Effects of Selective Left Ventricular Bypass
on the Left Ventricular Excess Lactate and Redox-Potential*

NORIHIRO YAMAMURA, M.D.†

Various types of "assisted circulation" have been considered as powerful measures for mechanical assistance to the failing heart. For the relief of left-sided heart failure, selective left ventricular bypass can be recommended.

Arterial and coronary sinus blood were analyzed for oxygen content, lactate, and pyruvate before and during bypass, with or without a left ventricular vent in 8 dogs.

Myocardial oxygen consumption, compared to controls, significantly decreased during bypass. Coronary sinus flow was not significantly changed. The decrease of excess lactate and increase of redox potential were significant during bypass with a left ventricular vent as compared with during bypass without such a vent.

The data seem to indicate that selective left ventricular bypass provides no myocardial anaerobiosis but some evidence of the adequacy of myocardial perfusion.

With the development of the technique using extracorporeal circulation to provide temporary systemic circulation and oxygenation during intracardiac surgery, efforts have been made to direct experiences gained in such techniques toward the treatment of medically uncontrollable central circulatory insufficiency.

Thus, mechanical assistance to the failing heart by extracorporeal circulation, i.e. assisted circulation, has been proved to improve a number of failing conditions affecting the right and/or left ventricle.

Acute myocardial infarction with shock, hemorrhagic and septicemic shock, pulmonary disease with right ventricular failure (pulmonary embolism), preoperative states (intractable failure prior to surgical correction of cardiac disease and to homograft transplantation or insertion of a mechanical heart) and postoperative states (low cardiac output syndrome after open-heart surgery) are examples of such conditions.

Through the serial experimental and clinical investigations by AKUNE and co-workers¹⁻¹⁴, various types of assisted circulation have been classified according to indicated disease states as follows:

(A) Assisted Circulation for Right-Sided Heart Failure
1) Selective right ventricular bypass
2) Veno-arterial pumping⁵⁻⁶,⁷,¹₂,¹₅
3) Partial cardiopulmonary bypass⁵,¹⁶

(B) Assisted Circulation for Left-Sided Heart Failure
1) Selective left ventricular bypass⁵,¹⁷⁻¹⁹
2) Synchronized arterial counterpulsation⁹⁻¹₃,¹₄,²₀,²₁
3) Combination of B₁ and B₂

(C) Assisted Circulation for Combined Left- and Right-Sided Heart Failure
1) Total cardiopulmonary bypass (Control-

(Received for Publication, February 27, 1968)
† The Second Department of Surgery, Nagoya University School of Medicine, Nagoya
(Director: Prof. Shin Hoshikawa)

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led circulation."

2) Combination of A and B.

With selective left ventricular bypass, the left atrial blood is drawn by gravity and pumped into the aorta by a pump, bypassing the left ventricle. Through this procedure, the volume work of the left ventricle can be diminished. This procedure was first developed and employed for assisted circulation by Salisbury and associates in 1960. They described beneficial effects of left ventricular bypass upon experimental heart failure and its clinical applicability to left heart failure. Edmunds et al. further studied left heart bypass both in dogs and in man to conclude that left heart bypass was tolerable by the arrested heart for periods of up to an hour and that it was a useful treatment of unexpected cardiac arrest. In the same year, Dennis and co-workers experimentally demonstrated reduction of myocardial oxygen utilization during left heart bypass without thoracotomy. In 1962, they used it clinically in the management of myocardial infarction with persistent hypotension, unresponsive to conventional modes of therapy. Baird and associates, 1963, concluded that selective bypass of the left ventricle was followed by a significant reduction in the oxygen consumption of the heart; but this reduction was not mirrored in the tension-time or the product of heart rate and blood pressure. Schenck and associates concluded that left ventricular bypass had to be a total bypass to be of assistance to the failing heart.

Thus, a number of authors presented experimental and/or clinical data suggesting that selective left ventricular bypass had a favorable effect on the left ventricular oxygen consumption and hemodynamics.

However, previous investigations of assisted circulation have paid little attention to the myocardial metabolism as compared with the hemodynamic assessment. Besides some reliable indexes are needed to assess possible benefit from cardiac assistance.

Consequently, this study was designed to investigate alteration in myocardial lactate and pyruvate metabolism for short periods of asynchronous selective left ventricular bypass using theoretically rational parameters such as myocardial "excess lactate" advocated by Huckabee and changes in redox potential across the heart by Guðbjarnason and Bing and also to evaluate the usefulness of these parameters on previously hemodynamically recognized selective left ventricular bypass.

**Materials and Methods**

**Experimental Preparation**

Ten experiments were performed on 8 healthy adult mongrel dogs, weighing 8.5 to 15.0 kg. Following anesthesia with intravenous sodium thiopental of 30 mg/kg of body weight and endotracheal cannulation with a cuffed tube, 100% oxygen and supplemental ether were administered through a Heidbrink anesthetic machine. After the induction of anesthesia, the animals were immersed in cold water until rectal temperature reached 33°C and maintained about 30°C throughout experiments. Bilateral femoral arteries and veins were exposed, as was the brachiocephalic artery. The chest was opened through the sixth intercostal spaces bilaterally and the pericardium widely incised. Two mg/kg of heparin was administered intravenously.

The physical characteristics of the experiments are illustrated in Fig. 1.

A polyethylene catheter with a flanged end was inserted through the right atrial appendage into the coronary sinus and sutured in place. This catheter is referred to as the coronary sinus catheter. A catheter is placed in the aorta and the catheter is connected to the pump system. The catheter is connected to the pump system through a reservoir and a pump. The pump is connected to the heart through a bypass circuit. The catheter is connected to the pump system through a reservoir and a pump. The pump is connected to the heart through a bypass circuit.

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**Fig. 1.** Schematic drawing of experimental methods for selective left ventricular bypass. C.S.—coronary sinus; F.V.—femoral vein; L.A.—left atrium; L.V.—left ventricle; F.A.—femoral artery; B.C. A.—brachiocephalic artery; A.—aorta.

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was connected via vinyl tubing to a catheter which was inserted into a femoral vein. A three way stopcock was placed in the coronary sinus-femoral vein circuit for periodic samplings of coronary sinus blood and for measurement of coronary sinus blood flow. The coronary sinus drains blood primarily from the left ventricle, consequently the coronary blood flow expressed as ml/100 g/min pertains chiefly to a unit of left ventricular tissue.

Pressures were monitored in the aortic arch via the femoral artery, the left ventricle and the left atrium. Aortic and left ventricular pressures were transmitted via strain gauge transducers to a four-channel recorder, on which the electrocardiogram was also recorded. Left atrial pressure was monitored by saline manometers.

For selective left ventricular bypass, cannulations were made as follows: a J-shaped arterial cannula (i.d. 4 mm) was placed either in the brachiocephalic artery or in the left femoral artery. An outflow catheter (i.d. 6 mm) with several side holes near the tip was inserted into the left atrium via the atrioc appendage. A Y-shaped cannula with a large bore was inserted into the left ventricle through the apex. One arm of this vent could either be shut off or be emptied into a pre-pump reservoir; the other arm was connected to a pressure transducer for left ventricular pressure. When required by the experiment, the left heart return and drainage from a left ventricular vent were channeled by gravity into an open reservoir. This arrangement permitted alternation between: (a) partial left ventricular bypass with a left ventricular vent occluded and return of oxygenated blood to the left atrium in a quantity sufficient to produce left ventricular ejection (group I); and (b) total left ventricular bypass with a left ventricular vent open, the left ventricle beating but empty (group II).

