THE INFLUENCE OF HALOTHANE ANAESTHESIA ON OXYGEN TOXICITY

BY

G. SMITH AND I. MCA. LEDINGHAM

SUMMARY

Twelve dogs were anaesthetized with halothane and allowed to breathe spontaneously gas comprising either 100 per cent oxygen at 2 ATA (the test group) or 40 per cent oxygen/60 per cent nitrogen at 1 ATA (the control group). The control group survived to 24 hours without undergoing any significant change in cardiac output, pulmonary shunt ratio or A-a Po\textsubscript{2} difference. The test group of animals died in respiratory failure at a mean time of 14.03 hours with a pulmonary shunt ratio of 32 per cent. At apnoea, the test group of dogs had adequate cardiovascular function (cardiac output 2.21 ± 0.30 l./min; mean arterial pressure 76 ± 9 mm Hg). It was concluded that respiratory failure was caused by a combination of halothane and the effects of high pressure oxygen.

Anaesthesia is known to have a profound effect on oxygen toxicity. Above 3 atmospheres absolute (ATA) of oxygen, convulsions are delayed in onset and often long enough to allow pulmonary changes to become manifest (Bean and Zee, 1965, 1966). Below 3 ATA, the onset of pulmonary oxygen toxicity is thought to be delayed (Jameson, 1966). Previous animal experiments relating to pulmonary oxygen toxicity are of limited usefulness in that in many instances the animals were conscious and therefore detailed study of the mechanism of oxygen toxicity was not possible. In a recent study, Clarke, Sandison and Ledingham (1969) developed a technique for inducing pulmonary oxygen toxicity in spontaneously breathing animals anaesthetized by neuroleptanalgesia. The manner of death did not differ significantly from that of conscious animals, and anaesthesia permitted the frequent measurements of cardiovascular and respiratory changes up to the time of death. These experiments, performed at 2 ATA, suggested that pulmonary oxygen toxicity was multifactorial in aetiology and that central nervous system, cardiac, pulmonary and possibly other factors were all present in the terminal stages; that is, the topical irritant effect of oxygen on the alveoli was less important than had been previously suggested.

Following the neuroleptanalgesic technique previously described, the effect of different anaesthetic agents was studied, the first of these being halothane, chosen because of its frequent clinical use in hyperbaric anaesthesia.

METHODS

Twelve pure-bred beagle hounds (weight range 11–18 kg) were randomly allocated to two groups. One group was exposed to 100 per cent oxygen at 2 ATA (test group) and the other to 40 per cent oxygen/60 per cent nitrogen at 1 ATA (control group). Anaesthesia was induced with fentanyl 0.003 mg/kg body weight. Tracheostomy was performed under intermittent thiopentone anaesthesia (dose range 150–450 mg) and the inspired gases were humidified by means of a simple Wolf’s bottle. The control group was then permitted to breathe spontaneously 0.75–1.25 per cent halothane (dial setting on a Fluotec Mk II) in 40 per cent oxygen/60 per cent nitrogen at 1 ATA and the test group of animals breathed 100 per cent oxygen at 2 ATA with the Fluotec dial registering a concentration of 0.5–1 per cent. The halothane concentration delivered by the Fluotec Mk II vaporizer was reduced to the minimum compatible with a very light level of anaesthesia and all the animals possessed a lash reflex throughout the experiment which was scheduled to last 24 hours.

## TABLE I
Respiratory data in two groups of dogs anaesthetized with halothane and breathing spontaneously gas comprising either 100 per cent oxygen at 2 ATA or 40 per cent oxygen/60 per cent nitrogen at 1 ATA. The results are expressed as mean values ± standard error of the mean.

