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PARAQUAT POISONING IN THE UNITED KINGDOM

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Introduction

Paraquat, a bipyridilium compound, was first put on the U.K. market as a contact herbicide by I.C.I. in 1962 (fig 1). By the late 1960's there were a significant number of fatal paraquat poisonings occurring each year (fig 2).

In the early 1970's a large amount of publicity was given by the press to deaths caused by paraquat poisonings, some of which involved very aggressive journalism (figs 3 & 4). This and the increased use of paraquat in the U.K. at this time, were probably significant factors in the number of deaths due to deliberate ingestion of paraquat (fig 5). The number of accidental deaths remained low, at about one or two a year.

Regulations following from the Poisons Act of 1972 stated that liquid formulations of paraquat (greater than 5% of paraquat ion, weight to volume) should only be used by professionals (that is, farmers, nursery gardeners and so on). This referred to the liquid concentrates such as Gramoxone and Dextrone. Granular formulations containing less than 5% of paraquat ion weight to volume, such as Weedol and Pathclear, were exempt from these regulations and could be used in domestic gardens.

In 1974, in response to the increasing number of poisoning incidents, I.C.I. published a booklet entitled "The Treatment of Paraquat Poisoning" (fig 6). This outlined the toxic effects of the herbicide, and advocated the use of Fuller's Earth, followed by haemodialysis or charcoal haemoperfusion, for the treatment of paraquat poisoning (fig 7). The booklet distribution was followed by the dispatch of Fuller's Earth, the mainstay of treatment, to hospitals throughout the United Kingdom. One year later, a stenching

agent was added to liquid formulations of paraquat in an attempt to prevent the small number of accidental poisonings occurring each year. Subsequently in 1977 an emetic substance was added to paraquat formulations (solid and liquid) in an attempt to reduce the acute toxicity of those formulations, by inducing vomiting before a potentially lethal dose could be absorbed.

Present Study

a) Aims

In 1980 a survey of paraquat poisoning in the U.K. was initiated jointly by the National Poisons Information Service at Guy's Hospital, London, and I.C.I. Plant Protection Division. There were three main aims of this study (fig 8):

- (i) To examine in detail the incidence of paraquat poisoning in the U.K.
- (ii) To evaluate treatment methods, especially charcoal haemoperfusion and any new treatments being used for paraquat poisoning.
- (iii) To evaluate the efficacy of the emetic added to paraquat formulations in reducing paraquat mortality.

b) Methods

Information about cases of paraquat poisoning was received from three sources (fig 9):

- (i) The National Poisons Information Service, including the four regional centres at Belfast, Cardiff, Dublin and Edinburgh.
- (ii) I.C.I. Plant Protection Division and Central Toxicology Laboratory.
- (iii) Newspaper articles, via I.C.I. Publicity Departments.

I.C.I. and the NPIS were usually contacted in the first instance by doctors requesting advice on the management of poisoned patients or measurement of plasma paraquat levels. Requests to I.C.I. for replenishment of Fuller's Earth stocks also brought several patients to our attention. In each case a note was made of the caller, the hospital, name of the patient and any symptoms present, and this information was filed at the NPIS in London.

Further information on subsequent symptoms, treatment given, results of laboratory analyses, and outcome for each patient was obtained by contacting doctors by telephone, usually between two and seven days after the poisoning incident, if possible. In some cases, for example those brought to our attention by newspaper articles, several months had elapsed before we contacted the relevant doctors.

Finally, questionnaires were sent to doctors to obtain a complete case history for each patient, including name, age and sex of the patient, amount of formulation of paraquat ingested, whether the formulation contained emetic, symptoms, treatment given, laboratory analyses and outcome (figs 10, 11 & 12).

Presence or absence of the emetic in the paraquat formulation involved had to be confirmed in each case as there are still significant amounts of old formulations (not containing the emetic) in stock. This could be done by:

- i) examination of the container (the presence of the emetic is indicated by a red chevron on the packets of Weedol and Pathclear, and by two black flashes on the Gramoxone label (fig 13).

- ii) analysis of urine samples for the emetic metabolites.
- iii) analysis of the original product for emetic parent compound.

Ideally, confirmation of the presence or absence of the emetic could be obtained by more than one of these methods.

c) Results and Discussion

i) Recovery of information

About 70% of the questionnaires sent out were returned with complete information. For a further 15% of patients, complete or almost complete information was obtained by telephone, leaving 13% about whom incomplete details were obtained, and 2% where hardly any information could be obtained at all (fig 14).

There were two main problem areas in the survey. The first was in estimating the amounts of paraquat taken: doctors could only report what they had been told by patients, and symptoms and laboratory analyses did not always confirm their report.

The second, and major difficulty of the study has been in confirming the presence or absence of the emetic in paraquat formulations. There are several reasons for this. Often the containers are not available for doctors to examine, and so there can be no positive identification of emetic formulations from the label or from analysis of the original product. For a urine analysis to detect the emetic metabolites a sample needs to be taken within 48 hours of ingestion of paraquat; a number of cases were notified after this time period. When urine samples were requested from hospitals they were not always sent, and, if sent, did not always arrive. We were able to confirm either presence or absence of emetic in only 39% of the cases in the survey.

ii) Mortality Statistics

Between the beginning of January 1980 and the end of February 1982, 262 cases of paraquat poisoning were reported. The two main formulations involved were Weedol (47% of cases) and Gramoxone (32%) (fig 15). The majority of patients were adults (94%) (fig 16), and male (76%) (fig 17). 83% of the poisonings were deliberate, 11% were accidental, and for 6% no intent was specified (although for most of the latter deliberate ingestion was implied at the time of the original call) (fig 18). 94 patients died, 143 survived, and for 25 the outcome was unknown (fig 19).

The commonest symptoms reported were spontaneous vomiting (in 55% of patients whose symptoms were specified) - in half of these patients vomiting occurred within half an hour of paraquat ingestion; irritation or ulceration of the fauces (47%); nausea (42%); renal damage (32%) and pulmonary damage (32%) (fig 20).

As would be expected, mortality increased as the reported amount of paraquat ingested increased. The mortality of patients who had ingested 2g to 5g of paraquat ion as Weedol or Pathclear was lower than that of patients who had taken equivalent amounts of the concentrates Gramoxone or Dextrone (figs 21 & 22). The reason for this apparent difference in relative mortalities is unclear. It may be that it is harder for patients to estimate the dose ingested of liquid formulations than for the sacheted solid products. The overall mortality from taking Weedol or Pathclear was 16%, while that from taking Gramoxone or Dextrone was 78%.

When the cases were analysed according to intent (that is, deliberate or accidental ingestion of paraquat) it was found that out of 208 patients about whom these details were known, there were five deaths reported as being accidental in origin (fig 23). All of these patients were adults.

No deaths of children under 12 were reported, either accidental or deliberate.

Monthly variation of paraquat poisonings was also studied (fig 24). It was thought that there may be a seasonal pattern to poisonings with Gramoxone and Dextrone, with peak numbers during the months when these products are most used, that is late August to October. However, no such pattern could be found during the two years of the study. Weedol and Pathclear are used by amateur gardeners most of the year, and no seasonal pattern of poisonings was expected or found with these.

Towards the end of 1981 when it became apparent that there were a large number of poisonings occurring involving Gramoxone, which legally should only be sold to professional users, an effort was made to determine the occupation of patients. The majority of patients taking Gramoxone seemed to be, or to have some connection with legitimate users, such as farmers, farm labourers or garden nursery workers.

iii) Treatment

Early treatment of paraquat poisoning is considered essential, because plasma paraquat concentration may reach a peak relatively quickly from the time of ingestion (certainly within six hours). In this study, this concept appears to be true for those cases involving 'Weedol' or 'Pathclear', but not for those involving 'Gramoxone' or 'Dextrone' (fig 25). As the solid formulations tend to be associated with relatively low doses of paraquat, this observation supports the one made by Dr Keir Howard in a previous meeting of this association, in which he concluded that early treatment is of benefit in cases swallowing between 1g and 6g of paraquat ion.

For several years now, the mainstay of treatment of paraquat poisoning has been the use of gastric lavage, followed by oral administration of Fuller's Earth and a suitable purgative. It is reassuring to see that 69% of the patients considered received Fuller's Earth as a treatment and 51% of patients received gastric lavage (fig 26). Unfortunately, due to the small number of patients not treated with Fuller's Earth and the large number of variables present, such as the time lapse between ingestion and treatment, the amount of paraquat taken and the amount of Fuller's Earth given, it is not possible to determine whether or not either of these methods influence the outcome.

Haemoperfusion through a charcoal column has been used for some time now for the treatment of paraquat poisoning, but has been received with a very much mixed response. In this study, 15% of the patients were haemoperfused. Most cases involved the use of haemoperfusion on one occasion only and for a period of up to 22 hours. The time lapse between ingestion of paraquat and the start of haemoperfusion varied greatly, from about four hours to over sixty hours. All cases were confirmed, by urine and plasma analysis, as involving paraquat. Although the number of patients haemoperfused was relatively small, the figures shown seem to indicate that this method is not associated with lower mortality, and may, in fact, have an adverse effect (fig 27).

