Influence of Oxygen on Hypothermic Cardiac Standstill in the Heart-Lung Preparation

By HENRY BADEER, M.D.

Administration of pure oxygen to denervated dog heart-lung preparation subjected to hypothermia does not affect the temperature that induces terminal ventricular fibrillation even when the progressive alkalemia that occurs is prevented. It is concluded that hypoxia of the myocardium is not a factor in the terminal cardiac arrest that supervenes in hypothermic of the heart-lung preparation.

SOME investigators suggest that cessation of the heart beat in acute severe hypothermia may be primarily due to hypoxia of the myocardium as a consequence of the marked shift of the oxyhemoglobin dissociation curve to the left. However, more recent work supports the view that at temperatures as low as 17 C the myocardium does not suffer hypoxia (relative to demand), as suggested by the finding that coronary arteriovenous oxygen difference remains unchanged, and that artificial respiration with oxygen does not alter the course of cardiac behaviour during hypothermia. Since no data on the effect of oxygen have been reported, this study was undertaken to determine specifically the influence of increased oxygen on the critical hypothermic temperature at which the heart ceases to beat in the Starling heart-lung preparation.

METHODS

All experiments were performed on unselected dogs weighing between 7.7 and 11.9 kgs. Defibrinated blood taken from animals anesthetized with chloroform was used to perfuse the denervated heart-lung preparation (HLP). Operations were performed under pentobarbital anesthesia. The systemic output at the start of each experiment was adjusted to around 600 cc/min. and the mean aortic pressure to around 100 mm Hg (mercury manometer). The peripheral resistance was unchanged throughout the experiment. The pH of arterial blood was determined by diverting the flow into a parallel circuit provided with a glass chamber into which the electrodes of a Beckman pH meter (model G) were inserted. Readings were made when the blood was excluded from the systemic circuit. The temperature of the S-A nodal tissue was recorded by the method described previously. Heart rate and disturbances in rhythm were recorded with a Sanborn direct-writing electrocardiograph. The heart was cooled gradually by adding ice to the water bath, starting with a blood temperature between 31.1 and 35.4 C. At about every two degrees lowering of temperature, readings of S-A and cannula temperatures and ECC were taken until 25 C was reached. Below this, readings were made with every degree cooling until the ventricles ceased pumping out blood, arterial pressure falling to near zero and remaining so for at least five minutes.

The first series consisted of control experiments with air-inflation of the lungs. In a second series, the same procedure was carried out with the exception that 100 per cent oxygen was used to inflate the lungs. In addition, this was supplemented by saturating the blood in the venous reservoir with 100 per cent oxygen by the method of gas dispersion. The foaming was effectively prevented by coating air-filled glass beads floating over the blood with Dow Corning Antifoam compound A.

In a third group of experiments the lungs were inflated with oxygen containing varying amounts of carbon dioxide to maintain the pH of aortic blood around 7.4. In all three groups of experiments artificial respiration was adjusted to keep aortic blood distinctly red.

RESULTS

Control Experiments. Cooling the heart in a HLP progressively slows its rate of beating in a linear fashion until the temperature reaches about 24 C, when sudden asystole with dilatation of the chambers appears. The standstill is not permanent and, within a minute or so, beats are resumed, usually from a ventricular focus. In five experiments the S-A temperature
at which sudden asystole appeared averaged 22.5°C, prior to which the sinus rhythm averaged 46/min. (table 1). There was a slight drop in the mean aortic pressure as recorded with the mercury manometer. The rhythm of the heart subsequent to sudden stoppage does not follow a definite pattern with further cooling. There may be several periods of asystole or periods of acceleration. As a general rule, however, there is gradual slowing until finally ventricular fibrillation supervenes. In all the experiments that could be carried to circulatory standstill the terminal event was ventricular fibrillation. The average S-A temperature at which this occurred in five experiments was 18.3°C, with a standard error of the mean of ±0.7 (table 1). The blood pH (corrected for temperature effects) showed progressive alkalinity reaching an average of 7.85 at the time of ventricular fibrillation (3 experiments). The terminal mean aortic pressure recorded with the mercury manometer is grossly inaccurate when the heart is beating very slowly and is therefore not reported. However, in most experiments there was a distinct drop in pressure.

**Oxygen Experiments.** In this group of experiments the results are practically the same as those of the control group. The mean temperature at which ventricular fibrillation occurred was 17.7°C, S.E. ±0.56 and the pH of blood progressively increased from an average of 7.46 to 7.96 (table 2).

**Oxygen with Carbon Dioxide Experiments.** In two of five experiments the sudden stoppage around 23°C did not occur. However,
Table 3.—HLP. Inflation of Lungs with Oxygen Containing Carbon Dioxide. Room Temperature 18-19 C.

