Acute Effects of Elevation of Coronary Sinus Pressure

By Richard W. Eckstein, M.D., J. Carl Hornberger, M.D., and Toyomi Sano, M.D.

The acute physiologic effects of the aorta to coronary sinus anastomosis of Beck have been studied. The evidence presented shows that arterialization of the coronary sinus results in a small retrograde flow from the sinus through capillaries into the occluded artery and that such retrograde flow supplies from 14 to 25 per cent of the normal myocardial oxygen requirement. It is suggested that this is insufficient to maintain normal myocardial contraction, but probably prevents ventricular fibrillation. However, when the sinus is arterialized in the presence of normal or reduced coronary flow electrocardiographic and coronary inflow data show that there is myocardial anoxia. This is probably due to the restriction in capillary outflow and results in an expansion of the coronary vascular bed.

This is a continuation of previous studies1-2 undertaken to investigate the acute and chronic effects of the operation developed by Beck and his associates3-7 to produce an anastomosis between the aorta and the coronary sinus with subsequent partial sinus ligation. The aim of the procedure is to revascularize the human heart in occlusive coronary artery disease. An examination of the evidence presented by our own acute experiments along with that concerning the chronic dogs of Beck7 leaves no doubt that elevation of coronary sinus pressure favorably modifies the generally fatal effects of the acute occlusion of a major coronary artery in the dog. Gross,8 Robertson8 and Ungerleider9 had previously shown that partial or complete sinus ligation or sinus pressure elevation resulted in a reduction in the size and number of infarcts and in the mortality following coronary artery occlusion. Roberts10 was able to maintain dogs for 26 hours after coronary occlusion by connecting an artery to the coronary sinus with a glass cannula. The work of others has been less optimistic.

Gregg and his associates17, 18, 19 studied this problem in detail and showed that elevation of sinus pressure augmented peripheral coronary pressure and retrograde flow, which changed from the normal arterial blood to venous blood containing only about 3 volumes per 100 cc. of oxygen. They were unable to demonstrate that sinus pressure elevation preserved myocardial contraction distal to a ligated artery even when arterial blood was forced into the sinus, and therefore, concluded that the acute procedure failed to benefit the coronary circulation. Likewise Shipley16 in acute experiments with the coronary sinus perfused by an artery was unable to demonstrate aid to the cardiodynamics following blockage of left coronary inflow.

Notwithstanding these pessimistic findings the reinvestigation of this problem is justified by the observations1, 2 that sinus pressure elevation serves to prevent the usual ventricular fibrillation following acute coronary occlusion. The explanation of acute benefit derived from sinus pressure elevation following coronary artery occlusion on the basis of improved myocardial oxygenation due to retrograde capillary flow requires certain evidence. First, it necessitates the demonstration that the anatomic connections between capillaries and veins actually allow retrograde flow. Such reversed flow may be impossible due to the effective action of venous valves or to

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peculiarities in the anatomic arrangement of capillaries and veins which results in blockage with venous pressure elevation. Second, there must be channels to serve as adequate drainage from the occluded artery. The observations of Wearn\(^{16}\) show that such an artery is not a dead end system, but does have potential drainage channels in the form of arterioluminal and arteriosinusoidal vessels. Evidence that these channels are functional is lacking. In addition there are large posterior veins opening into the ostium of the sinus or right auricle which do not share in sinus pressure elevation. Retrograde blood into the circumflex artery might escape into these veins through a second set of capillaries. Likewise the anterior cardiac veins may serve to drain the anterior descendens artery in a similar manner.\(^{17, 18, 19}\) Third, a suitable pressure differential between the coronary sinus and the artery must be present. Such is not the case in the normal dog whose coronary arteries are supplied from the aorta. However, after coronary artery occlusion an effective pressure differential is possible prior to the development of collateral vessels provided there is an escape route from the artery and the sinus pressure can be maintained at suitable levels. Fourth, in order for retrograde flow to benefit the myocardium it must be shown that such blood flows in sufficient quantities and gives up its oxygen during its capillary passage. That reversed flow of blood is accompanied by oxygen exchange has been shown by Heimbecker\(^{20}\) in the case of the gut, but has not been demonstrated in the heart.

