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PARAQUAT POISONINGS - UNITED KINGDOM - 1981

The following is a review of the paraquat poisoning statistics for 1981 in the United Kingdom. We do not anticipate notification of any new cases for this period and so the figures can be regarded as more or less complete.

1. GENERAL STATISTICS

	1978	1979	1980	1981
Total No. of cases (ingestion only)	?	?	121	120
Total No. of fatalities (ingestion only)	42	37	42	48
Total No. of survivors (ingestion only)	56	25	61	65

Initial examination of the above figures suggests that there is an increase in the number of paraquat fatalities since 1979. However consideration of statistics over the last seventeen years (Figure 1) shows that although there was a slight dip in the fatality number in 1976 and 1979, there appears to be little evidence of an increase over the last 6-7 years. The total number of fatalities due to paraquat poisoning remains between 40 and 50 fatalities per annum for this period of time.

2. DETAILED ANALYSIS OF PARAQUAT POISONING (1981) - INGESTION ONLY

2.1 ACCORDING TO INTENT

Outcome	Total	Suicide	Accident	Criminal	Unknown
Fatal	48	43	2	1	2
Non-fatal	65	44	3	1	17
Unknown	7	1	0	0	6

The above figures are consistent with the pattern seen over the last eight or nine years (see Figure 1), in that by far the majority cases (fatal and non-fatal) involve deliberate ingestion of paraquat. Both accidental fatalities involved storage of 'Gramoxone' in unlabelled drinks containers - a beer bottle and a wine bottle. The former case resulted from an old man, who was drunk at the time, mistaking 'Gramoxone' for beer, but in the second case there seems to have been a genuine and sober mistake made. The man involved stored the 'Gramoxone' in a wine bottle, placed in the garage with numerous other wine bottles containing home-made wine. In both cases the formulation appeared to be old and did not contain emetic.

Of the criminal cases, one was an attempted murder by a wife on her husband. Although she admitted adding 'Weedol' to his curry, she was acquitted on the grounds that she was not definitely trying to kill him. The other case is a much more sinister event and court proceedings are in progress. It is possible that member(s) of ICI CTL will be called as witnesses (as analytical experts).

In addition to the above, there were two larger scale criminal offences involving paraquat. The first involved Safeways food store chain being blackmailed by a person who admitted spiking certain foodstuffs (jars of pickles, sauce and tomato juice) with paraquat (probably 'Weedol'). No harm resulted directly from the incident, although the publicity given was substantial. The second case involved the impregnation of carrots with paraquat, which were then released onto the Dublin vegetable market. The incident was a protest against importation of foreign vegetables into Eire. As with the first case, no harm resulted, but a considerable amount of media scare-mongering ensued, which resulted in withdrawal of all vegetable produce from the market.

These latter two incidents are unique in the history of paraquat poisoning, although there have been 12 murders/attempted murders in the United Kingdom, since paraquat's introduction into the market.

2.2 ACCORDING TO AGE

Outcome	Adult	Child (<14 yrs)
Fatal	47	1 (suicide)
Non-fatal	64	1
Unknown	7	0

2.3 ACCORDING TO PRODUCT INVOLVED

	Total	Fatal	Non-fatal	Unknown	Mortality	
'Weedol'	47	11	33	3	25% (7%)	22%(10%)
'Pathclear'	16	2	13	1	13.3%(22%)	
'Gramoxone'	40	31	8	1	79.5%(80%)	
'Dextrone'	2	1	1	0	-	
'Dexuron'	1	0	1	0	-	
'Gramonol'	1	0	1	0	-	

1980 figures in brackets.

As can be seen from the above, there has been little change in overall mortality on a product by product basis compared with 1980, particularly in the case of 'Gramoxone'. Also it appears that approximately the same percentage of cases involved the use of 'Gramoxone', as was the situation in 1980. Where information is available, the majority of 'Gramoxone' cases have farming connections and therefore these poisonings are likely to be related to the legitimate use of the product. This supports the belief that the Poisons Regulations are being as effective as they can be, but with determined suicides there is little one can do to prevent them occurring.

2.4 MONTHLY VARIATION OF PARAQUAT POISONINGS

Figure 2 illustrates the montly variation of paraquat poisonings in the United Kingdom, over the last two years. Although there tends to be relatively more total poisonings with the products in the summer months, when each product is considered separately, no such seasonal pattern emerges. This may not be expected with 'Weedol' or 'Pathclear' as they are available all year round, but the availability/use of 'Gramoxone' is greatest in August to October.

This again suggests that the number of paraquat poisoning cases is not primarily related to the availability of product; other factors such as publicity and socio-economic pressures could well have a significant influence.

