Paraquat poisoning

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THIS IS an account of a case of suicidal poisoning with paraquat. Despite treatment by forced diuresis and peritoneal dialysis the patient died only 2 days after ingestion of the poison.

Paraquat (1,1′-dimethyl, 4,4′-dipyridilium) is a herbicide widely used in Britain. Its popularity is due both to its effectiveness and to the fact that it is rapidly inactivated on contact with the soil, leaving no poisonous residue. It is available for domestic use as Weedol (5% Paraquat) and for agricultural use as Gramoxone W (20% Paraquat). Fourteen cases of paraquat poisoning have now been reported (Bullivant, 1966; Leading Article, *Brit. med. J.* 1967; Almog & Tal, 1967; Mourin, 1967; Campbell, 1968; Duffy & O'Sullivan, 1968; Oreopoulos *et al.*, 1968; Kerr *et al.*, 1968; McKean, 1968; Fennelly, Gallagher & Carroll, 1968; Mathew *et al.*, 1968). Nine patients have died, all but one of respiratory failure; the ninth died of cardiac arrest (Duffy & O'Sullivan, 1968). At post-mortem the most striking abnormality has been cellular proliferation in the lungs: renal tubular and liver damage has also been commonly found. Five patients have had myocardial damage detected either by electrocardiography or by histological examination. The commonest initial symptoms have been vomiting, diarrhoea, sore throat and abdominal pain.

Case report

(Addenbrooke's Hospital No. 318357)

A previously fit 30-year-old man drank approximately 100 ml of Gramoxone W (20% Paraquat) at 17.00 hours on 15 September 1968 in an attempt to commit suicide. He had no symptoms until 18.30 hours when he took to his bed feeling ill. At 19.00 hours he vomited and at 20.40 hours was admitted to the North Cambridgeshire Hospital at Wisbech complaining of nausea vomiting, burning in the throat and aching in all muscles.

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Gastric lavage was performed and forced diuresis started. Frusemide 60 mg i.v. and intravenous fluids were given: over the next 12 hr he received 2 litres of normal saline, 1 litre of Darrow's No. 10 solution and 5 litres of 5% dextrose. At 23.00 hours he was given paraldehyde (6 ml) because of restlessness, and during the night he was given hydrocortisone (100 mg i.m.). The next day (16 September 1968) he received paraldehyde 10 ml at 13.15 hours and a further 10 ml at 14.15 hours. He was then transferred to Addenbrooke's Hospital, Cambridge, where he arrived at 17.00 hours. By this time he had received 8 litres intravenously and passed 5 litres of urine, although only 500 ml since 08.00 hours. He had also passed six large fluid stools. On arrival he was unconscious and smelled of paraldehyde but there were no other physical signs. He was anuric. Peritoneal dialysis was started and in all fifteen 1 litre exchanges were completed. The dialysis fluid contained 1·5% dextrose. He was given prednisone 20 mg i.m. at 19.00 hours and again at midnight. Paraldehyde (10 ml) was given at 23.00 hours. At midnight he was given Omnopon (15 mg i.m.) because he appeared to be in pain. At 05.00 hours he received a further 10 ml of paraldehyde and at 07.30 hours hydrocortisone (100 mg i.v.). At 09.00 hours he was still unconscious. He was now jaundiced. The respiratory rate was 40/min and the blood pressure unrecordable. From 09.30 hours onwards he was given intravenous metaraminol, 1 mg every 15 min, but he remained severely hypotensive and died at 13.00 hours only 44 hr after taking paraquat.

Investigations

Paraquat concentrations: Samples of blood, urine and dialysate were analysed for paraquat by Dr A. A. B. Swan of the Industrial Hygiene Research Laboratories. Four to 6 hr after ingestion of the poison the blood concentration was 1·5 mg/100 ml: after 24 hr it had fallen to 0·2–0·3 mg/100 ml (Fig. 1). Urine passed 4 hr after ingestion contained 90 mg/100 ml; 22 hr later no paraquat could be

detected. Concentrations in the dialysates were low (0·11–0·13 mg/100 ml) and the total amount removed by dialysis was only 16·5 mg.