In an effort to answer these and other questions these studies have been concerned with the influence of the elevation of coronary sinus pressure on normal coronary inflow, amount and nature of backflow, peripheral coronary pressure, electrocardiograms, coronary sinus pressure, cardiac output and in the microscopic appearance of the myocardium and coronary vessels. Due to the magnitude of the data and the fact that the findings in the acute experiments differ widely from the findings in the chronic dogs prepared by Beck, the observations are being reported separately. This then is a study limited to the acute effects of elevation of coronary sinus pressure.

**Methods**

Mongrel dogs were anesthetized with morphone and pentobarbital. Respiration was maintained by intermittent positive pressure applied through a tight fitting rubber tube placed within the trachea. The left jugular vein was exposed and a glass cannula passed to the level of the right auricle. This served to administer intravenous fluids and to return coronary sinus blood to the animal. A long metal cannula was passed through the right common carotid artery to the aorta for optical registration of aortic blood pressure and in some cases to perfuse either the descendens or the circumflex coronary artery. The left chest was entered between the fourth and fifth ribs which were widely spread. A ligature was passed about the coronary sinus near its origin and was tied about the tip of a cannula introduced through the tip of the right auricle. This cannula had either a double lumen as previously described,\(^{1}\) or had only a single lumen with a side arm for connection to the cannulated subclavian artery. In some instances an attempt was made to partially isolate the major venous drainage of the anterior descendens and circumflex arteries. In these cases a plastic tube was passed through the single lumen coronary sinus cannula. This tube was fixed in the great cardiac vein by means of a ligature. The blood from the great cardiac vein was led into the left jugular cannula. Arrangements were made so that pressure could be raised in either or both the great vein and the coronary sinus by clamping and/or perfusion from the subclavian artery. Usually the circumflex artery was cannulated and perfused through a Shipley recording rotameter\(^{21}\) to indicate the amount as well as the changes in inflow. In a few experiments the anterior descendens artery or the total left coronary artery was used. In the latter instance the special coronary cannula\(^{22}\) was employed. In certain experiments to study the mechanisms of coronary inflow changes, the constant perfusion pressure chamber\(^{22}\) was used. Optical recordings were made of coronary perfusion pressures, and coronary sinus pressure. The animals were given 150 to 200 mg. of heparin to prevent fibrin formation in the rotameter. Electrocardiograms were recorded usually from lead aV\(_R\).

Arrangements were made for measurements of peripheral coronary pressures distal to the point of clamping as well as the amounts of backflows at atmospheric pressure. In many instances the oxygen content of the back flowing blood was determined by the method of Neill and Van Slyke.\(^{23}\)

Finally, a series of experiments were performed to study changes in left ventricular output. The thoracic aorta was cut and the blood diverted through a large Shipley\(^{23}\) recording rotameter with the brachiocephalic and subclavian arteries supplied from the outflow side as described previously.\(^{24}\)
RESULTS

A. Effects of Sinus Pressure Elevation on the Source, Amount and Nature of Backflow

Figure 1 shows the salient anatomic arrangement of the coronary circulation. It also indicates the ligated circumflex artery which has been cannulated peripheral to the ligature. When the coronary cannula is open to atmospheric pressure, it has been shown that from 0.5 to 5.8 cc. of arterial blood flow from the peripheral artery. This backflow largely originates in nonocluded coronary arteries and reaches the cannulated artery through small normally present interarterial collaterals. In these present experiments the backflows from the circumflex artery ranged from 0.8 to 7.6 cc. with an average of 2.8 cc. When sinus pressure is elevated by partial or complete occlusion or by the connection of the sinus to a systemic artery the backflow increases and becomes venous in character. Table 1A shows that as the pressure in the arterialized sinus is increased from a mean pressure of 30 mm. Hg to 90 mm. Hg the backflow increases from 6 to 11.6 cc. per minute and the oxygen content decreases.

