REPORT ON THE THREE CASES OF SYPHILIS TREATED BY SALVARSAN ON AUGUST 29, 1914, SHOWING UNUSUAL REACTION, AND ONE OF WHICH PROVED FATAL.

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Case 1.—No. 9902 Lance-Corporal Sidwell, 2nd South Wales Borderers, aged 30. He had received a previous injection of salvarsan at Peking on March 10, 1914, and nine injections of mercurial cream (Hg. 9 gr.) He had no active signs and received this injection of salvarsan (0'6 grm.) in accordance with paragraph 9 of the "Instructions for the Diagnosis and Treatment of Cases of Syphilis," dated July, 1913. On the previous evening he received castor oil 1 oz., and his bowels acted frequently. On the morning of the operation his urine was tested and found free from albumin. At 7 a.m. he was given half a pint of milk; he walked into the theatre. The administration was begun at 10.45 a.m., a tourniquet having been placed round the upper arm and the bend of the elbow painted with iodine. There was no undue difficulty in introducing the needle into the vein chosen and there was a slight flow of blood into the tube at the observation glass. The flow of salvarsan was very slow and took about forty minutes. Patient complained of some numbness in the arm under treatment, and a sensation of cold in the lower limbs, he also felt inclined to vomit before leaving the table. A piece of sterile gauze was placed over the wound, the needle withdrawn, the arm bandaged and the patient carried back to bed. He complained of cold and was covered with four blankets. He dozed for about three hours and then vomiting and diarrhoea set in. His temperature was 102° F., falling to 101° F. at 6 p.m. He was given plain boiled water and soda water in small quantities. He complained of severe headache. He was seen by Majors Hartigan and Waters and myself, the same evening. At 1 a.m., August 30, the patient was in a collapsed condition, temperature 95° F., pulse 130, respirations 29; brandy was given and hot water bottles applied; patient improved towards morning but did not sleep. At 9.30 a.m., I saw the patient, although he was somewhat better the vomiting and diarrhoea continued. No urine had been passed, there was very little dullness over the bladder, but I thought it advisable to pass a catheter, which I did with slight difficulty, drawing off one ounce only of thick, whitish urine, which proved to be slightly albuminous. He was ordered egg and brandy flips, four hourly. At 6 p.m. his temperature was normal, pulse 98, respirations 18. Vomiting was less but diarrhoea continued. At 7.30 p.m. I saw the patient again, no urine had been passed, but there was no abdominal dullness. Patient had a fairly comfortable night, no vomiting or diarrhoea since evening visit, but he only slept about two hours. At 6 a.m., August 31, temperature 98°, pulse 72, respirations 20, herpes now present on the mouth and lips. No urine
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passed. At 9 a.m. a catheter was passed, but only a few drops of urine were withdrawn. Patient was fairly comfortable, no vomiting or diarrhoea. On consultation with the other medical officers it was decided to administer adrenalin, and at 1.20 p.m. adrenalin hydrochloride (1 in 10,000) dissolved in 5 minims of distilled water was given hypodermically. Temperature and pulse were practically normal. At 5 p.m. no urine had been passed and a further administration of 20 minims of adrenalin hydrochloride (1 in 1,000) in 1 drachm of distilled water was given by the mouth, this stronger dose being considered advisable. At 6 p.m. the patient passed voluntarily 15 oz. of urine, after which he felt much easier. A further dose of 20 minims of the 1 in 1,000 solution of adrenalin hydrochloride was given at 9 a.m. and again at 11 p.m. Forty-five ounces of urine were passed during the night. Patient slept well. September 1.—Temperature, pulse and respiration normal. Bowels not moved since yesterday morning. Egg-flips with brandy omitted, beef tea, weak tea and milk were given. The adrenalin solution was administered at 2, 6 and 10 p.m. Patient had a good night. September 2.—Temperature normal; bowels not moved; cascara sagrada liq. mixture given. Bowels moved at 6 p.m. Some abdominal pains complained of and fomentations applied. September 3.—Patient had a good night and spoke of feeling hungry, custard, milk, beef tea and calves'-foot jelly were given. Patient much better except for slight pain in the abdomen. September 4.—Patient continuing to do well and allowed up for a little while. Complains of feeling rather weak. September 9.—Patient is still complaining of slight weakness. Discharged to attend hospital.

