

# METHOXYFLURANE IN PAEDIATRIC CARDIAC SURGERY

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INHALATION ANAESTHESIA combined with hyperventilation is a suitable technique in children, especially for operations where controlled respiration is required but muscular relaxation is unnecessary. Halothane with  $N_2O-O_2$  and hyperventilation provides satisfactory maintenance anaesthesia for paediatric cardiac surgery. In addition, immediate recovery is easily achieved. Poor analgesia and cardiovascular depression, however, are two disadvantages associated with the use of this agent. For this reason, trichlorethylene has recently been substituted for halothane in neurosurgery using the same technique<sup>1</sup>. Results have been encouraging: the blood pressure is stable throughout anaesthesia, there is excellent analgesia in the postoperative period, but recovery is prolonged if this agent is not withdrawn well before the end of surgery. However, trichlorethylene is not sufficiently potent for use in cardiac surgery. Alternatively, methoxyflurane has about twice the potency of halothane<sup>2</sup> and is stated to provide considerable analgesia which persists into the postoperative period<sup>3-9</sup>. Clinical experiences with this agent in 50 children who underwent surgery for the correction of congenital heart defects are reported in this paper.

## METHOD

Of these children, 46 ranged in weight from 26 to 109 lb, and received pentobarbital 1 mg/lb, pethedine 0.6 mg/lb, and atropine 0.012 mg/lb as a premedication. Four children who weighed under 20 lb received only atropine. Thiopentone sodium 1-2 mg/lb, was used for induction in all but two cases, and suxamethonium chloride for intubation. The patients were then hyperventilated with a high flow of nitrous oxide and oxygen using a semi-closed system and Waters canister of appropriate size. Methoxyflurane was delivered from a Pentec vaporizer situated outside the circuit. When complete apnoea was required during surgery, additional suxamethonium chloride was used. In those cases where cardiac bypass was performed, a Pentec vaporizer was inserted in line with the oxygen inflow to the disks. A summary of the lesions operated upon is given in Table I.

## RESULTS

The depth of anaesthesia was sufficient in all patients to allow a venous cut-down to be performed within 5 minutes following the intravenous induction.

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TABLE I  
TYPES OF PATIENTS

Lesion	No of patients
Patent ductus arteriosus	13
Tetralogy of Fallot	12
Atrial septal defects	9
Ventricular septal defects	8
Aortic stenosis	5
Coarctation of aorta	1
Pulmonary stenosis	1
Aortic aneurysm	1

Only occasionally was it necessary to use concentrations of methoxyflurane in excess of 0.5 per cent

During maintenance anaesthesia and before surgical manipulation of the heart or great vessels, the systolic blood pressure remained relatively stable in 34 patients. In 10 patients there was a moderate fall and in 6 there was a severe fall. These results are recorded in Table II. The decrease in systolic blood pressure is expressed as a percentage of its preoperative value, or the value

TABLE II  
DECREASE IN SYSTOLIC BLOOD PRESSURE IN 50 CHILDREN WITH CONGENITAL HEART DISEASE DURING METHOXYFLURANE ANAESTHESIA

Percentage fall in blood pressure	0-10	10-30	>30
Number of patients	34	10	6

immediately before the introduction of methoxyflurane, if this was lower (4 patients). No one factor can be held responsible for the occurrence of hypotension during anaesthesia in such a variable group of patients. It is apparent from Table III that a fall of blood pressure in any one of the 6 patients would not be surprising regardless of the anaesthetic agent used.

No bradycardia or tachycardia that could be attributed to methoxyflurane was noted in any patient. Prior to manipulation of the heart two patients developed

TABLE III  
DATA OF 6 PATIENTS WHO HAD >30% FALL IN BLOOD PRESSURE

Maximum methoxyflurane concentration (%)	Relevant data
1.5	VSD shunt reversal by positive pressure
0.5	ASD secundum, induced hypothermia by surface cooling
0.5	Leaking aneurysm of the aortic arch
1.5	PDA 14 lb wt digitalized
0.3	Tetralogy Single ventricle Severe pulmonary stenosis Severe kypho scoliosis
0.5	Tetralogy

transient arrhythmias which consisted of an A-V dissociation and occasional supraventricular extrasystoles

