just before admission an attack of colic. Small stones were passed, and he produced these for inspection. When examined he was tender in the region of both kidneys. No kidney enlargement was felt. His general condition was good. The urine contained abundant pus, *Bact. coli*, and albumin, but no ova. His blood urea was 50 mg. per 100 ml. on July 11, and 34 mg. on July 17. An intravenous pyelogram showed a non-functioning left kidney containing a stone, a moderate hydronephrosis of the right kidney, a distended right ureter, and several small stones in the bladder.

Operation was performed on July 30 under general anaesthesia. The wall of the bladder was found to be replaced by a fibrous mass $\frac{1}{4}$ in. (1.9 cm.) thick. The abdominal contents were packed off and the bladder opened through the posterior surface. The cut surface showed that the fibrous mass extended down to an apparently normal mucosa. Three small stones and a quantity of calcareous material were so adherent to the mucosa that curetting was necessary. As removal of the fibrous mass would have involved cystectomy it was decided to wait for the result of a biopsy, and the bladder was closed with suprapubic drainage through an indwelling catheter.

The histological section of the bladder wall showed the bladder mucosa to be thin, disorderly, very variable in its nuclear staining, and ill-defined on its deep surface. Beneath it an abundance of chronic inflammatory cells were embedded in fibrous tissue containing groups of ova of *Schistosoma haematobium*. None of the ova was calcified and all contained recognizable miracidia. The mass beyond this inflammatory zone was a scirrhous carcinoma with strands and islets of deeply staining malignant cells embedded in dense fibrous tissue which also contained fragments of bladder muscle and occasional inflammatory cells.

On August 20, at a second operation, the right ureter was transplanted into the rectum, the left ureter was divided and tied off (as the left kidney was known to be functionless), and the bladder and prostate were removed entirely.

Discussion

The interest of the case is in its rarity. Ferguson (1911), who first drew attention to the frequent association between carcinoma of the bladder and bilharzia, did so in a detailed examination of 40 cases examined at necropsy. Ten of his cases were of general infiltration of the bladder wall with growth, and in only two of these were ova found mingled with the tumour cells.

An even smaller proportion of the 130 cases dealt with surgically by Makar (1942) were general infiltrations. He described six, but noted that these cases were likely to remain undiagnosed until operative treatment was no longer possible. The absence of cystoscopic evidence is always bound to deceive the clinician.

How far the presence of ova in the bladder wall contributes to the development of malignancy does not appear to be known. Girges (1934) said: "Although malignant disease of the bladder is met with more frequently in Egypt than elsewhere, it is very rare and is not so prevalent as stated by some authors (0.25% in my series)." He attributed to these authors the error of mistaking the exuberant inflammatory masses projecting into the bladder for malignant growth. Strong (1945), however, quotes an investigation by Sourour of 373 cases of urinary bilharzia in men, among whom 78 were found to have malignant disease. Willis (1948), reviewing the literature, observes that as practically all of the bladder reports originate from Egypt, in some parts of which the infestation rate is as high as 90%, the existence of both diseases in the one individual is bound to be a frequent occurrence. On these and other grounds he concludes that, although it is possible that bilharzial cystitis does predispose to carcinoma, the evidence is still not conclusive.

The prognosis in diffuse malignant infiltration of the bladder is gloomy in the extreme. Makar employed total cystectomy in three of his six patients and all died within a year.

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ACUTE ANTHISAN POISONING REPORT OF A FATAL CASE

BY

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In a critical review of antihistamine drugs Hunter and Dunlop (1948) state that in the five years of their therapeutic use no deaths or toxic effects leading to organic change have been reported. Toxic reactions severe enough to necessitate discontinuance of the drugs have been recorded by Kern (1947), Sternberg (1947), Sachs (1948), and others. Fatal cases have been very few; but in 1949 two were reported in the literature, both of which were in young children and were due to accidental ingestion of antihistamine preparations. Rives *et al.* (1949) reported a fatal case in a child aged 16 months following the accidental ingestion of 100 mg. of methapyrilene hydrochloride ("thenylene hydrochloride"). Tobias (1949) recorded another, also in a young child who accidentally swallowed six 0.1-g. tablets of "anthisan."

Below we record a fatal case of anthisan poisoning in which qualitative tests for the active principle of anthisan in the body fluids and the main organs were positive.

Case Report

On June 26, 1949, a healthy female child aged 16 months who was on holiday with her parents at a seaside resort was found in her cot about 10 a.m. playing with a box of anthisan tablets, which she had reached from a small bedside cabinet. Her hands, lips, and tongue were stained green from the tablets, which she had been sucking. Her general condition was unaffected and she continued to play. The tablets contained 0.1 g. of anthisan. The actual number eaten was unknown, but probably was not more than six. As the child appeared normal her mother took her out on the promenade from 10.15 a.m. until noon, when she was returned to her cot in the hotel. About 12.30 p.m. her condition had changed: she was moaning, was unconscious, had muscular twitchings and a profuse catarrhal discharge, was foaming at the mouth and nose, and probably had convulsions. She was taken to the local hospital, where she was found to be dead. Death probably occurred about three hours after eating the tablets.

Necropsy

The necropsy was performed about 24 hours after death. The body was that of a well-nourished female child showing

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