During the period of this study only one significant new treatment emerged - the use of ethacrynic acid. This treatment was used by intravenous injection at Ninewells Hospital, Dundee. Although initial success was claimed, further use of the drug in other patients did not succeed. Interest in this form of treatment has now largely subsided.

iv) Emetic

Despite the introduction of an emetic to paraquat formulations on the U.K. market in 1977, old stock not containing the emetic is still being involved in poisonings. Of the 103 cases in the study where emetic was identified as being present or absent, it was present in 62% and absent in 38% (fig 28). Of the 39 of these cases which involved Gramoxone, 20 (51%) were not emetic formulations. Weedol, which has a higher rate of stock turnover, was involved in 45 cases, only 13 (29%) of which were not emetic formulations (fig 29).

Although it is not possible to reach definite conclusions about the effectiveness of the emetic addition in reducing toxicity of paraquat formulations, the evidence clearly shows that this addition has increased the incidence of early spontaneous vomiting following ingestion of a paraquat formulation (fig 30).

Summary

Between January 1980 and January 1982, the number of fatal paraquat poisonings has been between 42 and 46 per annum, and has therefore remained fairly constant over the past six years (fig 2). Also over the last six years the majority of fatal poisonings have been associated with suicidal intent (approximately 95% in the last two years).

Statistics published by the Office of Population Censuses and Surveys show that the total number of deaths from suicide has remained fairly constant over the last decade, as have the number of deaths from suicide

associated with chemical poisonings. The latest figures, published for 1980, show that there were 4,321 deaths from suicide by any method and 4572 deaths from suicide associated with chemical poisoning. Suicidal deaths involving paraquat, therefore account for approximately 1% of all suicidal deaths and 2.5% of suicide deaths involving chemical poisoning. Fatal accidental poisoning with paraquat accounts for about 0.3% of all accidental fatalities involving chemicals.

The majority of patients involved with paraquat poisoning were male and adult. No children were involved in any fatal paraquat incidents. There appears to be no set monthly variation in the number of paraquat poisonings involving either liquid or solid formulations and most of the patients involved with 'Gramoxone' poisoning were reported to have connection with legitimate use of the product.

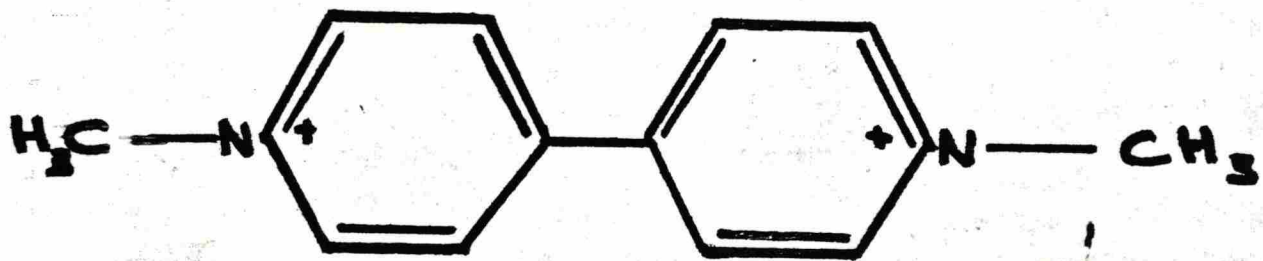
Early treatment of paraquat poisoning (up to 12 to 24 hours) appears to have some benefit when the dose of paraquat ingested is relatively low. We would recommend that although we cannot demonstrate an improvement in mortality with the use of Fuller's Earth or gastric lavage, these measures should be employed at the earliest opportunity, and are unlikely to be effective 24 hours or more after the time of ingestion. The results of using haemoperfusion through a charcoal column do not appear to be encouraging and it is unlikely that this method will be effective if used for single short periods of time. We would recommend that, if this method is to be used, it should be done within 24 hours of ingestion and should involve a different modus operandi.

We have not yet been able to evaluate fully the effectiveness of an emetic formulation in reducing mortality, but addition of the emetic significantly increases the incidence of early spontaneous vomiting. We are planning to continue to follow up paraquat poisoning cases, particularly those involving emeticised formulations. This continued follow-up will also attempt to study more cases involving early treatment with Fuller's Earth, and to evaluate any new treatment methods which may arise.

Finally, it is recommended that measures to prevent accidental paraquat poisoning are maintained and, if possible, improved upon. Widespread publicity of paraquat poisonings should be discouraged, because of its possible stimulus of suicide attempts with the chemical.

Fig. 1

PARAQUAT DICHLORIDE

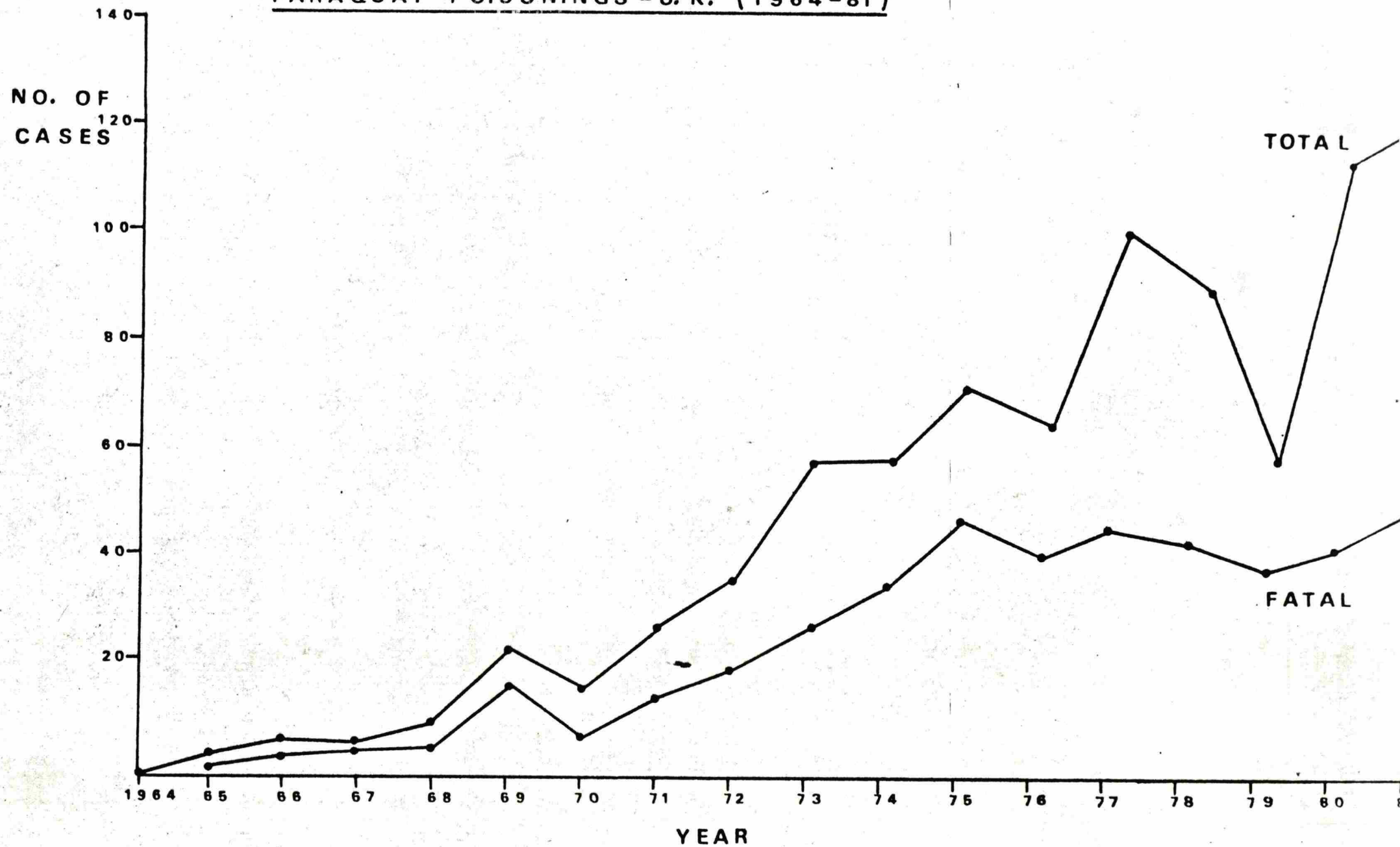


2 Cl⁻

permanent

fig. 2

PARAQUAT POISONINGS - U. K. (1964-81)



Not suicide, says jury

BH 45/74

SHOCK VERDICT IN PARAQUAT CASE

THE death of para-
quat victim Redacted - EU PII
Redacted - EU PII **was still a**
mystery last night.

For all the fatal accident
inquiry jury decided was that
Redacted - EU PII did NOT commit
suicide.

That was the unanimous verdict
of the four women and three men.

