Oxygen utilization by the heart bears an inconsistent relationship to its external mechanical work. Oxygen uptake of the heart lung preparation is influenced more by changes in intraventricular pressure than in minute volume of blood flow and is influenced by heart rate independently of changes in pressure or minute volume. These relationships have been amply confirmed in other types of preparations, in most instances either in open chest animals or in hearts isolated from the rest of the body where each hemodynamic factor could be controlled individually and its effect on oxygen utilization observed.

In the isolated heart a linear correlation has been demonstrated between minute oxygen consumption and the following two slightly different hemodynamic expressions: 1) mean systolic arterial pressure X heart rate, and 2) mean systolic arterial pressure X systolic ejection period, sec/min. The main purpose of this report is to examine the validity of these relationships under the following circumstances: 1) hearts of intact, anesthetized animals, 2) an extreme range of hemodynamic variables not attainable in isolated preparations, and 3) varied methods of altering hemodynamics. Experiments originally designed for varied purposes but which included a wide range of hemodynamic alterations should provide the most rigorous test of a possible correlation. Under the varied stimuli employed in these intact dogs, hemodynamic changes were less orderly than in isolated preparations, and simultaneous changes in more than one variable made analysis more difficult. These complicated adjustments, however, may more nearly resemble events naturally occurring in the unanesthetized animal.

Methods

Forty experiments were done in twenty-two dogs (18 to 26 kg) anesthetized with intravenous chloralose (50 mg/kg) plus urethane (500 mg/kg) or intravenous pentobarbital (20-25 mg/kg). Five dogs were premedicated with intramuscular morphine (50-150 mg) for depression of heart rate. Variations in heart rate, cardiac output and aortic pressure, in addition to those resulting from the type anesthesia used, were produced by blood removal, blood removal and volume replacement with dextran, obstruction of the ascending aorta with a balloon, injection of atropine (0.6 mg) and injection of methoxamine (4 mg).

The dogs' lungs were ventilated with a Harvard Respirator. Under fluoroscopic control, intravascular catheters were placed in the aorta, pulmonary artery and great cardiac vein. Observations were made over a four-minute period of steady aortic pressure and heart rate. Aortic blood pressure was measured by a P-23d Statham strain gauge recording on a Sanborn direct writer. Experiments were conducted with the dog in the supine position, and zero for aortic pressures was established at the estimated left atrial level. All blood oxygen contents were determined manometrically.

Cardiac output was calculated by the direct Fick method. Coronary blood flow was calculated by the nitrous oxide method. The left ventricle, including septum, was excised and weighed, and cardiac output and left ventricular mechanical work were expressed per 100 g of left ventricular muscle.

The following calculations have been made:

1. Left ventricular (LV) oxygen consumption (ml/100 g LV/min) = coronary arteriovenous oxygen difference (ml/ml) X coronary blood flow (ml/100 g LV/min).
## Table 1