On completion of anaesthesia 31 patients were awake while 19 were not awake (Table IV) The pharyngeal reflexes were present in all cases The patients were considered to have recovered when they responded correctly to a simple command or, in the case of younger children, when the eyes opened spontaneously

TABLE IV  
IMMEDIATE POST-ANAESTHETIC STATE

	Awake	Not awake
Number of patients	31	19

In this type of surgery the recovery time is influenced by a number of factors other than the effect of a single drug However, the percentage of the anaesthetic time during which methoxyflurane was being administered was a distinct factor determining whether or not the patient was awake at the end of surgery (Table V) The prospects of early recovery could have been increased either by

TABLE V  
IMMEDIATE POST-ANAESTHETIC STATE

	Number of patients	
	Awake	Not awake
Methoxyflurane on for >39% of anaesthetic time	17	17
Methoxyflurane on for <39% of anaesthetic time	14	2

$\chi^2$  test  $P < 0.01$

turning the methoxyflurane off at an earlier stage or by reducing the inhaled concentration This was found to be unsatisfactory because of the inadequate anaesthesia which often resulted Reference to Figure 1 will show that in only 9 patients was the methoxyflurane administered for more than 50 per cent of the operation

It can be seen from Figure 2 that the mean concentration of methoxyflurane delivered to the patients was over 0.4 per cent in only 13 cases The mean concentration includes a relatively high concentration (rarely over 0.5%) administered to the patient initially When anaesthesia was stable, concentrations of 0.2–0.3 per cent were used for maintenance

In general, any effort to further limit the amount of methoxyflurane administered impaired the quality of the anaesthesia Also, in cardiac surgery, a number of other factors may prolong the normally slow elimination of methoxyflurane Examples include reduction in pulmonary blood flow, reduction in systemic blood flow, and hypothermia In the postoperative period, respiratory depression may be an additional cause of slow elimination The following case report illustrates some of these points