Thus, selective left ventricular bypass was achieved by return of this blood into the aorta via the brachiocephalic or femoral artery by a metal finger pump (Sigamotor Cross Circulation Pump Model TM 2) except experiment No. 3 in which a kind of roller pump (Circulatory Assistor Model H-1) was used. The pump tubing and bypass circuit were primed with fresh, heparinized donor blood diluted with low molecular weight dextran solution. The pump used in these experiments was calibrated before and after each experiment. Care was devoted to prevent air embolism into the left heart.

Blood samples were simultaneously taken from the pulmonary artery, coronary sinus and aorta.

The oxygen content was measured after the method of Van Slyke and Neill. The lactate content was determined by the enzymatic method (UV-method with DPN)30, as modified by Oppè and associates31. The determination of pyruvate was done by the UV-method with DPNH using Biochemica Boehringer kits*. Measurement of the systemic oxygen consumption was accomplished by the originally designed device even under thoracotomy.

The control period was started after all cannulations were obtained. Recording of the control values in the parameters (left atrial pressure, aortic mean pressure, left ventricular pressure, coronary sinus blood flow, systemic oxygen consumption, ECG and rectal temperature) and samplings of the aortic, pulmonary artery and coronary sinus blood were made. The pump was then turned on. During left ventricular bypass, ten minutes after the start of the bypass, the same measurements as noted above were made.

After the experiment, a dye was injected retrogradely through the coronary sinus cannula, and the stained myocardium was weighed.

Definitions and Calculations

Myocardial extraction coefficient (A-V/A) was determined for oxygen, lactate and pyruvate. This is defined as the ratio of the coronary arteriovenous difference to the arterial level of each substance. It represents the per cent of each metabolite which is extracted from a unit of coronary blood during its passage through the myocardium.

The myocardial consumption of oxygen, lactate or pyruvate was obtained per 100 g of the myocardium as the product of coronary flow per 100 g of cardiac muscle and oxygen, lactate or pyruvate extractions, respectively.

Arterial lactate-pyruvate ratio and coronary venous pyruvate-lactate ratio was calculated from the analytical results.

Change in lactate/pyruvate ratio (ΔL/P) from arterial to coronary sinus blood was determined by applying the formula:

\[
\Delta L/P = \frac{\text{coronary sinus } L/P}{\text{arterial } L/P}
\]

Myocardial “excess lactate” in millimols per liter of whole blood was calculated with the HUCKABEE equation36:

\[
\text{myocardial } XL = (Lv - La) - (Pv - Pa) \times (La/Pa),
\]

where XL, excess lactate; v, CS; a, aorta; L, mM lactate; and P, mM pyruvate.

Change in redox potential (Eh) in the lactic dehydrogenase system in blood passing through the heart (ΔEh) was calculated from the formula of GUDJBRANSON and BING37.

\[
Eh = -204 - 30.7 \times \log (L/P) \text{mv}
\]

\[
\Delta Eh = Eh(\text{coronary sinus}) - Eh(\text{arterial})
\]

* The chemicals and enzymes for the determination of lactate and pyruvate were supplied by Boehringer and Soehne GmbH, Mannheim, Germany.

* * *

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\[ \Delta E_h = 30.7 \log \frac{L_a_1 \times Py_2}{L_a_2 \times Py_1}, \]

where 30.7 is a known constant, \( L_a_1 \) and \( Py_1 \) are the concentrations of lactate and pyruvate in the arterial blood; \( L_a_2 \) and \( Py_2 \) are the concentrations of lactate and pyruvate in the coronary vein blood.

Measurement of cardiac output was obtained by the Fick principle.\(^3\)

Left ventricular external work\(^{34}\). Practically, left ventricular work in kg m/min was obtained as the product of left ventricular output (aortic flow) in L/min divided by 100 and the planimetrically integrated mean systolic pressure recorded in centimeters of water (cm Hg/13.6).

Left ventricular internal work\(^{35}\) is,

\[ O_2 \text{ usage/min} \times 2.059 \times 0.8 \]

where 2.059 is the energy equivalent of 1 ml of \( O_2 \) at an R. Q. of 0.82, and 0.8 is the fraction consumed in contractile work.

The tension-time index (TTI) per minute\(^{36}\) is the product of mean systolic pressure, the duration of systole and heart rate. A variant of Sarnoff's TTI was determined from left ventricular pressure instead of the aortic pressure curve in all studies, because the left ventricular component commonly disappeared in the aortic pressure tracing when bypass was in force. Therefore, the author designates it "left ventricular TTI."

**RESULTS**

The experiments in 8 dogs have been divided into two groups. In the first group of five experiments, bypass flow was increased in stepwise fashion to near total bypass. In the second group of five experiments, blood was drained not only from the left atrium, but also from the left ventricle through a left ventricular vent. The values obtained apply directly to the metabolism of the left ventricle and may not pertain to the rest of the heart.

I. Circulatory Studies

The hemodynamic data of individual experiments are tabulated in Tables I and II.

Bypass rate on the dogs ranged between a low of 1040 and a high of 2320 ml/min or from 75 to 155 ml/kg/min in group I. In group II, bypass rate was between 680 and 1360 ml/min or from 68 to 147 ml/kg/min. In group I mean flow was 117 ml/kg/min during left heart bypass, and in group II mean flow was 102 ml/kg/min.

Both groups showed moderate reduction in cardiac rate during bypass.

Rectal temperature varied 23 to 32°C, and did not change in each case.

Cardiac output obtained by the Fick principle represents pulmonary artery flow which is similar to right ventricular output. Before bypass right and left ventricular output are mutually almost equal; left ventricular output, which is equivalent to the difference between right ventricular output and bypass flow during bypass, is zero in total bypass. All studies reported here were performed with the constant blood volumes being adjusted only by addition or sub-

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traction of blood from the circuit. In group I, right ventricular output increased in two experiments and decreased in three. It was increased in one, unchanged in two, and decreased in two in group II, showing a rather wide variation.

The average values of mean aortic pressure remained unchanged in both groups.

Left ventricular mean systolic pressure was reduced all but one exception (experiment No. 3 which showed an increase) in group I. It was reduced markedly due to the complete drainage of the left ventricular blood through a vent in group II, except experiment No. 8. Left ventricular mean systolic pressure was reduced by left ventricular bypass from 80 to 69 mmHg in group I and from 94 to 49 mmHg in group II. These represented a reduction of control systolic mean pressures from 25.8 to 37.5 per cent and from 0 to 87.5 per cent, with an average reduction of 13.8 per cent and 47.9 per cent, respectively.

In group I, left atrial pressure showed a significant reduction in three experiments and remained essentially unchanged during bypass in one. Especially, it fell from 95 to 0 mmHg in experiment No. 11. The fall in left atrial pressure was significantly noted in two cases.

Coronary arteriovenous oxygen difference was decreased in all in group I and corresponded in magnitude to the increase in coronary sinus oxygen content rather than the decrease in arterial one. It was uniformly reduced on bypass, with one exception in group II.

In group I, the response of coronary sinus blood flow showed a rather wide variation. It was increased in two experiments, unchanged in one, and decreased in two. But in group II, coronary sinus flow decreased noticeably in four experiments and was unchanged in the remaining one. Average coronary sinus blood flow remained relatively unchanged in group I and fell by approximately 37 per cent in group II (Fig. 2).