**Oxygen Uptake of the Left Ventricle and Related Hemodynamic Data**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Aneurysm &amp; subsequent manipulations</th>
<th>LV weight (g)</th>
<th>Heart rate (bpm)</th>
<th>SEP (sec/min)</th>
<th>AP (mm Hg)</th>
<th>Cardiac output (mL/100 g LV/min)</th>
<th>CBCP (mm Hg)</th>
<th>Oxygen consumption (mL/100 g LV/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>chlor-urethane</td>
<td>165</td>
<td>61</td>
<td>16.0</td>
<td>181</td>
<td>1.8</td>
<td>47</td>
<td>12.2</td>
</tr>
<tr>
<td>2</td>
<td>chlor-urethane</td>
<td>98</td>
<td>102</td>
<td>24.5</td>
<td>108</td>
<td>3.5</td>
<td>83</td>
<td>12.7</td>
</tr>
<tr>
<td>3</td>
<td>chlor-urethane</td>
<td>98</td>
<td>167</td>
<td>23.0</td>
<td>138</td>
<td>2.2</td>
<td>108</td>
<td>10.5</td>
</tr>
<tr>
<td>4</td>
<td>chlor-urethane</td>
<td>67</td>
<td>178</td>
<td>24.0</td>
<td>60</td>
<td>1.8</td>
<td>49</td>
<td>14.1</td>
</tr>
<tr>
<td>5</td>
<td>pentobarbital</td>
<td>160</td>
<td>180</td>
<td>21.0</td>
<td>247</td>
<td>1.5</td>
<td>32</td>
<td>14.2</td>
</tr>
<tr>
<td>6</td>
<td>pentobarbital</td>
<td>103</td>
<td>184</td>
<td>23.0</td>
<td>166</td>
<td>2.5</td>
<td>70</td>
<td>17.4</td>
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<tr>
<td>7</td>
<td>pentobarbital</td>
<td>81</td>
<td>190</td>
<td>22.8</td>
<td>138</td>
<td>2.2</td>
<td>104</td>
<td>17.4</td>
</tr>
<tr>
<td>8</td>
<td>pentobarbital</td>
<td>134</td>
<td>189</td>
<td>23.8</td>
<td>247</td>
<td>1.8</td>
<td>98</td>
<td>18.8</td>
</tr>
<tr>
<td>9</td>
<td>chlor-urethane</td>
<td>124</td>
<td>187</td>
<td>22.5</td>
<td>156</td>
<td>2.7</td>
<td>121</td>
<td>17.5</td>
</tr>
<tr>
<td>10</td>
<td>cardiac tamponade</td>
<td>121</td>
<td>143</td>
<td>25.7</td>
<td>29</td>
<td>0.3</td>
<td>26</td>
<td>17.0</td>
</tr>
<tr>
<td>11</td>
<td>m-chlor-urethane</td>
<td>144</td>
<td>54</td>
<td>9.7</td>
<td>128</td>
<td>2.3</td>
<td>50</td>
<td>15.1</td>
</tr>
<tr>
<td>12</td>
<td>hypovolemia</td>
<td>146</td>
<td>23.4</td>
<td>8.6</td>
<td>60</td>
<td>2.2</td>
<td>60</td>
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<tr>
<td>13</td>
<td>m-chlor-urethane</td>
<td>95</td>
<td>43</td>
<td>10.8</td>
<td>125</td>
<td>1.5</td>
<td>46</td>
<td>11.1</td>
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<tr>
<td>14</td>
<td>hypovolemia + anemia</td>
<td>120</td>
<td>14.4</td>
<td>122</td>
<td>1.2</td>
<td>109</td>
<td>7.9</td>
<td>8.6</td>
</tr>
<tr>
<td>15</td>
<td>chlor-urethane</td>
<td>102</td>
<td>180</td>
<td>22.5</td>
<td>151</td>
<td>2.3</td>
<td>96</td>
<td>14.5</td>
</tr>
<tr>
<td>16</td>
<td>anemia</td>
<td>166</td>
<td>26.6</td>
<td>175</td>
<td>4.7</td>
<td>366</td>
<td>4.7</td>
<td>17.2</td>
</tr>
<tr>
<td>17</td>
<td>m-chlor-urethane</td>
<td>100</td>
<td>75</td>
<td>14.3</td>
<td>165</td>
<td>2.4</td>
<td>84</td>
<td>16.2</td>
</tr>
<tr>
<td>18</td>
<td>anemia</td>
<td>100</td>
<td>180</td>
<td>184</td>
<td>6.6</td>
<td>222</td>
<td>7.4</td>
<td>16.4</td>
</tr>
<tr>
<td>19</td>
<td>m-chlor-urethane</td>
<td>157</td>
<td>51</td>
<td>12.2</td>
<td>155</td>
<td>1.0</td>
<td>50</td>
<td>15.9</td>
</tr>
<tr>
<td>20</td>
<td>anemia</td>
<td>73</td>
<td>17.5</td>
<td>160</td>
<td>1.3</td>
<td>133</td>
<td>8.7</td>
<td>11.5</td>
</tr>
<tr>
<td>21</td>
<td>chlor-urethane</td>
<td>112</td>
<td>196</td>
<td>26.5</td>
<td>158</td>
<td>2.6</td>
<td>182</td>
<td>8.0</td>
</tr>
<tr>
<td>22</td>
<td>anemia</td>
<td>129</td>
<td>200</td>
<td>21.0</td>
<td>188</td>
<td>1.8</td>
<td>93</td>
<td>17.1</td>
</tr>
</tbody>
</table>

LV = left ventricle  
SEP = systolic ejection period  
AP = mean arterial pressure  
CBP = coronary blood pressure  
A-VO \textsubscript{2} = arteriovenous oxygen difference  
\( \dot{V}_{\text{oxygen}} \) = oxygen consumption  
Chlor-urethane = chloralose-urethane mixture  
M-chlor-urethane = chloralose-urethane following morphine premedication
VENTRICULAR OXYGEN UTILIZATION

2. LV external mechanical work* (kgM/100 g LV/min) = mean systolic aortic pressure (mmHg \times \frac{1.36}{100}) \times \text{cardiac output (L/100 g LV/min)}

3. "AP \times HR" = mean systolic aortic pressure† (mmHg) \times \text{heart rate}.

4. PTM‡ = mean systolic aortic pressure† (mmHg) \times \text{systolic ejection period (SEP)} (sec/min). SEP = duration of systolic ejection measured on aortic pressure tracing† (sec/beat) \times \text{HR}.

