

PARAQUAT POISONING IS NOT ALWAYS FATAL

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SYNOPSIS

Of the nineteen cases of Gramoxone poisoning treated at the Medical Unit, Toa Payoh Hospital, three survived. The clinical data of these survivors is presented. The maximal ingested dose compatible with life in the present series is twenty millilitres of Gramoxone while the excretion rate of paraquat in urine in a non-fatal case is 0.92 mg/hr in the first 24 hours. In the follow-up of these survivors, there is some evidence to suggest that the pulmonary injury may be partially reversible.

INTRODUCTION

Paraquat (1,1 dimethyl 4,4 bipyridilium) was first synthesized in the 19th century and used by chemists as an oxidation-reduction indicator dye known as methyle nitrogen. It became commercially available as a herbicide in 1962. In 1966 two deaths resulting from ingestion of this compound was reported and by 1973 the toll increased to 232. In Singapore there were no deaths from paraquat poisoning prior to 1969. A report in 1972 recorded eleven deaths between 1969 — 1972. There has been no report of survivors in the local literature. This paper documents three survivors of paraquat poisoning to stress that paraquat poisoning is not always fatal.

CASE REPORT I

On 28.10.75, a 11 year old boy took a table-spoonful of Gramoxone (about 10 mls) after being chided by his mother. Eight hours later, he was admitted to hospital. At that time, he was not cyanosed or jaundiced. Respiratory rate 14/min and the lungs were clear. The following day, ulcers were seen in the mouth and the pharynx. These cleared five days later. Liver function tests including transaminases were normal. Blood urea was normal on admission but rose steadily to 72 mg% by the fourth day, and creatinine clearance reduced to 68 mls/min. Thereafter the blood urea gradually returned to normal. Arterial blood gas performed on admission revealed a Pa O₂ of 90 mm

Hg and a Pa CO₂ of 30 mm Hg. The first chest x-ray was normal. The urine in the first 24 hours contained 0.81 mg paraquat per 100 mls urine or an excretion rate of 0.92 mg/hr in the first 24 hours.

After stomach aspiration and gastric lavage, he was given Magnesium sulphate and Betonite suspension (7%) orally for next 2 days. Forced diuresis was also started and continued for 56 hours till the urine was negative for paraquat. He appeared well and comfortable on admission but by the fifth day was noticed to be tachypnoeic with a respiratory rate of 48/min. No crepitations were heard in the lungs. The pa O₂ had fallen to 59 mm Hg and pa CO₂ was 25 mm Hg. A repeated chest x-ray on 8th day showed opacities in right upper lobe. (Fig. 1—1). He was started on Imuran and Prednisolone. Six days later he became less dyspnoeic and pa O₂ was 63.4 mm Hg and pa CO₂ was 28.2 mm Hg. He continued to improve steadily and one month after admission the pa O₂ was 81 mm Hg and pa CO₂ 29.6 mm Hg. The chest x-ray showed early pulmonary fibrosis (Fig. 2). Lung Function Tests revealed a severe restrictive defect:

Determination	Predicted	Result
Vital Capacity (Litres)	1.95	0.85
Funct. Resid. Cap (Litres)	1.05	0.47
Residual Vol. (Litres)	0.56	0.32
Total Lung Cap (Litres)	2.55	1.17
Max. M. Flow Rate (L/sec)		1.70
Diffusing Cap. (Rest) cc CO ₂ /min. mm. Hg.	17	5.2

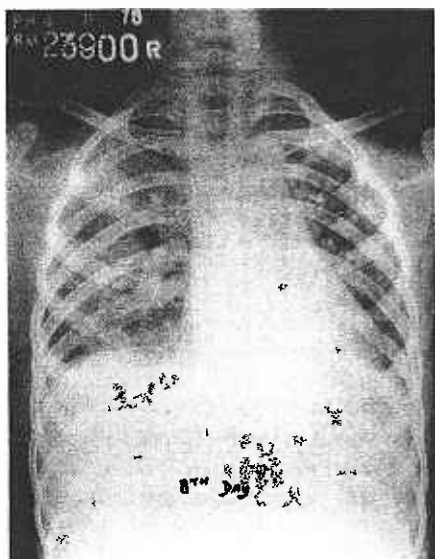


Figure 1. Patchy consolidation in the right lung and left mid zone.

