CORONARY ARTERY BLOOD FLOW IN THE HALOTHANE-
DEPRESSED CANINE HEART

BY

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SUMMARY

The effects of halothane in inspired concentrations of \( \frac{1}{2} \) to 3 per cent have been studied in Labrador dogs, using electromagnetic flow probes on the circumflex coronary artery, pulmonary artery and right femoral artery. Pressures were monitored from the central aorta and right atrium. Blood samples were taken from the aorta, coronary sinus and right atrium. Oxygen utilization and vascular resistances were calculated. The results indicate that myocardial blood flow falls in proportion to myocardial work and oxygen utilization.

Arterial hypotension has proved to be especially pronounced during the administration of halothane, and numerous reports expressing different opinions about the cause have been presented since the introduction of this anaesthetic in 1956. According to many authors the hypotension is combined with a reduction in cardiac output (Severinghaus and Cullen, 1958; Mahaffey et al., 1961). According to others a reduction of peripheral vascular resistance is the main cause (Raventós, 1956; Payne, 1963). A combination of causes was suggested by Beaton (1959) and Deutsch and associates (1962). According to Wyant and associates (1958) the administration of moderate concentrations of halothane causes hypotension owing to peripheral vasodilatation but the hypotension produced by overdoses of the anaesthetic was probably due to a myocardial impairment. Gordh (1964a, b), using the pericardium as an air plethysmograph for cardiometry in the rabbit, showed a dilatation of the heart which was attributed to a negative inotropic effect on the myocardium. Bagwell (1965), Saito and associates (1966) and Merin (1969) have demonstrated a fall in coronary blood flow with halothane anaesthesia. The present study was designed to estimate continuously and simultaneously, cardiac function, coronary blood flow and femoral blood flow.

METHOD

Fourteen Labrador dogs, weighing 17–24 kg were used in this study. With no prior premedication they were anaesthetized with sodium thiopentone (20 mg/kg) and ventilated with nitrous oxide and oxygen (ratio 2:1) through an endotracheal tube using a modified Starling pump. The pump rate was 28 strokes/min and the stroke volume was set at 10 ml/kg with an increase of 50 ml after thoracotomy. Further small adjustments were made to maintain the arterial \( \text{Pco}_2 \) at 40 mm Hg. Halothane was administered, using a Fluotec vaporizer and the inspired gases were continuously sampled through a Hook & Tucker ultraviolet analyzer. An intravenous infusion of 0.9 per cent sodium chloride was administered at a rate of approximately 100 ml/hour to replace insensible fluid loss. Muscle relaxants were not used. Oesophageal temperature was recorded so that adjustments could be made when necessary. Nylon cannulae were placed in the central aorta, by way of the left femoral artery and in the right atrium by way of the left jugular vein, and pressure recorded through Statham P239 transducers. A Cournand catheter was introduced via the left jugular vein to the coronary sinus under X-ray control and placed 4 cm into the great cardiac vein. The electrocardiogram was monitored, using needle electrodes.

Through a left lateral thoracotomy, previously calibrated Biotronex series 1000 flow probes of the appropriate size were placed around the
pulmonary artery, to measure cardiac output (Weaver, Bailey and Redding, 1970), and the circumflex coronary artery to estimate myocardial blood flow (Bailey, Redding and Weaver, 1970). A third probe was placed on the right femoral artery. Snares to produce zero flow were placed on the circumflex coronary artery and femoral artery, distal to the flow probes. Recordings were made on an eight-channel Sanborn direct writer, series 315. At intervals, blood samples from the coronary sinus, right atrium and central aorta were taken for haematocrit, haemoglobin content, and analysis of blood-gases using the Astrup microtechnique and the Siggaard-Andersen nomogram and an oxygen electrode. Po2 was converted to percentage saturation using the appropriate corrections for temperature (Kelman and Nunn, 1966), pH and base excess. Using haemoglobin content, the quantity of oxygen/100 ml blood was calculated for the three blood samples. It is appreciated that right atrial blood may not always be representative of mixed venous blood but samples compared favourably with right ventricular samples which were taken from four of the dogs.

It took between 60 and 90 minutes to prepare the dogs for study. Only when a satisfactory stable state had been achieved for at least 30 minutes were experiments carried out. Two dogs were excluded from the series because of blood loss. After satisfactory baseline readings, halothane was administered for a 15-minute period in concentrations of 0.5, 1, 2, 2.5 and 3 per cent v/v. Recovery was observed for up to 40 minutes after turning off the halothane. Only if blood pressure, right atrial pressure, cardiac output, coronary and femoral flow returned to previous control levels was the animal subjected to a different halothane concentration for a further 15-minute period. From the data obtained the following measurements were recorded or derived for analysis: mean aortic blood pressure; mean right and left atrial pressure; cardiac output; mean circumflex coronary blood flow; mean femoral artery blood flow; coronary vascular resistance; femoral vascular resistance; total body vascular resistance; quantity of oxygen used by heart muscle and percentage utilization; quantity of oxygen used by total body and percentage utilization; left ventricular stroke volume; left ventricular work and left ventricular power.

