Oxygen Consumption of the Nonworking and Potassium Chloride-Arrested Dog Heart

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SUMMARY In 21 dogs on cardiopulmonary bypass with ventricles kept empty, the mean beating but nonworking myocardial oxygen consumption (mV02) was 3.8 ml/min per 100 g at a heart rate of 158 beats/min. After subsequent potassium chloride arrest, the basal mV02 was 1.74 ml/min per 100 g. To compare these values with the working situation, we measured mV02 in these hearts before instituting bypass when the heart rate averaged 179 beats/min and arterial pressure averaged 108 mm Hg; mV02 was 9.2 ml/min per 100 g. Atrioventricular dissociation was induced in five beating, nonworking hearts; electrical pacing at increasing heart rates produced a linear increase in mV02. Extrapolation to zero heart rate yielded a value of 1.24 ml/min per 100 g, which was not significantly different from the KC1 arrest value of 1.25 ml/min per 100 g in these same hearts. These measurements permitted calculation of an energy expenditure per beat of 10.4 mJ/g. Subtraction of the basal value of 2.0 mJ/g yielded a value for energy of contraction of 8.4 mJ/g. The stress-independent component was estimated to be 2.7 mJ/g. The basal mV02 at normal perfusion pressure remained constant for arrest periods of at least 1 hour. Perfusion with modified Krebs-Henseleit buffer caused a 30% reduction in the basal mV02 in spite of maintained perfusion pressure, O2 supply in excess of consumption, coronary venous PO2 values above 60 mm Hg, and the addition of amino acids. It is possible that this finding indicates deficient oxygenation of myocardial cells in hearts perfused with solutions lacking red cells.


THE BASAL OXYGEN consumption of cardiac tissue is higher than that of skeletal muscle. Different groups of experiments, using a variety of techniques to induce cardiac arrest, have measured the basal metabolism in several species of animals (for reviews, see Lochner et al., 1968; Gibbs, 1978). There is a fairly wide scatter among the different estimates, presumably as a result of technique and species differences. It is desirable to measure the basal metabolism accurately so that the real energy cost of a single cardiac contraction can be determined. To calculate this value, the basal metabolism must be subtracted from the total metabolism of the working heart.

In the present investigation a cardiopulmonary bypass technique was used so that the oxygen consumption of arrested blood-perfused hearts could be followed in vivo for long periods of time (40 minutes and more). The per beat oxygen cost of (1) the beating working heart and (2) the beating nonworking heart was determined. We know of no other experiments on the in situ blood-perfused heart in which basal metabolism has been studied in this way.

An examination of published reports on this subject also suggests that hearts arrested with various cardioplegic solutions consume less oxygen than blood-perfused hearts (Bretschneider et al., 1975; Lochner et al., 1968). This suggests that such hearts are metabolically abnormal. An added complication is suggested by experiments with isolated hearts, perfused with physiological saline, where it has been shown that the oxygen consumption of the arrested heart falls with time (Arnold and Lochner, 1965; Penpargkul and Scheuer, 1969). A possibly related effect has been described for isolated quiescent papillary muscles where the resting metabolic rate, measured by recording heat production, falls for several hours and eventually reaches a value about one half that found originally (Loiselle and Gibbs, 1979).

Most of the information available concerning myocardial metabolism and electrophysiology has been obtained with salt solutions lacking red cells. We therefore have compared basal mV02 in hearts perfused with blood and then with modified (high-potassium) Krebs solution.

Methods

Twenty-seven mongrel dogs weighing from 14 to 26 kg were anesthetized with intravenous methohexitone sodium (10 mg/kg) followed by a standard dose of chloralose, 100 mg/kg (Arfors et al., 1971). A cuffed endotracheal tube was inserted and the lungs ventilated by an intermittent positive-pres-
sure ventilator. The left jugular vein was exposed through a small incision and a cardiac catheter was manipulated into the coronary sinus using a portable C.G.R. image intensifier. The position of the catheter was checked with a bolus injection of Urografin. Before the thoracic cavity was opened, respiratory movements were abolished by an intravenous injection of 80 mg of Flaxedil (gallamine triethiodiode, Burroughs Wellcome). The thoracic cavity was opened (see below) and a Silastic catheter filled with heparinized saline was inserted into the left atrial appendage. A cannula was inserted into the left femoral artery for measurement of arterial pressure. Arterial blood pressure (measured with an Elcomatic EM 750 transducer) and heart rate were monitored before and immediately after the microsphere injection (see below) and were essentially identical in all cases. Cardiopulmonary bypass was then achieved using one of two different surgical procedures, shown schematically in Figure 1. The two procedures are described separately. Both employed the bubble oxygenator described by Proctor and De Bono (1965).