Myocardial oxygen consumption was reduced with one exception (experiment No. 3) in group I from 3.6 to 2.4 ml per 100 g of the left ventricle per minute; and from 3.3 to 1.2 ml per 100 g of the left ventricle per minute in group II (Fig. 2). This represented from +2.5 to −56.3 per cent of the control in group I and from −20.0 to −81.3 per cent in group II, with an average reduction of 33.3 per cent and 63.6 per cent, respectively.

The mean coefficient of oxygen extraction by the myocardium showed a tendency to decrease in both groups but markedly reduced in group II.

In total bypass, left ventricular output was zero, and the calculated left ventricular external work was reduced to zero.

During selective left ventricular bypass a marked reduction occurred in the internal work

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<table>
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<tr>
<th>Left atrial pressure (mmHg)</th>
<th>Coronary arteriovenous O₂ difference (vol %)</th>
<th>Coronary sinus flow (ml/100 g/min)</th>
<th>Left ventricular O₂ consumption (ml/100 g/min)</th>
<th>O₂ Coefficient of extraction (%)</th>
<th>Left ventricular external work (kg m/min)</th>
<th>Left ventricular internal work (kg m/min)</th>
<th>Left ventricular TTI (mmHg sec/min)</th>
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TABLE II  HEMODYNAMIC EFFECTS OF SELECTIVE

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<tr>
<th>No.</th>
<th>Time</th>
<th>Bypass rate (ml/kg/min)</th>
<th>Cardiac rate (min)</th>
<th>Rectal temperature (°C)</th>
<th>Right ventricular cardiac output (ml/min)</th>
<th>Mean aortic pressure (mmHg)</th>
<th>Mean left ventricular mean systolic pressure (mmHg)</th>
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of the left ventricle in both groups, corresponding to the reduction of myocardial oxygen consumption.

Left heart bypass with a left ventricular vent reduced left ventricular TTI (68.6 per cent) more significantly than did bypass without a vent (20.8 per cent). The tension-time index per minute was reduced mainly by a decrease in mean systolic pressure, and no significant reduction in systolic ejection period was noted.

II. Metabolic Studies

The data on myocardial lactate and pyruvate metabolism in the two groups are presented in Tables III and IV.

Substrate Utilization

A slight rise followed bypass in three of five dogs in group I but in group II, there was no change in arterial lactate levels during bypass. Mean arterial lactate calculated for the control period was 2.436 mM/L of blood water in group I. During bypass, mean arterial lactate rose to 2.697 mM/L. In group II, the average lactate concentration changed from 2.376 to 2.493 mM/L by selective left ventricular bypass.

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Fig. 2. Coronary sinus blood flow and myocardial oxygen consumption before and during selective left ventricular bypass (SLVB).

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During bypass, arterial pyruvate levels increased in all of both groups. The mean arterial pyruvate concentration increased from the control value of 0.147 mM/L to 0.175 mM/L during bypass in group I and from 0.169 to 0.224 mM/L in group II.

Myocardial lactate extraction increased in three experiments, and remained unchanged in two in group I while it remained unchanged in four out of five in group II. The over-all average was increased from 0.343 to 0.386 mM/L and from 0.379 to 0.401 mM/L in group I and group II, respectively.

Myocardial pyruvate extraction was elevated in two experiments, unchanged in one, and decreased in two in group I. On the other hand, it was elevated in one, unchanged in one, and decreased in three in group II. The average value of myocardial pyruvate extraction did not alter in group I and fell from 0.019 to 0.016 mM/L in group II. Out of ten experiments studied, two experiments (No. 15 and 16) showed negative myocardial pyruvate balances before bypass. During bypass, however, positive pyruvate balances were observed in these cases.

During bypass, lactate extraction coefficient increased in one experiment, decreased in one, and remained unchanged in three in group I and increased in one, and remained unchanged in the remainder in group II. The mean level of the per cent extraction of lactate before bypass was 14.9 per cent in group I and 17.0 per cent in group II. The over-all average remained unchanged during bypass in both groups.

Pyruvate extraction coefficient increased in one experiment, decreased in three, and remained unchanged in one in group I. It increased in one, and decreased in four in group II. The mean level of the per cent extraction of pyruvate was 9.8 per cent and 11.4 per cent before bypass in group I and group II, respectively. It was reduced during bypass in both groups.

Myocardial usages of lactate and pyruvate during bypass were 2.385 mg per cent per 100 g of the left ventricle and 0.106 mg per cent per 100 g of the left ventricle in group I and 1.891 and 0.081 in group II. These meant 7.0 per cent and 7.1 per cent increase from the control in group I and 32.0 per cent and 47.1 per cent decrease from the control in group II (Fig. 3).

In group I the average ratio of lactate to pyruvurate in the arterial blood decreased by 6.0 per cent during bypass. The values averaged 16.54 before bypass and 15.55 during bypass. In group II, however, there was a 19.5 per cent decrease in the mean arterial lactate to pyruvurate ratio during bypass. The values averaged 14.16 before bypass and 11.40 during bypass.

Parameters of Anaerobic Metabolism

In group I the average ratio of pyruvurate to lactate in coronary venous blood increased by
5.4 per cent during bypass. In group II, however, there was a 32.1 per cent increase in the average coronary venous pyruvate to lactate ratio during bypass. Control values averaged 0.074 in group I and 0.078 in group II.

On the other hand, change in lactate/pyruvate ratio (\(4L/P\)) from arterial to coronary sinus blood varied from 0.946 to 0.934 for group I and from 0.937 to 0.897 for group II.

In group I, excess lactate in the portion of the heart drained by the coronary sinus blood varied from +0.054 mM/L to −0.331 mM/L during the control period. The control mean left ventricular excess lactate was −0.122 mM/L. After 10 minutes of left heart bypass, excess lactate produced by the heart increased in one experiment, did not change in one, and decreased in three. Values ranged from −0.036 mM/L to −0.335 mM/L with the average value of −0.172 mM/L (41.0 per cent decrease from control). In group II, excess lactate varied from −0.069 mM/L to −0.292 mM/L during the control period. The average of excess lactate was −0.144 mM/L. It was reduced in four ex-

### Table III  Effects of Selective Left Ventricular

<table>
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<tr>
<th>No.</th>
<th>Weight of left ventricle g</th>
<th>Time</th>
<th>Arterial level mM/L</th>
<th>Coronary arterial-venous difference mM/L</th>
<th>Coefficient of extraction %</th>
<th>Myocardial usage mg/100 g/min</th>
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<td>0.349</td>
<td>14.5</td>
<td>3.863</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.702</td>
<td>0.389</td>
<td>14.4</td>
<td>2.836</td>
</tr>
<tr>
<td>11</td>
<td>92</td>
<td>Before</td>
<td>2.021</td>
<td>0.435</td>
<td>21.5</td>
<td>2.858</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.139</td>
<td>0.423</td>
<td>19.8</td>
<td>2.655</td>
</tr>
<tr>
<td>16</td>
<td>93</td>
<td>Before</td>
<td>3.513</td>
<td>0.258</td>
<td>7.3</td>
<td>0.511</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>4.010</td>
<td>0.405</td>
<td>10.1</td>
<td>0.620</td>
</tr>
<tr>
<td>Average</td>
<td>77</td>
<td>Before</td>
<td>2.436</td>
<td>0.343</td>
<td>14.9</td>
<td>2.228</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.897</td>
<td>0.389</td>
<td>14.8</td>
<td>2.385</td>
</tr>
</tbody>
</table>