RESULTS

The average weight of the dogs used was 20 kg. In order to plot the results graphically with a meaningful statistical analysis, corrections for weight were made where necessary so that all referred to a standard 20-kg dog. A full table of numerical results is not included in this paper because of its size.* Mean values are expressed graphically with their standard deviations. The significance, derived from the Student t test, of the least significant part of each graph is quoted. The mean values of the maximum change in each parameter are also recorded as a percentage of the baseline values. The number of readings taken at the various points on the graphs are recorded in table I.

<table>
<thead>
<tr>
<th>Recovery time from halothane (% recovery)</th>
<th>0.5</th>
<th>1.0</th>
<th>2.0</th>
<th>2.5</th>
<th>3.0 and over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halothane (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>1.0</td>
<td>2.0</td>
<td>2.5</td>
<td>3.0</td>
<td>5 10 15 20</td>
</tr>
<tr>
<td>No. of results for each group</td>
<td>5</td>
<td>7</td>
<td>10</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

Although observations were made up to 40 minutes after halothane was discontinued, recovery was complete by 20 minutes in 9 of the 11 dogs observed and no further changes occurred beyond this point. Calculated values, corrections for weight and statistical analysis were carried out on an IBM 1800 computer. The Snedecor Variance Ratio (F test) of the results and the baseline values were computed, after applying Bessel's correction for small sample numbers. Where this was not significant at the 1% per cent level the Student t test was applied (Moroney, 1951). Mean and control values for the same animals were compared.

Figure 1 shows the typical effect of halothane as recorded on the chart. Figures 2, 3, 4, 5 show the results expressed graphically.

DISCUSSION

In a concentration of 0.5 per cent halothane had little cardiovascular effect apart from a reduction in heart rate (fig. 2). This has been previously shown (Shimosato, Li and Etsten, 1963; Price...

* Copies of data can be obtained on application to the authors.
and Price, 1966). In concentrations greater than this there is progressive depression of myocardial function seen in falling heart work, cardiac output and blood pressure (figs. 2, 3). Although a decrease in heart rate and fall in total peripheral vascular resistance does occur (fig. 4), the major effect appears to be on the heart itself and its progressive failure is underlined by a marked rise in right atrial pressure and an observed increase in heart size as emptying in systole deteriorates. Femoral artery and coronary artery blood flow fall by the same order as the blood pressure, there being little change in vascular resistance, particularly in the coronary artery. The quantity of oxygen used per minute by the myocardium falls by the same amount as the coronary artery blood

**FIG. 1**
The typical effect of halothane as recorded on the chart.

**Note:** The phasic pulmonary artery flow calibration was 0-6.7 L/min. Circumflex coronary artery flow calibration is identical with that of femoral artery flow.
The effects of halothane on the canine heart

The graphical representation of the changes in myocardial activity at different halothane concentrations.

Left ventricular work in Joules = (Mean aortic pressure - Mean left atrial pressure) \times \text{Cardiac output} \times F.

Left ventricular power in Watts = \text{Left ventricular work/second}.

Left ventricular stroke work in Joules = (\text{Mean aortic pressure} - \text{Mean left atrial pressure}) \times \text{Stroke volume} \times F.

(F = 1.36 \times 0.981 \times 10^{-4} \text{ and is the conversion factor for c.g.s. units.})
THE EFFECT OF HALOTHANE ON VASCULAR RESISTANCE

Total Body Peripheral Vascular Resistance
Fall to 50% of Control
0.001 < p < 0.01
Femoral Artery
Vascular Resistance,
Fall to 60% of Control
0.01 < p < 0.05
Coronary Artery
Vascular Resistance,
Fall to 70% of Control
0.01 < p < 0.05

Changes not significant
p > 0.05

PERIPHERAL RESISTANCE =

(Mean aortic pressure
—Right atrial pressure)
×100 × 22.2
(where 22.2 is a factor to
convert mm Hg/l./min to
c.g.s. units).

FIG. 4
Changes in peripheral resistance, pH and base deficit.
(Early experiments suggested parallel changes in these parameters. Subsequently, pH and base changes were found not to be significant.)

