

# POTENTIATED ANAESTHESIA (NEUROPLEGIA) WITH A NEW SHORT-ACTING MIXTURE CONTAINING HYDERGINE, ETAMON, PHENERGAN AND PETHIDINE

## A PRELIMINARY REPORT

N. L. WULFSOHN, M.B., B.Ch. (RAND)

*Registrar-Anaesthetist, Boksburg-Benoni Hospital, Transvaal*

The advantages (such as the prevention of shock) of carrying out operations on bad risk cases under 'potentiated anaesthesia' (neuroplegia) or hibernation represent one of the most interesting advances in anaesthesia. The principles of the method have been dealt with elsewhere.<sup>1-3</sup> It has been noted when neuroplegia or hibernation with the chlorpromazine (Largactil) 'lytic mixture' is applied, a more or less marked increase in pulse rate becomes manifest in most cases. To avoid this additional strain on the heart, particularly in long operations, a group of French research workers have investigated numerous drug combinations in experimental animals, and have found that Hydergine (which is a mixture of equal parts of 3 hydrogenated ergot alkaloids—dihydroergocornine, dihydroergocristine and dihydroergokryptine) in 'lytic mixtures' achieves similar effects to the original chlorpromazine mixture but does not cause tachycardia. This research group, led by J. Cahn<sup>4</sup>, reported that their Hydergine lytic mixture gave the following results as compared with the chlorpromazine lytic mixture:

The hypothermia achieved is at least as profound and as stable,<sup>4, 5</sup> and affords more complete inhibition of endocrine reactions to stress.<sup>6</sup>

In rabbits and dogs hibernation with either the chlorpromazine or the Hydergine mixtures led to identical electro-encephalographic tracings. However, generally speaking, the electrical activity of the brain remained greater with the Hydergine mixture. Normal EEGs were re-established earlier with chlorpromazine,

but on the day following the experiment no difference between the two methods could be discerned.<sup>5, 7, 8, 9</sup>

Hydergine had no depressant action on the myocardium as made evident by reduction of intracardiac systolic pressure and diminution of pulse pressure with chlorpromazine, and no tachycardia occurred, but on the contrary a reduction in the rate of heartbeat took place.<sup>5, 9, 10, 11</sup>

The two preparations, in combination with hypothermia, protected the animals equally well against the effects of ligation of a branch of the coronary artery.<sup>5, 11</sup>

Work carried out by Cahn *et al.*<sup>5, 9, 10, 11</sup> showed that good prospects for carrying out cardiac surgery without having to fear ventricular fibrillation lay in the use of a Hydergine lytic mixture in combination with infiltration of the sinus node with a local anaesthetic.

Based on the above experimental data, a number of operations on humans have been carried out with the Hydergine lytic mixture in combination with hypothermia. Huguenard<sup>12</sup> has reported on 17 cases of general surgery, and Campan<sup>13, 14</sup> on 54 neurosurgical cases. At these first clinical trials with Hydergine the following observations were reported:

The body temperature fell at the same rate as with chlorpromazine (1—1.5°C per hour) and the oxygen consumption dropped markedly. The heart rate was well controlled and tachycardia was much less frequent than with chlorpromazine. The blood pressure fell to the same extent, but the pulse pressure remained higher. By tilting the operating table controlled hypotension

could be achieved without the use of additional ganglionic blocking agents. Central sedation was less marked with Hydergine than is usual with chlorpromazine, and more anaesthetic had to be used in most cases.

#### PRESENT INVESTIGATION

The work referred to above was carried out by combining Hydergine with body cooling. Our endeavours were directed to carrying out 'potentiated anaesthesia' without body cooling. It was decided to try drug combinations which would not have an undesirable effect upon the heart; and because of the favourable reports referred to above, and because Hydergine has been reported to possess a protective effect against experimentally-induced ventricular arrhythmias during anaesthesia,<sup>15-18</sup> a drug combination containing Hydergine was selected.

Initially, Hydergine was used together with Phenergan and Pethidine. The finding of the French authors that slowing of the pulse rate occurred, was confirmed, but it was also found that an increased amount of anaesthetic drugs (Pentothal) was required. This was felt to be a drawback, and it was decided to add Etamon to this lytic mixture to potentiate its action. Etamon (tetra-ethylammonium chloride) is a potent ganglionic blocking agent. Further, it was expected that with the addition of Etamon a smaller amount of relaxing agent would be required, because of its curare-like effect.<sup>19</sup>

The combination of Etamon with the other ingredients of the Hydergine mixture produced the desired effect, which was not achieved when any one of the drugs was omitted.

In the course of our investigation the following combinations were tested:

- (a) Etamon with Pethidine and the following anaesthetic drugs: Pentothal, relaxant, and nitrous oxide.
- (b) Hydergine with Pethidine and the anaesthetic drugs mentioned in (a).
- (c) Hydergine with Phenergan, Pethidine and the same anaesthetic drugs.
- (d) Etamon with Hydergine, Phenergan, Pethidine and the same anaesthetic drugs. This final combination of 'neuroplegic drugs' (Etamon, Hydergine, Phenergan and Pethidine) produced, without addition of the anaesthetic drugs, a state of drowsiness and sleep rather resembling physiological sleep and from which the patient could readily be aroused. Furthermore, and this seems of importance, this state of 'artificial sleep' was of short duration, and could be terminated at will, as soon as the operation was concluded. Thus, a mixture allowing short-lasting neuroplegia was discovered by accident.

