The Relationship between Physiologic Shunt and Cardiac Output in Dogs under General Anesthesia

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Physiologic shunts during halothane-oxygen and ether-oxygen anesthesia were compared and their relationships to cardiac output analyzed. A-aD_{O_2} showed no significant change one hour after the start of halothane or ether anesthesia. The percentage of physiologic shunt during halothane anesthesia decreased significantly compared with the preanesthetic value. During ether anesthesia, however, no significant change in the physiologic shunt was observed.

Of the factors likely to cause a difference between halothane and ether, tidal volume was constant and Pa_{CO_2} and intratracheal pressure showed no significant differences. After halothane the cardiac index decreased markedly, but after ether it did not change significantly. A significant positive correlation was found between percentage of physiologic shunt and cardiac index regardless of the agent used.

AN INCREASE in physiologic shunt during general anesthesia has been observed by several investigators.[1-8] Major factors responsible for this change have been considered to be tidal volume, intratracheal pressure and the anesthetic agent itself.[1-8] Recently, it was suggested that the physiologic shunt may also be influenced by Pa_{CO_2} and cardiac output.[9-10] In addition, most calculations of physiologic shunt during anesthesia have been based on the measurement of the alveolar–arterial oxygen tension difference (A-aD_{O_2}) and on the assumption that the arterial–mixed venous oxygen content difference (a-$\bar{v}C_{O_2}$) is constant. It has been suggested, however, that the a-$\bar{v}C_{O_2}$ may change during anesthesia, especially when cardiac output is altered.[18]

The present study was undertaken, therefore, to evaluate the effect of change in cardiac output on the physiologic shunt during general anesthesia in dogs. The physiologic shunt was determined by measuring A-aD_{O_2} and the actual value of a-$\bar{v}C_{O_2}$. Halothane and ether were chosen for the study because they are believed to have different effects on cardiac output.[11-12]

Materials and Methods

Fourteen mongrel dogs weighing 10–18 kg were premedicated with 1 mg of atropine sulfate intramuscularly 30 minutes prior to induction of anesthesia. Anesthesia was induced with halothane, using the open-drop technique, and the tracheas were intubated with cuffed endotracheal tubes.

All dogs lay on their backs throughout the study. Light halothane anesthesia (0.3–0.5 per cent) was maintained during the preparations. A femoral artery was cannulated with a polyethylene catheter attached to a three-way stopcock to facilitate blood sampling and measurement of cardiac output. A femoral vein was cannulated for injection and infusion. A cardiac catheter was inserted through the jugular vein into the pulmonary artery under radiologic control for sampling mixed venous blood and injecting dye for measurement of cardiac output. Mixed venous blood samples were collected by the hydrostatic pressure from the catheter. The animals were heparinized by intravenous administration of heparin, 3 mg/kg, repeated after one hour.

At the completion of these preparations, halothane was discontinued and the awake

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condition, as confirmed by return of the ciliary reflex, re-established. Succinylcholine chloride, 30–40 mg, was then injected intramuscularly and the lungs were ventilated with a Harvard respirator using a nonrebreathing method at a rate of 25 per minute and a tidal volume 1.7 times larger than the value given by the Kleinman-Radford nomogram * for the dog. The tidal volume used was considered adequate, since it was possible to maintain Pa_{CO_2} between 35 and 39 mm Hg during the control period. Additional doses of succinylcholine chloride were injected intramuscularly when necessary.

Control measurements were made ten minutes after hyperinflation of the lungs by clamping the outflow from the pump during three breaths. This hyperinflation was performed to eliminate atelectasis, which might have occurred during the preparation period. Blood samples were taken from the femoral and pulmonary arteries and analyzed for oxygen saturation immediately. Oxygen tension, *p*H and hemoglobin concentration were also determined without delay. Intratracheal pressure was measured simultaneously with a pressure transducer (Nihon Kohden Co., Tokyo, Japan) and recorded on a Multiplex Monitor–Recorder (RM-150, Nihon Kohden Co., Tokyo). Cardiac output was determined by the dye-dilution method, using a densitometer (Model EN-6, Erma Optical Works Ltd., Tokyo, Japan) with indocyanine green as the indicator. Esophageal temperature was recorded electrically throughout the study.