**Procedure A**

This procedure, illustrated diagramatically in Figure 1A, was used successfully in nine experiments, and it involved either wide exposure of the thoracic cavity or the complete removal of the sternum and part of the rib cage. The right heart was bypassed and the flow of blood from the right side of the heart was monitored with an electromagnetic flow probe (Skalar 3 mm cannulating), before it entered the oxygenator. The right iliac artery was cannulated and supplied with blood from the oxygenator by a variable rate roller pump (Sarns peristaltic). Arterial pressure was maintained in the 40–80 mm Hg range. As soon as a satisfactory arterial pressure had been established, snared ties around the superior and inferior vena cavae and pulmonary artery were tightened to prevent any venous return to the right side of the heart, except via the coronary circulation. A left ventricular drainage tube (i.d., 6.5 mm), with many side holes, collected any residual pulmonary return to the left side of the heart, the Thebesian flow, and any blood escaping through the aortic valve. In actual practice the return of blood to the oxygenator via this tube during bypass was negligible.

The major disadvantage of procedure A was that there was no independent control of coronary flow rate. For this reason we adopted procedure B.

**Procedure B**

This procedure, which resembles a method described by Kahler et al. (1963), was used successfully in 12 dogs. In addition to cannulation of the right iliac artery, the right common carotid artery was cannulated with a long metal tube, the end of which was advanced into the aortic arch via the brachiocephalic artery. The long metal cannula was used for independent coronary perfusion. Coronary perfusion pressure was recorded with a suitable Cordis catheter, introduced from the left femoral artery, manipulated into the aortic arch, and positioned just outside the aortic valve; its position was checked with the image intensifier. The changeover to bypass was as described for procedure A except that a BYO 800 roller pump (Norris Industries Limited) supplied oxygenated blood separately to the coronary bed via the carotid cannula. We isolated the coronary circulation (soon after the start of bypass) by tying off snares around the brachiocephalic and subclavian arteries and aorta. The circuitry is shown diagramatically in Figure 1B. The isolation of the two circuits was checked by briefly arresting each pump separately while monitoring the coronary perfusion pressure. Total coronary venous flow was measured as described earlier with a flow probe in the coronary venous return line to the oxygenator. In the final eight experiments, two flow probes were used, one in the coronary perfusion line and one in the venous return line. The input probe gave readings about 10% higher than the probe on the venous return line.

**Perfusion Solutions**

The priming volume of the bypass apparatus was approximately 1.0 liter and consisted of a mixture
of 25% Lomodex 70 (Dextran 70 in 5% dextrose) and 75% Hartmann's solution with the following composition (mm): Na⁺, 131; K⁺, 5; Ca²⁺, 2; Cl⁻, 111; and lactate, 29. The solution in the bubble chamber of the oxygenator was warmed by a water-filled, stainless steel heat-exchanger to maintain body temperature as constant as possible. Within an experiment, the temperature regulation was within ±1°C, but the body temperature in different experiments varied between 35 and 38°C; the actual heart temperature could, when using procedure A, be 1°C cooler than the body temperature when the sternum and rib cage were removed if the incision was not covered. The gas flow into the bubble chamber was maintained at 6.1/min, and the CO₂ and O₂ content of the gas flow were varied until the Pco₂ and Po₂ of the arterial blood were approximately 40 and 100 mm Hg, respectively.

