

## Clinical and other Notes.

### TWO RARE TOXIC MANIFESTATIONS DUE TO TREATMENT OF SYPHILIS WITH ORGANIC ARSENIC PREPARATIONS.

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THE following cases are considered to be of sufficient interest to warrant publication.

*Case 1.*—R/m ———, 1/R.U.R., aged 22.

Diagnosis: Symptomatic toxic purpura.

Exposed to venereal infection at the beginning of December, 1936, and developed phimosis with a subpreputial discharge on December 22, 1936. A month later, on January 22, 1937, a slight rash was discovered on his body which, the next day, is described as "Rash more definite, resembles papulo-roseolar syphilide." On January 23, *T. pallida* were detected by dark-ground examination of exudate from sores on the penis. It is of interest that Wassermann and Kahn tests carried out at intervals from January 1, 1937, throughout treatment and during the surveillance period to date, have always been negative.

Antisyphilitic treatment was commenced on January 24, and subsequent treatment was very irregular; there were several breaks of varying duration, one being as long as four months.

For the first twenty-one injections sulphostab (Boots) and bismostab (Boots) were given. No toxic symptoms are recorded, his urine was normal, and his weight remained steady between 142 and 145 pounds.

He received his twenty-first injection on the H.T. "Nevasa" on December 1, and arrived in India during the Trooping Season, 1937-38. Treatment given at Rawalpindi was as under:—

Date	No. of injections	Arsenical dose	Bismuth dose	Urine	Weight
January 12, 1938 ..	22	0.45 gm.	0.2 gm.	N.	139
January 19, 1938 ..	23	0.45 "	0.2 "	N.	145
January 26, 1938 ..	24	0.45 "	0.2 "	N.	145
Rest.					
February 9, 1938 ..	25	0.6 "	0.2 "	N.	144
February 16, 1938 ..	26	0.6 "	0.2 "	N.	144

Both arsenic and bismuth were given by the intramuscular route and the patient was interrogated, clinically examined, and given sugar before each injection.

The arsenic preparation administered was sulpharsphenamine (May

and Baker), batch No. 0098, date of manufacture July, 1936, and the bismuth bismostab (Boots).

On February 17, 1938, he was admitted to hospital with a purpuric rash and, on being closely questioned, stated that he had had a faint rash after the injections on February 9, but had not mentioned it when he came for injection on February 16 because he thought it was nothing and possibly due to new khaki clothing. He further asserted that throughout his previous antisyphilitic treatment he had had no unusual symptoms or signs at any time.

On admission to hospital he was found to have a diffuse purpuric rash over the lower part of his body, legs, and feet. There was an extravasation of blood under the skin of the buttock round the site of injection of the arsenic but not on the other buttock, the site of injection of the bismuth. There were, also, submucous hæmorrhages on the palate, fauces, and the inner sides of the cheeks. The patient's general condition was excellent and he complained of no pain or other symptoms and stated that he felt quite well. Temperature 97° F.

Total white blood-cell count: 9,000 per c.mm. Differential count: Polymorphonuclears 67 per cent; lymphocytes 23 per cent; large mononuclears 7 per cent; basophils 3 per cent.

Abnormal red or white cells not seen.

Coagulation time: More than five minutes; end-point not reached.

The general appearance of the stained film suggested a very marked decrease in blood platelets.

The patient was put to bed on a milk diet and given 15 grains of sodium thiosulphate three times a day orally and 0.3 gramme in 12½ per cent sterile distilled water intravenously; campolon, 1 c.c. intramuscularly.

On February 18 the patient's temperature remained at 97° F. and he complained of cold, otherwise his general condition was excellent. At the sites of injection of the sodium thiosulphate and campolon, given on February 17, and of the bismostab, given on February 16, large extravasations of blood under the skin were now apparent; apart from this there was no extension of the rash and previous lesions were fading. Sodium thiosulphate and campolon were discontinued; collosol calcium, intramuscularly twice daily, and calcium lactate, by the mouth, were now commenced.

The patient continued to improve rapidly and, on February 24, the total white blood-cell count was 6,800 per c.mm. Differential count: Polymorphonuclears 63 per cent; lymphocytes 29 per cent; large mononuclears 5 per cent; eosinophils 1 per cent; basophils 2 per cent. No abnormal cells seen. More blood platelets than in previous film. Coagulation time (at room temperature), eleven minutes.

He was discharged from hospital to duty on February 28.