Either 1.5 per cent halothane in oxygen or 5 per cent ether in oxygen was administered for an hour using a calibrated vaporizer (Vapor: Dräger Werk, Lübeck, West Germany). After this, anesthesia was discontinued and ventilation maintained with pure oxygen until the awake condition was re-established. The other anesthetic was then administered for an hour after hyperinflation of the lungs as described. The order of administration of the anesthetic agents was alternated.

Measurements were made four times during the study, as follows:

before the start of the first experimental period of anesthesia
after one hour of anesthesia
after restoration of the awake condition
at the end of the second experimental period of anesthesia

Concentrations of halothane and ether employed in this experiment were within the range used in clinical anesthesia. Samples of halothane and ether vapor were drawn with a syringe at end-expiration from a polyethylene catheter inserted at the distal tip of the endotracheal tube and analyzed with a gas chromatograph (Ohkura Co., Tokyo, Japan).

Calculations

Alveolar oxygen tension was calculated according to the formula:

$$P_{A_{O_2}} = P_B - P_{H_2O} - P_{A_{CO_2}} - P_{anesthetic\ agent}$$
(assuming $P_{A_{CO_2}} = Paco_2$)[9,12]

where

$P_{A_{O_2}}$ = alveolar oxygen tension
P_B = barometric pressure
P_{H_2O} = vapor pressure of water
$P_{A_{CO_2}}$ = alveolar carbon dioxide tension
$Paco_2$ = arterial carbon dioxide tension
$P_{anesthetic\ agent}$ = partial pressure of anesthetic agent

This formula may be used since the effect of changes in respiratory exchange ratio becomes minimal at high oxygen concentrations. At oxygen tensions above 300 mm Hg, hemoglobin is 100 per cent saturated; the percentage of physiologic shunt was, therefore, calculated by the modified shunt equation [8-9]:

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{\alpha \cdot (P_{A_{O_2}} - Pa_{O_2})}{Ca_{O_2} - C\bar{v}_{O_2} + \alpha \cdot (P_{A_{O_2}} - Pa_{O_2})}$$

where

$\frac{\dot{Q}_s}{\dot{Q}_t}$ = proportion of cardiac output through right-to-left shunt
Pa_{O_2} = arterial oxygen tension
Ca_{O_2} = arterial oxygen content
$C\bar{v}_{O_2}$ = mixed venous oxygen content
α = solubility coefficient for oxygen in blood (vol per cent/mm Hg)

* This nomogram is attached to the Harvard respirator.

TABLE 1. Parameters Measured During the Control Period and One Hour after the Start of Halothane and Ether Anesthesia*

	Body Wt. (kg)	VT/BW (ml/kg)	P_{ACO_2} (mm Hg)	P_{AO_2} (mm Hg)	P_{aO_2} (mm Hg)	$A\text{-}aD_{O_2}$ (mm Hg)	C_{aO_2} (ml/100 ml)	$C_{\bar{v}O_2}$ (ml/100 ml)	$C_{aO_2}\text{-}C_{\bar{v}O_2}$ (ml/100 ml)	$\dot{Q}_T/\dot{Q}_I \times 100$ (per cent)	CI (l/min/m²)	Intratracheal pressure (cm H_2O)
Control	13.8 ±2.7	10.6 ±1.1	36.8 ±1.7	677 ±5	595 ±16	82 ±18	20.7 ±2.1	15.1 ±2.3	5.5 ±1.5	4.0 ±1.4	2.6 ±0.6	7.0 ±0.6
1.5 per cent halothane	13.8 ±2.7	10.6 ±1.1	35.1 ±3.5	672 ±6	589 ±15	84 ±13	19.8 ±2.0	11.4 ±3.0	8.4 ±3.3	3.3 ±1.0	1.5 ±0.5	8.0 ±0.7
Control	13.8 ±2.7	10.6 ±1.1	35.9 ±3.2	670 ±6	594 ±17	86 ±17	20.0 ±2.2	14.0 ±2.3	6.0 ±1.6	4.3 ±1.2	2.4 ±0.6	6.9 ±0.7
5 per cent ether	13.8 ±2.7	10.6 ±1.1	37.9 ±3.7	657 ±7	565 ±20	92 ±26	20.1 ±2.6	13.8 ±3.6	6.3 ±2.2	4.0 ±1.5	2.5 ±0.9	8.0 ±0.9

