mercury, and the discomfort and uncleanliness in the inunction method are disadvantages entirely got over by the employment of Ehrlich's remedy. The disadvantages of salvarsan are very trifling indeed in comparison with the potency of its therapeutic efficacy and the advantages it possesses over mercury. The constitutional effects of an injection, though in a few instances a little severe, are in most cases slight and easily borne by the patient, the manual dexterity necessary for administration is easily attained and the expense will in time be overcome. The greatest disadvantage that faces us at present is the alleged neurotropic action. If it turns out to be a fact that the new remedy has a toxic effect upon the optic and acoustic nerves, then this action is indeed a great disadvantage; but at present the evidence is overwhelmingly in support of the manifestation being a neuro-recurrence and not due to a neurotropic action, as explained under the heading of...
of toxicity. So valuable does one personally consider the new remedy, and so trifling the constitutional disturbances following an injection, that one would give every patient with even only a suspicious lesion on the genitals after exposure (where spirochaetes could not be found and the Wassermann reaction is negative) a full dose by intravenous injection as the best method of saving him from constitutional syphilis.

Though there are different procedures recommended by the various observers in the treatment of this disease, the most common and the one now recommended by Ehrlich himself is, to start with an intravenous injection of a full dose of salvarsan followed by the administration of mercury provided this drug has not been taken to excess already. If in 4 or 5 weeks the symptoms have not entirely disappeared and the Wassermann reaction has not been rendered negative, another intravenous injection should be given followed by more mercury; and this procedure is continued until all the clinical manifestations are absolutely healed and the Wassermann reaction - tested every 3 months - is rendered permanently negative.

How permanent the highly satisfactory results of/
of this new remedy will be, is beyond the power of any observer to answer at this stage, but judging by the observed phenomena we are undoubtedly upon a fairer road to bring about a cure than we were before Ehrlich made his beneficent discovery; time alone however can give to the profession, and to the world the answer they require.
SECTION XII

SUMMARY.
Summary.

The substance salvarsan is the dihydrochloride of the dioxydiamido-arsenobenzol. It is readily soluble in warm water forming an intensely acid solution, and if an alkali (such as NaOH) is added, the base (the dioxydiamido-arsenobenzol) is thrown down as a precipitate; if now, more alkali is added this precipitate redissolves forming an alkaline solution of the disodium salt.

The base (the dioxydiamido-arsenobenzol) is injected as the neutral suspension preparation, and the solution of the disodium salt as the alkaline solution. Both are injected subcutaneously or intramuscularly.

For the intravenous method of injection, the alkaline solution is diluted up to about 300 c.c. with distilled water or normal saline, and injected into one of the superficial veins of the body in exactly the same way as in intravenous transfusion of normal saline solution for shock. The dose is .6 grm.

The contra-indications to the use of salvarsan are chiefly advanced disease of the heart and circulatory system, and advanced degenerative conditions of the brain and spinal cord. Disease of the liver and kidneys are less serious contra-indications, but the functional/
functional activity of these organs should be ascertained if they are greatly degenerated.

The most comfortable and most advantageous way of giving the substance is by intravenous injection and it is astonishing how seldom one meets with contraindications to the use of salvarsan. For the following reasons I consider intravenous injection the best method of giving the drug.

1. Because the drug is in its most potent form, and brought more into contact with the spirochaetes. 
2. There is no continual absorption of arsenic. 
3. There is rapid elimination rendering a second injection safer. 
4. One is better able to regulate the dosage. 
5. The whole of the dose injected is brought into action. 
6. There is no inconvenience of a coagulated mass in the tissues. 
7. It is painless when compared to other methods. 
8. The by-effects of an injection are soon over and never return. 
9. The patient is out of the doctor’s hands quicker as there is no risk of necrosis etc.

The efficacy of an injection depends upon the ability of the salvarsan to reach the syphilitic lesions. If the lesion is a very sclerosed one and only/
only slightly vascular, healing is necessarily much slower than in soft vascular lesions. In primary sores the amount of sclerosed tissue varies considerably, hence some primary sores heal quickly in about a week, while others (very hard and sclerosed) may take nearly six weeks to heal. The same applies to enlarged lymphatic glands, and the papular rashes of secondary syphilis where induration is present in a more or less degree. In all other skin lesions such as condylomata, gummata and ulcerations where the circulating drug can get good access to the syphilitic part, healing is rapid and is at about the same rate in all patients.

Syphilis of the central nervous system usually greatly improves under treatment with salvarsan; although but little hope can be held out in advanced para-syphilitic cases, great benefit is got by an injection when the lesion, either in the brain or spinal cord, is due to presence of the spirochaete itself.

The influence of salvarsan upon the Wassermann reaction varies considerably, and depends upon the strength of the reaction at the time the test is done before an injection is administered. Sometimes the change towards haemolysis commences soon after an injection, other times it is very slow indeed or even may/
may not start at all; but when the change does take place the reaction slowly and gradually becomes negative in a regular manner, so that just before haemolysis is complete the reaction is neither negative nor positive.

After an experience of nearly three hundred cases treated with salvarsan - of which fifty were treated by myself and with the other two hundred odd I was closely associated - I am convinced that this drug is much more potent than mercury and should be given to every syphilitic patient who presents himself for treatment, provided he does not show distinct contraindications.

One injection however, is often not enough, and if after four or five weeks time all clinical manifestations have not disappeared and the Wassermann reaction not rendered negative, another injection should be given, - or if necessary another two or three injections.

In most cases also, treatment should be supplemented with mercury as this drug too exerts a specific action upon the Spirochaeta Pallida, and also by aiding the absorption of sclerosed lesions allows the salvarsan to gain better access to the infective organism.
Cases described - 45.

<table>
<thead>
<tr>
<th>Primary and Secondary</th>
<th>Tertiary</th>
<th>Malignant</th>
<th>Cerebral</th>
<th>Congenital (Interstitial Keratitis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>2</td>
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</table>

Primary and Secondary include: Chancres, Secondary rashes, Rupia, Psoriasis Syphilide, Lymphatic glands, and Iritis.

<table>
<thead>
<tr>
<th>Discharged clinically cured in less than three weeks</th>
<th>Discharged clinically cured in less than five weeks</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>9</td>
<td>1. kept in 91 days on account of complications. (case A. F.) 2, relieved after 28 days.</td>
</tr>
</tbody>
</table>

Tertiary Syphilis include: Gummata, gummatous ulcerations of the skin, larynx, and pharynx.

<table>
<thead>
<tr>
<th>Clinically cured in less than 3 weeks</th>
<th>Clinically cured in less than 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>3</td>
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</tbody>
</table>

Malignant Syphilis: Three cases; discharged (clinically cured) to return to work in 116 days, 36 days, and 13 days respectively.
Syphilis of the central nervous system includes: -
Tumour left side of pons, epileptiform seizures, and spastic paraplegia.
Discharged (clinically cured) to return to work in 12 days, 16 days, and 46 days respectively.

Congenital Syphilis - congenital interstitial keratitis.
Two cases; improvement in 103 days, and 54 days respectively.
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31. Neisser
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33. Fleming
34. Schwartz
35. James McIntosh
36. Paul Mildes
37. Ivy McKenzie

38. Finger


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43. Seeligson
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ERRATA.

Introduction, Nos. 24, 37, 97, and 103, should read.
"Recent Methods in the Diagnosis and Treatment of Syphilis".
- Browning and McKenzie.
NOTES ON CASES TREATED.
G. W. - Seaman - Age 30.

Admitted - 10th February, 1911.

History: Got infected about six months ago by a large chancre on prepuce causing phimosis. There was doubt as to whether the chancre was syphilitic or not.

Feb. 12th: Patient circumcised. The foreskin was tough and seemed indurated as though infected with syphilis.

March 6th: The circumcision wound will not heal, the stitches have all cut their way out and there is a profuse discharge. Though mercury has been given by the mouth for a fortnight and the penis dressed with antiseptics every day, there is practically no attempt at epithelium growing over the open ulcer that has formed. The glans penis are quite healthy. There are no appearances of secondary symptoms.

March 10th: Wassermann's reaction is positive. Mercury stopped.

March 12th: Intravenous injection of salvarsan .6 grn. in 300 c.c. solution at 9 p.m. By midnight the temperature had risen to 99 .8 , pulse not affected. Constitutional Effects: Nausea and later slight vomiting; headache but no rigor.

March 14th:
March 14th: - The discharge around the glans penis made slightly worse but to-day is beginning to dry up.

March 20th: - Wonderful improvement. The discharge has dried up and epithelium is rapidly growing over. The induration around about is practically all gone.

March 26th: - Completely healed and all induration gone. Epithelium has grown over the circular ulcer around the glans with great rapidity.

Wassermann reaction is weakly positive.

Discharged - 14 days after the injection.
PRIMARY SYPHILIS

J. E. - Seaman - Age 28.

Admitted - March 2nd 1911.

History: Infected by chancre seven weeks ago. He received treatment from ship's doctor for two weeks before admission. Only local treatment administered, and no mercury given by the mouth as condition was not considered to be syphilis.

State on Admission: A large sore size of a shilling on dorsum of penis, with a purulent discharge but no induration can be felt. No rash. Treated with black wash dressings.

March 18th: For sixteen days patient has been treated with black wash and fresh dressings daily. The ulcer is now quite clean, but no healing has taken place. Large pale granulations have sprung up but absolutely no sign of epithelium growing over them. Wassermann's reaction is weakly positive.

Patient has had no mercury.

March 20th: Intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 9 p.m. By 12-30 temperature rose to 100 but fell again by morning.

Constitutional Effects: Rigor, followed by shivering, at/
at midnight; headache (slight); no vomiting or diarrhoea.

March 25th: - Rapid improvement; the granulations have shrivelled up and epithelium is growing in from sides of sore.

March 30th: - Almost healed, only a very small piece to be covered by epithelium.

April 2nd: - Discharged - cured - ten days after the injection.

No secondary Syphilis had developed.

Wassermann reaction not taken again.
PRIMARY SYPHILIS.

S. B. - Seaman - Age 27.

Admitted - 20th July 1911.

History :- Got infected by chancre on corona two months ago. Hard, raised, discharging sore size of sixpence. No rash or other phenomena beyond chancre.

Wassermann reaction positive.

July 27th :- Given salvarsan .6 grm. in 300 c.c. solution at 9 p.m. Temperature rose at 12 midnight to 99.8° and then rapidly fell to normal.

Constitutional Effects :- Only slight rigor.

July 31st :- Discharge dried up from chancre.

Aug. 3rd :- Induration rapidly disappearing and epithelium growing over ulcer.

Aug. 10th :- Chancre completely healed.

Wassermann reaction slightly positive.

Discharged - 12 days after the injection.
PRIMARY and SECONDARY SYPHILIS

G. C. - Fireman - Age 40.

History: - Infected by chancre on foreskin near the fraenum - great swelling and oedema of prepuce.

Feb. 15th: - Patient circumcised and put on to mercury. Wassermann reaction negative.

Feb. 25th: - Circumcision healed except where chancre is situated - the region round about the fraenum has become very swollen and indurated.

March 26th: - Swelling and induration less but still sore is very slow in healing.

April 6th: - He has broken out into a diffuse papular rash - dull red in colour - in blatches all over body and face. The skin seems intensely indurated in parts. Wassermann reaction now positive.

Chancre completely healed.

May 4th: - Rash has become very scaly and is covering the body in every part except the scalp. Mercury stopped. Salvarsan injected intravenously .6 grm. in 300 c.c. solution at 8-30 p.m.

By 10 p.m. temperature had risen to 100, pulse to 108 " 12 p.m. " fell " 99.8, " 104 " 2 a.m. " normal, pulse 80.

Constitutional Effects: - Slight shivering attack; no/
no vomiting; no diarrhoea; no headache.

May 6th: - Rash certainly commenced to fade.

May 8th: - Rash much fainter and less scaly. It cannot be felt by running hand over body.

May 10th: - Improvement over body and especially the legs. Very little difference over the face.

Wassermann reaction positive.

May 15th: - Marked improvement all round. Rash on legs and body so faint, it can hardly be seen. On face, though greatly improved, it is still easily seen.

May 25th: - Rash on body absolutely gone. On face a few pigmented spots are still seen over malar prominences where rash was very thickly indurated.

Wassermann reaction weakly positive.

Discharged to go to sea - 21 days after the injection.
PRIMARY and SECONDARY SYPHILIS.

T.B. - Seaman - 21 years.

Admitted - 18th March, 1911.

History: - Infected two months ago by a large chancre on side of foreskin. Five days before admission a rash broke out.

State on Admission: - Large chancre on under surface of prepuce and latter swollen to an enormous degree.
Thick papular scaly rash on every part of the body.
He complains of severe headache. Temperature 99, pulse 100.

March 22nd: - Temperature rises every evening to 100 or 100.4 and falls to normal in the morning.
Injection of salvarsan .6 grm. in 300 c.c. solution at 11 a.m., temperature normal at the time.

By 1 p.m. temperature had risen to 101.2 pulse to 100
" 2 p.m. " " " 102 " 116
" 3 p.m. " " " 102 " 116
" 4 p.m. " " " 102.4 " 120
" 5 p.m. " fell " 101.8.
" 6 p.m. " " " 101

By midnight it had again fallen to normal, pulse to 80.

Constitutional Effects: - Rigor and vomiting at 4 p.m., bad headache but no diarrhoea.