At the end of the inquiry Mr
Redacted - EU PII and
Redacted - EU PII

Redacted - EU PII solicitors for
Redacted - EU PII and her
family, made a
formal statement.

They said: "We
point out that the
clear implication of
the verdict was that
while the jury did not
believe the death to
be suicidal, it could
well be accidental."

Bowed

"Even if it were
neither suicide nor
accidental, it was not
proved who might
have been responsi-
ble for his death."

There was no stir at
Kirkcudbright
Sheriff Court as the
foreman of the jury
read out the verdict
after two hours and
50 minutes delibera-
tion.

The foreman said:
Redacted - EU PII died
in Redacted - EU PII

Redacted - EU PII

"a terrible year."

Infirmity on the
Redacted - EU PII as
a result of poisoning
by paraquat which
was swallowed by
him at Redacted - EU PII
Redacted - EU PII on or
about the 12th of
July.

"We believe that
Redacted - EU PII did not
commit suicide.

"And we believe

Redacted - EU PII
... sat impassively.

the manufacturers
are taking all reason-
able precautions
against the misuse of
Gramoxone."

In the front row of
the public benches,
Redacted - EU PII widow.

Redacted - EU PII sat impas-
sively with her son
Redacted - EU PII and her
married daughter.

Redacted - EU PII

CONT/....

Irish Independent -

September 17, 1974 7

Paraquat: Most deadly killer since atom bomb'

A COUNTY physician last night called on the Government to put strict controls on "the most deadly killer since the invention of the atomic bomb"—paraquat.

Earlier, Redacted - EU PII Monaghan County Physician, had tried to raise the subject at the North Eastern Health Board, but the chairman, Senator D. Farrelly, asked him to put the item on the agenda for next month's meeting.

But Redacted - EU PII said that more people could die from paraquat poisoning and he wanted to warn the general public about the effects of using it. He suggested that the manufacturers should insert "a foul-smelling substance" into paraquat so that people would not mistake it for soft drinks.

He said: "I had the sad duty recently in Monaghan of sitting at the bedside of a perfectly healthy man who had taken paraquat. He asked when he was going home and I knew that he was going to his permanent home in about four days and that there was nothing I could do about it."

cc Mr J. S. L. Baker

.. K.D. Hughes

Legal Dept

Pub. Relats.

Mrs J. A. Whitaker (CTA)

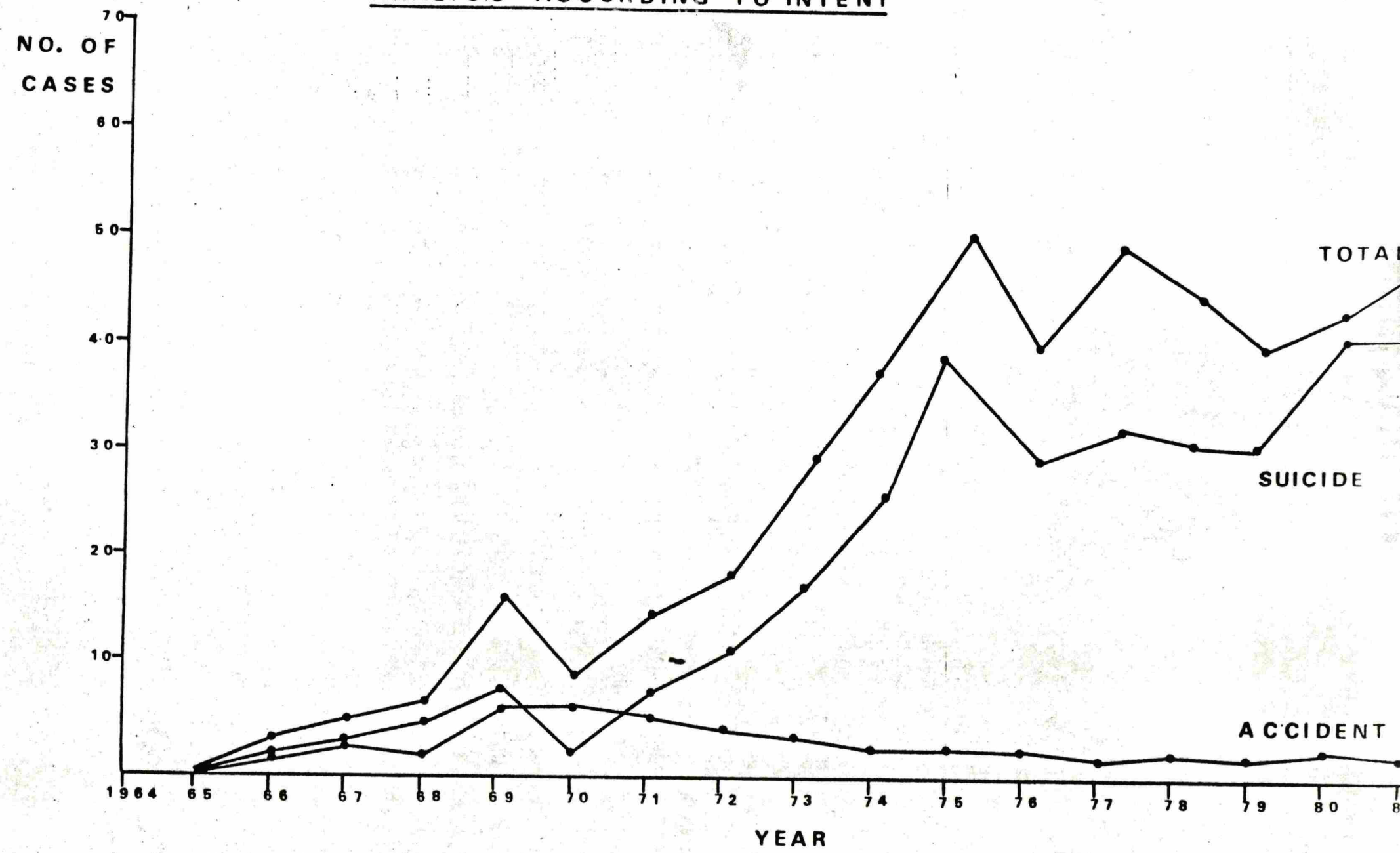
Dr E. G. Schumacher

Mr J. Swabey

paranant store for D Hart

fig. 5

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



119.0

THE TREATMENT PARAQUAT POISONING



1979

This supersedes all previous editions

TREATMENT OF PARAQUAT POISONING FOLLOWING INGESTION

First Aid

Induce vomiting if not already occurring and send patient to nearest hospital immediately.

Hospital Treatment

- 1 Give stomach washout and at the same time test both urine and gastric aspirate for the presence of paraquat (see Appendix 1).
- 2 It is important to purge the gastro-intestinal tract immediately; within four hours if possible. Give up to one litre of 15% Fuller's Earth (Surrey Finest Grade), including 200 ml 20% mannitol in water. Alternatively, sodium or magnesium sulphate can be used as the purgative. Administration should normally be orally but, if this is not tolerated, stomach or duodenal intubation can be used. Continue purgation until the stools are seen to contain adsorbent.
- 3 CONTACT NEAREST POISONS INFORMATION CENTRE FOR FURTHER ADVICE ON TREATMENT.
- 4 Maintain and monitor fluid and electrolyte status on a daily basis.
- 5 Carry out haemodialysis or haemoperfusion (using a charcoal column) to remove paraquat from the plasma (Refs 2, 3). This will only be of use if carried out within 48 hours of ingestion. In some cases renal failure may necessitate the use of haemodialysis at a later stage.
- 6 In the event of respiratory difficulties, delay the use of oxygen as long as possible as it enhances the toxicity of paraquat.
- 7 In severe cases, particularly where shock has supervened, consider additional supportive therapy such as the use of steroids.

AIMS OF U.K. PARAQUAT POISONING SURVEY (fig 8)

- 1 To examine in detail the incidence of paraquat poisoning in the U.K.
- 2 To evaluate treatment methods.
- 3 To evaluate the efficacy of the emetic in reducing paraquat mortality.

Sources of information about paraquat poisonings (fig 9)

- 1 National Poisons Information Service.

London

Belfast

Cardiff

Dublin

Edinburgh

- 2 I.C.I. Plant Protection Division
Central Toxicology Laboratory

- 3 Newspaper articles via I.C.I. Publicity Departments.