<table>
<thead>
<tr>
<th>Time</th>
<th>Control dogs at 1 ATA</th>
<th>Dogs at 2 ATA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time</td>
<td>before apnoea</td>
</tr>
<tr>
<td>Respiratory frequency (b.p.m.)</td>
<td>26.8 ± 2.2</td>
<td>23.3 ± 2.4</td>
</tr>
<tr>
<td>Alveolar ventilation (l./min)</td>
<td>1.49 ± 0.18</td>
<td>1.22 ± 0.15</td>
</tr>
<tr>
<td>Minute volume (l./min)</td>
<td>3.71 ± 0.70</td>
<td>2.83 ± 0.42</td>
</tr>
<tr>
<td>Dead space (ml)</td>
<td>75 ± 5</td>
<td>86 ± 7</td>
</tr>
<tr>
<td>Alveolar-arterial oxygen tension difference (mm Hg)</td>
<td>135 ± 20</td>
<td>275 ± 53</td>
</tr>
<tr>
<td>Pulmonary shunt ratio (%)</td>
<td>13.2 ± 1.8</td>
<td>15.2 ± 3.3</td>
</tr>
</tbody>
</table>

Arterial and central venous catheters were inserted via the femoral vessels and a pulmonary artery catheter was positioned via the external jugular vein under direct fluoroscopic vision. Oesophageal temperature was monitored continuously.

The following measurements were made at regular intervals throughout the experiment:

1. Arterial and mixed venous blood-gases. Oxygen tension was measured using a microelectrode (Radiometer type E5044). Readings were corrected for the difference in electrode response to blood and gas using a factor derived from dog’s blood tonometered to a known Po₂ (Torres, 1963). Carbon dioxide tensions were measured using a Severinghaus carbon dioxide electrode (Radiometer) and pH measurements were made with a glass electrode (Radiometer). All readings were corrected for temperature difference between the electrode and the dog using a Severinghaus slide rule.

2. Direct and mean systemic arterial, pulmonary arterial and central venous pressures were measured using appropriate transducers (Elaema-Schönander) and recorded on a Mingograf 81 inkjet recorder.

3. Cardiac output was measured using a dye-dilution technique employing indocyanine green and a Waters cuvette densitometer (XP-302).

4. Tidal volume (VT) was measured using a bell spirometer. The PCO₂ of mixed expired gas was measured using the Severinghaus electrode. Physiological deadspace (Vd) was calculated from the Bohr equation. Alveolar ventilation (VA) was derived:

\[ V_A = (V_T - V_D) \times \text{respiratory frequency}. \]

The alveolar arterial oxygen tension difference was calculated as follows:

\[ A-aD = P_{A_02} - P_{A_02} \]

where \( P_{A_02} = P_{T_02 - P_{A_02}} \frac{(F_{IO_2} - F_{EO_2})}{F_{EO_2}} \)

(Filley, Mcintosh and Wright, 1954).

Blood oxygen contents were calculated from the measurement of Po₂ and pH. Validation of this method in this laboratory has been described recently (Ledingham et al., 1970).

Pulmonary shunt ratio (Qs/Qt) was calculated as follows:

\[ Qs/Qt = (C_{C'O_2} - C_{A02})/(C_{C'O_2} - C_{V'O_2}) \]

## RESULTS
The control animals at 1 ATA survived to 24 hours at which time they were sacrificed. The test animals were exposed to 100 per cent oxygen at 2 ATA and five died in respiratory failure at a mean time of 14.03 hours (range 10.0–16.05 hours). One dog (HHB) was resuscitated from profound respiratory failure after 10 hours and allowed to proceed to 24 hours at 1 ATA.
INFLUENCE OF HALOTHANE ANAESTHESIA ON OXYGEN TOXICITY

Table II
Arterial \( P_{aO_2} \), \( P_{aCO_2} \) and pH in dogs exposed to 100 per cent oxygen at 2 ATA and 40 per cent oxygen/60 per cent nitrogen at 1 ATA. Mean values ± standard error of the mean.

<table>
<thead>
<tr>
<th>Time</th>
<th>( P_{aO_2} ) (mm Hg)</th>
<th>( P_{aCO_2} ) (mm Hg)</th>
<th>pH (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control dogs at 1 ATA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hrs</td>
<td>162 ± 12</td>
<td>44 ± 2</td>
<td>7.318 ± 0.014</td>
</tr>
<tr>
<td>12 hrs</td>
<td>188 ± 4</td>
<td>45 ± 4</td>
<td>7.343 ± 0.008</td>
</tr>
<tr>
<td>24 hrs</td>
<td>187 ± 8</td>
<td>47 ± 2</td>
<td>7.316 ± 0.026</td>
</tr>
<tr>
<td>Dogs at 2 ATA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hrs</td>
<td>1171 ± 35</td>
<td>54 ± 6</td>
<td>7.272 ± 0.042</td>
</tr>
<tr>
<td>2 hrs before apnoea</td>
<td>1184 ± 46</td>
<td>43 ± 4</td>
<td>7.334 ± 0.029</td>
</tr>
<tr>
<td>Apnoea</td>
<td>759 ± 156</td>
<td>150 ± 6</td>
<td>6.918 ± 0.014</td>
</tr>
</tbody>
</table>