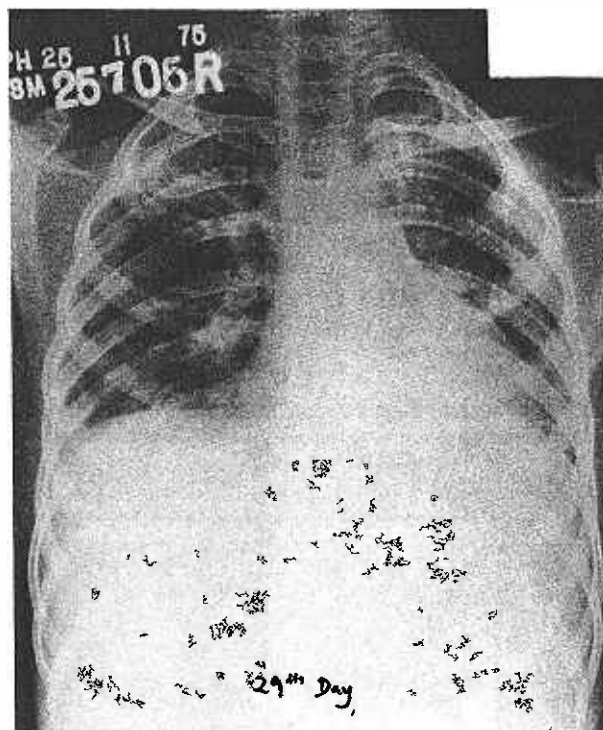


Figure 2. Fibrotic changes were seen in three areas where previously there were consolidation. The fibrosis was rather prominent in the right upper zone.

CASE REPORT II

A 32 year old male took 1 mouthful (10 mls) of Gramoxone by mistake on 30th January 1978. He tried to spit out as much of the weedkiller as he could. The next day, he had a sore throat but only sought medical attention on 2nd February. On admission, he was jaundiced and shallow ulcers were noted over the tongue, the gums and pharynx. The lungs were clinically clear. Serum bilirubin was 3.2 mg%, SGPT 100 IU/L. Alkaline phosphatase was 13.5 KA units. The blood urea was 100 mg%, serum creatinine was 4.7 mg%. Arterial blood gas analysis revealed a pa O₂ of 95 mm Hg, a pa CO₂ of 35 mm Hg. The first chest x-ray was normal. Stomach aspirate and urine were negative for paraquat. He was treated with hydrocortisone injections and over the next four days as the oral lesions improved oral corticosteroids were given. The transaminase rose steadily to 200 units, and was accompanied by a rise in serum bilirubin to 5 Mg%. After 10 days, the transaminase and bilirubin returned to normal. The renal impairment also continued steadily and by the end of the first week, the blood urea was 220% and creatinine clearance was reduced to 25.5 mls/min. Only protein restriction was required to treat the renal insufficiency. From the second week, there was gradual but definite improvement in the renal function. Serial arterial blood gas analysis did not reveal any significant changes in the pa O₂ and pa CO₂. Chest x-ray during the 2nd week showed small bilateral pleural effusion (Fig. 3). A full lung function test done showed that the vital capacity was diminished with relative fall in ventilatory capacity, and the diffusing capacity was slightly decreased, indicative of a restrictive ventilatory pattern:

Determination	Predicted	Result
Vital Capacity (Litres)	3.74	2.33
Funct. Resid. Cap (Litres)	3.11	3.18
Residual Vol. (Litres)	1.63	2.54
Total Lung Cap (Litres)	5.29	4.87
Mixing Efficiency %	64	66
Max. Br. Cap. (L/min)	117	85
Max. M. Flow Rate (L/sec)	4.12	4.72
Diffusing Cap. (Rest) cc CO ₂ /min./mm. Hg	20.8	15.0

