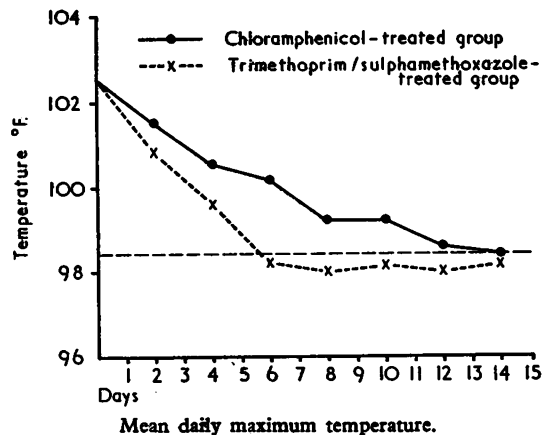


and mental changes occurred in one or other of the patients; all resolved within a few days, irrespective of the drug treatment given. There were no complications, and all patients made a very satisfactory and uneventful recovery.



Laboratory Findings.—On admission white cell counts were generally low, between 2,500 and 6,600/cu. mm. These values did not materially alter in any patients during the period of observation. E.S.R.s were raised on admission and fell slowly as the patients recovered. Chest x-ray examination showed that one patient in the chloramphenicol group had a mild pneumonitis of the left lower lobe: this resolved uneventfully during treatment. *Salm. typhi* was isolated on admission from the blood of all patients except one in the trimethoprim group in whom the organism was isolated from the stool. *Salm. typhi* was not isolated from any urine sample. In one patient in the trimethoprim group blood cultures were positive up to the sixth day of treatment, and thereafter became sterile. In all other patients *Salm. typhi* was isolated on the day of admission only; except in the case mentioned above, all stool samples proved negative for *Salm. typhi*.

Though the duration of illness before admission could not be exactly determined, all patients except the one with a positive stool culture complained of feeling definitely unwell for less than one week. The one patient with a positive stool culture

on admission gave a three- to four-week history of illness. It would seem, therefore, that the absence of *Salm. typhi* from the stools of all except the one patient reflects the early stage of their illness, during which faecal excretion of the organism is rare. *Salm. typhi* was isolated from the stool of the one faecal excretor on the day of admission only; subsequent stool samples were all negative. Long-term follow-up was not undertaken during this preliminary study, so no information is available regarding the possible later development of a carrier state in any of the patients.

All strains of *Salm. typhi* showed in-vitro sensitivity to chloramphenicol, sulphamethoxazole, and trimethoprim, with evidence of synergistic activity of the trimethoprim and sulphamethoxazole combination (Darrell *et al.*, 1968).

We would like to thank Mrs. G. Hamilton for her help in performing much of the laboratory work. We also wish to thank the Wellcome Research Laboratories for supplies of trimethoprim-sulphamethoxazole tablets.

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Medical Memoranda

Paraquat Poisoning in a Pregnant Woman

Brit. med. J., 1968, **3**, 722-723

At least eight deaths are known to have resulted from paraquat poisoning. Seven subjects died after oral ingestion of the liquid suspension and one after subcutaneous administration of 1 ml. of a 20% suspension. Survival has been reported after the ingestion of granules in one case. All eight patients appear to have passed through a phase of renal and hepatic insufficiency before expiring from respiratory failure associated with a specific type of pulmonary proliferative lesion (Bullivant, 1966; *Brit. med. J.*, 1967; Almog and Tal, 1967; Campbell, 1968; Duffy and O'Sullivan, 1968; Oreopoulos *et al.*, 1968). We wish to report the case of a 27-year-old pregnant woman who died 20 days after ingestion of paraquat. The antimetabolite fluorouracil was used in an attempt to depress the proliferative lesion, but without success.

CASE REPORT

On 4 March 1968 a married woman accidentally swallowed a teaspoonful of paraquat mixture from an old wine bottle. Pharyngitis and oesophagitis developed, and she was treated with antibiotics and corticosteroids. On 14 March she was transferred to a Dublin hospital, where initial studies showed renal- and hepatic-cell damage without evidence of respiratory involvement, as follows: haemoglobin 90%; serum sodium 163, potassium 4.8, chlorides 119 mEq/l.; blood urea 490 mg./100 ml.; urine volume at this stage exceeded 1 litre a day; the electrocardiogram was normal. Serum lactate dehydrogenase 700 units, alanine aminotransferase 80 units, aspartate aminotransferase 83 units, alkaline phosphatase 26 K.A. units, and serum bilirubin 1.1 mg./100 ml. indicated low-grade liver-cell damage. Over the next seven days the renal function improved, as shown by a fall in blood urea to 103 mg./100 ml. and a return of serum electrolytes to normal. On 19 March, some 14 days after the ingestion of paraquat, the patient complained of dyspnoea, and a repeat chest x-ray examination showed a diffuse miliary mottling pattern. In spite of hydro-