Case 2.—No. 10735 Private G. Lloyd, 2nd South Wales Borderers, aged 24. Service five years. This man had also received a previous dose in Peking in February, 1914, and nine weekly injections of mercury, one grain. Patient, also, had no active signs and was treated under similar circumstances to case 1. The patient was prepared as in the former case, except that the oleum ricini was given at 12 midnight, because the patient came late to hospital. Bowels moved frequently. On the morning of the operation, the urine was tested and found normal. The administration was successfully carried out, lasted about twelve minutes, and no unusual symptoms were observed. Patient was carried back to bed and extra blankets applied. Vomiting and diarrhoea began about four hours after. Temperature at 4 p.m. was 102° F., at 10 p.m. temperature was 100° F.; pulse 100 and respirations 20. Diarrhoea and vomiting was still troublesome during the night. August 30.—Vomiting and diarrhoea better at 6 a.m.; temperature 100-8° F.; milk and weak tea given. At 10 a.m. temperature the same; diarrhoea decreasing. At 6 p.m., temperature 100-4° F.; pulse 90 and respirations 18. Herpes began to appear about the lips, nose, mouth and tongue. Patient had a restless night, herpetic eruption causing considerable irritation. Patient vomited once during the night. Urine was passed normally. August 31.
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-A 6 a.m. the temperature was 99·6° F., pulse 83 and respirations 20. At 6 p.m., temperature 100·2° F. The eyes had a curious glistening appearance, pupils dilated and some conjunctivitis present. Adrenalin hydrochloride (1 in 1,000 solution) 20 minims given by the mouth at 7 p.m. Shortly afterwards patient passed 45 oz. of urine. Patient had a good night, perspired freely, no vomiting or diarrhooa. September 1.—At 6 a.m. the temperature was 99·4° F.; pulse 80; respirations 20. Herpes of the lips and mouth more marked. Treated with glycerine and borax and frequent bathing with hot water. Adrenalin hydrochloride (1 in 1,000) 20 minims was administered at 2, 6, and 10 p.m. At 6 p.m. the temperature was 100·6° F. Patient had a good night. September 2.—The temperature at 6 a.m. was 99·2° F. Egg-flips taken well, no vomiting or diarrhooa. At 6 p.m., the temperature was 99·6° F. Bowels normal. Patient had a good night. September 3.—At 10 a.m., the temperature was 99° F.; pulse 58 and respirations 18. At 6 p.m., temperature normal. No adrenalin given since September 1. Patient doing well. September 9.—Patient discharged to duty.

Case 3.—No. 10366 Private P. Cox, 2nd South Wales Borderers, aged 23.

Previous History.—Patient was admitted to hospital at Tientsin, on June 27, 1914, with a large indurated sore on the body of the penis. No examination for Treponema pallidum was made. The sore was treated with pure carbolic, lotio nigra and local baths. On July 27, the sore had healed and the patient was discharged from hospital to attend weekly for observation. On August 20 a macular rash was noticed, slight at first, which the patient attributed to bug bites. On August 24 a definite diagnosis of syphilis was made and the patient admitted to hospital. On August 27 the patient attended the medical inspection room with other syphilitic patients. The macular rash was then noticed on the body, limbs and face, the mucous membranes were unaffected, with the exception of a small mucous patch on tonsil. The lymphatic glands were shotty. No mercury was given, but the patient's name was taken for the administration of salvarsan at the earliest possible opportunity. Patient was sent back to hospital and a course of iodide of potash ten grains three times a day ordered. On Saturday, August 29, salvarsan 0·6 grm. was administered intravenously, after two other cases had been similarly treated. On the previous evening oleum ricini one ounce had been given, the bowels subsequently moving four times. On the morning of the operation the patient received half a pint of milk at 7 a.m., and the salvarsan was administered at about 12.30 noon.

Condition of Patient before administration of Salvarsan.—Patient was a muscular, well-nourished man of medium height. Heart and lungs apparently healthy. There was a profuse raw ham colour macular rash on the body, face and limbs, especially marked on the face, where the spots were somewhat raised and flat on the top. On the limbs in places
they showed signs of desquamation. The usual injection of 0·6 grm. of salvarsan, neutralized, dissolved in distilled water and normal saline solution added to 250 c.c. was injected into one of the veins on the inner side of the bend of the elbow. The administration, terminated by a few cubic centimetres of normal saline solution, lasted about twelve minutes (about the average time).

Condition after Administration of Salvarsan.—Patient was carried back to bed on a stretcher and remained quiet, no symptoms were noticed until about 4 p.m., when the rash appeared to be more pronounced. The temperature was 103·6° F., and patient began to vomit. Between 4 and 6 p.m., the bowels moved frequently, and urine was passed. At 6 p.m., the temperature was 103·8° F. During the night the patient slept a little, but vomited frequently bile-stained material, and also complained of some pain in the abdomen. Turpentine supes were applied which gave relief. On August 30, temperature at 6 a.m. was 97·8° F., and at 7.30 a.m., some warm milk was given. Temperature at 9 a.m. was 99° F. Patient vomited twice during the morning.