Cardiac arrest was produced by infusing 3 M KCl into the oxygenator or, in the case of procedure B, into the coronary perfusion line. The arterial potassium concentration, which was measured several times during the period of arrest, needed to be between 20 and 35 mmol/liter to produce arrest. With these concentrations the heart could be kept quiescent. If the K⁺ level was allowed to fall, the heart resumed electrical activity. The blood pH was maintained as close as possible to pH 7.4 by the addition of sodium bicarbonate (8.4% wt/vol) to the oxygenated blood. In nine experiments there was a total replacement of an animal's blood by a modified Krebs-Henseleit solution. The composition of the solution in mmole/liter was as follows: NaCl, 118.0; NaHCO₃, 24.8; CaCl₂·2H₂O, 2.54; MgSO₄·7H₂O, 1.18; KH₂PO₄, 1.18; KCl, 25.00; glucose, 5.00; and L-lactate (neutralized to pH 7.4) 5.00. Insulin, 2 U/liter, was added to this solution, together with bovine serum albumin (fraction V) to a concentration of 2 g/liter. To produce a physiological solution which contained the essential (and some non-essential) amino acids in concentrations close to their in vivo values (see Schreiber et al., 1977; Banos et al., 1978) 10 ml of Aminosol-Vitrum 10% (Vitrum, Sweden) were added to each liter of the above-described solution.

Coronary Blood Flow Measurement with Microspheres

The pre-bypass coronary blood flow of the normally working heart was measured by the method of Domenech et al. (1969). A minimum of 1.26 × 10⁴ of 15 μm 3 M radioactive carbonized microspheres was injected into the left atrium via the implanted catheter. Prior to injection, the microspheres were disrupted sonically for 10 minutes and flushed into the left atrial catheter through a mixing vial. The microspheres thoroughly mix in the left ventricle before being distributed to the myocardium and all organs of the body where they become trapped in the capillary bed. The distribution of the microspheres between organs is in direct proportion to the blood flow reaching those organs. More details of the microsphere technique have been given recently (Drake et al., 1978). The myocardial blood flow (MBF) was calculated from the following equation: MBF = myocardial counts × (reference flow/reference sample counts).

The reference sample was obtained from the femoral artery cannula at a preset flow rate (reference flow) using a peristaltic pump (BYO 800, Norris Industries Limited). The sampling was started before the microsphere injection and continued for 70 seconds. The flow rate was measured by a timed collection of blood into a preweighted counting vial.

At the completion of an experiment, the hearts were excised and the fat and connective tissue removed: they were then blotted and weighed. The hearts were fixed overnight in 10% formalin and the next day were cut into small pieces (approximately 3 g) and the entire heart counted for radioactivity (myocardial counts). The reference blood sample was counted at the same time (reference sample counts), removing the necessity for decay corrections, using a Nuclear Enterprises automatic-spectrometer, model 8312.

The validity of this microsphere method has been determined by comparison with direct measurements of total coronary venous return during right heart bypass (Domenech et al., 1969; Utley et al., 1974).

Immediately prior to the microsphere injection, samples were taken from the arterial and coronary sinus catheters for analysis of oxygen content.

Blood Analysis

The Po₂, Pco₂, and pH of 2-ml blood samples were measured with a Corning Eel pH/Blood Gas Analyzer. The oxygen content of the samples was determined with a Læx-O₂-Con, TL. The accuracy of this method in our hands was checked against spectrophotometric measurement of oxygen saturation. Oxygen consumption per g tissue (mVO₂) was calculated from the formula: mVO₂ = MBF × [(arterial O₂ content - coronary venous O₂ content)/total heart weight]. Throughout this paper, the results are expressed in ml O₂/min per 100 g.

Protocol

Prior to initiating cardiopulmonary bypass, microspheres were injected to calculate MBF. Simultaneously, arterial and coronary venous blood samples were taken for calculation of the mVO₂ of the working heart. After bypass had been instituted, the heart was beating but not working and the arterial Po₂ and Pco₂ values were adjusted toward normal. When these values were satisfactory, arterial and coronary venous blood samples were taken and, at the same time, the now directly measured
coronary flow was displayed, together with pressure and ECG traces on a Gould Brush 480 pen recorder.

In five experiments, the nonworking heart was paced at different rates by means of a Digitimer Mark IV stimulator via electrodes sutured into the right ventricle. Prior to pacing, atrioventricular dissociation was produced by 0.5–1.0 ml of 40% formaldehyde injected into the bundle of His, using the groove between the right atrium and aorta as described by Steiner and Kovalik (1968).

After the heart had been in the beating, nonworking condition for 20–40 minutes, cardiac arrest was induced by infusing 3 M KCl, as described in the section on Perfusion Solutions. Arterial and coronary venous blood samples were taken at intervals of up to 60 seconds following arrest.

