HALOTHANE AND CIRCULATORY OCCLUSION: SOME EXPERIMENTAL AND CLINICAL OBSERVATIONS

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Three aspects of halothane anaesthesia form the basis for this presentation and are discussed separately. The first phenomenon is a fall in blood pressure. Hypotension is not marked in light halothane anaesthesia but as the concentration of halothane is increased more severe hypotension develops. In the opinion of some this results primarily from a direct depression of cardiac activity (Severinghaus and Cullen, 1958). Secondly, halothane has the reputation of reducing cardiac irritability although there have been reports of disturbances of cardiac rhythm during its administration (Chang, Macartney and Graves, 1957). Thirdly, the administration of halothane is associated with a reduction in the body oxygen consumption (Severinghaus and Cullen, 1958).

Reduction in cardiac output and in body oxygen consumption are properties which are common to a number of anaesthetic agents and narcotics (Price and Helrich, 1955). It is probable that much of this reduction is due to the decrease in muscular and respiratory work associated with anaesthesia. The observations on reduced oxygen consumption during halothane anaesthesia prompted us to undertake this work.

The tolerance of an animal to complete circulatory interruption produced by occlusion of both venae cavae is limited by its continuing metabolism, particularly that of the heart and brain. Using standard anaesthetic techniques periods of up to 3 minutes of circulatory occlusion have been used to permit open cardiac operations (Varco, 1957; Lam, 1957; Bjork, 1957). This period may be safely extended by depression of the rate of metabolism with hypothermia and considerable experience with this technique has shown that a period of 8 minutes of circulatory occlusion at 30°C is well tolerated.

A previous communication from this centre (Orton and Morris, 1959) discussed a possible alternative method of prolonging the safe period of circulatory occlusion and presented the early results of the clinical application of deep halothane anaesthesia to open cardiac surgery using inflow occlusion at normal body temperature. This work was based on experimental and clinical observations which suggested that halothane administration was accompanied by a profound reduction in body oxygen consumption.

Claims have been made that at least two other factors are of importance in conferring protection on an animal submitted to circulatory occlusion. The first arose from the work of Crowell, Sharpe, Lambright and Read (1955) from which it was concluded that the administration of heparin to dogs before a period of circulatory arrest would enhance their chances of survival. This conclusion was questioned by Read, Lillehei and Varco (1956) who also pointed out that the incidence of survival and of neurological damage after circulatory occlusion are favourably influenced if the circulation is promptly re-established by vigorous cardiac massage. This would seem self-evident as it results in a total period of ischaemia which is usually much less than that which follows occlusion when massage is not used.

Our investigations are presented in some detail because they have led to a modification of the opinions expressed by some of us in a former publication and because our results differ from those obtained by Read, Lillehei and Varco (1956).

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I. FACTORS AFFECTING TOLERANCE TO CIRCULATORY OCCLUSION

Method

Eighty dogs, weighing from 5 to 25 kg were used in this study. Premedication always involved the use of atropine sulphate (0.6 mg). Morphine sulphate was added in some experiments in a dose of 1 to 2 mg/kg body weight and, in other experiments, in a dose of 4 mg/kg body weight. Anaesthesia was induced with 2.5 per cent thiopentone, an endotracheal tube was passed and anaesthesia was continued with nitrous oxide and oxygen, in equal amounts, using controlled respiration and a standard soda-lime canister. Occasional small supplements of thiopentone were needed in most experiments. A right thoracotomy was carried out by resecting the fifth rib. The azygos vein was ligated and tapes were passed around the superior and inferior venae cavae and threaded through rubber tubes. The pericardium was widely opened. In some experiments heparin was administered by intravenous injection in a dose of 2 mg/kg body weight or 10 mg/kg body weight 10 minutes before venous occlusion was commenced.

