Effect of Hypothermia on Oxygen Consumption and Energy Utilization of Heart

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The oxygen uptake of the denervated dog's heart doing constant work in a modified HLP appears to vary logarithmically with temperature between 36 and 26 C. Under these conditions hypothermia increases the mechanical efficiency of the heart. It is concluded that cold does not interfere with the conversion of aerobic energy into useful work done by the myocardium.

Edwards and colleagues noted a reduction of 47 per cent in the oxygen consumption of the left ventricular myocardium in anesthetized dogs cooled from 37.5 to 26.4 C, when the work of the left ventricle was reduced by 79 per cent. There was a fall in the mechanical efficiency from 20.3 per cent to 7.8 per cent, suggesting that cold induces a failure in aerobic energy utilization of the myocardium. However, in the intact animal, factors other than the direct effect of cold might reduce the efficiency of the heart during hypothermia, e.g., reduced work of the heart or possible neurohumoral changes. These factors can be eliminated by resorting to the heart-lung preparation (HLP).

Evans has observed in a few closed circuit heart-lung preparations that mechanical efficiency of the heart is increased as the temperature is lowered when the work of the heart is kept constant. He determined the oxygen uptake of the heart by the so-called “external method.” In this method the total oxygen uptake of the HLP is found and from this value the consumption of isolated perfused lungs is subtracted.

Since coronary sinus blood and Thebesian venous blood do not have the same oxygen content and coronary sinus flow is not a constant fraction of total coronary flow, the use of direct Fick method to determine total cardiac oxygen consumption imposes a serious difficulty. This was overcome by adapting the technic of Rodbard, Graham and Williams to the HLP in which a sample of mixed coronary venous blood could be obtained from the pulmonary artery. Thus, direct Fick principle may be applied (with only slight inaccuracy) to determine the total gaseous metabolism of the heart. The present report deals with a study of the effect of hypothermia on cardiac oxygen consumption and mechanical efficiency in such a modified HLP under conditions of constant work.

Methods

Modified heart-lung preparations were performed as described in a previous communication on unselected dogs weighing 9.4 to 17.0 Kg. The lungs were inflated with 100 per cent oxygen and the blood in the venous reservoir saturated with oxygen by gas dispersion. Left ventricular output was maintained at about 460 ml./min. and mean aortic pressure at 80 mm Hg. Heart rate was recorded with a Sanborn Viso-Cardiette. In some preliminary experiments the left pulmonary arterial pressure was recorded with a mercury manometer. Total coronary flow was measured with a recording rotameter in the left pulmonary artery using a dampening chamber. Samples of arterial blood were taken into syringes moistened with normal saline from a point just beyond the cannula in the brachiocephalic artery and mixed coronary venous blood taken from the left pulmonary artery about 10 cm. beyond the pulmonary valve. For purposes of stirring the blood before analysis, some mercury was drawn into the syringe which was then sealed with a needle stump soldered at its tip. Samples of blood were immediately refrigerated until duplicate analyses were done with the Van Slyke manometric apparatus on the same day. The cooling extended from 37 to 26 C., and in some experiments the heart was rewarmed to 37 C. At the end of each experiment the right atrium was examined for the presence of septal defect and anomalous venous drainage. The oxygen consumption of the heart was calculated by

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TABLE 1.—Modified HLP Subjected to Hypothermia, Mean of Ten Experiments

<table>
<thead>
<tr>
<th>S-A temp. C</th>
<th>Heart rate/min.</th>
<th>Arterial O₂ content vol. %</th>
<th>Coronary O₂ Diff. vol. %</th>
<th>Coronary blood flow ml/100 Gm./min.</th>
<th>Myocardial O₂ Consumption cc/100 Gm./min.</th>
<th>Left vent. output ml/min.</th>
<th>Right vent. output ml/min.</th>
<th>Work of heart Kg. A·M. /min.</th>
<th>Mechanical efficiency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>36.4</td>
<td>151</td>
<td>21.0</td>
<td>11.1</td>
<td>59</td>
<td>5.90±0.24</td>
<td>0.089</td>
<td>485</td>
<td>62</td>
<td>0.54</td>
</tr>
<tr>
<td>32.6</td>
<td>120</td>
<td>20.0</td>
<td>6.6</td>
<td>76</td>
<td>4.47±0.19</td>
<td>0.038</td>
<td>470</td>
<td>78</td>
<td>0.22</td>
</tr>
<tr>
<td>29.3</td>
<td>92</td>
<td>21.5</td>
<td>6.3</td>
<td>69</td>
<td>4.02±0.26</td>
<td>0.044</td>
<td>458</td>
<td>70</td>
<td>0.51</td>
</tr>
<tr>
<td>26.1</td>
<td>65</td>
<td>21.5</td>
<td>5.4</td>
<td>64</td>
<td>3.17±0.36</td>
<td>0.048</td>
<td>446</td>
<td>65</td>
<td>0.49</td>
</tr>
<tr>
<td>36.2*</td>
<td>134*</td>
<td>20.0*</td>
<td>4.9*</td>
<td>122*</td>
<td>5.36±0.13*</td>
<td>0.044*</td>
<td>472*</td>
<td>88*</td>
<td>0.54*</td>
</tr>
</tbody>
</table>

Aortic pressure kept constant at 80 mm Hg throughout all experiments.