March 29th: -/
March 29th:-- Each day since the injection, temperature has risen in the evening, and down again in the morning, but each evening rise is less than the previous one. 24th - 101, 25th - 100.8, 26th - 100, 27th - 99.8, 28th - 99.2, 29th - 98.4.

The induration of the chancre began first to disappear on the 24th. To-day there is no induration left, leaving only an open sore to be covered by epithelium. The prepuce is still somewhat oedematous and can't be retracted. Rash changed definitely on the 26th, i.e. became paler, more scaly, and smaller. The rash was very marked over his chest, some of the heaped up masses of epithelium being as large as a threepenny piece and very red in colour. They are now paler, flatter and less induration round about.

April 4th:-- Patient is feeling well. The rash is disappearing especially from chest. Face is now clean. Chancre nearly healed, only a very small piece left to be covered by epithelium. Prepuce easily retracted.

April 8th:-- Chancre healed. Remainder of rash slowly fading. Mostly pigmented spots left.

April 11th:-- The rash has practically disappeared, only one or two pigmented spots left - no induration to be felt anywhere.

April 19th:-- Discharged to go back to sea - 28 days after injection.
PRIMARY and SECONDARY SYPHILIS.

A. M. - Seaman - Age 24 years.
Admitted - 22nd March, 1911.

History: - He contracted syphilis and gonorrhoea six
weeks ago and a rash appeared four or five days later.
He has taken no mercury.

State on Admission: - Hard chancre on under surface of
foreskin - collar shaped - no abrasion of epithelium.
Distinct enlargement of both inguinal glands.
Rash, macular scaly syphilide all over body.
No sore throat; no headache; feels well. One or two
mucous patches in his mouth.

March 31st: - Intravenous injection of salvarsan .6 grm.
in 500 c.c. solution. Temperature rose to 101 F but
fell to normal in about three hours.

Constitutional Effects: - Only a slight shivering attack.

April 4th: - Sore on penis softer and rash distinctly
paler.

April 8th: - Sore on penis about half gone - induration
rapidly disappearing. The rash too has greatly
improved - the fine scales have gone and the remaining
spots are quite pale.

April 16th: - The chancre has completely melted away.
The rash is still visible in parts, but needs close
inspection to detect it. Goes back to sea to-morrow.
Discharged - 16 days after the injection.
PRIMARY and SECONDARY SYPHILIS.

A. F. - Seaman - Age 44 years.

Admitted - 14th May, 1911.

History: - Infected seven weeks ago. Three chancres, one on side of foreskin; one on corona; diamond shaped one on fraenum. All three with septic infection and discharging profusely. The one on the fraenum is the most indurated.

Rash: - marked in blotches, each blotch the size of a threepenny piece all over trunk, back and front - and also slightly on arms.

Complaining of constant headache.

May 16th: - Injected with salvarsan .6 grm. in 300 c.c. solution at 9-30 p.m. By midnight temperature had risen from normal to 101.6, pulse to 100, but by 6 a.m. it fell to normal again and pulse to 80.

Constitutional Effects: - Slight rigor; slight nausea; headache - very severe.

May 23rd: - Headache, which lasted for a day or so, has completely gone. A sore throat of which he had been complaining is also cured.

Chancres: - The coronal chancre is cured; the one on foreskin has only a very small piece left to be covered by epithelium - induration completely gone. The diamond/
diamond shaped one on the fraenum is the least affected
but the induration is disappearing.
Rash :- Over the arms it has gone and on the body it is
now so faint it can hardly be seen. This rash has
disappeared quicker than any yet seen even though in
large blotches.
Wassermann reaction positive.
June 8th :- The two chancres have completely healed.
The indurated one is much smaller, though the induration
is slow to disappear- the floor of the ulcer is clean.
June 16th :- Fraenum chancre has still induration
around its edges. It is disappearing very slowly.
Wassermann's reaction is positive.
June 27th :- Fraenum chancre is still indurated
though the raw surface is now covered with epithelium.
It is in the form of a deep pit with hard rolled edges
and quite dry.
Patient is put on to mercury to see if this induration
will resolve
Wassermann's reaction is negative.
July 3rd :- Induration is still present.
July 10th :- Induration slowly disappearing and edges
of pit contracting. He is now complaining of severe
headache, and pain running through his left eye and
keeps this eye closed to get relief from pain.
July 13th :-
July 13th: He has developed a very definite paralysis of the left sixth nerve with considerable diplopia and pain over left temporal region. No inflammation however in the left eye. Retina is healthy and length of vision normal. Wassermann reaction still negative.

July 16th: Left eye is still the same as on the 13th. Induration has completely disappeared from chancre, leaving in its place a tiny round hole running for a quarter of an inch up into the glans penis.

July 20th: No change in left eye and paralysis of left external rectus muscle same as on July 13th.

July 24th: Eye condition is somewhat better, the paralysis is still present but the pain has gone and he can stand the light better.

July 31st: Hole in glans penis contracting.

Aug. 3rd: In statu quo; he is still taking mercury.

Aug. 16th: Punctured shaped hole in penis closed up. There are no scars to show where any of the chancre were situated. The eye condition is much the same though the examining oculist considers the paralysis is a little less. There is absolutely no pain and he stands the light well. On a whole patient feels extremely well and wants to return to work. Wassermann's reaction is negative.

Discharged - 91 days after the injection.
PRIMARY and SECONDARY SYPHILIS.

J. B. - Seaman - Age 33.
Admitted - May 20th, 1911.
History :- Infected six weeks ago - he has taken no mercury.
State on Admission :- An indurated mass in the region of the fraenum; a discharging and indurated ulcer on the dorsum of the glans penis; balanitis. No rash, no sore throat. Epitrochlear, sternoc mastoid, and sub-maxillary glands slightly enlarged.
May 25th :- A papular rash has developed all over the body - very fine and only slightly indurated.
Given mercury 1 gr. thrice daily.
June 6th :- Rash, which had become more marked since May 25th, has now faded to a considerable extent, but is still easily seen.
The indurated mass around the fraenum is, but little, if at all affected. Ulcer on the glans penis is healing, and the discharge stopped with local treatment.
Mercury increased to one and a half gr. thrice daily.
June 10th :- Mercury stopped. Salvarsan injected .6 grm. in 300 c.c. solution at 4 p.m. By 8 p.m. temperature rose to 101°, pulse from 80 to 96.
Temperature fell to normal at midnight.
Constitutional Effects :-
Constitutional Effects: - Slight rigor; vomited once; no headache; and no diarrhoea.

June 16th: - Rash almost entirely gone; ulcer on glans penis is rapidly healing, epithelium can be seen growing in from edges over the granulations.

The indurated mass near the fraenum, though still marked is considerably reduced.

June 23rd: - The rash has entirely gone and the ulcer on the dorsum healed. The induration under the fraenum is still further reduced, and should not be long before it too is entirely gone. Lymphatic glands are but slightly affected.

June 27th: - Ulcer healed and all induration entirely disappeared. No clinical evidence of syphilis left. The Wassermann reaction has remained positive, but is greatly reduced in strength.

June 29th: - Discharged - 18 days after the injection.
M. H. - Seaman - Age 33.

Admitted - 1st June, 1911.

History: - Infected ten weeks ago by a large mixed sore near fraenum. In three or four days time another started on foreskin. In four weeks a rash appeared.

State on Admission: - The two sores have almost joined and both are hard and indurated, with a profuse discharge. Small papular scaly rash all over body. Throat red and sore but not ulcerated. Left inguinal glands about the size of a two shilling piece.

June 3rd: - Intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 1 p.m. By 6 p.m. temperature had risen to 100.6, and pulse to 88.

Constitutional Effects: - Practically nil.

June 8th: - Throat cleared up on second day. Rash certainly fainter.

Wassermann reaction positive.

Sores on penis much drier and little less indurated.

June 16th: - Sores on penis rapidly healing. The one on foreskin is almost cured. The other on fraenum is about half its original size, clean, and healthy. Rash still evident, though fading and desquamating.

Inguinal/
Inguinal glands not yet influenced by the injection.

June 21st: Both sores on penis healed. Desquamation of skin ceased, and only faint brown pigmented spots left, where rash was; these too are fading away. Wassermann reaction positive.

Discharged - 17 days after the injection.
PRIMARY and SECONDARY SYPHILIS - PHAGEDAENA.

G. K. - Seaman - Age 24.
Admitted - 7th June 1911.

History: - Infected seven weeks ago by a sore on fraenum of penis. A rash appeared two weeks afterwards. Then ulcerations broke out over both legs - three on the right leg and one on the left. Next rupeia developed over the shoulders and one large patch on right nipple.

State on Admission: - Half of the glans penis have ulcerated and sloughed away. The sore having started near the fraenum has spread around the glans and over the meatus, destroying completely more than the anterior half of the glans. There is a profuse discharge.

Legs: - On the right leg a large shallow ulcer - ecthyma - the size of the palm of one's hand is situated over the inner surface of the calf. Two smaller ones, and a shilling, (size of two shilling piece, respectively) are over the anterior surface of the tibia, and outer aspect of the knee joint.

Left leg: - One small ulcer size of a shilling on outer aspect of the ankle joint.

All these named ulcers are shallow, but discharge a dirty purulent material.

Rash/
Rash: - A sparsely scattered papular rash all over body but not infiltrating the skin to a great extent.

Patient looks extremely ill; very anaemic and thin. He complains of a sore throat, great weakness and loss of appetite. Small hard glands in left groin and submaxillary region.

Temperature fluctuates to 101°F daily.

Patient has taken no mercury whatever.

Wassermann's reaction is positive.

June 20th: - Intravenous injection of salvarsan 0.6 gm. in 300 c.c. solution at 9 p.m., temperature being 100°F.

By 10 p.m. temperature rose to 101°F pulse to 96, but gradually both fell to normal by 4 a.m.

Constitutional Effects: - Rigor and shivering at 10 p.m. for one hour; nausea; rather severe diarrhoea, lasting from the time of the injection to the following evening; no vomiting; no headache.

June 21st: - Temperature rose again this morning to 101°F and it is keeping up all day. The diarrhoea is rather troublesome.

June 22nd: - Temperature fell again to normal this morning - coming down by lysis.

June 23rd: - The red and inflamed throat has cleared up. Patient has enormous craving for food whereas before/
before the injection (apart from the inability to swallow on account of the throat symptoms) he had absolutely no appetite at all.

June 27th:— Swelling and oedema of penis — which before the injection was intense — has now absolutely disappeared. It is receiving local treatment with hydrogen peroxide and black wash. The discharge too has gone leaving a clean granulating ulcer size of a two shilling piece. All the sores on his legs are clean and granulating, though of course they are dressed with antiseptics. Healing has commenced slowly in all the ulcers from the margins. The rupia is not yet influenced. Rash is slightly fainter and changing colour to brown.

Temperature has remained normal since the 22nd June. Patient is much stronger, eating well, sleeping well, and putting on weight.

Wassermann's reaction is positive.

July 3rd:— He has come out in an erythematous rash all over the body, very itchy and irritating.

All the ulcers are granulating well, especially the one on the penis, and the large one on inner side of right calf. The latter is now only half the original size. The rash is fading, though some of the spots are still distinctly seen.

July 10th:
July 10th:— All the sores are healing and epithelium is growing over the granulations.
Penis healing well and epithelium growing in over the granulations from the glans. Rash is still visible.
The erythema has gone.
Wassermann's reaction is positive.

July 13th:— Still rapid improvement, especially of penis.
He complains of difficulty in micturating due to obstruction at the meatus which is in the centre of the ulceration.

July 17th:— Wassermann's reaction is positive.

July 20th:— Very great improvement since July 13th.
Sore on penis almost healed, only a piece the size of a millet seed left to be covered by epithelium.
All the ulcers on the legs have completely healed, except the large one on the right calf, which is now only the size of a shilling. The rupia has dropped off, leaving well marked highly coloured scars. The secondary rash has practically gone. The submaxillar glands are scarcely palpable, but the groin glands have hardly been influenced at all.

July 24th:— Still improving. The penis has healed, except for a very slight serous discharge, coming from the meatus. This too is becoming less and should disappear in a day or two. All the skin lesions are healed/
healed except the one on the right calf, which has only a very small piece left to be covered by epithelium. No vestage of the rash remains. The scars are firm and flexible.
Patient is looking a new man having become very fat. Wassermann's reaction is still positive, but becoming weaker.
Discharged - 34 days after the injection.
F. E.

Admitted - June 26th, 1911.

History: - Infected with syphilis two months ago.

He declares that when the sores first appeared he had seventeen chancre on the prepuce and glans. They were all very small and in one place on the corona five ran together and formed one moderate size sore. Rash appeared four weeks ago. He has taken no mercury, but burnt the sores with caustics and applied black wash.

State on Admission: - Several pits and scars of healed chancre are easily seen. On the corona there is one sore about the size of a threepenny piece, where he says five have run together.

Rashes: - 1. Ordinary roseola.

2. Papular - with red bases and pustular tops.

Both rashes are fairly distributed over the body, arms, and legs, but none on the face.

June 28th: - Intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 9 p.m. Temperature 98, pulse 82.

By 10 p.m. temperature rose to 103 and pulse to 116.

" 12 midnight " fell to 101 " " 112

" 4 p.m. " " " 96.6 " " 80.

Constitutional Effects: - Severe rigor and shivering for half an hour; heavy feeling in his head; slight vomiting/
vomiting, and violent action of the bowels.

**July 3rd**: Marked improvement in both rashes, especially the pustular, which is drying up.

A subcutaneous gumma on the thigh, size of a two shilling piece, (previously very tender) is now greatly reduced in size. The chancre is drying up and rapidly healing. The induration is markedly less.

