Med. J. Malaysia Vol. XXXII No. 4, June, 1978

PARAQUAT POISONING

Ng Tian Seng
M.B., B.S. (S'pore), M.R.C.P. (UK), M.R.A.C.P.

Physician
District Hospital
Kuala Pilah

Thong Kok Wai
M.B., Ch.B. (Manch)

Medical Officer
General Hospital
Seremban

INTRODUCTION

PARAQUAT (1,1 di-methyl 4,4' bi pyrilium chloride) a potent herbicide was introduced to Malaysia in 1961. Since then the number of fatal cases due to accidental or suicidal consumption of paraquat has been increasing. It is sold under various trade names – e.g. (Gramoxone (I.C.I.) Gramixel Priglone weedol etc) and is available in two forms – the granular form containing 5% paraquat and the liquid concentration containing 20% to 40% solution of the herbicide. Ingestion of large amounts of paraquat is invariably fatal even though the minimum lethal dose has not been ascertained. It appears that as little as 7 ml. may be fatal (Materson and Rodie, 1970) and a subcutaneous injection of 1 ml. has also proved to be fatal (Almog and Tal, 1967). Severe poisoning due to large doses of paraquat may kill within 24 to 72 hours with extensive necrosis of heart, liver and kidneys at autopsy, whilst small amounts produced variable degrees of damage of renal or hepatic function which may be reversible. Death is usually due to progressive respiratory failure; the onset of pulmonary oedema and haemorrhage bearing a temporal relationship to the amount of paraquat ingested, smaller doses being associated with a slower development of pulmonary lesions. In general, after a small dose there is an initial asymptomatic period of several days then respiratory functional impairment sets in which hypoxaemia, decreased lung volumes, low lung compliance and impaired DLCO (Carbon monoxide diffusing capacity). Chest roentgenograms will show pulmonary infiltrates and electrolyte studies reveal renal impairment.

When pulmonary manifestations appear, the prognosis is poor and while few cases have recovered (Douglas *et al.*, 1973) in this series it has proved invariably fatal. The local effect of paraquat on contact have included nail loss, epistaxis due to toxic effect on the nasal mucosa, eye injuries and in one of our cases (not reported here) necrosis, dermatitis and desquamation of the scrotal skin due to accidental splashing. For those of us who have used paraquat this is understandable as we can see that within 8 to 10 hours after paraquat is sprayed, the leaves turn brown and within 3 days, the weeds have died. The contact with the oral mucosa sometimes takes up to 48 hours to develop with ulceration and desquamation. The most remarkable effect is the complete inactivation of paraquat when clay is present and Fullers earth or bentonite when given very early after gastric lavage may save a life.

The following is a report of five fatal cases admitted over the period 1/6/76 to 1/6/77 to the Seremban General Hospital and while this is written several more have died. No blood gas estimation or respiratory volumes measurement were done in our cases.

CASE I

An Indian boy of 18 years was referred from Tampin District Hospital on 27/8/76 with a history of fever, sore throat, hoarseness of voice and cough productive of yellowish sputum of about a week's duration. His sputum was blood tinged and he had dysphagia with epigastric pain and dyspnoea. He admitted to have taken paraquat after prolonged questioning even though he denied intentional suicide.