The respiratory frequency, tidal volume, alveolar ventilation, alveolar/arterial oxygen tension difference and pulmonary shunt ratio are indicated in Table I. At 2 hours, the two groups are comparable, other than that the alveolar/arterial oxygen tension difference in the test group was 275 ± 53 mm Hg compared with 135 ± 20 mm Hg in the control group (\( P<0.025 \)). In the control group at 12 hours, there was an apparent increase in respiratory rate of 15 per cent, which was not significant. There was no significant alteration in alveolar ventilation and A–a \( P_{O_2} \) difference and pulmonary shunt ratio were unchanged. At 24 hours, no further significant changes had occurred.

In the test group, 2 hours prior to apnoea (i.e. range 8–14 hours), respiratory frequency was unchanged whilst alveolar ventilation had increased by 39 per cent (\( P<0.025 \)). The alveolar-arterial oxygen tension difference and the pulmonary shunt ratio had risen slightly but not significantly.

Immediately prior to apnoea in the test group, respiratory rate, tidal volume and alveolar ventilation had all fallen substantially and a marked increase had occurred in the A–a \( P_{O_2} \) difference and pulmonary shunt ratio. Table II shows the arterial \( P_{aO_2}, P_{aCO_2} \) and pH values at times corresponding to those in Table I. In the control animals, there was a significant rise in \( P_{aO_2} \) from 2 to 12 hours (0.025 < \( P < 0.05 \)) probably related to a minor fluctuation in the \( F_{iO_2} \). There was no significant change in \( P_{aCO_2} \). In the test animals, there was a fall in \( P_{aCO_2} \) from 54 to 43 (\( P > 0.05 \)) and no change in \( P_{aO_2} \) between the initial readings and 2 hours before death and no significant difference in \( P_{aCO_2} \) between control or test animals in this time.

The cardiovascular measurements are shown in Table III. At 2 hours, the two groups are again essentially comparable, the only difference being a lower cardiac output in the test group (1.91 l./min ± 0.15 compared with 2.40 ± 0.29) and a small increase in mean pulmonary artery pressure.

Table III
Cardiovascular data in two groups of dogs anaesthetized with halothane and breathing spontaneously gas comprising either 100 per cent oxygen at 2 ATA or 40 per cent oxygen/60 per cent nitrogen at 1 ATA. The results are expressed as means ± standard error of the mean.