Results

Data for all experiments are presented in table 1. Marked differences in aortic pressure, cardiac output and heart rate were produced by variation of anesthesia alone; therefore, initial observations have not been classified as a control group distinct from observations subsequent to further manipulations. Although the type of anesthesia had a pronounced influence on myocardial oxygen utilization, this influence appeared to be entirely indirect and dependent upon the effect of the anesthetic agent on systemic hemodynamics. The relationship of myocardial oxygen consumption to hemodynamic factors was unaffected by the type of anesthesia.

The relationship between oxygen consumption and external mechanical work of the left ventricle is represented in figure 1. The low level of correlation (r = 0.30) was not random but depended upon instances of relatively isolated alterations in separate hemodynamic factors. Myocardial oxygen consumption increased less than mechanical work when elevation of cardiac output was the predominant hemodynamic alteration and more than mechanical work when elevation of aortic pressure or of heart rate was the major alteration. Results in the six dogs exhibiting the most disproportional changes in separate hemodynamic factors are illustrated in figure 2. In these experiments changes in myocardial oxygen consumption and external mechanical work were never parallel. During hypovolemia with marked increase in heart rate, myocardial oxygen consumption as well as coronary blood flow actually rose despite substantial reductions in cardiac output and left ventricular mechanical work.

Even with the diverse hemodynamic alterations in these six dogs, oxygen consumption had a constant relationship to the product of mean systolic aortic pressure and systolic ejection period (PTM), whether PTM was increased mainly by arterial pressure (dogs 21 and 22) or systolic ejection period (dogs 10 and 11), and irrespective of concomitant marked changes in cardiac output (dogs 12 and 13). The relationship between oxygen consumption \( (\dot{O}_2) \) and PTM for all experiments (fig. 3) was linear from PTM 1000 to 8800 (r = 0.93). The \( \text{PTM} / \dot{O}_2 \) ratio (mean = 222, SD = 56) was constant at high and at low PTM and when systolic ejection period

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*Velocity work has been disregarded since it constituted always less than 2% of total work.
†Mean value over a full respiratory cycle.
‡Equivalent to tension time index.

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ANEMIA

Obstructed Aorta

Hyponemia

FIGURE 2

Per cent change from control values for individual hemodynamic factors and left ventricular oxygen utilization. Changes in oxygen utilization were proportional to changes in PTM despite widely divergent alterations in the individual factors in these six dogs. HR = heart rate, AP = mean systolic aortic pressure, CO = cardiac output, W = LV external mechanical work, PTM = pressure time per minute, \( V_02 \) = LV oxygen consumption.

was high (Δ, fig. 3) or low (X, fig. 3) in relation to arterial pressure. The PTM/\( V_02 \) ratio was independent of the relationship between coronary blood flow and myocardial oxygen consumption. In seven experiments with anemia, in which the mean coronary arteriovenous oxygen difference was reduced to 7.2 VPC, the mean PTM/\( V_02 \) ratio was 234. In the two dogs with aortic obstruction and comparably elevated PTM levels, two-fold differences in coronary blood flow were matched by reciprocal differences in their coronary arteriovenous oxygen extraction so that their left ventricular oxygen consumptions and PTM/\( V_02 \) ratios were nearly equal.

The overall correlation of left ventricular oxygen consumption to the product of mean systolic aortic pressure and heart rate (AP × HR) was comparable to the correlation of oxygen consumption to PTM (fig. 4, r = 0.93). Elevation of aortic pressure and elevation of heart rate, however, did not appear to cause equal changes in oxygen consumption, in contrast to the result of separation of the PTM components. Experiments with heart rate high relative to aortic pressure and those with heart rate low relative to aortic pressure had different AP × HR/\( V_02 \) ratios.
TABLE 2
Relative Effects of Changes in Heart Rate and Systolic Ejection Period per Minute on the Rate of Left Ventricular Oxygen Utilization

<table>
<thead>
<tr>
<th>Per cent change from initial value</th>
<th>Dog</th>
<th>Heart rate</th>
<th>SEP</th>
<th>AP</th>
<th>LV $V_o_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11</td>
<td>+179%</td>
<td>+33%</td>
<td>-2%</td>
<td>+65%</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>+217%</td>
<td>+96%</td>
<td>+1%</td>
<td>+122%</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>+224%</td>
<td>+137%</td>
<td>-4%</td>
<td>+85%</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>+207%</td>
<td>+89%</td>
<td>-2%</td>
<td>+90%</td>
</tr>
</tbody>
</table>

Abbreviations are the same as in table 1.

(0.001 < P < 0.005, figure 4). Although changes in heart rate and systolic ejection period usually were approximately parallel, in three experiments (one each of hypovolemia, anemia and atropine) these changes were different enough from each other for a comparison of the separate effects of heart rate and systolic ejection period on myocardial oxygen consumption (table 2). In these three instances duration of systolic ejection per beat shortened so that systolic ejection period (per minute) increased significantly less than heart rate. Blood pressure was essentially unchanged. The increases in oxygen consumption were consistently less than those in heart rate and were closer to the increases in systolic ejection period.