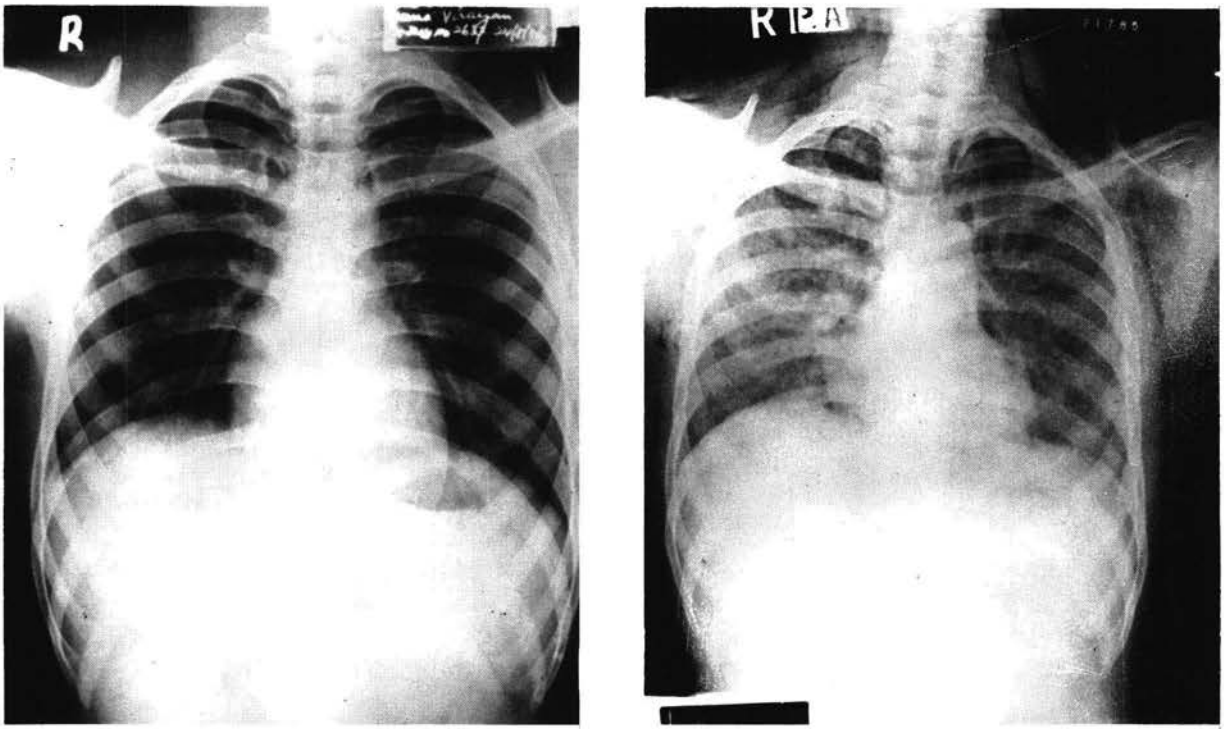
General examination revealed a very ill boy with dyspnoea, jaundice and fever. His tongue was swollen, coated and congested and so were the oral mucosa, lips and the pharyngeal wall.

Other salient features included gross surgical emphysema extending from the neck to the subscapular areas on both sides, slightly impaired chest expansion but adequate air entry and without adventitious sounds. The respiration was 40/min, pulse 102/min and blood pressure was 130/80. The liver was palpable and there was epigastric tenderness. Investigations revealed a leucocytosis of 16,400, a erythrocyte sedimentation rate of 48/hour, a raised urea of 276 mg % and normal electrolytes. X-rays of the chest showed extensive mottling of the lung fields and surgical emphysema on 27/8/77 compared with the film taken in Tampin on 24/8/77 (both shown in Fig. 1 for comparison). Serum creatinine was 6.6 mg %, serum bilirubin 21 mg % and alkaline phosphatase 48 K.A. Units. A barium swallow was done to look for any perforation and was essentially normal.

Over the next 3 days inspite of steroids and attention to fluid balance the patient deteriorated with increasing dyspnoea, crepitations in both lungs and succumbed on 30/8/76. Autopsy revealed a deeply jaundiced man with extensive necrosis of the fauces and tongue; the kidneys showed bilateral cortical haemorrhage, and the liver was enlarged, yellow and haemorrhagic. Both lungs were oedematous and showed haemorrhages. Examination along the trachea and oesophagus reveal no area of perforation.

CASE II

A Malay lady of 21 years was admitted on 10/12/76 with a history of consuming 1 teaspoonful of a 'Coffee coloured' weedkiller by mistake. She was slight drowsy but had reactive pupils. There was oral ulceration but no chest signs or jaundice. On 11/12/76 the blood urea was 54 mg %, electrolytes were normal and there was a trace of albuminuria. Chest X'ray was normal. There was paraquat in the urine. She was given Fuller's earth 30% suspension (200 ml. every 2 hours × 5 doses) and intravenous fluids but the urine output was poor and blood urea was 90 mg % on 12/12/76. Later the same day she became dyspnoeic with bilateral chest crepitation and inspite of high dose lasi she deterio-



1a 1b

Fig. 1 Chest X-Rays of case 1 showing the effect of paraquat on the lung. 1a before and 1b after the ingestion of paraquat.

rated with the 'Paraquat' lung syndrome with mottling of bases shown on chest X'ray. Urine for paraquat on 14/12/76 was negative but she deteriorated further and died in the early hours of the next day.