<table>
<thead>
<tr>
<th>Time</th>
<th>Heart rate (beat/min)</th>
<th>Mean arterial pressure (mm Hg)</th>
<th>Cardiac output (l./min)</th>
<th>Central venous pressure (mm Hg)</th>
<th>Mean pulmonary artery pressure (mm Hg)</th>
<th>Haemoglobin (g/100 ml)</th>
<th>PCV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control dogs at 1 ATA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hrs</td>
<td>129 ± 8</td>
<td>97 ± 6</td>
<td>2.40 ± 0.29</td>
<td>-1.5 ± 0.9</td>
<td>6.9 ± 1.2</td>
<td>14.5 ± 0.5</td>
<td>42 ± 2</td>
</tr>
<tr>
<td>12 hrs</td>
<td>142 ± 10</td>
<td>94 ± 5</td>
<td>3.0 ± 0.5</td>
<td>-2.3 ± 0.7</td>
<td>10.1 ± 1.7</td>
<td>15.3 ± 0.9</td>
<td>47 ± 3</td>
</tr>
<tr>
<td>24 hrs</td>
<td>138 ± 8</td>
<td>97 ± 5</td>
<td>2.34 ± 0.30</td>
<td>-3.0 ± 1.1</td>
<td>10.1 ± 1.4</td>
<td>14.5 ± 1.1</td>
<td>44 ± 3</td>
</tr>
<tr>
<td>Dogs at 2 ATA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hrs</td>
<td>122 ± 6</td>
<td>93 ± 6</td>
<td>1.91 ± 0.15</td>
<td>-0.7 ± 0.7</td>
<td>10.3 ± 1.8</td>
<td>14.5 ± 0.7</td>
<td>40 ± 0</td>
</tr>
<tr>
<td>2 hrs before apnoea</td>
<td>111 ± 14</td>
<td>81 ± 8</td>
<td>2.43 ± 0.6</td>
<td>-1.7 ± 0.9</td>
<td>12.1 ± 1.5</td>
<td>15.7 ± 1.1</td>
<td>48 ± 1</td>
</tr>
<tr>
<td>Apnoea</td>
<td>118 ± 14</td>
<td>76 ± 9</td>
<td>2.21 ± 0.30</td>
<td>-1.8 ± 1.0</td>
<td>13.7 ± 2.3</td>
<td>16.3 ± 0.9</td>
<td>48 ± 2</td>
</tr>
</tbody>
</table>
in the test group (10.3 ± 1.8 mm Hg compared with 6.9 ± 1.2 mm Hg), neither of these changes being significant (P > 0.05). In the control group of animals at 12 hours, the only changes of note were a small increase in cardiac output and in mean pulmonary artery pressure. At 24 hours, there was no further significant change in any of the measurements. In the test group at 2 hours before apnoea, the only significant change was again a small increase in cardiac output (P < 0.01). The arterial oxygen tension, carbon dioxide tension and pH and mean arterial pressure immediately prior to the onset of apnoea are shown in Table IV and confirm that all six animals were in ventilatory failure. One animal (dog HHC) showed a marked degree of hypotension.

The terminal events in two of the animals (dog HHB and dog HHE) were examined in more detail and in dog HHE the changes are described in Figure 1. At time 11.00 p.m., the blood-gas and haemodynamic values had not changed from the initial recordings 12 hours previously in this animal. In particular, arterial Pco₂ was 40 mm Hg. By 1.00 a.m. (2 hours later) minute ventilation had fallen from over 6 l./min to less than 2 l./min and arterial carbon dioxide tension had reached 30 mm Hg.

<table>
<thead>
<tr>
<th>Dog</th>
<th>Pao₂ (mm Hg)</th>
<th>Paco₂ (mm Hg)</th>
<th>pH (units)</th>
<th>Mean systemic b.p. (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHA</td>
<td>940</td>
<td>140</td>
<td>6.900</td>
<td>75</td>
</tr>
<tr>
<td>HHB</td>
<td>1040</td>
<td>125</td>
<td>6.980</td>
<td>90</td>
</tr>
<tr>
<td>HHC</td>
<td>380</td>
<td>160</td>
<td>6.890</td>
<td>30</td>
</tr>
<tr>
<td>HHD</td>
<td>620</td>
<td>125</td>
<td>6.900</td>
<td>100</td>
</tr>
<tr>
<td>HHE</td>
<td>820</td>
<td>150</td>
<td>6.920</td>
<td>85</td>
</tr>
<tr>
<td>HHF</td>
<td>820</td>
<td>150</td>
<td>6.920</td>
<td>85</td>
</tr>
</tbody>
</table>

**Table IV**

Arterial blood gases, pH and mean systemic pressure in dogs exposed to 100 per cent oxygen at 2 ATA immediately prior to the onset of apnoea.

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Oxygen toxicity—halothane series. Terminal events in dog HHE (100 per cent oxygen at 2 ATA).
140 mm Hg. The arterial oxygen tension, however, was still elevated at 1,200 mm Hg. Gentle manual intermittent positive pressure ventilation of the dog over a period of 20 minutes succeeded in reducing the arterial carbon dioxide tension to a value of 55 mm Hg (with a pH of 7.350 units). At this time, the dog had a lash reflex and eye movement but no gross voluntary movement. On cessation of the intermittent positive pressure ventilation, the animal was unable to sustain adequate alveolar ventilation and, despite by now a minimal level of anaesthesia (supported by the rise to almost 4 l./min in cardiac output), returned to a state of respiratory failure.