**July 10th**: Gumma gone; sore on penis healed; rash improving.

Wassermann reaction positive.

**July 13th**: Further improvement in rash.

**July 15th**: He refuses to stay in hospital any longer.

The roseola rash has gone. The papular rash has greatly improved though still present in parts.

Wassermann's reaction is still positive.

Discharged - seventeen days after the injection.
PRIMARY and SECONDARY SYPHILIS.

C. M. - Seaman - Age 32.

Admitted - 1st July, 1911.

History: He got infected by a sore on foreskin in June and soon a bubo developed in the left groin. At first it was doubtful if the sore was syphilitic, but the bubo increased in size. Mercurial inunctions were administered in case syphilis was present also. In a week however a rash developed and the sore showed more definitely the characteristics of a chancre. Severe headaches and aching all over his body soon followed, and the temperature fluctuated between 99° and 101°. A papular rash covers the whole body but is thickest on the face and in the hair. Over the legs and trunk some of the papules have become pustular and running together have formed small open sores. His head is very bad, hair being full of desquamating skin and indurated patches.

July 29th: Given salvarsan .6 grm. in 300 c.c. solution at 9 p.m. By midnight temperature rose from normal to 99.2 F, but by 2 a.m. had fallen to normal. Constitutional Effects: Slight shivering attacks lasting for two hours; slight diarrhoea but no vomiting. The bad headache was made much worse for three or four hours.
July 30th: He feels very fit. Headache absolutely gone and periosteal pains practically gone also, only slight aching left in the left tibia.

Aug. 3rd: Great improvement, especially in the head, which is practically clean excepting for one rupial patch. Rash fainter all over body and the small pustular sores are rapidly drying up. Sore on penis is almost healed.

Aug. 16th: Clinical evidence almost gone. Head and face which were so bad, are now absolutely clean. On the body only a few pigmented scars left by the healing ulcers and a few of the more indurated spots are to be seen. Chancre healed.

Patient discharged - 18 days after the injection.

Sept. 2nd: Patient seems absolutely cured as far as clinical evidence is concerned, there being only a few faintly visible scars left.

Wassermann's reaction is negative.
PRIMARY and SECONDARY SYPHILIS - PHAGEDAENA.

J. J. - Seaman - Age 32.

Admitted - 5th July, 1911.

History: Got infected twenty months ago by chancre on dorsum at junction of glans and reflection of foreskin.
He has taken mercury by mouth on and off ever since.
The chancre healed in five months but broke down again in three weeks and has had a spreading ulcer ever since.

State on Admission: - Hard chronic ulceration of prepuce which has ulcerated completely through its dorsal aspect and around corona, leaving glans absolutely bare.
- Profuse discharge. Slight shotty glands in groins but none elsewhere. The dorsal lymphatics of penis are very hard and feel like whip cord under the skin.
Marked rash - papular and scaly - all over trunk and legs. No sore throat; hair not coming out.

Wassermann reaction negative.

Aug. 9th: - Given salvarsan .6 grm. in 300 c.c. solution at 11 a.m., temperature 97.8, and pulse 76 at time of injection.

By 12 Midday Temperature rose to 99 pulse to 92.

" 1 p.m. " " 100 " " 96
" 3 p.m. " " 101.8 " " 96

From 3 p.m. temperature began to fall and by 9 p.m. had/
had reached the normal. Next evening however it rose again at 10 p.m. to 100.8° but fell suddenly at 2 a.m. to normal.

Constitutional Effects: Rigor and shivering at 2 p.m. for one hour, till temperature began to fall. Another rigor at 10 o'clock next evening when temperature rose the second time. Vomited twice after first rigor. Very bad headache till morning of the 11th. No diarrhoea.

Aug. 16th: Improvement in every way. Ulceration much drier and looks as though it were going to heal rapidly. Indurated lymphatics on dorsum completely subsided. Rash considerably improved. Much less indurated and pealing off in scales, especially over the shoulders.

Sept 2nd: Ulceration of penis healed by drying up. Glands in groins only slightly affected. Rash completely gone.

Wassermann reaction negative - was never positive by the Fleming method.

Discharged - 22 days after the injection.
PRIMARY and SECONDARY SYPHILIS.

W. S. - Seaman - Age 29.

Admitted - 6th July, 1911.

History: - Got infected nine weeks ago with a round raised chancre at junction of prepuce and fraenum. Rash appeared six weeks afterwards.

State on Admission: - Chancre in the above named position; moderately indurated, perfectly round, flat topped, and with glazed epithelium covering it.

Rash: - A dark papular rash all over the body, excepting the face; very thickly placed and skin markedly indurated - lichenoid.

July 10th: - Salvarsan injected intravenously 0.6 grm. in 300 c.c. solution at 9 p.m. Temperature 98, pulse 78.

By 11 p.m. temperature rose to 101°.

" 12 midnight " fell " 100
" 4 a.m. " " normal.

Constitutional Effects: - Rigor at 11 p.m., vomited, no headache, no diarrhoea.

Wassermann reaction positive.

July 13th: - Chancre slightly less indurated and not so raised above the skin surface. Rash is fainter in colour and beginning to desquamate.

July 16th: - Rash is just the same as on the 13th, chancre/
chancre a little softer.

July 20th: Rash a little fainter and less indurated than when last seen, but can be easily felt above the skin surface. Can detect no improvement in the chancre. Wassermann reaction positive.

July 24th: Considerably improved as regards rash, which is certainly fainter, less indurated, and not so raised above the skin surface. Chancre seems a little softer than when last examined.
Wassermann reaction positive.

July 31st: Rash still fading, on the legs and arms it is scarcely seen. Over the body however it is still quite visible. Chancre is disappearing, but extremely slowly. This seems strange as other chancre much harder and more indurated, have disappeared much more quickly.

Aug. 2nd: Rash is just the same as when last examined: the great induration is probably the cause of the delay but though the rash over the front of the body cannot now be felt the spots are quite visible. The chancre too looks much the same as when last examined. The patient is of a very neurotic nature and not only refuses a second injection, but also to stay in hospital any longer. He therefore goes out in a much less relieved condition/
condition than any of the other cases treated. Wassermann reaction positive. Discharged - 21 days after the injection.
PRIMARY and SECONDARY SYPHILIS.


Admitted - 16th July, 1911.

History: - Infected ten weeks ago by a chancre at the meatus. He has never taken mercury.

State on Admission: - Small ulcerated chancre on the meatus with a purulent discharge. Slight sore throat and a few slightly indurated papular spots scattered over his body and legs.

Aug. 8th: - Intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 11-30. Temperature 98.0, pulse 80.

By 4 p.m. temperature rose to 102° and slowly fell to normal at 10 p.m.

Constitutional Effects: - Prolonged shivering, starting at 1 p.m. and lasting till 4 p.m., and severe headache lasting for the same four hours. Vomited once; he felt very heavy all next day.

Aug 16th: - Most rapid improvement. The chancre has completely healed by rapidly drying up, and on the body there is absolutely no sign of the rash.

Wassermann reaction indéfinintely positive.

Discharged - eight days after the injection.
PRIMARY and SECONDARY SYPHILIS.

L. J. L. - Fireman - Age 36.

Admitted - 27th July, 1911.

History: - He got infected three months ago by a chancre under the foreskin, so that the latter cannot now be retracted, and a purulent discharge is coming from under it. Penis swollen and oedematous and a papular rash all over his body. This rash is of a very severe type the papules being considerably raised above the skin and with intensely infiltrated bases. In both axillae and in both groins are crops of condylomata, each individual condyloma being about the size of a threepenny piece. Also in several other parts of the body such as the flexures of the elbows and knees rash is merging into condylomatous looking infiltrations. Wassermann's reaction is positive.

Aug. 1st: - Given salvarsan .6 grm in 300 c.c. solution at 9-30 p.m. temperature normal and pulse 92.

By 2 a.m. temperature rose to 102 F and pulse to 120.

By 6 a.m. temperature became normal but at 10 a.m. again rose to 100 and took all day to return to the normal.

Constitutional effects: - Violent shiverings for one hour; violent sickness and severe abdominal pain; slight/
slight diarrhoea.

Aug. 3rd: -- Considerable improvement in his condition. The penis is cleaner and much less oedematous, although the foreskin cannot be drawn back the discharge is less. The condylomata too are much drier, and rapidly shrivelling up.

Aug. 8th: -- Still improving; the condylomata have gone, leaving very deeply pigmented areas, and the rest of the rash is fading.

Aug. 16th: -- At first sight, improvement, not so advanced one since August 8th, as would have liked to have seen. Under arm pits and in groins the condylomatous areas are very pigmented, and over the body surfaces rash has not faded much, but on running the hand over it, one can easily feel that the induration has greatly receded.

Sept 3rd: -- All oedema and discharge from penis have disappeared and no induration - such as a hard sore - can be felt. The rash is fading but slowly ever since August 16th. The pigmentation is deeper than one has ever seen before. Another injection would probably hasten matters.

Wassermann reaction positive.

Discharged - 33 days after the injection.
PRIMARY and SECONDARY SYPHILIS.

O. O. - Seaman - Age 28.

Admitted - July 31st, 1911.

History: Infected in May by a chancre on penis and a rash appeared soon afterwards.

State on Admission: Chancre almost healed but a papular rash scattered all over his body. He has taken mercury constantly for two months and although the sore is healing there seems to be no improvement upon the rash by the mercurial treatment. He came in especially for salvarsan.

Aug. 11th: Given .6 grm. of salvarsan in 300 c.c. solution at 10 p.m. By 1 a.m. temperature had risen to 101.6 and slowly fell to normal again by six in the evening. Pulse did not rise above 92.

By effects: Rigor at 1 a.m., vomiting (slight), nasty headache for two hours.

Aug. 16th: Chancre completely healed; rash greatly improved. It has gone from his legs and front of the body, and only faintly seen on the back.

Wassermann reaction positive.


Discharged - nine days after the injection.
Admitted 28th November 1911.

History: - Got infected with a soft sore eight weeks ago. At first there seemed to be no sign of syphilis. To-day however a papular rash has appeared - much like measles in appearance - all over his body, but is not very indurated. Two hard chancre can now be felt, one under the foreskin, the other on the dorsum of the shaft of the penis; each is about the size of a split pea.

Nov. 29th: - Intravenous injection of salvarsan .6 grm. in 500 c.c. solution at midday.

Constitutional Effects: - Rigor about 4 p.m. lasting for half an hour, with nausea and vomiting three times; slight headache, no abdominal pain, no diarrhoea. At 4 p.m. the temperature rose to 103 F but fell to normal again at six the next morning.

Dec. 2nd: - The rash has considerably improved and has become much fainter all over his body.

The dorsum chancre is much softer than when the injection was given - in fact hardly any induration is left. But the chancre under the foreskin is still hard and indurated, and the prepuce cannot be retracted.

Dec. 4th: -
Dec. 4th :- Both chancres rapidly disappearing.
Dec. 6th :- No sign of the rash.
Dec. 13th :- Both chancres completely healed and the prepuce is easily retracted.
Discharged - 15 days after the injection.
SECONDARY SYPHILIS.

W. S. - Seaman - Aged 28.

Admitted 14th July, 1911.

History: - Infected six months ago - chancre healed in five weeks.

State on Admission: - Scar of healed chancre.

Dusky rash, irregularly distributed in large blotches all over body and limbs. Enlarged glands in both groins. Snail track ulcers all over posterior wall of pharynx.

July 17th: - Salvarsan .6 grm. in 300 c.c. solution at 4 p.m. By 6 p.m. temperature had risen to 102 and pulse to 96.

Constitutional Effects: - Rigor at 6 p.m. and shivering continued for nearly one hour afterwards.

Vomiting, fairly severe; No diarrhoea; No headache. Temperature fell to normal at midnight.

July 21st: - Rash beginning to fade. Mercury as well given, one grain three times a day.

July 27th: - Rash disappearing to a considerable degree, and desquamation taking place.

July 31st: - Desquamation finished and only pigmentation left of the rash.

Aug. 3rd: - Pigmentation disappearing.

Wassermann reaction positive.

Aug. 16th: -
Aug. 16th: Pigmentation only faintly seen. Glands in groins greatly reduced in size, but can still be felt.

Wassermann reaction indefinitely positive.

He was discharged to-day - 30 days after injection.
SECONDARY SYPHILIS - SQUAMO-PAPULAR.

C. V. - Seaman - Age 32.

Admitted - 21st May, 1911.

History: - Infected ten months ago and he took mercury. The sore healed but later broke out again in the same place. In three weeks after infection a large squamous rash appeared all over the body including the face. Later a papular rash appeared on the top of the squamous especially over the arms and legs. Around both wrists and ankles the rash became pustular and desquamation of the skin took place all over the body.

State on Admission: - Patient is in a shocking state. The two rashes are distinctly visible covering the whole body. Both forearms, wrists, backs of both hands, and the lower parts of both legs, including the ankles, are thickly covered with large scales, underneath which pus can be found in places. Shallow ulceration all around the right elbow. The other parts of the body though thickly covered are not so bad.

He had mercury for three or four months but none for the last six weeks, yet the Wassermann's reaction is negative.

May 24th: - Intravenous injection of salvarsan .45 grm. - the vein thrombosed and no more could run in.

Constitutional Effects: -
Constitutional Effects: - Temperature rose to 100 but there were no other constitutional effects.

May 27th: - No improvement.

May 31st: - Slight improvement in the squamous rash - scales loosening.

