EFFECT OF HALOTHANE ON LYMPH FLOW


SUMMARY

The thoracic lymph duct was cannulated at the root of the neck in seven anaesthetized, artificially ventilated dogs. The mean control lymph flow was 1.51 ml kg\(^{-1}\) h\(^{-1}\) (SD ± 0.35). The administration of 1% halothane caused a 59% decrease in mean lymph flow (to 0.62 ml kg\(^{-1}\) h\(^{-1}\)) within 20 min, which returned to control values 30 min after the discontinuation of the administration of halothane.

The lymphatic system appears to perform a homeostatic function by removing proteins, lipids and other materials from the interstitial spaces (Milnor, 1980). Normally, interstitial fluid is formed by physiological transudation from the capillaries, the amount of interstitial fluid formed and the potential lymphatic flow depending on the balance between hydrostatic forces, the colloid osmotic pressure and capillary permeability. Ultimately, all lymphatics converge on the two main trunks, the thoracic duct and the right lymph duct (Wiederhielm, 1974). In the dog lymph flow is principally via the thoracic duct, which enters the venous system at the junction of the left subclavian and jugular veins; only around 5% of the total lymph flow enters the right lymph duct (Vrein, Ohkuda and Staub, 1977).

Quinn and Shannon (1975) demonstrated that thiopentone–halothane anaesthesia caused a 25% decrease in lymph flow from the legs of sheep, when compared with the conscious animal. More recently, Schad and Brechtelsbauer (1977) demonstrated that the administration of halothane (1%) caused a 50% decrease in lymph flow in the thoracic duct in dogs, immobilized with pancuronium and ventilated artificially. P\(_{\text{aCO}_2}\), P\(_{\text{aO}_2}\), pH and core temperature were maintained in the ranges 4.5–5.5 kPa, 24–26 kPa, 7.32–7.34 unit and 37.5–38°C, respectively. Cannulae were inserted to the inferior vena cava via a femoral vein for the infusion of drugs, to the superior vena cava via the right external jugular vein to record venous pressure and to a femoral artery. The ECG, beat-by-beat heart rate, and femoral arterial pressure were recorded and displayed on an ultraviolet recorder (SE Laboratories type 2112).

The lymphatic vessels draining into the venous system at the root of the neck were dissected and exposed on the left side without opening the pleura. The thoracic duct was identified and cannulated with a thin plastic tube (internal diameter 1 mm). Satisfactory cannulation of the thoracic lymph duct was achieved in six out of seven preparations.

MATERIALS AND METHODS

Experiments were carried out on seven dogs weighing between 23 and 30 kg. They were anaesthetized with methohexitone 15 mg kg\(^{-1}\) followed by α-chloralose, initially in a bolus of 30 mg kg\(^{-1}\) i.v. followed by an infusion of 15 mg kg\(^{-1}\) h\(^{-1}\). Suxamethonium 2 mg kg\(^{-1}\) h\(^{-1}\) was administered and the lungs ventilated artificially. P\(_{\text{aCO}_2}\), P\(_{\text{aO}_2}\), pH and core temperature were maintained in the ranges 4.5–5.5 kPa, 24–26 kPa, 7.32–7.34 unit and 37.5–38°C, respectively. Cannulae were inserted to the inferior vena cava via a femoral vein for the infusion of drugs, to the superior vena cava via the right external jugular vein to record venous pressure and to a femoral artery. The ECG, beat-by-beat heart rate, and femoral arterial pressure were recorded and displayed on an ultraviolet recorder (SE Laboratories type 2112).

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The cannula inserted to the superior vena cava was connected to a vertically mounted column of physiological saline solution and the end of the tube draining the thoracic duct was continually adjusted to the mean height of the saline column. Thus, the lymph flow occurred against a pressure equivalent to that present in the veins at the root of the neck.

The present study was undertaken to determine the possible acute effects of halothane on lymph flow in the thoracic duct of the dog under carefully controlled conditions.

approximately the same as the control values. Lymph was collected every 5 min for a 30-min period, after which the halothane was discontinued and further observations made on return to the control situation. In two preparations sodium nitroprusside (SNP) was administered until the decrease in mean arterial pressure was the same as that caused by the halothane and the effect on lymph flow observed, after which the nitroprusside was withdrawn and the subsequent changes observed. In one of these two preparations, SNP was administered before halothane and in the other after the withdrawal of halothane on the return of lymph flow to control values. In addition observations were made on the effect of infusing a solution of 5% dextrose alone at the same rate as the volume infused during the administration of SNP (50 mg in 30 ml of 5% dextrose solution infused at a rate of 60 ml h⁻¹).