% Change

\[ +10.7 \quad +12.5 \quad -0.7 \quad +7.0 \]

Abbreviations: \(4L/P\)-change in lactate/pyruvate ratio from arterial to coronary sinus blood;

---

**MYOCARDIAL UTILIZATION FOR LACTATE**

<table>
<thead>
<tr>
<th></th>
<th>Before SLVB</th>
<th>During SLVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td>GROUP II</td>
<td>2.8</td>
<td>1.9</td>
</tr>
</tbody>
</table>

---

**MYOCARDIAL UTILIZATION FOR PYRUVATE**

<table>
<thead>
<tr>
<th></th>
<th>Before SLVB</th>
<th>During SLVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>GROUP II</td>
<td>15</td>
<td>16</td>
</tr>
</tbody>
</table>

---

Fig. 3. Myocardial utilization for lactate or pyruvate before and during selective left ventricular bypass (SLVB).
EXCESS LACTATE AND REDOX POTENTIAL DURING LEFT VENTRICULAR BYPASS

BYPASS ON CARDIAC METABOLISM IN GROUP I

<table>
<thead>
<tr>
<th>Arterial level</th>
<th>Coronary arteriovenous difference mM/L</th>
<th>Coefficient of extraction %</th>
<th>Myocardial usage mg/100 g/min</th>
<th>Arterial lactic acid: pyruvic acid ratio</th>
<th>Coronary venous pyruvic : lactic acid ratio</th>
<th>ΔL/P mmol/L</th>
<th>ΔEh mv</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.151</td>
<td>0.027</td>
<td>17.9</td>
<td>0.164</td>
<td>20.36</td>
<td>0.048</td>
<td>1.022</td>
<td>+0.054</td>
</tr>
<tr>
<td>0.170</td>
<td>0.020</td>
<td>15.3</td>
<td>0.217</td>
<td>18.38</td>
<td>0.055</td>
<td>0.986</td>
<td>-0.036</td>
</tr>
<tr>
<td>0.142</td>
<td>0.012</td>
<td>8.5</td>
<td>0.055</td>
<td>8.16</td>
<td>0.132</td>
<td>0.925</td>
<td>-0.079</td>
</tr>
<tr>
<td>0.185</td>
<td>0.017</td>
<td>9.2</td>
<td>0.117</td>
<td>8.15</td>
<td>0.129</td>
<td>0.955</td>
<td>-0.062</td>
</tr>
<tr>
<td>0.147</td>
<td>0.010</td>
<td>6.8</td>
<td>0.108</td>
<td>16.40</td>
<td>0.066</td>
<td>0.918</td>
<td>-0.183</td>
</tr>
<tr>
<td>0.170</td>
<td>0.007</td>
<td>4.1</td>
<td>0.050</td>
<td>15.89</td>
<td>0.070</td>
<td>0.893</td>
<td>-0.278</td>
</tr>
<tr>
<td>0.149</td>
<td>0.027</td>
<td>18.1</td>
<td>0.173</td>
<td>13.56</td>
<td>0.077</td>
<td>0.950</td>
<td>-0.069</td>
</tr>
<tr>
<td>0.180</td>
<td>0.023</td>
<td>12.8</td>
<td>0.142</td>
<td>11.88</td>
<td>0.091</td>
<td>0.920</td>
<td>-0.150</td>
</tr>
<tr>
<td>0.145</td>
<td>-0.003</td>
<td>-2.1</td>
<td>-0.006</td>
<td>24.23</td>
<td>0.045</td>
<td>0.908</td>
<td>-0.331</td>
</tr>
<tr>
<td>0.171</td>
<td>0.003</td>
<td>1.8</td>
<td>0.004</td>
<td>23.45</td>
<td>0.047</td>
<td>0.915</td>
<td>-0.335</td>
</tr>
<tr>
<td>0.147</td>
<td>0.015</td>
<td>9.8</td>
<td>0.009</td>
<td>16.54</td>
<td>0.074</td>
<td>0.946</td>
<td>-0.122</td>
</tr>
<tr>
<td>0.175</td>
<td>0.015</td>
<td>8.6</td>
<td>0.106</td>
<td>15.55</td>
<td>0.078</td>
<td>0.934</td>
<td>-0.172</td>
</tr>
</tbody>
</table>

ΔEh—change in redox potential across the heart.

Experiments and unchanged in one. Values ranged from -0.142 mM/L to -0.344 mM/L. At 10-minute-interval during assistance, the average of excess lactate was -0.235 mM/L (63.2 per cent decrease from control). In summary, during left heart bypass the average left ventricular excess lactate remained the same as the control value or became more negative, and the tendency in decrease of excess lactate in group II was quantitatively more marked than that in group I (Fig. 4).

During ventricular assistance change in the redox-potential across the heart (ΔEh) increased in three experiments, did not change from control level in one, and decreased in one in group I. In group II, coronary venoarterial difference in oxidation-reduction potential showed no change in one experiment, and increased in four. The average value of ΔEh changed from 0.75 to

![Fig. 4](image1.png)  
**Fig. 4.** Effects of selective left ventricular bypass (SLVB) upon left ventricular excess lactate.

![Fig. 5](image2.png)  
**Fig. 5.** Effects of selective left ventricular bypass (SLVB) upon changes in the redox potential (ΔEh) across the heart.
Table IV  Effects of Selective Left Ventricular

<table>
<thead>
<tr>
<th>No.</th>
<th>Weight of left ventricle</th>
<th>Time</th>
<th>Arterial level mM/L</th>
<th>Coronary arteriovenous difference mM/L</th>
<th>Coefficient of extraction %</th>
<th>Myocardial usage mg/100 g/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>75</td>
<td>Before</td>
<td>2.426</td>
<td>0.519</td>
<td>21.4</td>
<td>4.605</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.512</td>
<td>0.522</td>
<td>20.8</td>
<td>3.758</td>
</tr>
<tr>
<td>10</td>
<td>92</td>
<td>Before</td>
<td>2.021</td>
<td>0.435</td>
<td>21.5</td>
<td>2.858</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.092</td>
<td>0.420</td>
<td>20.1</td>
<td>2.759</td>
</tr>
<tr>
<td>12</td>
<td>70</td>
<td>Before</td>
<td>1.732</td>
<td>0.275</td>
<td>15.9</td>
<td>1.559</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>1.806</td>
<td>0.293</td>
<td>16.2</td>
<td>0.554</td>
</tr>
<tr>
<td>13</td>
<td>47</td>
<td>Before</td>
<td>2.245</td>
<td>0.453</td>
<td>20.2</td>
<td>3.995</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.434</td>
<td>0.467</td>
<td>19.2</td>
<td>1.891</td>
</tr>
<tr>
<td>15</td>
<td>93</td>
<td>Before</td>
<td>3.454</td>
<td>0.213</td>
<td>6.2</td>
<td>0.594</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>3.623</td>
<td>0.303</td>
<td>8.4</td>
<td>0.491</td>
</tr>
<tr>
<td>Average</td>
<td></td>
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<td>2.376</td>
<td>0.379</td>
<td>17.0</td>
<td>2.782</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During</td>
<td>2.493</td>
<td>0.401</td>
<td>16.9</td>
<td>1.891</td>
</tr>
<tr>
<td>% Change</td>
<td></td>
<td></td>
<td>+4.9</td>
<td>+5.8</td>
<td>-0.6</td>
<td>-32.0</td>
</tr>
</tbody>
</table>

Abbreviations: See Table III.

