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SUBJECT:-

"Treatment of Syphilis by Arylarsonates  
with special reference to recent research."

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## INTRODUCTION.

Throughout the entire range of diseases there is not one malady, not excluding cancer, which is more deadly and yet so common as Syphilis. There is no region of the body which is not liable to be permanently deranged by it. There are but few regions in the world where its ravages are unknown. The far-reaching effects of this disease on the health of the individual and the welfare of the nation have not received appropriate recognition, nor the extent to which it should be held responsible for physical degeneration has been fully realised.

When we come to consider syphilis in its relation to other diseases, its importance is even more enhanced. So protean are its effects that it may be affirmed, without fear of exaggeration, that any advance in our knowledge of the disease will clear many mysteries attaching to other diseases, and will provide clues to their prevention, diagnosis and treatment.

So much has mankind to gain by its extermination that every effort in this direction should be encouraged.

Any/

Any efficient addition to the therapeutic measure at our disposal to successfully combat this disease is a great advance and ought to be welcomed by the medical profession.

So far mercury has been considered the only specific remedy in the treatment of syphilis, and iodides in certain cases. But the discovery of the specific organism by Schaudirm & Hoffmann in 1905, has led to a great deal of research. Since that date experimental work has led many to advocate the use of Arsenic, especially its organic compounds. It is these - the Arylarsonates - that form the subject of this communication. Recently a lengthy controversy regarding the value of these preparations ensued in the British Medical press. It is the object of this paper to examine all the evidence for and against the use of these drugs in the treatment of syphilis, based upon sixty cases treated at the London Lock Hospital and all the cases of Amyblyopia due to these preparations, reported in the medical press during this year.



MICRO-BIOLOGY.

That *Spirochaeta pallida* is the specific organism of syphilis as claimed by Schaudinn and Hoffmann in 1905, is now an undoubted fact. They proved that this organism is found in all cases of syphilis and is never found in any other affection. They also discovered spirochaetes in fresh preparation, not only on the surface of the chancre and papules, whether of the skin or mucous membranes, but also in deep tissues and the enlarged inguinal glands of syphilitic cases. Metchnikoff & Roux, have demonstrated the presence of the organism in chancre on the penis and face of monkeys; they have also found the spirochaetes in papules. Levaditi, demonstrated large numbers of spirochaetes in the fluid contained in the bullas in congenital syphilitic child and other observers have found the organisms in the spleen and liver of children with congenital syphilis. An ever increasing army of workers have supported the discovery of Schaudinn.

The objections urged by Seigel and his school that the spirochaete is merely a saprophyte and that the spirochaetae which stain by the silver method are in reality/



reality spirally arranged tissue elements, have been disproved repeatedly. Recent discovery of the spirochaeta pallida in aertitis and osteo-chondritis is of special interest and one observer has even found it in the dental germs of syphilitic fetuses, which probably explains Hutchinson's teeth. According to Metchnikoff, this organism has been shown in every possible lesion which is definitely syphilitic.

The spirochaeta pallida examined in fresh preparation, taken from the scraping of a primary sore or secondary papules of mucous surfaces, under the ultra-microscope, may be recognised by its size, shape, and movements.

SIZE & SHAPE - It appears in fine silvery spirals 5-25" in length, with very regular, steep and closely set spirals, the height of which diminishes at the ends. The organism oftener looks like a row of luminous dots resembling a chain of streptococci but which on careful focussing is seen to be a spiral.

MOVEMENTS - The spirochaeta pallida is freely motile compared to the other varieties met with. The movements consist of -

- (1) Bending, which are most marked;
- (2) Snake-like undulations;
- (3) Cork-screw rotation around its long axis;
- (4) Concertina/

- (4) Concertina like movement;
- (5) Local wave of contraction which flattens out the spirals.

They have to be differentiated from larger spirochaetes found in the mouth, mucous membranes and superficial sores; these are thicker, have more open spirals and are less active. The only other sprochaeta very like the pallida is the Spirochaeta dentium found in carious teeth but it is shorter and the depth of the wave is considerably less.

I have examined one hundred scrapings under the ultra-microscope, seventy were from undoubted syphilitic cases and thirty from doubtful sores. Of the former, I found the organism in sixty seven cases, most of them within five minutes. In the remaining three I made repeated examinations on three successive occasions but found the organism only in one, on the third trial after a long search.

Of the latter thirty cases the spirochaeta pallida was found in nineteen and all of them showed induration of the sore and later on secondary manifestations. Of the remaining eleven, eight turned out to be syphilis and three merely septic sores (chancroids).

I have also examined puncture fluid from enlarged glands in the groin, in fifteen cases of undoubted syphilis; but have not discovered the organism except in one single case.

Lately, Burri, has introduced a very simple method of detecting the spirochaeta pallida. One drop of Grublers Indian ink diluted eight to ten times is mixed well with the scraping from the sore or papule and then rapidly covered with a cover-glass and examined with an oil immersion before it has dried. The spirochaetes appear as white threads on a black ground. The method is good in the absence of an ultra-microscope but has the disadvantage that the organisms do not display their characteristic movements.

Other methods which require skill and experience and involve a great deal of time are the staining of smears by the Giemsa method or the silver process of Levaditi. These are only applicable in laboratories and hence not helpful in making a diagnosis on the spot.

All methods of cultivation of the spirochaeta pallida outside the body failed until Muhlens obtained a pure culture of a spirochaet indistinguishable from the/  
the/



the pallida. The material was taken from a syphilitic inguinal gland and the organism was grown anaerobically for many generations on horse serum agar. But all attempts to produce syphilis by inoculation with it have failed and it is impossible to state definitely that the culture was one of spirochaeta pallida or of an organism closely resembling it.

Hoffmann, believes it possible that, though the spirochaeta may be cultivated, it soon loses its virulence on artificial media. This view is supported by Metchnikoff's observation that syphilitic material loses its virulence outside the body in a few hours, long before the spirochaetes have lost their motility.

In spite of the fact that the spirochaeta pallida does not fulfil all Koch's postulates, it is certain that it is the causative organism of syphilis.

Neisser, says, "we may assume with certainty that these spirochaetes are the cause of syphilis; we may say that where we find spirochaetes we have to do with syphilitic processes. In short for myself the question is settled - Schaudinn's spirochaetes are the cause of syphilis."

CLINICAL PATHOLOGY.

After inoculation the organism remains for a short time, a few hours, in the lymphatic spaces and clefts of the tissue and there multiplies. It then gets into the lymphatic glands and produces histological changes though yet no naked eye changes are observed. This opinion has been arrived at by inoculating monkeys with syphilitic virus and finding the specific histological changes before any sore developed. Levaditi & Yamanouchi, have endeavoured to find some explanation for the length of the incubation period in syphilis by the study of lesions produced experimentally in the cornea of rabbits and the eyebrow of anthropoids and monkeys. They find that the incubation period corresponds to the slowly progressing development of the histological lesions which are set up by the multiplication takes place only slowly at the beginning owing to the difficulty the parasites find in assimilating the new nutritive medium. The active multiplication of the parasite and the concomitant termination of the incubation period is due to the completion of those changes in the vessels and newly formed cellular elements which/

which assure for the *spirochaeta pallida* a plentiful supply of nutritive material. When the organisms penetrate the surrounding tissue and infiltrate these the formation of the typical hard sore takes place.

After leaving the chancre the organisms take various routes. In man and the anthropoids they pass to the nearest lymphatic glands, where they multiply and cause adenitis and then passing into the general lymph stream they set up polyadenitis and infection of glands remote from the site of inoculation.

When the parasites pass out of the lymphatic system, the infection extends to the blood circulation and a roseolar eruption results. The generalisation of infection takes place at this stage. Though the organism has been found in nearly every tissue and organ in the body it has greater affinity for certain tissues. The organisms might disappear from the blood entirely, yet they would be found in the juice of lymphatic glands, in a condition of acute swelling. It is well known that the secondary eruptions, mucous tubercles and condylomata, contain immense number of spirochaetes and hence are most infective. Neisser, was unable to inoculate animals with the virus by injecting it into the blood/



blood or into organs, though he succeeded in doing so by causing abrasion of the skin or mucous surface and rubbing in the virus. Lingard, in his report on Dourine disease in horse, which may really be considered syphilis in the equines, (the similarity between mal de coit and human syphilis being very great) observes that he succeeded in inoculating animals more readily by scarifying the genitals and rubbing blood from papules or vaginal discharge than when he injected blood into animals. Mott, thinks that this habit of Trypanosomata and Spirochaetes of selecting the skin and mucous membrane is acquired to preserve and perpetuate the species.