June 8th: - Though slow in commencing improvement has gone on extremely rapidly since June 1st. The squamous rash has cleared up more quickly than any squamous rash yet seen. Over the trunk - back and front - the rash has gone, leaving only large faintly pigmented areas. The papular rash has also improved, but induration is still present. The backs of both hands have almost completely cleared up. The desquamation of both ankles has finished, (the skin is smooth but deeply coloured) and only two open sores (size of sixpence) remain. The right elbow is the slowest of all, large scales all around the joint and one or two open sores still remain, though this part too has greatly improved since the injection. Wassermann reaction still negative.

June 16th: - Still further improvement in every direction. The backs of both hands and wrists are cured. Right elbow, though still red and scabby, has greatly improved and the small ulcers on both ankles are healing. The induration of the papular rash is still present/
present in parts, but in others nothing but brown pigmented areas remain.

The squamous rash has gone from all parts of the body, leaving faint brown patches over both arms.

Wassermann reaction has now become positive.

June 23rd: - Still improving. The right elbow has almost cleared up and only two small scabs (size of threepenny piece) remain of the ulcers; these are dry and should soon fall off. The ulcers around the ankles are healed, except for one the size of sixpence, which is covered by a dry scab. Both rashes have now gone, but plenty of brown pigmentation, where the papular rash was, remains.

Patient is feeling very fit and anxious to return to work.

Wassermann's reaction is still positive, but only weakly so.

Given mercury to take and discharged - 29 days after the injection.
SECONDARY SYPHILIS - PSORIASIS SYPHILIDE.

H. H. - Seaman - Age 30.

Admitted - 1st August, 1911.

History :- Infected by chancre six months ago.

State on Admission :- He has the whole of the anterior surfaces of both legs from the knees to the ankles closely covered with large dull red patches, varying in size from a shilling to a penny. Some of the patches are confluent forming much larger areas. The skin is intensely infiltrated and the areas stand out well beyond the remaining healthy skin. The areas affected are for the most part closely covered with silvery scales.

Aug. 5th :- Intravenous injection of salvarsan (at 11-30 a.m.) .6 grm. in 300 c.c. solution.

By 2 p.m. temperature had risen to 100.4, pulse to 92.

" 4 p.m. " fell " 100.2 " " 90
" 6 p.m. " " 100 " " 88
" 8 p.m. " " 98.2 " " 88

Constitutional Effects :- Slight rigor about 2 p.m., slight headache, no vomiting, no diarrhoea.

Aug. 8th :- Some small ulcers, present in the mouth at the time of the injection, have healed. A slight change in the colour of the infiltrated masses, not so red/
red, becoming a little browner, and desquamation is beginning to take place.

Aug. 16th: Considerable improvement. The affected masses are much less indurated and not so raised above the skin. The skin too seems more flexible, but still there is a tremendous lot of induration to be removed, especially on the left leg where improvement has been slower in starting.

Wassermann reaction positive.

Sept. 2nd: Improvement slow since Aug. 16th especially in left leg, though desquamation in both legs has been considerable. There is no doubt however that the areas are in no way so raised as they were at the time of the injection.

It looks as though another injection would have had a marked effect, but patient left hospital to return to work - 28 days after the injection.

Wassermann reaction positive.
SECONDARY SYPHILIS - RUPIA.

H. S. - Seaman - Age 32.

History:—Infected by chancre on penis twelve months ago. Treated in this hospital for three weeks and three days with mercury pills. He went out with chancre healed and no sign of any rash. A fortnight later he was treated in Hull Infirmary for seven weeks for sore throat. He returned to this hospital in November 1910 with gummatous infiltrations and ulcerations on different parts of the body - was vigorously treated with iodides and mercury for ten days and greatly improved. At the beginning of December mercury was stopped and .6 grm. of salvarsan was injected subcutaneously under the left breast. An enormous swelling ensued, which was fomented. In about fourteen days it was reduced to the size of a small egg and very hard. As it would get no smaller it was incised, and the wound made was practically dry. Swelling would get no smaller, nor would incision heal, so it was scraped out under gas and a small improvement followed. A fortnight later it was again scraped out under gas, and this time healed in two weeks, leaving a red scar size of half a crown but no induration around about.

Patient was given no mercury after this subcutaneous injection.
injection and the lesions present, not only did not heal, but became considerably worse. He was therefore put on to mercurial inunctions and potassium iodide, and by February 18th, 1911, all the ulcerations had healed. - discharged.

May 6th, 1911. Re-admitted. It is ten weeks since he was last discharged and for four of these he took mercury and potassium iodide regularly. For the last six weeks he has taken nothing at all, and now he comes back to hospital with sixteen places of rupial eruptions, varying in size from half a crown to a crown piece. They are situated over the neck, back and front of chest. Injected intravenously with 0.6 grm. of salvarsan in 300 c.c. solution. Temperature rose to 100, pulse to 86.

Constitutional Effects: - Practically nil - only a slight rigor.

May 8th: - Not much improvement to look at except some of the patches are drier and less tender.

May 10th: - Four large masses have become so dry that they have dropped off, leaving an absolutely painless scar. When knocked off by accident while at work before the injection, an open sore was left, which was extremely painful. All other masses about the body are loosening.
A scaly eruption which was present over the face is rapidly clearing up. A sore throat too has completely healed.

May 15th: All rupial masses except a small one on right shoulder have dropped off, leaving dry, painless, and non indurated scars.

May 23rd: Mass on shoulder has dropped off also. Nothing is now left. Face is clean, throat healed, and all rupia gone. Patient feels extremely well and wishes to return to sea from which, (except for one trip) he has been absent since his illness began.

The Wassermann reaction however has remained positive all through.

Discharged - 17 days after the injection.
SECONDARY SYPHILIS - Rupia.

P.G. - Seaman - Aged 30.
Admitted April 26th, 1911.

History: Got infected with Syphilis in June 1910, and treated in Buenos Ayres for one month with mercury. He has taken mercury on and off ever since until he came to hospital.

State on Admission: Rupia over face and forehead - nine patches, one size of half-a-crown, three the size of a shilling, and one size of sixpence. The rest are about as big as a split pea. They are raised nearly half an inch above the skin level.

Thick crusts in his beard, and a small ulcer on his right thigh. Throat very sore and can’t eat - snail tracks about tonsils and uvula. He has suffered from palpitation of the heart for at least six months.

Temperature fluctuating to 100.

May 6th: Given salvarsan .6 grm. in 300 c.c. solution at 2-30 p.m.

By
4 p.m. temperature rose to 103.4 pulse to 128 Resp. 26
6 p.m. " fell " 102 " 126 " 24
8 p.m. " " 101.6 " 120 " 24
10 p.m. " : " 101 " 20 " 24
Midnight " " 100 " 88 " 24

Next day/
Next day temperature rose again to 102° and gradually fell by lysis to normal.

Constitutional Effects: - Rigor severe at 4 p.m. on 6th. Vomiting (painful) four times; great feeling of exhaustion.

May 7th: - Very exhausted all day and could not get up.

May 8th: - Temperature and pulse normal. Much stronger and brighter than yesterday. Throat made much worse for a day by the injection, though to-day it has improved again and he can eat fairly comfortably. Rupial crusts have begun to get loose at their attachments and one has almost dropped off. The skin round about is not so indurated.

May 10th: - Feeling quite well. All patches on face getting loose and one has completely dropped off leaving a painless scar. He can eat any kind of solid food. Wassermann reaction positive.

May 15th: - Improvement is not proceeding at the same rate since the 10th, and patient is a little disappointed. However the patches are certainly smaller and the skin of forehead and face much healthier looking. Beard however is practically clean. This case is in contrast with H. S. where the rupial patches dried very quickly and dropped off. In this case they have not/
not dried so quickly and a discharge comes from underneath the scabs.

May 23rd: Slight improvement since May 15th. Patient has pulled the scabs off himself, leaving small ulcers which are slowly healing from the margins. Wassermann reaction still positive. Put on to mercury by mouth to-day.

May 30th: Ulcers still slowly healing and drying up. The mercury is now given as an inunction. Wassermann reaction still positive.

May 31st: Another .3 grm. of salvarsan injected intravenously. Temperature rose to 99 but there were no accompanying effects.

June 8th: Very evident influence upon sores on forehead, which are again rapidly healing up. The scars where the other masses have come off are now not so bright in colour as on the 31st. To-day the Wassermann reaction is negative.

June 16th: All sores on face healed up. Ulcer on thigh also healed. Patient looks extremely well and has put on considerable weight and is a marked contrast to when he was first admitted. Wassermann reaction still negative.

Discharged - 26 days after first injection.
SECONDARY Syphilis - Onychia.

W. W. - Fisherman - Age 34.

Admitted - April 22nd, 1911.

History: - Was in this hospital for three weeks during October 1910 for Syphilis - treated with mercury vapour baths and mercury pills. Left hospital greatly improved but with a few spots of rash still present. Continued mercurial treatment.

Soon after leaving hospital the nails of his left hand became affected. The affection slowly advanced so that in April he had to stop work and return to hospital.

State on Admission: -

Left hand: - Deep ulceration under thumb nail, half the nail already gone. Profuse discharge and extremely painful to the touch.

Second and third fingers are in much the same condition, but more acutely inflamed. Great excavation down into the nail bed so that the portion of nail not eaten away stands out as a shelf over the pulp of the fingers.

The disease seems to start in the quick and ulcerates towards the centre of the nail.

Right hand: - Second finger just commencing. Greatly inflamed with a slight purulent discharge. In this finger it has started under the nail raising it up from the rest of the finger.

Small/
Small gumma on top of scalp size of sixpence.

Wassermann reaction positive.

Patient declares he has taken mercury continuously, except for the last month, since he first became infected.

May 9th:— Injected with salvarsan intravenously .6 grm. in 300 c.c. solution at 9 p.m.

By 2 a.m. temperature rose to 99.4 pulse to 104.

By 6 a.m. both were normal again.

By Effects:— No rigor, headache or vomiting, but severe diarrhoea and abdominal pain. Pain in both arms and in all the affected fingers.

May 10th:— Two of the fingers have dried a great deal since the injection, but two others have become much more inflamed and tender— they ache considerably.

May 15th:— The second and third fingers of the left hand have completely dried up. There is nothing now but a dry excavation between the remainder of the nail and top of the finger in each case. They are in no way tender or sensitive to the touch. The other fingers to look at don’t seem much improved by the treatment, though the patient says they are less tender when handling anything.

May 23rd:— Wassermann reaction still positive.

The thumb of the left hand is slowly healing by drying up.
up but is still a little painful if squeezed.

The second finger of right hand, the most recently affected, and most inflamed at the time of the injection is still very swollen, inflamed, and painful. The ulceration of the nail is still spreading, so local treatment is applied.

May 27th: - The thumb of left hand has healed, the excavation being quite dry. To-day the nail of second finger on right hand was removed by operation to allow the local antiseptic treatment to get at the ulceration under it.

May 30th: - The above finger greatly improved, less swollen and inflamed.

June 6th: - The second finger on right hand practically healed, only a very slight discharge on dressings. The other fingers being absolutely well, patient considers he is quite fit to return to work.

Wassermann reaction still positive.

Discharged - 28 days after the injection.
SECONDARY SYPHILIS, (Lips, throat, and lymphatic glands)

W. F. - Seaman - Age 30.

Admitted - June 6th 1911.

History: - Infected with Syphilis four months ago.
Treated with black wash and mercury by the mouth and chancre healed in three weeks. Continued with mercury until admission to hospital.

State on Admission: - Condylomate round anus. Snail tracks and ulcers on fauces and tonsils; red inflamed throat; three ulcers on lips - very sore; faded rash on both arms.

Lymphatic Glands: - Sterno - Mastoid glands both sides about the size of a shilling. Submaxillary glands both sides size of a two shilling piece. Submental glands, small; Inguinal glands left side only, size of two shilling piece.

June 7th: - Injection of salvarsan .6 gms. in 300 c.c. solution at 2 p.m. In six hours temperature rose to 99.3°.

Constitutional Effects: - Slight shivering; vomited twice, and slight headache.

June 11th: - To-day there is no sign of any of the ulcers on the lips, tonsils or fauces, and the throat looks/
looks quite natural.
June 16th :- Most of the glands are getting smaller, especially the submaxillary - now only about three quarters of the size, when injection was given. The Sterno - Mastoid too, are much smaller; the submental are slightly smaller; the inguinal glands, however, are not affected at all. The faint rash on the arms is still present.
June 23rd :- The rash has entirely gone and the glands in the submaxillary, Submental, and Sterno - Mastoid regions are now only just palpable. The inguinal glands however seem to be almost as large as at the time of the injection. Patient got no mercury while in hospital.
Goes back to sea to-morrow - 16 days after injection.
SECONDARY SYPHILIS (Iritis)


Admitted - May 12th, 1911.

History: - Infected by a chancre on penis three months ago, which was burnt out by caustics. Later a coppery rash developed, and iritis in right eye soon followed. On April 5th he was injected in the left buttock (intramuscular) with salvarsan at Marseilles and sent back to sea the same day - no by-effects followed. After the injection the rash cleared up a great deal from his body, but never really left his arms and legs. The iritis, however, rapidly healed, and in ten days all pain and symptoms had completely left his eye. After landing in England he drank heavily for three or four days, and all the symptoms suddenly returned. In thirty one days after first injection he was admitted to Seamen's Hospital.