Features of Paraquat Poisoning

	Age and Sex	W.B.C.	Duration of Illness	Blood Urea (mg./100 ml.)	Serum		E.C.G.	Chest X-ray Examination
					Bilirubin	AsT/Alt		
Bullivant (1966)	23 M	26,000	8 days	150 (NPN)*	3	66/160	B.B.B.† Myocarditis	Consolidation
Bullivant (1966)	28 M		15 days	112 (NPN)	13	162/—	B.B.B. Myocarditis	Mottling
Almog and Tal (1967)	30 M		18 days	140	4.6	250/—	Normal	Bilateral opacities
Duffy and O'Sullivan (1968)	45 M	10,300	18 days	124	0.8	300/—	Normal	Pneumonia
Campbell (1968)	6 M	11,000	7 days	240	6.0	—	—	Bronchopneumonia
Present case	27 F	13,000	20 days	490	1.1	80/83	Normal	Mottling
Irish (unreported) .. .	Child							
Oreopoulos <i>et al.</i> (1968)	44 M	19,400	8 days	310				Hypervascularization

*NPN = Non-protein nitrogen. †B.B.B. = Bundle-branch block.

cortisone 100 mg. eight-hourly and fluids intravenously the dyspnoea increased in severity and she was cyanosed at rest.

On the 16th day of illness she was given fluorouracil 15 mg./kg. intravenously daily for three days. There was no deleterious effect in terms of marrow toxicity (W. B. C. 14,000 at end of treatment) or fresh gastrointestinal ulceration, but her condition continued to deteriorate and she died in respiratory failure 20 days after the ingestion of paraquat.

Necropsy.—There was a small ulcer on the tongue (present from time of paraquat ingestion). One hundred ml. of yellowish fluid was present in both pleural cavities. Both lungs were solid and oedematous, and showed numerous subpleural bullae. The alveolar walls were thickened owing to proliferation with spindle-shaped cells and infiltrated with multinucleated giant cells which reduced or obliterated the alveolar lumina. An inflammatory exudate present consisted mainly of lymphocytes. The kidneys showed patchy necrosis of the proximal tubules. There was some fatty infiltration in the centrilobular areas of the liver; bone marrow was within normal limits. Sections of the foetal lungs, kidneys, pancreas, liver, and spleen, and the bone marrow showed no abnormalities.

COMMENT

This patient passed through a similar sequence to that found in the cases already described (see Table). Though a severe degree of renal failure appears to have developed in most of the reported cases none of the patients seems to have died from this complication. A similar statement holds true for the liver-cell damage, though this does not appear to have been so severe. It is to be expected that some electrocardiographic changes must be noted in patients who are passing through a phase of renal failure, so it is difficult to assess the significance of the E.C.G. changes which have been observed. The multinucleated giant cells noted in the present case had not been observed in previous reports. The lack of changes in foetal tissues is probably a reflection of absent pulmonary function and minimal renal tubular function of the foetus.

Treatment with an antimetabolite was tried for a number of reasons: (a) all patients who died have shown a proliferative lesion in the terminal bronchioles that was constricting the lumen; (b) Ackerman and Regato (1954) commented on similar lesions to those following administration of carcinogens to

animals; and (c) Duffy and O'Sullivan (1968) suggested that immunosuppressive treatment be considered. The unique circumstance of this poisoning in a 28-week pregnant woman raised the question of damage to the foetus should the mother survive. Methotrexate and mercaptopurine were precluded because of the maternal hepatic and renal-cell damage already present. Alkylating agents were not considered, because in optimal dosage a prolonged depressive effect on the bone marrow would result. It is important to stress that in this case fluorouracil was given at a stage when the respiratory complications of paraquat poisoning had fully developed. To achieve any possible effect an antimetabolite would have to be given at a much earlier phase of the illness.

We feel there should be little occasion to stress the need for rigorous care in the sale and distribution of this, and, indeed, any other weedkiller. The fact that five of the eight recorded deaths attributed to paraquat have occurred in Ireland—one death a year since 1964—should be adequate cause for grave concern.

Since this report was prepared a further death has been mentioned at a coroner's inquest in Dublin. The Minister for Health has as a result issued restrictions on the sale and labelling of paraquat in Ireland.

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Cholecystogastric Fistulae

Brit. med. J., 1968, 3, 723-724

Fistulae between the biliary tree and the alimentary tract are not uncommon. Of these the rarest are those between the gall bladder and the stomach. Wakefield *et al.* (1939), in a series of 176 such fistulae, reported 101 to the duodenum, 33 to the colon, 24 direct to the peritoneal cavity, 11 to multiple sites, but only 7 to the stomach. Judd and Burden (1925) reported 153 cases, of which six were to the stomach, and Hicken and

Coray (1946) reported 272 cases, with 12 to the stomach. This gives an overall incidence of 4.2% cholecystogastric fistulae.

The discovery of gall stones in the stomach is also rare. Cases have been reported by Miles (1861), Naunyn (1892), Demole *et al.* (1950), McLaughlin and Raines (1951), and Hoskins (1962). The portal of entry was usually the pylorus, the gall stone having previously entered the duodenum via the common bile duct or a cholecystoduodenal fistula. In these cases the stone must have been small, and many such stones are probably passed per rectum without symptoms. Small stones entering the stomach via a cholecystogastric fistula may also be passed, and several cases of cholecystogastric fistulae