<table>
<thead>
<tr>
<th>Exp No.</th>
<th>Initial Heart Rate/Min.</th>
<th>Cannula Temp. °C</th>
<th>M.A.P. mm Hg</th>
<th>Temporary Asystole Heart Rate/Min. Prior to S-A Temp. at Onset of °C.</th>
<th>M.A.P. mm Hg</th>
<th>Terminal Event</th>
<th>S-A Temp. at Onset of °C.</th>
<th>M.A.P. mm Hg</th>
<th>Terminal Fibrillation Heart Rate/Min.</th>
<th>S-A Temp. at Onset of °C.</th>
<th>M.A.P. mm Hg</th>
<th>Aortic Blood pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>112</td>
<td>33.8</td>
<td>94</td>
<td>27</td>
<td>20.1</td>
<td>90</td>
<td>V.F.</td>
<td>16.6</td>
<td>7.4</td>
<td>7.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>126</td>
<td>32.9</td>
<td>112</td>
<td>27</td>
<td>19.3</td>
<td>106</td>
<td>V.F.</td>
<td>18.1</td>
<td>7.48</td>
<td>7.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>91</td>
<td>34.5</td>
<td>98</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>V.F.</td>
<td>19.6</td>
<td>7.35</td>
<td>7.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>150</td>
<td>34.5</td>
<td>100</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>V.F.</td>
<td>18.8</td>
<td>7.42</td>
<td>7.43</td>
<td></td>
<td></td>
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<tr>
<td>22</td>
<td>118</td>
<td>35.1</td>
<td>94</td>
<td>39</td>
<td>24.7</td>
<td>86</td>
<td>V.F.</td>
<td>20.0</td>
<td>7.56</td>
<td>7.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>119</td>
<td>34.1</td>
<td>100</td>
<td>94</td>
<td></td>
<td></td>
<td>18.6</td>
<td>±0.6</td>
<td>7.45</td>
<td>±0.03</td>
<td>±0.05</td>
<td></td>
</tr>
</tbody>
</table>


S.E. = \( \sqrt{\frac{\sum \delta^2}{n(n-1)}} \)

the terminal event in all five experiments was ventricular fibrillation. The average critical temperature at which fibrillation set in was 18.6 C, S.E. ±0.6 even though blood pH was kept almost constant (table 3).

**Discussion**

From the data it is clear that the presence of increased oxygen physically dissolved in the blood does not lower the critical hypothermic temperature which produces ventricular fibrillation in the HLP. The inhalation of 100 per cent oxygen increases the quantity of physically dissolved oxygen in blood at 38 C from 0.25 vol per cent to about 2 vol per cent.10 Besides, cooling blood from 38 C to 20 C further increases the dissolved oxygen by about 50 per cent.10 It is reasonable to expect that such an increase in oxygen supply would have a detectable effect on the critical hypothermic temperature if hypoxia played a role in the onset of hypothermic cardiac arrest.

In the air-inflated HLP, blood becomes distinctly alkaline, presumably as a result of washing out of carbon dioxide.14 Since alkalinity shifts the oxyhemoglobin dissociation curve to the left and may aggravate possible hypoxia of the myocardium due to cooling, it was necessary to maintain blood pH around normal. This was accomplished by inflating the lungs with oxygen containing adequate amounts of carbon dioxide. The results show clearly that alkalinity of blood in the control and oxygen experiments did not contribute to the onset of ventricular fibrillation and standstill.

These findings support the view that hypoxia does not contribute to the arrest of the heart in hypothermia. Hegnauer has reviewed the evidence against the hypoxia theory and the recent work of Berne and Hegnauer also provide additional evidence.

In connection with the theory of hypoxia, the interesting experiments of Lutz may be discussed briefly. Lutz found that guinea-pigs subjected to high pressures of oxygen during severe lethal hypothermia could be revived after much longer periods of "apparent" death than control animals breathing air and concluded that hypothermia causes death by inducing hypoxia of tissues. However, these results may be interpreted differently in the light of recent work. Assuming that hypothermia inhibits the functional activity of tissues by direct action, the presence of greater amounts of oxygen in cooled tissues should favor their viability since tissues continue to use oxygen after the cessation of circulation and respiration before "irreversible" damage is done. Obviously, the presence of greater amounts of O2 available would postpone the "irreversible" damage. According to this concept, if the body is cooled below the lethal hypothermic temperature, resuscitation should be further enhanced because of the reduced demand for oxygen. This is borne out by other experiments of Lutz in which he obtained...
recovery in some guinea-pigs subjected to excess oxygen and cooled to 0–1 C rectal temperature after the heart had stopped for as long as 72 minutes (the average lethal hypothermic temperature being around 14 C). Likewise, if the flow of oxygenated blood to the myocardium and tissues is maintained during severe hypothermia, recovery should be further enhanced. This has been demonstrated recently by Gollan by means of a pump-oxygenator with which he obtained survival in dogs after cardiac arrest of one hour duration during hypothermia of 0 C. The above concept also explains why resuscitative measures are more effective after hypothermic death than normothermic death following cardiorespiratory arrest.

SUMMARY AND CONCLUSIONS

The mean hypothermic temperature at which the dog heart stopped beating in five air-inflated heart-lung preparations was 18.3 C, S.E. ±0.7, and the mean terminal blood pH was 7.85. When the lungs were inflated with 100 per cent oxygen, the mean temperature at which ventricular fibrillation occurred in seven experiments was 17.7 C, S.E. ±0.56, and the mean terminal blood pH was 7.96. When the lungs were inflated with oxygen containing carbon dioxide to maintain blood pH around 7.4, ventricular fibrillation occurred at a mean temperature of 18.6 C, S.E. ±0.6, in five experiments.

It is concluded that hypoxia of the myocardium is not a factor leading to hypothermic fibrillation of the ventricles in the dog heart-lung preparation.

REFERENCES

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