* Values are means ± standard deviations. VT/BW is the ratio of tidal volume to body weight.

Blood oxygen content was calculated from the formula:

$$\text{Blood } O_2 \text{ content} = \text{Hb (grams per cent)} \times 1.34 \times \frac{\text{per cent saturation}}{100} + (\alpha \cdot P_{O_2})$$

(Hb: red blood cell; $\alpha \cdot P_{O_2}$: dissolved)

$A\text{-}aD_{O_2}$ was obtained by subtraction. Cardiac index was calculated from body surface area with the equation of Rubner.[14] The significances of differences in results obtained were tested by Student's *t* test.

Blood Samples

Blood samples were immersed in a mixture of ice and water in a vacuum bottle[15] and analyzed for P_{O_2}, P_{CO_2} and *p*H within 15 minutes in an I.L. Meter (Model 113-S, Instrumentation Laboratory Inc., Boston, Massachusetts). The oxygen electrode was calibrated with a sample of each animal's blood which had been equilibrated with a known oxygen concentration in a tonometer (Ichikawa Shiseido Co., Tokyo, Japan).

Blood gas tensions were corrected for temperature according to the nomogram of Kelman and Nunn.[16] After sampling in heparinized glass capillary tubes, oxygen saturation was estimated by a spectrophotometric method[17] in an oxygen saturation meter (Type OSMI, Radiometer, Copenhagen, Denmark). Hemoglobin concentration was determined by the cyanmethemoglobin method with a hemoglobin meter (Model 101, Erma Optical Works Ltd., Tokyo, Japan).

Results

Table 1 summarizes mean values and standard deviations of the parameters measured. Statistical analyses of effects of the two anesthetics on $A\text{-}aD_{O_2}$, percentage of physiologic shunt, P_{aCO_2}, intratracheal pressure and cardiac index are listed in table 2.

$A\text{-}aD_{O_2}$

An hour after the start of halothane anesthesia, the mean value of $A\text{-}aD_{O_2}$ was 84 mm Hg (±13 SD), compared with the control value of 82 mm Hg (±18 SD) (table 1).

TABLE 2. Statistical Analysis of Effects of Halothane and Ether on A-aD_{O_2}, Percentage of Physiologic Shunt, Pa_{CO_2}, Intratracheal Pressure and Cardiac Index

	Control versus halothane	Control versus ether	Halothane versus ether
A-aD_{O_2}	NS*	NS	NS
$\frac{\dot{Q}_s}{\dot{Q}_t} \times 100$	Control > halothane $P < 0.01$	NS	Halothane < ether $P < 0.05$
Pa_{CO_2}	NS	NS	NS
Intratracheal pressure	Control < halothane $P < 0.05$	Control < ether $P < 0.05$	NS
Cardiac index	Control > halothane $P < 0.001$	NS	Halothane < ether $P < 0.005$

* NS = No significant difference.

An hour after initiation of ether anesthesia, A-aD_{O_2} was 92 mm Hg (±26 SD), compared with a control value of 86 mm Hg (±27 SD). During both halothane and ether anesthesia, A-aD_{O_2} showed no significant changes.