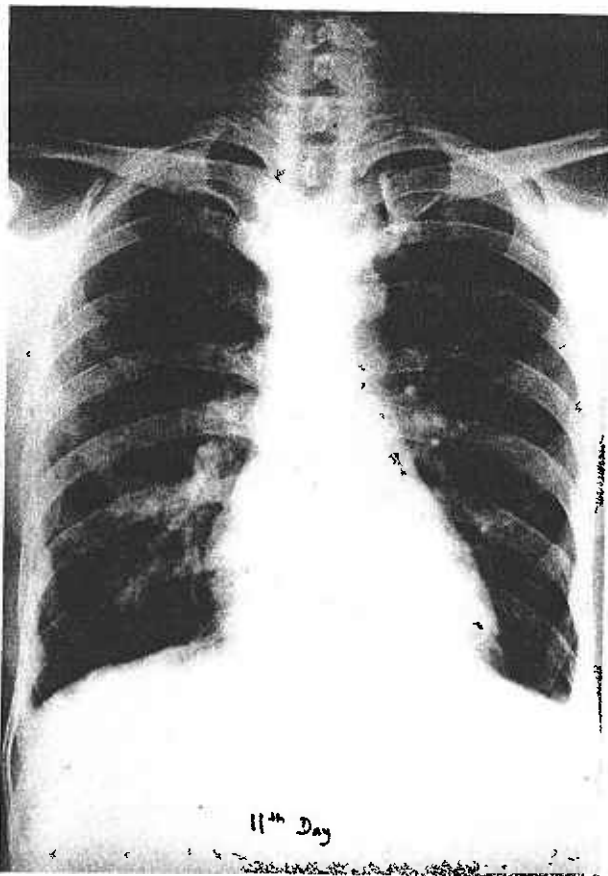


Figure 3. Day 11 after ingestion of paraquat. Note the blunting of both costo-phrenic angles indicating the presence of some pleural fluid.

CASE REPORT III

A 56 year old male took about 20 mls of Gramoxone mixed with beer in an attempt to commit suicide. About eight hours after ingestion of the weedkiller, a burning sensation in the throat prompted him to seek medical advice. On admission, the pharynx was injected; no ulcers were seen, blood pressure was 130/80 mm Hg, pulse rate was 72/min and the lungs were clear. The blood urea, conventional liver function tests, arterial blood gas analysis and chest x-ray were normal on admission (Fig. 4). A qualitative test for paraquat using sodiumdithionite showed the urine to contain paraquat. After gastric lavage, he was given betonite suspension and magnesium sulphate orally. Forced diuresis was started and continued for thirty-six hours. Neither steroids nor cytotoxics were used. Two days later, ulcers were noted in the mouth and pharynx and these healed by the end of the first week. The liver function remained normal throughout the hospital stay. The blood urea began to rise on the third day and by the seventh day it was 50 mg% and serum creatinine was 2.6mg%. During the second week, it returned to normal without any active treatment given. On the sixth day, the patient was noticed to be febrile and dyspnoeic, crepitations were heard over both lung bases. Chest x-ray at that time showed patchy consolidation in the right lower zone with streaky markings in the right middle zone and left lower zone (Fig. 5). By then, the arterial oxygen tension had dropped to 53 mm Hg with a $pa\ CO_2$ of 35 mm Hg. The patient was treated with antibiotics and was on ambient air. The oxygen tension remained between 50 — 60 mm Hg without oxygen therapy. Serial chest x-rays showed extensive confluent opacities in both lungs predominantly in the mid and lower zones. (Fig. 6). A right pleural effusion developed by the eighth week. (Fig. 7). Over the next two months, the effusion resolved spontaneously and pulmonary fibrosis became established in the mid and lower zones (Fig. 8). Both diaphragmatic leaves were elevated as a result of the fibrosis. Lung function test showed a restrictive ventilatory pattern:

Determination	Predicted	Result
Vital Capacity (Litres)	3.36	1.44
Funct. Resid. Cap (Litres)	3.18	2.18
Residual Vol. (Litres)	2.17	1.41
Total Lung Cap (Litres)	5.29	2.85
FEV ₁ (Litres)	2.76	1.48
Max. M. Flow Rate (L/sec)	3.12	2.76
Diffusing Cap (Rest) cc CO ₂ /min./mm. Hg	14.3	7.03

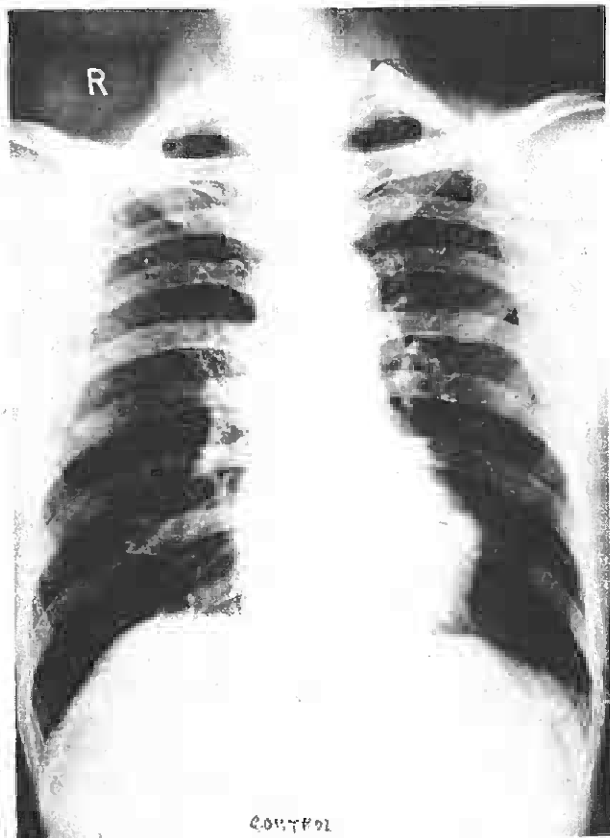


Figure 4. Control — taken before changes were seen. Film was essentially normal.

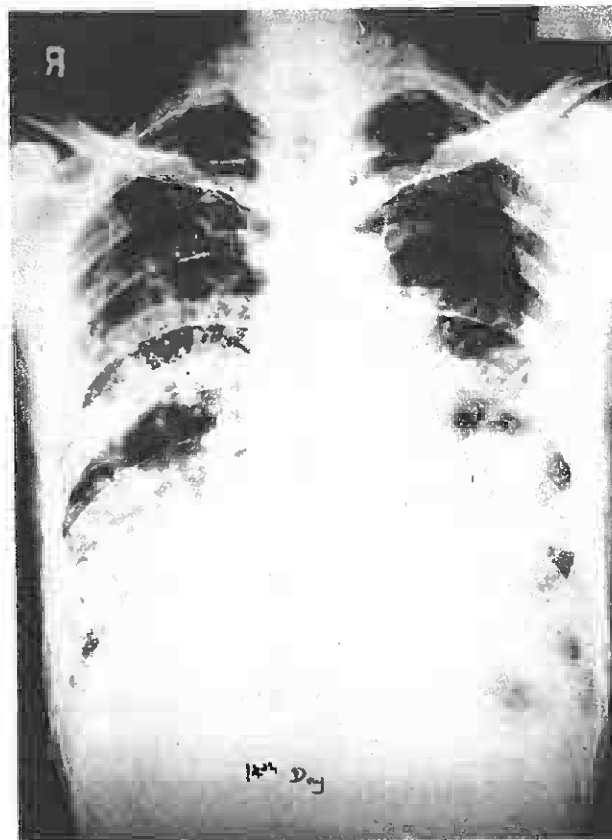


Figure 6. 14th day: The consolidation became worse with confluence of some areas. Some effusion was suspected in the right costo-phrenic angle.

