Reduction of the Oxygen Utilization of the Heart by Left Heart Bypass

By Clarence Dennis, M.D., Ph.D., David P. Hall, M.D., Juan R. Moreno, M.D., and Åke Senning, M.D.

Reports of support of the heart in acute failure both in man and in experimental animals have been published. The means investigated include: (1) heart-lung bypass, from the cava through an oxygenator and pump to the aorta; (2) veno-arterial pumping without oxygenator; (3) aortic synchronized counter pulsation to lower the pressure during left ventricular ejection and to raise it when the valves are closed; and (4) left heart bypass, from left atrium to aorta.

The studies here reported have been done simultaneously with our development of a simple method of nearly complete left heart bypass without thoracotomy, adaptable to clinical acute left heart failure whether from coronary occlusion, mitral disease, or aortic stenosis too severe to respond to the usual conservative measures. It is essential, therefore, to settle the disputed question as to whether partial cardiac bypass can reduce the oxygen utilization of the heart. Left heart bypass has been investigated here for the further reason that it is basically less complicated than heart-lung bypass, or the Harken method, more physiological than veno-arterial pumping, and appears to us more susceptible to performance under precise control in the laboratory.

Methods

Seventeen mongrel dogs (18 to 27 Kg.) were anesthetized with intravenously administered thiopental sodium (300 to 400 mg.), supplemented as needed with thiopental or pentobarbital sodium, and placed on the left side. Thirty to 50 per cent O₂ was given with an Engström respirator. The established technique consisted in securing a cannula in the coronary sinus by a ligature just distal to the vena magna cordis, from which a Y-tube led either back to the right atrium or to a condom attached at the level of the top of the atrium and supported distally by one pan of a balance. Sinus blood flow was measured by stopwatch and clamp occlusion of the atrial return tube at physiological pressures (6 mm. Hg throughout cannula and 40 cm. of tubing) (fig. 1).

For the bypass circuit, blood was drained from the transseptal cannula, a cannula in the left atrial appendage (abandoned because of poor maximum flows), or a cannula in the upper end of the left atrium (abandoned because of air embolism). It passed by siphonage through an AGA flowmeter* to a flexible-walled chamber placed 80 to 90 cm. below the atrium, from which a roller pump returned it to a proximal femoral artery (fig. 1). A large side tube permitted rapid addition or removal of blood. There was no blood-air contact.

Blood and blood circuits were prepared aseptically; the surgical technique was clean, not aseptic; and penicillin and streptomycin were given before dissection. Heparin (3 mg./Kg.) was given after preliminary dissections.

A mercury manometer was used for arterial blood pressure eight times, an Elema Mingograf 42B with 1-mm. polyethylene cannulas, nine times; the latter was also used for left ventricular and left arterial pressures four times. A water manometer permitted maintenance of central venous pressure during experiments always within 3 cm. of the control, and always below 10 cm., except once when it was deliberately raised. Temperature was held between 36 and 39 C. The electrocardiograph was used to record pulse rates at times.

Coronary sinus blood samples were taken through a stopcock in the tube to the condom after two or more flow measurements. Arterial samples were drawn through a 1-mm. polyethylene catheter in the aortic arch. Blood was drawn into standardized siliconized syringes, which were sealed and refrigerated until O₂ determination (maximum three hours). Although early experi-

*Aktiebolaget Gas Accumulator, Lidingö, Sweden.
LEFT HEART BYPASS

Coronary sinus drainage

Return to right atrium

Clamp & stopwatch for flow measurement

To femoral artery

Roller pump

Flexible siphon chamber

FIGURE 1

Extracorporeal circuits. A cannula is secured in the coronary sinus by a snug purse-string suture just distal to the vena magna cordis. Blood from this returns to the right atrium. A Y-connection with condom attached permits flow determination by balance, stopwatch, and occlusion of return to the right atrium. The major circuit drains the left atrium through a transseptal jugular cannula, through an AGA flowmeter, to a flexible-walled chamber 80 to 90 cm. below the left atrium. Blood is pumped back to a femoral artery without contact with air. Transfusion connection not shown.

Experiments used the Kipp method, all conclusive ones employed the Van Slyke or the spectrophotometric method (Beckman). All blood O\textsubscript{2} determinations were in duplicate; all flow determinations were multiple (two to five runs, usually three).

