little doubt that it can be overdone. Blalock and Mason (*Arch. Surg.*, 1941, **42**, 1054) have found that exsanguinated and traumatized animals survive longer if they are cooled rather than warmed, and our own observations show that soon after the application of heat the blood pressure falls. Vasodilatation of the skin and enlargement of the vascular bed may well be harmful in shock. Some experimental work is being carried out to elucidate this point, but there is need for more observations on shocked patients.

Summarized Instructions for Use of the Shielded Cradle.—

(1) Place the upper end of the cradle at the level of the lower end of the sternum. (2) Cover the cradle and its open ends with two blankets, and do not disturb these unless absolutely necessary. (3) Leave the patient naked except for a small hand towel to protect the groins, and if the patient is restless insert the guard (see above). (4) At first turn on all 12 bulbs. (5) After not more than 30 minutes reduce the bulbs to the number required to maintain the air temperature at the desired level (see Fig. 6). (6) Determine the oral temperature at least every 15 minutes.

Summary

The heat cradle issued by the Ministry of Home Security has been modified by shielding the bulbs and blackening the reflector.

As a result of the conversion of the short-wave infra-red radiation into long-wave infra-red the risk of burns is almost eliminated and the patient can be heated at least twice as rapidly.

The danger of overheating the patient is emphasized.

Instructions are provided for using the new cradle.

We should like to thank Prof. Witts for his interest and suggestions. Our thanks are also due to the volunteers who were used in the experiments, and to Mrs. V. Launchbury, who gave technical assistance.

SYPHILIS TREATED WITH DAILY MULTIPLE INJECTIONS OF MAPHARSIDE

BY

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When Norway was invaded by Germany in April, 1940, a large part of the Norwegian Merchant Navy was isolated from its bases and eventually made its way to this country. In spite of dangers and hardships these ships continue their hazardous work, and it is not difficult to understand why, under prevailing conditions, the crews become easy victims to venereal disease when they are in port. There has been a serious increase in syphilis and other venereal diseases amongst the crews of these vessels; this constitutes a grave problem for the authorities at the present time and points to future difficulties in our social welfare. Before the war fresh cases of syphilis in Norway were very rare, and in 1938 there were only about 200 new cases amongst the whole population.

Routine treatment of syphilis is possible only if a sailor stays ashore for any length of time; but in most cases this cannot easily be arranged; and, furthermore, life ashore often has a demoralizing effect upon the men. Many who contract venereal disease come to the clinics only at irregular intervals, and treatment is necessarily unsatisfactory. These conditions obtain not only in the Merchant Navy but also in the smaller vessels of the Navy proper, and the smaller Army groups, none of which has a doctor on the staff.

At the beginning of 1942, following a review of syphilitic cases treated in the clinic, it was found that less than 30% of the patients were being adequately treated, and it was decided to start intensive arsenical treatment at the Norwegian Naval Hospital. Continuous intravenous drip therapy, using neoarsphenamine, has been tried in America (Chargin *et al.*, 1935), but the drug proved to be too toxic, peripheral neuritis being one of the most frequent complications. Later it was found that "arsenoxide" (mapharside), given in massive doses by the intravenous drip method, caused appreciably fewer toxic effects than neoarsphenamine (Chargin, 1940). Even so, the

method presented difficulties, and massive arsenotherapy, using multiple-divided doses, eventually came into use. Gordon (1941), and later O'Malley (1941), in South Africa, employed a course of treatment consisting of five doses, each of 0.02 g., of mapharside at two-hourly intervals daily for a period of five days. At the same time 25 oz. of a 10% solution of glucose by mouth, spread over the day, were given during the period of treatment. Similarly, other workers in America have administered the drug by multiple doses, but, for the most part, have given two injections daily for a period of five days.

Method of Treatment

It was decided to follow the South African method, but to give larger doses of mapharside. On Feb. 2, 1942, treatment was begun, and by June 25 one hundred patients had completed the course. In this preliminary report consideration will be given to five groups of patients, all of whom have received the intensive course, special reference being made to the complications and reactions noted during treatment.

At the outset only untreated cases of syphilis in the first and second stages were given massive arsenotherapy. As the earlier patients tolerated the treatment so well it was decided to use the intensive method in cases in which either neoarsphenamine had been given previously and had not been well tolerated or the conditions were such that the patient was unable to follow routine treatment with weekly injections. Before starting the course the patients were carefully examined clinically and the urine investigated. On the day preceding the beginning of treatment each patient had an enema, and 300 to 500 c.cm. of glucose (6%) was given orally.