PARAQUAT QUESTIONNAIRE

Fig 10

A. PATIENT DETAILS

1. Name
2. Age
3. Sex
4. Hospital No.
5. Name of Doctor
6. Hospital

B. PRODUCT INGESTED

1. Formulation

- Liquid: Gramoxone
Dextrone
Other (please state)
- Solid: Weedol
Patholear
Other (please state)

2. Amount ingested
3. Time and date of ingestion
4. Time and date of admission
5. Ingestion

Accidental

☐

Suicidal

☐

Other

☐

6. Did product contain emetic? YES/NO

7. If yes, how was this ascertained

- a) from original container
- b) from gastric aspirate analysis
- c) from urine analysis

SIGNS AND SYMPTOMS

	YES	NO	TIME AFTER INGESTION
Irritation/ulceration of fauces	<input type="checkbox"/>	<input type="checkbox"/>
Epigastric pain	<input type="checkbox"/>	<input type="checkbox"/>
Nausea	<input type="checkbox"/>	<input type="checkbox"/>
Vomiting - spontaneous	<input type="checkbox"/>	<input type="checkbox"/>
" - after treatment	<input type="checkbox"/>	<input type="checkbox"/>
Diarrhoea	<input type="checkbox"/>	<input type="checkbox"/>

Disturbance in:

Time after ingestion & duration

Renal function

Hepatic function

Pulmonary function

D. TREATMENT

	YES	NO	TIME AFTER INGESTION
Gastric lavage	<input type="checkbox"/>	<input type="checkbox"/>
Emetic	<input type="checkbox"/>	<input type="checkbox"/>
Fuller's earth	<input type="checkbox"/>	<input type="checkbox"/>
Haemodialysis	<input type="checkbox"/>	<input type="checkbox"/>
Haemoperfusion	<input type="checkbox"/>	<input type="checkbox"/>
Forced diuresis	<input type="checkbox"/>	<input type="checkbox"/>
Steroids	<input type="checkbox"/>	<input type="checkbox"/>
Other	<input type="checkbox"/>	<input type="checkbox"/>

E. OUTCOME

1. Survival (date of discharge)
2. Fatal (date of death)
3. If fatal - cause of death
4. Is (3) based on clinical judgement? . . . post-mortem result?

F. TOXICOLOGICAL ANALYSIS

	<u>Date & Time</u>	<u>Result</u>
Urine
Gastric aspirate
Serum/plasma

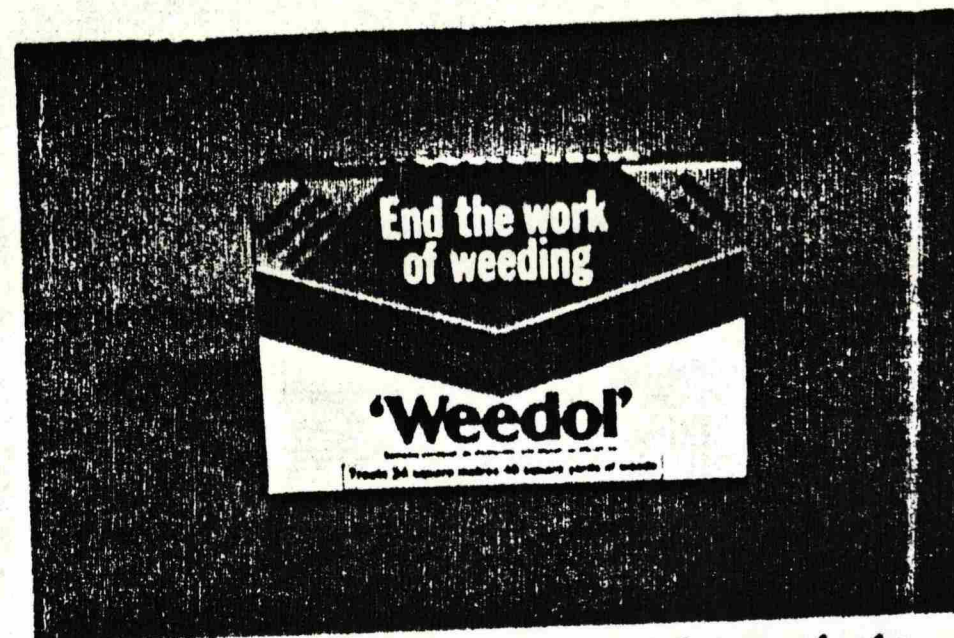
G. COMMENTS

.....
.....
.....
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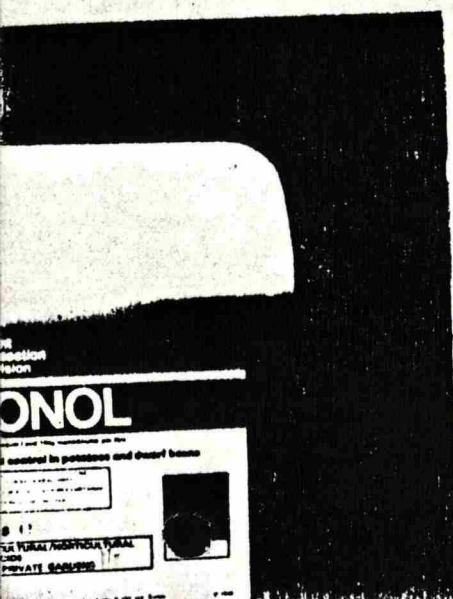
Fig. 13



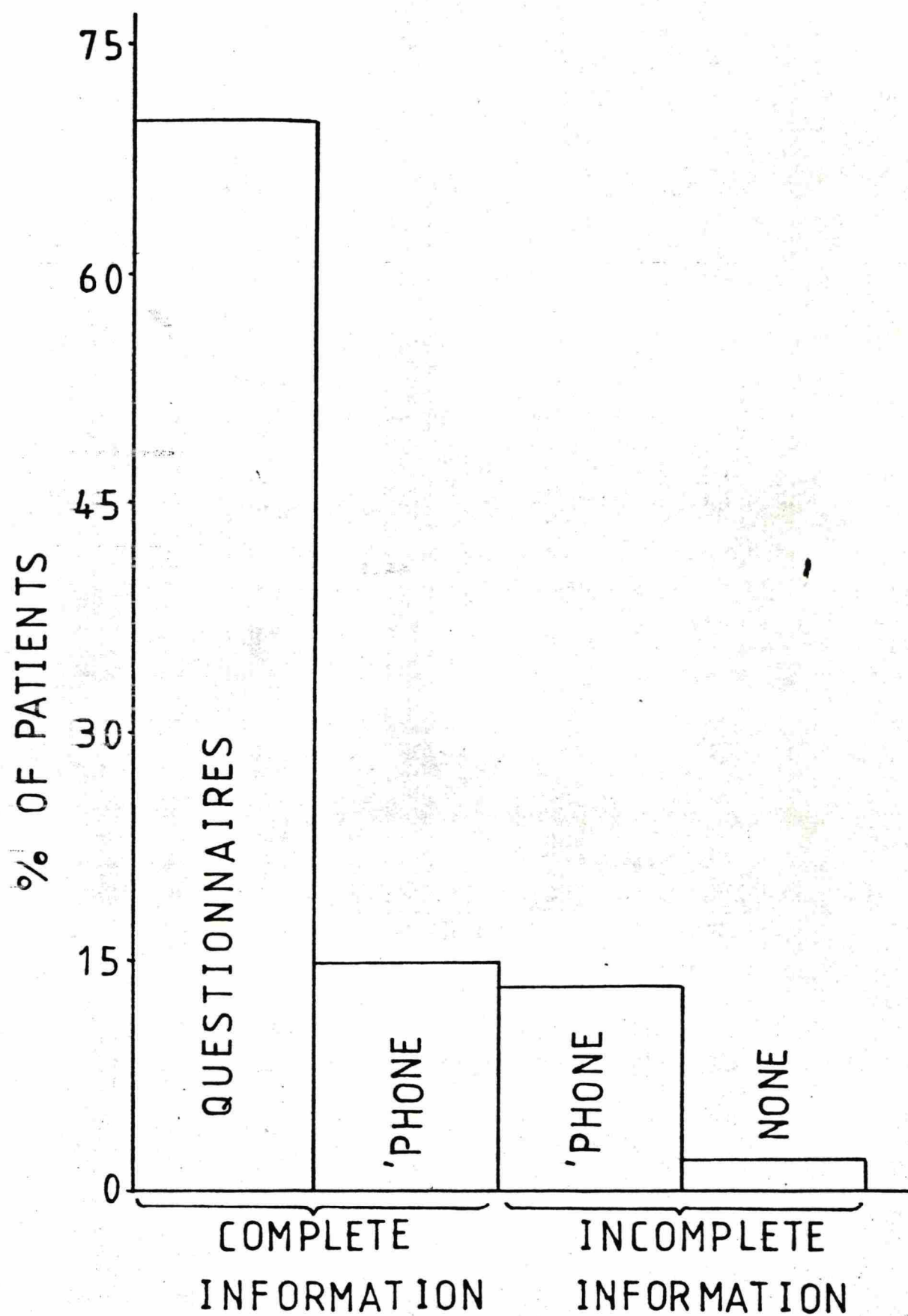
Light brown granules in 56g sachets.
(Paraquat 2.5% w/w: Diquat 2.5% w/w:
Simazine 5% w/w.)