Venous inflow occlusion was effected by traction on the caval tapes. The periods of occlusion varied from 4 to 15 minutes: during this period the respirator was disconnected from the endotracheal tube. At the end of the period of occlusion the respirator was reconnected, the caval tapes were slowly released and, if there was not a prompt rise in arterial blood pressure, cardiac massage was begun. If the tone of the heart muscle was poor after 1 minute of cardiac massage 1 ml of 1 in 20,000 adrenaline was injected into the right atrium. In many cases ventricular fibrillation occurred and electrical defibrillation was necessary. If heparin had been given, protamine sulphate was given to counteract heparin activity, the dose being twice that of heparin.

In some experiments halothane was administered through a vaporiser,* in high concentration up to 4.5 per cent, for 15 to 20 minutes before the cavae were occluded, and this resulted in a fall in arterial blood pressure. When this reached 50 mm Hg halothane was discontinued and venous occlusion was commenced. Halothane was occasionally reintroduced after release of occlusion to lessen hypertension and tachycardia if these developed.

When the circulation had been satisfactorily re-established the chest wound was closed with a drain tube connected to a water seal drainage bottle. Continuous observations of the arterial blood pressure, the electrocardiogram and, occasionally the electroencephalogram were made throughout the experiment.

The 10 dogs submitted to occlusion during hypothermia were anaesthetized with intravenous pentobarbitone in sufficient dosage to control shivering while they were cooled down to an oesophageal temperature between 26.5°C and 30°C by the application of crushed ice in plastic bags. Rewarming was accomplished by the use of a standard laboratory table heater. In 5 dogs an atriotomy was made during the period of circulatory occlusion.

Criteria of Evaluation

(1) If the animal survived the procedure and continued in apparent good health without evidence of cerebral damage it was regarded as having tolerated the period of circulatory occlusion. This is indicated in the accompanying diagram (fig. 1) by an open rectangle placed above the base line.

(2) If the animal died after the procedure, or, if it survived and manifested any signs of severe or permanent neurological damage, then it was regarded as having not tolerated the procedure. These dogs were usually sacrificed during the first 3 days for humanitarian reasons. Both results are represented by a rectangle below the base line. The letters “N” and “C” respectively indicate that the dog survived for a time with evidence of neurological damage or that the dog succumbed from circulatory failure. Neurological damage was assessed clinically from evidence of blindness, ataxia, spasticity or even coma.

Results and Conclusions

A. Control study (fig. 1).

Group 1a. Of 7 dogs submitted to 4 minutes of circulatory occlusion without any premedication other than atropine 5 survived the procedure without evidence of neurological damage.

* British Oxygen Co. “Fluothane” vaporizer.
SURVIVAL AFTER CIRCULATORY OCCLUSION.

1. No drugs.

   1a. 4 min

   1b. 6 min

2. Heparin.

   2a. 8 min M.2,H.2.

   2b. 8 min M.2,H.10.

3. Morphine.

   3a. 8 min M.4,(s.c.).

   3b. 8 min M.4,(s.c.),H.2.

   3c. 8 min M.4,(s.c.),H.2.

4. Halothane.

   4a. 6 min M.2,H.2.

   4b. 8 min M.2,H.2.

   4c. 10 min M.2,H.2.

   4d. 15 min M.2,H.2.

   4b'. 8 min M.4,H.2.

   4c'. 10 min M.2,H.10.

5. Hypothermia. 26.5-30°C.

   5a. 10 min

   5b. 10 min & atriotomy.

Fig. 1

Schematic representation of occlusion experiments. Rectangles above the base line represent dogs who survived occlusion without evidence of neurological damage. The rectangles below the line represent dogs who died or were sacrificed because of severe neurological damage (N), or circulatory failure (C). M = morphine sulphate; H = heparin. The figures adjacent to these symbols refer to the dose of the drug in mg/kg body weight.
One dog was still blind after 3 weeks and was destroyed and another had impaired vision which recovered after a few days. There was no difficulty in cardiac resuscitation in any of these dogs.

Group 1b. Five dogs were submitted to 6 minutes of circulatory occlusion under similar conditions to those in group 1a. Of these, 1 survived with transient slight neurological damage, 2 survived with severe damage, and were destroyed, and 2 died of circulatory failure.

It is clear that even 4 minutes of circulatory occlusion is not tolerated by all dogs who are not protected by special techniques and that after 6 minutes of occlusion the incidence of severe damage is high.