CHANGES IN PERCENTAGE OF PHYSIOLOGIC SHUNT

One hour after starting halothane anesthesia the mean physiologic shunt decreased significantly from the control value of 4.6 per cent (±1.4 SD) to 3.3 per cent (±1.0 SD) ($P < 0.01$). During ether anesthesia, however, no significant change occurred, 4.3 per cent (±1.2 SD) to 4.6 per cent (±1.5 SD). The difference between the percentages of physiologic shunts in the two anesthetic conditions was significant ($P < 0.05$).

CHANGES IN Pa_{CO_2}

The mean value of Pa_{CO_2} during halothane anesthesia was 35.1 mm Hg (±3.5 SD), compared with the control value of 36.8 mm Hg (±1.7 SD). During ether anesthesia, the value changed to 37.9 mm Hg (±3.7 SD) from a control value of 35.9 mm Hg (±3.2 SD). Neither change was significant. When halothane and ether anesthesia were compared, no significant difference in Pa_{CO_2} was observed.

CHANGES IN INTRATRACHEAL PRESSURE

The mean value of intratracheal pressure an hour after the start of halothane anesthesia was 8.0 cm H_2O (±0.7 SD), compared with the control value of 7.0 cm H_2O (±0.6 SD). An hour after the start of ether anesthesia, the value changed to 8.0 cm H_2O (±0.9 SD) from a control value of 6.9 cm H_2O (±0.7 SD). In both cases, significant increases in the intratracheal pressure ($P < 0.05$) occurred. There was no significant difference between intratracheal pressures found with halothane and with ether.

CHANGES IN CARDIAC INDEX

A comparison of changes in cardiac index showed a remarkable difference between the two anesthetics ($P < 0.005$). The mean value following halothane decreased significantly from 2.6 l/m²/min (±0.6 SD) to 1.5 l/m²/min (±0.5 SD), ($P < 0.001$), whereas ether did not change the value significantly. Percentages of physiologic shunts were plotted against cardiac indexes in all cases (fig. 1) and a positive correlation was found ($\gamma = 0.792$, $P < 0.001$). Regardless of the agent administered, the percentage of physiologic shunt decreased whenever cardiac index decreased.

Discussion

This study demonstrates that a decrease in physiologic shunt is associated with a reduction in cardiac index during general anesthesia. Further, the percentage of physiologic shunt during halothane anesthesia decreased significantly compared with the preanesthetic value.

The physiologic shunt refers to the quantity of venous blood added to the arterial blood

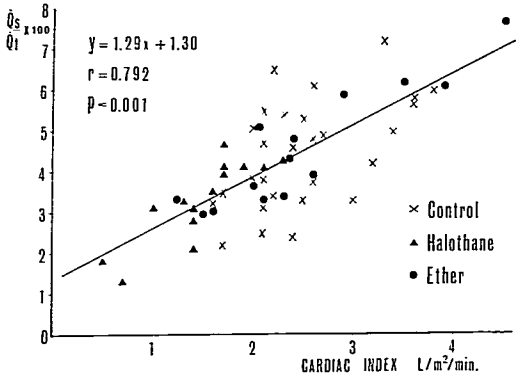

FIG. 1. Relationship between percentage of physiologic shunt (ordinate) and cardiac index (abscissa) in 14 dogs. Total correlation coefficient (γ) 0.792 ($P < 0.001$).

emerging from the lungs. Low ventilation/perfusion ratio and impaired diffusion have been considered responsible for the change in physiologic shunt.[5] If a high concentration of oxygen is given, however, as in the present study, these effects are eliminated.

But other sources of venous admixture remain, even when pure oxygen is given: shunting of venous blood into the left heart from bronchial, pleural or Thebesian veins, or from those pulmonary vessels which have no contact with alveoli, and the effective shunt caused by unoxygenated blood from nonventilated alveoli. Further, the degree of the physiologic shunt is affected not only by the amount of mixed venous blood passing through the shunt but also by the oxygen content.