In figure 2 are shown the changes which dog HHB underwent. This animal proceeded in a steady state for just over 10 hours with a $P_{a\text{CO}_2}$ of 1,100–1,200 mm Hg and an arterial $P_{\text{CO}_2}$ of 50–55 mm Hg. Then, within the space of half an hour, ventilatory failure became established, the $P_{a\text{CO}_2}$ rising to 125 mm Hg and the $P_{\text{CO}_2}$ falling slightly from 1,160 to 1,040 mm Hg. The mean arterial pressure at this time was 70 mm Hg and cardiac output 1.3 l./min. Halothane administration was discontinued and the animal ventilated gently by hand and the chamber decompressed. On reaching 1 ATA and having reduced the $P_{a\text{CO}_2}$ to 38 mm Hg in half an hour, halothane was reintroduced in 40 per cent oxygen/60 per cent nitrogen at a concentration of 0.5 per cent and the dog recommenced spontaneous ventilation which persisted until sacrifice at 24 hours. During the period of intermittent positive pressure ventilation, the dog possessed a lash reflex and eye movements, but no gross voluntary movements. For the remainder of the time spent at 1 ATA, arterial $P_{O_2}$ varied between 140 and 160 mm Hg, $P_{a\text{CO}_2}$ dropped from the high initial value of 78 to 53 mm Hg and cardiac output varied between 1.6 and 1.8 l./min.

**Pathology**

Macroscopic examination of the lungs revealed only a small amount of congestion in the dependent lung in both groups. In particular, there was no apparent difference in appearance between the two groups. Histological examination of the lungs after fixation by inflation of the lungs with 10 per cent neutral buffered formalin revealed a substantially normal appearance.

**DISCUSSION**

The major findings in this study are that dogs anaesthetized with halothane at 1 ATA revealed remarkable cardiovascular and respiratory stability over a period of time as long as 24 hours; at 2 ATA with 100 per cent oxygen, there was similar stability for a mean time of 12 hours following which acute ventilatory failure occurred in the space of $\frac{1}{2}$–2 hours, with no other significant changes. An impression was also gained that animals at 2 ATA on 100 per cent oxygen required less halothane for the same level of anaesthesia as animals on oxygen/nitrogen at 1 ATA.

There is now considerable evidence to show that during conventional general anaesthesia, there is no progressive rise in the alveolar-arterial oxygen tension difference. Panday and Nunn (1968) found steady $P_{a\text{O}_2}$ values in patients breathing spontaneously for about 2 ½ hours, and in spontaneously breathing horses no change was found in A–a $P_{O_2}$ differences over a few hours (Hall, Gillespie and Tyler, 1968). This work confirms that over a period of time as long as 24 hours, in dogs anaesthetized with halothane in oxygen/nitrogen, there are no progressive changes in A–a $P_{O_2}$ differences or pulmonary shunt ratios.
Clarke, Sandison and Ledingham (1969) obtained similar findings in dogs anaesthetized with a neuroleptanalgesic technique. It should be emphasized that the level of anaesthesia was much lighter than that associated with surgical anaesthesia and the consequent minimal cardiovascular depression was probably a major factor in preservation of normal arterial oxygenation.

Cardiovascular and respiratory measurements in the animals exposed to 100 per cent oxygen at 2 ATA were indistinguishable from those at 1 ATA during the first 12 hours of anaesthesia. The lack of depression of cardiovascular function contrasts with a previous report of cardiovascular depression occurring after some 4 hours exposure at 2 ATA to 100 per cent oxygen in animals anaesthetized with trichloroethylene and subjected to intermittent positive pressure ventilation (Smith and Ledingham, 1970); the development of acute respiratory failure as the mechanism of death contrasts with a previous report of cardiovascular depression occurring after some 4 hours exposure at 2 ATA to 100 per cent oxygen in animals anaesthetized by neuroleptanalgesia (Clarke, Sandison and Ledingham, 1969).

