METHYL-N-PROPYL ETHER

By G. J. Rees and T. Cecil Gray

METHYL-N-PROPYL ETHER is an isomer of di-ethyl ether and possesses the formula CH₃-O-(CH₂)₃-CH₃. The physical properties of the two drugs are similar, and the vapour pressure curve of methyl-n-propyl ether is such that it may be used in the Oxford Vaporizer No. 1 without any alteration in the calibration of the instrument (see Figure).

Methyl-n-propyl ether has a very unpleasant pungent odour. This was found to prevent its use as an analgesic agent for women in labour, and it is unpleasant in operating theatres when the drug is administered in open circuits as an anaesthetic agent.

The use of methyl-n-propyl ether as an anaesthetic agent was first described in 1946 by White et al. This paper is based on the experiences of the authors in a small series of twenty cases in which it was used as an anaesthetic agent. The series is small but was abandoned when it was appreciated that the drug had no outstanding advantages. In none of these cases was the drug used in combination with any of the muscle relaxant drugs, as it was our intention to investigate the basic effects of the ether, and not to develop a technique for its use.

ANALGESIC EFFECTS

Methyl-n-propyl ether produces a remarkable degree of analgesia without loss of consciousness. This was discovered when trying to assess the degree of recovery in one of the patients by pressure on the supra-orbital nerve. The patient
Graph showing the vapour pressure curves of di-ethyl and methyl-n-propyl ether. It will be seen that at the operating temperature of the Oxford Vaporizer No. 1 the vapour pressures are 605 mm. Hg and 515 mm. Hg respectively. Therefore if the machine is used with methyl-n-propyl ether the vapour concentration delivered will be the percentage shown on the di-ethyl ether calibration $\times \frac{515}{605} = .85$ (approx.) which, for practical purposes, over the range of the machine may be regarded as 1.
Methyl-n-Propyl Ether

tolerated this very painful stimulus without sign of discomfort, although able to phonate.

As a result of this observation, experiments were carried out on volunteers to see if practical use could be made of this property of the drug. The experiments consisted of the inhalation of the vapour from one of the standard obstetrical analgesia inhalers commonly used to administer trichlorethylene. The stimulus used was the application of a cross-action towel clip to the skin of the fore-arm. It was found possible to carry out this procedure without discomfort under the analgesic effect, but without this the pain was hard to tolerate.

As a result of these findings one of our colleagues exhibited the vapour to women in labour, but the unpleasant odour of the drug caused it to be unacceptable to these patients.

INDUCTION OF ANAESTHESIA WITH METHYL-N-PROPYL ETHER

As compared with di-ethyl ether the induction of anaesthesia with methyl-n-propyl ether is smooth, both with nitrous oxide-oxygen-ether and with thiopentone-ether sequences, and with open-drop administration.

Using a standard Boyle's machine it has been found possible in all but the most refractory cases to change over from thiopentone narcosis to the full vapour concentration of methyl-n-propyl ether which the machine will deliver without bubbling the gases through the liquid, in three quite short stages, and this without any signs of intolerance of the vapour on the part of the patient.

It has also been found quite feasible to administer the drug from the ether vaporizer of the Coxeter-Mushin circle absorber following a normal induction dose of thio-
pentone, without any intermediate saturation of the patient with a nitrous oxide-oxygen mixture, a feat which is difficult to perform with di-ethyl ether.

MAINTENANCE OF ANAESTHESIA

**General Remarks.** Endotracheal intubation is readily performed under methyl-n-propyl ether anaesthesia. It is possible to maintain a light plane of anaesthesia with it more smoothly and with less risk of untoward occurrences than is the case with di-ethyl ether. This is illustrated by Case No. 3, where the patient was conscious and talking during the recovery period, but at the same time tolerating a Waters metal airway without any retching!

**Relaxation.** The drug has been found to be most unsatisfactory for those operations which call for more than the minimal amount of muscular relaxation. Spasm of the laryngeal muscles or of the masseter was not seen in any of the cases.