TABLE I.—Scheme of Dosage

Mapharside				
	8 a.m.	12 noon	4 p.m.	8 p.m.
1st day	0.04 g.	0.04 g.	—	0.04 g.
2nd	0.04 g.	0.04 g.	0.04 g.	0.04 g.
3rd	0.04 g.	0.04 g.	0.04 g.	0.04 g.
4th	0.04 g.	0.04 g.	0.04 g.	0.04 g.
5th	0.04 g.	0.04 g.	0.04 g.	0.04 g.

Glucose Solution 6%				
Daily for 5 days (total per day, 1,500 c.cm.):				
7 a.m.	250 c.cm.	2.30–3.30 p.m.	..	300 c.cm.
8 a.m.	250 c.cm.	6–7 p.m.	..	200 c.cm.
10.30–11.30 a.m.	300 c.cm.	7–8 p.m.	..	200 c.cm.

The total amount of mapharside administered over a period of five days was 0.76 g., but in the 83rd and subsequent cases each dose was increased to 0.06 g. on the third, fourth, and fifth days, making a total of 1 g. of the drug given during the five-day period. In the earlier cases the patients received 1,500 c.cm. daily of a 6% solution of glucose orally, and they were instructed to sip the solution over a period of one hour. When the dosage of mapharside was increased the amount of glucose was also increased to 1,800 c.cm. daily, in 6 doses of 300 c.cm. On the first day of treatment the 4 p.m. dose of mapharside was not given because this period of the day usually coincided with the time at which a Herxheimer reaction might occur. During treatment the patients were kept in bed and the urine was tested every morning and evening.

TABLE II.—Complications and Reactions occurring in Five Groups of Patients

Group	No. of Patients	Pyrexia	Nausea	Vomiting	Headache	Dizziness	Dermatitis	Cerebral Symptoms	Jaundice after Hospitalization	Albuminuria	Serological and Clinical Relapse
I ..	70	36	17	8	20	2	—	—	—	1	1
II ..	10	—	—	—	—	—	1	1	—	—	—
III ..	14	—	2	—	4	—	—	—	1	—	—
IV ..	1	—	—	—	—	—	1	—	—	—	—
V ..	5	—	—	—	—	1	—	—	—	—	—
Total ..	100	36	19	8	24	3	2	1	1	1	1

Results

Group I: Primary and Secondary Cases not Previously Treated.—In 36 of the 70 cases pyrexia occurred on the first day of treatment only. Occasionally the temperature rose to 103.4° F., but in the majority of cases it lasted only from three

to five hours and did not exceed 100° F. Generally this increase in temperature caused no inconvenience to the patient and was so slight that it was recognizable only by taking hourly thermometric readings. Nausea, vomiting, and headache were experienced in those cases in which the temperature exceeded 100° F. One of the patients showed a trace of albumin in the urine on the last day of the course.

Group II.—These 10 patients had previously had one injection of neoarsphenamine at a clinic, where syphilis had been diagnosed. This group had no reactions or complication, with the exception of one patient (No. 82) who developed dermatitis and cerebral symptoms. Nevertheless, some of these patients had had a Herxheimer reaction before being admitted to this hospital.

Group III.—Five of the patients in this group were given intensive treatment with mapharside because they were intolerant to neoarsphenamine. The remaining 9 were unable to follow routine treatment with weekly injections.

Groups IV and V.—These two groups consisted of 1 patient with tertiary syphilis and 5 patients with latent syphilis.

Comments on Individual Cases

Case 7.—This patient had sero-positive primary syphilis. He differed from the other patients as he developed general lymphadenitis and exanthema macula papulosa; but recently he has been given a fresh intensive course of mapharside.

Case 13.—An initial course of neoarsphenamine was interrupted owing to dermatitis, nausea, and vomiting, and the persistence of severe headaches after each injection. On the completion of the course the patient developed jaundice. A fortnight after the jaundice had disappeared he was given a complete intensive course of mapharside without ill effects.

Case 19.—This patient had been given a course of neoarsphenamine in a V.D. clinic, but each injection was followed by severe vomiting, headache, and pyrexia. Towards the end of the course he developed a severe dermatitis with pyrexia, and was seriously ill for two weeks. After an interval of three months he was given a further injection of neoarsphenamine 0.3 g. and bismuth 0.2 g. at a V.D. clinic, but the dermatitis recurred. He came into this hospital a fortnight later and, although dermatitis still persisted, was given an intensive course of mapharside, which was completed without reactions.

Cases 35 and 96.—Both these patients were very sensitive to neoarsphenamine, and trouble occurred after each injection. One had previously had a course of mercury inunctions. This patient had slight vomiting on the first day of the intensive treatment with mapharside, but the other finished the course without reactions.