It has been known for some time that at pressures much higher than those employed in the present study, different anaesthetic agents modify oxygen toxicity in different ways (Bean and Zee, 1965) and also that hyperbaric oxygen may cause respiratory failure in rats (Jamieson and Cass, 1967). It is generally accepted that lung pathology occurs in the absence of convulsions at oxygen pressures below 2 ATA (Bean, 1945; Wood, 1969), although this dividing line may vary according to differences in species susceptibility (Smith, 1899). In conscious dogs, death occurs from pulmonary changes at oxygen pressures of 2 ATA whilst elevation of the pressure to 2.5 ATA induces convulsions (Winter et al., 1967). The unusual feature of the results presented here is the demonstration of a c.n.s mechanism of death at this relatively low pressure and its existence is supported in part by some of the results reported by Clarke, Sandison and Ledingham (1969). The existence of c.n.s. disturbances caused by oxygen at subconvulsive pressure is not a new concept; it has been advocated that symptoms in man of paraesthesiae, malaise and fatigue might result from a c.n.s. response to oxygen at 1 ATA (Welch, Morgan and Clamann, 1963).

The reduction in buffering capacity of haemoglobin when fully saturated, as occurs in venous blood when the inspired gas is 100 per cent oxygen at high pressure, leads to a rise in tissue carbon dioxide tension and a fall in tissue pH (Gesell, 1923). Data obtained of brain carbon dioxide tensions under high pressure oxygen conditions have been reviewed recently by Wood (1969) who concludes that such changes are small —of the order of 5 mm Hg. It is likely that this loss of the dual role of haemoglobin in combination with the respiratory depressant effect of halothane plays a contributory role in the production of respiratory failure but that the main mechanism lies in direct depression of central nervous system enzyme systems (Haugaard, 1968).

That overdose with halothane was responsible for the onset of respiratory failure is unlikely for several reasons:

1. Clinically, the dogs were in a very light state of anaesthesia throughout the duration of the experiment and the test dogs possessed a lash reflex whilst developing respiratory failure.

2. The terminal events described in the Results section for dog HHE would imply irreversibility of ventilatory failure, whilst ventilation with 100 per cent oxygen at 2 ATA continued. In contrast to this in dog HHB, a change to oxygen/nitrogen at 1 ATA permitted the re-establishment of adequate spontaneous ventilation, the reason for this being either the cessation of hyperbaric oxygen or the introduction of nitrogen which is known to offer protection against oxygen toxicity at pressures lower than 3 ATA (Smith, Ledingham and Sandison, 1970).

It would appear that the test animals required less halothane than the control animals for the same level of anaesthesia. In the Appendix is given the concentrations of halothane delivered by the Fluotec Mk II at the flow rates in use during the experiment at 1 and 2 ATA. There was a reduction in delivered concentration of halothane at 2 ATA compared with the results of McDowall (1964), although different flow rates have been used here. A full analysis of the performance was not undertaken at this time as our interest was in ensuring that excessive halothane was not being delivered at 2 ATA.

In view of the induction with thiopentone and fentanyl and the possibility of c.n.s. toxicity at 2 ATA after several hours, it is not possible to
state from this work that the m.a.c. value is lower with 100 per cent oxygen at 2 ATA than oxygen/nitrogen at 1 ATA. This hypothesis is the subject of a further investigation at present in progress.

Pulmonary oedema has been described as a major feature in the classical Lorrain Smith effect (Binger, Faulkner and Moore, 1927). In this experiment, pulmonary oedema has not been apparent. There was no oedema obvious on pathological examination and the relatively low pulmonary artery pressures in the terminal stages would not support such a diagnosis. In figure 1, the high terminal $P_aO_2$ with complete ease of reversal of ventilatory failure would also mitigate against pulmonary oedema which in the unanaesthetized dog is present by 14 hours (Karasewitch, 1961, unpublished observations). Absorption atelectasis has been implicated for many years as a contributory factor in pulmonary oxygen toxicity (Morgan, 1968; Penrod, 1956) and this may explain the moderately raised $Qs/Qt$ of 32 per cent.

It is felt that this work supports the concept that oxygen toxicity at relatively low pressures involves many systems and is not primarily a pulmonary toxic process.

APPENDIX

The halothane concentrations delivered by the Fluotec Mk II used in this experiment are shown below, expressed as a percentage of 1 ATA. At 1 ATA, a flow rate of 10 l./min of oxygen was used whilst at 2 ATA the flow rate was 12 l./min. Measurements were made using a Riken-Joburg Type 17 portable refractometer on loan from Cyprane Limited.

