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ARSENICAL DERMATITIS TREATED WITH SODIUM-THIOSULPHATE.

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CASE I.

Previous History.—The patient, a man, aged 37, had suffered almost continuously for two months from "diarrhoea," which had developed in the autumn of 1924 during a stay in the hills. He had been kept under observation since the onset of the diarrhoea, which had failed to yield completely to various forms of treatment, including purgatives and a course of emetine hydrochloride, one grain hypodermically for ten days.

History of Present Condition.—When this case was first seen by me he was confined to bed for a short period, and given a low diet and saline treatment, and this resulted in a definite improvement. On December 6, a few days after his return to duty, the patient had a relapse, which came on after some rather vigorous exercise. Blood and mucus appeared in the stools, and these were found on examination to contain the vegetative forms of Entamoeba histolytica.

Treatment.—On December 14 it was decided to try whether or not stovarsol in daily doses of eight grains by the mouth for ten days would be of any benefit. His diet for the first six days of this course was beef-tea, arrowroot, sago, puddings, cocoa, tea and toast. On the seventh day he was given a light diet, but "felt off colour," and he began to have burning pain in the stomach, and in the evening he complained of headache and continuance of abdominal pain.

On December 22 his temperature was 99° F., and rose to 102° F. later in the day. Repeated blood-examinations revealed no malarial parasites. The bowels were confined in spite of the large doses of magnesium sulphate which had been given.

On the morning of December 23 he took his daily dose of eight grains of stovarsol at 8 a.m., and about two hours later a profuse rash appeared all over the body. This rash was a rosy erythema with mottling. It was generalized over the whole body, but more intensely marked over the trunk, and disappeared on local pressure. The rash corresponded to the description of arsenical dermatitis recorded by other workers. The urine contained a thick suspension of uric acid and urates, but no albumin.

At 3 p.m. on the same day his symptoms became urgent. His tempera-
ture was found to be 104° F., his pulse very feeble, and he showed severe dyspnœa and complained of a feeling of impending death. Movement of the bowels, produced by magnesium sulphate, given as soon as the rash was first observed, caused an immediate relief of the distressing symptoms. He was given two grammes of chemically pure sodium-thiosulphate in solution by the mouth, and about two and a half hours later his temperature had fallen to 101.8° F. (vide temperature chart).

At 6 p.m. he was given 0.5 gramme of sodium-thiosulphate intravenously. Similar injections were repeated at 6 p.m. on December 24, 25 and 27, and the patient was firmly convinced that they afforded him almost immediate relief.

After the first intravenous injection of sodium-thiosulphate the patient began to improve, and the rise of temperature was controlled (vide chart).

Progress.—The next day branny desquamation commenced on the face, ears and feet. The hair of the head was brittle and fell out in quantities.

On the following day the rash was extending on to the upper extremities, but was fading on the thighs and becoming less prominent on the back. The rash continued to fade during the next two days, and peeling of the skin of the hands and feet was noticeable.

By December 29 the rash had completely disappeared, having lasted six days, but branny desquamation continued for some days.

Fourteen consecutive daily microscopical examinations of the stools
were then made, and all proved to be negative to vegetative forms of amebæ or their cysts.

The "anchovy sauce" character of the stools was lost, but some mucus was still passed. Daily rectal injections of normal saline solution improved the latter condition.

The slow pulse rate noted in the temperature chart was probably accounted for wholly, or in part, by the fact that under normal conditions this patient had a low rate, rather than by any effect of the arsenic.

**Case II.**

Signaller W., aged 23, a case of chronic benign tertian malaria, relapsed on September 22, 1926. After receiving three grains of calomel on the evening of September 22, followed next morning by 60 grains of magnesium sulphate, he was given three four-grain pills of quinine-stovarsol at 10 a.m. and three pills at 3.30 p.m. daily. Each four-grained pill contained 2·008 grains of quinine and 1·6 grains of stovarsol, so that the daily dose of quinine was 12·048 grains, and of stovarsol 9·6 grains.