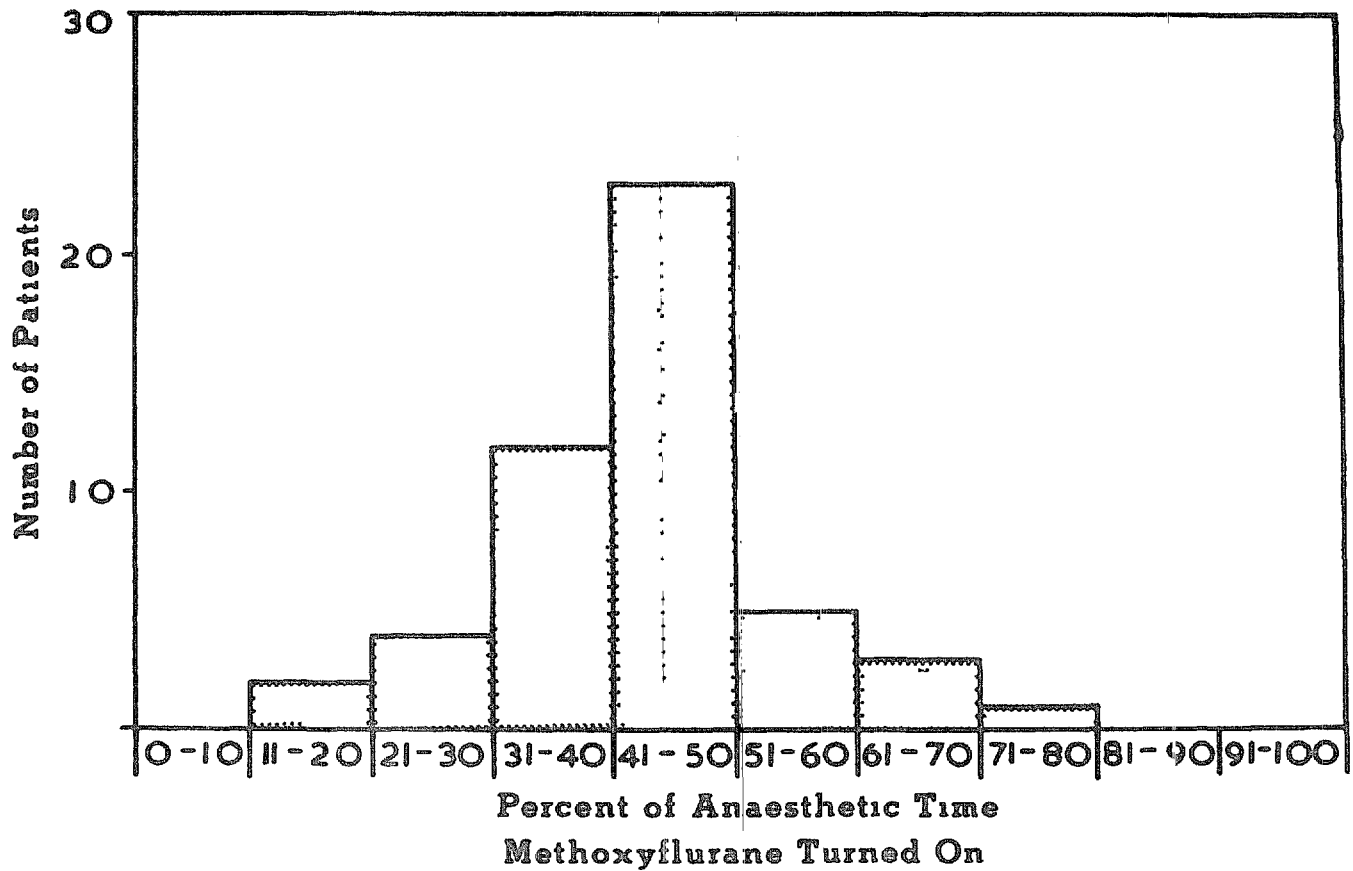


FIGURE 1

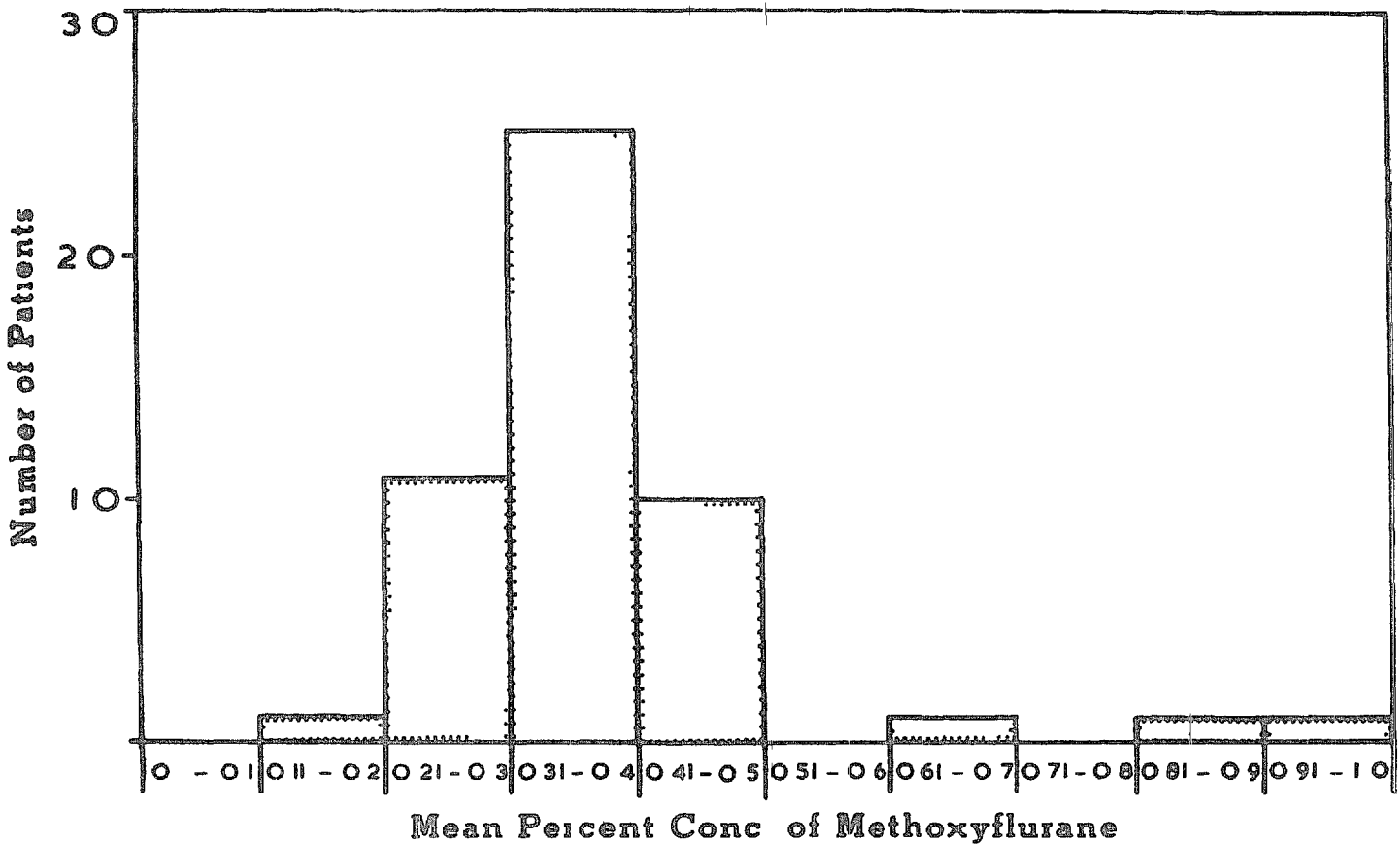


FIGURE 2

A Blalock anastomosis was performed under hypothermia on a child with cyanotic Tetralogy of Fallot, severe pulmonary stenosis, severe kypho-scoliosis, and a single ventricle. A poorly functioning anastomosis was effected. During a large part of the operation there was considerable hypotension. On the cessation of anaesthesia, the pharyngeal reflexes were present but the patient was not awake. The blood pressure was 50-60 mm Hg systolic and there was a supraventricular tachycardia of 200/min.

The patient was extubated. It was noted that the odour of methoxyflurane in the patient's breath was unexpectedly strong. The patient was, therefore, re-intubated and artificially ventilated and awakened an hour later.

It is not suggested that methoxyflurane was responsible for the prolonged recovery but only that it contributed to the patient's precarious postoperative condition. This occurred despite the fact that the drug was only administered for 15 per cent of the total anaesthetic time at a mean concentration of 0.23 per cent.

Table VI records the postoperative analgesic requirements of 23 patients. These patients are chosen because they received a high dose of methoxyflurane relative to the anaesthetic time (The dose was calculated on the assumption that 0.5% for 5 min  $\equiv$  0.1% for  $5 \times 5$  min). This selection serves to exclude the more ill patients, including all those who required IPPR in the postoperative period. Persistent restlessness, interference with physiotherapy, and persistent irritability, all due to pain, were indications for giving pethidine 1–3 mg i.v./10 lb, or morphine 0.1–0.3 mg i.v./10 lb. Doses repeated within one-half hour were regarded as being single.