State on Admission: - Slight ulceration on both tonsils. Lymphatic glands - submaxillary, epicondylar, and sternomastoid, enlarged and tender. Thick coppery rash on both thighs and slightly over abdomen. Intense iritis in right eye with pain, photophobia and lachrymation. All these symptoms returned during a drinking bout of three or four days, when he thought he had/
had been completely cured.

May 15th:— Wassermann reaction positive.

Injected intravenously with .5 grm. salvarsan (150 c.c. solution) instead of .6 grm. on account of his eye condition. Injection was given at 4-30 p.m.

By 7-50 his temperature had risen to 101 F and remained so till 10 p.m., and pulse rose from 80 to 120. At 7-30 he had a rigor for half an hour, and vomited every half hour from 7-30 till 10 p.m. By 6 a.m. next day temperature was again normal, and pulse dropped to 100 but did not become normal till 10 a.m.

The constitutional effects in this case are severe, both the rigor and the vomiting upsetting the patient considerably. A bad headache followed and patient felt altogether quite ill.

May 23rd:— Considerable impression upon rash which now consists only of a few scaly syphilides size of a split pea, scattered over both thighs and back. Submaxillary lymphatic glands greatly reduced in size and now not tender as previously. Throat quite healed. Eye much better. Local treatment has been continued all through, but still the pain, photophobia and lachrymation have disappeared with remarkable rapidity. He can see to read as well with right eye as with left.
The right iris however is still quite a different colour to the left; the cedema and exudations are still quite visible and the pupil dilates irregularly.

Wassermann reaction still positive.

May 30th: - Eye has improved immensely since the 23rd. To-day it looks perfectly normal and dilates quite regularly.

Very little improvement on rash since the 23rd - seems to be in statu quo.

June 2nd: - Second injection .15 grm. to clear up rash. Some spots are still quite indurated and typically raw ham in colour.

June 8th: - The desired effect somewhat attained. The remaining papules are much less indurated and flatter.

June 16th: - Mostly brown patches in place where these papules were - scarcely any induration left. A little circumcorneal injection has reappeared in the affected eye. Atropine continued.

Wassermann reaction still positive.

June 27th: - Scarcely any remains of rash whatsoever, one or two faintly pigmented spots alone remain. The ciliary injection which only lasted for a day has again completely disappeared.

Discharged.

Wassermann/
Wassermann reaction still positive.

July 10th: Returned to report himself. Patient has been drinking very heavily for the last week, yet improvement has continued. Absolutely no trace where rash was, and right eye is as healthy as the left. Wassermann reaction weakly positive.
SECONDARY SYPHILIS.


Admitted - June 27th, 1911.

History: - Contracted Syphilis about Easter 1911, and four chancres developed on the penis. In four or five days he began to feel extremely ill and weak as though he had caught a severe cold. Admitted to hospital in Montreal and treated there with mercury for five weeks. Severe pains in his head, arms and legs developed which were not at all relieved by the medicine, so after five weeks, he left hospital to come to England. On the voyage over he was too ill to work, being so weak he could hardly stand. The chancres were still present so he was treated with mercurial inunction by the doctor on board. A rash now appeared for the first time and enlarged glands developed in both groins. He was also greatly troubled with severe abdominal pains and diarrhoea, with some blood appearing in the motions.

State on Admission: - Weak emaciated man; complaining of marked pain and stiffness in his arms and legs, and severe headache. He has diarrhoea with blood in the motions. His mouth is in a filthy condition, teeth loose, gums swollen and spongy, and sores all over the buccal surfaces of both cheeks and gums. On his penis are the remains of four healing chancres/
chancre. His weight is nine stones.

June 28th:- As mercury evidently did not agree with him it was immediately stopped. This evening he was given an intravenous injection of salvarsan 6 grm. in a 300 c.c. solution at 9 p.m. By 2 a.m. his temperature rose to 100.2 and pulse to 116 but both were normal again by 4 a.m.

**Constitutional Effects** :- Rigor and shivering for one hour at midnight; vomiting; severe headache; and diarrhoea.

June 29th:- To-day he is much brighter in every respect, the injection has acted as a strong tonic. His mouth and throat are, however, worse, having a burning sensation in them.

June 30th :- To-day he is delighted with himself. The pains have disappeared from his head and legs, though the latter are still a little stiff. His mouth too has greatly improved nearly all the ulcers have entirely disappeared.

July 3rd.:- Allowed up. The pains and stiffness in his legs (he says) are gone. Mouth cured; teeth tightened up and gums gone down. All the mucous patches have disappeared. The rash too is disappearing and the diarrhoea has stopped.

July 7th :- Goes out of hospital on his own accord to-day saying he is quite well and no need to stay in any longer. The rash however, can still be seen, though/
though certainly fainter than when he came in, and is the only symptom left out of these present when he was admitted.

Wassermann's reaction is positive. Discharged to-day - nine days after injection.
TERTIARY SYphilis.

R. H. - Seaman - 35 years.
Admitted - January 10th, 1911.
State on Admission: He came to the hospital with a hard mass about the size of a bantams egg on inner side of right thigh, just above the knee. The centre has softened and a discharging ulcer formed. Around about is old scarring due to previous infection and signs of a previous operation.

Previous Illnesses: He has been in this hospital twice (in the last three years) for the same trouble, and twice has the condition been treated by excision. Strenuously denying syphilis and giving the history of a previous injury to this part, the condition was considered to be non-syphilitic.

Jan. 15th: The whole lump excised to-day as twice previously, and stitched up.

Jan 30th: The wound has not done well; a discharging ulcer has formed the size of a crown piece. It is dressed every day with antiseptic lotions but seems to be practically stationary, neither spreading nor healing. Wassermann's reaction (done for the first time) is positive.

Feb 4th:-
Feb. 4th: - Given .6 grm. of salvarsan intravenously in 300 c.c. solution at 8-30 p.m. By midnight temperature had risen to 100°.

Constitutional Effects: - Rigor at midnight; nausea, but no vomiting; no diarrhoea.

Feb. 7th: - Improvement has set in rapidly. The very next day the ulcer seemed to dry up, and to-day epithelium can be seen growing in from the margins.

Feb. 12th: - Rapidly healing. Ulcer about half its original size.

Feb. 19th: - Completely healed - smooth flexible epithelium covering the place where the ulcer was.

Healing has been rapid.

Wassermann reaction not taken again after the injection.

Feb. 20th: - Discharged - fifteen days after the injection.
TERTIARY SYPHILIS. (Ulceration of the ventricular bands; very severe pains in head.)

S. DeC. - Portuguese seaman - Age 35.
Admitted - February 2nd, 1911.
State on admission: - Patient can speak very little English - date of infection not known. When admitted he showed ulcerations over the Tibial surfaces of both legs. Numerous small ulcers and mucous patches on the buccal surfaces of both cheeks. Ulceration of right ventricular band (R. false cord)
Very severe pains in head and down both legs. Refused to take food.
Temperature 101 F.
Patient was immediately put on to mercurial inunctions and a mouth wash.
March 1st: - No improvement seems to have resulted from the treatment. Mouth has not healed; larynx is in the same condition as on admission. Has suffered from constant and severe diarrhoea since treatment began. (Periosteal) pains in head and legs are so severe that he has to be kept on aspirin or antipyrin etc; their severity suggests an early meningitis.
Catechu is used for the diarrhoea.
March 20th: - Practically no improvement. Complaining constantly of pains in head, legs and throat. Refuses to/
to eat. Mercury stopped.
Wassermann reaction strongly positive.
Salvarsan injected intravenously .6 grm in 300 c.c. solution at 5 p.m. The temperature though fluctuating greatly since admission was normal at the time of the injection. By 8 p.m. it had risen to 99.4 remaining at this for a few hours; fell to normal again at 4 next morning.
Constitutional Effects: - Nil.
The night of the injection he slept soundly all night, the first time since admission to hospital.
March 22nd: - The effect of the injection seems to have been immediate. All pains about the head and legs have gone. Slept well the last two nights and needed no hypnotics. He started to take food to-day with a certain amount of success.
March 24th: - Ulcers in the mouth healing. Some are already gone, while those left seem to be much more anaesthetic, for he took a full meal at dinner to-day.
March 30th: - Allowed up. Ulcers on legs healed and only scaly marks left. Only one or two ulcers in mouth left. Before injection no one could understand what he said but now his voice is much more powerful and distant.
April 4th: - No signs of ulcers in mouth.
Laryngoscopic/
Laryngoscopic examination showed the right ventricular band - once considerably ulcerated - to be now completely healed.

April 15th: No clinical signs of Syphilis.
Wassermann reaction still weakly positive.
Discharged to go to sea - 15 days after the injection.
TERTIARY SYPHILIS. (Gummatous Ulceration of the Larynx)

A. W. - Seaman - age 47.

Admitted - March 14th, 1911.

History: About two months ago throat became very sore, and voice rapidly began to fail. After about a fortnight he could speak only in a whisper. He was treated with mercury and iodides for five weeks without any improvement to his voice whatsoever.

State on Admission: Patient can only speak in a faint whisper.

By laryngoscopic examination the epiglottis is seen to be swollen about twice its normal size, with several ulcerations scattered over it, especially near its upper rounded margin.

Patient denies syphilis.

March 17th: Salvarsan injected .4 grm. intravenously.

Constitutional Effects: Practically nil.

Temperature did not rise above 98.8 F.

March 18th: Throat very bad, too painful to eat or drink. The exacerbation is probably due to the injection.

March 19th: Throat greatly improved, he can now eat soft foods. Voice still a whisper.

March 25th: Beginning to take solid foods. Voice greatly/
greatly improved and he can easily be heard by those in the beds near him.

March 30th: - Can now eat with perfect ease and comfort. Voice is becoming stronger daily. Sometimes it is quite loud but every now and again it fails him. He can easily make himself heard across the ward.

April 15th: - Voice has so much improved that patient declares he is fit for work. When speaking with him his voice sounds almost natural, but every now and again it becomes husky or gruff. However the improvement is most marked; on admission he could hardly make himself heard, now he can make himself heard from the end of the ward.

Examining his throat again; the epiglottis has returned almost to its natural condition, except for a small part at its junction with the larynx, where it is still a little swollen.

Discharged April 15th - 28 days after the injection.

Still to come as an out patient.
TERTIARY SYPHILIS. (Marked Ulceration of the Pharynx)

J. E. - Seaman - Age 39.

Admitted - May 6th, 1911.

History: In August 1910 he got infected with Syphilis by a chancre situated on the lower lip - probably infected from a shipmate suffering with severe Syphilis at the time. A rash developed in three weeks and after nine weeks treatment with mercury all clinical symptoms cleared up. Soon afterwards, while still taking mercury, mouth, gums, and teeth become extremely sore and about Xmas time his throat became so inflamed and sore, that he could hardly swallow even fluids.

State on Admission: - Deep ulceration and excavation of both tonsils until almost nothing is left of them. Ulceration of anterior and posterior pillars of the Fauces. Ulceration of the soft palate with complete loss of the uvula.

In connection with the ulcerated parts are nasty white sloughs with profuse foul smelling discharge; the surrounding parts being extremely red and inflamed.

Voice very gruff.

Temperature swinging irregularly between 97° and 101°. Wassermann reaction positive.

May 8th: - Salvarsan injected intravenously. .6 grm.
in 300 c.c. solution at 6-30 p.m.

By 8 p.m. temp. rose from 99.4° to 104.2° pulse to 120.

"10 p.m. " fell to 102 " " 120
" midnight " " " 101 " " 118
" 2 a.m. " " " 100 " " 100
" 6 a.m. " " " 98.6 "

Next day rose again to 100.6 but fell to normal by night.

Constitutional Effects :- Severe rigor and shivering

at 8 p.m. on the 8th; nausea, but no vomiting.

May 10th:-
Temperature still normal. For last two days throat
has been made worse by the injection, both the pain and
discharge being increased, but to-night both are better
again.

May 11th :- Throat not so painful but feels extremely
dry and tight. He is certainly not spitting so much.
The constant headache present before the injection has
now gone and he feels much better personally.

Yesterday he complained of tenderness all day over the
abdomen but to-day says it is better. Also complained
of severe aching along arms and legs especially the
two ulcerations on one leg (size of 2/6) which were
very moist and discharging, but now rapidly drying up.
A faint rash all over body, arms, and legs, has not yet
been influenced by the injection.

May 15th :/
May 15th: Throat has immensely improved. All redness and inflammation has entirely disappeared. The discharge stopped and sloughs separated; the cavities left by the deep ulcerations are practically clean. A hacking cough has stopped and the normal taste has returned to his mouth. Patient declares it is a great relief to be free from the constant spitting which prevented him from sleeping at night. He can now eat any kind of solid food.

May 23rd: Throat now completely well. It looks extremely healthy and clean. Says he can eat as well as ever he could.

Rash gone from arms and back of neck. Three crusted ulcers once about the size of half a crown and discharging, are now reduced to the size of a shilling. They have however been at this stage for some days, and patient is afraid they have ceased to heal.

Wassermann’s reaction is still positive.

June 8th: Feeling so well he wants to go out.

Throat well; rash gone except for a few pigmented spots, and the scales have fallen off the rupial patches on right leg, leaving highly coloured pigmented scars. Wassermann’s reaction is still positive.

Discharged - 28 days after the injection.
TERTIARY SYphilis. (Gummatous Ulcerations)

F. W. — Seaman — Age 44 years.

Admitted — May 16th, 1911.

History:— Began seven or eight years ago by a painless lump appearing on the sternum; in a week this broke down forming a deep ulcer, which ultimately healed in fourteen days by local treatment.

Several similar places have broken out since—in the head, neck and face—all leaving marked scarring.