#### BIOCHEMISTRY.

With this general invasion by the spirochaetes a profound biochemical change occurs in the blood and fluids of the body. As the result of the activity of spirochaetes the fixed cells proliferate, which by their destruction, form the nutritive material for the spirochaetes. The dissolution of these young cells rich in nuclein is the cause of the production of certain substances of a lipid nature in great abundance. These lipoids, the so-called "antibodies", are produced/

produced in the animal body infected with syphilis in such a large quantity that they become demonstrable by the method of serum diagnosis called Wassermann's reaction. In the normal body the lipoids exist in such small quantity that they are not demonstrable by the same method of examination. It appears that they are not new specific syphilitic substances, but they are normally present, which under the influence of the disease increase in the manner of a re-action product. This re-action of Wassermann is positive only, with the serum of a syphilitic person. Neisser, asserts that in spite of many thousands of examinations these substances have never been found in healthy men. He takes up the position that, where we find these anti-bodies, we have to do with a man who has had syphilis, and we may even say, with one who still harbours the syphilitic virus.

#### WASSERMANN METHOD.

This method can be carried out in the following manner either for testing the serum or cerebro-spinal fluid. It is necessary to immunise an animal against the blood corpuscles of some other animal - for example, by injecting the blood corpuscles of an ox into the circulation/

circulation of a rabbit. After several injections the serum of the rabbit becomes haemolytic to the corpuscles of the ox by virtue of the presence in the serum of an immune body plus the normal complement. This latter can be removed from the rabbit's serum by heating it in vitro to  $56^{\circ}\text{C}$  for thirty minutes. The rabbit's serum with the immune body alone in it will not dissolve the red blood corpuscles of the ox. Its haemolytic property could be restored by adding a small amount of guinea-pig serum which contains complement.

The experiment consists in mixing the serum of cerebro-spinal fluid to be examined in varying dilutions with a watery or alcoholic solution of the liver of a syphilitic foetus; a small amount of the serum of a guinea-pig is added, and the bulk made up to a constant volume (about 2 c.c.) with saline solution. The series of tubes containing these mixed solutions are placed in an incubator for one hour at  $37^{\circ}\text{C}$ , and then the sensitized corpuscles are added. The mixtures are again placed in an incubator for two hours at  $37^{\circ}\text{C}$ , then removed and placed on ice over night. The next morning the amount of haemolysis in each tube can be estimated. If, on the one hand, antigen (contained in the extract of/



of syphilitic fetal liver) and antibody (in the syphilitic serum or cerebro-spinal fluid) have been present, they have united with the complement (provided by the guinea-pig serum) and no haemolysis will have taken place, because the complement has been fixed before the addition of the sensitized corpuscles. If however, the antibody was not present in the serum or cerebro-spinal fluid, then the complement in the guinea-pig serum has remained free to act on the sensitized corpuscles and to lead to their solution.

A control experiment using normal serum or cerebro-spinal fluid, namely, one which contains no antibody, must be made at the same time.

This test of Wassermann is very elaborate and a large number of tests have been suggested which are simpler in their application, though just as reliable, being based on the same re-actions. Among others, Hecht's process improved by Fleming, Forge's and Nogouchi test may be mentioned.

Fleming's method differs from Wassermann's original method in the following respects:-

1. An alcoholic extract of normal heart muscle is used instead of a saline extract of syphilitic liver.
2. The/

2. The natural haemolytic power of human serum for sheeps corpuscles is made use of, thus doing away with the necessity for the haemolytic serum of a rabbit immunised against ox's corpuscles, and the guinea-pig's serum (complement).

3. The amount of blood which can be collected in an ordinary blood capsule will furnish an ample supply of serum for the test.

The value of Wassermann re-action has been differently estimated by Continental and English authorities. Lesser and Boas', figures might be taken as a fair average and they give the re-action as positive in primary syphilis in 60 per cent of the cases examined; in secondary in all the cases, and in 97 per cent of the untreated tertiary cases. In G.P.I. it was present in all cases, whilst it was positive in 80 per cent of the cases of tabes.

Flashman & Butler are of opinion that negative results with the serum of syphilitics are diminishing as the technique of the experiments is improving. Mott, still considers Wassermann's original test more reliable than any of its modification. Lane, places great faith in Fleming's modification and Bassett-Smith who/

who at first got less reliable results with Fleming's method than with Wassermann's, later on confirms the equal reliability of both methods.

Mr. H. W. Bayly, the pathologist to the London Lock Hospital gives the following figures as the result of his observations. He finds 100 per cent positive results in cases of untreated congenital syphilis; all negative in cases of primary syphilis, in which the lesion was present less than a fortnight and 75 per cent positive when lesion was present over a month. In secondary syphilis he gets positive results in 90 per cent and 75 per cent in untreated cases of tertiary syphilis. In para-syphilitic affections, he obtains 90 per cent in G.P.I. and 50 per cent in tabes.

His observations on the effects of anti-syphilitic treatment on the Wassermann re-action are most noteworthy. Out of twelve cases treated with full courses of soamin and orsudan, he found the re-action negative only in one case and he doubts if that one case was not one of those 9 per cent of undoubted cases of secondary syphilis which fail to give a positive Wassermann./



Wassermann. On the other hand the effect of mercurial treatment is clearly shown by him. He finds that cases with treatment of six months to one year record 43.5 per cent negative re-actions, while those with eighteen months treatment give 72 per cent negative Wassermann.

Porge's test, as recorded by Campbell, appears very simple and according to the author it is as reliable as Wassermann; 1 to 2 c.c. of blood are taken from the finger and transferred to a small test tube. The corpuscles are allowed to sink, and the upper serous portion is drawn off. This is then centrifugalised, and the serum again drawn off and heated in a water-bath for half an hour to a temperature of 56°C. By means of a finely-graduated pipette, 2 to 10 c.c. of the heated serum is transferred to a test tube A, and a similar quantity to a test tube B. (control). To the test tube A. is added 2 to 10 c.c. of a freshly prepared solution of sodium glyccolate (1 per cent of the salt in distilled water), the two fluids being mixed by carefully inverting the tubes a few times, and to the test tube B. is added a similar quantity of normal saline solution. The two tubes are kept at the ordinary temperature/

temperature of the laboratory for about twenty hours. In the event of a positive re-action, at the end of this time a flocculent precipitate will be observed in the test tube A, floating in the upper portion of the fluid, the fluid in the test tube B remaining, on the other hand, quite clear.

Porge maintains that this test is not only simpler and more easy of application than the Wassermann test, but that it gives better results.

Though I have carried out this test only in twelve cases, in which Wassermann was also done, I found that it gave identical results to the more elaborate test, namely, positive in nine cases and negative in three.

A very simple method introduced by Noguchi, and recommended strongly by Mott, consists in boiling two parts of the cerebro-spinal fluid with five parts of a 10 per cent solution of butyric acid in saline solution for a few seconds and then adding one part of a normal sodium hydrate solution and again boiling. A floccular precipitate is obtained on standing in parasymphilitic affections, due to the presence of a globulin.

EARLY DIAGNOSIS OF SYPHILIS.

The above re-actions and the ultra-microscope mark a great advance in the diagnosis and therapeutics of syphilis. They confirm immediately the diagnosis of lues even where symptoms are wholly obscure and clinically give no support to the diagnosis of syphilis, or especially where nothing is known of a syphilitic history.

Much more often than before can we finally prove the fact that an infection with syphilis has taken place. For merely we had either to wait for weeks for the development of primary induration, or in very many cases we had to wait even for months until the appearance of a secondary eruption on the skin or mucous membranes. Whilst we were still in doubt, the spirochaetes were extending over the body and forming metastases in the different organs. The experiments of Levaditi and Yamanouchi, referred previously, have conclusively proved, that a long time, fourteen to sixteen days, before the appearance of the primary sores, the virus had spread to the internal organs. Further, the generalisation/



generalisation of the virus is complete, as a rule, as soon as the primary lesion appears. Thus up to the present our treatment had only commenced when the syphilitic infection had been already generalised. It has been shown, however, in many protozoal diseases and particularly by researches on trypanosome diseases that treatment is effective to a greater degree if applied before general dis-semination.

The principle that the treatment of syphilis should not be commenced before the diagnosis has been settled beyond doubt will no longer oblige medical men to wait till the onset of secondary symptoms. By the demonstration of the spirochaetes we are now able to determine in good time whether an erosion is the beginning of a primary lesion. By the serum diagnosis we can determine whether a general infection is developed.

We are thus in a position to institute as soon as possible a local radical treatment, excision of the primary lesion, as strongly advocated by Neisser, and undertake the earliest possible commencement of an energetic general treatment. We are also by means of the serum diagnosis able to ascertain whether general syphilis has developed or whether the treatment has yet succeeded in removing the syphilitic virus from the body as the result of treatment.

TREATMENT OF SYPHILIS BY ARYLARSONATES

Arylarsonates are salts of Arsonic Acids, which are derived from Arsenic acid by the substitution of an organic radicle for a hydroxyl group. The organic radicle may belong either to the aromatic or fatty series; when it belongs to the former the acid derived thereby is called "arylarsonic." A salt derived from this acid is called an "arylarsonate", a good example of which is atoxyl, or soamin, which is atoxyl free from impurities.