TABLE VI  
POST-OPERATIVE ANALGESICS REQUIRED BY 23 PATIENTS WHO  
RECEIVED A RELATIVELY HIGH DOSE OF METHOXYFLURANE

Doses of analgesic in first 12 hours postop		Time from end of operation until first dose of analgesic (min)	
Patients awake (8)	Patients not awake (15)	Patients awake (8)	Patients not awake (15)
4	5	25	20
6	4	10	300*
4	5	15	5
4	4	5	5
5	1	15	75*
4	4	5	300
3	5	25	55
5	5	5	25
	5		10
	4		165*
	5		50
	0		90
	6		25
	2		350*
	2		35
Mean 4.4	3.8†	13.1	65.6‡

\*See text

† $t^2$  test not significant

‡ $t^2$  test  $P < 0.01$

During the first 12 postoperative hours there was no significant difference in the number of doses of analgesic required by the patients who were awake and those who were not awake at the cessation of anaesthesia. This occurred despite the fact that the first dose was not given for an average of 65 minutes after the completion of surgery in the latter group. The patients who were awake required

an analgesic an average of 13 minutes after the completion of surgery. Methoxyflurane could easily be detected in the exhalations of all these patients. These results suggest, firstly, that following chest surgery in children, methoxyflurane exerts little or no analgesic action once the patients are awake, and secondly, that the analgesia it does give is at the expense of a reduced level of consciousness. The 4 patients in Table VI marked with an asterisk could only be roused after considerable stimulation in the early postoperative period, and did not awaken for periods of 60 minutes, 45 minutes, 120 minutes, and 50 minutes, respectively.

