HYPOTENSION DUE TO HALOTHANE

BY

J. H. BURN
The Department of Pharmacology

AND

H. G. EPSTEIN
The Nuffield Department of Anaesthetics, University of Oxford

In the pharmacological section of the report to the Medical Research Council on Fluothane by the Committee on Non-explosive Anaesthetic Agents (1957), the conclusion was drawn that the hypotensive action was made up of a central depressant action, together with some weakening of the heart and possibly a small contribution of peripheral ganglion block. One further possibility remained which had not been thoroughly examined, namely that halothane might have a direct relaxing action on the smooth muscle of the arteries. We have therefore carried out some observations to test whether such an action was exerted, and in addition have made observations on the spleen and on the intestines.

METHODS

Experiments were performed in which the hind leg of a dog was perfused with blood made incoagulable with heparin. One dog was anaesthetized with ether, after which tracheotomy was performed and cannulae were inserted in the left common carotid artery and in the right external jugular vein. The dog was then bled into a polythene beaker containing heparin, 800-900 ml being collected. The front part of the bony thorax was removed and cannulae were tied into the pulmonary artery and into the left auricle. A ligature was tied round the ventricle near its base. Blood was then pumped from a Dale-Schuster pump into the pulmonary artery while the lungs were ventilated with oxygen and 5 per cent carbon dioxide. The blood leaving the left auricle was collected in a reservoir and, until the second dog was prepared, was recirculated through the lungs.

The second dog was also anaesthetized with ether, a tracheal cannula and a carotid cannula were inserted, and about 150 ml blood was withdrawn for addition to the blood reservoir. The dog was then eviscerated and cannulae were tied in the external iliac artery and vein of one side pointing towards the aortic bifurcation. The aorta was ligatured below the origin of the external iliac arteries, and ligatures were passed round the aorta and vena cava just above the bifurcation. At a given moment these ligatures were tied and perfusion was begun from the Dale-Schuster pump through the cannula in the external iliac artery from which blood passed to the leg of the opposite side. The venous effluent from the leg was passed to an outflow recorder and was carried to the reservoir from which it was pumped once more through the lungs. A side arm of the cannula tied in the external iliac artery was connected to a mercury manometer. In this way the resistance to flow of the leg vessels was recorded, as well as the venous outflow. In other experiments observations on spleen volume were made in spinal cats which were prepared by cutting the cord at the second cervical vertebra under ether anaesthesia. The spleen was brought out through the body wall on the left side and placed in a plethysmograph so that variations in its volume could be recorded.

In other experiments observations on intestinal motility were made in spinal cats. An incision was made into the upper end of the jejunum through which was inserted a small balloon attached to the end of a catheter. The balloon was then pushed up into the duodenum. The balloon and catheter
had been filled with water, and the contractions of the duodenum were transmitted to a piston recorder.

In order to administer halothane or ether, the outlet from a Palmer "Ideal" pump was connected by tubing to a T-adaptor close to the tracheal cannula. The appropriate quantitative inhaler was connected to the intake of the pump and the tubing mentioned above was kept fairly narrow in order to reduce the time lag between altering the setting of the concentration control and the arrival of the new mixture in the lungs. The expirations were led from the side branch of the T-adaptor through the mechanical valve on the pump onwards through an exhaust tube to the outer air.

In all experiments the rotary drive to the pump was set to a fixed rate of inflation—25 per minute. The stroke volume was adjusted according to requirements to a few spaced values: 100 ml, 150 ml and 200 ml. The peak inflation pressures were recorded on a dial manometer in a side branch of the tubing leading to the tracheal connector. For cats, the peak inflation pressures were in the region from 9 to 15 cm H₂O for tidal volumes of 100 to 150 ml. Often a deterioration of the preparation was apparent from a steadily rising inflation pressure while the tidal volume remained unaltered.

When halothane was used the apparatus connected to the intake of the pump was a modified E.M.O. halothane inhaler. It had been modified so that even for the low minute volumes (2 l litres) used the concentrations delivered were not far away from the settings of the control for human anaesthesia. The inhaler had been calibrated in the laboratory with a similar Palmer pump. Variations in output were reduced to a small value by immersing the inhaler in a water bath, although it contained the usual thermo-compensator, which automatically reduces effects of external temperature fluctuations. The range of halothane concentrations available from this inhaler was up to 4 per cent by volume.

For ether an Oxford vaporizer, modified for animal work, was attached to the intake of the pump, although a standard ether E.M.O. inhaler would have been equally suitable. The range of concentrations which can be delivered from the latter apparatus is up to 20 per cent by volume.