0.92 mv for group I (22.7 per cent increase) and 0.87 to 1.46 mv for group II (67.8 per cent increase) (Fig. 5).

Correlation of Excess Lactate or Redox Potential with Hemodynamic and Metabolic Changes

No correlation was found between left ventricular excess lactate and measured left ventricular mean systolic pressure as well as left ventricular external work. For example, even though left ventricular mean systolic pressure decreased, no significant decrease of left ventricular excess lactate was observed.

As shown in Fig. 6 left ventricular excess lactate could be related to myocardial oxygen consumption. In both groups in which left ventricular excess lactate was markedly decreased, myocardial oxygen consumption was significantly reduced. The alterations in change in the redox potential across the heart were similar in general to those for left ventricular excess lactate (Fig. 7).

Discussion

Generally, assisted circulation is often applied to critically ill patients in which all conservative treatments have been exhausted. The
<table>
<thead>
<tr>
<th>Bypass on Cardiac Metabolism in Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pyruvic Acid Metabolism</strong></td>
</tr>
<tr>
<td>Arterial level</td>
</tr>
<tr>
<td>mM/L</td>
</tr>
<tr>
<td>0.207</td>
</tr>
<tr>
<td>0.296</td>
</tr>
<tr>
<td>0.149</td>
</tr>
<tr>
<td>0.222</td>
</tr>
<tr>
<td>0.126</td>
</tr>
<tr>
<td>0.144</td>
</tr>
<tr>
<td>0.185</td>
</tr>
<tr>
<td>0.227</td>
</tr>
<tr>
<td>0.176</td>
</tr>
<tr>
<td>0.229</td>
</tr>
<tr>
<td>0.169</td>
</tr>
<tr>
<td>0.224</td>
</tr>
<tr>
<td>+32.5</td>
</tr>
</tbody>
</table>

Influence of this therapeutic procedure on cardiac failure states should therefore be investigated under the conditions which permit continuous observations of all important indexes to cardiac function. Such metabolic and physiological parameters with a high degree of accuracy should also be obtained without burdening the patients.

Listed as these indexes are general conditions, the external and internal work of the heart, the tension-time index (TTI), myocardial oxygen consumption, excess lactate (XL), redox potential ($\Delta Eh$) and the isometric time-tension index ($\frac{dp}{dt}/IIT$) 37.

Among various parameters for the evaluation of myocardial condition, myocardial oxygen consumption has been the most reliable parameter 36,38, which is relatively difficult to determine at the bedside. Consequently various factors bearing a closer relation to myocardial oxygen consumption should have been investigated.

It has been shown that selective left ventricular bypass lowered the pressure in the left atrium markedly by reason of the characteristic of this procedure and maintained an adequate aortic pressure 15,16 but did not necessarily result in significant changes in left ventricular pressure or in the oxygen utilization of the

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Fig. 7. The relationship between myocardial oxygen consumption and changes in the redox potential across the heart. Arrows show direction of changes during selective left ventricular bypass.

*Japanese Circulation Journal Vol. 32, April 1968*
heart\textsuperscript{15,39,40}. The aortic pressure curve during this procedure was almost completely replaced with the pump-induced pressure curve and mean aortic pressure tended to elevate. Pulsatile arterial blood flow is thought to be more physiological than nonpulsatile one\textsuperscript{41}. It is desirable for left ventricular work to return the blood to the arterial tree in diastole by a synchronous pulsatile pump. More clarification of the role of the pulse is required.

Schenk and associates\textsuperscript{19} have observed that left ventricular pressure was not always reduced during even total left ventricular bypass. The observation made by these authors was similar to the results of experiments in the author's laboratory\textsuperscript{5,11}. In one experiment of group I, a reduction in left ventricular pressure and myocardial oxygen consumption were not remarkable. This phenomenon is understandable since under these circumstances not only the continuing accumulation of the thebesian drainage but also the blood which flowed into and collected in the left ventricle result a significant left ventricular pressure and tension load. The trapping of blood in the left ventricle (a phenomenon well known from open heart surgery) may result in a highly undesirable state since the left ventricular myocardium would continue to contract against the trapped bolus of blood.

In all experiments of group II, those two parameters were markedly reduced by removing the residual blood in the left ventricle through a left ventricular vent. The findings suggest that left ventricular bypass should be total and include a left ventricular vent.

Left ventricular pressure was considered to have some relationship to myocardial oxygen consumption, but not linear\textsuperscript{5}.

On institution of left ventricular bypass in a normal heart, left ventricular output should be reduced in proportion to the amount of blood removed from the left atrium.

Left ventricular minute work was advocated by Sarnoff and Berglund\textsuperscript{44} as one of the expressions of left ventricular external work which means the mechanical work of the heart. And left ventricular work should be reduced primarily as a result of reduction in left ventricular output, rather than by a reduction of the pressure component of work. When selective left ventricular bypass was achieved to total or near total bypass, left ventricular output was decreased to near zero level, so was left ventricular external work. Khouri et al.\textsuperscript{45} reported that oxygen usage was a linear function of left ventricular work. However, Lüthy and Bing\textsuperscript{45} described no direct relationship between the change in oxygen consumption and the work of the left ventricle. When the heart is allowed to contract at a given frequency with its cavities empty of blood, i.e., without producing any external hemodynamic work, the oxygen consumption of the myocardium, though is considerably reduced, but still amounts to a considerable part of the total consumption under normal condition of activity. Therefore left ventricular external work can not be adopted as a direct parameter of myocardial energy and oxygen metabolism when the mechanical work of the heart is performed by a pump. The reduction of left ventricular external work is the necessary but not sufficient condition.

It is to be desired that one should measure not only left ventricular external work but other cardiac indexes (myocardial oxygen consumption, the tension-time index, and the internal to work of the heart).

When systemic blood pressure cannot be maintained at its normal level and, as a result, coronary perfusion pressure is presumably reduced, the myocardium begins to deteriorate and this might alter unfavorably the balance of myocardial oxygen demand and supply, leading to a relative myocardial hypoxia.

One would suppose a decrease of oxygen supply to the myocardium (i.e., myocardial oxygen consumption) when arterial oxygen content is low. The fact is that the first response to an increased oxygen demand is normally an increase in coronary flow and the acquired balance between oxygen supply and demand renders. The oxygen lack acts either directly or through some intermediate substance to increase the caliber of the coronary vessels, thereby increasing the coronary flow to maintain the performance of the heart.

About coronary flow during pumping, Liotta and co-workers\textsuperscript{44} found an increase in the coronary flow but Schenk and associates\textsuperscript{19} reported a reduction of coronary flow when total left ven-

\textit{Japanese Circulation Journal Vol. 32, April 1968}
Excess lactate and redox potential during left ventricular bypass

The bypass was carried out. Coronary flow measurements in the present report is based principally on the amount of the coronary sinus drainage. For the coronary sinus was found to drain approximately 60% of the total coronary flow and represent all or a constant portion of the venous drainage from the left ventricle. The findings in this report indicate that selective left ventricular bypass has no appreciable effect upon left ventricular coronary flow. It is easy to understand on considering that this form of assistance does not preferentially elevates the diastolic pressure. Left ventricular bypass lowers the work load and the metabolic requirements of the left ventricle, thus reducing the amount of coronary blood flow required for that ventricle. However, in the presence of coronary lesions or myocardial damage, flow rates may not adequately increase for the demand of induced stress and increased extraction of oxygen is initiated as the second adaptive mechanism.

