THE EXPERIMENTAL USE OF HALOTHANE ANAESTHESIA IN OPEN-HEART SURGERY WITH CARDIO-PULMONARY BYPASS*

A. B. BULL, M.B., CH.B. (CAPE TOWN), F.F.A.R.C.S.; G. J ROSSOUW, M.B., CH.B. (CAPE TOWN); J. E. KENCH, PH.D., D.SC. (BRISTOL), M.B., CH.B. (MANCH.), F.R.I.C.; and C. N. BARNARD, M.D., M.MED. (CAPE TOWN), M.S., PH.D. (MINNESOTA)

Departments of Anaesthesia, Chemical Pathology and Surgery, University of Cape Town

During open-heart surgery with cardio-pulmonary bypass, the anaesthetist is faced with the problem of maintaining anaesthesia without access to the lungs whilst extracorporeal circulation is in progress. In addition, markedly altered blood circulation raises problems with regard to the intravenous route of anaesthetic administration.

At the commencement of bypass, one is faced with the mixing of two blood volumes—that of the anaesthetized patient and that used to prime the pump oxygenator. This mixing inevitably causes marked alteration in the level of anaesthetic agents in the patient's circulation unless some means of equalizing anaesthetic levels in the two blood volumes can be achieved. In the lightly anaesthetized patient, dilution of anaesthetic concentration may have the undesirable effect of causing excessive movement on the part of the patient; even return of consciousness is not unknown. The addition of intravenous anaesthetic agents to maintain an even level of anaesthesia becomes extremely difficult to judge and, as these agents are eliminated relatively slowly from the body, control of anaesthesia may be far from accurate. This makes the desired rapid post-operative recovery from the influence of anaesthetic agents difficult to achieve unless extremely fine judgment in their useis exercised.

Further, the very light plane of anaesthesia usually employed in these procedures in order to promote rapid recovery may to a large extent be responsible for the metabolic acidosis described by DeWall *et al.*[1] It is felt that the unopposed sympathomimetic stimuli brought about by the trauma of surgery under light anaesthesia, perfusion pressures which are considerably below normal blood pressures, and relatively low perfusion rates as compared with normal cardiac output, play a significant part in causing the accumulation of organic acids in the body during cardio-pulmonary bypass. The effect of adrenalin on the production of organic acid has been described by Griffith *et al.*[2]

The following properties of halothane (Fluothane) led us to believe that this agent might be of some help in overcoming these difficulties, and so it was decided to investigate its usefulness in this respect:

1. The clinical use of halothane for cardiac and thoracic surgery not requiring cardio-pulmonary bypass has shown it to be capable of providing adequate and safe anaesthesia. In children we use it regularly as the sole anaesthetic agent

* Paper presented at the 42nd South African Medical Congress, (M.A.S.A.) East London, C.P., September–October 1959.

with nitrous oxide and oxygen for these procedures without the use of relaxants or other intravenous agents.

2. The controllability of depth of anaesthesia with small changes in inhaled concentration and the potency of this agent would seem to indicate that blood-anaesthetic levels are readily alterable in either direction.

3. Burn and Epstein[3] have shown that halothane produces a direct effect on blood vessels giving vaso-dilatation and diminished peripheral resistance.

4. Severinghaus and Cullen[4] and Krantz *et al.*[5] have produced evidence of depression of total oxygen consumption and myocardial oxygen consumption during halothane anaesthesia. Most recently, Orton[6] and Orton *et al.*[7] have described the use of this property in producing brief circulatory occlusion in cardiac surgery and have shown a decreased production of carbon dioxide as measured from alveolar air samples during halothane anaesthesia for ordinary surgical procedures.

With these factors in mind, it was decided to attempt to use halothane with nitrous oxide and oxygen as the sole anaesthetic agent on experimental animals for cardio-pulmonary bypass procedures with the object of providing easily controllable anaesthesia which might have the added benefit of minimizing or avoiding metabolic acidosis by virtue of depressing tissue metabolism and providing better peripheral tissue perfusion through the vasodilator action of halothane. Also, Dobkin[8] has shown that no accumulation of fixed acid occurs with halothane anaesthesia.