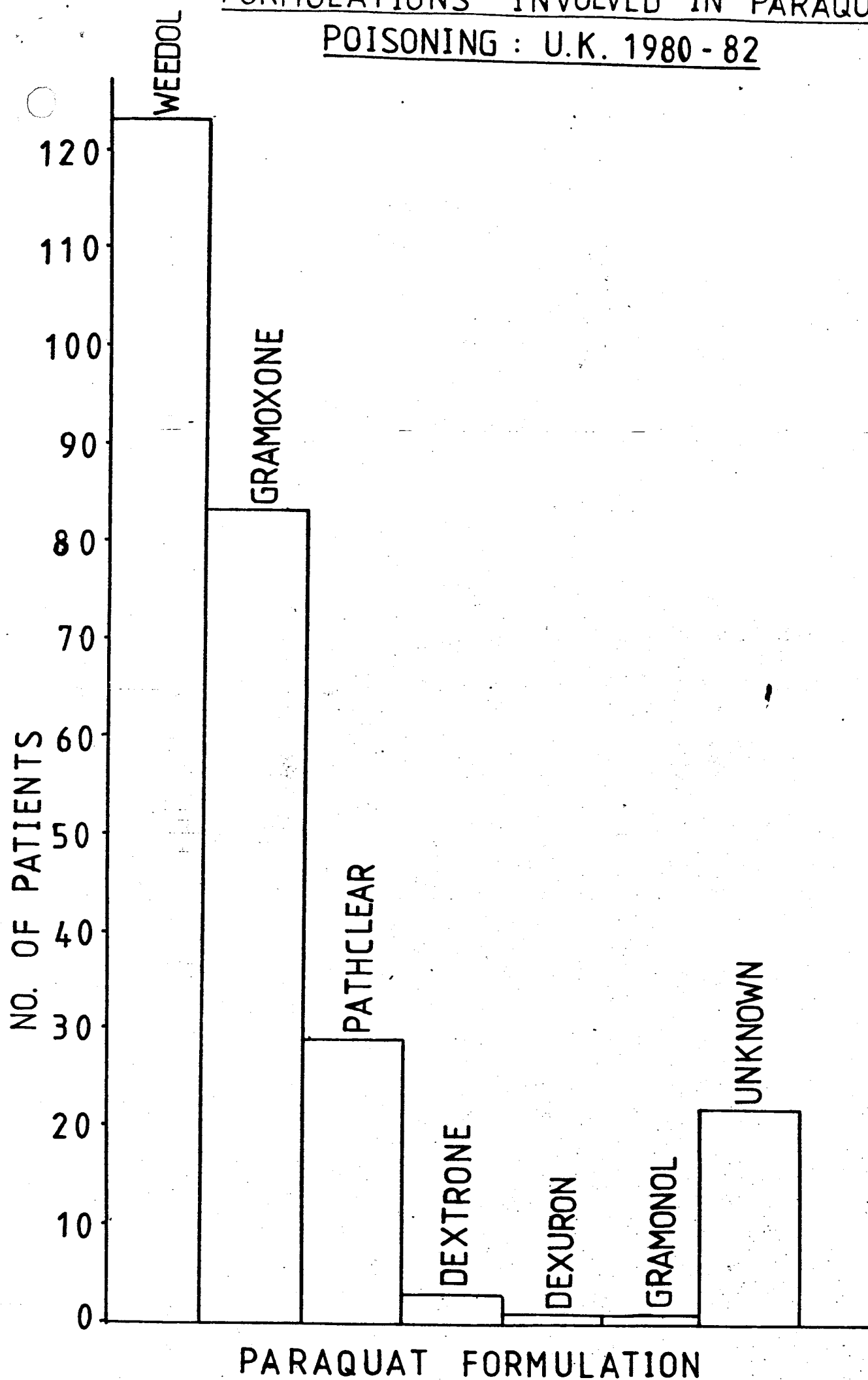
Light brown granules in 56g sachets.
(Paraquat 2.5% w/w: Diquat 2.5% w/w.)