In some experiments, the perfusing blood was then replaced by a modified Krebs solution. To accomplish this, the two venous return lines to the oxygenator were interrupted so that the blood drained into a container. At the same time, prewarmed modified Krebs-Henseleit solution was infused directly into the bottom of the oxygenator from a reservoir. There was no interruption in the perfusion of the dog, although the perfusion rate had to be increased greatly in an attempt to maintain perfusion pressure. When the fluid in the venous return lines was practically clear, the original circuitry was reestablished. The arterial PO2 was raised to about 500 mm Hg rather than the value of 100 mm Hg in the blood-perfused dog.

**Effect of Arrest of the Heart during Bypass**

Even after several hours on bypass and, in some cases, after 2 hours of perfusion with Krebs-Henseleit buffer rather than blood, the hearts resumed electrical activity if the extracellular potassium levels were allowed to fall toward normal. It was our distinct impression that the hearts were more flaccid when there was independent coronary perfusion (procedure B). Procedure A sometimes resulted in the hearts being slightly mottled in appearance when the bypass duration was 2 hours or more. In only one heart was there evidence of edema due to perfusion. This occurred in an experiment in which our pressure catheter blocked and the selected coronary perfusion rates were probably increased, producing edema as described by Pogatsa et al. (1978).

**Lactate and Other Substrate Concentrations.**

Under chloralose anaesthesia, arterial lactate and free fatty acid concentrations (FFA) were both below 1 mmol/liter, whereas glucose averaged 4.6 mmol/liter. In these experiments there was no reason to expect a rise in FFA concentration; FFA was also excluded from all priming and perfusion fluids. However, there was a marked rise in lactate concentration (up to 10 mmol/liter). In separate experiments, such levels of arterial lactate at neutral pH were found to have no effect on mVO2 of the working heart.

**Statistical Analysis**

Paired data were tested by the paired sign test of Dixon and Mood (1946) as described by Snedecor and Cochran (1973).

**Results**

**Oxygen Consumption of Working and Nonworking Hearts**

The oxygen consumption of the working heart was measured by the microsphere technique to determine coronary blood flow. In 21 dogs the calculated mVO2 was 9.2 ml O2/min per 100 g. The relevant circulatory variables are given in Table 1. This mVO2 value compares well with others in the literature (see Discussion), but several cardiovascular variables were higher than they would be in the conscious dog. Presumably as a result of the chloralose anesthesia, sympathetic tone and, therefore, the heart rate and mean blood pressure (108 mm Hg), were elevated.

In 21 dogs it was possible to obtain an estimate of the metabolism of beating but nonworking hearts. The hearts were in sinus rhythm, but since both the left and right sides of the heart were kept

<table>
<thead>
<tr>
<th>Variables</th>
<th>Working vs. Non-working Circulatory Data</th>
<th>Nonworking procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Working</td>
<td>A</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>179 ± 23</td>
<td>156 ± 37</td>
</tr>
<tr>
<td>Mean perfusion pressure (mm Hg)</td>
<td>108 ± 16</td>
<td>56 ± 12</td>
</tr>
<tr>
<td>Coronary flow rate (ml/min per 100 g)</td>
<td>63 ± 24</td>
<td>71 ± 35</td>
</tr>
<tr>
<td>mVO2 (ml O2/min per 100 g)</td>
<td>9.17 ± 2.92</td>
<td>3.40 ± 1.1</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD; n = 21.
drained, no blood could be ejected. The mean \( mV_02 \) under such conditions was 3.40 ml O\(_2\)/min per 100 g for procedure A and 4.13 ml O\(_2\)/min per 100 g for procedure B (overall mean = 3.8 ml O\(_2\)/min per 100 g). Thus, the lower perfusion pressure and coronary blood flow in procedure A resulted in a lower \( mV_02 \) than in procedure B. These measurement were made with the hearts on bypass and, hence, with a lower hematocrit than usual (hemoglobin concentration 53% of pre-bypass value). Under these conditions, the coronary flow rate was not altered much; heart rate had declined slightly and the coronary perfusion pressure was about half the working (pre-bypass) value (see Table 1). In a few of the early experiments, where our technique was less secure, the hearts fibrillated. The \( mV_02 \) data from fibrillating hearts have not been included in Table 1, but it was possible to measure the oxygen consumption rate. The mean value was 4.8 ± 1.5 ml/min per 100 g (mean ± 1 sd, \( n = 5 \)), a value considerably higher than that obtained in the arrested or nonworking states. As will be shown in the next section, it was possible to increase the oxygen consumption of the nonworking heart preparations by pacing them at higher rates.