To avoid excessive changes in blood-anaesthetic levels at the start of and during cardio-pulmonary bypass, a method of administering halothane *via* the oxygenator of the heart-lung machine was attempted. This consisted of introducing Fluothane vapour into the DeWall bubble oxygenator with the oxygen stream. So as to interfere as little as possible with standard procedure, it became necessary first to obtain some rough idea in theory whether anaesthetic levels were likely to be achieved and maintained. A blood-halothane level of 20-25 mg. per 100 ml. of blood in animals has been reported to give a fairly deep level of anaesthesia, and is achieved after inhalation of 1·5 - 2% halothane vapour. If we then take this level of 20 mg.% as an arbitrary target to be reached in the oxygenator we can make some guess at the minimum amount of halothane which must be offered to the blood with the oxygen stream. We have found that 2% concentration of halothane administered *via* the lungs maintains deep anaesthesia in dogs and so again took 2% as our arbitrary concentration to be introduced with the oxygen to the oxygenator.

Now, by Avogadro's law, 197 g., i.e. the molecular weight of halothane in g., is the weight of 22·4 litres of halothane vapour at S.T.P.;

or, corrected to average room temperature, 24 litres;

or 1 g. of halothane = 0·12 litres of halothane vapour;

or 1 mg. of halothane = 0·12 ml. of halothane vapour;

or 1 mg. of halothane is contained in 6 ml. of 2% halothane vapour.

Therefore, using 2% halothane *via* the oxygenator, each ml. of blood must be offered the halothane contained in 1·2 ml. of 2% halothane vapour if introduced with the oxygen. This is a basic minimum possible if all the halothane is accepted by the blood. It falls well within the standard gas/blood flow ratio employed in the DeWall oxygenator, this being 3 : 1, which gives an available 0·5 mg. of halothane to each ml. of blood. Raventós gives the solubility of halothane in blood at 37°C as 1·16 g. per 100 c.c. This saturation figure is some 58 times the amount of our arbitrary target figure of 20 mg. per 100 ml. for anaesthesia. It seemed quite possible then that a satisfactory blood level of halothane might be achieved through the bubble oxygenator with 2% halothane vapour; also that this low percentage would cause little or no effect on the oxygenation of the blood.

As a preliminary, 5 dogs were subjected to standard cardio-pulmonary bypass procedures as described by McKenzie and Barnard[9] but with the addition of 2% halothane vapour introduced with the oxygen. To achieve this, a 'Fluotec' vaporizer was placed in the oxygen line. Both during priming of the machine with blood and during the time of bypass, this vaporizer was maintained at a 2% setting. All these dogs survived for a minimum period of 7 days. No EEG or pressure studies were performed. All the animals were awake within 20 minutes of the end of the operation. The duration of bypass, perfusion rates, operative procedure and results of blood-gas analysis are given in Table I.

TABLE I

Dog No.	*Duration of Bypass (minutes)*	*Operative Procedure*	*Art. O_2 Ven. O_2 (Vols.%)*	*Art. CO_2 Ven. CO_2 (mEq./litre)*
1	54	Y	100 73	26 30·5
2	52	RA	100 65	23 30
3	23	RV	100 64	26 32
4	50	RA	98 75	29 35
5	51	Nil	105 74	20 26

RV=Right ventriculotomy. RA=Right atriotomy. Y=Right ventriculotomy with induced cardiac arrest with potassium citrate.

From clinical observation in these 5 dogs it appeared that the procedure was entirely practical, that satisfactory anaesthesia could be easily maintained, and that recovery was rapid and uneventful and without post-operative sequelae which could be attributed to the anaesthetic.

An attempt was next made to determine blood-halothane levels when 2% halothane was introduced with the oxygen during priming and bypass without in any way interfering with 'standard procedure' regarding oxygen/blood flow ratios and perfusion rates. Samples were taken during bypass as indicated in Fig. 1 and subjected to analysis for halothane content by a modification[10] of the method described by W. A. M. Duncan of I.C.I. Laboratories. In each experiment, Sample I at '0' on the graph ordinate (Fig. 1) represents the arterial blood-halothane level of the dog before bypass is commenced. Sample II was taken from the arterial line of the pump during the first minute of bypass in an attempt to get the level attained during priming and after the blood had stood in the helix reservoir during placing of catheters in the dog. Subsequent samples were taken from the arterial line at the times of bypass indicated in Fig. 1.