An ulcer in the right upper arm formed about a week before admission, starting on the sight of an old healed scar. Also a lump over the right elbow now breaking down and forming a softening under the skin—but the latter is still whole.

On admission:—The scarring from previous ulcerations is very evident. Starting from the back of the neck and running round on to the left side of face is one big white arborencscent scar. Also stellate scarring all over sternum.

Big red scar on right side of neck. In the mid deltoid region of the right arm there is a deep sloughing ulcer about the size of a shilling, the edges of which are sharp cut and raised about the skin surface. Around about is scar tissue due to previous ulceration.

Over/
Over the external condyle of right humerus there is a soft fluctuating subcutaneous swelling not hot or painful but slightly tender to the touch.

Hair very thin - falling out readily.

Patient is extremely debilitated.

Previous illnesses: - Scarlet fever when young; malaria and black water fever eight years ago; Bright's disease seven years ago - ill for nine months.

Denies Syphilis: - Has never had a rash or sore throat.

He lived nine years in Nigeria and was there when the disease started.

Urine: - 1022 Sp.G.

  Acid
  Albumen and blood.
  Hyaline, granular and blood casts.

Wassermann's reaction is positive.

He has never taken any mercury but has taken plenty of other medicines as the disease was never thought to be Syphilitic.

May 21st: - Patient has only been in hospital a few days but the subcutaneous softening has rapidly increased and to-day it burst, leaving a deep ulcer the size of a crown piece. Getting very weak - temperature constantly swaying to over 100 F.

May 28th: - Intravenous injection of salvarsan. .6 grm in/
in 300 c.c. solution at 8-30 p.m. Temperature being 103 at the time did not rise higher but gradually came down, and was normal by 6 a.m.

Constitutional Effects: Nil - no nausea, no rigor, no headache.

May 29th: The discharge of both ulcers made worse for two days with great aching of whole limb. Aching and discharge has gradually got less. To-day the ulcers are much cleaner, hardly any discharge at all now; gradually granulating from the bottom and not so tender as previously - dressed daily with boracic lotion.

Urine: Albumen and blood were both present at the time of the injection, but were not made worse by it. On 23rd albumen alone remained, while to-day the 29th no albumen at all is present.

June 5th: The small ulcer has healed, while the larger one is now only half its original size.

June 15th: Almost healed.

June 20th: Completely healed - firm epithelium coming over both ulcers.

Discharged - 28 days after injection.
TERTIARY SYphilis. (GUMMATOUS ULCERATIONS)

S. G.

Admitted - June 1st, 1911.

History: - Infected twelve months ago by a chancre which healed in a few days. Two months later rash appeared over the body which healed in three weeks. Later another scaly syphilide appeared and some of these areas formed into ulcers. He started mercury for the first time, some of the ulcers healed but some did not.

State on Admission: - Two ulcers, one on the left leg and the other over the inner aspect of the right elbow. Both are almost the size of a crown piece, deep and discharging profusely. Also several areas of dull red induration scattered over the body.

June 2nd: - Intravenous injection of salvarsan. 0.6 grm. in 300 c.c. solution at 8 p.m.

Wassermann reaction positive.

Temperature remained normal after the injection till next day when it suddenly rose to 100.2

Constitutional Effects: - Absolutely nil.

June 4th: - Pain and aching of the ulcers were eased straight away - not made worse for a few hours.

Healing in both ulcers started next day, by the discharge becoming less, and is now going on rapidly.

June 8th: -/
June 8th: Leg ulcer almost healed. Before the injection it was very deep with hard rotted edges but now it has granulated to a level with the surrounding skin, with a layer of glassy epithelium covering it - discharge completely stopped.

The ulcer on right elbow is healing almost as fast and in the same way, i.e. the discharge stopping immediately and healthy bleeding granulations springing up almost at once.

The papular rash has also greatly improved by becoming less indurated, flatter and changing colour from red to brown.

June 16th: Ulcer in left leg healed. Firm epithelium now covering the place where the ulcer was. Right elbow not quite healed - covered by a dry scab.

June 23rd: All ulcers are now completely healed - covered by a firm epithelium - the rash not gone, but becoming very faint.

June 27th: Rash absolutely gone. No clinical evidence of active syphilis.

Wassermann reaction still positive.

Discharged - 19 days after the injection.
P. A.
Admitted - 26th June, 1911.

History :- Infected four years ago. Has had various rashes and ulcers at different times.

On Admission :- He had three or four small tertiary ulcers on his face and three on his legs, two of the latter being each the size of a five shilling piece. A thick scaly dull red rash all over his face, which being extremely sore has prevented him from shaving. He has taken mercury continuously for the last twelve months.

June 27th :- Intravenous injection of salvarsan. 0.6 grm. in 300 c.c. solution at 9 p.m.
By 10 p.m. temperature rose to 100.2 ° pulse to 116.°
" 12 midnight " " " 101.2 " " 116.°
But normal again by 6 a.m.

Constitutional Effects :- Vomiting; slight diarrhoea; no headache; no rigor.

July 3rd :- Sore throat cleared up first day after the injection. Rash on forehead commencing to heal on the second day has now gone, leaving only brown pigmented spots. The scaly syphilide of beard also gone; he can now shave with comfort. Only three sores left on face./
On the legs all ulcers are rapidly healing; commenced on second day. Feels excellent in health.

July 10th:— Face healed, also the large sore on left leg completely healed. Two on right leg almost healed. Wassermann's reaction is positive.

July 13th:— All lesions completely healed, feeling very fit — enormous appetite. Wassermann's reaction is positive.

July 18th:— Feeling extremely well and ready for work. The tired indolent feeling which he had had so long before the injection has entirely gone. Discharged — 21 days after the injection.
G. T. - Seaman - Age 31.
Admitted - July 10th, 1911.

History: Infected two years ago by chancre on scrotum. He has been troubled almost ever since with the disease in some form or other, although he has taken mercury continuously right from the beginning pills, liquor hydrarg; and hypodermic injections.

He was in this hospital for 13 weeks about fifteen months ago, and also later, for thirteen weeks as an out patient, taking mercury all the time. Whenever he stopped taking his medicine for a week or fortnight a lesion broke out somewhere, especially swelling and oedema of penis and scrotum, or ulcerations on arms or legs.

State on Admission: Penis immensely swollen and oedematous - three times its normal size, and intensely red with desquamating and broken skin all over its surface. Scrotum also swollen with oedema but to a slightly less extent, and covered with small discharging sores where skin has given way.

Gummatous ulcerations completely surrounding left ankle and greatly swollen. Broken down gumma over right tibia. Two patches of hard gummatous infiltrations over/
over flexor surface of left forearm. Two similar infiltrations over small of back.

Slight coppery papular rash all over body and limbs.

Nasty red sore throat, but no ulcerations.

Temperature 98.5

July 13th: Salvarsan injected .6 grms in 300 c.c. solution at 8-30 p.m. Temperature 98.8 pulse 84.

At 12 midnight temperature rose to 100.6 pulse to 96

" 2 a.m. (14th) " " 101.4 " 88
" 4 a.m. " fell " 99 " 80
" 8 a.m. " " " 98.6 " 74
" 10 a.m. " rose " 100.4 " 94
" 2 p.m. " fell " 99.8 " 86
" 6 p.m. " rose " 101.4 " 90
" 10 p.m. " fell " 99 " 88
" 2 a.m. (15th) " " 97.8 " 80

Constitutional Effects: Severe rigor at 2 a.m. on 14th and shivering for two hours afterwards.

Another slight shivering attack at 10 a.m., when temperature rose to 100, and another rigor when temperature rose again for the third time to 101.4. Shivering this time lasted for half an hour.

Vomited with first rigor, six times; diarrhoea (intense watery motions) three times; bad headache for two/
two days.

July 16th:— No improvement during the last three days, except that he feels much better in himself and sore throat is gone.

July 20th:— Considerable improvement. Penis greatly reduced in size - less oedematous, skin of penis almost healed up - desquamation finished and only one or two clean granulating sores left.

Scrotum:— Oedema completely gone, the skin has rapidly healed leaving only one granulating sore. 

Penis is soaked in boracic lotion for one and a half hours daily.

Gummatous infiltration of extensor and flexor surfaces of left elbow nearly healed - only a few scabs to come off. The broken down gumma over right tibia is also healing well, but still discharging - is now about the size of a two shilling piece. The diffuse ulceration and desquamation, and scabbing around left ankle is still very bad, but it is drier, not so inflamed, and less painful.

The diffuse infiltration over small of back and upper part of buttocks is greatly improved - is less red and desquamation nearly finished.

The papular rash is still present over back and chest, but/
but much fainter over legs.

July 24th:— Still further great improvement during the last four days. Penis reduced to its normal size, only one superficial sore to heal.

Scrotum completely healed and of normal size.

Left elbow, both surfaces of which were once so bad, is now practically healed. The scars are firm and not bound down to the underlying bones. Only a little scabbing left to peel off.

Left ankle:— Improvement here has been rapid also, only one or two ulcers, each the size of sixpence covered with scabs left to heal. Desquamation here too has finished.

Gummatous infiltration over upper parts of buttocks healed, only supple scaring remains.

The broken down gumma over right tibia is the slowest to heal, but is decidedly making good progress - a clean superficial ulcer now remains to be healed.

The papular rash is also slow to disappear, but is certainly becoming fainter.

Wassermann's reaction is positive.

July 31st:— The rapid improvement still progressing everywhere. Left ankle, now scarcely recognisable compared to time of injection, has only one ulcer, size of a shilling, left to heal. Left elbow healed except for/
for one or two dry scabs. Gummatous ulcer over right tibia now the size of a shilling.
All induration over back gone, nothing but dark supple scars left.
Penis healed; scrotum healed.
Aug. 3rd :- All parts should now be healed in a few days. Rash is practically gone.
Aug. 16th :- Clinically, every affected area of body is now completely healed. The scars that are left are all flexible and healthy, but darkly pigmented.
Patient took no mercury while in hospital.
Wassermann reaction weakly positive.
Discharged - 20 days after injection.
TERTIARY SYPHILIS (Gumma of the Nose)

E. W. - Female - Age 32.

History: Has been ill for four years; began by sore throat and hair coming out soon after birth of first child. Treated for nine months in Charing Cross hospital and soft palate ulcerated away while in there. From there she went to the London hospital attending there for three or four months. Was told in November last that nothing could be done for her. Came to Greenwich in November 1910 and treated with potassium iodide and mercury in the same way as at the Charing Cross and London hospitals. Has taken these drugs continually for four years. Soon after coming to Greenwich, nose broke out into a gummatous fungating mass, size of a Tangarine orange, starting around the whole circumference of the left nostril.

April 5th, 1911 :- When examined to-day patient was both looking, and feeling, extremely ill and in a very serious condition. The whole of the soft palate had ulcerated away and a hole in hard palate size of a pea. Also the fungating mass, size of a Tangarine orange, described above.

April 7th :- Salvarsan injected intravenously. .45 grm. at 11 a.m.

By/
By 1 p.m. temperature had risen to 104°.

9 p.m. "fell" 99°.

Patient did not stay in hospital the night but was treated as an out patient and at 9 p.m. returned to her home.

Constitutional Effects:— Slight shivering and headache.

No vomiting, but when she got home she felt a little sick.

April 8th:— Much brighter; not feeling so ill as she did before the injection.

April 10th:— Marked effect upon nose and palate—both much drier. Before the injection mass was very moist, covered with serum and a nasty foul smelling purulent discharge coming down nostrils and also passing back into the throat. This discharge has now to a large degree dried up. The mass itself is drying and shrivelling up.

April 17th:— Mouth condition has greatly improved and she herself considers it has all healed because it is now not a bit sore. The discharge too, that she constantly spat up—extremely foul and bad tasting—has stopped. Gummatous mass on nose has dried and shrivelled up to at least a third of its original size.

April 24th:— Only a dry sore around left nostril remains.
remains of the fungation and a slight mucoid discharge coming down the same nostril as she exhales.

April 29th:— It is three weeks since the injection and all lesions are practically healed. The nose condition has entirely healed and epidermis has covered over the dry sore seen on the 24th. No discharge from nose at all now. The left nostril is greatly reduced in size however due to cicatricial contraction but looks wonderfully dry. The oral parts before so inflamed and sore have now quite returned to their natural colour, though the loss of the soft palate is markedly evident. The hole in the hard palate has ceased to ulcerate and margins are healed, though the aperture is very little smaller.

Patient looks extremely well, and where as before she was too ill to work, can now work as actively as before she became ill.

Wassermann reaction not examined.
Mrs. A. - Age 33.

Treated as an out patient.

History:— Infected by a chancre eight years ago and treated for eight months with mercury, during which time the chancre healed. She remained quite well for about six years, then ulcers broke out over her right eye lid, over the left breast, one on the groin and one on the back. For these she came into hospital and again treated with large quantities of mercury. Then seventeen months ago her head broke out in gummatous ulcerations, for which she has been treated on and off ever since with large doses of mercury. Once it healed for three weeks but she started drinking, and all broke out afresh.

She has had seven still born children, and once when the pain in her head was so severe she attempted suicide by drowning.

State on Admission (as out patient):— She has six big gummatous ulcerations over her scalp.

One, over the right eye, size of a five shilling piece.

Two, over the frontal region, each the size of a five shilling piece. These two are practically run together.

Three, over the occipital region, one the size of a five shilling/
shilling piece, the other two each the size of a two shilling piece.