This salt, which is sodium-para-amino-phenyl-arsenic acid, was the first of the arylarsonates used extensively. It was discovered by a French chemist, Béchamp, over fifty years ago; but a few years ago was introduced by a German firm under the trade name of "atoxyl." Fourneau, another French chemist, pointed out that atoxyl was identical with Béchamp's substance, and the credit generally given to Ehrlich for this discovery was wrong. His work, as well as the works of Moore, Nierenstein, and Todd, consisted only in showing the true constitution of the substance, in that/

that the arsenic was directly on the benzene ring.

After its discovery the drug had only a short career, being used in some skin diseases. It was soon abandoned owing to its toxic effects which led to blindness in cases where its use was long continued. Its use was revived by the discovery of Thomas and Breinl that it had a marked destructive action on the trypanosomes. They suggested its use as a drug in cases of sleeping sickness.

In Liverpool, as well as, in other places its use was well known to the workers and it was recognised, long before Koch used it in Africa, that in all cases of trypanosomiasis life was prolonged by the administration of atoxyl. It was known that the parasite could be driven out of the circulation by its use and that attacks were often cut short; but that ultimately a fatal issue was unavoidable. Koch's share in the work consisted in applying it on a large scale in an expedition of which he then happened to be in command in Africa.

Koch, as the result of his observations, gave glowing accounts of the curative powers of atoxyl in sleeping sickness and since that time the drug has been/



been extensively used for that most fatal malady, in Uganda and other parts of Africa where sleeping sickness is prevalent. But the high anticipations raised by Koch's statements have not been fulfilled, as shown by the last quarterly report of the Sleeping Sickness Bureau; indeed from somewhat diverse reports of the medical officers in charge of the different segregation camps in Uganda, it appears that most of them have discontinued its use owing to cases of optic atrophy following its continued administration.

Besides sleeping sickness, atoxyl has been tried in other protozoal diseases. Trincas, finds that atoxyl is not a satisfactory substitute for quinine in malaria. In undoubted cases of malaria, as determined by the examination of blood, atoxyl seems of quite secondary value, and its high toxicity makes it a dangerous remedy. But the experience of Schacht, is quite the reverse of this; he finds atoxyl in small doses given intra-muscularly of great benefit in anaemia following malaria.

In another protozoal disease, relapsing fever, Iversen, used Arsacetin (acetyl-atoxyl) and atoxyl. He treated 104 patients by intramuscular injections, the average/

average total quantity given to each patient was 2.8 grains. Those treated with atoxyl showed less severe symptoms after its use. Of those treated with arsacetin (104); 52 per cent did not have recurrence of symptoms; the relapses between the first and the second attack had longer intervals and the fever was only slight. In one of the cases permanent blindness set in.

The use of arylarsonates has been made in such other protozoal infections as spirillosis in hen, tsetse fly disease, dourine disease of horses and in pellagra.

The results of atoxyl in the treatment of sleeping sickness and the analogies in structure between the organism of that disease and that found in syphilis, both being presumably protozoal, led many pathologists to try the drug in the treatment of syphilis. Atoxyl was first used in the treatment of syphilis by Uhlenhuth, Hoffmann, Roscher and Salmon, after extensive animal experiments. Professor Hallopeau collected the cases treated at the St. Louis Hospital, Paris, by himself and his colleagues Professor Lassar, M. Salmon/

M. Salmon and M. Balzer, which amounted to 150 cases, and made an important communication on the treatment of syphilis by atoxyl at the meeting of the Academie de Medecine, in June 1907. His conclusions may be given here briefly:-

1. Atoxyl has a powerful action on the infective agent of syphilis, it acts as a microbicide; mercury and iodides should be administered at the same time, according to the prescribed rules.
2. We now possess, against syphilis, a third specific agent equal, if not superior to its predecessors.
3. Secondary associated infections such as vegetating condylomata appear refractory to the treatment; so also leucoplasia of tongue and hemiplegia. The drug has no influence on tabes and general paralysis.
4. After a long continued use of the drug, which is necessary for the cure of syphilis, toxic symptoms make their appearance, owing to which the treatment has to be discontinued. These symptoms are general malaise, pains in the limbs, gastro-intestinal pains, nausea, vomiting, painful micturition. These can be avoided by using large doses for the first two injections, /



injections, by having intervals between them and stopping them as soon as toxic symptoms appear.

5. Old people, people of small stature and patients with organic affections, should be given smaller doses.
6. It is highly probable that atoxyl breaks up into toxic products and therefore a more stable product should be looked for.
7. The direct local action has not yet been established but injections should be given near a hard chancre or gumma.

Hallopeau advises that treatment should be carried out as follows:- A patient with average constitution, weighing about twelve stones, should be given two injections of 75 cg. of 10 per cent solution, at two days interval, then four further injections of 50 cg. each with three days interval between each.

The investigations of Igersheimer and Rothmann, on the behaviour of atoxyl in the body and its fate in the organism elucidated good many points of great value. The experiments were carried out on rabbits, cats, dogs and man. They found that elimination was completed in five or six hours (for rabbits) and in nine hours (for men/

men.) As the total arsenic recovered was generally greater than the atoxyl recovered, some chemical change must have taken place to a small extent. They found contrary to Ehrlich's opinion, that though there were negligible quantities of reduction products in urine, the substance eliminated was mostly atoxyl.

The blood of rabbit was examined after injection of atoxyl, and it was found to be present almost exclusively in the serum for as long as two hours and a half and only in traces in the corpuscles. In their opinion this protracted stay of atoxyl in the serum has some bearing on its therapeutic value in diseases caused by haematozoa.

In the rabbit and the dog they found considerable quantity of atoxyl in the internal organs and also in the central nervous system of the cat. Traces were found in the eye of the cat and dog, whereas corresponding dose of sodium arsenate did not show least trace of arsenic in the eye. They therefore concluded that atoxyl had specific attraction for nerve tissues and the eye.

No toxic symptoms were observed, unless there was evidence of retention in the body. The poisonous symptoms/

symptoms of atoxyl, were in their opinion, due to reduction products on the one hand and to inorganic arsenic on the other.

At the meeting of the International Medical Congress at Berlin, Metchnikoff thus described his experiments:- "Seven monkeys (*macacus*) were inoculated with the same syphilitic virus; during the incubation period of syphilis, two of these animals were given injections of 10 grains of atoxyl. While the chancre appeared in the five monkeys not subjected to the arsenical treatment, the two monkeys treated did not show any visible sign of syphilis." He concluded that besides its curative properties on the established lesions of syphilis, arsenic shows preventive properties as well.

Neisser, confirms Metchnikoff's experiments and speaks very favourably of a number of Arsenic preparations in the treatment of syphilis. He emphasises the fact that mercury is a true specific for this disease, and he does not suggest that it should be replaced by arsenic. He is able to show, by animal experiments, that arsenic is also capable of curing syphilis. Some animals even re-act better to certain arsenic preparations than to mercury. In his experiments, atoxyl exhibited/



exhibited both preventive and curative actions. But he thinks that the action of atoxyl on the virus of syphilis is different from that of mercury; the latter kills the germ directly, while the former exerts its influence in strengthening the phagocytic defence of the host.

He speaks very highly of Arsacetin, a preparation of atoxyl, which owes its existence to Ehrlich. It is sodium-acetyl-para-amino-phenyl-arsenate, is less toxic than atoxyl and stable even at high temperature. In animal experiments Neisser, found it as powerful a curative agent as atoxyl. He has therefore successfully used it in a number of his patients. So far none of his patients have exhibited any undesired effects from arsacetin, save a slight gastro-intestinal disturbance, which are at once allayed by the simultaneous use of alkaline drinks.

He gives injections of six grains of arsacetin on two consecutive days each week, for a period of ten to twelve weeks. He advises 10 or 15 per cent warm solution intramuscularly but thinks it can be given by mouth. He is of opinion that arsenic preparations and/

and mercury can be employed simultaneously with advantage. He cautions the use of atoxyl and arsacetin in patients suffering from kidney disease.

G. Heymann, used arsacetin in a number of cases of primary, secondary, and tertiary syphilis and succeeded in obtaining a rapid and obvious curative action of the drug. Broad condylomata, mucous patches, and various forms of rashes disappeared in a short time under the treatment. The rapid beneficial influence, however, did not persist, and recurrence of the symptoms within a fortnight were met with. The repetition of the treatment proved of no value, and mercury was employed in the recurrences. In 23 per cent of his cases he found symptoms of intoxication. He came to the conclusion that arsacetin acted rapidly in influencing the symptoms for the time, but that this action was not durable.

In this country the officers of the R.A.M.C. have utilised to the utmost the splendid opportunities they possess in studying the effects of different methods of treatment of syphilis in the army. Colonel Lambkin's name stands out most prominent among a host of other workers in the army. He started treatment of/

of syphilis by atoxyl in August 1907, soon after Hallopeau published his results, and has since carried on the treatment with different preparations, scamin, Orsudan and Arsacetin, with brilliant results. He reported the result of his treatment on 54 cases at the meeting of the British Medical Association held at Leeds in July 1908 and again at the Belfast meeting in July 1909, on 130 cases.