Three ounces of sugar mixture, containing one and three-quarter ounces of sugar, and fifteen grains of sodium bicarbonate, flavoured with three drachms of lime juice, as recommended by Harrison (1926), were given with each dose of three pills to protect the liver cells, together with sixty grains of magnesium sulphate to promote free elimination of the arsenic by the bowel.

The quinine and stovarsol produced the usual rigor on the first day at 4·20 p.m., the temperature rising to 103·2° F. The patient's temperature was normal the next morning, September 24, and thereafter remained normal till the evening of October 1, the ninth day of treatment with quinine and stovarsol pills. At 7.15 p.m. on October 1 he came to hospital with a temperature of 104° F. and pulse 128 per minute. No malaria parasites could be found in his blood by the thick-drop method on that evening, nor on the following morning. He was given his usual three pills of quinine and stovarsol at 10 on the morning of October 2, making a total of fifty-seven pills since the commencement of treatment. The patient had thus received a total of 114·456 grains of quinine and 91·2 grains of stovarsol.

On the morning of October 2 a rash appeared, consisting of a very faint rosy mottling on the lower part of the back, over the lower part of the chest wall in the axillary and mammary line, and over the sternum and epigastrium. There was no sign of rash on any other part of the body. The urine contained no albumin or crystals, and there was no deposit on standing.

The quinine and stovarsol treatment was stopped, and he was given one gramme of sodium thiosulphate intravenously at 11 a.m. The temperature remained at 103° F. until 6 p.m., but at 9.30 p.m. it had fallen to 101° F., with a relief of the symptoms of headache and general malaise. By
7 a.m. on the next morning the temperature was normal and thereafter remained normal. There was a slight increase in intensity of the rash of October 3, but the distribution was the same as on the previous day.

On October 4 there was a fine branny desquamation of the skin over the area of distribution of the rash. On the 5th this branny desquamation was less marked, and the rash had begun to fade. On the 6th very little desquamation or rash remained, and on the 7th both had entirely disappeared.

The temperature chart shows the striking effect on the temperature of the intravenous injection of one gramme of sodium-thiosulphate, in spite of the fact that three pills of quinine-stovarsol had been given one hour before.

After an interval of six days the quinine-stovarsol pills were again administered. Three pills were given on the first day, September 9, six on September 10 and subsequent days, and three on September 31, with the usual dose of magnesinm sulphate and sugar. On September 9 he received 1·5 gramme of chemically pure sodium thiosulphate by the mouth, as recommended by Myers, Marples, Groehl, and Throne (1926). This, however, was followed by severe colic, so the drug was not repeated till the morning of September 11, when 8·5 grains of sodium thiosulphate were given in three ounces of water, producing abdominal pains from 10.30 a.m. to 3.30 p.m. The dose of sodium thiosulphate tolerated without undue colic was found in this case to be 5·6 grains, and this was given every alternate morning up to the end of treatment on October 31.

The patient thus received, during this second course, a total of 132 pills containing 265·056 grains of quinine and 211·2 grains of stovarsol. As this is rather more than double the amounts which originally produced the arsenical dermatitis, and symptoms of arsenical poisoning, it may be concluded that sodium thiosulphate prevented their recurrence.

Daily examination during this second course revealed no further sign of any rash; there was no further rise of temperature, and no symptoms of malaise.

COMMENTS.

(1) Reasons for Stovarsol Treatment.—Stovarsol was given in Case I, because emetine had definitely failed to cure the condition, vegetative amœbæ being passed in the stools.

(2) Effect of Stovarsol.—In Case I, oral stovarsol apparently cured the amœbiasis, but in both cases its gradual cumulative effect produced an arsenical dermatitis. This may have been due to deficient elimination of arsenic by the kidneys and bowel, and therefore an attempt of the body to excrete arsenic by the skin producing the dermatitis, or to some unexplained susceptibility or idiosyncrasy towards the drug. Ten cases of chronic benign tertian malaria treated about the same time as Case II, but who were treated continuously for twenty-eight days with quinine-
stovarsol in the same daily amounts, experienced no ill-effects whatever from the treatment.