CASE III

A Chinese child of 11 years was referred from Jelebu District Hospital on 23/2/77 with history of taking 1 teaspoon of paraquat after her father had reprimanded her, and she was given a stomach washout before referral. Her main complaints were of intractable nausea and vomiting, sore throat, and several loose motions over the previous evening. General condition was satisfactory with haemorrhagic spots over the tongue and palate (which progresses to ulceration later) but no jaundice or chest signs. Paraquat was found in the urine and a trace of albuminuria was detected but urea and electrolytes were normal. Bilirubin was 1.1 mg % with leucocytosis. On 3/3/77 the urea rose to 237 mg % with urinary output of 600 – 700 mls. daily and a swinging prexia and chest crepitations. A dialysis was contemplated but her urea decreased to 122 mg % with serum potassium 5.1 meq/L on 8/3/77 with increased urinary output. However her chest X'ray had features typical of the 'Paraquat' lung syndrome and inspite of steroids, controlled oxygen therapy, she died on 12/3/77 after a total of 18 days in hospital.

CASE IV

A 34 years Chinese male apparently drank one mouthful of paraquat on 27/5/77 in a bout of depression over family and financial problems. He was admitted to Kuala Pilah District Hospital the next morning with complaints of sore throat, vomiting and retrosternal discomfort and referred to Seremban on 11/6/77 with severe jaundice, severe ulceration of the oral mucosa and moist sound in both lungs. Fuller's earth and prednisolone was administered in Kuala Pilah but the bilirubin had increased from 11.3 mg % to 24.6 mg %. Investigations revealed leucocytosis of 29,000, a trace of albuminuria, blood urea of 93 mg %, serum sodium 118 meq/L, serum potassium 3.1 meq/L and serum chloride 69 meq/L. There was no paraquat in the urine and urinary output was adequate and 1500 ml. of 3% saline corrected his electrolyte over 3 days. The urea on 18/6/77 was 104 mg %. However he was hypoxic, delirious and went into shock and coma and died on 19/6/77.

CASE V

One example of fulminating poisoning involved a self confessed heroin addict. This Malay boy, 20 years old drank half a gallon of diluted 'GRAMOXONE' at 4.30 p.m. on 21/7/77 and was admitted to Jelebu District Hospital where a stomach washout was performed and he was referred to us. He was in very poor condition with severe retching and in shock. Intravenous fluid, atropine and 100 gm. of Fuller's earth 2 hourly was given but he deteriorated, becoming cyanotic, delirious and later comatose. Paraquat was present in large amounts in the urine but except for leucocytosis and a trace of albuminuria, other investigations were negative. He had cardiac arrest 23 hours after taking the paraquat.

DISCUSSION

The above cases illustrate most convincingly the methodical precision with which paraquat kills and that the salvage rate is nil in our cases and that any desperate measure which has even the remotest chance of success is worth trying. Successful treatment will depend on very early intervention by the repeated administration of 30% suspensions of Fuller's earth orally to inactivate paraquat and rapid reduction of the circulating compound using haemoperfusion through a charcoal column. One effective substitute for Fuller's earth is bentonite suspension consisting of 70 gm. of bentonite in 100 mls. of glycerine and made up to 1 litre with water. Haemodialysis and peritoneal dialysis have not shown any success in removing paraquat and recent reports have shown that the charcoal column is not as effective as when first reported probably because the lung appears to concentrate the paraquat from the blood and thereby produce an alveolitis before the blood levels can be lowered. Steroids, azathioprine and other drugs have been used to suppress the severe alveolitis but have not been successful. Case I also demonstrates that subsequent to the alveolar membrane damage (our contention) the patient can develop extensive surgical emphysema without any perforation of the trachea or the oesophagus.