In his first report he advised intramuscular injection of 10 per cent solution of scamin every other day. He laid great stress on fresh preparation of solution every time it was used, as the drug was liable to undergo decomposition on standing, and might produce toxic symptoms. He gave ten such injections, namely, 100 grains in all. He forbade the use of arylarsonates by mouth, as they were broken up by the acid contents of the stomach, and the toxic effects of over dose of arsenic were thus produced. He also advised that these preparations should not be used simultaneously with mercury, as the latter dissociated the ingredients of the arylarsonates, giving rise to accidents. Before beginning <sup>\*</sup>mercurial treatment or vice versa he advised to wait for fifteen days until either/



either drug was eliminated from the system. He concluded finally that in these salts we were in possession of a second specific for syphilis, the importance of which could not be exaggerated.

In his second communication he gave effects of treatment of 130 cases by arsacetin. He used the same technique but only 70 grs. of preparation in all. He found simultaneous use of arsacetin and mercury very useful.

He has now completed over 300 cases at the Rochester Row Hospital, with excellent results not only in primary and secondary manifestations but in late secondary and tertiary cases of syphilis. He has not had any case of optic atrophy, though several of his cases have exhibited temporary toxic symptoms which disappeared without stopping the course of treatment.

I have visited the military hospital at Rochester Row on two occasions and have seen the technique used. It is identical to the one pursued at the London Lock Hospital. I have also had facility given me for independent examination of some fifty of the patients; but I did not hear report of any toxic effects or mishaps/

mishaps from a single patient in spite of a very careful scrutiny.

Mr. Lane, who began the use of arylarsonates some time before Colonel Lambkin, gave up the use of these preparations owing to early disappointment; but he resumed it in 1908 and published a very excellent account of his experience of the preparations. He supported Colonel Lambkin's views fully and strongly advocated the use of arylarsonates in the treatment of primary and secondary stages of syphilis.

He continued the use of the drug until the end of 1909 when the occurrence of amblyopia in one of his patients as the result of this treatment made him refrain from further use of this drug. It is through Mr. Lane's courtesy that I am able to make use of the cases treated in his ward at the Lock Hospital.

#### ARYLARSONATES AND THEIR DERIVATIVES IN USE.

1. ATOXYL - is the original compound of arsenic used in sleeping sickness and later in syphilis. Chemically it is sodium-para-amino-phenyl-arsenate, the trade name given by the German firm being "atoxyl". It contains 29.10 per cent of arsenic; it is a white powder, soluble in ten times its weight of water.
2. SOAMIN /

2. SOAMIN - is a production of Burroughs Wellcome & Co. In its chemical composition it is sodium-amino-phenyl-arsenate and almost identical with atoxyl, except that being of a definite chemical composition and arsenical strength, (22.5 per cent) can be administered with greater safety. It is soluble in three parts of water at body temperature, giving a neutral solution which can be sterilised by boiling for five minutes. This preparation was used in case 45, as well as in cases 45 to 53 and 54 to 56 in the list of cases appended.
3. KHARSIN - also a production of B.W. & Co. It is sodium-trimethyl-tetra-amino-phenyl-arsenate. It is an amorphous powder, soluble in 5 parts of water at body temperature. It contains 23.7 per cent of arsenic. It has not been used at either this hospital or any other place.
4. ORSUDAN - also a production of B.W. & Co. It is an acetyl derivative of atoxyl, being chemically sodium-tri-methyl-tetra-acetyl-amino-phenyl-arsenate. It is a white anhydrous powder, soluble in  $2\frac{1}{2}$  parts of water at body temperature, it contains 25.4 per cent arsenic and is less toxic than soamin. This preparation was used in the majority of the cases treated in the Lock Hospital (40 cases).



5. ARSACETIN - introduced by Professor Ehrlich and produced by a German firm. It is an acetyl derivative of atoxyl, like orsudan, but different in chemical composition, being acetyl-amino-phenyl-arsenic sodium. It is a crystalline white powder, soluble in ten parts of water; the solution can be kept for a long time without any decomposition, even repeated heating to 100 degrees for sterilisation does not dis-associate the preparation. The preparation is free from arsenious and arsenic compounds and contains 21.25 per cent of arsenic and hence of lower toxicity than any other preparation though equal in therapeutic effects. Professor Neisser speaks very favourably of this preparation. In the series of cases quoted, four were treated with this compound.
6. ARSENO-PHENYL-GLYCIN - produced by a German firm on the recommendation of Ehrlich. It is a liquid solid in small capsules in which it is sealed in vacuo. Colonel Lambkin, is yet uncertain about this drug, though looks with suspicion on the fact that being easily decomposable the preparation has to be sold in capsules. Wendelstadt who experimented on trypanosomiasis in rats and monkeys believes that this is the most/

most stable, least toxic and best drug as regards its effects on destroying trypanosomes in these animals. This preparation has not been used at the London Lock Hospital.

7. Various other new compounds prepared by Ehrlich and experimented upon by him and other workers are (a) para-oxy-benzylidin-arsanilic acid; (b) tri-oxy-benzylidin-arsanilic acid and (c) arseno-phenyl-glycin prepared in flasks. These compounds are not stable and give rise to toxic symptoms if not used immediately after they are manufactured.
8. ATOXYLATE OF MERCURY - this preparation was suggested and employed by Uhlenhuth in some experiments. The compound is prepara-amino-phenyl-arsenic acid salt of mercury, and contains 24.2 per cent of arsenic and 32.3 per cent of mercury.

Meikley, has treated a number of syphilitic patients with this preparation. He used a 1 to 10 emulsion in olive oil, and injected .5 gm. intramuscularly in males and .3 gm. in females; later he gave 1 gm. in both till they received a course of 5 grms. in males and 4.8 grms. in women. This observer thinks it a better preparation than either mercury of arylarsonate/

arylarsonate simply. The rapid effects in papular and ulcerative processes were most marked and beyond a glimmering of the eyes in two cases, no toxic effects were observed.

In this country no records are yet published of the use of this preparation.

9. HYDRYL - this is a tabloid hypodermic product of W.B. & Co. each tabloid containing .01 grm. of this compound. The manufacturers thus describe this preparation:-

"The compound contains 50% mercury and 7.5% arsenium; the tabloids Hypodermic products, therefore, contain 25% of mercury or 0.005 grm. and 3.75% of arsenium or 0.00075 grm. The proportion of arsenic to mercury in the compound is as 1 to .6."

Its chemical name is, sodium-oxy-mercury-acet- amino-tolyl-arsenate. It is a white amorphous powder soluble in an equal weight of water at 20°C, giving a solution strongly alkaline to litmus; the substance is insoluble in alcohol. An aqueous solution may be boiled without decomposition, and the substance appears to be quite stable.

.01 grm. ought to be a safe initial dose for man, since/



since five times this dose does no harm to a dog or goat.

I have given this quantity (.01 grm.) dissolved in 15 minims of distilled water and then boiled to make the solution sterile. It was given with all aseptic precautions intramuscularly in the glutial region, on every alternate day, in five cases quoted in the series.

#### TECHNIQUE EMPLOYED.

It was practically the same as recommended by Lambkin. A 10 or 15 per cent solution (usually 10 per cent) was made fresh as required. It was then boiled to make it sterile. It was given intramuscularly at the body temperature, the syringe and the needle being sterilised and kept warm. The skin was prepared by thoroughly washing it first with castille soap, then with methylated spirit and finally with ether. The site of injection was in the glutial region, about half an inch above the mid point between the anterior superior iliac spine and the tuberischium; this situation as pointed out by Lane is comparatively free from blood vessels and nerves.

A/

A dose of 10 grains of Orsudan was injected every alternate day till 100 grains were administered, this quantity constituting one full course. In case of soamin the same quantity was used, except in cases of tertiary syphilide, in which 2 grs. were given bi-weekly until altogether 10 grs. were administered; this quantity usually cleared the skin lesion, failing which a second or a third course of 10 grs. were given after a week's interval till the desired effect was obtained. In case of arsacetin 7 grs. were injected every alternate day till a total of 70 grs. was reached. Hydryl was used in three weekly injections till 10 injections were given, that is, altogether .1 grm.

CLINICAL RESULTS

Although there was no induration or pain at the site of injection in any case, the patients suffered from pains in the limbs in 3.3 per cent of cases. It generally amounted to slight aching but at times it was sufficient to disturb their rest at night. It generally appeared from four to five hours after the injection and subsided in ten to twelve hours. Our experience in this respect was different from those recorded by the officers of the R.A.M.C. (See Cases 2 and 43).