RECOVERY OF INFORMATION

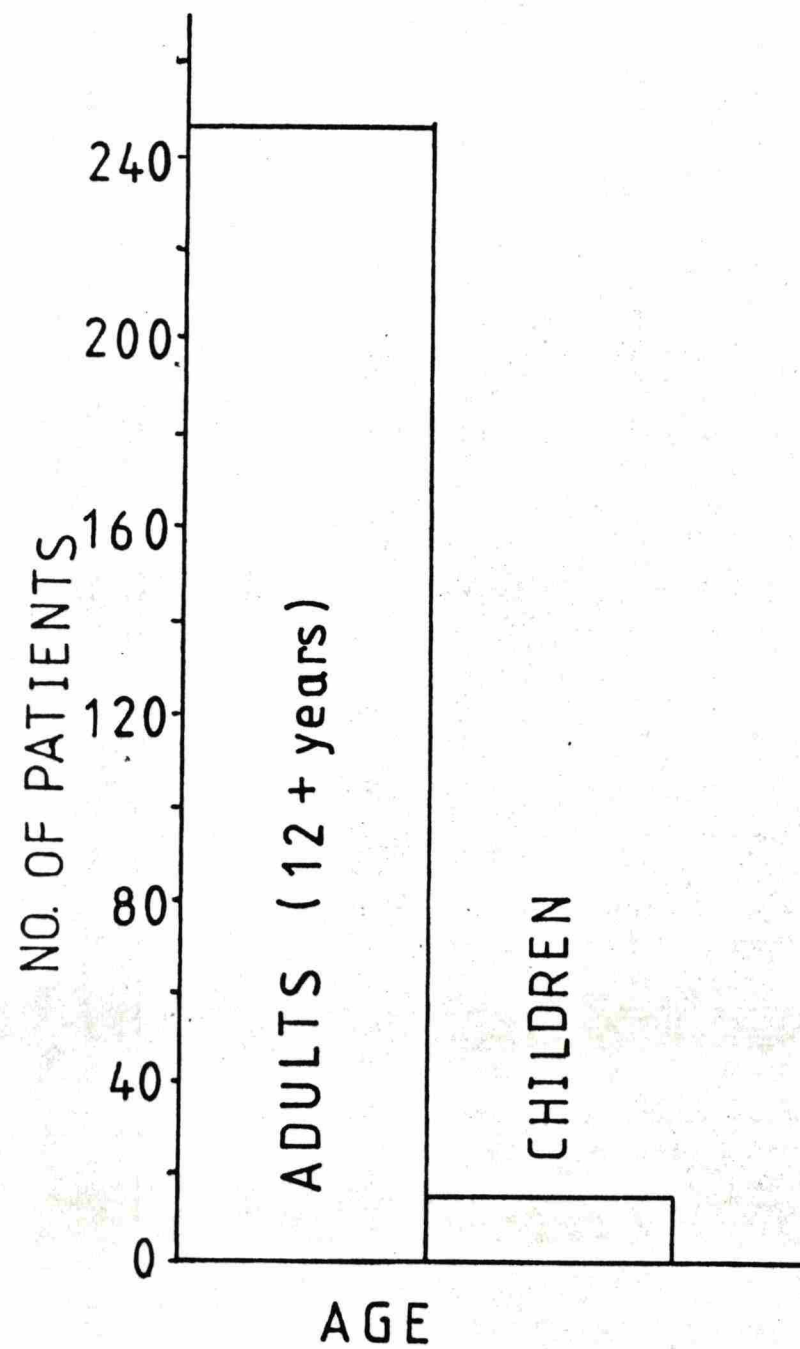


FORMULATIONS INVOLVED IN PARAQUAT POISONING : U.K. 1980 - 82 fig.1



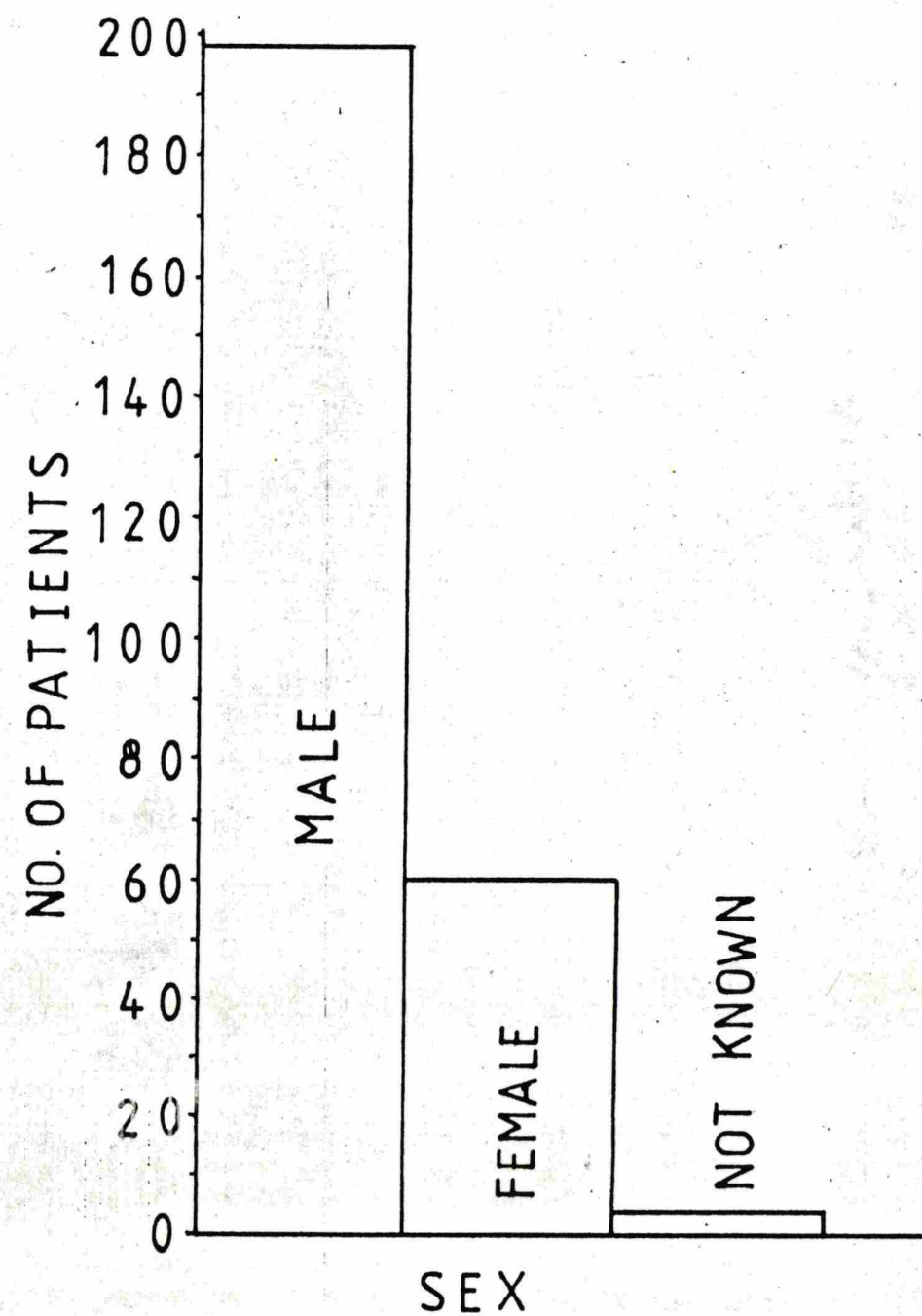
AGE OF PATIENTS

fig.16



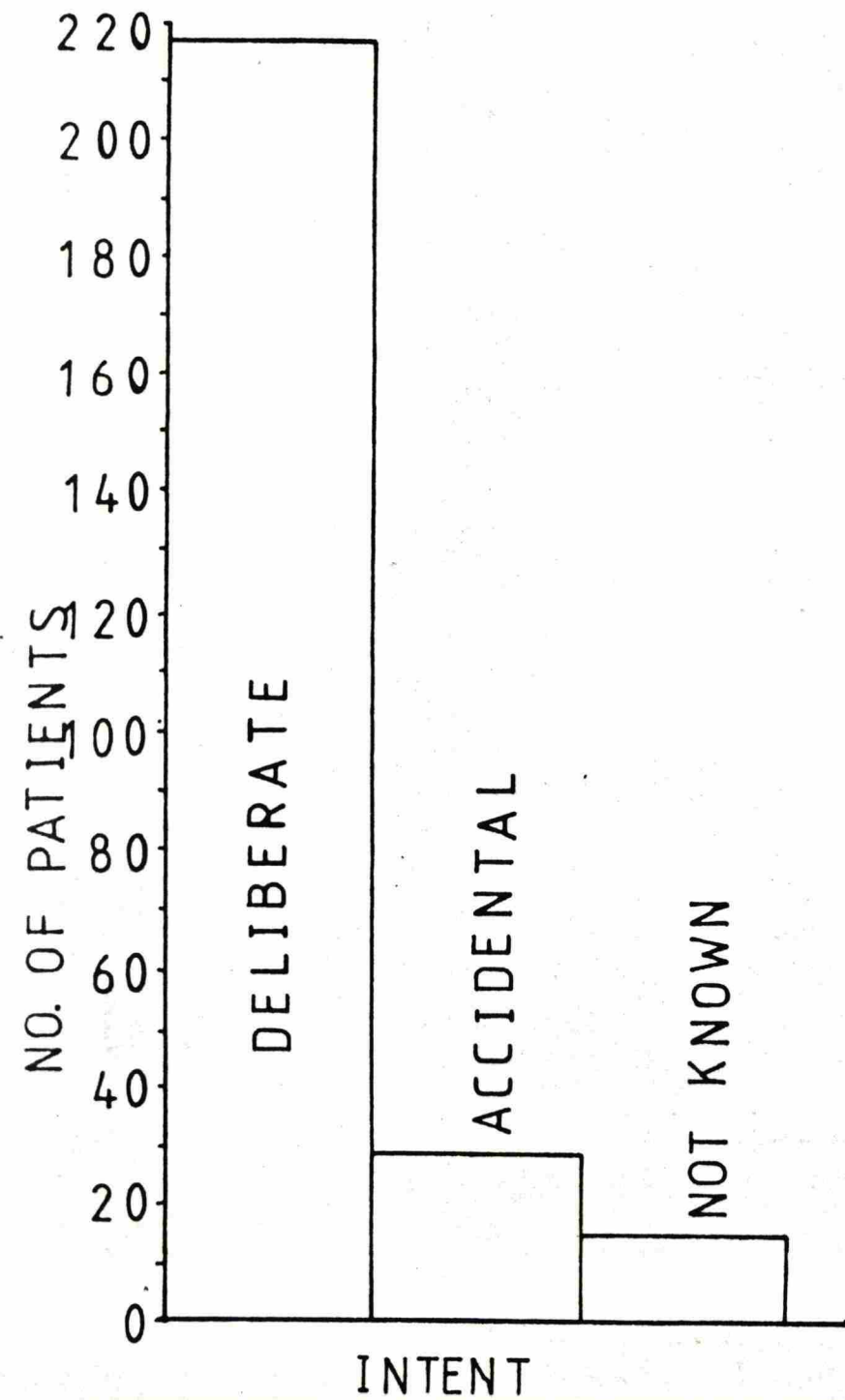
SEX OF PATIENTS

fig.17



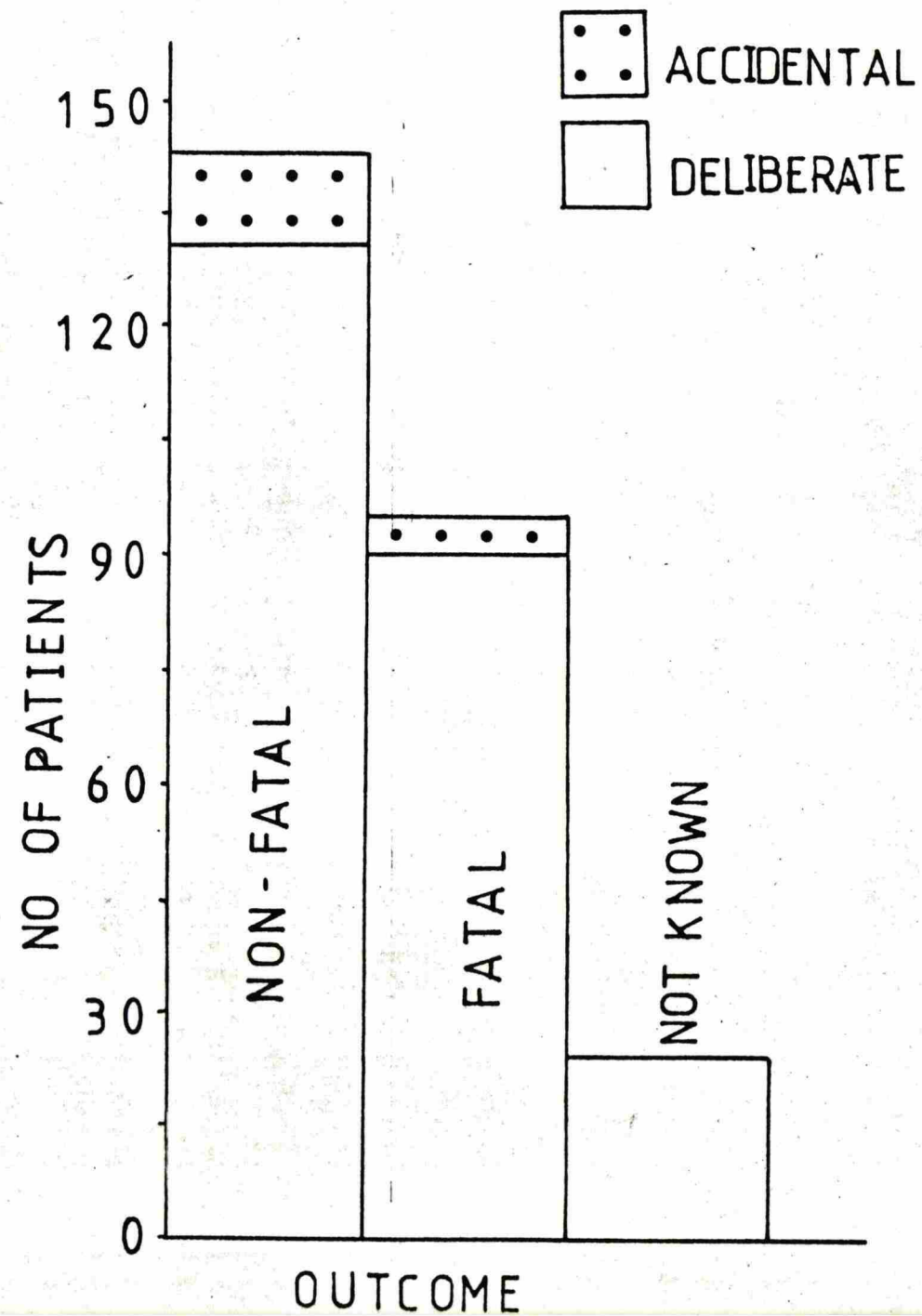
INTENT

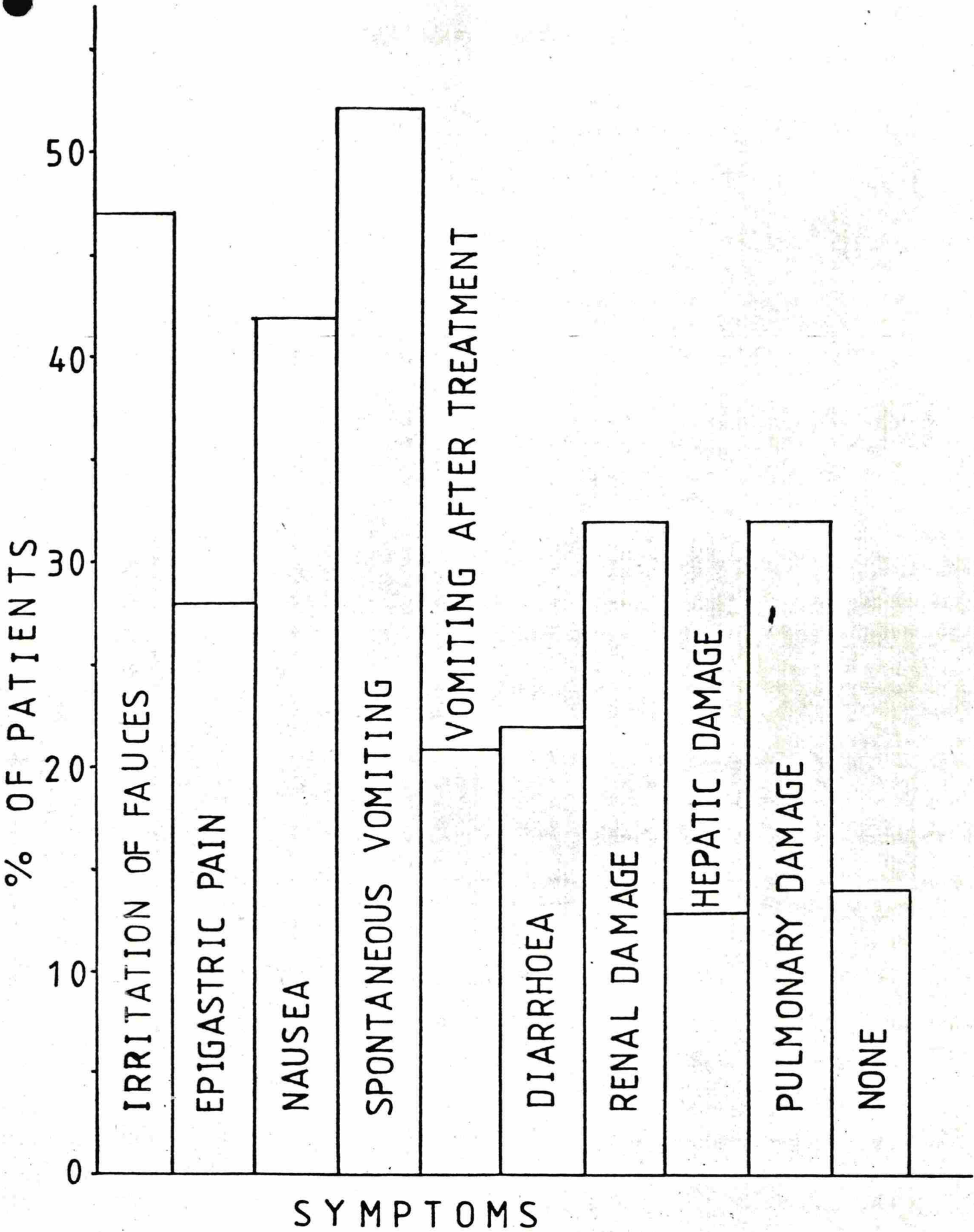
fig.18



OUTCOME

fig.19





AMOUNT OF PARAQUAT TAKEN V. MORTALITY