Paraquat poisoning has been said to represent adult respiratory distress syndrome (Mantelow, 1967) and the mechanism of its toxicity has been ascribed to the formation of superoxide ion (02^-) (Gaje, 1968, Conning *et al.*, 1969). Paraquat seems to act as an electron acceptor when nicotinamide adenine dinucleotide phosphate is oxidised in cellular and subcellular fractions of rat or rabbit lung and then reoxidised by oxygen to molecular paraquat with subsequent formation of superoxide ions (02^-) which is highly unstable and thought capable of tissue damage. Superoxide ions are decomposed to hydrogen peroxide and oxygen in the presence of free H^+ radical, catalysed by a tissue enzyme, superoxide dismutase ($20^- + 2H^+ \rightarrow H_2O_2 + O_2$). H_2O_2 is thought to damage the lipid cell membrane. In an attempt to preserve lung function and maintain oxygenation, lung transplantation was performed by

several investigators (Cooke *et al.*, 1973) but it was found that the transplanted lung also showed signs of paraquat poisoning which was confirmed at autopsy. At the time of operation paraquat was still present in the blood and in the intact lung but on postmortem no paraquat was detected in the transplanted lung suggesting an inexorable progress of the pathological process once initiated. Animal studies also suggest that oxygen administration may accelerate the development of lung lesions. Our own management is as follows:-

1) Gastric lavage

2) Oral administration of 200 ml. of 30% Fuller's earth every two hours for 48 hours.

3) Intravenous fluid with careful monitoring of output and peritoneal dialysis where indicated.

4) Steroids and other symptomatic therapy. We are now considering haemoperfusion. The kidneys excrete paraquat and maintaining a good diuresis is most helpful as paraquat has been detected in the urine 31 days after ingestion.

CONCLUSION AND SUGGESTIONS

Paraquat is of great economic value as planting can proceed a few days after spraying and has resulted in 3 crops per annum instead of 2 in places like Sri Lanka but it is lethal to man. We would advise that Fuller's earth be given immediately if paraquat has been taken and gastric lavage done before transferring the patient from a district hospital as this offers the only hope of survival in Negri Sembilan. In the hope that the number of accidental poisoning be lowered we hope the manufacturers of GRAMOXONE I.C.I. (MALAYSIA) will 'stench' the compound as many labourers and their family refer to GRAMOXONE as coffee and have drank it accidentally with fatal results as there is no strong smell.

ACKNOWLEDGEMENTS

We are indebted to Dr. John Loh Kim Yew without whose help this report would never have been published. Mr. Tan, Biochemist, Hospital Besar, Seremban was most gracious to have carried out for us the urine test for paraquat and his ingenuity in getting the sodium dithionite. We also wish to express our sincere thanks to Cik Kasimah bt. Hj. Abdul Karim for typing the manuscript and Mr. C. Gnaneswaran, Administrator of Kuala Pilah District Hospital for his help. Dr. Charanpal Singh very kindly carried out the barium swallow studies.

REFERENCES

Almog, C. and Tal, E. (1967) Death from paraquat after subcutaneous injection, *Br. Med. J.* **3,** 721–724.

Conning, D.M. *et al.* (1969) Paraquat and related bipyridyls, *Br. Med. Bull.*, **25,** 245–248.

Cooke, N.J., Fenley, D.C. and Matthew, H. (1973) Paraquat poisoning serial studies of lung function, *Quarterly J. Med. New Series,* **168,** 683–692.

Daves, R.E. (1976) Management of paraquat poisoning, *New Zealand Med. J.*, **83,** 244.

Douglas, J.F., McGeown, M.G. and McEvoy, J. (1973) Treatment of paraquat poisoning: three cases of recovery, *Ulster Med. J.*, **42,** 209–211.

Fairshter, R.D. and Wilson, A.F. (1975) Paraquat poisoning: manifestation and therapy, *Am. J. Med.*, **59,** 751–753.

Gaje, J.C. (1968) The action of paraquat and diquat on the respiration of liver cell fractions, *Biochem. J.*, **109,** 757–759.

Manktelow, B.W. (1967) The loss of pulmonary surfactant in paraquat poisoning, *Br. J. Exp. Pathol.*, **43,** 366–369.

Masterson, J.G. and Rodie, W.J. (1970) Another paraquat fatality, *Br. Med. J.*, **2,** 282–284.

Teare, R.D. (1976) Poisoning by paraquat, *Med. Sci. Law* **16,** 9–12.