In 60 per cent of all the cases the secondary skin rashes disappeared and in most of these cases before the full course was finished, generally between the 6th and 8th injections. One of the cases treated was probably only a skin disease (Case 27), as no other sign of syphilis was present but even in this case the skin lesion disappeared. It is a great pity that Wassermann's reaction was not tried in this case before treatment commenced. It is a very common experience at the Lock Hospital that patients suffering from skin disease come up for treatment thinking it was syphilis and in some cases, where a sore is present, and the patient is unable to give a definite information, it/



it becomes a matter of great difficulty to diagnose syphilis from some skin diseases without the aid of ultramicroscope and serum re-action.

The arylarsonates not only remove the secondary skin rashes more rapidly than any other drug but they also remove tertiary skin lesions especially when given in conjunction with mercury. For skin lesions only small doses of the arylarsonate are sufficient when given with mercury (Vide Cases 46, 47, 48, 51, 52, 54 and 58). In our experiments five injections of soamin two grs. were generally sufficient to remove secondary as well as tertiary skin lesions. The new preparation of Burroughs Wellcome & Co., Hydryl, exactly fulfils these requirements; (Vide Cases 53, 56, 57, 58, 59 and 60.) It seems irrational to apply large doses for the skin lesions and expose the patients to risks when small doses of these preparations combined with mercury answers the same purpose without any risks whatsoever. Mr. Gibbs, always applies the latter method in persistent skin lesions whether secondary or tertiary, with excellent results.

In 5% of the cases secondary rashes did not disappear/

disappear after the completion of the course and all these cases had orsudan or arsacetin alone and in full doses, (Vide Cases 14, 17, and 39.)

The most infectious secondary lesions, namely ulcerated throat, mucous patches and condylomata, are very rapidly affected by the injection of arylarsonates and even more quickly when combined with mercury, (Vide Cases 53, 57, 58, 59, and 60). In 33.3 per cent of the cases, the throat, mucous patches and condylomata disappeared; but in 5% the condition persisted after the course of treatment.

The healing of the primary sore, as well as the softening and disappearance of the gland took place in all the cases except one. This would point, in the light of what has been previously pointed out regarding the spread of the spirochaeta pallida, that arylarsonates have a destructive action on the virus of syphilis and they act much more rapidly than mercury. For it is a well-known fact that it takes months before the induration of the sore and the glands subside under mercurial treatment.

The improvement in the general health of the patient during and after the course of these preparations  
the/

the noticeable change in colour and the substantial increase in the body weight of the patients are such marked features that they cannot be ignored or denied. In this again the contrast with mercurial treatment alone is very favourable; though some syphilologists assert that the weight increases on mercurial treatment our experience at the Lock Hospital is different. It is exception rather than the rule for any increase in weight to take place and the anaemia during mercurial treatment is a marked feature. Combination of arylarsonates, in small doses with mercury, would, in my opinion, be an excellent tonic in cases of syphilis.

In 5% of the cases secondary symptoms persisted after a full course of treatment with arylarsonates was given. This shows that the drug is not successful in every case of syphilis. It may be that there are different varieties of spirochaetes and some resist the action of this drug. Should however mercury be combined with these arsenic compounds as in the newer preparation, atoxylate of mercury and Hydryl, it is probable that the secondary symptoms would soon subside and the disease would be quickly got under hand. But it is too soon to say much about these preparations, as/



as they are still under experiment, (Vide Cases 14, 17, and 39).

The occurrence of relapse in 8.3 per cent of the cases clearly shows that syphilis is not curable by a single course of these drugs; that as soon as the drug is stopped the virus which was diminished in number and strength gradually multiplies and in from a week to eight months' time the disease re-appears. It demonstrates the necessity for the so-called "chronic intermittent treatment." After a lapse of a fortnight, to allow the complete elimination of the accumulated drug from the system, another course should be given. How many courses would be sufficient to cure a patient, is a difficult question to answer. But just as the treatment of syphilis by mercury is now tested as regards its efficacy by taking a serum re-action, so also it should be done in case of aryl-larsonates. After the repeated negative re-actions (provided the drug has not been used for a fortnight at least before the serum is examined) the patient, in absence of any lesions, may be considered free from disease, (Vide Cases 10, 18, 20, 22 and 43).

Out of the twelve cases, in which serum re-action was/

was tested, only one gave negative result and the pathologist was not quite sure of that. This corroborates the <sup>remarks</sup> mentioned above. The experience of Lambkin is very similar as regards recurrence of disease after the course, (Vide Cases 32 - 34 and 36 - 43).

As regards prophylaxis, as claimed by Metchnikoff, in aborting syphilis if injections are started after the appearance of the sore up to a week or even a fortnight, our experience varies from those of the officers of the R.A.M.C. and Colonel Lambkin. In 11.66 per cent of the cases primary sores alone were present and they were diagnosed as syphilitic by the help of the ultra-microscope. The sores healed after a course of injections of orsudan and in one of these seven cases the patient reported himself after a month and was found without any signs. There might have been a relapse afterwards even in this case; but at any rate it proves that though not absolute, at least a slight degree of prophylaxis.

#### TOXIC SYMPTOMS

The most common toxic symptom that occurred in the series of cases was gastro-intestinal disturbance. It occurred in 11.6 per cent of the cases. It generally/

generally made its appearance about ten to twelve hours after the injection and lasted for an hour or two, (Vide Cases 16, 29, 43). The symptom was usually allayed by the use of alkaline drinks but in two cases the injections were postponed and in one case had to be completely stopped, (Vide Cases 4, 5, and 1).

Iritis was present in 6.6 per cent of the cases, in half the number it subsided after the injections, but in the remaining half, other measures were found necessary to allay the condition, (Vide Cases 14, 23, 33 and 34.)

The gravest and most alarming symptom and one which has been the chief cause of bringing the arylarsonates into disfavour is amblyopia, either temporary or permanent. It occurred in 5% of the cases, temporary in one third and permanent in two thirds of the number. Here again our experience unfortunately does not agree with that of Lambkin, though it corresponds with Hallopeau, Heymann, Neisser, and other continental syphylographers. Considering the experiments of Igersheimer and Rothmann on animals which show the special selective action of atoxyl on the eye and its specific action on the central nervous system, it is not/



not surprising that optic atrophy due to retro-bulbar neuritis should in some cases take place, due either to individual idiosyncrasy, excessive dose, or accumulation of the drug in the system.

But the explanation of the discrepancy between the civil and military hospital results is simple. In the army the patients are in the prime of life and except for syphilis are in the best condition of health. Their surroundings are salubrious; they live in most hygienic conditions, and lead a healthy, active, outdoor life. They are thus placed in the best possible conditions to cope with disease or withstand the toxic effects of any medicament. In the civil hospital practice, the conditions are often just the reverse, as regards age, health, occupation, surroundings and food.

Optic atrophy has never been reported in a patient in the prime of life (20-30 years); the cases quoted in the series (Vide Cases 30 and 45) as well as all the reported cases, have happened in persons above the age of 45. The only case in which it occurred in a man of 27, was a patient whose constitution was much undermined due to his having contracted syphilis of a severe kind and in whom treatment was delayed till late secondary manifestations appeared. Even in this case the loss/

loss of vision was only temporary, (Vide Case 44).

Numerous cases have been recorded of optic atrophy due to continued use of atoxyl in sleeping sickness; but it would be of interest to record briefly those cases published during this year in the medical press. It would make clear the point made out above that amblyopia generally occurs in people above 45 in age.

Case 1. Drs. Lundie and Blaikie, describe a case of optic atrophy following ten injections of soamin grs. X in a patient aged 51, suffering from pemphigus foliaceus. After how many injections the vision failed, is uncertain; but the patient proved totally blind on examination. Ophthalmoscope showed that both discs were pale and the retinal vessels considerably diminished in calibre.

Case 2. A gentleman (age unknown) suffering from tabes and tertiary skin trouble, was treated by Dr. Heard, with a course of soamin injections. The skin trouble disappeared after 45 grains, but the ataxic pains increased. Visual disturbances began after 35 grs. and progressed till the vision became greatly impaired.

Note. Though the age of the patient is not given, tabes suggests/

suggests middle age.

Case 3. Iveraen, records a case of an old patient suffering from relapsing fever, whom he gave .7 gr. + 1.5 grm. of arsacetin after a week's interval. Permanent blindness due to toxic retro-bulbar optic neuritis resulted.

Cases 4,5,6. Eckard, reporting the result of treatment of sleeping sickness, in German East Africa, records three cases of total blindness, in aged patients; first after taking 11.025 grms. of arsacetin, in five months; the second after 14.25 grms. in four and a half months; and the third after 9.6 grms. of arsacetin, in three months.

Besides these and the two cases mentioned in the list, (Cases 30 and 45), Mr. Lane mentioned two other cases of optic atrophy in his first letter in the B.M.J. March 5th 1910; I found on enquiry they were both elderly people.

In none of the cases quoted, any urinary disorder was noticed.