**Respiratory Effects.** In light planes of methyl-n-propyl anaesthesia the respirations are quiet and slow. This depression of the respiration is never so marked as that seen during cyclopropane anaesthesia, and the rate appears to be more affected than the depth of respiration. When an attempt is made to produce any great degree of muscular relaxation by increasing the concentration of the ether, the respiration becomes extremely rapid. Unlike the tachypnoea of deep trichlorethylene anaesthesia, the tidal volume remains fairly high. This tachypnoea, combined with the poor muscular relaxation, produced difficult operating conditions and evoked many complaints from surgeons.

**Cardiovascular Effects.** The colour of patients anæsthe-
Methyl-n-Propyl Ether

tized with methyl-n-propyl ether indicates a degree of vasodilatation. They are pink, flushed, and usually sweat freely at deeper levels of anaesthesia.

The pulse rate is not greatly affected but the effect on the blood-pressure is very marked. Alarming degrees of hypotension have been seen when attempts have been made to procure muscular relaxation by deepening anaesthesia (Fisher and Whitacre, 1947). In such cases a change to di-ethyl ether was accompanied by an immediate improvement in cardiovascular function. This improvement has been taken to indicate that the depression was due to the ether and not to incidental causes.

Recovery. The recovery from light anaesthesia with this agent has been very pleasant. The major cases all required supplementation with di-ethyl ether so that the recovery has been as from that drug.

The remarkable analgesic properties of the drug have been observed during recovery of patients from anaesthesia. Two of the cases demonstrated this very clearly. The first was a man of fifty-four who had been operated on for the excision of a hydatid of Morgagni. This man recovered consciousness to such a degree that he was able to carry on a coherent conversation before the suturing of the scrotal incision was complete. He made no complaint of any discomfort, even when interrogated, whilst the operation was being completed.

The second case which demonstrated this effect was a female who had been operated on for the radical cure of varicose veins. She opened her eyes shortly after the completion of the operation, and was asked how she felt. She replied that she felt very good, and her smile showed that this was no exaggeration, despite the fact that she still retained a Waters-type metal airway in her pharynx.
The following specimen records of cases illustrate some of the properties of methyl-n-propyl ether when used as an anaesthetic agent. The incidence of vomiting is noted but, as would be expected from the nature of the operative procedures, no post-operative pulmonary complications were encountered.

Case No. 1
M. N., male, aet. 44. Renal calculi. 
Operation performed: Nephrolithotomy. 
Pre-operative B.P.: 130/90. 
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.) given one hour before operation. 
10.45: Thiopentone 0.5 g. administered slowly. Put on closed circuit with CO₂ absorption and pure oxygen, 300 ml. per minute. Methyl-n-propyl ether introduced to circuit from vaporizer. 
10.50: Oro-tracheal intubation easily performed. Oral pack—face-piece re-applied. 
11.05: B.P. 100/70. Respirations 30 per minute. Surgeon complained of poor relaxation. Airway good. 
11.30: B.P. 110/75. 

Case No. 2
A. P., male, aet. 52. Renal calculi. Chronic bronchitis. 
Operation performed: Nephrolithotomy. 
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.). 
Induction: Thiopentone 0.5 g. at 10.58 N₂O 4 l. per minute, O₂ 2 l. per minute. Methyl-n-propyl ether introduced to gases from vaporizer. Some coughing during induction. 
11.00: B.P. 130/70. 
11.05: B.P. 150/90. Intubation easily performed, no reaction to tube—mouth packed, rapid recovery and coughing on tube before mask could be replaced. Quickly re-stabilized.
Methyl-n-Propyl Ether

11.10: B.P. 160/90. Moved into theatre.
11.15: B.P. 110/65. Respirations 28 per minute.
11.20: B.P. 92/60. Respirations 30 per minute.
   Positioned in kidney position. Bridge up.
11.25: B.P. 90/55. Respirations 30 per minute. Incision made.
   Respiration assisted with view to control. Pulse good in volume. Anesthesia lightened.
11.30: B.P. 100/60. Pulse 90.
11.32: Breathing rather gasping in type.
11.35: B.P. 120/80. Pulse 92. Respirations 48 per minute (quite deep).
11.40: B.P. 120/90. Pulse 96. Respirations 42 per minute.
11.45: B.P. 110/90. Pulse 100. Respirations 40 per minute.
11.46: Hiccough a nuisance.
11.49: Cyclopropane 400 ml./min. added.
   Reflexes not back in theatre. Seen one hour later, full consciousness and comfortable.