3. EMETIC CASES

As for 1980, this part of the follow-up has proved to be the most difficult to achieve successfully. The reasons for this have already been explained in a previous communication (TBH to J T Braunholtz - 25.6.81).

Of the 120 cases followed-up in 1981, the presence or absence of emetic involvement was confirmed in 53 (44.2%) of cases. It was present in 39 (33%) of cases and absent in 14 (11.2%) of cases. The recovery of this type of information is by no means perfect, but is an improvement over 1980 figures, which were:- present - 23%: absent - 15.7% and present/absent - 38.7%.

3.1 EFFICACY OF THE EMETIC

Some of this information has already been communicated in an interim report (10.3.82), but the following gives a more complete picture of the effect of emetic addition to paraquat formulations.

3.1.1 PP796 As An Emetic

The data so far collected leads to the definite conclusion that PP796 added to paraquat formulations causes spontaneous vomiting if that formulation is swallowed. Keir Howard in a review of 68 cases of paraquat poisoning (non-emetic)[1] in the United Kingdom estimated that just over 50% of patients vomit spontaneously. I have reviewed the raw data of this study, but selected out only those patients swallowing more than 1.5 sachets 'Weedol'/'Pathclear' or 10 ml 'Gramoxone', ie the amount that would contain an emetic dose with PP796 present. Out of 45 patients selected in this

way, 35 (67%) of them vomited spontaneously.

Studying 45 cases involving emeticised formulation, and using the same selection criteria, 43 of these patients (95%) vomited spontaneously. Most of these cases vomited within half an hour of ingestion.

3.1.2 Delay In Gastric Emptying And PP796

There was good evidence produced from animal data, to show that

i) the main site of paraquat absorption was beyond the stomach[2,3,4]
and
ii) PP796 had the ability to delay emptying of the stomach and thus slow down the rate at which paraquat was absorbed into the blood stream[5,6]

If the same were true for man and paraquat was swallowed in the presence of P796, it would take longer for the paraquat to enter the blood stream and effectively buy more time for treatment. It is not possible to say from paraquat poisoning data in humans whether paraquat is absorbed from man's stomach or whether PP796 delays gastric emptying. Some idea can be gained, however, of the success of the overall objective, ie increasing time available for treatment, by studying the time from ingestion to the peak plasma concentration in 'emetic' cases.

In cases involving non-emeticised paraquat formulation, and where early blood samples have been taken, it has been estimated that the peak plasma paraquat concentration occurs certainly between 0 and 6 hours from the time of ingestion and possibly between 0 and 3 hours. The table below summarises six cases of paraquat poisoning involving emeticised product and estimates the time to peak plasma concentration.

Identity	Sex	Formulation	Dose (Approx)	Estimated time of peak plasma concentration	Outcome
M.B.	M	'Dextrone'	70 ml	0-7 hours	Survived
M.M.	F	'Gramoxone'	20 ml	0-5 hours	Died
D.O.	M	'Weedol'	1 sachet	0-6 hours	?
J.I.	M	'Weedol'	<1 sachet	0-6.5 hours	Survived
M	M	'Weedol'	1 sachet	0-8 hours	Survived
E.H.	F	'Weedol'	4 sachets	0-3.5 hours	Died

Of the above, the last case provides perhaps the best example that the addition of emetic to paraquat formulations, does not affect the time to peak plasma concentration. It is possible that the presence of surfactants in paraquat formulations is affecting this situation, but for the present there is no evidence to support the claim that PP796 will delay gastric emptying in man and thereby reduce the rate of paraquat uptake into the

body. Further work is being considered at CTL to investigate possible interaction of surfactants and the emetic.

3.3 OVERALL EFFECTIVENESS OF PP796 ADDITION TO PARAQUAT FORMULATIONS IN REDUCING MORTALITY

The claims on the emetic's effectiveness, which were made prior to the poisoning follow-up programme, were based on animal toxicology data. In summary a 3-5-fold increase in the potentially lethal dose was predicted from the studies. This would mean that accidental death from swallowing a paraquat formulation should be preventable with the emetic's presence and in addition some suicide cases may be helped.

The following table summarises mortality data on a product by product basis, in the United Kingdom for the period 1970 to 1977 (incl), ie it involves non-emeticised products.

1970-1977 (incl)

	Fatal	Non-fatal	% Mortality	
'Weedol'	38	131	22.5	]21.5
'Pathclear'	1	11	8.3	]
'Gramoxone'	119	18	87	]84
'Dextrone'	4	5	44	]
'Dexuron'	1	0	(100)	
'Gramonol'	1	0	(100)	
'Preeglone'	4	0	(100)	

The above figures agree well with Dr Howard's review of 68 cases, in which he states that mortality from ingestion of solid paraquat formulations is 18.5% and for liquids 87.8%.