During the afternoon and the evening he appeared much brighter. At 6 p.m., temperature was 101° F., at 6.45 p.m. he was seen by Major Hartigan at his evening visit, and by Major Waters who happened to be in the hospital. He complained of slight pain and was ordered turpentine supes by Major Hartigan, R.A.M.C. At 7.45 p.m., I, myself, saw the patient, as I had gone to the hospital especially to visit the three salvarsan cases; he continued to complain of slight pain in his abdomen, but said it was not very severe but was afraid he could not sleep, so I ordered him potassium bromide twenty grains. He then showed no alarming symptoms. At 8.35 p.m. he complained of severe pain in the abdomen and white a stipe was being prepared he suddenly expired. The potassium bromide was not given. I was at once telephoned for and reached the hospital at about 8.50 p.m. The patient was then quite dead, lying with his left hand raised above his head on the pillow. A post-mortem examination was made on August 31, at 9 a.m.

The body was that of a well-developed man, well nourished and of medium height. Hypostatic congestion marked posteriory. A pronounced macular rash on body, limbs and face, especially on the face, spots circular, raised and flattened on the top; left testicle enlarged. On opening the chest a small quantity of frothy yellow fluid was noticed on the surface of the pericardium, and a slight excess of fluid within. Heart 12½ oz., very pale, fatty and flabby. Small punctate haemorrhages could be seen immediately beneath the epicardium, giving the appearance of a "thrust's breast," most marked in the left ventricle, but present all over the base of the heart and also on the appendices auriculre and the wall of the aorta. Lungs: No adhesions; right lung 23 oz., left lung 22 oz., both congested. Liver: Weight 51½ oz., very pale, bile-stained (dark green) on lower margin, most marked over the right lobe;
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gall bladder containing bile. Spleen: Enlarged, of abnormal shape, acutely pointed at upper end; weight 9 1/2 oz., congested, very soft and friable. Kidneys: Right kidney 5 1/2 oz., left kidney 5 1/2 oz., normal in appearance, capsule non-adherent. Bladder: Normal in appearance, empty. Brain: On opening the dura mater the surface of the brain was noticed to be markedly congested and the superficial blood-vessels greatly dilated. On making sections of the brain substance, the interior of the brain appeared normal, but the whole of the surface extending over each of the lobes showed marked dilatation of the superficial blood-vessels constituting the condition known as encephalitis hæmorrhagica (Ehrlich). It was concluded that death was due to this condition. Other organs of the body were normal. Smears were taken from the surface of the brain for examination for Spirochæta pallida. The smears were stained by the Giemsa’s method and S. pallida were discovered.

RÉSUMÉ.

In considering the foregoing cases certain features are of interest:—
All three suffered much more severely after the injection than any I have previously treated. This naturally points to the presence of some unusual condition connected with the drug or its administration, rather than of any idiosyncracy on the part of the patient. Bearing this in view, I have gone carefully over the whole procedure from its commencement and have summed up as follows:—

The phials or capsules were in sealed cases opened by myself as each was required. The phial showed no sign of crack or damage, which might have permitted deterioration of its contents. The distilled water was prepared the previous day by Dr. Thorpe’s method, the saline solution (0‘5 per cent) was prepared on the morning of the operation, and both that and the distilled water, after filtration, were boiled.

Except for the following minor points of detail, the procedure was the same as that adopted in all previous cases.

First.—In Case 1 the administration lasted nearly forty minutes, instead of twelve minutes, the average duration. This may have been due to partial blocking of the needle with blood-clot, or impaction of the point against the wall of the vein; short of withdrawing the needle, I tried to rectify this but without success. This case was the only patient whose condition subsequently gave cause for alarm.

Second.—In Case 2, as I was called away, the solution was allowed to stand about five minutes in the Erlenmeyer’s flask, which was plugged with sterile wool. On my return I added the neutralizing agent (NaHO). This case, however, was the least affected of the three, so that any consequence of this delay appears to be negligible.

Third.—Case 3, the fatal case, though suffering from diarrhœa and vomiting, like the others, had no anuria like Case 1, and gave no cause for uneasiness until he suddenly expired. The duration of administration
in Cases 2 and 3 was about twelve minutes. It was Case 1 which gave cause for anxiety, both on account of his collapsed condition during the night, and also on account of his anuria, which only yielded on the exhibition of adrenalin which acted like magic.