### Oxygen Consumption of the Arrested Heart

**Blood Perfused (Basal \( mV_02 \))**

The complete oxygen consumption, pressure, and flow data, obtained with both procedures, are given in Table 2, and an example of the experimental data is shown in Figure 2. Notice that, regardless of the experimental procedure employed, the basal oxygen

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**Table 2 Metabolism of Blood-Perfused Arrested Hearts as a Function of Time**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Procedure A</th>
<th>Procedure B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>at 5 min*</td>
<td>at 10 min</td>
</tr>
<tr>
<td>Pressure (mm Hg)</td>
<td>101 ± 40</td>
<td>86 ± 27</td>
</tr>
<tr>
<td>Flow rate (ml/min per 100 g)</td>
<td>38 ± 11</td>
<td>32 ± 15</td>
</tr>
<tr>
<td>( mV_02 ) (ml O(_2)/min per 100 g)</td>
<td>2.04 ± 0.46</td>
<td>1.91 ± 0.68</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 sd.

* \( n = 8; \) † \( n = 6; \) ‡ \( n = 12.\)
consumption of the arrested hearts was essentially constant for arrest periods of up to 1 hour. There was no significant difference in the means of the different time bins. The mean coronary flow rate for procedure A, where autoregulatory mechanisms determined flow, was about two-thirds of that obtained with procedure B, where the flow rate was adjusted to maintain coronary perfusion pressure in the 80–120 mm Hg range. When the mean basal mVO2 value for each experiment was calculated and the results were pooled, an overall value of 1.92 ± 0.50 ml/min per 100 g (mean ± 1 SD) for procedure A and 1.61 ± 0.72 ml/min per 100 g for procedure B (overall mean = 1.74 ± 0.56 ml/min per 100 g (n = 21) was obtained.

To test whether these levels of potassium were stimulating or depressing metabolism, the oxygen consumption of the beating but nonworking hearts were assessed while hearts were paced at 1.0, 2.0, 3.0, 5.0, and 6.0 Hz after induction of atrioventricular dissociation. Myocardial oxygen consumption was plotted against heart rate and the data fitted by linear regression, as shown in Figure 3. The oxygen consumption intercept at zero heart rate provides an estimate of the basal metabolism. This value can be compared with the mean KCl arrested value. In five experiments, the rate technique gave a basal metabolic value of 1.24 ± 0.22 ml O2/min per 100 g (mean ± 1 SD, n = 5), whereas the KCl estimate was 1.25 ± 0.13 (mean ± 1 SD, n = 5); this difference is not significant (0.50 < P < 0.75).

In addition, the mVO2 values measured at low (15–25 mmol/liter) and high (30 to 65 mmol/liter) K levels were compared. Only paired data were used in this comparison. The mean mVO2 values obtained in the high and low extracellular potassium were 1.69 ± 0.20 and 1.52 ± 0.37 (mean ± 1 SD, n = 8), respectively. The difference is not significant (0.5 > P > 0.25).

Oxygen Usage per Beat

The oxygen cost per beat of both the working and nonworking heart was calculated by subtracting the average basal oxygen consumption from the total mVO2 values found in the two conditions and dividing the remainder by the heart rate. This was done for each dog, and the results of all experiments were averaged. The mean per beat oxygen consumption of the working heart was 0.042 ± 0.014 ml/100 g, whereas the value for the nonworking heart was 0.013 ± 0.007 ml/100 g.

Perfusion with Physiological Solution

With procedure A, basal mVO2 fell to a mean value of 0.55 ± 0.16 ml/min per 100 g with a corresponding mean value for oxygen supply of 0.75 ± 0.21 ml/min per 100 g. Coronary venous values for oxygen content were 0.04 ± 0.12 ml/100 ml and for PO2 were 84.0 ± 45 mm Hg.