On August 4 his total white blood-cell count was 5,800. Differential count: Polymorphonuclears 58 per cent; lymphocytes 30 per cent; large mononuclears 11 per cent; basophils 1 per cent. Coagulation time: Five and three-quarter minutes. No abnormal cells seen.

Up to the time of writing, May, 1939, he has remained in good health and is, in fact, now serving on active operations in Waziristan.

Case 2.—Pte. ———, 1/Devons, aged 24.

Diagnosis: Hæmorrhagic encephalitis.

Exposed to venereal infection at Rawalpindi about Christmas, 1938. Admitted to hospital on March 29, 1939, with a granulating, indurated sore, about  $\frac{1}{4}$  in. in diameter on the left side of the inner surface of the prepuce. Dark-ground examinations of the exudate from the sore were negative on the day of admission and again on March 30, but on March 31 *T. pallida* was detected. The Wassermann reaction and Kahn test were negative on March 29 and on March 31.

The patient denied having any previous illnesses and there were no entries in his medical history sheet. He was a well-built, muscular, and healthy young man; urine normal; weight 132 pounds.

On March 31, after physical examination and administration of sugar, he was given 0.45 gramme of sulphostab (Boots) batch No. S87, date of manufacture August 17, 1937, and 0.2 gramme of bismostab (Boots), both intramuscularly.

On April 5, 1939, the sore was clean and healthy and his general condition was good; he complained of no untoward effects from the first injections and exhibited no signs of intolerance; his urine was normal and his weight 130 pounds.

After administration of sugar he was given a second dose of 0.45 gramme of arsenic and 0.2 gramme of bismuth, intramuscularly, the same drugs being given as before. Blood taken before his injection on April 5 was strong positive, 0/0 to the Wassermann test; he was, therefore, diagnosed "Syphilis, fresh, medium primary."

On the morning of April 7 he complained of slight nausea and headache and stated that he had felt "feverish" the evening before but did not report it. On examination he was found to have a definite rash on the trunk, limbs, palms of the hands and soles of the feet; there was no irritation. Temperature 102° F., pulse 100.

He was placed on a milk diet and kept in bed; sodium thiosulphate, 15 grains, four-hourly, orally, and calciostab (Boots), 0.6 gramme, intravenously, were given. In the evening of the same day his temperature went up to 104° F., pulse 100. He complained of nothing and stated that he did not feel uncomfortable. The rash was now more marked and was, definitely, of the scarlatiniform type. He was tepid sponged and given aspirin, 10 grains.

On the morning of April 8 the scarlatiniform rash was even more marked, especially on the chest and abdomen, and on the dependent parts of the back was petechial. There was also well-marked œdema of the hands and arms but none in the feet or ankles. Apart from nausea and vomiting of clear fluid, the patient complained of no discomfort and stated that he felt quite well; there were no mental or nervous symptoms. The temperature

had dropped to 100·4° F., pulse 92 ; he was constipated. Given 0·6 gramme of calsiostab intravenously, and magnesium sulphate 2 ounces orally ; sodium thiosulphate continued by mouth.

During the day his condition gradually worsened and vomiting became a marked feature.

The temperature dropped to 95° F. and remained there to the end. He was given 0·5 c.c. of 1 : 1,000 adrenaline hydrochloride intramuscularly, and 1 : 1,000 adrenaline hydrochloride, 10 per cent in glucose D solution, one drachm four-hourly, by the mouth (Kromberger's adrenaline syrup). Sodium thiosulphate by the mouth was discontinued and sodium bicarbonate and sodium citrate substituted.

During the afternoon and evening he complained of feeling cold ; extra blankets and hot-water bottles were applied. Later in the evening he broke into a cold, clammy sweat, and complained of numbness of the feet. At this time the rash was frankly purpuric and had extended, including the mucous membranes. There was no loss of sensation and reflexes were present ; no mental symptoms.

At 8.30 p.m. he became restless but soon settled down again. At 12 midnight mental symptoms developed for the first time ; even then they were only mild—he tried to get out of bed and refused to take his medicine ; otherwise his mental outlook was clear and he was quite rational up to about five minutes past twelve, when he suddenly dropped back on his pillows, his breathing became loud and stertorous, and he became unconscious ; conjunctival reflexes were now absent.

He never recovered consciousness and died at 12.20 a.m. on April 9. He had no fits, twitchings, or convulsions of any kind at any time ; just before death supervened his breathing became shallow and irregular.

Post-mortem examination, carried out by the D.A.D.P., Rawalpindi District, on the morning of April 9, revealed very marked congestion of the pia arachnoid membrane, marked œdema of the brain, and multiple hæmorrhages throughout the brain substance.