Johns and Jamison (1925) state that the only untoward effect attributed to stovarsol was dull headache in one case, mild rash in another, and rash with slight temperature in a third.

Willmore (1926), however, says that at least one death from this drug has been heard of. He records one case under treatment that developed intense dermatitis with purpuric spots after only eight grains of stovarsol.

Vialatte (1926) describes a case of benign tertian malaria which he treated with two courses of sodium stovarsol as follows: 4·5 grammes were given intravenously in four days, from January 22 to 25, 1926. After an interval of five days, the administration of 1·5 grammes on the morning of January 31 was followed in the afternoon by severe rigor, vomiting, and later sweating, and a rise of temperature to 40·3° C. (104·5°F.) in the evening. The blood was found to be negative to malaria parasites by the thick-drop method. One gramme given on February 1 was followed on February 2 by a morbilliform papulous eruption all over the body. It was more marked over the sternum, on the back, on the outer aspect of the arms, and on the front of the thighs. On the face the eruption was confluent and of a deep red colour, and the case was suspected to be one of scarlet fever. The stovarsol was accordingly stopped, but the erythema increased in intensity on February 3, and thereafter gradually faded during subsequent days.

On February 7 one gramme of sodium-stovarsol was administered intravenously, and on the next day the erythema broke out again, became more red and intense than in the previous attack, and took on the form of diffuse erythematous patches. Stovarsol was stopped and replaced by quinine, when the erythema gradually disappeared.

Duperie and Cadenaule (1926) report a case in a child, aged 5½, to whom 3·75 grammes of stovarsol were administered in March, 1926. During the course of this treatment a morbilliform eruption appeared simulating measles. In May, 1926, 4·75 grammes of stovarsol were administered, but there is no mention of any further rash.

(3) The effect of the sodium-thiosulphate was to produce an immediate and rapid improvement in the signs and symptoms. It had a marked tendency to reduce and control the temperature, which tended to rise again next morning when its effects had worn off.

Chen (1926) treated three cases of arsphenamine dermatitis with intravenous injections of sodium-thiosulphate in doses of from 0·3 to 0·6 gramme, repeated at daily intervals until improvement occurred. In each case there was rapid improvement in the signs and symptoms.

Myers, Marples, Groehl, and Throne (1926) advise a dose of one gramme of fresh crystals of sodium-thiosulphate three times daily before meals for adults, and the ingestion of large volumes of fluid. In order to secure the best results the daily intravenous administration of 0·5 gramme of sodium-
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thiosulphate is advisable. They state that the only contra-indication to the use of the drug is intestinal irritation. There are no evidences of disturbance of kidney function, but there is diuresis. The same authors state that Nyiri has shown that when sodium-thiosulphate is introduced into the blood-stream sixty to seventy per cent of it is oxidized to sodium sulphate, while the remaining thirty to forty per cent remains unchanged in the urine, provided there is a normal kidney function. They explained the mode of action of sodium-thiosulphate as follows: The continued use of fresh crystals of this drug releases the arsenic that has been deposited either in the skin, or along the nerve trunks until a gradual return of normal conditions is observed.

I have to thank Lieutenant-Colonel W. S. Nealor, I.M.S., Officer Commanding No. 7, Indian General Hospital, Dera Ismail Khan, for permission to publish the first of these two cases.

REFERENCES.

NOTES ON A CASE OF SWALLOWED DENTURE.

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BANDSMAN B., 1st Battalion the Border Regiment, was admitted to York Military Hospital, about 6.30 a.m., on November 22, 1926, stating that he had swallowed his upper denture whilst laughing in the barracks.

He was ordered to bed by the O.M.O., and attempts to tickle the fauces and produce the denture by regurgitation failed to effect the desired result.

On arrival at hospital I found the man in great pain across the chest. A skiagram located the denture lying in the oosophagus about an inch below the sterno-clavicular articulation—the vulcanite with serrated edge and the attachment, wire-angulated and dangerous-looking, produced a formidable picture.