Total protein concentration in the lymph was measured by the Biuret method using a Boehringer kit. Most of the lymph collected during each 30-min period was reinfused into the dogs before commencing the next phase of the investigation.

Statistical analyses were performed using analysis of variance and paired \( t \) tests.

### RESULTS

The effect of halothane on the flow of lymph in the thoracic duct is illustrated in figure 1. The control mean lymph flow was 1.51 (±0.35) ml kg⁻¹ h⁻¹ (these and all other values are mean ± SD) and this decreased to 0.67 (±0.41) ml kg⁻¹ h⁻¹ in response to the administration of 1% halothane (fig. 1). The decrease in lymph flow during the administration of halothane was statistically significant after 10 min. On discontinuation of the halothane the preparation returned to control values within 30 min (fig. 1). The mean femoral arterial pressure (MAP) decreased from 155 (±21.4) mm Hg to 94 (±16.0) mm Hg in response to the administration of the halothane (table I).

The mean dose of SNP required to produce a decrease in MAP of approximately 60 mm Hg was 6.6 \( \mu \)g kg⁻¹ min⁻¹. In the two preparations in which SNP was administered, there was no significant change in lymph flow although there were decreases in MAP from 160 mm Hg to 90 mm Hg and from 155 mm Hg to 85 mm Hg; that is, decreases similar to those witnessed during the administration of halothane. In addition, there was no change in lymph flow in response to the infusion of a solution

### TABLE I. Lymph flow (individual preparations) and cardiorespiratory measurements (mean ± SD) before, during and after the administration of 1% halothane (six preparations).

<table>
<thead>
<tr>
<th></th>
<th>A (Control)</th>
<th>B (After 30 min of 1% halothane)</th>
<th>C (30 min after hal. withdrawal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph flow (ml kg⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dog No. 1</td>
<td>1.44</td>
<td>0.00</td>
<td>2.24</td>
</tr>
<tr>
<td></td>
<td>1.16</td>
<td>0.61</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>1.12</td>
<td>1.06</td>
<td>1.47</td>
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<tr>
<td></td>
<td>1.95</td>
<td>0.47</td>
<td>1.57</td>
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<tr>
<td></td>
<td>1.52</td>
<td>0.77</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>1.89</td>
<td>1.11</td>
<td>1.20</td>
</tr>
<tr>
<td>Mean</td>
<td>1.51</td>
<td>0.67*AC</td>
<td>1.33</td>
</tr>
<tr>
<td>SD</td>
<td>±0.35</td>
<td>±0.41</td>
<td>±0.57</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>155.0</td>
<td>94.0*AC</td>
<td>131.0</td>
</tr>
<tr>
<td></td>
<td>±21.4</td>
<td>±16.0</td>
<td>±17.2</td>
</tr>
<tr>
<td>HR (beat min⁻¹)</td>
<td>145.0</td>
<td>119.0*AC</td>
<td>138.0</td>
</tr>
<tr>
<td></td>
<td>±22.6</td>
<td>±23.7</td>
<td>±29.4</td>
</tr>
<tr>
<td>pH</td>
<td>7.324</td>
<td>7.323</td>
<td>7.322</td>
</tr>
<tr>
<td></td>
<td>±0.037</td>
<td>±0.060</td>
<td>±0.044</td>
</tr>
<tr>
<td>PaCO₂ (kPa)</td>
<td>5.03</td>
<td>4.78</td>
<td>4.91</td>
</tr>
<tr>
<td></td>
<td>±0.30</td>
<td>±0.84</td>
<td>±0.51</td>
</tr>
<tr>
<td>PaO₂ (kPa)</td>
<td>25.36</td>
<td>26.15</td>
<td>24.73</td>
</tr>
<tr>
<td></td>
<td>±5.21</td>
<td>±5.25</td>
<td>±3.61</td>
</tr>
</tbody>
</table>
HALOTHANE AND LYMPH FLOW

FIG. 1. Effect of 1% halothane on lymph flow (ml kg⁻¹ h⁻¹) and its total protein content (g litre⁻¹) (mean ± SD from six preparations).

DISCUSSION

In this study the flow of lymph was decreased by 59% in response to the administration of 1% halothane, and on withdrawal of this agent lymph flow returned to control values. The thoracic duct does not drain all the pulmonary lymphatic flow nor flow from the right upper part of the animal (Vrein and Ohkuda, 1977; Nakahara et al., 1983). However, it represents over 90% of the total lymph flow in the dog (Vrein, Ohkuda and Staub, 1977).