In his letter in the B.M.J. of March 5th, Mr. J.E. Lane, by quoting the cases of amblyopia, has warned the profession against the use of the drug. Two of/



of his cases (Case 30 and 45) which are appended in the list, show that although both the patients were above forty-five in age, they were otherwise quite healthy. They had no kidney disease, nor were their arteries diseased; they had no eye disease previous to this loss of sight. The technique described by me was the one used in case 30; the other patient was treated elsewhere, and yet optic atrophy took place. It would thus appear that there is cause for some apprehension. The only probable explanation of this mishap is that he was a man of over 45 and the dose should not have been given in full quantity.

Against this are the 308 cases of soldiers treated at the Rochester Row, Military Hospital without a single mishap. As I have personally examined a large number of these patients, I am quite satisfied as regards the absolute veracity of the statements. It is thus obvious that in healthy robust young men with active life, the drug produces most beneficial results, without any attendant dangers.

In giving Professor Hallepeau's conclusions, I have mentioned the fact that he lays great stress that the/  
the/

the dosage should be regulated according to the body weight. As pointed out by Mr. Wray, a man of eight stones should receive only two thirds of the dose which a man of 12 stones would receive. Similarly the age factor ought to be considered and due allowance made for it. One cannot help feeling that after making these deductions to suit particular cases and if one always examined the vision and looked for other signs of toxicity, no untoward results would happen.

There is no doubt that the arylarsonates are of great value in the treatment of syphilis and to abandon them in a panic would be a great mistake. In smaller doses and in combination with mercury, I do not think this drug could be surpassed especially regarding its effects on secondary manifestations.

CONCLUSIONS.

1. That arylarsonates are most valuable in primary and secondary syphilis.
2. That they are best administered in conjunction with mercury but cannot replace it.
3. That their effect being temporary, their combination with mercury would produce a lasting result.
4. That they are best administered in young men of good physique.
5. That in old and feeble, the dose should be decreased according to age and weight.
6. That the excretory organs and eyes should always be tested before and during treatment.



NOTES OF CASES TREATED BY INTRAMUSCULAR IN-  
JECTIONS OF ARYLARSONATES AT THE LONDON LOCK HOSPITAL.

Case 1. Alfred Wilkinson, - aet 28 - admitted 24th March 1907. He gave a history of syphilis of twelve months duration. He had very extensive destruction and ulceration of nose and face, exposing the pharynx which was deeply ulcerated.

Five weekly injections of calomel cream gr. 1 were given without any benefit; mercury and iodide did not stop the destructive process.

Twenty-four intramuscular injections of Iodipin zil given daily proved useless.

Injections of Orsudan given, first one of grs. V and four of gr. X., 45 grains in all; but discontinued due to urgent vomiting. This course had checked the ulceration and the patient had put on weight. Died on November 23rd, of inanition.

Case 2. George Spokes - aet 22 - admitted 14th September 1908 with swollen and oedematous penis and a desquamating papular rash all over his body. He received the injections of Orsudan, the first one of grs. VI. the others of/

of grs. X. He suffered from pains after the first three injections; the rash disappeared before the last injection. He was discharged on 3rd November free from symptoms. He reported every fortnight for four months and was well when last seen at the end of February 1908.

Case 3. Robert Duke - aet 20 - admitted September 1908, with a hard indurated sore of three weeks duration but without any other signs of syphilis. He was given ten injections of Orsudan grs. X. He was discharged free from any symptoms on October 13th 1908. He was under observation till November 11th without any further sign.

Case 4. William Lovey - aet 25 - admitted September 29th 1908, had concealed sores of two and a half months duration for which he had two weeks treatment. On admission he had enormous swelling of the prepuce, inguinal adenopathy and ulceration of fauces. He was treated with ten injections of Orsudan grs. X. on alternate days, with an intermission of six days after the ninth injection due to gastric pain, vomiting and diarrhoea. Discharged on November 30th 1908 free from any symptoms. Reported himself on December 28th when no sign of disease was discovered.

Case 5. Wm. Brady - aet 22 - admitted 6th October 1908, with/

with indurated sore of eight and a half weeks, phimosis of seven weeks duration and left inguinal adenopathy was given ten injections of Orsudan grs. X on alternate days, with one omission after the eight injection due to diarrhoea. Discharged on December 18th free of all symptoms.

Case 6. Wm. Bastick - aet 20 - admitted October 7th.

Treated first at another Hospital and told he had Syphilis. On examination it was found he had a small indurated sore round corona, faint macular rash, condylomata ani and ulcerated throat; was given ten injections of Orsudan grs. X. After seventh injection rash disappeared, and throat and condylomate after the ninth. He was discharged on November 4th, free from any sign of disease. Re-examined on November 11th found without any signs.

Case 7. Thomas Parrish - aet 22 - admitted 17th October 1900, with a history of five weeks phimosis and sore; examination revealed superficial sores on foreskin, left inguinal gland and macular rash. He received ten injections of Orsudan on alternate days of grs. X. He was discharged free from any visible sign of Syphilis on November 8th and was advised to report every fortnight for examination.

Case 8. John Howell/



Case 8. John Howell - aet 20 - admitted October 17th 1908 with phimosis and swelling of foreskin of three weeks duration and macular syphilid on face and abdomen of two weeks duration; was given nine injections of Orsudan grs. X and left on November 4th before his time but quite free from all signs of syphilis. Has not reported himself again.

Case 9. James Sanders - aet 23 - admitted 27th October 1908. He had sores of three weeks duration and phimosis two weeks, glands in both groin; on circumcision indurated sore on corona. He received ten injections of Orsudan grs. X. vomited the day following first injection. When he left on November 18th he was free from symptoms but advised to be examined at intervals.

Case 10. Geo Carter - aet 22 - admitted November 2nd 1908, with history of sore three weeks before, phimosis two weeks and bleeding from under foreskin for the last four days. Examination showed large oedematous penis still slightly bleeding; suppurating glands in left groin; faint macular rash on chest and abdomen. On circumcision a phagedoenic ulcer disclosed, which had destroyed/

destroyed most of glans penis and had extended into the urethra, causing a fistula posteriorily. He had pustular eruption on back and ulceration of fauces. Given ten injections of Orsudan grs. X. He left on December 18th free from symptoms. Came back May 8th with papular rash on abdomen, extensive destruction of glands, complete perforation of palate; put on mercurial treatment.

Case 11. Morris Brooks - aet 30 admitted 9th November 1908 with a phagedoenic sore on the under surface of penis forming urinary fistula. He was given six injections of Orsudan grs. X. The sore healed up after the fourth injection and he had no signs left when he was dismissed for fighting on November 22nd 1908.

Case 12. Wm. Smith - aet 48 - admitted on 14th November 1908, giving a history of seven weeks sore and phimosis for four weeks; treated at a general hospital for a few days. He had oedema of penis and sinus opening at the base of prepuce on the dorsum, concealed indurated sore on inner surface of prepuce. Received ten injections of Orsudan grs. X; discharged on January 26th/

26th 1909 completely free from symptoms.

Case 13.

George Rowland - aet 33 - admitted 16th November 1908. Gave a history of sore of over four weeks duration and phimosis of about a month's; right inguinal adenopathy, distinct papular rash. He was given ten injections of Orsudan grs. X on every alternate day; week after the tenth injection rash had disappeared. He was discharged on December 18th free of any sign and advised to call at intervals.

Case 14.

James Emery - aet 23 - admitted 23rd November 1908. Had sore on glands, papular rash of ten days duration, glands in both groins and sinus in the left; had received treatment at an Infirmary for seven weeks. He was given ten injections of Orsudan grs. X on alternate days; the rash on the day of the last injection was still well-marked on the face but was becoming scaly. He suffered from sore throat and later from iritis in the left eye which subsided on treatment. He was then given a course of six calomel cream injections gr. 1 every week, fully one month after Orsudan. The patient left on February 24th without a trace of any symptoms and was advised to become an out-patient, which he failed to carry out.

Case 15.

Thomas Wood/



Case 15.

Thomas Wood - aet 26 - admitted 23rd November 1908. Gave a history of discharge eight weeks, phimosis six weeks, and rash of five weeks duration; treated with pills and capsules. Had papular rash, swollen red prepuce ulcerated superficially; glands in the right groin. He received ten injections of Orsudan grs. X and when discharged on January 7th was without any signs.

Case 16.

Alfred Bannister - aet 22 - admitted 9th December 1908 with phimosis and swollen penis and a hard concealed sore. He received three injections of Orsudan grs. X. on alternate days; had vomiting on the day following the first injection and pain in the stomach and aversion to food after the third. He was given in continuation four injections of Arsacetin grs. VII on alternate days, suffered from gastric symptoms on the night following the first injection of arsacetin, but had no symptoms after that. When dismissed on December 23rd 1908 he had no symptoms but was prescribed Pill Hydrar gr. 11 td; p.c. and was advised to be treated as an out-patient. Has never been seen since.

Case 17.