It will be noted that the widest variation in concentrations occurs immediately after the start of bypass in the samples taken from the arterial line during the first minute. These samples should reflect the halothane levels in the helix

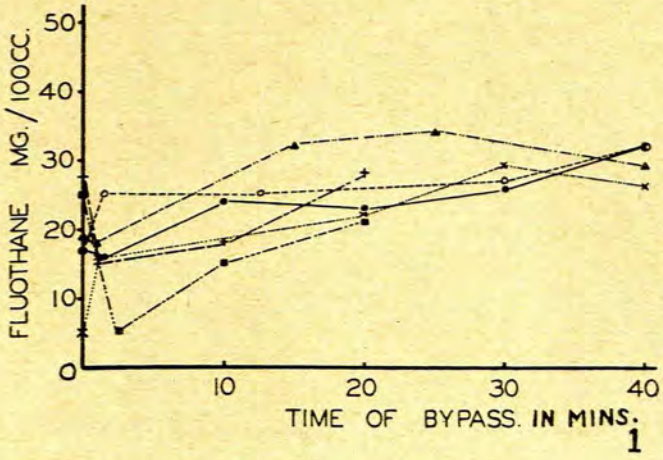

Fig. 1. Values of samples at '0' minutes indicate halothane levels of femoral-artery samples just before start of bypass. Other points indicate time and halothane level of samples from arterial line during bypass.

after priming and standing, and the variation is probably due to:

(*a*) The low rates of oxygen flow used during priming, i.e. less than 2 litres per minute, which is known to be the lowest flow at which the 'Fluotec' vaporizer used will function accurately according to its settings.

(*b*) Inconstant gas/blood flow ratios through the oxygenator during priming.

(*c*) The probability that some halothane may be taken up by the plastic tubing of the pump oxygenator system.

(*d*) Dilution of helix reservoir blood with saline used during the de-bubbling process.

(*e*) Difficulty in accurate timing of sample-taking during this critical phase of bypass.

The levels obtained from femoral-artery samples taken before bypass reflect the concentration attained by giving halothane 2% *via* the dogs' lungs during preliminary thoracotomy and preparation for bypass. Their variation may, in some part, be due to the duration of anaesthesia—and to variations which occurred in minute volume of manual pulmonary ventilation—up to this point in the surgical procedure.

Throughout bypass, adequate anaesthetic levels were maintained and in no case did the upper limit of concentration reached give any indication that a safe level was exceeded.

Information regarding oxygen uptake and the effect on acid/base balance has not yet become available and investigation on this aspect is proceeding.

This technique of anaesthesia has recently been carried into clinical use and is at present standard practice during open-heart procedures, both at the Red Cross War Memorial Childrens' Hospital and at Groote Schuur Hospital, Cape Town. Up to the time of writing 20 consecutive cases have been anaesthetized by this method, with excellent results. This will form the subject of a further communication.

We wish to thank I.C.I. South Africa (Pharmaceuticals) Ltd. for the supply of Fluothane, and for assistance in making available reagents for blood-halothane estimations. Our thanks are also due to Mr. E. J. Duncan for his valuable practical assistance in the analysis of halothane.

REFERENCES

1. DeWall, R. A., Warden, H. E., Gott, V. L., Read, R. C., Varco, R. L. and Lillehei, C. W. (1956): J. Thorac. Surg., **32**, 591.
2. Griffith, F. R., Lockwood, J. E. and Emery, F. E. (1939): Amer. J. Physiol., **127**, 415.
3. Burn, J. H. and Epstein, H. G. (1959): Brit. J. Anaesth., **31**, 199.
4. Severinghaus, J. W. and Cullen, S. C. (1958): Anesthesiology, **19**, 113.
5. Krantz, J. C., Park, C. S., Truitt, E. B. and Ling, A. S. C. (1958): *Ibid.*, **19**, 38.
6. Orton, R. H. (1958): Med. J. Austral., **1**, 830.
7. Orton, R. H. and Morris, K. N. (1959): Thorax, **14**, 39.
8. Dobkin, A. (1959): Anesthesiology, **20**, 10.
9. McKenzie, M. B. and Barnard, C. N. (1958): S. Afr. Med. J., **32**, 1145.
10. Kench, J. E. and Duncan, E. J.: *A Note on Determination of Bromochlorotrifluoroethane (Halothane) in Blood.* To be published.