#### COMMENTARY.

Both purpura and hæmorrhagic encephalitis are, fortunately, rare toxic manifestations. One case of fatal purpura has been recorded in this Journal (Buist, 1925). David Lees stated that nine cases of hæmorrhagic encephalitis, five of which recovered, came under his notice (Lees, 1931). These conditions, however, appear to be more common in America than in this country ; Padget and Moore (Johns Hopkins University) reviewed 264 articles on syphilis which appeared between July, 1936, and July, 1937, and found that dermatitis, amblyopia, jaundice, encephalitis, and purpura, were the most frequently reported complications. Hæmorrhagic encephalitis appeared to be due to arsenical overdosage in the 135 cases collected by Cormia (Wise and Sulzberger, 1938). It cannot, however, be charged that there was any overdosage in the cases under review.

The conditions were undoubtedly due to toxic action of the organic arsenic preparations given, but it is not considered that they were in any way the result of extra toxicity of the drugs used. The particular batch of sulpharsphenamine had been used in hundreds of cases without producing toxic symptoms and the batch of sulphostab had, similarly, caused no symptoms in other cases; moreover, a case of medium primary syphilis, admitted the same day as Case 2, was treated at the same times with the same batch and is quite well. Both batches were reported to the Medical Directorate, Simla, and it has been ascertained that no further report as to the toxicity of these batches has been received from other stations in India.

In a number of reported cases general debility, alcoholism, intercurrent influenza (especially the latter), etc., are undoubtedly contributory causes, but in a large number (as in the cases under review) the victims are, apparently, physically fit and healthy individuals. It would seem that there must be in each case some other factor present, such as insufficient adrenaline in the blood (Milian and Erlich) or other endocrine disturbance (Lees, 1931). In the case of hæmorrhagic encephalitis a reaction in the nature of a Jarisch-Herxheimer has been suggested (Memoranda on Venereal Diseases, 1936). It has been pointed out by Harrison and by Anwyl Davis and Mellanby that arsenobenzol reacts with fibrinogen and delays blood coagulation. Rabut and Oury suggest that it is the benzol radicle which causes toxic symptoms (Buist, 1925).

The two conditions are closely allied. As a general rule they occur twenty-four to forty-eight hours after the second or third injection of the resumed course in old-standing cases in which treatment has been intermittent.

Case 1 illustrates the danger of intermittent and irregular treatment. Fortunately this case was mild and reacted well to appropriate treatment.

Case 2 was in many ways unusual. The patient was an early case of syphilis in which the disease had only just become generalized; he had had no previous antisyphilitic treatment and was physically fit. There was, therefore, no reason to anticipate any serious toxic disturbance, especially as all precautions were taken against any such event.

Almost up to the time of his death his general condition was excellent and he presented no symptoms which pointed to involvement of the brain or meninges.

Lumbar puncture and/or venesection were considered, but at first his general symptoms and signs were not sufficiently grave to warrant this procedure; later the progress of the disease was so rapid—twenty minutes only—that there was no time. Post-mortem findings, moreover, make it doubtful whether such treatment would have been of any avail.

It is for consideration whether, in the light of these two cases, it would not be advisable to perform lumbar puncture and drainage and/or venesection in every case of toxic purpura due to organic arsenic compounds whether they have mental or nervous symptoms or not. By such prophylactic treatment, severe "serous apoplexy" might be avoided.

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## NEW APPLIANCES FOR THE RECOVERY AND TRANSPORT OF CASUALTIES IN FORWARD AREAS UNDER FIRE.

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THE stretcher bearers, whether regimental or R.A.M.C., have a difficult, laborious, and dangerous task. They deserve any assistance that may be given by the provision of new and improved appliances.

The special problems which confront the regimental stretcher bearers are: (1) How to bring in a man from no-man's-land in the dark and under fire. (2) How to carry a loaded stretcher down a narrow trench with frequent traverses.

The R.A.M.C. bearers have a longer carry, they may have to take cover on the journey, conservation of man-power is important, and the time factor comes into play.

### THE GROUND-DRAG (figs. 1 and 2).

A special grip (claw) has been devised which can be rapidly attached to the collar of the man's tunic or battle-dress (fig. 1). The stretcher bearer



FIG. 1.



FIG. 2.

FIG. 1.—The "claw" grip. The man's blouse or tunic is loosened and the claw applied. The spare cloth is pulled up allowing protection for the patient's head as he is dragged along.

FIG. 2.—The ground-drag in action, showing concealment.