Case No. 3
Pre-operative B.P.: 120/90.
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).
Induction: Thiopentone 0.4 g. N₂O 4 l. per minute, O₂ 2 l. per minute.
Methyl-n-propyl ether started.
Duration of operation: 20 minutes. Breathing slow throughout (12 per minute). Pulse regular. B.P. fell to 90/80. Rapid recovery. Patient tolerated Waters pharyngeal airway after recovery to consciousness. No vomiting. In this case at one time there was a noticeable waxing and waning of the pulse with respiration.

Case No. 4
E. M., female, aet. 36. Haemorrhoids.
Operation performed: Haemorrhoidectomy.
Pre-operative B.P.: 130/90.
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).
Induction: Thiopentone 0.5 g. N₂O, O₂, methyl-n-propyl ether.
   At time of dilatation of sphincter B.P. 100/70, laryngeal
Crow occurred. Anaesthesia lightened after dilatation and maintenance was smooth with respirations at 14 per minute. Recovery time: 10 minutes. No vomiting.

Case No. 5
M. C., male, aet. 55. Hydatid of Morgagni. Bronchitis.
Operation: Exploration of testicle.
Pre-operative B.P.: 140/100.
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).
Induction: Thiopentone 0.5 g. N₂O, O₂, methyl-n-propyl ether. Induction difficult with coughing, laryngeal spasm and cyanosis. Operation lasted 30 minutes. Some tachypnoea and tachycardia. B.P. fell at one point to 100/70 and the ether was withdrawn. Recovery was very rapid, and patient was talking and moving as the skin was being sutured, but complained of no pain, even on interrogation, and demonstrated clearly the analgesic properties of methyl-n-propyl ether.

Case No. 6
G. T., male, aet. 30. R.I.H. Radical cure.
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).
Induction: Thiopentone 0.5 g.
Maintenance: Closed circuit methyl-n-propyl ether. Induction smooth, maintenance satisfactory, respirations 18 per minute throughout, pulse volume good throughout. Recovery time: 10 minutes following withdrawal of ether. Vomited once on return to ward.

Case No. 7
F. S., female, aet. 32. Laparotomy.
Operation performed: Oophorectomy.
Pre-operative B.P.: 125/85.
Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).
Induction: Thiopentone 0.5 g. at 10.15 a.m.
Maintenance: N₂O-O₂=methyl-n-propyl ether.
11.35: Relaxation poor, anaesthesia deepened.
11.45: B.P. 105/70. Respirations becoming shallower. Apnoea—artificial respiration by compression of bag filled with O₂ only.
11.50: Return of spontaneous respiration.
11.55: Operation completed. Vomited twice on return to ward.
Methyl-n-Propyl Ether

Case No. 8

N. A., male, aet. 2. Varicose veins.

Operation performed: Radical cure.

Premedication: Morphia gr. 1/6 (11 mg.) and atropine gr. 1/100 (0.65 mg.).

Induction: Thiopentone 0.5 g. N₂O, O₂, methyl-n-propyl ether.

Maintenance satisfactory—respirations 16 per minute throughout.

Recovery time: 6 minutes. No vomiting.

CONCLUSIONS

There appears to be only one outstanding and possibly valuable property exhibited by methyl-n-propyl ether as opposed to the di-ethyl homologue. That is the well-marked state of analgesia which it produces in low concentrations. This property could not be utilized to produce analgesia in conscious patients because the odour makes the drug unacceptable to them. It might, however, give the drug a certain value in a balanced anaesthetic when a relaxant is used to complete the triad of relaxation, narcosis and analgesia.

In anaesthetic practice it could never supplant di-ethyl ether as the “universal drug”. It could be used satisfactorily in minor surgery, but possesses no properties which would make it more useful than trichlorethylene for such purposes.

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REFERENCES
Fisher and Whitacre (1947). Anesthesiology, 8, 156.
White et al. (1946). Anesthesiology, 7, 663.