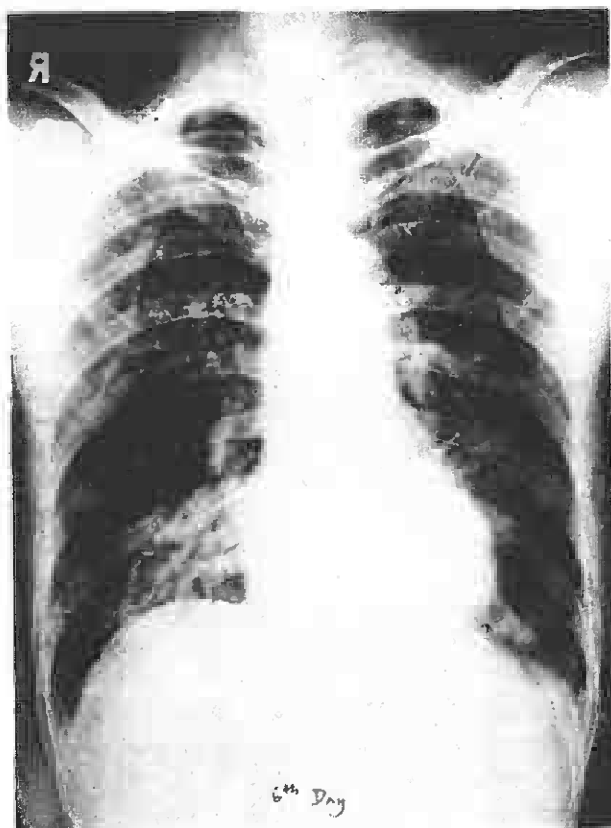


Figure 5. 6th day: As in the first case, patchy consolidation developed within a week. The upper zones appeared to be spared.

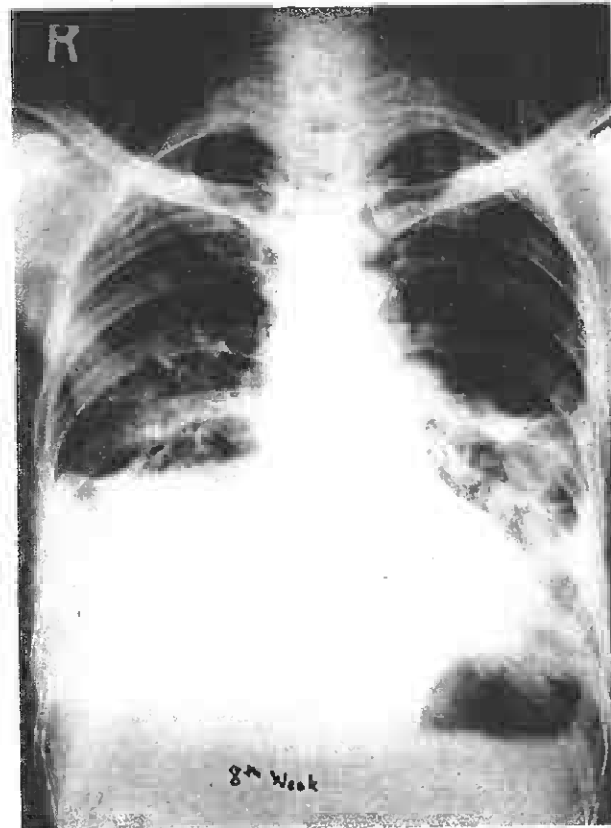


Figure 7. 8th week: The abnormal shadows had become streaky suggesting fibrosis. More fluid had accumulated in the right pleural cavity.