### DISCUSSION

It is well known that methoxyflurane causes cardiovascular depression, but in a healthy patient a significant fall of blood pressure is not likely to occur if overdosage is avoided.<sup>3</sup> There may be a considerable fall of blood pressure, however, if the patient's compensatory mechanisms are inadequate. This is apparent from our results and those of other clinical studies.<sup>5 6 10 11,12</sup>

Methoxyflurane has little tendency to induce spontaneous cardiac arrhythmias.<sup>3 13 14</sup> There is evidence that it sensitizes the heart to the action of adrenaline.<sup>15 16</sup> This drug is not infrequently used in cardiac surgery as a circulatory stimulant. Any disadvantages that methoxyflurane may have in this respect in cardiac surgery are difficult to evaluate and are not within the scope of this study.

The drawback of the slow rate of uptake of methoxyflurane can largely be offset by the use of an intravenous induction. Although recovery times in the many published reports on the clinical use of methoxyflurane have varied considerably, all authors are agreed that prolonged recovery is a special feature of anaesthesia with this agent.<sup>5 6 10 11 12</sup> This constitutes a distinct disadvantage to its use in cardiac surgery with the described technique. Efforts to have the patient awake at the end of surgery by reducing the inhaled concentration or by earlier withdrawal of methoxyflurane can easily result in unsatisfactory anaesthesia during the procedure. Should this occur, it is difficult to remedy owing to the inflexible nature of the agent. Factors which adversely affect elimination are not infrequently present and further add to the difficulty of having the patient awake immediately postoperatively.

It is highly debatable whether methoxyflurane possesses a specific analgesic action of any significance. Torda<sup>17</sup> concludes from analgesimetry studies that it "appears" to have. His results, however, are not very consistent. Dundee and Love,<sup>18</sup> also using analgesimetry, state that methoxyflurane in subnarcotic doses has no significant analgesic action. The results of this study support their view. Many authors of reports regarding the clinical use of methoxyflurane are of the opinion that it exhibits a prolonged analgesia in the postoperative period.<sup>4-9</sup> Few of the patients involved were awake at the end of surgery. There was a gradual emergence until at varying periods of time after the operation the patients were able to obey simple commands. Following this, many of the patients remained drowsy or somnolent, but pain-free and easily aroused. There is no objection to somnolence in a co-operative patient after cardiac surgery, and this is a side-

effect of many analgesic drugs. The analgesia provided by the opiate drugs, however, is superior to that offered by methoxyflurane to the extent that it is controllable, dependable, can be adjusted to the requirements of the patient, and is easily achieved. Using methoxyflurane with the above technique in paediatric cardiac surgery, to consistently provide an awake patient, who is also in such a state of emergence as to be analgesic and co-operative, is practically impossible. It is sufficiently difficult even to have the patient awake at the end of surgery.

#### CONCLUSIONS

From our results in children, it is doubtful that methoxyflurane possesses a specific analgesic action. Because of its slow elimination and associated prolonged recovery, this agent is contraindicated in paediatric cardiac surgery, using the technique described.

#### SUMMARY

Methoxyflurane in nitrous oxide and oxygen was administered to 50 children who underwent surgery for the correction of congenital heart defects. The patients were hyperventilated using a semi-closed system and Waters canister, incorporating a Pentec vaporizer outside the circuit. The results suggest that following anaesthesia with methoxyflurane in children, there is little analgesia in the awake patient. Because of the prolonged recovery associated with methoxyflurane anaesthesia, this agent is regarded as being unsuitable for use in paediatric cardiac surgery.

#### ACKNOWLEDGMENTS

We gratefully acknowledge the assistance given by our anaesthetic colleagues, the surgical residents, and Dr W T Mustard and Dr G T Trusler, under whose care the patients were admitted.

#### RÉSUMÉ

Nous avons administré du méthoxyflurane avec du protoxyde d'azote et de l'oxygène à 50 enfants qui devaient être opérés pour corriger une anomalie congénitale du cœur. Nous avons hyperventilé ces malades en employant un circuit semi-fermé et l'absorbeur de Waters, et nous avons utilisé le vaporisateur Pentec en dehors du circuit. Les résultats, nous portent à croire que, à la suite de l'anesthésie au méthoxyflurane chez les enfants, il persiste une légère analgésie chez le malade réveillé. À cause du réveil tardif à la suite de l'anesthésie au méthoxyflurane, nous considérons que cet agent n'est pas approprié pour la chirurgie cardiaque chez les enfants.

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