Case 63.—The first course of neoarsphenamine given at a V.D. clinic had to be interrupted several times owing to severe reactions following each injection. During treatment the patient lost weight and his condition deteriorated. A second course was started two months later, but again a severe reaction followed the first injection. He was admitted to this hospital, and the routine intensive course of mapharside was given. Slight vomiting occurred on the first day of treatment and the patient complained of headache, but he finished the course without further reactions until eight days later, when he developed jaundice.

Case 82.—The only patient amongst the series of 100 cases who had a serious reaction was Case 82, a rating aged 20 who had been exposed to infection about April 20. On May 25 he presented himself at a V.D. clinic on account of a penile ulcer of eight days' duration. *Spirochaeta pallida* was found by dark-ground illumination, and he was given neoarsphenamine 0.3 g. and bismuth 0.2 g. He reached this hospital about three hours after receiving the injections. On arrival he had a marked Herxheimer reaction. The presence of *Sp. pallida* was confirmed, and a blood test taken on May 27 showed a strongly positive Meinicke clarification reaction and a negative Wassermann. On May 29 the patient began intensive treatment with mapharside, the course being continued without reactions until the fifth day. That evening his temperature rose to 100° F., but he made no complaint and the full course was completed. On June 3 his temperature rose to 101.2° F. and he developed a morbilliform erythema. The temperature was 102° F. on June 4; during that day he complained of severe headache, and became more and more lethargic, and at times confused. At 8.30 p.m. the same evening he suddenly shrieked and exhibited strong convulsions of the clonic type which lasted about three minutes. There were no further convulsions, but he remained unconscious until 10 a.m. the following day. During the next 24 hours the condition cleared up and the

temperature fell to normal. The erythema which had made its appearance on June 3 disappeared 48 hours later, but severe headaches persisted for some days. The cerebrospinal fluid, collected shortly after the convulsions, was not under marked pressure, and contained 3 cells per c.mm. and protein 160 mg. per 100 c.cm. Gold test, 0012321000. The Wassermann reaction was very weak or doubtfully positive. On June 11 protein in the spinal fluid had decreased to 60 mg. per 100 c.cm. Possibly in this case the erythema was of a type that usually appears about the ninth day after starting arsenical treatment, and toxic encephalitis combined with this form of dermatitis is occasionally seen. Concerning the reaction in this patient it should be noted that the mapharside was dissolved in distilled water, which was almost certainly contaminated owing to a leakage in the distilling apparatus.

Serological Results

Thomas and Wexler (1941) found that on an average it requires 4 to 6 months after massive arsenotherapy for the blood Wassermann test to become negative, and in some instances it may be a year or more before complete serological reversal is achieved. According to these workers the longer a patient has had syphilis the longer it takes for the Wassermann reaction to become negative, although there are exceptions to this rule.

The serological findings for the first 100 cases in this series are shown in Table III. It has been the custom in this hospital to use the Wassermann and the Meinicke clarification reactions.

TABLE III.—Serological Results

Group	Total No.	Wassermann Negative			Meinicke Negative			Serological Relapse	Untraced
		Before Course	Immediately after Course	4 to 24 Weeks after Course	Before Course	Immediately after Course	4 to 24 Weeks after Course		
I ..	70	23	16	49	14	8	29	3	6
II ..	10	7	6	9	4	3	6	—	—
III ..	14	10	11	12	8	9	10	—	—
IV ..	1	1	1	1	1	—	—	—	—
V ..	5	3	2	2	1	—	—	—	—
	100	44	36	73	28	20	45	3	6

Among the first 100 patients there were 3 serological and clinical relapses.

Discussion

Experience in this hospital has demonstrated that *Sp. pallida* disappears from the chancre in less than 24 hours after treatment with mapharside. Primary and secondary lesions heal very quickly. In no instance during treatment of these 100 cases has there been any difficulty in giving 19 injections over a period of five days. Only males have been treated, and in many cases the patients also had gonorrhoea. With one exception there have been no serious reactions, and in most cases pyrexia occurred only for a few hours on the first day. The procedure has been to dissolve the mapharside in redistilled sterile water in the proportion of 0.01 g. in 1.5 c.cm., according to the number of cases to be treated. With this intensive treatment it is necessary to have nurses who are acquainted with the procedure, and the patients should be under their constant observation.

Summary

A series of 100 cases of syphilis treated with multiple injections of mapharside is described.

The first 82 cases received 0.76 g. of mapharside within a period of five days. The remaining 18 received a total of 1 g. during this period. These injections were combined with the oral administration of glucose.

The reactions, which with few exceptions were mild, are described. Only in one case was there a serious reaction.

This series of cases is too small for any definite statement to be made regarding this method of treatment, but these results indicate that in a time of emergency massive arsenotherapy is of the utmost value, although the method is fraught with more risk than the orthodox treatment.

I wish to express my appreciation of the services of my assistant, N. Bonsaksen, and the nursing staff of the hospital.

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