Energy available from myocardial anaerobic metabolism appeared to be negligible in these experiments. A small net lactate production by the heart (0.03 mEq/min) occurred in one of the ten dogs in which blood lactate and pyruvate levels were determined.

Discussion
The validity of correlating any one figure for myocardial oxygen utilization with some other factor depends, of course, upon the accuracy of the oxygen utilization figure. A large group of oxygen values could be falsely correlated with some hemodynamic factor if errors in the oxygen values were systematically related to the factor. Although the inaccuracy of determining coronary blood flow in intact animals may cause considerable error in any of the myocardial oxygen uptake figures, these errors should be random among the different experiments and not lead to a false correlation.

Left ventricular oxygen consumption was proportional to PTM throughout the range of hemodynamics studied. A change either in systemic arterial pressure or in systolic ejection period per minute was associated with a proportional change in the rate of oxygen consumption. The mean PTM/$V_o_2$ ratio was similar to that observed for normal human subjects, but lower than those found for isolated hearts and for intact dogs studied over a narrow PTM range. The difference in ratio from these latter studies is unexplained.

Although there was also a close overall correlation between left ventricular oxygen consumption and AP x HR, increase in heart rate caused a proportionately smaller increase in left ventricular oxygen consumption when duration of systolic ejection per beat diminished (table 2, fig. 4). Oxygen consumption per beat then fell. In other studies also the increase in oxygen consumption per minute...
was approximately half the rise in heart rate when the rate was changed by altering vagal tone,\textsuperscript{2} electrical stimulation\textsuperscript{3,11} or atropine.\textsuperscript{12} Nevertheless, excepting extreme heart rate changes, oxygen requirements of the left ventricle could be estimated accurately in these experiments, as well as in others,\textsuperscript{13} from the product of blood pressure and heart rate (fig. 4) without the less convenient determination of systolic ejection period.

The relationship between oxygen consumption and PTM (or AP \times HR) is best regarded as empirical. It seems inappropriate to assign to any combination of systemic arterial hemodynamics a direct role in regulation of oxygen uptake of the left ventricle. Heart muscle energy requirements presumably are influenced directly by the force exerted by myocardial fibers and only indirectly by systemic arterial and intraventricular fluid pressure. Since the relationship between arterial pressure and myocardial fiber force varies as the heart changes its size and shape, the relationship of myocardial oxygen consumption to arterial pressure must vary under different environmental conditions and during the course of each contraction period. Systolic ejection period, the other component of PTM and also independently correlated with left ventricular oxygen consumption, can be regarded, on the one hand, simply as the duration that systolic pressure is maintained. It is, however, actually a complex factor influenced by the rate and extent of fiber shortening, fiber force and heart size. Each of these factors might have a more fundamental relationship to myocardial oxygen consumption which was responsible for a secondary coincidental correlation between oxygen consumption and systolic ejection period.

If oxygen consumption is related to myocardial fiber force, the PTM/\(V_02\) ratio might be increased when the left ventricle is smaller and decreased when the left ventricle is dilated, since wall tension of a sphere with constant internal pressure is proportional to its radius. In five dogs with acute anemia the PTM/\(V_02\) ratio rose when stroke volume increased and fell when stroke volume decreased. One explanation of these small changes in PTM/\(V_02\) ratio would be increased left ventricular systolic emptying and decreased mean systolic chamber size accompanying increases in stroke volume, and decreased emptying and increased mean systolic size accompanying decreases in stroke volume. However, neither hypovolemia with decreased stroke volume and systemic arterial pressure nor aortic obstruction with marked increase in intraventricular pressure and diminished stroke volume had a demonstrable net effect on the PTM/\(V_02\) ratio. It appears that acute volume changes of the left ventricle generally are not of sufficient magnitude in the intact dog to produce detectable changes in the myocardial oxygen requirements for generating systemic arterial pressure.

**Summary**

The influence of acute changes in systemic hemodynamics on the rate of oxygen utilization by the left ventricle has been studied in intact anesthetized dogs. Certain types of hemodynamic changes caused reproducible alterations in the relationship between oxygen consumption of the left ventricle and its external mechanical work. The relationship of left ventricular minute oxygen consumption to the product of mean systolic aortic pressure and systolic ejection period per minute was constant over an extreme range of varied types of hemodynamic alterations. Changes in oxygen consumption were proportionately less than concomitant changes in heart rate. These findings are in accord with previous studies of isolated heart preparations.

**References**


Left Ventricular Oxygen Utilization in Intact Dogs: Effect of Systemic Hemodynamic Factors

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doi: 10.1161/01.RES.12.2.163

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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