B. Effect of heparin (fig. 1).

Ten dogs were submitted to periods of 8 minutes of circulatory occlusion using morphine sulphate (1 to 2 mg/kg body weight) premedication. Five of these (group 2a) were given heparin in a dose of 2 mg/kg body weight whilst the rest (group 2b) were given heparin in a dose of 10 mg/kg body weight. None of these 10 dogs survived without stigmata of neurological damage. This series of experiments was prompted by the observations of Crowell, Sharpe, Lambright and Read (1955) which led them to consider that heparin would protect an animal under the conditions of circulatory arrest. We cannot support this view and would agree with the conclusions of Read, Lillehei and Varco (1956) that heparin has no significant protective effect. Read, Lillehei and Varco also state that “interference with the circulation for 8 minutes resulted in 1 out of 18 dogs showing persistent brain damage”; it is clear that our results are in marked contrast to theirs.

We consider that a possible factor of significance was the high dose of morphine sulphate (4 mg/kg body weight) used by Read and his colleagues in their experiments.

C. Effect of morphine sulphate (fig. 1).

Group 3a. Eight dogs failed to recover completely from 8 minutes of circulatory occlusion when morphine sulphate was administered subcutaneously as pre-anaesthetic medication in a dose of 4 mg/kg body weight.

Group 3b. One dog, of a group of 5, survived 8 minutes of circulatory occlusion after pre-anaesthetic medication with morphine sulphate (4 mg/kg body weight) and the administration of heparin (2 mg/kg body weight).

Group 3c. Five dogs were given an intravenous injection of morphine sulphate (4 mg/kg body weight) 5 minutes before they were submitted to 8 minutes of circulatory occlusion. In all a profound hypotension resulted and, although they all survived the procedure, all manifested severe signs of neurological damage.

We were therefore unable to reproduce the results of Read, Lillehei and Varco, and were unable to demonstrate that morphine sulphate conferred significant protection on dogs submitted to 8 minutes of circulatory occlusion.

D. Effect of halothane.

Orton and Morris (1959), on the basis of certain theoretical considerations and a small laboratory experience, suggested that halothane, by reducing the metabolic rate, might protect animals from damage during circulatory occlusion. The results of thirty experiments in which the halothane-heparin technique has been used are presented in figure 1.

In these experiments, except where indicated, the dogs received pre-anaesthetic medication with morphine sulphate (1 to 2 mg/kg body weight) and were given heparin (2 mg/kg body weight) 10 minutes before venous occlusion for periods of 6, 8, 10 and 15 minutes (groups 4a, 4b, 4c, 4d).

Certain observations of interest were made during these experiments. Spontaneous ventricular fibrillation was encountered on only two occasions. The general pattern was that after 6 to 10 minutes of occlusion the heart rate slowed markedly and finally atrioventricular dissociation occurred. In 3 of 5 dogs occluded for 15 minutes (group 4d) asystole occurred after 11 to 12 minutes.

Cardiac resuscitation was usually possible but most of the surviving dogs showed evidence of severe neurological damage and were destroyed. As can be seen from the figure there were isolated survivors, without evidence of neurological damage after periods of occlusion of 6, 8, 10 and 15 minutes. Unfortunately these occurred preponderantly in our early laboratory experience.
If groups 4b and 4c are studied it is clear that increasing the morphine dosage to 4 mg/kg body weight or the heparin dosage to 10 mg/kg body weight made no significant difference to these results.

Finally it should be clearly stated that the halothane-heparin technique does not confer sufficient protection to make occlusion of the dog's circulation for 6 minutes a safe procedure.

E. Effect of hypothermia.

The tolerance of experimental animals to circulatory occlusion under conditions of hypothermia is far better documented than is the tolerance of the same animals to occlusion at normal temperatures. We do not wish to add to this already voluminous literature.

In our laboratory occlusion of the dog's circulation for 10 minutes at 26.5°C to 30°C was well tolerated by 5 dogs (group 5a) and 4 of 5 dogs who were occluded for 10 minutes, during which time an atriotomy was performed, also survived (group 5b).