Since the introduction of the emetic, the picture has altered very little as can be seen from the table below. This reviews mortality statistics for paraquat formulations from 1978 until the present time.

1978-182 (incl)

	Fatal	Non-fatal	Mortality (%)	
'Weedol'	33	126	21	]21
'Pathclear'	7	25	22	]
'Gramoxone'	95	24	80	]79
'Dextrone'	4	2	67	]
'Dexuron'	1	1	(50)	
'Gramonol'	0	2	(0)	
'Cleansweep'	1	0	(100)	

Admittedly studying the statistics in the above fashion, does not take into account the fact that a substantial proportion of cases still involve non-emeticised product despite the introduction of emetic into the United Kingdom market in mid-1977. In 1980, we estimated that 23% of cases involved emeticised product and 15.8% non-emeticised product. In 1981 the number of 'emeticised' cases had increased to 33% of cases, whereas 'non-emeticised' cases have reduced to 11.2%. To reduce this variable, the following table considers only those cases, which involve emeticised product.

'Emetic' Cases

	Fatal	Non-fatal	% Mortality	
'Weedol'	6	24	20	]21
'Pathclear'	3	10	23	]
'Gramoxone'	15	6	71.5	]68
'Dextrone'	0	1	(0)	]

There appears to be very little evidence to show that the addition of emetic to paraquat formulations has altered the mortality statistics overall. This must, of course, be considered in the context of the fact that the population studied involves predominantly suicides (see section 2.1). It is unfortunate that both accidental fatalities in 1981 involved non-emeticised product, thus we are not able to comment from the above or from those two cases on the effectiveness of PP796 in saving life in cases of accidental ingestion.

3.4 EFFECTIVENESS OF PP796 ADDITION TO PARAQUAT FORMULATIONS IN REDUCING ORAL TOXICITY IN HUMANS

The approximate lethal oral dose in humans for paraquat has often been quoted as being between 2 and 3 g of ion (equivalent to 10-15 ml non-emeticised 'Gramoxone' or 1.5 sachets non-emeticised 'Weedol'/'Pathclear'). The following table, compiled of cases from 1970 to 1977, confirms that statement.

Dose reported to have been swallowed	Fatal	Non-fatal	Mortality %
<2 g pq ion	10	93	9.4
2-5 g pq ion	29	23	56
>5-10 g pq ion	18	2	90
>10 g pq ion	43	0	100

If the same analysis is done for emeticised cases the following is seen:-

Dose reported to have been swallowed	Fatal	Non-fatal	Mortality %
<2 g pq ion	7	26	21
2-5 g pq ion	4	6	40
5-10 g pq ion	9	3	75
>10 g pq ion	16	1	94

No definite conclusions can be drawn from the above, except that there does not seem to be a large shift in the potential lethal dose as a result of the addition of emetic. More cases involving emeticised product need to be studied, especially in the dose range 2-10 g paraquat ion.

OVERALL ASSESSMENT OF PARAQUAT POISONING IN THE UNITED KINGDOM

The number of cases of paraquat poisoning in the United Kingdom for 1981 was recorded at 120, out of which 48 were fatal and 65 non-fatal. Over the past 6 years, the number of fatal paraquat poisonings has remained relatively constant and as has been the case over the last eight years most poisonings (fatal and non-fatal) have been associated with suicidal intent. This total of fatal poisonings, as was the case in 1980, represents 1% of the total number of suicidal deaths and 2.5% of suicidal deaths due to chemicals. The number of accidental fatalities (2 in 1981) represents a very low percentage (0.3%) of all accidental fatalities due to chemicals (household, drugs, pesticides etc).

Factors influencing the number of paraquat poisonings appear to be many and complex. No seasonal variation appears to be readily identifiable and it is probable that publicity plus socio-economic factors have most influence.

The addition of emetic to paraquat formulations (solid or liquid) has not affected the overall mortality of paraquat poisonings, but insufficient evidence is available to judge whether it has made difference at all. PP796 itself certainly appears to be an effective and reliable emetic, when present in paraquat formulations, but its ability to delay gastric emptying and reduce the rate of paraquat absorption into the blood from the gastrointestinal tract, has not been shown to be true for man as it was in certain animal models. More cases involving emeticised product need to be evaluated, particularly those involving an ingested dose of between 2 and 10 g paraquat ion, to show any small difference the addition of emetic may have made.