Observations were divided into two categories. In category I, all preparations were made, but no bypass was used; the effects of changes in blood pressure secondary to withdrawal or addition of blood, and the effects of minute gas embolism and of manipulation were assayed.

In category II, observations were made in pairs, one during bypass and the other without it. Except for two instances (see table 2), the control either immediately preceded or followed the experimental run. Control and experimental runs were less than 10 minutes apart in half the experiments, as long as 26 minutes once, when flows were run in quintuplicate (here controls both preceded and followed the experimental run). The mean blood pressure was held nearly constant in the two runs of each paired observation, that in the experimental run lying below the control five times (maximum 4 mm., mean 2 mm.), and never more than 8 mm. Hg above the control. All data were continuously dictated into a tape recorder to permit a timed full record. The same

Circulation Research, Volume X, March 196X

Results

Coronary sinus flows were not detectably altered by changes in level of the junction of tubing to condom between -3 and +3 cm. above the top of the right atrium. Resistance to flow through the circuit or into the condom at the rates measured was less than 1 cm.

In the absence of bypass, both coronary sinus flow and O\textsubscript{2} utilization vary with changes in blood pressure brought about by altering the blood volume (fig. 2). There was slow variation in control coronary sinus flows and O\textsubscript{2} utilization rates done serially with intervening bypass runs even though the blood pressure was held constant (table 1). On the other hand, O\textsubscript{2} utilization was increased following minimal air embolism (25 per cent on two observations), manipulation of the heart (25 per cent once), or fibrillation and defibrillation (15 per cent once), even though the blood pressure was controlled.

CATEGORY II

In six dogs, experiments were performed on bypass with orderly control of all factors. In all of 21 paired observations, the oxygen utilization of the portion of the heart drained

FIGURE 2

Effect of changes in blood pressure on coronary sinus blood flow and oxygen utilization of the coronary sinus drainage area. Blood pressure changes were produced by addition of blood to, or removal of blood from, the circulating blood volume. The highest two flow rates are the final observations, and the numbers indicate the order in which the oxygen utilization data were gained.

O\textsubscript{2} determination method was used for both the experimental and control determinations of each paired run.
by the coronary sinus was reduced below the control levels by institution of bypass (fig. 3). Coronary sinus blood oxygen saturation was higher on bypass than on control in 17 experiments, lower in four.

Striking effects of bypass on coronary flow and on \(O_2\) utilization were observed without significant pulse rate changes (table 2).

In one experiment, manipulation caused a septal tear sufficient to permit right-left shunt and a drop in arterial oxygen saturation on high rates of bypass flow. \(O_2\) utilization by the heart fell sharply here, but rose with the arterial \(O_2\) saturation when a lower rate of bypass pumping reduced the interatrial gradient and shunt (table 3). A similar, but unproved, shunt may have occurred in another experiment, in which arterial saturation of 83 per cent was noted (61 ml./Kg./min., fig. 3). In all other dogs (except one observation of 92 per cent in a control run), the arterial saturation was 94 per cent or above.*

Tracings made on high bypass show an aortic pressure curve with complete left ventricular pulse deficit, and reflecting only the pulsations from the pump. The left ventricular systolic pressure was only a fraction of the aortic, which was sustained by the pump (fig. 4) (104 ml./Kg./min., fig. 3). In all other dogs (except one observation of 92 per cent in a control run), the arterial saturation was 94 per cent or above.*

TABLE 1

<table>
<thead>
<tr>
<th>Time (min.)</th>
<th>Bypass (ml./Kg./min.)</th>
<th>Blood pressure (mm. Hg.)</th>
<th>Oxygen utilization (ml./min.)</th>
<th>Coronary sinus flow (ml./min.)</th>
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<td>0</td>
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<td>118</td>
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</tr>
<tr>
<td>137</td>
<td>15</td>
<td>106</td>
<td>112</td>
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</tr>
</tbody>
</table>

*Male shepherd dog, 26 Kg. Coronary sinus flow: mean of four or more determinations. This preparation was used thereafter for studies of effect of blood pressure without bypass shown in figure 1, and remained relatively stable throughout.