Arthur Sly - aet 27 - admitted 21st December 1908 He had a marked macular rash of three weeks duration, phimosis/

phimosis over six weeks, phagedenic ulcer on the under surface of prepuce exposing the glans. Had been treated for six weeks in a hospital. He received ten injections of Arsacetin grs. VII on alternate days. As the rash was still marked and some papules were becoming pustular, it was thought advisable to give mercury. A week after the arsacetin course, injections of calomel cream gr.1 weekly was started and ten injections given. He was discharged on March 18th free from symptoms and advised to become an out-patient.

Case 18.

George Williams - aet 24 - admitted December 22nd 1908. He had a discharge of about three months duration; phimosis six weeks and glands in left groin; meatual chancre found on circumcision. He developed a macular rash on the day the injections commenced. Given ten injections of Arsacetin grs. VII every other day. Discharged on January 27th 1909, the only remaining sign left was slight ulceration of the right fauces. Advised to report himself occasionally. Came back on September 27th 1909, with large spreading sore on foreskin, rash on body and excavated ulcer on leg and put on mercury.

Case 19.

Wm. Mulcock - aet 21 - admitted on 23rd December 1908/

1908, with history of discharge for nearly two months, phimosis, papular rash all over and inguinal adenopathy. Was treated for a week at a general hospital. He was circumcised and a hard indurated frenal chancre discovered. He received ten injections of Arsacetin grs. VII. When discharged on January 20th 1909 he had no sign of syphilis. Not seen since.

Case 20.

Walter Marston - aet 23 - admitted 3rd April 1909. Had large chancre, ulcerated throat, roseolar rash glands all over the body, hard and shotty. Received ten injections of Orsudan grs. X. Discharged on 5th May absolutely free from symptoms; advised to visit the hospital occasionally for inspection. Came back 14th June, with rash, sore-throat and deafness and put on mercurial treatment.

Case 21.

Charles Brown - aet 28 - admitted 13th April 1909, with a deep frenal sore, discharge from under foreskin and macular rash and sore throat. He received ten injections of Orsudan grs. X. Discharged on 15th May, without any sign except slight redness of the throat. Has not reported himself again.

Case 22.

Alexander Allen - aet 29 - admitted 10th April 1909, with chancre, swollen penis, sore-throat and papular rash./



papular rash. Received ten injections of Orsudan grs. X and left on 5th May 1909 free from symptoms. Came back a week later to out-patients with sore, rash and throat and put on mercurial treatment.

Case 23.

Alfred Lovell - aet 20 - admitted 6th May 1909 with a very extensive chancre on glans and penis of six weeks duration, ulcerated throat, faint macular rash and iritis on the right eye. Received ten injections of Orsudan grs. X., the iritis subsided after the 2nd injection and there was no other sign left on the day after the last injection. Sent out on 5th June 1909 without any sign of disease.

Case 24.

Arthur Lovell - aet 20 - admitted 10th May 1909, with extensive phagedonic ulceration around corona, inguinal adenopathy and ulcerated throat. He received nine injections of Orsudan grs. X and when sent out on 5th June 1909 had no sign of disease.

Case 25.

Henry Davison - aet 28 - admitted 11th May 1909, with indurated concealed sore, general adenopathy, roseolar mottling of the body and ulcerated throat. Received nine injections of Orsudan and discharged on 29th May 1909 without a trace of disease.

Case 26.

Ernest Wellag/

- Case 26 Ernest Wellag - aet 21 - admitted 26th May 1909. Had oedematous phimosed prepuce with a hard lump concealed underneath, which on circumcision proved to be a chancre; scattered papular rash and gland in groins. Received nine injections of Orsudan grs. X and discharged on 15th June 1909 free from all symptoms.
- Case 27. Edward Dialis - aet 30 - admitted 8th June 1909. Came with an eczematous rash on neck, feet and hands, without any signs of syphilis; wife suffered from similar condition seven years ago, it was called syphilis. Treated with seven injections of Orsudan grs. X and discharged free from rash on 23rd June 1909.
- Case 28. William Keen - aet 21 - admitted 11th June 1909. He gave a history of sore of four months duration and rash which had gone two months ago. He had phimosis, indurated lump under foreskin, discharge, inguinal glands, and mucus patches on tonsils. He received ten injections of Orsudan grs. X and was sent out on 7th July 1909 free from disease.
- Case 29. Thomas Watson - aet 24 - admitted July 14th 1909, with a sore of one weeks duration, enlarged and hard glands and papular rash. Was given ten injections of Orsudan grs. X. He had diarrhoea and vomiting after the second injection. Discharged on 19th August free from symptoms.

Case 30.

Frederick Hemson - aet 49 - admitted 11th September 1909, with a typical hard sore which came three weeks after connection, discharge and a papular rash on face and trunk. Was given nine injections of Orsudan grs. X on alternate days. On the day after the 7th injection he noticed general fogginess of vision in both eyes which went on growing worse, but he did not report the condition till the day after the ninth injection. On examination there was found tremor in both eyes, difficulty in counting fingers in strong light at a distance of twelve inches. Ophthalmoscope showed the discs pale and indistinct in outline and the vessels of normal calibre. A very careful general examination showed absence of disease of vessels, kidneys or skin, and a very good physique and general health.

He received treatment with large doses of strychnine hypodermic without any improvement of sight. Examination of the eyes four months after by an ophthalmic surgeon revealed perception of hand movements at a distance of one sixth metre, equal in both eyes. Both discs markedly atrophic atrophy not suggesting previous neuritis; with marked pigmentary changes at both maculae suggesting of inflammatory or degenerative changes taking/



taking place.

Patient kept under observation and eight months after the Orsudan treatment, showed no signs of syphilis.

Case 31.

W.A. Hogg - aet 22 - admitted 28th July 1909 with a history of indurated sore, papular rash and sore throat. He received the injections of Orsudan grs. X and was discharged free from any sign of syphilis on 31st August 1909. He was advised to report himself every fortnight, but failed to do so.

Case 32.

Albert Lambert - aet 20 - admitted 28th July 1909, with a sore of four months duration, discrete squamous rash and sore throat. He had nodes on right ulna both tibiæ and swelling of both legs. Treated outside for a week. He received ten injections of Orsudan grs. X on alternate days. After the fifth injection the rash, bony thickening and oedema of legs gone. He left on 31st August 1909 free from disease. Not seen since. Wassermann re-action, taken just before leaving, gave positive result.

Case 33.

James Buchanan - aet 26 - admitted 2nd August 1909 with a sore of eleven weeks duration; extensive papular/

popular rash of four weeks duration, slight sore throat, general adenopathy. He was given ten injections of Orsudan grs. X. He got iritis after the second injection which was treated with atropim. When he left on the 31st August 1909, free from disease, the pigmentation on the body was well marked where rash existed. Has not been seen since. Wassermann serum reaction gave positive result.

Case 34. Charles Hunt - aet 22 - admitted August 21st 1909. Gave a history of sore nine months ago and rash on the body. Examination showed scar at the site of the sore, scattered scaly rash and some pigmentary patches on the body and general enlargement of glands. Iritis in both eyes. He received ten injections of Orsudan grs. X and was discharged free from any symptoms on 5th October 1909. Not been seen again. Wassermann was found positive.

Case 35. Alfred Blackwell - aet 30 - admitted 4th September 1909. Gave a history of discharge from underneath the prepuce of over two weeks duration, phimosis and swelling of foreskin and probable concealed sore. He received injections of Orsudan grs X every other day; had /

had diarrhoea after the first injection; absconded after four injections on 16th September 1909.

Case 36.

George Woods - aet 22 - admitted 10th September 1909, with a history of sore around corona and discharge of six weeks duration. Eversion of foreskin revealed a serpiginous discharging sore; small abscess of the scrotum and papular rash. He received ten injections of Orsudan grs. X and was sent out quite free from disease on 2nd October 1909, but Wassermann re-action was positive.

Case 37.

Samuel Varndale - aet 20 - admitted 16th September 1909 with a phagedoenic sore in coronal sulcus, oedema of penis and a bubo. Ultra-microscope revealed presence of spirochoeta pallida. He received ten injections of Orsudan grs. X and was discharged free from any signs on the 5th of November 1909; but Wassermann was positive.

Case 38.

Daniel Gorman - aet 36 - admitted 28th September 1909. Had coitous two months previous to admission, multiple discharging sores a few days after. On examination found a large indurated sore on the glans and well marked papulo-squamous rash and general adenopathy. He received ten injections of Orsudan grs. X/



X on alternate days; was discharged free from symptoms on 25th October 1909. Wassermann was found positive.

Case 39.

George Lovey - aet 24 - admitted 14th October 1909. Gave history of a sore ten weeks before, now healed and left a scar; very extensive rash raised indurated red areas, general adenitis, mucous plaques on throat and condylomata round arms and in groin. He received ten injections of Orsudan grs X; there were still some rash after the course of Orsudan, but the mucus patches and condylomata had quite healed. He left four days after the last injection without any symptoms, on the 8th November 1909, and was advised to take mercurial treatment after a fortnight and report himself occasionally. Has not been seen. Wassermann positive.