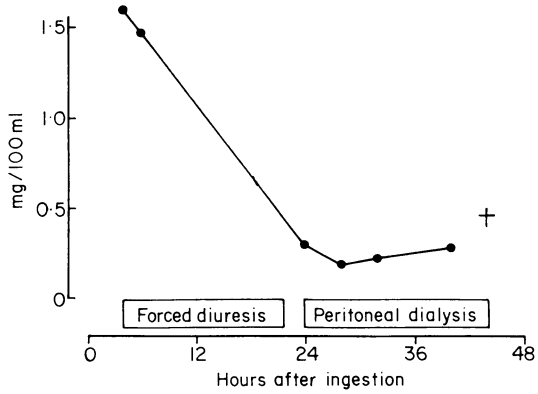

FIG. 1. Concentrations of paraquat in blood.

Other biochemical findings: On the 2nd day plasma concentrations were as follows: bicarbonate 8 mEq/l, sodium 128 mEq/l, potassium 3·8 mEq/l, bilirubin 11·5 mg/100 ml, alkaline phosphatase 12 King Armstrong units, SGOT 133 units, SGPT 122 units; and blood urea was 56 mg/100 ml. Arterial blood gases and pH were unfortunately not measured.

Electrocardiograms: The first record, taken 5 hr after ingestion of paraquat, showed no abnormality. During the next 24 hr increased 'T' wave voltage was noted in right chest leads (TV_2 19 mm).

Chest X-rays (portable): soon after admission the lung fields were clear; the right diaphragm was elevated and the stomach markedly dilated. The next day there appeared to be areas of basal collapse.

Necropsy (P 68–613)

He was a rather plump subject (body weight 84 kg). The skin and conjunctivae were faintly yellow. The lips were pale yellow and the buccal mucosa bright red and purple fluid filled the mouth. The tongue and pharyngeal mucosa were discoloured purple; the oesophageal mucosa was smooth and grey though slightly oedematous towards the lower end; there were purple areas in the stomach but no evidence of ulceration. The liver weighed 1990 gm and had patches of yellow discolouration throughout the cut surface. There was 700 ml of dialysis fluid in the peritoneal cavity but no other abnormality in the alimentary tract. Each pleural sac contained almost 200 ml of cloudy yellow fluid and both lungs had a few petechial haemorrhages over the posterior parts of the lower lobes which were deep purple and appeared collapsed. Apart from slight dilatation of the cardiac chambers the heart was normal. The urogenital, endocrine, lymphoreticular and central nervous systems were normal.

Various tissues and fluids were sent for toxicological analysis. No paraquat was found in the stomach contents, liver, urine nor in the small bowel contents. A search for other poisons was also unrewarding.

Histological examination: The only abnormalities were in the lungs (Fig. 2) and kidneys. In the lungs amorphous pink material thickened the interstitium

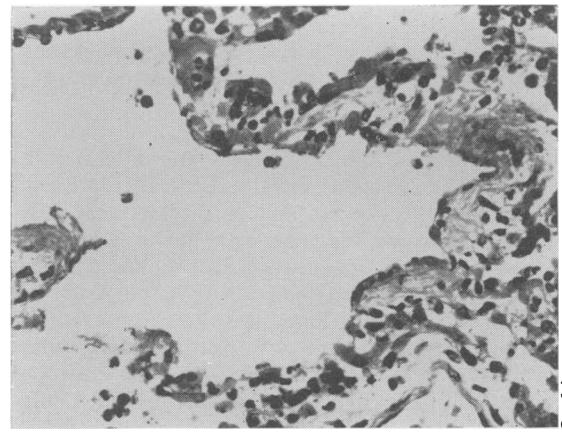

FIG. 2. Lung: amorphous material in the interstitial tissue. H & E, ×280.

of some alveoli and also lined some alveoli. Occasional fibroblasts contributed to the interstitial thickening. The kidneys showed occasional pyknotic nuclei in the convoluted tubule cells and many pyknotic nuclei in the cells of the loops of Henle. Sections of liver, pancreas, thyroid, suprarenal, pituitary, bone marrow, heart and quadriceps muscle were histologically normal.

Discussion

It is difficult to know how much paraquat was absorbed. In rats it has been found that about 80% of an oral dose is excreted in the faeces (Daniel & Gage, 1966). In this case it is likely that most of the ingested paraquat was lost by vomiting and diarrhoea and following the stomach washout. Most of the material absorbed was probably removed by the forced diuresis since none was detected in the tissues at post-mortem. Only 16·5 mg of paraquat was removed by peritoneal dialysis. During the dialysis the blood paraquat concentration remained at about 0·29 mg/100 ml (Fig. 1) while the average concentration in the returned dialysis fluid was only 0·12 mg/100 ml. This is not surprising since a high

degree of protein binding is predictable from the highly ionized state of the molecule.