Myocardial oxygen extraction ratio, which remains constant under certain conditions, has been frequently used as an useful index of oxygen demand and supply balance in the left ventricular myocardium. This ratio correlates inversely with the oxygen partial pressure in the coronary venous blood, which is accepted to reflect the oxygen partial pressure in the myocardium. Hence a high value of this ratio means the disturbance of oxygen demand and supply, that is, the presence of intracellular hypoxia. As shown in the present data, the percentage of oxygen extraction by the myocardium decreased greatly during bypass. On the other hand, this ratio is significantly reduced in cardiac muscle exposed to a solution of sodium cyanide and shows deleterious myocardial metabolism with which are associated a decrease of myocardial oxygen consumption and lactate production.

Consequently this ratio only means the relationship between oxygen demand and supply in the myocardium, and cannot be an index to estimate the myocardial metabolism.

The marked reduction in oxygen consumption by the myocardium during cardiopulmonary bypass is a reflection of the decreased work load of the heart during bypass.

Dennis and co-workers have shown that left heart bypass decreases myocardial oxygen consumption in proportion to the degree of bypass. Determination of the oxygen consumption of the left ventricle also have been based on the same assumptions as stated in coronary flow. This reduction in oxygen utilization is usually the result of a decrease in arteriovenous oxygen difference rather than of a decrease in coronary sinus blood flow. The significant decrease in myocardial oxygen consumption, also observed in the cases of selective left ventricular bypass with a vent, strongly suggests that this procedure is effective in substantially unloading the left ventricle. The less significant decrease in the left ventricular pressure in the cases of selective left ventricular bypass without a vent is thought to be due to the presence of the blood which flowed into and collected in the left ventricle, because the complete withdrawal of the blood from the left atrium is difficult. These findings are in agreement with the previous work of Schenck and associates. These results imply that left heart bypass should be beneficial in reducing the internal work of the left ventricle in acute left heart failure.

Sarnoff found that myocardial oxygen consumption was dependent primarily upon the pressure generated by the left ventricle. The average systemic pressure exerted by the left ventricle per min. was termed the "tension-time" index by his group. Neill, Levine, Wagman, and Gorlin showed that there was a linear correlation between the tension-time index and the oxygen consumption of the left ventricle. Although a good correlation between the tension-time index and the oxygen consumption of the left ventricle was observed at a lower oxygen consumption level, no significant correlation was observed in a higher range (not less than 15 ml).

Studies by the authors have shown that the tension-time index was reduced accompanying a reduction of myocardial oxygen consumption, but was in direct proportion to the latter. Baird and associates also described that this reduction in oxygen consumption was not mirrored by the tension-time index or heart rate times blood pressure. Therefore, it was suggested from these results that the tension-time index could not be adopted as a principal clini-
cal parameter to evaluate myocardial oxygen consumption.

Thus, the importance of myocardial oxygen consumption has been confirmed by a number of authors. The use of oxygen metabolism as an index of the production of energy by the heart probably represents the best direct method of evaluating the effectiveness of any procedure to assist the heart.

The normal heart functions as an aerobic organ, deriving the bulk of its energy through extraction and oxidative metabolism of glucose, free fatty acids, lactate and pyruvate and, to a lesser extent, acetate, ketone bodies and amino acids. Thus the heart has been considered primarily an aerobic organ, recent work has emphasized the possibility that measurement of oxygen alone might not be adequate to define the total energy utilization under all conditions. If the above-mentioned mechanism fails to yield sufficient oxygen, the metabolism of the myocardial cell no longer can remain completely aerobic. The most feeble point is aerobically acting tricarboxylic acid cycle and the cells, therefore, increase glycolysis in excess of oxidation in order to derive small amounts of high-energy phosphate from glucose or glycogen for the maintenance of cellular activity. This source of cellular energy is limited and cannot provide full myocardial function for a longer period.

Hence determination of myocardial efficiency by the oxygen consumption of the heart cannot be made unless one is sure that anaerobic glycolysis in the heart muscle is absent.

Previous investigations\(^{46}\) have indicated that, after cardiopulmonary bypass and profound hypothermia, metabolic acidosis frequently occurred presumably as the result of decreased perfusion of tissues and glycolysis of anaerobic metabolism. A meager cardiac output leads to an impoverished tissue perfusion in which the heart itself participates. Aerobic metabolism gives way to anaerobic glycolysis and metabolic acidosis ensues. As shown by Bing, the oxidative reactions in the heart muscle are pH-dependent, and acidosis, therefore, further reduces the cardiac output. Metabolic acidosis decreases ventricular contraction which in turn leads to further decrease in cardiac output and a self-propagating vicious cycle is established.

Although such metabolic acidosis is evidenced by arterial pH, buffer base, blood lactate and pyruvate concentrations, lactate-pyruvate ratio, excess lactate and so on, lactate and excess lactate are thought to indicate prognosis more accurately than pH and buffer base.

The metabolism of the myocardium differs from one of the skeletal muscles, normally utilizing lactic acid as a substrate; however, during protracted perfusions, myocardial metabolism appears to resemble the skeletal muscles closely, and produces lactic acid as a metabolic end-product. Lactic acid, as the end-product of cytoplasmic glycolysis, tends to lower cellular pH, and if it increases for prolonged periods may institute cellular autolysis. From the metabolic viewpoint, the most convenient means of assessing the sequelae of intracellular hypoxemia in the present study appears to be the analysis of lactate and pyruvate concentration in arterial blood.

A rise in lactate due to the failure of effective supply of oxygen to tissues to keep pace with metabolic needs reflects a serious defect in metabolic function, whether the relative lack of oxygen might have its origin in circulatory, respiratory, hematologic or cellular dysfunction. Whether pyruvate rises or falls has no apparent effect on oxygen debt. But if a rise in pyruvate occurs which accounts entirely for the rise in lactate, then there is no evidence of cellular hypoxia\(^{19}\). As shown in Tables III and IV, the rise in lactate can be accounted for the rise in pyruvate and can be regarded as relatively benign situation.

There is little information on the myocardial metabolism during assisted circulation as compared with the cardiopulmonary bypass. Edmunds et al.\(^{25}\) first showed that slight increase of pyruvate levels by left heart bypass during cardiac arrest was not account for the acidosis nor it consistent in all dogs. Jacobson, 1965, also found no significant changes in the lactate or pyruvate levels from the base line during partial left heart bypass. Kennedy and his group\(^{35}\) reported that when left heart bypass was ineffective in the presence of ischemic left ventricular failure, anaerobic glycolysis, as the results of an inadequate tissue perfusion, gradually supplanted aerobic metabolism and lac-
tic acidemia progressed. On the other hand, Brief and Berkeley found reduced values of blood lactate and pyruvate during counterpulsation in the dogs with hemorrhagic shock. Callaghan et al. also reported that in the early stage of myocardial augmentation, there was a marked rise in blood lactate level and as the assistance to the circulation continued, the blood lactate level fell. This paradoxical behavior of blood lactate in those treated by the pumping seemed to indicate benefit of the peripheral perfusion by a lactate "washout" from the tissues, i.e., although the blood level was high, the intracellular lactate, which must be at a higher concentration, was washed out by the increased perfusion.