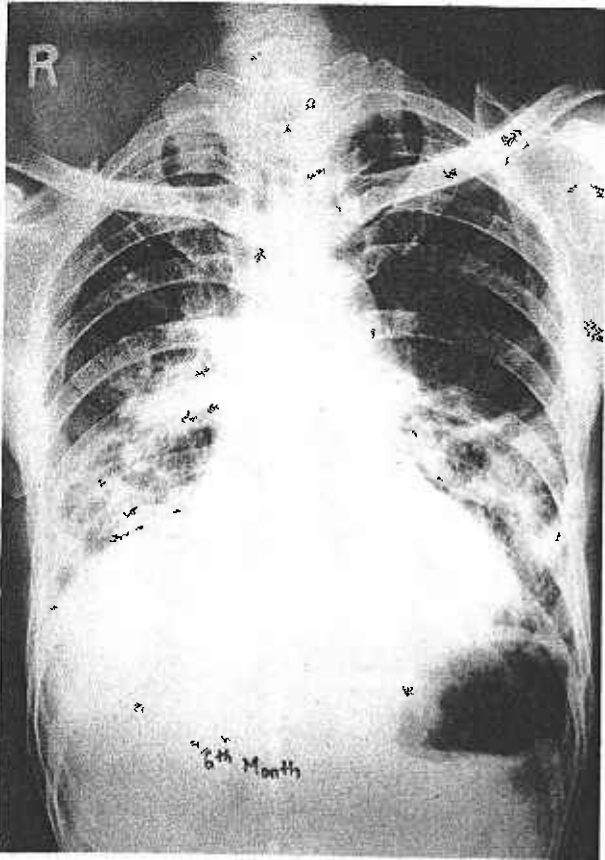


Figure 8. 6th month: The fibrosis was established. Note also the pleural thickening in the right lower zone.

DISCUSSION

Paraquat (1,1, dimethyl 4,4 bipyridilium) is a para substituted quaternary bipyridyl cation. It is available as dichloride or dimethyl salts, both of which are water soluble. In Singapore, it is available as a 20% solution in "Gramoxone" and a 2.5% solution in "Weedol". Both products are readily available. Paraquat exerts its herbicidal activity by interfering with the electron transfer system and thereby inhibits the reduction of NADP to NADPH during photosynthesis. The superoxide and peroxide ions produced in the process destroy membranes by polymerizing their unsaturated lipid components. In man, most poisonings have occurred as a result of accidental or deliberate ingestion. The careless storage of the liquid in empty beer, soft drink bottles have resulted in many unfortunate accidents as the liquid is odorless and has a reddish brown colour which resembles root beer or coca-cola. One unfortunate victim sprinkled paraquat on French fries thinking it was vinegar. He paid for the mistake with his life 25 days later. Dermal absorption of paraquat is usually poor but systemic toxicity following it has been reported. Inhalation of the spray has apparently never been associated with human fatality. Although transient hepatic, renal, myocardial and adrenal damage can occur, the chief cause of death is respiratory failure resulting from pulmonary oedema, haemorrhage or fibrosis.

In the period 1975 — 1979 there were altogether 19 cases of paraquat (Gramoxone) poisoning seen at the Medical Unit, Toa Payoh Hospital. Of these only three patients survived. The mortality rate is 84%. Survival after paraquat poisoning was first reported in 1968 in Europe. By 1971, with more than 60 survivors, it was estimated that the mortality rate from paraquat was in the region of 33 — 50%. As these figures include patients who have taken Gramoxone (constituting 20% paraquat) and Weedol (containing 2.5% paraquat), the mortality rate may be diluted by patients who have taken Weedol. In 1979, Proudfoot reported a mortality rate of 78% with Gramoxone alone, a value more in line with our experience.

The outcome of paraquat poisoning depends on the amount ingested and the treatment given. Ten millilitres of Gramoxone is generally considered the minimum lethal dose. With treatment using Fuller's earth, forced diuresis, haemodialysis and charcoal haemoperfusion, survival after ingestion of 50 millilitres or more have been reported. The maximum excretion rate of paraquat via the kidneys that is compatible with life is 1 mg/hr, after the first 8 hours. From the data available from these three case reports, it can be seen that using our present mode of (betonite, forced diuresis, oral magnesium sulphate with treatment or without steroids and immunosuppressants,) the maximal ingested dose compatible with life is 20 ml and the maximal excretion rate via the kidneys in a survivor is 0.92 mg/hr.

Our three patients have been regularly reviewed since discharge. They have shown clinical improvement; their chest x-rays and lung function tests, while still abnormal, have shown considerable return to normal. This would suggest that paraquat-induced pulmonary injury may be partially reversible, an encouraging note to clinicians everywhere.

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