● EEDOL/PATHCLEAR (Pg. 21.)

Amount (g. p - ion)	Total	Fatal	Non-Fatal	Mortality
< 2	82	12	70	15%
2 - 5	12	1	11	8%
5 - 10	1	1	-	-
10+	1	1	-	-
TOTAL	96	15	81	16%

GRAMOXONE/DEXTRONE (Pg. 22)

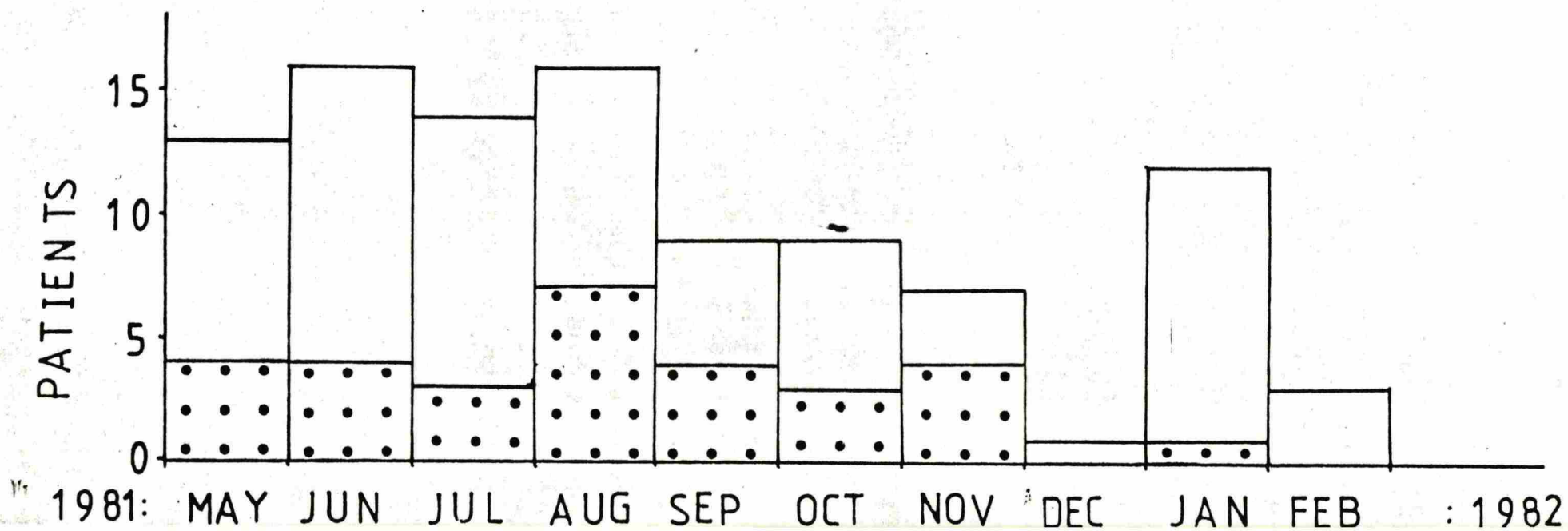
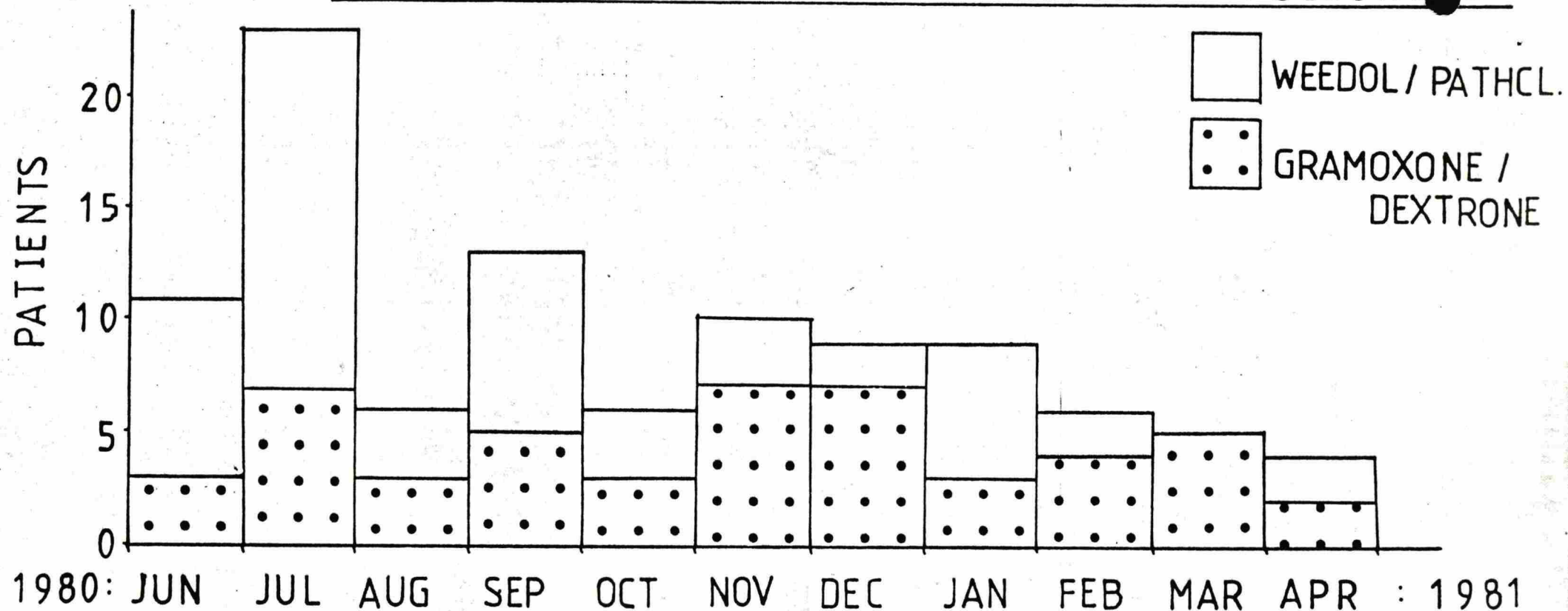
Amount (g. paraquat on)	Total	Fatal	Non-Fatal	Mortality
<.2	5	-	5	-
2 - 5	11	7	4	64%
5 - 10	14	12	2	86%
10 +	28	26	2	93%
TOTAL	58	45	13	78%