Clinical Experiences

The technique and results of the first 14 patients operated on with the halothane-heparin technique were reported by Orton and Morris (1959). Twenty-eight patients have now undergone direct vision open heart surgery using this technique.

Valvular pulmonary stenosis.

In 11 cases of valvular pulmonary stenosis there have been no deaths. The times of circulatory occlusion have ranged from 1 min 45 sec to 2 min 40 sec.

In one case of pulmonary stenosis associated with hypoplasia of the right ventricle and atrial septal defect death occurred suddenly 18 hours after operation. The pulmonary stenosis had been inadequately relieved and the atrial septal defect had been completely closed. This patient had his circulation occluded for 5 min 15 sec. A typical foramen ovale type of defect was found and closed by direct suture. The operation was uneventful but on recovery from the anaesthetic the patient manifested signs of cerebral irritation which persisted for 12 hours. She then made a prompt and complete recovery from this episode and left hospital 3 weeks later with no evidence of neurological damage.

Aortic stenosis.

Thirteen cases of aortic stenosis have been submitted to open operation using this technique. The periods of occlusion ranged between 1 min 45 sec and 3 min 15 sec. Three children with congenital aortic stenosis have already been cited by Orton and Morris (1959). The remaining 10 cases have been adults with calcified aortic stenosis. There have been 3 deaths in this group. We have attributed death to inadequate relief of the aortic stenosis in 2 of these cases and to the creation of aortic incompetence in the third. Nick's of Sydney (1959) has reported successful results in operations on 13 of 14 cases of aortic stenosis.

Atrial septal defect.

Three cases of atrial septal defect have been submitted to operation using the halothane-heparin technique. Two of these have been described in detail in an earlier publication. Our experience with the third case detailed below has caused us to reverse the opinion expressed by Orton and Morris (1959)—"it is considered that, under these circumstances, periods of circulatory arrest of at least 5 minutes, and probably longer, can be achieved with safety."

J.B., a 17-year-old girl had the typical features of an atrial septal defect with a large left to right shunt. This was confirmed by cardiac catheterization. She was submitted to open operation for closure of the atrial septal defect using the halothane-heparin technique during which her circulation was occluded for 5 min 15 sec. A typical foramen ovale type of defect was found and closed by direct suture. The operation was uneventful but on recovery from the anaesthetic the patient manifested signs of cerebral irritation which persisted for 12 hours. She then made a prompt and complete recovery from this episode and left hospital 3 weeks later with no evidence of neurological damage and with signs suggesting that her atrial septal defect was completely closed.

Despite the successful end result we feel that this experience was a salutary indication that, under these circumstances, 5 minutes must be regarded as the upper limit of tolerance to circulatory occlusion in the normothermic human subject.

II. THE CIRCULATORY EFFECTS OF HALOTHANE

The administration of moderate to high concentrations of halothane to man or dog is accompanied by a progressive fall in systemic arterial blood pressure. Two series of experiments were carried out in order to determine whether this hypotension resulted from cardiac depression or from peripheral vasodilatation or both.

Right Ventricular Performance During the Administration of Halothane

Method.

Six dogs, the weights of which ranged from 15 to 20 kg, were used in this study. Premedica-
Experimental arrangement used for study of right ventricular function. Venous blood siphoned from both venae cavae (S.V.C., I.V.C.) drains into a reservoir which is emptied at a series of known rates of flow by a pump which returns the blood to the right atrium (R.A.) through a cannula introduced through the azygos vein (Az.V). Pressures are continuously recorded from the right atrium and the pulmonary artery (P.A.).