A thick profuse yellow discharge exudes from all the ulcers and bare bone can be felt in most of them with the probe. Over the rest of the scalp is a thick scabby rash; hair of course is very scanty. She complains of very severe pain in her head and has got no sleep at night for weeks. She is very weak and emaciated and looks extremely ill.

Jan. 10th. 1912: - Intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 3 p.m.

Temperature rose to 100.8 F.

Constitutional Effects: - Violent rigor at five o'clock; no vomiting; severe diarrhoea for three or four days, but no abdominal pain along with it.

Patient went home same day the injection was given at eight o'clock.

Jan. 11th: - She came back to hospital to be dressed.

The yellow discharge has begun to dry up, and the pains in her head have gone. Patient has a very much better complexion this morning. Her head is dressed with green protective and dry gauze.

Jan. 15th: - It is now five days since the injection. Excepting for one small patch the size of a threepenny piece/
piece all the ulcers are dry. The discharge has entirely stopped and bare bone can be distinctly seen in four ulcers dry and clean. Patient looks wonderfully improved and declares she has an enormous appetite, since the injection was given.

Jan. 17th:— Her head is now clean of the scabby rash—hair shaved off. All the ulcers on the scalp are clean and dry and nothing is left but the damage that was done. On her forehead, (over the right eye) where granulation tissue had formed there is still a small patch to be covered by epithelium.

Jan. 27th:— The five holes in her scalp have entirely filled up with practically no scarring. The ulcer on the forehead is the only one that has left a scar. Patient has wonderfully improved; she has put on a considerable amount of flesh since the injection, and her face has quite a healthy normal expression.
MALIGNANT SYPHILIS.

A. R. - Seaman - Aged 28 years.
Admitted - 20th April 1911.

History: - Got infected 24 months ago with chancre on penis, and was treated at Seaman's Hospital, as an out patient, with mercury. In two months however, sores developed on body, head and legs, and he was admitted to hospital for six months, and treated with large quantities of mercury; discharged in April 1910 apparently cured. He kept pretty well for eight months taking mercury all the time, then throat began to get sore and he could hardly swallow; next large gummatous ulcerations broke out on both sides of the neck - three ulcers on right side and one large one on the left side. At the same time a perforation occurred at the junction of hard and soft palate about the size of sixpence.

Re-admitted on April 20th 1911 with the following lesions:

- Badly inflamed throat.
- Perforation of Palate.
- Bad stomatitis and superficial ulcers over both cheeks.
- Deep ulceration on both sides of the neck.
- Syphilitic/
Syphilitic synovitis of the right knee joint.

Temperature 100.4.

April 22nd:— Salvarsan injected intravenously .6 gms. in 300 c.c. solution at 8-30 p.m. Temperature normal at the time; pulse 96.

By 10 p.m. temperature had risen to 101 Pulse to 104.

12 midnight " still 101 " 104.

2 a.m. " fell " 99 " " 80.

4 a.m. " " " normal " " 76.

Constitutional Effects:—Rigor at 11 p.m., vomiting severe headache.

April 29th:—His constant headache disappeared on the first day and the chronic tired feeling of which he so often complained disappeared on the second day after the injection. His throat got well on the third day while the ulcers on both sides of his neck began to heal on the second day. The swelling and fluctuation of the right knee joint disappeared on the fourth day, and to-day, seventh day, the hole in his palate is rapidly healing.

May 14th:—The ulcerations on neck which were very deep and spreading, have healed rapidly. Though local applications were used the discharge decreased phenomenally fast; at this date they are mostly covered by soft scar tissue from which exudes a serous discharge.

The/
The stomatitis and ulcers in mouth have all gone. Says he can still feel his throat a little sore. 

May 29th:-- The ulcers on his face and neck have practically healed, leaving large scars on both sides. The margins of these scars are hard but their centres are soft and inclined to break down, and a slight serous discharge exudes from these soft portions. The perforation in the palate is now absolutely healthy. The margins being completely covered by healthy mucous membrane. He says he does not notice it so much, as fluids do not now pass up into the nose when drinking, as they did previous to the injection. Wassermann's reaction is strongly positive. 

June 22nd:-- Patient in statu quo since May 29th. The drug seems to have spent itself and the condition of patient seems to be stationary. Another injection administered .45 gms. intravenously at 2 p.m. In four hours time the temperature had reached 100 , and pulse 104. The after effects were not so severe this time - the dose however was smaller - but there were Bad headache; nausea, but no vomiting; slight shivering, but no rigor. 

June 5th:-- Improvement has followed the injection. The scars are harder and drier, especially the right side which is practically dry. From the left side there/
there is still a slight serous discharge.

Wassermann's reaction is positive.

June 16th: Condition same as on June 8th.

June 26th: Still a slight serous discharge from the center of scar on left side. Says he feels perfectly well however except for a slight sore throat.

July 10th: Still in much the same condition; the serous discharge still oozes from left side of neck, though fluctuates a good deal, some days it appears and other days dries up. He has been taking grs. $\frac{\text{iii}}{\text{v}}$ of mercury per day for the last month.

Wasserman reaction positive.

July 20th: No improvement.

Wassermann reaction positive.

July 26th: Wassermann reaction much less positive.

Aug. 3rd: In statu quo. Still compelled to wear a bandage over left side of face, because of the intermittent discharge. For the last few days, however, it has been very slight. Still complaining of his throat being a little sore.

Aug. 16th: An improvement seems to have set in as he does without the bandage on the side of his face, though the scar is still a little soft in the centre. Throat is better again; it has never prevented him from eating, but says he has felt it less for the last few days/
Of all the conditions for which he came into hospital the above is all that remains. The stomatitis and small ulcers in his mouth have healed. The palate has healed and the knee feels quite well. The clear serous discharge only comes from a place about the size of a threepenny situated just in front of left ext. auditory meatus. This too is less now than it has ever been. He says he feels better than he has done since he first contracted the disease, and wishes to return to work.

The Wassermann reaction is only indefinitely positive. Discharged to-day to return to sea - 116 days after injection.
MALIGNANT SYPHILIS.


History: - Contracted Syphilis in August of this year; 1910, in India. Chancre healed by local treatment about beginning of September, but soon afterwards a lump appeared in the left groin.

Previous Venereal Disease: - In 1902 he contracted a soft sore which healed in seven weeks after treatment by cautery.

State on Admission: - Scar on penis, remains of the soft sore, but no evidence of the recent syphilitic infection. Swollen glands in the left groin, about the size of a hen's egg, soft and breaking down. Epitrochlear glands size of pea, hard and firm.

No other glands; no rash; no sore throat.

Wassermann reaction negative.

Given 1 gr. mercury by mouth thrice daily.

Nov. 22nd: - Rash developed, whole body is covered in a rose coloured rash.

Wassermann reaction is now positive.

Dec. 20th: - Complaining of a lot of pain in the head, and along the long bones of the body. Has a rise of temperature up to 101 F or 102.6 F. most evenings but/
but down again in the morning. Profuse sweating all night. Rash however is fading. Put on to daily injections of benzoate of mercury.

Dec. 26th: Patient feeling very ill. Mouth very sore, gums swollen and teeth loose. A fresh scaly rash has broken out over back and chest.

Jan. 25th 1911: Patient is better. The second rash has faded a good deal and his temperature is much steadier.

Jan. 27th: A third rash has suddenly developed - a rose coloured papular rash all over his body and face. He has now had 33 daily injections of the benzoate of mercury. To-day the injections are stopped, and mercurial inunctions prescribed.

Feb. 4th: Patient is suffering from violent diarrhoea. He declares he will not stay in hospital any longer and is determined to go home to-day. He has been in hospital three and a half months.

Re-admitted: March 27th, 1911.

Since patient has been out of hospital he has been in bed practically the whole time. He has persevered with the mercurial inunctions daily. His mouth is so bad that he cannot take solid food of any kind whatsoever. On re-admission he weighed eight stone and seven pounds, he looks extremely thin and weak.
His face, back and shoulders are covered with a bright coloured papular rash, which in parts is pustular, and scattered over the same areas, apparently where the previous rashes have disappeared, are a large number of small pigmented pitted spots. In the neck are large glands running down the posterior border of the Sterno-Mastoid, and the skin over them is very red.

On the penis near the fraenum is an ulcer about the size of sixpence, with a sloughy base and hard sharp edges. His mouth is in a filthy state, the gums are soft, spongy and sore, with the teeth all loose, throat red and congested, breath foul and profuse salivation.

Temperature 100°, pulse 78.

Wassermann reaction is negative.

March 30th: Patient's condition is much about the same, but his mouth is cleaner and he can take his food better. His temperature is normal in the morning, but every evening it rises to 101°. Mercury stopped.

April 4th: Salvarsan injected intravenously .6 gms in 300 c.c. solution at 8.30 p.m. Patient felt quite fit during the injection.

By 10 p.m. temperature rose to 102.3° Pulse 104 Resp. 32
12 midnight " fell " 102.4 " 112 " 20
2 a.m. " " " 100.4 " 104 " 20
4 a.m./
4 a.m. temperature fell to 99.4° Pulse 92 Resp. 16
6 a.m. "  "  " 99 "  92 "  16
8 a.m. "  "  " 98.2 "  88 "  16

Constitutional Effect: Slight rigor at midnight.
No headache, no nausea

April 6th: Declares he is much better. Rash is certainly fading, and the enlarged glands are smaller, and the skin over them not so red. The throat and mouth show marked improvement. The sore on his penis shows positive signs of healing and his temperature is still normal.

May 8th: Without further treatment improvement has been going on all the time. He declares he feels absolutely well; he has gained 15\(\frac{1}{2}\) pounds, weight now being nine stone eight pounds. The sore on penis which was four weeks old on re-admission, has been completely healed a week. The glands behind the Sterno-Mastoid muscles are now absolutely gone.

Rash: All the induration of the skin at the time of the injection has completely disappeared and nothing is now left but tiny pigmented spots, closely covering the whole body. These show up very plainly being the remains of three definite rashes.

His mouth is in splendid condition, gums normal, teeth tightened.
tightened up, and throat healed. He can eat any kind of food.

May 10th: Careful examination of the skin shows that no rash is present. The markings are only pigmented areas, and the skin is now quite healthy. Patient says he feels better than he has felt since August 1910. His weight has now increased to ten stone. He has been put upon the working gang of the hospital for some days, and has been booked to go back to sea on August 15th.

Wassermann's reaction is negative.

Discharged to return to work - 36 days after injection.
R. S. - Age 30.

History: Infected twelve years ago by chancre which healed in six weeks without treatment and no rash developed.

In a month or so, sore throat and ulcers on his legs appeared, so vigorous mercurial treatment was started and the condition greatly improved. Then he went to South Africa and there developed a chronic cold in the head and running from his nose. Small pieces of bone soon began to come away, and though taking mercury and iodides all the time nearly the whole nasal septum came away in about two and a half years. So he returned to England and was sent over to Germany - shown at cliniques, vigorously treated with mercurial inunctions and later by mercurial injections. After three months he returned to England improved. In about a month nasal discharge became very profuse and he had to undergo another course of inunctions when the condition again improved considerably. He returned to South Africa and was fairly well for a time but soon broke down in health. Left eye now became very inflamed and he could see double, and the bridge of his nose/
nose sunk in. He came back to England and thence to Germany for three weeks mercurial inunctions. He could not take mercury now as he used to; a few weeks inunctions made him feel very ill. Was fairly good for twelve months but got bad again, the discharge from his nose increased and more bone came away. He was this time advised to have salvarsan.

On December 25th 1910 he was injected under the scapular region - dose not known - and a big swelling developed lasting for two months. There was severe pain - had morphia - but no constitutional effects. The condition improved for a bit, especially his left eye which had been very inflamed before the injection. In March, however, more bone came away and nose went right in. In June the discharge was very bad and the fleshy septum ulcerated away.

He came to hospital October 18th, 1911.

State on Admission: Practically nothing but the soft parts of the nose remains. The bridge has entirely sunken in on a level with the face. The whole of the septum has gone and the nose has the appearance of a big round hole in the centre of his face. There is a profuse evil smelling discharge.

Given .6 grm. salvarsan intravenously on admission at 11-30 a.m. Temperature rose to 99.8.

Constitutional effects:
Constitutional effects:— Nausea, but no vomiting; shivering, but no rigor; headache and heaviness next day. The effects however were more marked than after the intramuscular injection.

Oct. 30th:— Great improvement. The profuse discharge has greatly dried up and most of the filthy granulations lining the nasal walls have disappeared. One can look right back into sphenoidal sinus. Since the injection he has felt much better, his appetite has returned and he takes a much greater interest in life.

Dec. 20th:— Patient has not been seen since the 30th October till to-day. Nose is now quite dry and healthy and giving him no trouble in any way. He says it is better now than it has ever been, since the disease started. Paraffin has been injected under the skin, thereby raising the bridge of his nose to a respectable height. Taking him all round patient has wonderfully improved and he is very delighted with the result.
C. B. - Seaman - Age 31.

Admitted - July 12th, 1911.

History: - Contracted Syphilis five years ago. One morning about the New Year he waked up with mouth twisted to right side and difficulty in closing left eyelid, and with severe headache. Before long the condition became worse; he could not move left side of face; constant headache localised to left side of head and face, and increasing deafness in left ear.

Condition on Admission: - Complete left sided facial paralysis. Ocular movements normal; slight nystagmus on extensive lateral fixation. Unsteady in walking. No aural discharge, moderate degree of deafness in left ear, slight tenderness over left mastoid, but no smelling. Knee jerks present but reduced; achilles jerks present but reduced.