FIG. 5
The effect of halothane on oxygen utilization by the whole animal and by the myocardium. This is expressed as a percentage of available oxygen and as an absolute figure in ml of oxygen used per minute, which takes into account perfusion.
BLOOD FLOW IN THE HALOTHANE-DEPRESSED CANINE HEART

flow. There was no significant change in arterial oxygen saturations while coronary sinus blood oxygen saturations rose, reducing the arteriovenous oxygen difference (fig. 5). These findings are contrary to those of Saito and associates (1966) who found increases in coronary arteriovenous oxygen difference. Eberlein (1965) demonstrated decreasing coronary blood flow with increasing halothane concentrations, but saw no change in coronary sinus oxygen saturation and felt that there had been a concomitant decrease in oxygen consumption.

The recovery phase of our experiments gave no indication of an oxygen debt. Oxygen consumption returned to the control level over 20 minutes as did the arteriovenous oxygen difference. Bagwell (1965) and Merin (1969) were unable to find evidence of excess lactate production in dog coronary sinus blood under halothane anaesthesia. Merin actually demonstrated a change of excess lactate from positive (indicating anaerobic metabolism) to negative (indicating aerobic metabolism). The concept of excess lactate as an indicator of anaerobic metabolism and hypoxia was put forward by Huckabee (1961) but has since been questioned by Olsen (1963). Using mouse heteroploid monolayer cultures, Fink and Kenny (1968) showed that in the presence of halothane, glucose uptake and lactate output increase and the oxygen consumption is inhibited. At whatever level halothane interferes with the myocardium, it would seem that compensation by anaerobic metabolism is slight if it occurs at all.

Total body oxygen consumption fell by 60 per cent (half the fall shown in coronary blood) and like the heart, recovery occurred over 20 minutes with no increase in demand. There was no significant change in pH or base deficit but if the anaesthetic was given for longer periods of 30 minutes or more a fall in pH and increase in base deficit was seen, suggesting a degree of tissue hypoxia due either to low flow and pressure, the direct effect of halothane or a combination of both.

Graphs recording the percentage oxygen utilization of available oxygen derived from blood-gas estimations alone are included in the results. There was a 20 per cent fall in percentage utilization in the coronary blood and no significant change in the systemic blood. Systemic oxygen utilization gives a guide to the state of the animal during the experiment, for surgical shock associated with blood loss will give rise to significant increases in the percentage oxygen utilization. Further evidence of stability of the prepared dog is that the haematocrit and haemoglobin estimations fell by no more than 12 per cent in any animal under study.

Since this work was submitted for publication, similar experiments were undertaken on two dogs anaesthetized solely with halothane, nitrous oxide and oxygen. The results fell within the limits of those reported here. It is considered, therefore, that induction of anaesthesia with thiopentone had little or no effect on the circulatory changes associated with halothane inhalation.

A thoracotomy was necessary in each of the acute experiments described. Similar effects of halothane on the heart have been found in two dogs with implanted aortic flow probes investigated two weeks after full recovery from surgery.

CONCLUSIONS

The most significant effect of halothane on the canine cardiovascular system is seen to be on the myocardium itself. The fall in coronary artery blood flow is equal to the fall in femoral artery flow and proportional to the decrease in blood pressure and myocardial work. The amount of oxygen used by the heart also falls by the same amount as the blood flow but oxygen availability was always found to be adequate. The amount of oxygen used by the whole body fell, but by only half as much as the fall seen in oxygen used by the heart.

ACKNOWLEDGEMENTS

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REFERENCES


FLUX SANGUIN DANS LES ARTERES CORONAIRES DU COEUR DE CHIEN, DEPRIME PAR HALOTHANE

SOMMAIRE

Les effets d'halothane en concentrations de 0,5 à 3 pourcent ont été étudiés chez le chien thoracotomisé, en utilisant des sondes électromagnétiques du flux dans l'artère fémorale droite. Les pressions ont été enregistrées dans l'aorte centrale et l'oreillette droite. On a prélevé des échantillons de sang de l'aorte, du sinus coronarien et de l'oreillette droite. La consommation d'oxygène et la résistance vasculaire ont été calculées. Les résultats indiquent que le flux sanguin du myocarde se réduit en proportion au travail du myocarde et à sa consommation d'oxygène.

CORONARDURCHFLUSS DES HUNDEHERZENS NACH DEPRESSIONEN MIT HALOTHAN

ZUSAMMENFASSUNG


FIFTH INTERNATIONAL CONGRESS ON ANAESTHESIOLOGY

The Congress will take place in Kyoto, Japan, from October 2 to 8, 1972. The Belgian Professional Association of Specialists in Anaesthesia and Reanimation is to organize a three-weeks group tour from Brussels to the Far East, open to all anaesthetists of Western Europe and their families. The journey can thus be accomplished on the most advantageous terms. Booking is done on guaranteed periodical payments in advance. For further particulars apply to

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