TRIALS OF PERPHENAZINE IN THE PREVENTION OF POST-OPERATIVE VOMITING

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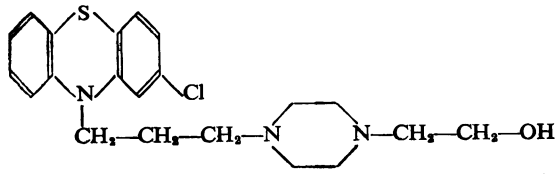
Numerous drugs with anti-emetic activity have been introduced during the past few years. Most of these compounds are derivatives of the antihistamine group, but Robson and Keele (1956) state that there is no relation between antihistaminic potency and protection against motion sickness. Many of these agents have been used to reduce the incidence of post-anaesthetic vomiting or in the treatment of this complication. In this application it is dangerous to assume that vomiting in the post-operative period is due to the anaesthetic or to analgesic drugs, for it can be due to surgical complications—dilatation of the stomach, intestinal obstruction, raised intracranial tension, etc. These possibilities must especially be kept in mind when anti-emetic drugs are given in treatment, as some agents are powerful enough to mask such dangerous complications.

Burtles and Peckett (1957) noted that both chlorpromazine and promethazine given with the premedication were equally effective in reducing post-operative vomiting. They stated that chlorpromazine had undesirable side-effects, including delayed recovery of consciousness, hypotension, dizziness, vasodilatation, occasional restlessness, and pain at the site of the intramuscular injection. They considered promethazine preferable, as these side-effects were largely avoided, but occasional mild dizziness and a cerebral depressant action (additive to anaesthetic and premedicant agents) were still noted. In our experience promethazine leads to undesirable prolongation of the recovery period.

A new compound, perphenazine (Sch 3940, "trilafon"), has 24 times the anti-emetic activity of chlorpromazine when tested against apomorphine-induced vomiting in dogs (Rosenkilde and Govier, 1957). Perphenazine is 1-(2-hydroxyethyl)-4-[3-(2-chloro-10-phenothiazinyl)-propyl]-piperazine; the structural formula is:



Early experiments in dogs (Rosenkilde and Govier, 1957) seem to indicate that the specificity of this agent, for its competitive action with the emetic agent on the chemoceptive trigger zone, is almost akin to ablating this centre. The drug is prepared as an injection containing 5 mg. per ml., and may be given intramuscularly or intravenously. There is no pain after intramuscular injection; the *p*H is 5.9, and therefore much less acid than chlorpromazine (*p*H 3.9). The adult dosage ranges from 2.5 to 5 mg. Significant hypotension seems to be rare, but perphenazine does produce some adrenergic blockade. There is some potentiating effect on barbiturates and other narcotics, but this effect is much less than with chlorpromazine. With intensive dosage (unlikely in the present application) there may be extrapyramidal stimulation. The main danger is perhaps that this drug, like chlorpromazine, can obscure the cause of vomiting due to organic disease.

Present Investigation

We have investigated the efficacy of perphenazine against post-operative vomiting in 200 consecutive patients undergoing various operative procedures (gastrectomies and patients with stomach tubes were omitted from the series).

Alternate patients received perphenazine, 5 mg., by intramuscular injection in the right thigh at the end of operation, the remainder serving as controls. All vomiting occurring in the first six hours after operation was recorded; this period was chosen because six hours is stated to be the duration of action following a single injection of perphenazine. The recovery period was assessed by the return of rational response to questioning.

Results and Conclusions

For all the statistical conclusions the χ_c^2 test was used—that is, χ^2 with Yates's corrections for continuity.

Of the 100 patients treated with perphenazine, 7 vomited (6 women and 1 man); of the 100 controls, 21 vomited (14 women and 7 men) (see Table I). The difference between

TABLE I

	Control Series	Perphenazine Series
Males	49 (7 vomited)	51 (1 vomited)
Females	51 (14 ,,)	49 (6 ,,)
Mean age	44·32 years	43·23 years
Premedication (in addition to atropine or hyoscine):		
Opiates (papaveretum and morphine)	75 (14 vomited)	74 (5 vomited)
Pethidine	24 (7 ,,)	24 (2 ,,)
Other	0	2
None	1	0
Anaesthetic agents:		
Thiopentone and nitrous oxide	12 (4 vomited)	12 (1 vomited)
Thiopentone, nitrous oxide, and halothane	19 (3 ,,)	33 (3 ,,)
Thiopentone, nitrous oxide, and pethidine	50 (11 ,,)	37 (3 ,,)
Others	19 (3 ,,)	18 (none vomited)

the two series in the incidence of vomiting is significant at the 1% level—that is, the result might be expected by chance in less than 1 in 100 trials.

In the 200 cases the number of vomits was significantly greater in the female sex in the ratio of 2.5 : 1, but in the 100 control series the ratio was not significant, although the figures were highly suggestive of such a bias. There was no indication that perphenazine reduced the incidence of vomiting in one sex more than the other.

It can be seen from Table I that there was a similar mean age and an even distribution of sex and premedication, and

TABLE II

	Intra-abdominal and Lumbar Operations		Other Operations	
	Control	Perphenazine	Control	Perphenazine
Vomiting	5	—	16	7
No vomiting	21	12	58	81
Total	26	12	74	88

Test for significance in difference in vomiting rates between control and perphenazine groups in other operations:
$\chi_c^2 = \chi^2$ with Yates's correction for continuity.
$\chi_c^2 = 5{\cdot}0928$; $P < 0{\cdot}05$.

that the anaesthetic agents had no significant effect on the vomiting rate.