It has been reported that during general anesthesia the A-aD_{O_2} is greatly increased for a given Pa_{O_2}, but the cause has not been clearly established.[1-8] Bendixen *et al.*[1-2] advanced the hypothesis that the increased A-aD_{O_2} was caused by progressive miliary atelectasis which was eliminated by periodic hyperinflation of the lungs and accentuated by shallow tidal volume. In the present experiments, the A-aD_{O_2} did not increase significantly for at least an hour after the start of anesthesia, even though the lungs were not hyperinflated. This finding suggests that atelectasis may not have occurred during controlled ventilation with an adequate tidal volume.

Kelman *et al.*,[18] in a theoretical study, reported that for any given oxygen consumption and pulmonary venous admixture, the A-aD_{O_2} is inversely related to cardiac output. Further, Prys-Roberts *et al.*[19] demonstrated that a sudden fall in arterial P_{O_2} resulted from the acute reduction of cardiac output following the administration of intravenous thiopental in man.

If the cardiac output is reduced with the oxygen consumption remaining constant, there must be a fall in the oxygen content of the mixed venous blood. Therefore, the blood passing to the left heart through the shunt would also have a lower oxygen content, and this would be expected to cause an increase in A-aD_{O_2}. The present results, however, indicate that during halothane anesthesia the A-aD_{O_2} does not increase, although there is a fall in mixed venous oxygen content secondary to a significant reduction in cardiac output. This finding suggests that the amount of blood passing through the shunt is reduced when cardiac output decreases.

During ether anesthesia, Pa_{O_2} fell significantly, compared with the control value, but the A-aD_{O_2} was unchanged as in halothane anesthesia. A fall in $P_{A_{O_2}}$ owing to alveolar ether concentration may account for this fall in Pa_{O_2}.

The calculated percentages of physiologic shunts following halothane and ether anesthesia showed a significant difference, the

value for halothane being lower than that for ether. The following factors are considered in determining the reason for the difference. First, tidal volume was constant and probably not responsible. Second, intratracheal pressures with halothane and with ether anesthesia were not significantly different. Third, Pa_{CO_2} values did not show a significant difference between the two anesthetic conditions. Finally, determination of cardiac output showed a highly significant difference between halothane and ether anesthesia, and is considered to be a dominant factor influencing the change in percentage of physiologic shunt.

When percentage of physiologic shunt was plotted against cardiac index, a significant positive correlation was found. The percentage physiologic shunt decreased consistently with either agent whenever cardiac index decreased. Figure 2 shows two typical cases in which percentage physiologic shunt and cardiac index varied in the same direction regardless of agent administered. This relationship between the shunt and the cardiac output was also suggested by Hedley-Whyte *et al.*,[10] who observed that high-percentage physiologic shunts occurred when cardiac indexes increased in patients with cardiopulmonary disease.

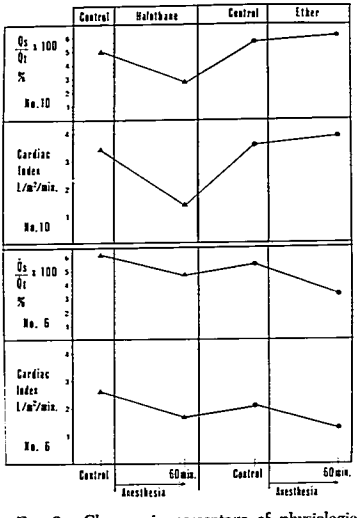

FIG. 2. Changes in percentage of physiologic shunt and cardiac index in two dogs during the control period and one hour after the start of halothane and ether anesthesia (dog 10 above; dog 6 below). Changes in these parameters are in the same direction in both cases.

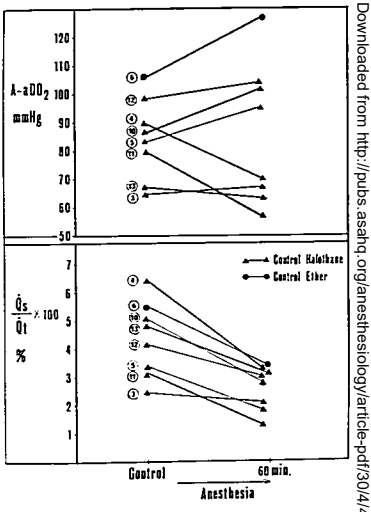

FIG. 3. Changes in $A\text{-}aD_{O_2}$ and percentage of physiologic shunt in the cases where cardiac indexes fell more than 50 per cent of the control value. The changes in these two parameters are not always in the same direction. (Numbers of the lines indicate identifying numbers of the dogs.)