FUTURE PARAQUAT FOLLOW-UP

Miss Amanda Bramley (Poisons Information Officer) has now completed her 2-year contract and has effectively left the Poisons Unit. ICI PPD have negotiated a new 1-year contract with the Poisons Unit starting 1 July 1981 and Miss Bramley's replacement is Miss Alexandra Whitehead. I plan to review the situation versus the emetic again in January 1983 to determine how we need to modify paraquat poisoning follow-up for the future. At this stage, it seems unlikely that we need to continue the type of follow-up we have been doing over the last 2 years, but, for political and regulatory reasons, it is advisable to continue some form of follow-up. A possible alternative is to fund half an Information Officer's salary for a less detailed follow-up. This would involve a cost to the Division of £4000-4500 per annum, but would obviously need the agreement of Dr Volans, the Poisons Unit Director.

Bernard Hart.

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U. K. PARAQUAT POISONINGS - FATAL (1964-81)
ANALYSIS ACCORDING TO INTENT

FIG. 1.

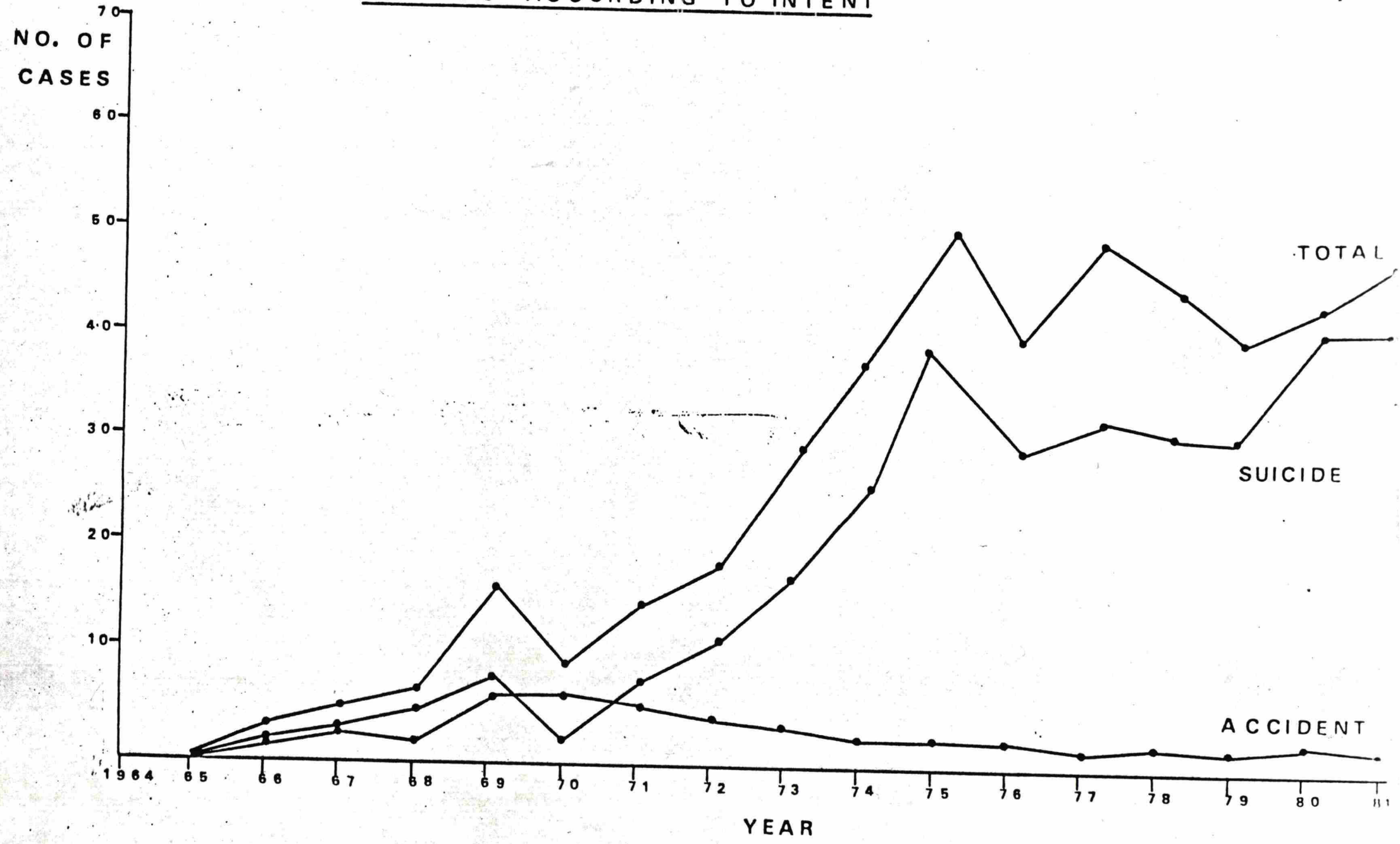

fig.2

MONTHLY VARIATION OF PARAQUAT POISONINGS