With procedure B, basal mVO2 during Krebs-Henseleit buffer perfusion was 1.18 ± 0.45 ml/min per 100 g with a corresponding mean value for oxygen supply of 2.63 ± 0.75 ml/min per 100 g. Coronary venous values for oxygen content were 1.1 ± 0.3 ml/100 ml and for PO2 were 147.4 ± 41.9 mm Hg.

With procedure B, it was possible to maintain the coronary perfusion pressure in the 80–100 mm Hg range using a flow rate of 120 ml/min per 100 g, but with procedure A we were unable to increase the flow enough to maintain perfusion pressure which was in the 30–60 mm Hg range. In the latter situation, the drop in oxygen consumption was more dramatic (Table 3), the mean basal mVO2 value being about one-fourth of the blood-perfused control. The basal oxygen consumption remained fairly constant over the measurement period (Table 3). There was no evidence that provision of the essential amino acids had any effect on basal oxygen consumption, irrespective of which procedure was employed (Table 3). In three experiments, two using procedure A and one using procedure B, a period of
perfusion with modified Krebs-Henseleit buffer was followed by a period in which much of the original blood was returned to the animal. The hemoglobin concentration of the blood solution was now only 25-30% of the original pre-bypass value. The oxygen content was still 2 to 3 times higher than that of the physiological solution. With procedure A, the return to blood perfusion produced a rapid and sustained increase in both basal oxygen consumption and mean perfusion pressure. With procedure B, the return to blood perfusion produced a much less clear-cut result (see Fig. 4), as the decline upon switching to physiological saline was less marked and there was no evidence of an improvement in basal metabolism upon returning to a blood perfusion.

Discussion

This study shows that basal metabolism accounts for about one-fifth of the total myocardial oxygen consumption. The remaining three-fifths of total myocardial oxygen consumption is therefore the proportion attributable to mechanical activity. By basal metabolism, we mean the oxygen consumption of the arrested blood-perfused heart, and by metabolism of activation, we mean the oxygen consumption of the beating, nonpressure-developing heart. There are necessary reservations about these methods (see below).

Basal Metabolism

In experiments with dogs, several investigators have paced hearts at different rates and extrapolated to zero frequency to estimate the basal oxygen consumption, with values in the range 2.0-2.3 ml/min per 100 g being obtained (Cohn and Steele, 1935; Laurent et al., 1956; Van Citters et al., 1957). This method has the advantage that no agents have to be administered that might themselves alter metabolism. Its disadvantage is that it will be accurate only if circulatory variables such as end-diastolic volume and arterial blood pressure are kept constant (see Gibbs, 1978). We used an extrapolation technique (Fig. 3) with which this disadvantage was avoided because the heart was kept empty and unloaded so that there was no external work and no pressure development. The mVO₂ of the nonworking, beating heart therefore should depend on heart rate only. The mean value we obtained of 1.25 ml/min per 100 g is lower than that obtained by the other extrapolation method described above.

Blood-perfused dog hearts have been arrested by administration of high potassium in several earlier studies (McKeever et al., 1958; Beuren et al., 1958; Monroe and French, 1960). The mVO₂ values for the arrested heart range between 1.5 and 4.8 ml O₂/min per 100 g. Our mean value for hearts in which we also used the extrapolation technique (above) was 1.24 ml/min per 100 g (Fig. 3). Our overall mean value was 1.74 ml/min per 100 g. The reliability of our K⁺ arrest method is confirmed by the agreement with the extrapolation technique and the lack of effect of varying K⁺ concentration.

### Table 3

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Krebs</th>
<th>Krebs and amino acids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>at 10</td>
<td>at 20</td>
</tr>
<tr>
<td>Procedure A</td>
<td>1.93 ± 0.42</td>
<td>0.57 ± 0.25</td>
</tr>
<tr>
<td>Procedure B</td>
<td>1.72 ± 0.82</td>
<td>1.20 ± 0.38</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

* Mean of all blood arrest values.

† In both procedures A and B, three preparations were exposed to both treatments. In procedure A, there was one experiment with Krebs only and one with Krebs plus amino acids only. With procedure B, there were two experiments with Krebs only and two with Krebs plus amino acids only.