The lethal dose seems to be variable. In the past death has occurred after ingestion of 1 ml of Gramoxone W and after spitting out a mouthful ingested accidentally. In the present case the amount ingested and the concentration in the blood were high compared with other fatal cases.

Paraquat is remarkable for the distinctive lung changes it causes and for the 'hit and run' manner in which it appears to act (Clark, McElligott & Hurst, 1966). In this case even though death occurred within 48 hr early proliferative changes were found in the lungs; and it seems highly probable that he would have succumbed to respiratory failure if he had survived long enough. It follows that if treatment designed to inhibit cellular proliferation is to have any chance of success it should be started as soon as possible after ingestion of the poison.

Jaundice and raised serum transaminase concentrations were interpreted as evidence of liver damage although histologically the liver was normal. In accord with previous reports the renal changes were predominantly those of tubular damage affecting the loops of Henle more than the convoluted tubules.

The mode of death was not typical. In most reported cases death has resulted from respiratory failure some 10–20 days after taking paraquat. In this case death occurred from circulatory failure within 48 hr: whether this represented a direct toxic affect of paraquat on the myocardium or the effects of severe metabolic disturbance is uncertain. Paraldehyde may have been a contributory cause since the drug has been reported as a cause of metabolic acidosis (Hiemcke, 1964) particularly in the presence of liver damage.

Acknowledgments

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References

ALMOG, C. & TAL, E. (1967) Death from paraquat after subcutaneous injection. *Brit. med. J.* **3,** 721.

BULLIVANT, C.M. (1966) Accidental poisoning by paraquat: report of two cases in man. *Brit. med. J.* **1,** 1272.

CAMPBELL, S. (1968) Death from paraquat in a child. *Lancet,* **i,** 144.

CLARK, D.G., MCELLIGOTT, T.F. & HURST, E.W. (1966) The toxicity of paraquat. *Brit. J. industr. Med.* **23,** 126.

DANIEL, J.W. & GAGE, J.C. (1966) Absorption and excretion of diquat and paraquat in rats. *Brit. J. industr. Med.* **23,** 133.

DUFFY, B.S. & O'SULLIVAN, O.J. (1968) Paraquat poisoning. *J. Irish med. Ass.* **61,** 97.

FENNELLY, J.J., GALLAGHER, J.T. & CARROLL, R.J. (1968) Paraquat poisoning in a pregnant woman. *Brit. med. J.* **3,** 722.

HIEMCKE, T. (1964) Metabolic acidosis caused by paraldehyde. *Ned. T. Geneesk,* **108,** 2165.

KERR, F., PATEL, A.R., SCOTT, P.D.R. & TOMPSETT, S.L. (1968) Paraquat poisoning treated by forced diuresis. *Brit. med. J.* **3,** 290.

LEADING ARTICLE (1967) Poisoning from Paraquat. *Brit. med. J.* **3,** 690.

MCKEAN, W.I. (1968) Recovery from paraquat poisoning. *Brit. med. J.* **3,** 292.

MATHEW, H., LOGAN, A., WOODRUFF, M.F.A. & HEARD, B. (1968) Paraquat poisoning—lung transplantation. *Brit. med. J.* **3,** 759.

MOURIN (1967) Paraquat poisoning. *Brit. med. J.* **4,** 486.

OREOPOULOS, D.G., SOYANNWO, M.A.O., SINNIAH, R., FENTON, S.S.A., MCGEOWN, M.G. & BRUCE, J.H. (1968) Acute renal failure in a case of paraquat poisoning. *Brit. med. J.* **1,** 749.

Diquat poisoning

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DIQUAT, like paraquat, is a dipyridilium compound used as a herbicide, and sold under the trade name of 'Reglone'. The severe toxic effects of paraquat have been well documented (Oreopoulos *et al.*, 1968; Matthew *et al.*, 1968; Kerr *et al.*, 1968), but there is little known as yet of the effects of diquat ingestion.

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We present here what we believe to be the first case of diquat poisoning The patient recovered after treatment with forced diuresis.

Case report

An 18-year-old man accidentally took a mouthful of undiluted 'Reglone', from a Coca Cola bottle at 08.00 hours on the 7 September 1968. Although he