It was thought that the change in $A\text{-}aD_{O_2}$ could reflect the percentage of physiologic shunt with constant-volume ventilation. In the present study, however, the changes in $A\text{-}aD_{O_2}$ and percentage of physiologic shunt were not always in the same direction when cardiac output was reduced; *e.g.*, with a decrease in cardiac index of more than 50 per cent of the control value, as shown in figure 3.

In interpreting these findings, it must be noted that the percentage of physiologic shunt was calculated by substitution of derived or

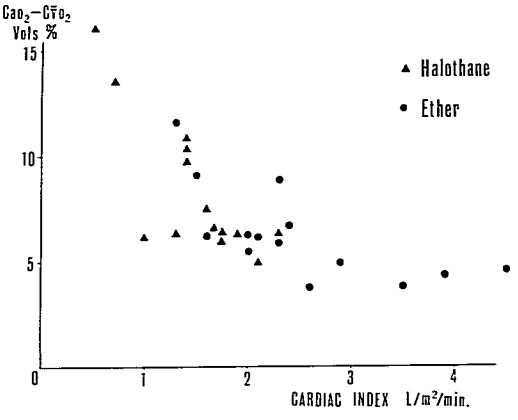

FIG. 4. Relationships between arterial–mixed venous oxygen content difference (ordinate) and cardiac index (abscissa) in 14 dogs under halothane or ether anesthesia. The fall in cardiac index is associated with the increase in arterial–mixed venous oxygen content difference.

measured values of A-aD_{O_2}, Ca_{O_2} and $C\bar{v}_{O_2}$ in the shunt equation. In our study, a marked reduction in cardiac output resulted in an excessive desaturation of the mixed venous blood, whereas the arterial blood was fully saturated, since the Pa_{O_2} remained at a high level. The resultant increase in a-$\bar{v}C_{O_2}$ was, therefore, associated with a reduction in cardiac index, as shown in figure 4. This marked increase in a-$\bar{v}C_{O_2}$ differences offsets the change in A-aD_{O_2} when the percentage of physiologic shunt is calculated from the shunt equation. Thus, even in cases in which A-aD_{O_2} increased, the percentage of physiologic shunt decreased in the present study. An analysis of the oxygen content of mixed venous blood, therefore, is important in calculating the percentage of physiologic shunt.

We conclude that change in cardiac output is an important factor in determining the alteration in physiologic shunt under general anesthesia with controlled ventilation using an adequate constant tidal volume.

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Anesthesia

BIDIRECTIONAL PLACENTAL TRANSFER EEG electrodes were placed in the brains of fetal guinea pigs and their mothers. Administration of meperidine to the mother by the intravenous, intramuscular or intraperitoneal route produced EEG evidence of meperidine depression in both mother and fetus. These changes included the appearance of high-voltage slow waves and the presence of 15-to-25-second waveforms. Maternal intravenous administration produced rapid changes in the maternal and fetal EEG, the fetal changes appearing 69 seconds after maternal administration. Maternal intraperitoneal administration produced the slowest effect, 178 seconds being required for fetal changes to occur. In other preparations, meperidine was given intraperitoneally and intramuscularly to fetal guinea pigs. Maternal effects required 217 and 182 seconds, respectively. These studies demonstrate a bidirectional transfer of meperidine across the placenta. (*Rosen, M., and Bleyer, W.: Bidirectional Transfer of Meperidine Across the Guinea Pig Placenta, Amer. J. Obstet. Gynec. 101: 918 (Aug.) 1968.*)