OUTCOME VERSUS INTENT AND AGE

OUTCOME	TOTAL	SUICIDE	ACCIDENTS	ADULTS	CHILDREN
FATAL	82	77	5	82	—
NON-FATAL	119	105	14	109	10
NOT KNOWN	7	7	—	7	—
TOTAL	208	189	19	198	10

fig.24

MONTHLY VARIATION OF PARAQUAT POISONINGS



TIME UNTIL TREATMENT VERSUS MORTALITY

Weedol/Pathclear

Time until treatment (hrs)	Fatal	Non-Fatal	Mortality
0 - 6	6	32	16%
6 - 12	2	13	13%
12 - 24	1	3	25%
24 - 48	3	-	100%

Gramoxone/Dextrone

Time until treatment (hrs)	Fatal	Non-Fatal	Mortality
0 - 6	23	8	74%
6 - 12	4	3	57%
12 - 24	2	2	50%
24 - 48	2	1	67%

% OF PATIENTS

60

50

40

30

20

10

0

GASTRIC LAVAGE

EMETIC

FULLER'S EARTH

HAEMODIALYSIS

HAEMOPERFUSION

FORCED DIURESIS

ETHACRYNIC ACID

NONE / SUPPORTIVE ONLY

TREATMENTS

HAEMOPERFUSION / MORTALITY (fig 27)

Patients haemoperfused

Amount (g. paraquat ion)	Total	Fatal	Non-Fatal	Mortality
< 2	11	3	8	73%
2 - 5	5	2	3	60%
5 - 10	6	-	6	100%
10 +	6	1	5	83%
TOTAL	28	6	22	79%

Patients not haemoperfused

Amount (g. paraquat ion)	Total	Fatal	Non-Fatal	Mortality
< 2	67	64	3	5%
2 - 5	15	11	4	27%
5 - 10	9	2	7	78%
10 +	19	2(?)	17	89%
TOTAL	110	79	31	28%

FORMULATIONS TAKEN

fig.28

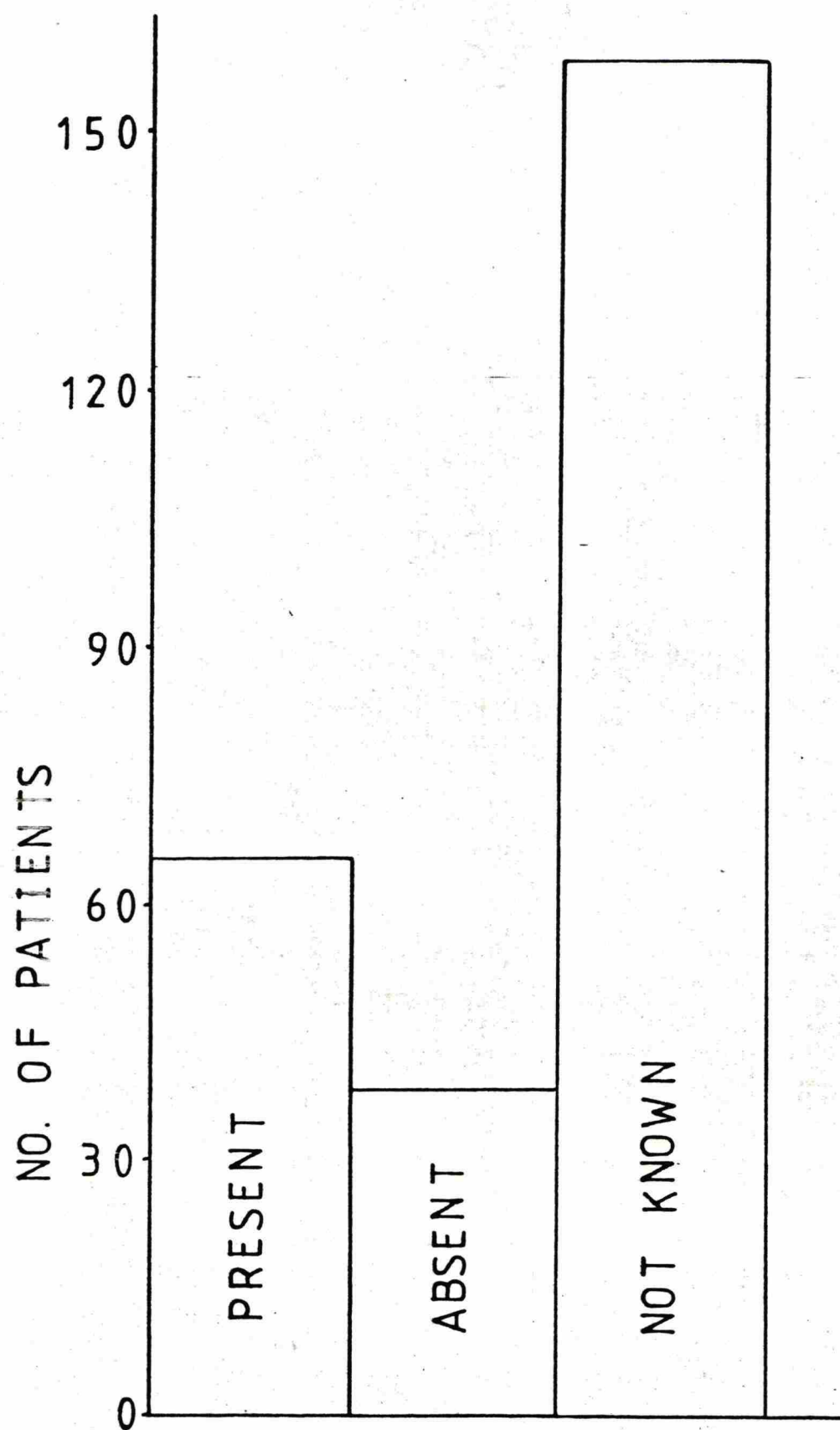


Fig. 29

Emetic - Present or Absent in Formulations

	Total	Weedol	Pathclear	Gramoxone	Dextrone	Dexuron	Gramonol	Not Known
Present +	64	32	12	19	1	-	-	-
Absent -	39	13	2	20	1	1	1	1
TOTAL	103	45	14	39	2	1	1	1

SPONTANEOUS VOMITING AFTER INGESTION OF EMETIC/NON-EMETIC

FORMULATIONS OF PARAQUAT

Emetic present

Amount (g. paraquat ion)	Early Vomiting ($< \frac{1}{2}$ hr p.i.)*	Late Vomiting	No Vomiting
< 2	16 (55%)	8	5
2 - 5	3 (75%)	1	-
5 - 10	1 (100%)	-	-
10 +	6 (100%)	-	-
TOTAL	26 (65%)	9	5

* p.i. = post ingestion

Emetic absent

Amount (g. paraquat ion)	Early Vomiting ($< \frac{1}{2}$ hr p.i.)*	Late Vomiting	No Vomiting
< 2	1 (10%)	2	7
2 - 5	1 (25%)	1	2
5 - 10	-	1	1
10 +	2 (40%)	-	3
TOTAL	4 (19%)	4	13