TABLE 2

<table>
<thead>
<tr>
<th>Bypass (ml./Kg./min.)</th>
<th>Pulse rate (ppm.)</th>
<th>Coronary sinus flow (ml./min.)</th>
<th>Mean blood pressure (mm. Hg.)</th>
<th>Arterial (O_2) saturation</th>
<th>Oxygen utilization (ml./min.)</th>
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<tr>
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<td>48.5</td>
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<td>57.0</td>
<td>115</td>
<td>94</td>
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</table>

*Blood, 100 ml., was removed on institution of bypass to maintain the blood pressure at the control level.
Graphic presentation of 21 determinations of oxygen utilization on left heart bypass. The adjacent control determination (without bypass) is indicated in solid black just to the left of the experimental value if it preceded it, just to the right if it followed it in time. The overlaid lower graph indicates arterial oxygen per cent saturation and also the arteriovenous difference in volumes per cent, for each experimental observation and for each control. Flow rates as such are not presented, but may be calculated.

With increasing bypass flow is demonstrable in the entire data by expressing each experimental determination of $O_2$ utilization as a fraction of the adjacent control, especially if one considers only the 17 observations without arterial desaturation (below 94 per cent) (fig. 5). The 9 runs with bypass below 61 ml./Kg./min. present a mean $O_2$ utilization of 82 per cent of the controls, and the difference of this mean from the controls is statistically significant ($P < 0.00001$). The 8 bypass determinations above 61 ml./Kg./min. present a mean $O_2$ utilization of 67 per cent of the controls. The mean $O_2$ utilization of the high bypass group is significantly less than that of the low bypass group ($P < 0.004$). The 5 determinations with highest bypass flows have a mean utilization significantly less than the next 5 or the next 8 observations, suggesting a somewhat greater $O_2$-sparing as nearly total bypass is achieved ($P < 0.001$). The mean of control values of $O_2$ utilization for high bypass runs was higher than that for the low bypass experiments. Controls immediately following periods of high bypass showed no elevation above controls just preceding (three of four runs). The difference between means of low flow controls and of high flow controls is, therefore, coincidental.

Probabilities of statistically significant differences calculated both by "chi-square" test and by calculation of relative deviates on the normal frequency curve.
In two dogs, the "time-tension index" (T.T.I.) of Sarnoff et al. was determined. The areas were measured under the left ventricular pressure tracing on paper moving 100 mm. per second. The T.T.I. showed no decrease on partial bypass until disappearance of the left ventricular component from the aortic pressure tracing (table 4). The slope of the steepest portion of the ascending limb of the systolic rise changed similarly with increase in bypass flow. Oxygen studies were not done on these dogs.

**Discussion**

The mechanism by which reduction in left ventricular work is accomplished by left heart bypass appears to be through reduction of left atrial pressure to such a level that left ventricular filling is reduced or eliminated (fig. 4). That left ventricular filling does not occur under full left heart bypass with the transseptal cannula in the absence of thoracotomy is demonstrated by angiocardiographic studies to be reported. Late in some experiments, there was difficulty in holding...
Effect of Left Heart Bypass on Time-Tension Index and on Slope of Ascending Limb of Left Ventricular Pressure Curve*

<table>
<thead>
<tr>
<th>Bypass flow (L/min.)</th>
<th>Pulse rate (per min.)</th>
<th>Stroke of left ventricular contraction (mm. Hg./0.01 sec)</th>
<th>Initial increase (mm. Hg/sec.)</th>
<th>Pulse deficit</th>
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</thead>
<tbody>
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</tr>
<tr>
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<td>140</td>
<td>5.5</td>
<td>9.2</td>
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</tr>
</tbody>
</table>

*Male shepherd dog, 19.5 Kg.

The blood pressure up during control periods, even with transfusion of 100 to 200 ml., so that withdrawal of blood was then necessary to maintain constancy of blood pressure when generous bypass was instituted. The blood pressure drop seen for a few seconds during termination of high bypass may be due to the loss in systemic blood volume incident to refilling of the pulmonary veins and left heart sufficiently to lead to effective left ventricular ejection into the aorta (fig. 4 lower). The rapidity of this response is a good index of the stability of the experimental preparation.15

The sensitivity of the O₂ utilization rate to multiple factors (air embolism, manipulation, time) led us to the employment of the pairing of experimental runs with adjacent controls which we have described. The possibility that air micro-emboli might be a factor in raising cardiac O₂ utilization confirmed our decision to use left bypass, and therefore no oxygenator, and to use a completely closed system, for this study.