Although this is substantial evidence that elevation of sinus pressure produces a true reversed capillary flow which originates in the sinus, Gregg noted that the increased backflow following sinus occlusion could largely be abolished from the descendens simply by clamping the circumflex artery. However, he makes no reference to possible changes in sinus pressure.) It was found in these experiments that sinus pressure previously elevated by complete sinus occlusion dropped considerably when the second major branch of the left coronary artery was clamped. This is understandable, since clamping of the total left coronary largely removes the last remaining source of sinus blood. However, no drop in sinus pressure occurs when the sinus is perfused by a systemic artery. Table 1B shows the results of such an experiment. Clamping of the anterior descendens artery in the presence of the arterialized sinus results in a decrease in backflow from 12.4 to 8.8 cc. per minute due to removal of the normal interarterial backflow. This results in no change in sinus pressure. However, clamping of anterior descendens artery in the presence of sinus occlusion without arterialization, reduces the backflow from 11.6 to 3.2 cc. per minute and is accompanied by a considerable reduction in sinus pressure. These and the results of similar experiments (see table 2B, experiment 115) support the conclusion that the coronary sinus is the immediate source of the increase in backflow which occurs when coronary sinus pressure is elevated.

The final two observations in table 1C show averages of eight experiments with the coronary sinus occluded to produce a mean sinus pressure of 50 mm. Hg and averages of eight experiments in which the coronary sinus was arterialized to produce a mean sinus pressure of 50 mm. Hg. Although both groups had equal mean sinus pressures, the backflow in the arterialized group is substantially higher. Examination of the optically recorded actual sinus pressures provides the reason since arterialization of the sinus results in a sinus diastolic pressure of 28 mm. of mercury as compared with 16 mm. of mercury found in the
### Table 1.—Pressure Relationships Affecting Retrograde Flow

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Condition of Sinus</th>
<th>Anterior Descending Artery</th>
<th>Pressures mm. Hg</th>
<th>Backflow at Occluded Circumflex Artery cc./min.</th>
<th>Oxygen from Occluded Circumflex Artery Vol. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-111</td>
<td>Arterialized at 30 mm. Hg</td>
<td>Normal</td>
<td>112/96</td>
<td>30/?</td>
<td>40/23</td>
</tr>
<tr>
<td></td>
<td>Arterialized at 50 mm. Hg</td>
<td>Normal</td>
<td>100/80</td>
<td>38/?</td>
<td>70/36</td>
</tr>
<tr>
<td></td>
<td>Arterialized at 85-90 mm. Hg</td>
<td>Normal</td>
<td>99/79</td>
<td>46/22</td>
<td>100/52</td>
</tr>
</tbody>
</table>

**A. Effect of Arterialization at Various Pressures**

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Arterialized at 50 mm. Hg</th>
<th>Normal</th>
<th>122/90</th>
<th>50/18</th>
<th>68/40</th>
<th>12.4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arterialized at 50 mm. Hg</td>
<td>Ocluded</td>
<td>130/82</td>
<td>45/15</td>
<td>70/43</td>
<td>8.8</td>
</tr>
<tr>
<td></td>
<td>Occluded at 50 mm. Hg</td>
<td>Normal</td>
<td>122/88</td>
<td>40/14</td>
<td>83/14</td>
<td>11.6</td>
</tr>
<tr>
<td></td>
<td>Occluded at 50 mm. Hg</td>
<td>Ocluded</td>
<td>133/98</td>
<td>30/8</td>
<td>50/22</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>112/72</td>
<td>25/10</td>
<td>12/3</td>
<td>6.0</td>
</tr>
</tbody>
</table>

**B. Effect on Anterior Descendens Artery with Arterialized and Occluded Sinus**

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Arterialized (Ave. of 8)</th>
<th>Normal</th>
<th>125/97</th>
<th>35/13</th>
<th>72/16</th>
<th>5.9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arterialized (Ave. of 8)</td>
<td>Normal</td>
<td>119/84</td>
<td>47/17</td>
<td>68/28</td>
<td>9.2</td>
</tr>
</tbody>
</table>

**C. Comparison of Arterialized and Occluded Sinus**

<table>
<thead>
<tr>
<th>Condition of Sinus</th>
<th>Normal</th>
<th>Arterialized</th>
<th>Occluded</th>
<th>Normal</th>
<th>Arterialized</th>
<th>Occluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-115</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Arterialized</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Arterialized</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Arterialized</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

### Table 2.—Studies of the Source of Retrograde Flow

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Conditions of Sinus</th>
<th>Anterior Descending Artery</th>
<th>Pressures mm. Hg</th>
<th>Backflow at Occluded Circumflex Artery cc./min.</th>
<th>Oxygen Vol. % from Occluded Circumflex Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-115</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>93/66</td>
<td>37/15</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>ArterIALIZED</td>
<td>Normal</td>
<td>92/60</td>
<td>35/13</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>90/58</td>
<td>46/18</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>ArterIALIZED</td>
<td>Normal</td>
<td>95/62</td>
<td>46/19</td>
</tr>
</tbody>
</table>