Figure 4: A plot of basal mVO₂ as a function of time in three hearts perfused sequentially with blood, Krebs solution, blood, all containing high (25 mmol/liter) K⁺ levels. One preparation was perfused using procedure A (Fig. 1): the arterial perfusion pressure with Krebs solution was in the 50-60 mm Hg range. The other two preparations were perfused using procedure B (Fig. 1): the coronary perfusion pressures were in the 80-100 mm Hg range during perfusion with Krebs-Henseleit solution.
When working isolated heart preparations are arrested, there is a decline in basal metabolism with time (Arnold et al., 1968; Penparagkul and Scheuer, 1969). Evidence for such a decline in a blood-perfused preparation was not obtained in the present study but, before arrest, our hearts had been in a beating but nonworking condition for 30-40 minutes. There is some evidence that the extent of the decline in basal metabolism depends on the rate of energy expenditure at the time of arrest (see Fig. 3, Arnold and Lochner, 1965). We therefore raised the nonworking metabolic rate several-fold by pacing at high rates prior to arrest, but this did not reveal a consistent effect. In myothermic studies on isolated papillary muscles there is a progressive decline in the basal heat production, (Loiselle and Gibbs, 1979). It is not certain, however, that the same phenomenon is being studied, since the decay occurs over a much longer time course than in isolated heart preparations. The present study throws some doubt on the physiological importance of these decay phenomena.

There have been some measurements of the basal oxygen consumption of dog hearts arrested while perfused with cardioplegic solutions. The reported mVO₂ values are much lower than for blood-perfused hearts (Hoffmeister et al., 1959; Bonhoeffer and Standfuss, 1964; Bonhoeffer, 1967). At temperatures close to normal body temperature mVO₂ values in the range 0.6 to 1.0 ml/min per 100 g have been reported.

Even with procedure B, where coronary perfusion pressure could be maintained at normal levels, the switch to Krebs-Henseleit solution caused an immediate fall in basal metabolism of some 30%. Duvelleroy et al. (1976) found that oxygenated physiological solutions may not be able to supply adequate amounts of oxygen to working cardiac preparations. The energy demands of the arrested heart are only one-quarter to one-fifth of those of the working heart, and the flow rate was twice normal, so that oxygen supply exceeded consumption by 123% for procedure B. However, this oxygen was delivered in solution at high Po₂ instead of being carried by hemoglobin. As a result, the oxygen content of coronary venous blood was less than 1.5 ml/100 ml despite Po₂ values over 60 mm Hg. The coronary arteries and veins run alongside one another in the epicardium so that oxygen can diffuse directly from arteries (Po₂ over 500 mm Hg) to veins. Thus, venous Po₂ and oxygen content values may exceed tissue values and mask the presence of tissue hypoxia. We suggest that the low mVO₂ implies such tissue hypoxia during Krebs-Henseleit perfusion, even under basal conditions. Such considerations cannot be excluded completely from the values obtained during blood perfusion, but the effect is likely to be much smaller because of the presence of normal arterial Po₂ values and normal arterial to venous Po₂ gradients.

The viability of hearts arrested with high potassium has been demonstrated for arrest periods between 30 and 160 minutes (Arnold et al., 1968; Hearse et al., 1975; Schrieber et al., 1977) and was confirmed in our hearts, which regularly resumed sinus rhythm if the potassium level was allowed to decline. We have shown that variations in the extracellular potassium between 15 and 65 mmol/liter have little effect per se on basal metabolism. This is at variance with other authors, who find an influence of high potassium on metabolic rate (Blond and Whittam, 1965; Crone, 1966; Arnold et al., 1968; Bonhoeffer, 1967).

A basal mVO₂ close to 2.0 ml/min per 100 g implies an aerobic energy expenditure of 6 mW/g at normal body temperature. What biochemical processes might underwrite this flux rate? The sodium pump is an obvious candidate, since the basal oxygen consumption of both rat and dog hearts is reduced further by lowering the sodium concentration of the perfusing fluid (Bonhoeffer and Standfuss, 1964; Lochner and Dudziak, 1965). However, the Na⁺ flux data of Langer (1968) and the calculated energy used by an electrogenic sodium pump (see Gibbs and Chapman, 1979) account for only about 10% of the basal cardiac metabolism. Depolarization by KC₁ should greatly accelerate the sodium pump so that this 10% would be an underestimate in hearts arrested with KCl. It is possible that there are other ion pumps consuming energy and, in particular, the energy flux needed for intracellular calcium homeostasis may be important, even though variations in extracellular calcium have little effect on basal metabolism. Another factor (Gibbs, 1978) is the fraction of the basal metabolism needed for amino acid transport and protein synthesis and degradation (Chapman and Gibbs, 1979; Millward et al., 1975; Everett et al., 1977; Baños et al., 1978; Earl et al., 1978; Burns and Reddy, 1978; Schrieber et al., 1977).