As defined by Sarnoff et al.,20 "the time-tension index (T.T.I.) per beat in mm. Hg seconds was obtained from the area under the systolic portion of the aortic pressure curve and is equal to the mean systolic pressure times the duration of systole." They concluded that "in any given functional state of the beating heart, the T.T.I. (mean systolic pressure times duration of systole) is the principal, if not the sole, determinant of myocardial O₂ utilization." Their work was concerned with cardiac outputs of 1 L. per minute or more, whereas ours in considerable measure has involved bypass flows sufficient to reduce the calculated left ventricular minute output to less than 1 L. In some of our experiments, bypass flow was sufficient so that some or all left ventricular contractions failed to eject blood into the aorta, a situation in which Sarnoff's T.T.I. would be zero, but in which the oxygen utilization is more than half the control level. We have, therefore, calculated the T.T.I. from the area under the left ventricular pressure tracing, using the end-diastolic pressure as base line. Although full bypass produces comparable decreases in O₂ utilization and in T.T.I., our results show definite and consistent reductions in O₂ utilization at lower bypass flow rates not accompanied by drops in T.T.I. (cf. fig. 3, fig. 5, table 4).

The mechanism of decrease in O₂ utilization in the absence of decrease in T.T.I. is not
clear. Sarnoff et al. suggest that variations in $O_2$ utilization might arise from changes in the rate of development of systolic tension while holding the other hemodynamic factors constant. Measurements of the slope of the steepest part of the rising limb of the left ventricular tracing also failed to show correlation with oxygen utilization, as it did not drop with increasing bypass until the left ventricular component partially or wholly disappeared from the aortic pressure curve (full bypass), while $O_2$ utilization decreased with less than 25 per cent bypass (table 4).

We have not measured mean diastolic left ventricular volume during left heart bypass. It is possible that institution of bypass may diminish this value and, therefore, fiber length and thus favor a decrease in $O_2$ utilization, as Sarnoff suggests.

In spite of the conclusions of others that bypass less than the full cardiac output does not reduce $O_2$ utilization by the heart, our use of left bypass without the complications of an oxygenator, the precision of our control of variables such as respiration, blood volume, blood pressure, venous pressure, temperature, and manipulation, the elimination of gaseous micro-embolism, and the statistical significance of our findings, lead us to the belief our conclusions are valid.

We have measured total coronary sinus flow only. It is suspected that the reductions in $O_2$ utilization, here reported, might be more striking if one could measure blood drained from the left ventricular muscle only, without admixture of blood which has perfused the right ventricle, which is reported to use approximately as much $O_2$ as the working left ventricle. It is possible, on the other hand, that the proportion of total coronary flow drained by the coronary sinus varies with institution of left bypass, and this is a possibility we have not yet studied.

We are proposing to use left heart bypass without thoracotomy by means of atrial septal puncture for such catastrophes as major coronary arterial occlusion, or severe mitral disease or aortic stenosis which cannot be handled more conservatively with success.

The method has been used for 24-hour runs with survival of 9 of 10 dogs. The results here reported indicate a reduction in oxygen need on left bypass with an increase in oxygen tension in the myocardium (as reflected by that in the blood from the coronary sinus), a drop in left atrial and pulmonary vein pressure (anticipating relief of pulmonary edema), while maintaining a sound arterial blood pressure to assure good perfusion of the still patent coronary arterial tree. Whether a few hours of support might permit enough muscular recovery for patient survival without definite surgical procedure, as past experience suggests, or whether left bypass be used a few hours as preparation for definitive operation, as we have once so far employed it clinically, is a question which must await further experience for resolution.

**Summary**

Full left heart bypass reduces the oxygen utilization of the heart to about half the control levels, as measured by coronary sinus flow and arteriovenous oxygen differences. All measured lesser degrees of bypass reduce the oxygen utilization less markedly, but with high statistical significance of the reductions below controls. The reduction in oxygen utilization upon institution of partial or complete left bypass is usually the result more of a decrease in arteriovenous oxygen difference than of a decrease in coronary sinus blood flow. These results support the thesis that left heart bypass should be beneficial in reducing the internal work of the left ventricle in acute left heart failure with competent aortic valve.

**Acknowledgment**

The authors wish to express their thanks to Dr. William Dock, Professor of Medicine, State University of New York Downstate Medical Center, for his many valuable suggestions in the preparation of this manuscript.

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Reduction of the Utilization of the Heart by Left Heart Bypass
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Circ Res. 1962;10:298-305
doi: 10.1161/01.RES.10.3.298

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