*Technique.* The following mixture was prepared:

Hydergine	(0.6 mg.)	2 ml.	} 7 ml.
Etamon	(0.2 g.)	2 ml.	
Phenergan	(50 mg.)	2 ml.	
Pethidine	(50 mg.)	1 ml.	

Of the above mixture an initial dose of 2 ml. was administered intravenously. If the patient had not fallen asleep after 10 minutes a further 2 ml. was injected. Blood pressure and pulse rate were recorded every 5 minutes (the blood pressure fell and the pulse rate, after a short initial increase, started to fall within 20 minutes

from the first injection, and then remained at a stable rate throughout).

Twenty minutes after the first injection the patient was usually asleep, and at this stage 2 ml. of 5% Pentothal, and 6 mg. of curare or 50 mg. of Scoline, were given intravenously. Oral intubation was then performed, and nitrous oxide and oxygen (5 : 3) were administered. Immediately before the surgical incision a further 2 ml. of Pentothal was given in order to 'settle' the patient. During the operation, Pethidine in doses of 10 mg. was given, whenever the breathing tended to become more rapid. The re-breathing bag was squeezed repeatedly, in order to prevent carbon dioxide building up. Whenever the blood pressure rose appreciably, or the heart rate increased, a further dose of 1 ml. of the neuroplegic mixture was injected. If the patient moved, 1 ml. of 5% Pentothal was given.

The above technique was applied in 12 cases. See Table I.

*Results.* The general condition of the patients operated on under Hydergine-Etamon-Phenergan-Pethidine neuroplegia appeared to be good throughout. The pulse rate was reduced in all cases. The general impression gained was that Hydergine exerts a bradycardic effect in the initial stages, and in the further course of the operation,

TABLE I

Race Sex Age	Operation	Duration of operation (minutes)	Amounts of drugs used (total)
CM42	Appendectomy	50	7 ml. mixture, 9 ml. Pentothal, 12 mg. curare.
EM50	Lobectomy	158	11 ml. mixture, 4 ml. Pentothal, 15 mg. curare, 60 mg. Pethidine.
BM59	Biopsy Carcinoma Tongue	17	7 ml. mixture, 25 mg. Scoline, 3 ml. Pentothal.
BM22	Skin-graft leg	38	8 ml. mixture, 6 ml. Pentothal, 3 mg. curare.
EM70	Cholecystectomy + Pancreatectomy	160	10 ml. mixture, 3 ml. Pentothal, 60 mg. Scoline, 10 mg. Pethidine.
EF58	Cholecystectomy	138	6 ml. mixture, 4 ml. Pentothal, 15 mg. curare, 10 mg. Pethidine.
BF26	Dilatation + Curettage	10	4 ml. mixture, 6 ml. Pentothal, 25 mg. Scoline.
EF63	Cholecystectomy	90	7 ml. mixture, 6 ml. Pentothal, 30 mg. Pethidine, 150 mg. Scoline, 21 mg. curare.
BM36	Bronchoscopy + Lobectomy	±180	14 ml. mixture, 7 ml. Pentothal, 125 mg. Scoline.
BF34	Dilatation + Curettage	10	3 ml. mixture, 5 ml. Pentothal.
EM73	Artificial bladder from caecum + ileum and transplant. of ureters	70	12 ml. mixture, 6 ml. Pentothal, 60 mg. Pethidine, 70 mg. Scoline, 21 mg. curare.
BM?	Intestinal obstruction	72	4 ml. mixture, 4 ml. Pentothal, 50 mg. Pethidine, 18 mg. curare.

C=Coloured; E=European; B=Bantu.

Mixture=Mixture of Hydergine, Etamon, Phenergan and Pethidine, as specified under the heading *Technique*.

does not reduce the heart rate further, but rather prevents it from rising. The pulse rate, once settled, remained almost constant throughout the operation, and never became very rapid. Usually, it was between 60 and 80, and rarely above 95 per minute.

At the end of the operation, the patient could usually be wakened easily by shouting, slapping his face gently, or moving him. If left alone he went back to sleep immediately. The action of the neuroplegic mixture was short-lived, no matter how long the operation had lasted. Nevertheless the patients required little or no sedation in the first few post-operative hours. Throughout the operation, the skin was dry, cool and pink. In some cases sweat appeared, and the administration of 10 mg. of Pethidine terminated this reaction.

The body temperature usually dropped by 3–4°F. (experiments on white mice with this mixture resulted in a drop of temperature of 7–9°F over a period of  $\frac{1}{2}$  to  $\frac{3}{4}$  hours.)

It was observed when this neuroplegic mixture was used that much less relaxant had to be used than was otherwise expected. Some cases could be intubated with as little as 3 mg. of curare and 1 ml. of Pentothal.

The amounts of neuroplegic mixture varied from case to case. One patient who had received only 4 ml. of neuroplegic mixture was asleep and analgesic for about  $\frac{1}{2}$  hour.

A point of particular importance is the remarkably good post-operative condition of the patients, on which the house surgeons commented.

#### SUMMARY

1. This is a preliminary report on the use of a new short-acting neuroplegic mixture for use in 'potentiated anaesthesia' (neuroplegia).

2. The neuroplegic mixture consisted of Hydergine, Etamon, Phenergan and Pethidine.

3. Anaesthesia was maintained with Pentothal, nitrous oxide, Pethidine, and relaxants.

4. In all cases the pulse rate was reduced.

5. The amount of relaxant required was markedly reduced.

6. The state of neuroplegia produced was of short duration, lasting as long as the patient was given just sufficient anaesthesia to keep him asleep.

7. This method seems to afford good protection from shock, as evidenced by a dry, cool and pink skin throughout operation, and a remarkably good post-operative course.

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