Anaesthesia consisted of morphine sulphate (1 mg/kg body weight) and atropine sulphate (0.6 mg). Anaesthesia was induced with thiopentone and continued using nitrous oxide and oxygen in equal amounts with constant volume positive pressure ventilation through an endotracheal tube. Small supplements of thiopentone were used during the course of the experiment. The right pleural cavity was opened by excising the fifth rib. The azygos vein was then dissected free and tapes were passed around the superior and inferior venae cavae. The pericardium was widely opened and two wide-bore cannulae were introduced through the atrial appendage. These were guided into the superior and inferior venae cavae respectively whilst a third shorter cannula was introduced through the azygos vein and directed into the cavity of the right atrium (fig. 2). The two caval cannulae were used to siphon the returning venous blood to a reservoir which, in turn, was emptied by a pump which propelled the blood through the inflow cannula back into the right atrium. When the tapes around the cavae were tightened snugly around the cannulae the whole of the venous return to the heart, with the exception of the coronary return, was forced to traverse this extracorporeal circuit. Before each experiment the pump* was carefully calibrated to produce a series of known rates of flow which ranged from 40 ml/kg/min to 200 ml/kg/min. It has been found that these flows are reproducible with an error of less than 5 per cent. In other words, a preparation was constructed which enabled the operator to present the intact dog's heart with a graded series of known rates of

cardiac inflow. Fine polyethylene catheters were introduced into the right atrium, the pulmonary artery and the aorta and these were connected to Cambridge electromanometers. Full pulse tracings and electronically integrated mean pressures were continuously monitored and recorded whilst the rate of cardiac inflow was changed by adjustment of the pump to a series of predetermined rates. The pressure readings used in the calculations were those obtained after the system had reached equilibrium following a change in flow rate. This was evidenced by stable pressures and a constant volume in the venous reservoir. In most experiments equilibrium was reached 2 minutes after a change in rate of inflow. Care was taken to ensure that tricuspid regurgitation was not present by constant reference to a fast pulse tracing. The pressure responses to at least five different rates of inflow were used to construct a "control" right ventricular function curve.

At this stage the preparation was maintained at a constant flow rate and a halothane vaporizer* was fitted into the anaesthetic circuit so that concentrations of 0.5 to 2.5 per cent halothane could be added to the nitrous oxide and oxygen mixture. After 15 minutes of halothane administration a stable situation was reached and a further series of pressures was recorded in response to the same graded series of rates of cardiac inflow. From these data a second right ventricular function curve was constructed and compared with the control curve.

Right ventricular minute work was calculated from the following formula:

\[ W_{\text{min}} = \frac{(P.P.A. - P.R.A.)F}{100} \]

where \( W_{\text{min}} \) = minute-work of right ventricle (gram-metres)

\( P.P.A. \) = mean pulmonary artery pressure (cm water)

\( P.R.A. \) = mean right atrial pressure (cm water)

\( F \) = minute volume (ml)

It should be noted that the coronary venous return to the right atrium has not been included in the minute volume, nor has the acceleration component of right ventricular work been included in the calculations (Sarnoff and Berglund, 1954).

**Results.**

The results of these experiments are presented as right ventricular function curves which relate the minute work of the right ventricle to its filling pressure or mean atrial pressure. The normal curve is found to be almost a straight line with a steep gradient (Stirling, Stanley and Lillehei, 1957). Impairment of right ventricular function is indicated by a shift of the curve to the right and by a flattening of the curve at higher right atrial pressures. Consistent results were obtained in all six experiments and two examples of these are illustrated in figure 3. In all cases the administration of halothane resulted in an impairment of right ventricular function. The degree of impairment was proportional to the concentration of halothane in the ventilating gases. When concentrations of greater than 1.5 per cent were used the impairment of ventricular function was severe.

**The Effects of Halothane Administration on the Peripheral Circulation.**

Awareness of the depressant effect of halothane on ventricular performance prompted us to design experiments in which the cardiac and peripheral actions of halothane could be divorced.

**Method.**

In a series of three experiments the preparation already described for the study of right ventricular function was used to submit a dog to a constant rate of cardiac inflow (100 ml/kg/min). Mean pressures in the aorta, pulmonary artery and right atrium were continuously recorded. After a period of 15 minutes, during which the dog was ventilated with nitrous oxide and oxygen in equal proportions, halothane was introduced into the gas mixture and its concentration rapidly increased to 2 per cent. A steadily progressing fall in mean aortic pressure was observed and this was accompanied by a progressive rise in the mean pressures in the pulmonary artery and right atrium. The results of one of these experiments are illustrated in figure 4. It is assumed, but not established, that the cardiac output was main-

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* British Oxygen Company "Fluothane" Vaporizer. The authors do not wish to infer that the concentrations referred to in this text are absolutely accurate.
HALOTHANE AND CIRCULATORY OCCLUSION

HALOTHANE - RIGHT VENTRICULAR FUNCTION.