**Energy Utilization per Heart Beat**

Gamble et al. (1970) report an average value for total mVO₂ of 9.1 ml O₂/min per 100 g at 100 mm Hg left ventricular pressure which compares favorably with our value of 9.2 ml/min per 100 g; a lower range of values (4.9-8.6) was reported in unanesthetized resting dogs by Gregg et al. (1965).

Such values depend on wall stress, stroke work, and heart rate. Estimates of the mVO₂ of the beating but nonworking dog heart in the range 3.0-4.2 ml O₂/min per 100 g were reported by McKeever et al. (1958), Glaviano et al. (1977), and Weber and Janicki (1977); these results are similar to ours. Published values are variable because of the dependence of mVO₂ on the_ios, in these circumstances, on heart rate (Fig. 3) and perfusion pressure and coronary flow (Table 1, Kahler et al., 1963). Several investigators have reported that during fibrillation there is a marked increase in cardiac mVO₂ to values...
above that recorded in quiescent or beating but nonworking preparations (McKeever et al., 1958; Monroe and French, 1960; Hashimoto et al., 1960). Our mVO₂ value of 4.8 ml/min per 100 g is the mid-range of the published values.

Values of 9.17 ml O₂/min per 100 g for the oxygen consumption of the working heart and of 1.74 ml O₂/min 100 g for the basal oxygen consumption yield a value for the oxygen cost of contraction of 7.43 ml O₂/min per 100 g. If we take the energy generated from 1 liter of oxygen to be 20.2 kJ, this represents a total energy expenditure of 150 J/min per 100 g.

With a knowledge of the basal and the working mVO₂ plus the heart rate, it is possible to calculate the oxygen cost per beat. In the present series of experiments, the oxygen consumption of the working heart varies. This value yields an oxygen cost of contraction per beat at a mean arterial pressure near 100 mm Hg of 0.42 μl O₂/g, a value within the range 0.35–0.55 reported by McKeever et al. (1958) in the conscious dog. This represents an energy expenditure of 8.4 mg/l per beat (10.4 mJ/g total minus 2.0 mJ/g basal). Knowledge of the metabolism of the nonworking but beating heart allows calculation of the stress-independent energy component (see Gibbs, 1978). This component has a mean value of 2.7 mg/l in these experiments. As there is still some wall stress development and performance of internal work even in an empty beating heart (see Weber and Janicki, 1977), this component is due to the equivalent of the activation heat of skeletal muscle (Hill, 1949) plus the contribution of this internal work. There is, however, good agreement between the energy estimates for the stress-dependent and stress-independent terms obtained in myothermic and oxygen consumption studies as recently reviewed in some detail by Gibbs and Chapman (1979).

References


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In the first days and weeks after birth of the rat, there is a rapid increase in the mean arterial pressure (Burlingame et al., 1942; Litchfield, 1958; Rackus et al., 1965; Gerrity and Cliff, 1975), and the thickness of the aortic wall increases as a result of an accumulating mass of smooth muscle cells, elastin, and collagen (Looker and Berry, 1972; Gerrity and Cliff, 1975). Aortic smooth muscle cells are the source not only of cellular growth but also of the extracellular components of the media (Ross, 1971; Ross and Klebanoff, 1971) that determine the changing mechanical properties of the aorta (Berry et al., 1975). To understand the dynamics of cellular growth and function in this tissue we used morphometric techniques to measure absolute values of tissue and cellular components in the thoracic aorta of the rat at 1, 5, and 11 days after birth.
Oxygen consumption of the nonworking and potassium chloride-arrested dog heart.
C L Gibbs, D E Papadoyannis, A J Drake and M I Noble

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