There were a greater number of intra-abdominal and lumbar operations in the control group, but the difference in the incidence of vomiting was still significant if these were eliminated (see Table II). The distribution of the other operative procedures was satisfactory.

The mean recovery time was 26.75 ± 3.69 minutes in the perphenazine series and 17.30 ± 2.26 minutes in the control series, a difference of 9.45 ± 4.33 minutes; this difference is significant at the 5% level—that is, the results might be expected by chance in less than 1 in 20 trials. An increase in recovery time of this order is not unacceptable.

No side-effects were observed, and there was no complaint of discomfort at the site of injection in any case.

Table III compares the reduction in vomiting rate with similar reports upon other agents.

TABLE III

Report	Series	Post-operative Vomiting Rate
Albert and Coakley (1954)	Control	28·8%
	Chlorpromazine	13%
Burtles and Peckett (1957)	Control	32%
	Promethazine	18%
	Chlorpromazine	18%
Present report	Control	21%
	Perphenazine	7%

Summary

A trial has been made of the efficacy of perphenazine in the prevention of post-operative vomiting in a group of 200 patients. The vomiting rate was 21% in the controls and 7% in those receiving perphenazine.

The mean recovery time was 17 minutes in the controls and 27 minutes in the perphenazine series.

More females vomited than males in the ratio of 2.5:1.

There was no indication that any differences between control and perphenazine-treated groups regarding premedication, anaesthetic agent, or operation contributed significantly to the difference in vomiting rate.

No side-effects of the drug were observed.

Our thanks are due to Dr. Brian Lacey for the statistical calculations. We are indebted to our colleagues and to the nursing staff for their co-operation. The perphenazine was generously supplied by the Schering Corporation, Bloomfield, New Jersey, U.S.A.

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The ninth Annual Report of Family Service Units states that during 1956–7 Family Service Units worked with over 700 families, or an equivalent of about 4,500 men, women, and children. It is often through a telephone call from a housing manager, hospital almoner, or probation officer that a family needing long-term assistance is heard of by F.S.U. The help which "problem" families need varies greatly: material aid, such as clothing, bedding, or furniture, is often required, and specialized help, such as medical treatment, may well be necessary. Constant collaboration is essential with all the many agencies concerned with the different aspects of the family's welfare. The F.S.U. worker's task is to mobilize all the resources available and to enable the family to make the best of them. So that each family can be given the time and attention it needs, each worker is in touch with 12 to 15 families only at one time. Some 39,000 visits were made to families during the year.

BEMEGRIDE AS AN ACTIVATOR IN ELECTROENCEPHALOGRAPHY

BY

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Bemegride (β-ethyl-β-methylglutarimide) was introduced in 1954 as a barbiturate antagonist. Its first clinical application was in the treatment of barbiturate poisoning (Shaw *et al.*, 1954; Shaw, 1955; Shulman *et al.*, 1955). Shulman *et al.* (1955) suggested that treatment should be carried out with electroencephalographic control, and an investigation of the electroencephalographic examination of the effects of bemegride in barbiturate narcosis was made in animals (Peacock, 1956).

Delay *et al.* (1956a, 1956b, 1956c), Drossopoulo *et al.* (1956), and Courjon and Bonnet (1956) published papers on the use of bemegride as an activating agent in electroencephalography. They compared bemegride with leptazol, using roughly equivalent techniques in normal, psychiatric, and epileptic patients. The drugs were given by slow intravenous injection until a convulsion was produced. The amount of bemegride used to produce a convulsion was often of the order of 250 mg., the maximum dose being 630 mg. Normal subjects showed, at the most, "slight activation in the electroencephalogram." Subjects with temporal lobe epilepsy sometimes produced focal discharges, and other epileptics had generalized convulsive discharges. The fits produced by bemegride were slow in onset and of short duration, recovery being quick. Subjective side-effects were few, and consisted usually of muscular twitchings. These workers considered bemegride to be equal to leptazol as an activator in electroencephalography, and that it was safer because the convulsions were milder and more easily controlled.

An experimental study of the effects of bemegride in the antagonism of barbiturates and other narcoleptics was carried out by Cass (1956) in animals with electroencephalographic control. That author concluded that bemegride had a specific effect against the electroencephalographic changes produced by barbiturates, and that this change was not seen with other narcoleptics. The effect of bemegride was greater than that of other analeptics in antagonizing the changes brought about by barbiturates.

The present paper reports the use of bemegride as an activator in electroencephalography in 40 patients, most of whom had temporal lobe epilepsy, and also in 10 normal subjects. The bemegride activation was used with routine recordings and also in addition to a standard technique for investigation of temporal lobe epilepsy (Pampiglione and Kerridge, 1956), in which sphenoidal needle electrodes were inserted. Following the bemegride activation in the majority of patients in whom sphenoidal recordings were carried out, sleep was induced with intravenous thiopentone.

Technique

The subjects studied had been referred for electroencephalography because of the clinical suspicion that an epileptogenic lesion was present. Apart from occasional exceptions, patients were off anticonvulsants for one or two days before recordings. One or more routine recordings