The myocardial extraction of lactate and pyruvate is ordinarily proportional to their arterial concentrations, but in the presence of hypoxia, hemorrhagic shock, or a block in pyruvate metabolism, there is a diminution in their extraction at elevated arterial concentrations.

Kuel and co-workers reported that the extraction of lactate and pyruvate by non-working, resting human heart was small in spite of a very high arterial concentration. On the other hand, Goodale and Hacket have demonstrated that myocardial extraction of carbohydrate metabolites (expressed either as the coronary arteriovenous difference or as an extraction ratio) was independent of coronary blood flow and cardiac work.

From results presented in this paper, it appears that the myocardial extraction of lactate and pyruvate remained rather constant during bypass. A decrease in oxygen utilization of the canine myocardium during cardiopulmonary bypass was noted and an increase in the production of lactic acid by the myocardium was not detected except during the perfusion of an hour or more.

Wallace et al. have observed a marked increase in oxygen consumption as well as an increase in lactate and pyruvate utilization of the myocardium during extracorporeal circulation.

Since selective left ventricular bypass causes no significant alteration in coronary flow, it can be assumed that myocardial usages of lactate and pyruvate likewise remained unchanged, or rather decreased. The myocardial usages of lactate and pyruvate decreased in proportion to the fall of myocardial oxygen consumption. It is thought to be due to the decreased external and internal work of the normal heart. Increase in lactate and pyruvate utilization during the procedure is thought as the result of the improvement of the myocardial carbohydrate metabolism in a failed heart.

However, such extractions of substrates reflect only balances and give little information of intermediary metabolism.

The arterial lactic-pyruvic acid ratio is an important index to the function of glycolysis which operates to produce energy from carbohydrate sources. And this ratio is regulated with considerable constancy within a wide range of activity of the normal condition. The rise of the ratio is considered to mean the anoxia.

The mean percentage fall from control ratio was 6.0 per cent for group I and 19.5 per cent for group II. The reduction of this ratio during the procedure indicates no hypoxia.

The increase in lactate and pyruvate in the coronary sinus blood after ischemia has been demonstrated previously but not for such brief ischemic periods and it was regarded as an expression of anaerobic carbohydrate metabolism. However it has been emphasized by Huckabee that lactate might rise as a result of an increase in pyruvate, as described later.

As mentioned above, the development of metabolic acidosis due to incomplete glycolysis, with resulting accumulation of lactic and pyruvic acid metabolites during bypass has been known for several years. Litwin and associates indicate an inverse relationship between the rise in blood lactate concentration and the adequacy of perfusion. Such factors as hyperventilation or increased pH or glucose concentration can be present during cardiopulmonary bypass, and therefore one cannot ascribe the rise in blood lactate to anaerobic metabolism alone. Away out of this dilemma Huckabee advocated the term systemic "excess lactate" to consider only that lactate produced by anaerobic metabolism, and derived a formula for its calculation. A measurement of overall excess lactate does not differentiate be-

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tween the excess lactate of large nonvital tissue masses and that of smaller but more essential organs. Later HUCKABEE developed the concept of myocardial "excess lactate" as a quantitative parameter, that is, the number of molecules transferred in the lactic dehydrogenase system in bringing about an alteration in ratio rather than the estimate of intensity or potential given by lactate-pyruvate ratio.

Attention is also directed toward the publications by HARRIS, BATEMAN and GLOSTER, as well as by OLSON, which criticize the basis for the derivation of "excess lactate", together with the correlation between changes in lactate-pyruvate ratio (which are not utilized in HUCKABEE's equation). Furthermore, HERMAN, ELLIOTT and GORLIN used neither the calculation of myocardial excess lactate nor comparison of arterial and venous lactate to pyruvate ratio due to the problem inherent to accurate measurement of small arteriovenous pyruvate differences.

However, in the heart muscle itself, a very close agreement has been established between the redox potential changes in the lactic dehydrogenase and the DPNH to DPN system during progressive hypoxia, whereas the potential of the alpha-glycerolphosphate to dihydroxyacetonephosphate (the participation of other systems than lactate to pyruvate) system lags more and more behind the other two. From these findings the conclusion seems justified that HUCKABEE's concepts and their further development by GUDJARNASON and BING are basically correct qualitatively in the sense that the lactate to pyruvate ratio in blood adequately reflects at least the cytoplasmic DPNH to DPN ratio. Thus excess lactate is a more accurate and sensitive indication of the status of tissue oxygenation than blood gas. BESSINGER, JR. et al. reported that excess lactate values increased during left ventricular bypass at a high flow rate (bypass of 55 to 98 per cent of blood). KUHN and his associates have indicated that a mechanically induced rise in aortic pressure and systemic vascular resistance (by balloon obstruction of the abdominal aorta) in experimental acute myocardial infarction with shock was associated with a sharp increase in coronary flow, an increase in cardiac output and left ventricular mechanical efficiency, and a decrease in left ventricular "excess lactate" production. SKINNER et al. have reported that systemic excess lactate showed almost no change during mechanical ventricular assistance in three of five dogs. So far as this study is concerned, the decreased excess lactate in the bypass animal is indicative of an improvement in tissue oxygenation.

The other available qualitative parameter is the redox potential Eh of the system. Whereas the excess lactate represents only the hydrogen transferred to one redox system and does not permit quantitative estimation of hypoxia, it has been suggested that the change of the redox potential across the heart, referred to as $\Delta$Eh and calculated from the lactate to pyruvate ratios in arterial and coronary sinus blood, reflects the aerobic and anaerobic metabolic conditions in the heart muscle. When $\Delta$Eh is positive, there is active cellular oxidation, and the energy required is supplied by oxidative phosphorylation. When $\Delta$Eh is negative, there is glycolysis, and anaerobic phosphorylation becomes an important process of energy production.

Therefore it is possible to interpret alterations in $\Delta$Eh across the heart as reflecting change of oxygen supply in the myocardium. And it is believed to become abnormal on inadequate blood supply and to reflect tissue ischemia much earlier than other indexes reach their abnormal levels. MANTINI et al. reported that both normal and shocked animals following 30 min of counterpulsion developed progressive acidosis but the lactate/pyruvate ratios revealed no tendency in either group to the development of anaerobic metabolism and all Eh values in both groups were within the normal range. The data presented here indicate that the lactate-pyruvate redox potential gradient across the heart muscle was consistently positive although coronary blood flow and oxygen consumption of the myocardium were reduced by the bypass of the left heart. The shift of redox potential to a more positive value (from a mean of $+0.75$ to a mean of $+0.92$ in group I and from a mean of $+0.87$ to a mean of $+1.46$ in group II) was observed. The metabolic pathways therefore appeared to be oxidative,

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and during the procedure there was no indication of anaerobic metabolism.

As shown in Fig. 6 and 7, some correlation was found between change in ΔEh (or myocardial excess lactate production) and myocardial oxygen consumption during selective left ventricular bypass by the author.

In some instances (Tables III and IV), the myocardial extraction of pyruvate was negative during the control period in which the cannulated heart was rhythmically contracting in the open chest animal. Similar negative myocardial pyruvate balance had been previously found in hemorrhagic shock and artificial myocardial infarction. In one experiment, positive excess lactate and negative redox potential were seen at control, suggesting the anaerobic metabolism.