<table>
<thead>
<tr>
<th>Fluotec setting</th>
<th>Refractometer readings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 ATA</td>
</tr>
<tr>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>0.75</td>
<td>0.63</td>
</tr>
<tr>
<td>1.0</td>
<td>0.88</td>
</tr>
<tr>
<td>1.25</td>
<td>1.12</td>
</tr>
</tbody>
</table>

ACKNOWLEDGEMENTS

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REFERENCES


Smith, J. L. (1899). The pathological effects due to increase of oxygen tension in the air breathed. J. Physiol. (Lond.), 24, 19.


L'INFLUENCE DE L'ANESTHESIE A L'HALOTHANE SUR LA TOXICITE DE L'OXYGENE

SOMMAIRE
Douze chiens ont été anesthésiés à l'halothane; ils respiraient ensuite spontanément un gaz contenant soit 100 pour cent d'oxygène à 2 ATA (groupe d'essai), soit 40 pour cent d'oxygène/60 pour cent de nitrogène à 1 ATA (groupe-contrôle). Le groupe-contrôle à survécu les 24 heures sans modification significative du débit cardiaque, du rapport shunt pulmonaire ou de la différence A-a Po2. Les animaux de groupe d'essai ont succombé en insuffisance respiratoire en moyenne après 14.03 heures avec un rapport shunt pulmonaire de 32 pour cent. Le groupe d'essai présenta à l'apnée une fonction cardiovasculaire défaillante (débit cardiaque 2,21 ± 0,30 l/min; pression artérielle 76 ± 9 mm Hg). On en conclut que l'insuffisance respiratoire était due à l'association de l'halothane et les effets de l'oxygène sous pression élevée.

DER EINFLUSS HALOTHANANESTHESIE AUF DIE SAUERSTOFFTOXIZITAT

ZUSAMMENFASSUNG
12 Hunde wurden mit Halothan narkotisiert bei Spontanatmung von 100% Sauerstoff von 2 ATA (Testgruppe) oder 40% Sauerstoff/60% Stickstoff von 1 ATA (Kontrollgruppe). Die Kontrollgruppe überlebte, ohne daß es innerhalb von 24 Stunden zu signifikanten Veränderungen im Herzminutenvolumen, der pulmonalen Shuntverhältnisse oder der A-a Po2-Diffe-

BOOK REVIEW

This is a collection of thirty-three papers given at the annual meeting of the International Society of Parenteral Nutrition. The papers are collected under three main headings: advances in complete parenteral nutrition; advances in the use of amino acids for parenteral nutrition; and physiological and special clinical findings. Slightly less than half of the papers are printed in English, papers mainly given by American, English, Scandinavian and Japanese authors; the rest of the papers are in German.

On the whole, the English papers are the more interesting ones and this book can, therefore, be recommended to doctors who cannot read German.

Progress in this specialty has been so rapid that the subject matter of most of the important papers has, in the meantime, appeared somewhere else in the medical literature.

In the many papers dealing with long-term parenteral nutrition there are relatively few cases where parenteral nutrition was given for more than one or, at the most, two weeks and in many of the examples listed one wonders whether it was of much use at all. Anaesthetists and surgeons working with these patients would like to know how the dreaded complications of this therapy such as septicaemia and pulmonary embolism can be overcome; unfortunately, there is little mention of these complications in these papers. In fact, the influence of the Americans, who are not allowed to use intravenous fat emulsions and have, therefore, always to resort to vena cava infusions when giving parenteral infusions, pervades most of the papers. The routine setting up of central infusions regardless of the length of time and the substances used for intravenous alimentation is frequently advocated.

Another subject which has worried medical men using intravenous fat infusions is the possible danger of thrombocytopenia and haemorrhages. The results reported at this meeting were somewhat conflicting. Huth and Hasenkopf, using Lipofundin in animal experiments, could produce some thrombocytopenia, although not as bad as that seen in former times with Lipomul. On the other hand, Halmagyi could not demonstrate any thrombocytopenia when giving Lipofundin in long-term infusions to patients.

It is impossible in a few words to do justice to the many excellent contributions. Any anaesthetist, surgeon or physician interested in intensive therapy should read this book, which is well illustrated and printed.

P. P. Rickham