Right ventricular function curves obtained during the administration of halothane in concentrations of approximately 1 per cent (left) and 2 per cent (right). Both curves, when compared with their respective control curves, show significant impairment of ventricular function.

EFFECT OF HALOTHANE - CONSTANT CARDIAC INFLOW.

Changes in pressure recorded in the femoral artery (F.A.), pulmonary artery (P.A.) and right atrium (R.A.) before and during the administration of 2 per cent halothane to a dog with a fixed rate of cardiac inflow of 100 ml/kg body weight/min.
maintained constant during this experiment and therefore that the changes in aortic pressure reflect a progressive fall in systemic vascular resistance.

In another series of experiments involving 5 animals total cardiopulmonary bypass was established in the standard fashion using a rotating disc type of oxygenator* and sigmamotor pumps. The perfusion rate for each dog was kept constant throughout the experiment but the rates of flow used in the five experiments varied from 50 to 108 ml/kg body weight/min. The ventilating gas in the oxygenator consisted of 95 per cent oxygen and 5 per cent carbon dioxide and was delivered at a rate of 10 l./min. A halothane vaporizer was inserted in the gas line to the oxygenator but halothane was not administered until the animal had been on bypass for 15 to 20 minutes and had been in a stable state for at least 10 minutes.

Commonly the aortic pressure and the volume in the extracorporeal circuit stabilized after 5 to 8 minutes. During this stable period samples of arterial and venous blood were taken from the lines of the oxygenator for determination of oxygen content by the method of Peters and Van Slyke.

Halothane was then introduced with the ventilating gases into the cylinder of the oxygenator and serial measurements of the aortic blood pressure and the volume in the extracorporeal circuit were made. After a period of 15 to 20 minutes of halothane administration further blood samples were taken for oxygen determination. Halothane was then discontinued and after a further 20 minutes further blood samples were taken.

Results

In all experiments the administration of halothane resulted in a progressive fall in aortic pressure and a progressive fall in the volume of blood in the extracorporeal circuit. The significance of the former observation is that halothane caused a fall in systemic vascular resistance; the latter observation indicates that the volume of blood in the dog increased during halothane administration but gives no indication of the distribution of the blood in the animal. When halothane was discontinued these parameters returned to the control levels in a period of 10 to 15 minutes. Figure 5 is an illustration of the blood pressure changes in a typical experiment.

It was concluded from these experiments that halothane, when administered in high concentration, produces a profound depression of ventricular function and also a profound reduction in systemic vascular resistance.

III. THE EFFECT OF HALOTHANE ON THE OXYGEN CONSUMPTION OF THE DOG DURING TOTAL CARDIOPULMONARY BYPASS

Severinghaus and Cullen (1958) observed that the induction and maintenance of anaesthesia with halothane in human subjects was accompanied by a reduction in total body oxygen consumption. The factors responsible for this are many and include reduced respiratory, muscular and cardiac activity. To exclude these variables, in an attempt to determine the effect of halothane on the rate of metabolism of the body tissues in general, a series of five experiments was undertaken in which the total body oxygen consumption of the dog, under the circumstances of total cardiopulmonary bypass, was determined before, during and after the addition of halothane to the ventilating gases of the oxygenator. The experimental method has already been described in the previous section.

The oxygen consumption of an animal during bypass is influenced by a number of factors. Two of these, blood flow rate and temperature, were carefully controlled during these experiments. Oxygen consumptions were calculated using the Fick principle; the flow rate was controlled at a known level and the arteriovenous oxygen differences were measured. The results are presented in table I. For purposes of com-

* Kay-Cross oxygenator. Pemco Inc., Cleveland, Ohio.
EFFECT OF HALOTHANE ON ARTERIAL PRESSURE.