Thus the control may be considered a chemically deteriorating heart due to the results of complexities in manipulation such as thoracotomy and cannulation and, especially, the administration of barbiturates for anesthesia. For this reason the author paid attention to the shift of these parameters from slight heart failure of control state during the bypass of the left ventricle. The results might become more obvious if this procedure would be applied to failing animals.

Thus lactate and pyruvate have provided a valuable index of the metabolic disturbance that followed the critical reduction in tissue perfusion and of assessment of the effect of assisted circulation. Progress in application of this procedure was limited by laborious complexity and by limited reliability of the classical techniques. Marbach and his co-workers employed a modified enzymatic method for rapid determination of lactate and pyruvate. Though it is simple and can be reliably completed within 20 minutes, we will need any method which is attractively simple, timesaving, and requires no special equipment nor skilled hand. Further investigation into this problem is warranted.

As stated above, it is mandatory to gain a proper quantitative evaluation of the patient's myocardial capacity during performance of assisted circulation. Any of the above-mentioned parameters, however, can not meet all the demands on their reliability, simplicity and in-

Recently, the ratio between the maximum rate of development of isometric tension (dp/dt) and a constant fraction of the integrated isometric tension developed (IIT), based on the time to maximum dp/dt, has been shown by Siegel and Sonnenblick to be a reliable index to myocardial contractility which is independent of alterations in end diastolic pressure, aortic pressure, or cardiac work.

This index obtained during synchronized arterial counterpulsation has shown a significant correlation with myocardial oxygen consumption and the changes in redox potential across the heart.

The isometric time-tension index, \( \frac{dp}{dt}/IIT \), is obtained with greater ease by computer analysis of left ventricular pressure and thought to be a more useful measure in patients who are in a serious condition or after cardiac surgery than other hemodynamic parameters, since it is possible to quantify myocardial contractility and to predict cardiac failure prior to its manifestation with this type of "on-line" analysis of the information.

Although a number of basic questions remain to be answered about the validity of this parameter in many pathological states and this is one direction under investigation in the author's laboratory, this parameter is thought to be available as an useful index as well as excess lactate or redox potential.

It has been confirmed both hemodynamically and metabolically that synchronized arterial counterpulsation and selective left ventricular bypass are the most promising procedures in the treatment of left heart failure.

Although synchronized arterial counterpulsation, as selective left ventricular bypass, provides the marked reduction of left ventricular work, there is a substantial difference in their mechanism between these methods. In selective left ventricular bypass, the reduction in left ventricular external work is caused by the remarkable reduction in the volume work as a result of the reduction in cardiac output; while, in synchronized arterial counterpulsation, it results from the reduction of the pressure work (Table V).
Synchronized arterial counterpulsation can be instituted with only one arterial cannulation for pumping without thoracotomy. However, an efficient mechanical pumping unit combined with a precise electrical triggering circuit and a bigger artery (for example, external iliac artery) for cannulation are essential to accomplish the desired effects\(^\text{19}\).

Selective left ventricular bypass possesses many advantages over other types of mechanical assistance to the heart. More notable of these are the simple device like a veno-arterial pumping, and the independence from any extracorporeal oxygenator. This can avoid mechanical trauma to blood during oxygenation which may be responsible for the subsequent pulmonary injury\(^\text{50,53}\). In order to attain a total or near total drainage of the blood from the left atrium and to render the technique of selective left ventricular bypass clinically useful, it appears necessary to position the cannula tip in the left ventricle through the mitral valves or to use a left ventricular vent.

The target date of 1972 set by the National Institutes of Health for whole-heart replacement disappeared because of the need for more basic research and greater problem of the project, and studies of left ventricular assist devices have revived.

Recently, modification of the principles of synchronous counterpulsation and left heart bypass has resulted in the developments of mechanical pumping devices which can be implanted in the thorax and powered from an external energy source for assistance of the failing heart\(^\text{54,55}\) for a longer period.

Furthermore, it is reported that, in most instances, the hemodynamic improvement did not last beyond termination of the procedure although closed-chest and open-chest left heart bypass have been successfully applied clinically\(^\text{53,56}\).

To produce more efficient assistance to the failing heart, a combined form of these two procedures, that is, a synchronized left ventricular bypass, is advisable than either the one reducing the volume work or the one reducing the pressure work alone.

**Summary and Conclusions**

1. Selective left ventricular bypass was performed on 8 dogs.

2. Myocardial extractions of oxygen, lactate and pyruvate, production of left ventricular excess lactate as defined by HUCKABEE, and change in lactate/pyruvate ratio and in redox potential of the lactic dehydrogenase system in blood passing through the heart according to

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**Table V. Comparison of Two Types of Mechanical Assistance for Left Heart Failure**

<table>
<thead>
<tr>
<th></th>
<th>Selective left ventricular bypass</th>
<th>Synchronized arterial counterpulsation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Indication</strong></td>
<td>left atrial and/or ventricular failure</td>
<td>left ventricular failure</td>
</tr>
<tr>
<td><strong>2. Mechanism</strong></td>
<td>reduction of the volume work, sec. of the pressure work</td>
<td>reduction of the pressure work</td>
</tr>
<tr>
<td><strong>3. Coronary blood flow</strong></td>
<td>inappreciable</td>
<td>augmented</td>
</tr>
<tr>
<td><strong>4. Flow characteristics</strong></td>
<td>usually, low amplitude</td>
<td>high amplitude</td>
</tr>
<tr>
<td><strong>5. Difficulties</strong></td>
<td>left atrial drainage</td>
<td>synchronisation esp. in the presence of tachycardia and/or arrhythmia</td>
</tr>
<tr>
<td><strong>6. Procedure required</strong></td>
<td>throracotomy or transseptal cannulation</td>
<td>exposure of an artery with a large bore</td>
</tr>
<tr>
<td><strong>7. Analogous techniques</strong></td>
<td>synchronous external pulsation (Dennis)</td>
<td>intrathoracic auxiliary ventricle (Kantrowitz)</td>
</tr>
<tr>
<td></td>
<td>intraaortic balloon pumping (Moulopoulos)</td>
<td></td>
</tr>
<tr>
<td><strong>8. Contraindication</strong></td>
<td>aortic insufficiency, patent ductus arteriosus</td>
<td></td>
</tr>
</tbody>
</table>

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GUDBJARNASON and Bing were determined before and during this procedure of which benefit to left heart failure has previously been confirmed hemodynamically.

3. Control value of myocardial excess lactate in dogs was negative and became more negative by selective left ventricular bypass. Lactate extraction and positive change in redox potential were also observed with this procedure performed.

4. Selective left ventricular bypass affords some evidences of the adequacy of myocardial perfusion.

5. In selective left ventricular bypass with a left ventricular vent, the tendency in changes of the parameters was similar to that in selective left ventricular bypass without a left ventricular vent but, in most instances, it was quantitatively more marked.

6. The findings suggest that selective left ventricular bypass should favorably be total and include a left ventricular vent.

7. A significant correlation between percent decrease in myocardial oxygen consumption and changes in both redox potential and myocardial excess lactate was also found.

8. The results suggest that change in redox potential or myocardial excess lactate formation is, at the present time, one of the most reliable measures in order to evaluate the effectiveness of assisted circulation on failing cardiac function.

9. To produce more efficient assistance to a failing heart, a synchronous left ventricular bypass is recommended.

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REFERENCES

Japanese Circulation Journal Vol. 32, April 1968


84. Hall, C. W., Liotta, D., Henly, W. S., Crawford,

Japanese Circulation Journal Vol. 32, April 1968