Normally, the lymph flow into the venous system is a closed loop draining against the venous pressure. In the present study the lymph drainage occurred at a hydrostatic pressure equivalent to that in the veins at the root of the neck and, hence, it may be assumed that the observations are relevant to the normal rate of lymph flow under these experimental conditions.

The change in lymph flow observed in the present study is similar in degree to that observed by Schad and Brechtelsbauer (1977) but, whereas in their study the observed change occurred over 2 h, in the present study the decrease in lymph flow was complete within 20 min (fig. 1). Quinn and Shannon (1975) observed a decrease in lymph flow of 50–75% in the leg of spontaneously breathing ewes in response to anaesthesia induced with thiopentone and maintained with an undisclosed concentration of halothane. However, again there was no reference to the rate of onset of the effect of halothane. In the present study the rate of lymph flow returned to control values within 25 min of discontinuing the administration of halothane, but neither Shad and Brechtelsbauer (1977) nor Quinn and Shannon (1975) made any comment on the rate of recovery.

Several authors have observed that pentobarbitone causes a decrease in lymph flow in dogs (Polderman, McCarrell and Beecher, 1943; Schad and Brechtelsbauer, 1977) and rats (Hungerford and Reinhardt, 1950), whereas ether has been observed to increase lymph flow (Polderman, McCarrell and Beecher, 1943; Hungerford and Reinhardt, 1950). However, in none of this previous work was there any reference to pressures within the cardiovascular system, or blood-gas tensions.

The mechanisms whereby halothane causes a decrease in lymph flow are not clear. It could be postulated that the preliminary observations reported here are simply a result of the decrease in arterial pressure, caused by halothane, with a consequent alteration in the normal balance in hydrostatic and oncotic pressures, and a decrease in the capillary filtration flow. However, the fact that comparable decreases in mean arterial pressure produced by sodium nitroprusside did not decrease lymph flow makes this hypothesis untenable. The lymphatic vessels have an intrinsic pumping mechanism (Hall, Morris and Wooley, 1965) and it could be that this is affected by anaesthesia but not by sodium nitroprusside, but at present there is no study to support this possibility. The mechanisms involved in the ob-
served changes in lymph flow caused by halothane are probably complex and, apart from any direct effect on lymph vessels, are possibly more dependent on changes in metabolism and cardiac output than on intravascular pressures.

Further research is required into this subject, which could have interesting clinical and pharmacokinetic implications.

REFERENCES


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EFFET DE L’HALOTHANE SUR LE DEBIT LYMPHATIQUE

RESUME
Le canal thoracique a été cathétérisé à la racine du cou chez sept chiens anesthésiés et en ventilation contrôlée. Le débit lymphatique moyen de base était de 1,51 ml kg⁻¹ h⁻¹ (DS±0,35). L’administration d’halothane à 1% provoquait une baisse de 59% du débit lymphatique moyen (jusqu’à 0.62 ml kg⁻¹ h⁻¹) en 20 min, et le débit retrouvait sa valeur de base en 30 min après arrêt de l’administration d’halothane.

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EFFEKT VON HALOTHAN AUF DEN LYMPHFLUSS

ZUSAMMENFASSUNG
Bei sieben narkotisierten und künstlich beatmeten Hunden wurde der Ductus lymphaticus im Nacken kathertiert. Der mittlere Kontroll-Lymphfluß lag bei 1,51 ml kg⁻¹ h⁻¹ (SD±0,35). Die Gabe von 1% Halothan setzte den mittleren Lymphfluß innerhalb von 20 Minuten um 59% auf 0,62 ml kg⁻¹ h⁻¹ herab. Innerhalb von 30 Minuten nach Absetzen des Halothans kehrte er wieder auf den Kontrollwert zurück.

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EFECTO DEL HALOTANO SOBRE LA CORRIENTE DE LINFA

SUMARIO
Se canuló en la raíz del cuello el conducto torácico de linfa de siete perros anestesiados y ventilados artificialmente. La corriente promedio de control de linfa era de 1,51 ml kg⁻¹ (SD±0,35). La administración de halotano al 1% tuvo por efecto un descenso del 59% de la corriente promedio de linfa (hasta 0,62 ml kg⁻¹) dentro de 20 min, la cual volvió a valores de control 30 min después de interrumpir la administración de halotano.