greenish discoloration of the lips and fingers. On moving the body, greenish-coloured watery fluid poured from the nose and mouth.

Internal examination revealed no evidence of organic disease. The main signs were those of acute passive congestion. The meninges, spleen, kidneys, and liver were congested. The stomach contained 6 oz. (170 ml.) or more of watery undigested food showing a marked greenish tinge. The contents of the duodenum, jejunum, and ileum were also tinged with the same colour.

On histological examination both lungs showed acute passive congestion, intra-alveolar haemorrhages, and small extravasations of red blood cells into the alveoli; many of the alveoli contained oedematous fluid. The heart appeared normal except for capillary hyperaemia. The liver showed marked cloudy swelling. The red pulp of the spleen was also congested.

Chemical examination of the box of tablets found in the child's cot, and of the stomach and duodenal contents, urine, blood, liver, and kidneys, was made by one of us (E. P.). Information regarding methods of assay and chemical tests for anthisan was kindly furnished by Messrs. May and Baker, Ltd., the manufacturers of the tablets, such information not then being available from the literature.

Anthisan, or mepyramine maleate, is the maleic acid salt of N-2-dimethylaminoethyl-N-methoxybenzyl- α -aminopyridine, and is a creamy-white solid, soluble in water and having a melting-point between 98° and 101° C. In the pure form it may be assayed for mepyramine by hydrolysis, and extractions of the base with chloroform and direct weighing of the residue after removal of the solvent. Maleic acid may be determined by direct titration with N/1 sodium hydroxide, using phenolphthalein as an indicator. The nature of this assay, however, precludes its use for the determination of the drug in biological materials, and in the absence of any other method a quantitative determination was not attempted in the present case.

A solution of the base in dilute hydrochloric acid gives a yellowish-green precipitate with Mayer's reagent, and a trace of the dry base gives a bright cherry-red colour with concentrated sulphuric acid.

The identity of the tablets was established by these tests and by a further test involving identification of the maleate radical.

The necropsy material was submitted to the classical Stas-Otto extraction process. As anthisan is a basic substance it was expected that it would be extracted at the caustic-soda/chloroform stage—and this extract, on evaporation, did in fact give the reactions with Mayer's reagent and sulphuric acid as mentioned above. This, however, applied to the stomach contents only, and no such reactions were obtained from similar extracts from the liver, kidney, urine, or blood.

The diagnosis in this case was acute poisoning due to mepyramine maleate.

Comment

Although the clinical observations were incomplete the main features were similar to those described by Tobias. The onset of symptoms was about two and a half hours after ingestion of the tablets, and the survival period was about three hours. The principal features were unconsciousness, catarrhal discharge, and muscular twitchings, followed probably by convulsions. The naked-eye and microscopical appearances at the necropsy revealed acute passive congestion only. In the case reported by Rives *et al.* the antihistamine drug was methapyrilene, which differs from anthisan in chemical structure, the methoxybenzyl portion of the nucleus being replaced by the sulphur ring. This drug is said to be less active than anthisan. The symptoms and their time of onset were similar to those observed in the two fatal anthisan cases, but the survival period of fifteen hours is much longer. This may have been due to the less active nature of the methapyrilene preparation.

Summary

A fatal case of anthisan poisoning in a child aged 16 months is described.

A positive reaction for mepyramine maleate was obtained from the stomach contents but not from the liver, kidneys, blood, or urine.

We wish to thank Messrs. May and Baker Ltd. for technical information regarding the chemical tests for mepyramine maleate, and Mr. E. B. Love for details of the structure of methapyrilene.

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TRICHOMONICIDAL ACTION OF DINAPHTHALENE METHANE SILVER DISULPHONATE

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Dinaphthalene methane silver disulphonate in 1% aqueous solution ("viacutan") has a pH value of 4.5 to 5; it contains a wetting agent to assist spreading and a water-soluble yellow dye to indicate the areas treated. It has the property of attaching itself to and penetrating animal tissue. Sixty hours after painting living skin, silver deposits can be demonstrated in the epithelium at an average depth of 0.3 mm. It inhibits the growth of both Gram-positive and Gram-negative organisms (for example, *Staphylococcus aureus*, *Bacterium coli*, *Salmonella enteritidis*, and *Proteus*) in twenty-four-hour broth cultures in a dilution of 1 in 16,000—an antiseptic power twenty times that of phenol. Its activity is enhanced by the presence of blood, pus, or serum.

The multiplicity of remedies recommended for the treatment of trichomonal vaginitis is some indication of the complexity of the problem; relapses or recurrences are all too frequent. While recognizing that a fair proportion of recurrences are due to reinfection by the male during intercourse, it is known that relapses without reinfection do occur. An example of the latter is the case of a virgin aged 15 years who had four six-week courses of treatment within twelve months for recurrent trichomonal vaginitis, using gentian violet, 1% aqueous solution, together with acetarsol compound powder insufflations and acetarsol compound pessaries.

Some authorities believe that the *Trichomonas vaginalis* organism has a life cycle, part of which is spent in the deep vaginal epithelium, though as yet the non-flagellate stage has not positively been demonstrated (Trussell, 1947). In theory, then, for a complete and rapid cure of trichomonal vaginitis an antiseptic with a penetrating power is essential. Dinaphthalene methane silver disulphonate, having this power, was tried in over twenty resistant cases, and all, including the above-mentioned case, were found to be free from the symptoms and signs of the condition after one course of treatment. This consisted of six weekly paintings of the vagina with 1% dinaphthalene methane

silver disulphonate without any preliminary cleaning, followed, as with all other antiseptics hitherto employed, by the insufflation of acetarsol compound powder in non-pregnant cases, together with the use of acetarsol compound pessaries daily during the course of treatment. In none of the cases was a relapse reported within six months.