RESULTS

Observations in the perfused hind leg

In the course of experiments in which the hind leg of a dog was perfused with blood by way of a cannula tied in the left external iliac artery, we observed the effect of ventilating the lungs with 1.5 per cent halothane. Figure 1 illustrates the effect. The upper record is that of the venous outflow from the common iliac vein, and when halothane was administered the outflow increased. The lower record is that of the pressure in the perfusion cannula, and when halothane was administered the pressure fell because the arterial resistance diminished. The pressure recovered when halothane was stopped and the venous outflow declined. The results in two experiments in which halothane was compared with ether are given in table I.

<table>
<thead>
<tr>
<th>Anaesthetic</th>
<th>Duration (min)</th>
<th>Fall in arterial resistance (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exp. 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Halothane 1.5%</td>
<td>5</td>
<td>170 to 132</td>
</tr>
<tr>
<td>(b) Halothane 1.5%</td>
<td>5</td>
<td>153 to 119</td>
</tr>
<tr>
<td>(c) Ether 6.0%</td>
<td>5</td>
<td>no fall</td>
</tr>
<tr>
<td>Exp. 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Halothane 2.0%</td>
<td>4</td>
<td>119 to 98</td>
</tr>
<tr>
<td>(b) Ether 8.0%</td>
<td>4</td>
<td>106 to 100</td>
</tr>
</tbody>
</table>

Observations on intestinal contractions

The effects of halothane and of ether on intestinal contractions recorded by a balloon in the duodenum are shown in figure 2. The adrenal glands were excluded from the circulation. The contractions were vigorous because of the injection of 0.1 mg eserine sulphate 30 minutes previous to the taking of the record. During the administration of halothane, 0.7 per cent, there was complete inhibition of the contractions. During the administration of ether, 10 per cent, there was no inhibition. Three experiments were performed with a similar result, although the difference between halothane and ether was greatest in the experiment of figure 2.

Observations on spleen volume

The sympathetic nerves to the spleen accompany the arteries, and impulses passing along
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FIG. 1

Record from an experiment in which the hind leg of a dog was perfused with blood. The blood on leaving the leg was pumped through the lungs of another dog which were ventilated with O₂ and 5 per cent CO₂. The blood was then pumped back to the leg. When halothane was added to the ventilating mixture in 1.5 per cent concentration, the arterial resistance in the leg fell, and the outflow from the leg increased.
Record from an experiment in a spinal cat in which the contractions of the duodenum were recorded from a balloon inside it. The adrenal glands were excluded. When the cat was ventilated with halothane 0.7 per cent the contractions were arrested. When the cat was ventilated with ether 10 per cent the contractions were not arrested.
them cause the spleen volume to shrink. Figure 3 shows in (a) the effect of ventilating a spinal cat with ether, 20 per cent by volume. The adrenal glands had been excluded. The blood pressure was low and was not affected, but the spleen volume declined during administration of ether, recovering again when ether was discontinued. In figure 3 (b) halothane was given in 2.5 per cent concentration. The volume record was slowly rising, and when halothane was given there was a slight fall, the volume recovering when halothane was discontinued. Similar results to these were obtained in three other experiments. The conclusion was drawn that under ether the sympathetic impulses to the spleen were increased and as a result the volume diminished. Under halothane there was also some diminution in volume but it was much smaller. Either the increase in sympathetic impulses was much less under halothane, or the impulses were counteracted by a direct action on the spleen, causing relaxation.

**DISCUSSION**

The observations on the intestine and on the perfused vessels of the hind leg indicate that halothane has an inhibitory action on smooth muscle greater than that of ether, even when given in a concentration of less anaesthetic potency. Ether has previously been shown to cause contraction of the spleen volume (Bhatia and Burn, 1933) and this effect indicates that ether causes an increase in the flow of sympathetic impulses since it occurs when the adrenal glands are excluded. Halothane was observed to have some effect in causing contraction of the spleen but usually less than ether, as shown in figure 3. In one experiment it was recorded that a contraction of the spleen began when halothane was given, but ceased and the spleen dilated while halothane was still acting. This observation suggested that there were two effects; first, contraction due to increased sympathetic impulses, and then dilatation because the sympathetic action was overcome by direct action on the muscle.
When all the results are taken together they point to halothane having a relaxing or dilating action on the smooth muscle of the vessels, of the spleen and of the intestine, from which the conclusion may be drawn that the fall in blood pressure during halothane anaesthesia is in part, at least, due to this direct effect. The observations on the spleen suggest that sympathetic impulses are increased, although not to the same extent as they are under ether. The inhibition of the intestine could indeed be sympathetic in origin.

SUMMARY

Halothane has a direct relaxing action on smooth muscle which probably contributes to its action in lowering blood pressure.

REFERENCES


"Fluothane": a report to the Medical Research Council by the Committee on Non-explosive Anaesthetic Agents (1957). Brit. med. J., 2, 479.