Plantar reflex - flexor.

Ophthalmoscopic Examination: - Inner side of both discs blurred, left, more extensively than the right, and more congestion of veins on this side, suggesting an early optic neuritis.

Cranial Nerves: - 3rd, 4th, 5th, 6th are normal 7th/
7th paralysed; 8th, nerve deafness; 12th tongue deviated to left side.
Patient is left handed and left grip is less than the right.
Urine: normal.
Wassermann reaction positive.
July 23rd: Salvarsan intravenously 0.6 gram in 300 c.c. solution at 11 a.m. Temperature rose to 100.6°F, pulse to 96.
Constitutional Effects: Rigor, vomiting. By 4 p.m. temperature was normal again.
July 25th: The constant headache has gone. Facial paralysis still well marked.
July 31st: Greatly improved. The facial paralysis is markedly less. Eye shuts nearly naturally. Tongue almost straight. Walks more firmly, and feels much better.
Aug. 3rd: Still improving. The facial paralysis is hardly evident at all even on laughing. No headache; Walks well.
Goes back to sea to-morrow - 12 days after injection.
CEREBRAL SYPHILIS. - Fits.

C. W. - Seaman - Age 38.

History: - He had an accident to his head on November 11th 1910 and remained unconscious for thirty hours. On December 17th 1910 he had an epileptiform seizure and was admitted to this hospital for probable cerebral tumour, complaining of severe headache, and vomiting. Fits returned on December 21st and on every fifth day till January 24th. They were general and no localising diagnostic signs could be found.

On Examination: - Nothing was found wrong with his nervous system beyond a girdle of anaesthesia around his chest; contracted pupils, sluggish in reaction to light; apathetic in temperament; a distant gaze and sunken eyes, with dark rings around them. He had syphilis some years ago. He was now thought to be developing General Paralysis.

Fits stopped on January 24th for three weeks under bromides so he went out of hospital.

Re-admitted - March 23rd, 1911. The fits have continued once a week all the time he was out. It was now noticed that the fits were much worse than when he was in hospital last. For, instead of occurring on regular days they were very irregular in their time.
On some days he would have two or more and on one day he had ten in succession. Instead of being general they now started on the left side of the face by twitching and travelled on to the left arm and left side of the body, before the right side became affected. There was marked opisthotonos too. Bromides seemed to have no effect and syphilitic remedies continuously administered were also without avail. There was altered sensation down the left side of the body, face, arms and legs. Sensation to light touch abolished. Differentiation between sharp and blunt points also abolished. Differentiation between heat and cold is very indefinite. No optic neuritis; no reaction of pupils to light; knee jerks and plantar reflexes normal. Wassermann reaction positive.

June 12th:— The last fit was on June 9th. To-day intravenous injection of salvarsan .6 grm. in 300 c.c. solution at 9 p.m. Temperature rose at 4 a.m. to 99.4 but fell again by 10 a.m. same day to normal. At six the same evening rose again suddenly to 100 and gradually fell to normal by 2 a.m.

Constitutional Effects:— Rigor and shivering at midnight on the 12th. Severe headache, severe vomiting, and diarrhoea. A second rigor on evening of the 13th when/
when temperature rose to 100° accompanied by severe cramping pains in both legs, which lasted for two days. June 28th:—No fits since the injection. He seems much brighter and not so despondent and is determined not to stay in hospital any longer.

Discharged—16 days after the injection.

Sept. 23rd:—Patient was seen again to-day. He is better in every way; it is now one hundred and three days since the injection of salvarsan, and no fits have occurred.

Wassermann's reaction is still positive.
SPASTIC PARAPLEGIA.

J. E. - Seaman - Aged 30.

History: Patient contracted Syphilis five years ago and had the ordinary secondary symptoms. He was treated with mercury and all the manifestations passed off. Then seven weeks ago he noticed a numbness in the left foot and leg below the knee. Soon his toes scraped along the ground, and four weeks later a similar condition began in the right leg - viz, numbness, stiffness and dragging of the toes.

State on Admission: -

Nervous System: - Numbness from both knees downwards, but no pain. He walks with the aid of sticks. Very spastic gait; drags both feet, the left being the worse. He waddles to avoid the ground, sways when standing with eyes shut.

Anaesthesia: - (Slight) over chest and around the body, and also from both knees downwards.

Knee jerks exaggerated.

Achilles jerks exaggerated.

Abdominal reflexes absent.

Cremaster absent; No Babinski; No nystagmus.

Bladder and Rectum reflexes very weak, often suddenly passing urine and faeces in bed.

Lumbar Puncture: - Pressure much increased, and 250 lymphocytes/
lymphocytes in the field.

Eyes: - Left disc normal; right disc shows striation and filling up of physiological cup, with oedema of retina.

Wassermann reaction strongly positive.

Oct. 5th, 1911: - Intravenous injection of salvarsan .3 grm in 150 cc of solution at 10 p.m. Temperature did not rise until next day when it rose to 100 at seven o'clock in the evening. It fell again to subnormal next morning. The pulse rose from 96 to 120. At the time when the temperature was highest (7 p.m. Oct 6th) there was nausea and headache, but no diarrhoea or vomiting.

Oct. 30th: - Patient has improved very much. The anaesthesia is much less and he walks a good deal better.

Wassermann reaction still positive but Lumbar puncture revealed 94 cells to the field.

Nov. 1st: - A second intravenous injection of salvarsan .6 grm. in a 300 c.c. solution, at 12.15 a.m. In three hours temperature rose to 100 and the pulse from 84 to 140.

Constitutional Effect: - Rigor, headache (severe), vomiting and diarrhoea.

Nov. 20th: - Patient has made considerable further improvement/
improvement. He can now walk about the wards and around the hospital grounds without aid of any description whatsoever and without dragging the toes, though there is still evidence of a little stiffness. Rectal symptoms have now quite disappeared. The bladder reflexes too, have also greatly improved, but he has still an occasional precipitate passage of urine. The deep reflexes have almost returned to the normal condition, while the knee jerks, however, are still slightly exaggerated. The anaesthesia around the chest and down the legs has gone.

Eyes :- Veins not so swollen and the oedema has completely gone.

Wassermann reaction weakly positive.

Lumbar puncture shows 78 cells to the field.

The patient was to-day discharged - 46 days after injection.
CONGENITAL INTERSTITIAL KERATITIS.

T. S. - Male - Age 18.

History:— Admitted April 24th, 1911. Suffering from severe pain and redness; intense lachrymation and photophobia of left eye, and on forcing the lids apart interstitial flakes could be seen in the cornea. Right eye is healthy. Soon after admission the disease became further advanced; iritis developed with marked ciliary injection.

The patient was put on to the usual treatment of atropine and argyrol accompanied with twelve inunctions with Ung: Hydrargyri. Very little improvement followed this treatment; the lachrymation and photophobia continued just as severely, while the flakes over the cornea appeared to be spreading.

On June 10th the condition was:—

Left eye

1. Marked Interstitial Keratitis.

2. Severe iritis - the iris being greatly discoloured and fixed in moderate position.

3. Conical Cornea.

4. Raised tension.

5. Ciliary injection, lachrymation and photophobia, though improved, are still present.

All/
All mercurial and local treatment stopped.

At midday .6 grm. of salvarsan injected in 300 c.c. solution.

By 5 p.m. temperature rose to 100 ; pulse to 88.
By 2 a.m. " fell to 98.4 ; pulse to 72.

Constitutional Effects :- Practically none, slight nausea but no vomiting, no rigor and no headache.

June 16th :- For a few days after the injection the ciliary and circumcorneal injections became much worse, and lachrymation more marked but both have now somewhat subsided. Can see no difference in the keratitis, while the perception of light to the patient is almost nil.

June 28th :- The exacerbation has settled down though there is still a little circumcorneal injection. The perception of light has improved and the photophobia has gone. He can detect something in front of the eyes when the hand is held up against the light at ten inches distant.

July 3rd :- Left eye in same condition as on June 28th, but now complaining of pains in the right eye.

July 10th :- A definite patch of keratitis has developed in right eye at upper boarder of sclero corneal junction. Intense injection and also a little irido-cyclitis in region of keratitis.

July 13th :-
July 13th: Great pain in right eye. No pain in left eye, and is certainly clearer than on June 28th. July 14th: As right eye had become so seriously affected, salvarsan was again injected - .6 grm. in 300 c.c. solution at 9 p.m.

By 12 midnight temperature was 100.6 F Pulse 96
By 6 a.m. temperature fell to 99 F Pulse to 96.

Constitutional Effects: Vomited three times; painful diarrhoea twice; very severe pain in right eye all night, slowly subsiding next day. He felt very ill for many hours after. These disturbances were much worse after the second injection.

July 16th: Right eye very painful though not so severe as yesterday, but very red and injected.

Photophobia marked and the keratitis increasing.

July 20th: Left eye in much the same condition as when last seen; still a little injection but absolutely no pain. Right eye worse than has yet been.

Extremely red and inflamed - intense injection of all blood vessels. Marked photophobia and the keratitis is spreading all over pupil.

Wassermann reaction examined for the first time showed positive result.

Left eye much improved.

Right eye: Acute stage seems over. Pain practically gone/
gone though photophobia still present. Vessels still very injected and keratitis all over the pupil - the well known salmon coloured patches ofInterstitial Keratitis beautifully exhibited.

Aug. 16th: - Left eye considerably improved - the keratitis being much less. He has been able to count fingers at twelve inches for nearly a week.

Right eye quite settled down after the acute attack, no pain, the salmon patches are turning white, but there is a great deal of keratitis to be cleared up however.

Sept. 21st: - Condition of both eyes seems much the same as when last seen on Aug. 16th.

Left eye Corneal opacity has now become patchy though still shows traces of vascularization. No circum-corneal injection however and no pain. Can bear light better and vision improving.

Right eye: - No improvement since Aug. 16th. The salmon coloured patches slowly turning white, still completely cover the whole cornea with marked vascularization. Marked ciliary congestion. Photophobia present but no pain.

Patient had no treatment other than salvarsan from June 10th till Sept. 21st. After this date was not seen again.
DOUBLE CONGENITAL INTERSTITIAL KERATITIS

C. D. - Male - Age 19.

History: Right eye became affected first about 5th December, 1910 by severe pains behind the eyeball accompanied with photophobia, and objects quickly became dim. After a few weeks and before any treatment was administered the left eye became suddenly affected in a similar way to the right.

Admitted to hospital on December 22nd, 1910.

State on Admission: Double Interstitial Keratitis; severe pain marked conjunctival injection, and intense photophobia in both eyes.

From December 22nd 1910 till June 29th 1911 he was treated by the ordinary methods for Interstitial Keratitis with considerable improvement regarding the pain and photophobia, but still both corneae remained opaque especially the left. With the right eye he could just count fingers held up at three feet distant but with the left could see nothing at all - at this stage it was decided to try salvarsan.

Wassermann reaction positive.

June 29th: Salvarsan injected; .6 grm. intravenously at 3 p.m., Temperature 98 F; pulse normal. By 3-30 temperature rose to 103 F accompanied by a rigor lasting one/
one hour. Pulse rose to 88. After rigor temperature began to fall and by twelve midnight it had reached the normal line; pulse 78.

Constitutional effects:—Bad headache; vomiting (slight), and severe diarrhoea lasting till next day.

*July 3rd:* Though it is only five days since the injection there seems considerable improvement in the left eye, he being able to read fingers at three feet. The left eye has therefore improved to the extent of the right. The latter has remained the same as before the injection there being no lengthening in the power of vision of this eye. The two corneae are both about equally opaque, the improvement in the left eye is therefore probably due to the clearing up of some ciliary injection which was present at the time of the injection.

Some rheumatoid pains from which he had previously been suffering in the arms and legs have entirely disappeared.

*July 13th:* Right eye has improved considerably since last examined and is less opaque. Says he can see better now, than since the disease started. Left eye has improved since July 3rd, but only slightly. Wassermann reaction taken to-day was found to be negative.

*July 20th:*
July 20th: - Still improving in vision, especially in right eye but not so much as expected to find because corneae are still too opaque.

Aug. 3rd: - Thinks he can see better than when last examined, but on close examination of the eyes, the opacities of the corneae look much the same as on July 20th.

Aug. 16th: - Further improvement is seen to-day in the right eye. The opacity of cornea is much less than that of left. With the right eye he can see to read very large print, but not a newspaper. Can dimly see objects across the road. The left cornea still has a fairly thick nebula across it.

Sept. 21st: - Patient not seen again until this date. Improvement still taking place but very slow. Both corneae appear a little clearer than on Aug. 16th. The right is still better than the left. He can read large print, but only with difficulty the small print of a newspaper.

Patient has not been seen from this date. He had no mercury between the dates Dec. 22nd 1910 and Sept. 21st 1911.
Case E. W. - Female - Age 32.

Photographed three days after the injection of salvarsan. Gumma drying up and becoming smaller rapidly.

Photographed ten days after the injection. The gumma has dried up, leaving a healing ulcer only.
Mrs. A. - Age 33.

Photographed just before the injection of salvarsan was administered. The photograph shows six ulcerating gummata of the scalp from which exudes a profuse purulent discharge.
Photographed on the fifth day after the injection of salvarsan. The discharge from the ulcers has dried up entirely and only the damage due to loss of tissue remains. Bare bone can be seen in some of the ulcers.
Mrs. A. - Age 33.

Photographed on the seventeenth day after the injection of salvarsan. The hair has been shaved off and the holes in the scalp are seen to be filled up, leaving practically no scarring.