Comparing the Cases.—Cases 1 and 2 had both received salvarsan 0·6 grm. previously. Case 3 had received no treatment beyond potassium iodide 30 gr. daily for about three days previously, with a view to modifying any degenerative changes which might be taking place in the arteries. He was covered with a profuse rash, but there was no indication of any idiosyncrasy to the action of arsenic, and accordingly the prophylactic administration of adrenalin, so strongly recommended, was not indicated.

In regard to the use of adrenalin, advocated by Milian (Paris), I should like to add my testimony to its value. In case 1 where no urine had been passed for twenty-four hours, 20 minims of a weak solution (1 in 10,000) was injected subcutaneously at 1.30 p.m. and at 5 p.m. a dose of 20 minims of 1 in 1,000 was given by the mouth, an hour later the patient passed 45 oz. of urine. I continued the administration of the drug by the mouth in the same doses two hourly for the first day and four hourly on the second. Adrenalin was also administered to Case 2.

The post-mortem examination in Case 3 showed a great dilatation of the vessels on the surface of the brain, a condition described by Professor Ehrlich in an article in the British Medical Journal of May 9, 1914, and to which he has given the name of encephalitis haemorrhagica. He says: "The dilatation of the vessels is, in my opinion, in close connexion with the salvarsan injection." He also speaks of the formation of an extremely toxic oxidation product (paraminoarsenoxide) "favoured by all forces which cause a delay in salvarsan excretion," but this would apparently occur later; in this case death occurred about thirty-two hours after the injection.

In addition, he speaks as follows of another factor which he thinks may be the most significant: "The irritated vessels only undergo dilatation of so colossal a character under the influence of the arsenical substance, when the normal regulator of the vascular system, adrenalin, is present in insufficient quantities in the blood." As I have previously shown, adrenalin was given with great benefit in Cases 1 and 2, but in case 3, there being no indication for its administration before the sudden and fatal result, none was given.

In regard to this case, which was an early secondary one, further remarks of Ehrlich are particularly interesting, "the patients specially threatened with encephalitis haemorrhagica are, as is known, those in whom the brain in the early secondary period of syphilis is flooded with spirochetes." Smears from the brain of this case treated by Giemsa's method showed spirochetes present. In these cases Ehrlich says: "A thorough course of mercury should precede the salvarsan treatment, and the dose chosen for the first injection should not be high." The difficulty appears to be to recognize these cases beforehand. Except for the
profusion of the rash there was nothing in this case to suggest any unusual features. The condition of the heart, which showed epicardial petechial haemorrhages, is worthy of note, and in this connexion a death occurring in Guy's Hospital and quoted in the British Medical Journal of May 2, 1914, is of interest. Here in addition to bleeding in other organs, petechial haemorrhages beneath the pericardium were present.

A NEW PATTERN STRETCHER.

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The new pattern stretcher (figs. 1 and 2), particulars of which are given below, has been designed for use more particularly in those cases where the patient is liable to experience, in transit down line of communication, considerable pain or discomfort when of necessity he is repeatedly lifted on and off the regulation stretcher, which, owing to its length, etc., may not be placed directly into (or, in the majority of cases, even on) the cot in hospital or on shipboard. It is also pointed out that the width in the case of this new stretcher may be reduced from the standard to a given minimum without unloading, which greatly facilitates the transport of the patient through passages, railway carriage doors, and confined spaces generally. Fig. 1 illustrates the "traverses" locked at the reduced width by the use of pins, which are attached to the bars by means of chains.

The stretcher, as will be observed from the illustrations, consists of two parts, i.e.: (a) the frame complete; (b) the loose canvas bed. The total weight of the stretcher complete, with its special metal fitments, reinforcing plates, etc., is approximately 21 lb. only.

The frame is so constructed that the handles can be pushed home (fig. 2), giving a total overall length not exceeding five feet nine inches, which length at a trial on a hospital ship recently proved amply sufficient for a man six feet two inches in height. The special metal feet also, with the utmost ease, collapse on release from the trigger and fold up flush against the poles—thus enabling the frame with the traverses eased to be placed directly over the patient, who it is assumed is resting upon the loose canvas bed mentioned above. This canvas "bottom" (which has been placed under the patient in the same manner as a sheet) is now readily fastened to the frame by means of the eyelets and spring hasps illustrated—see figs. 3 and 5—and the traverses having been pressed home the patient is ready for removal.

The "bottom" or bed was originally made of the Army regulation canvas, but it has since been found more satisfactory to employ a somewhat smoother material. In any case the canvas "bottom" is strengthened by the use of web bands which extend beyond the bed and serve as hand grips (see fig. 2).