Case 40.

Stanley Decker - aet 20 - admitted 20th October 1909. Gave a history of connection three months previous to admission; warts five weeks later; indurated sore on glans of ten days duration; general adenitis and ulcerated fances. Was given ten injections of Orsudan grs. X and when he left on 21st November 1909, he was free from signs. Wassermann positive.

Case 41.

Herbert Woolridge - aet 28 - admitted 25th October 1909/

1909, with sore on penis of seven weeks duration, general papular rash and condylomata ani. He received ten injections of Orsudan grs. X. The rash and condylomata disappeared after the course but chancre spread round the glans. Wassermann re-action one week after last injection, positive. He went out on 1st December 1909 to be treated with mercurial pills in the out-patient department.

Case 42. Ernest Brown - aet 19 - admitted 27th October 1909 with oedema of the prepuce; sore near frenum; papular rash, and general adenopathy. Received ten injections of Orsudan grs. X. Patient discharged on December 1st 1909 free from any signs. Wassermann taken two days after last injection and was positive.

Case 43. Alfred Clarke - aet 24 - admitted 2nd November 1909 with a history of coitus ten weeks ago; discharge ever since, sore one week later and epididymitis of two weeks duration. On examination found a general papular rash, general adenopathy and mucous patches on tonsils. He received seven injections of Orsudan grs. X; all signs of syphilis had disappeared after the sixth injection; after the seventh injection he complained of pain/

pain in his stomach, malaise and pain in knees. He went out on 1st December 1909 free from symptoms of syphilis but with slight urithritis and gononhoral rheumatism. Came back to out-patient with a relapse on 13th December 1909 and put on mercurial treatment. Wassermann was found positive.

Case 44. James Jones - aet 27 - admitted 12th November 1909.

Gave history of sore on penis of four months duration, still unhealed, rupial patches all over the body and remains of a bronzed syphilide. He had general adenopathy. Received six injections of Orsudan grs. X; the injections were discontinued as he complained of some fogginess in his eyes at night time. He could read all right and see objects at a distance, pupils dilated but re-acting to light. He left on the 1st December without any signs of the disease and with perfect vision; advised to report every week. Wassermann was negative.

Case 45. Antonio Toniolo - aet 46 - admitted 7th January, 1910. He gave a history of having contracted syphilis in the previous August; had sore on penis (now a scar) sore throat and rashes. On admission he had some sore-throat/



throat, pigmented areas on the body at the side of rash, a scar on penis and amblyopia following treatment by injections of soamin.

He had received ten injections of soamin grs. V. (given by a medical man outside) on alternate days. After the third injection (patient is quite definite about it) without any warning he noticed slight haziness, more marked in the right eye. After the sixth injection foginess became definite, but he could still see objects at a distance, though definition was not good. After the first course all signs of syphilis has disappeared and treatment was stopped for two months. He again was given five injections of soamin grs. X on alternate days. At the end of it the darkness became so obvious that he became alarmed and requested to stop injections.

Examination. No signs of syphilis; good general health, no arterial disease, skin and kidneys acting well.

Eyes. Examined by an expert who found perception of hand movements at sixth of a metre in right eye and half a metre in left eye. Both discs showed typical primary/

primary optic atrophy, no alteration in the state of vessels, no disturbance at maculae. Discharged on 2nd March, after a course of ten injections of calomel cream, gr. 1, weekly, free from any signs of syphilis and advised to continue treatment.

Case 46.

Arthur Woolley - aet 32 - came to out-patient department 2nd February 1910, with a history of syphilis contracted seven years ago. He had coppery coloured indurated patches of syphilide on face and trunk; left elbow was covered with deep-eaten red ulcers, breaking down gummata. He was put on mercury and iodide and was given five bi-weekly injections of soamin grs. 2; all syphilide on face and trunk disappeared after the fifth injection.

Case 47.

Victor Carrer - aet 27 - admitted to out-patient 2nd February 1910. He had chancre five years ago, sore throat and rash and took pills for seven months. About a week after connection, there was a superficial raised erosion, yellow in colour, on the site of this old chancre. On 16th February 1910 he developed dark red coloured papular syphilide all over the face and neck. He received two courses of soamin injections, with/

with an interval of a fortnight between them; five injections of soamin 2 grs. on alternate days consisted a course. The rash on the face entirely disappeared after the second course. Patient was on mercurial treatment all the time.

Case 48.

Albert Newmann. - aet 31 - been on treatment for syphilis since October 31st 1908; developed a lupoid syphilide on nose and forehead. Two courses of five injections of soamin grs. 2 given with a week's interval between the two. At the end of second series the skin lesion disappeared. The patient was on mercury and iodide all the time.

Case 49.

Charles Franklin - aet 39 - been on treatment for syphilis since February 9th 1910; but the papular rash on the face still persisted. Received five injections of soamin grs. 2, on alternate days, at the end of which the rash entirely disappeared.

Case 50.

James Chandler - aet 30 - treated for syphilis by mercurial pills since 16th February 1910. Had bad papular rash on face and deep-eaten circular papules on legs. Received five injections of soamin grs. 2 every alternate day, and simultaneously weekly injections/



injections of calomel cream gr. 1, with the result that all the papules disappeared at the end of the course. He was then placed on mercurial injections alone.

Case 51. George Pearman - aet 30 - contracted syphilis in 1905, treated at the London Lock Hospital for three years, and again for a year since March 1909. On April 6th 1910 had circinate rash on arms and neck. Two weekly injections of calomel cream gr.  $\frac{3}{4}$  with five injections of soamin grs. 2, every alternate days, absolutely cleared the rash.

Case 52. George Marriott - aet 25 - syphilis two years treated with pills for eighteen months. Had on 6th April 1910, large circinate rash on serotum, also raised papular ulcers. Received five weekly injections of soamin grs. 2, at the end of which all the skin lesions had disappeared.

Case 53. Philip Brownstone - aet 17 - admitted in out-patients 30th March 1910 with chancre, roseolar rash, glands in groin and ulcerated fances. He was put on mercurial pills. On 20th April he developed a maculo-papular rash on face and neck. He was given five injections/

injections of Hydril, grm. 0.01 on alternate days. At the end of which all signs of syphilis had disappeared and the patient had put on eight pounds in weight. He was put on mercurial pills after that.

Case 54. Herbert Marsh - aet 35 - syphilis five years ago. On 9th January 1909 admitted to out-patients with lencoplasia on lower lip and a warty syphilide on the chin. Was put on mercurial treatment and also received five injections of soamin grs. 2, after which both the warty lesion and lencoplasia disappeared.

Case 55. Edward Collins - aet 25 - admitted to out-patients 9th March 1910 with sore on penis, ulcerated throat, roseolar - macular rash all over the body but most marked on the face. He was put on mercury pills and received a course of five soamin injections grs. 2, at the end of which the rash had disappeared as well as the throat had cleared.

Case 56. George Thurnan - aet 39 - admitted to the out-patients 16th March 1910. He had syphilis five years ago for which he received injections at the Lock Hospital. When examined he was covered over with huge rupial scabs, some on the face mixed with papules. He was/

was put on injections of calomel cream gr. 1 weekly and received three courses of five injections of eosamin grs. 2, with a week's interval between each course. At the end of the third course his skin lesion had healed up.

Case 57.

John Webb - aet 29 - admitted in the out-patients on 25th April 1910, with indurated sore, inguinal adenopathy, papulo-squamous rash, ulcerated throat, and condylomata on the under surface of penis and scrotum. He was given six injections of Hydryl, grm. .01, every alternate day. After the fourth injection, his rash disappeared and he had put on four pounds in weight. After the sixth injection his throat had cleared, sore and condylomata had healed up. No toxic symptoms seen yet.

Case 58.

Fred Lamming - aet 48 - admitted to out-patients with chancre, adenitis and peculiar peticheal pin point rash. He also had a sharp clean cut ulcer on his soft palate. He was given six injections of Hydryl, grm. .01, every alternate day; at the end of it the patient had put on six pounds in weight and felt very well. All his symptoms had also disappeared/  
ed/



disappeared; but he is now on mercurial pills.

Case 59.

Richard Ball - aet 31 - has been on treatment for syphilis in the out-patients since 14th September 1908. Came back on April 4th with fissured tongue, and breaking down gummata on the legs. He was given ten injections of Hydryl grm. .01 on alternate days, at the end of which the tongue healed, the gummatous ulcers dried up. The patient felt better than he had done for years and he put on three pounds in weight.

Case 60.

George Smith - aet 28 - admitted to out-patients 29th March 1910 with sore which had healed up and a suspicious scattered papular rash. Wassermann reaction was found positive. The patient a week later developed sore throat, and condylomata ani. He was given ten injections of Hydryl, grm. .01, after which the rash, sore throat and condylomata disappeared. There were no toxic symptoms. The patient had gained eight pounds in weight and felt well. He was put on mercurial pills.

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