* Mean of four experiments.
† Mean of values obtained from individual experiments.
± = Standard error of the mean.

multiplying the coronary flow with the A-V oxygen difference. Cardiac work was calculated as follows:

L. V. work (Kg. N M./min.) = L. V. output (L./min.) × aortic pressure (meters) × 13.6
R. V. work (Kg. N M./min.) = R. V. output (L./min.) × 3/4 aortic pressure (meters) × 13.6

Mechanical efficiency (%) = Work of two ventricles (Kg. N M./min.) × 100
Myocardial O₂ uptake (cc/100 Gm./min.) × 2

The oxygen uptake is multiplied by 2 to convert it into energy units, as 1 cc. oxygen consumed represents 2 Kg. N M. of work.

RESULTS

Data obtained from ten satisfactory experiments are shown in table 1. Arterial blood oxygen contents varied between 17.8 and 25.7 vol. per cent, thus ruling out any possibility of hypoxia of the myocardium as a result of hypoxemia. The work of the heart was maintained between 0.5 and 0.55 Kg. N M./min. in all the experiments. This low level of work was intended to avoid overloading the heart during hypothermia which causes marked bradycardia.

In contradistinction to the intact dog's heart,1 hypothermia in the HLP caused a distinct drop in the coronary A-V oxygen difference (table 1), probably as a result of the relatively high coronary blood flow as compared to that in the intact animal. Hypothermia in the denervated HLP with constant aortic pressure and left ventricular output causes an increase in coronary blood flow, confirming the observation of Nakagawa.8

The oxygen uptake of the heart exhibited an exponential decrease with reduction in temperature although the work of the heart was kept practically unchanged (fig. 1). The bars indicate the standard error of the mean. The Q₁₀ between 36 and 26 C. is about 1.83 which represents a reduction of about 45 per cent in the oxygen consumption. However, the oxygen

Fig. 1. Effect of hypothermia on myocardial oxygen consumption in the modified HLP performing constant work.
uptake per beat increases at low temperatures (table 1).

The low mechanical efficiency of the heart in our experiments is probably due to the low level of cardiac work. During hypothermia efficiency is increased (table 1), confirming the observations of Evans.3

The data in table 1 also show that the changes in heart rate, oxygen consumption and mechanical efficiency of the heart are reversible upon rewarming to 36°C. However, coronary blood flow undergoes a marked increase compared to initial values, a change that results in a proportionate lowering of A-V oxygen difference.

**DISCUSSION**

The relationship between the oxygen uptake of the mammalian heart and temperature has not been carefully studied. The recent statement that it is linear, similar to that of the brain,9 is not based on adequate data. Although Penrod10 found that the coronary A-V oxygen difference remains unchanged during hypothermia in the anesthetized animal, he did not measure coronary flow to determine the oxygen consumption of the heart. Furthermore, in the intact animal there is no possibility of maintaining the work of the heart constant; this in itself would markedly alter the metabolic rate. Such considerations necessitated the use of our HLP, however, an important drawback of this preparation is that the right ventricle is pumping only the coronary flow and therefore is doing much less work than normal.

Our data show that there was no change in the oxygen consumption after a period of cooling and rewarming which averaged 100 min. in 4 experiments. The exponential relation between temperature and myocardial oxygen uptake and a Q10 of 1.83 are in general agreement with van't Hoff's rule. A similar relation has been obtained for the total oxygen consumption of intact dogs during generalized hypothermia from 37.5 to 23.5°C.11 In our experiments, the reduced cardiac metabolism during hypothermia is due to at least two factors, (1) direct effect of temperature, and (2) slowing of the heart. The relative influence of each of these factors requires further study.

The greater oxygen consumption per beat at 26°C indicates that the direct effect of cold in lowering the metabolic rate is outweighed by the rise in metabolism due to increased diastolic ventricular volume secondary to the bradycardia. The prolongation of the period of contraction and relaxation in hypothermia may have also contributed to this increase.

With regard to mechanical efficiency, it is clear that a drop in oxygen consumption doing the same work implies an increase in efficiency of the heart (fig. 2). This finding confirms the early work of Evans2 and does not support the conclusion of Edwards and colleagues1 that hypothermia causes a partial loss of the ability of the myocardium to convert aerobic energy into useful work. There is no evidence that cold induces a failure in the utilization of aerobic energy by heart muscle. The fall in the mechanical efficiency of the heart in the intact animal is probably secondary to the greatly diminished work caused by the drop in cardiac output and arterial pressure. However, it is possible that other factors such as changes in nervous and humoral influences on the heart (stimulation of cardiac sympathetics, secretion of adrenaline, etc.) may also be partly responsible for the lowered myocardial efficiency in the hypothermic animal.

**SUMMARY AND CONCLUSIONS**

In the modified dog, heart-lung preparation, cardiac oxygen consumption can be reliably determined by applying the Fick principle.
In such a preparation where the work of the heart is kept constant, hypothermia produced a decline in the oxygen uptake. Between 36 and 26°C, the relationship appears to be logarithmic, with a Q_{10} of 1.83. The decrease in oxygen consumption is attributed to at least two factors, the direct effect of cold on metabolic rate of myocardium and to bradycardia. The rise in mechanical efficiency during hypothermia under these conditions indicates that cold does not interfere with the conversion of aerobic energy into useful work.

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