Dinaphthalene methane silver disulphonate in 1% solution is now used as a routine in all cases of trichomonal vaginitis and also for pre-operative and post-operative sterilization of the skin in obstetrical and gynaecological operations.

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Medical Memoranda

Schistosoma Mansoni Infection

The success which attended the treatment of urinary schistosomiasis in African school-children with a short concentrated course of miracil D (Blair *et al.*, 1949) suggested that the drug might be given a trial in two cases of *Schistosoma mansoni* infection in European children in Kenya. Both cases had previously been resistant to treatment with antimony preparations. The children probably contracted the infection in 1946, when paddling in a stream within the Nairobi Municipal Boundary.

CASE REPORTS

Case 1.—A boy aged 10½, weight 37 kg. on May 20, 1949, had had 108 injections of various antimony preparations at different times in the past three years. Examination of his faeces in May, 1949, still showed large numbers of viable eggs. Following the advice of Dr. Blair he was given miracil D orally, 27 mg. per kg. of body weight daily, for three days. The drug was dispensed in gelatin capsules, each containing 200 mg. to minimize the gastric irritation sometimes produced by the plain powder or tablet. In spite of this precaution he vomited repeatedly after the third dose. Some milk was given, which seemed to allay the sickness, and the treatment was continued. The remainder of the course was marked by only a little nausea and vomiting on the third day. Some discoloration of the skin was apparent, reminiscent of that seen during mepacrine prophylaxis of malaria, but this faded and disappeared within a week. There was no jaundice and neither the liver nor the spleen was enlarged. The urine during treatment was an orange-yellow colour. For a week after treatment he was lethargic and uninterested in his food, but thereafter became his usual cheerful self.

Case 2.—A brother of the patient in Case 1, aged 12, weight 33.6 kg. on June 5, 1949, also had viable eggs present on examination. He had not had as many injections as his younger brother, as at one time he was thought to have been cured. He was given "tabloid nilodin," an enteric-coated preparation of miracil D, in the same dosage—that is, 27 mg. per kg. of body weight daily for three days. Apparently nilodin causes much less gastric irritation than miracil D in capsules, for he had very little nausea and no vomiting during the course.

Weekly stool examinations for two months disclosed no ova. The Cercarial antigen test (Blair and Ross, 1948) was performed on both cases in July, 1948, with locally prepared antigen (after the formula of Blair *et al.*) and was then strongly positive. The tests were repeated on July 27, 1949, some two months after treatment, and were found to be negative. Many further samples of stools have been examined since then, the last occasion being in March, 1950. All have been negative, so one may take it that the cure is complete.

S. mansoni infections in the past have been notoriously resistant to treatment with antimony. While miracil D

(ni'odin) has produced a most satisfactory percentage of cures with *S. haematobium* infections it has not been as successful with *S. mansoni*.

Our thanks are due to Dr. D. M. Blair, of the Schistosomiasis Research Laboratory, Salisbury, for his helpful advice, and to Messrs. Burroughs Wellcome and Co. for a supply of tabloid nilodin.

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Association of Achalasia of Cardia with Oesophageal Carcinoma

In view of the fact that I have seen a second case of this condition so soon after reporting a similar case (Baer and Sicher, 1947) it seems desirable to record the details.

Although two such cases hardly show that the condition is a frequent one, the rapid appearance of this second case does lend weight to the previous suggestion that achalasia produced conditions favourable to the subsequent development of carcinoma, and that if the possibility of its occurrence was more widely recognized it would be discovered more often. The difficulties of diagnosis are certainly very real, and the importance of oesophagoscopy in checking any doubtful cases cannot be over-emphasized.

CASE REPORT

A married woman aged 49 had panhysterectomy on November 27, 1947, for carcinoma of the body of the uterus; this was followed by deep x-ray therapy. The pathological report revealed a highly differentiated papillary adenocarcinoma. She was followed up and found to be progressing satisfactorily. On her visit in April, 1949, she reported "tightness across the chest" and difficulty in swallowing solid foods. On closer interrogation she admitted that she had had this swallowing difficulty on and off for about 10 years; recently, however, it had been increasing in severity, and the periods free from it had become shorter. She could take fluids and semi-fluids with ease, but the solid food caused the discomfort. In the last six months she had lost several pounds in weight.

On examination, her general condition was found to be good; no abnormal signs were found on physical examination, and a straight x-ray film of the chest was normal. The report on the barium swallow was as follows: "Marked dilatation in the oesophagus due to cardiospasm. Constriction in the oesophagus at the junction between mid and lower thirds with ? filling defect on the right below this."

Oesophagoscopy was performed on May 27, 1949, with the following findings: "Oesophagus full of food: ulcerating growth at about 7 cm. from cardia: cardia in spasm. Dilated with bougies and a Negus hydrostatic bag." A biopsy was carried out and the pathological report was: "Section shows the features of an exceedingly cellular and anaplastic squamous carcinoma."

The patient was then referred to Mr. J. Leigh Collis for the opinion of a thoracic surgeon, and was admitted to the Queen Elizabeth Hospital, Birmingham. Pre-operative investigations revealed a secondary anaemia with haemoglobin at 68%. Electrocardiography indicated no cardiac defect. A further oesophagoscopy showed a "typical appearance of achalasia: massive growth seen at 31½ cm." She was given a blood transfusion, and oesophagectomy and gastro-oesophagostomy was performed on June 18.

A large growth was found midway between the arch of the aorta and the diaphragm. It was resected and continuity of the alimentary tract was established by an anastomosis between the stomach and the oesophagus. The whole operation went satisfactorily and the patient was in fair condition in the