Fig. 5
Changes in aortic pressure of a dog on total cardiopulmonary bypass before, during and after the administration of 2 per cent halothane. The perfusion was maintained at a constant level of 110 ml/kg body weight/min.

Comparison the results have been expressed in terms of millilitres of oxygen consumed per minute per kilogram of body weight. They reveal no consistent and significant effect of halothane administration on the oxygen consumption of the dog during cardiopulmonary bypass.

DISCUSSION

Unsupported circulatory occlusion is now an established technique allowing direct vision intracardiac surgery. Curiously the limits of tolerance of both the experimental animal and the human subject to circulatory occlusion under the circumstances of general hypothermia have been extensively investigated and well documented whilst tolerance at normal body temperature is less well defined. The basic hypothesis that the time of permissible circulatory occlusion is inversely proportional to the metabolic rate, is now fairly well established. Thus, while the limit of permissible circulatory occlusion at a body temperature of 38°C is probably about 4 minutes, lowering the temperature to 30°C allows this time to be doubled at least. At present the induction of general hypothermia seems to be the only practical technique whereby the resting metabolic rate of the anaesthetized subject may be significantly lowered. We must look to the researches of the biochemist and the pharmacologist for alternative methods of achieving this end.

The attraction of techniques of venous inflow occlusion lies in their relative simplicity whilst their main disadvantage lies in the fact that the time of the intracardiac procedure is strictly limited. Their beneficial application to intracardiac surgery is dependent on the exhibition of sound surgical judgment based on experience which has been intelligently interpreted.

We have found the clinical technique described by Orton and Morris (1959) to be satisfactory, enabling the surgeon to perform pulmonary or aortic valvotomy. Indeed three cases of atrial septal defect have been successfully managed by this technique although this is no longer recommended for the reasons already stated in detail.

The factors in this success proved difficult to evaluate. We have demonstrated in the laboratory animal that neither halothane nor heparin nor morphine has any marked effect in prolonging the safe period of circulatory occlusion. Although halothane effects a reduction in total body oxygen consumption, it does not appear to
produce this by any specific action other than the reduction in cardiac, respiratory and muscular work which follows the induction of deep anaesthesia. The attractive hypothesis of Crowell et al. (1955) that the damage incurred during circulatory occlusion may result, in part, from intravascular thrombosis during circulatory stasis receives no support from our work although, on a priori grounds, it would seem reasonable to administer heparin before circulatory occlusion if this is not attended by any increased morbidity. Clearly an important factor in our success has been that human tolerance to circulatory occlusion at normal body temperature has been underrated.

The hypotension which accompanies deep halothane anaesthesia has been of inestimable value during the performance of aortic valvotomy. The side excluding clamp is applied to a relatively flaccid aorta before valvotomy is carried out. After valvotomy, when the clamp is reapplied, the aortic blood pressure may be rapidly controlled by the exhibition of further halothane should hypertension develop following circulatory occlusion. We feel that this endows the technique with a considerable safety factor. Apart from these technical considerations it is possible that moderate hypotension immediately following circulatory occlusion is, in itself, beneficial in so far as the potential work load of the heart is reduced.

SUMMARY

Some of the factors affecting the tolerance of the dog to circulatory occlusion at normal temperature have been studied.

The limit of safe circulatory occlusion in the dog was found to be less than 4 minutes.

The administration of morphine and of heparin did not significantly prolong the safe period of occlusion.

The use of the halothane and heparin technique did not significantly improve the results, although occasional survivals after periods of up to 15 minutes of occlusion were obtained.

The hypotension of deep halothane anaesthesia has been analyzed. It was found that halothane produces a depression in ventricular function and also results in a profound reduction in systemic vascular resistance.

Halothane was found to have no significant effect on the oxygen consumption of the dog during total cardiopulmonary bypass.

The use of circulatory occlusion for open heart surgery at normal body temperature is discussed in relation to a clinical experience with 28 cases using the halothane-heparin technique.

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