**A. Effects of Arterialization of Sinus and/or Great Cardiac Vein**

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Normal</th>
<th>Arterialized</th>
<th>Normal</th>
<th>80/56</th>
<th>32/14</th>
<th>18/0</th>
<th>18/0</th>
<th>7.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Arterialized</td>
<td>Normal</td>
<td>69/44</td>
<td>45/20</td>
<td>70/44</td>
<td>70/44</td>
<td>18.8</td>
</tr>
<tr>
<td></td>
<td>Arterialized</td>
<td>Normal</td>
<td>Normal</td>
<td>67/49</td>
<td>37/18</td>
<td>70/53</td>
<td>70/53</td>
<td>9.0</td>
</tr>
</tbody>
</table>

**B. Effects of Arterialization of Sinus and Great Vein and Descendens Occlusion**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>R-120</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>1.2</td>
</tr>
</tbody>
</table>

**C. Retrograde Circulation Time with Amount and Oxygen Content of Retrograde Flow**

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Normal</th>
<th>Arterialized</th>
<th>Normal</th>
<th>Peripheral anterior descendens bleeding to air.</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-126</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Ant. descend. 0.8 Ant. descend. 10 Great vein 2.3</td>
</tr>
</tbody>
</table>
sinus occlusion group. (See also fig. 2 B and C.) Since cardiac diastole provides optimum conditions for intramural flow the interpretation of these results becomes obvious.

Although no mention has been made of the changes in peripheral circumflex pressure it can be stated in general, as shown in table 1 and figure 2 that these pressures follow the direction of the changes in backflows and sinus pressures under the conditions of these experiments, namely, following brief periods of circumflex occlusion and sinus pressure elevation. Peripheral coronary pressure is always elevated by elevation of sinus pressure and in these acute experiments is always less than coronary sinus pressures. However, in the case of the normal sinus, the peripheral coronary pressure exceeds the sinus pressure.

B. Results of Attempts to Isolate Venous Drainage of the Circumflex Artery

In these experiments the great cardiac vein was drained separately through the long plastic cannula as shown in figure 1. The drainage from the circumflex artery in some instances was reasonably well isolated from that from the anterior descendens artery. Such a situation served two purposes: (1) It permitted more definite information as to the source of coronary backflow with coronary venous pressure elevation. (2) It provided conclusive evidence as to the pathways concerned in the retrograde flow.

Table 2 shows the results of typical experiments. In A it can be seen that arterIALIZATION of the great cardiac vein raised the backflow from 7.6 to but 8.0 cc. per minute, that arterIALIZATION of the coronary sinus augmented the backflow to 14.0 cc. per minute while arterIALIZATION of both sinus and great vein resulted in an addition of only 2 cc. per minute to the backflow. Table 2B shows that elevation of pressure in both the great cardiac vein and the coronary sinus increased the backflow from 7.2 to 18.8 cc. per minute, and clamping of the anterior descendens artery reduced the backflow to 9 cc. per minute, which is expected since anterior descendens clamping removes about 7.2 cc. per minute, which is the normal interarterial collateral flow. These experiments are further evidence that the source of the increased backflow is the venous system which drains the artery in question.

In table 2C nearly complete isolation of the circumflex artery and its venous drainage was attained since clamping of the circumflex artery reduced the flow from the sinus cannula to only 3.6 cc. per minute. In this experiment blood containing P³² and 14.7 volumes of oxygen per 100 cc. of blood which was introduced into the sinus was identified with a Geiger counter and recovered from the circumflex artery within 13 seconds. The fact that the blood was reduced to contain but 3.2 volumes of oxygen per 100 cc. is proof of its capillary passage and provides equally substantial evidence that blood flowing in a retrograde fashion through myocardial capillaries does give up its oxygen. The final experiment in table 2D provides similar evidence in the case of the anterior descendens artery.

C. The Question of Retrograde Flow When Backflow to Atmospheric Pressure Is Prevented

The fact that sinus pressure elevation produces reversed capillary flow with the peripheral artery bleeding does not prove that such retrograde flow will occur when the artery is clamped and not allowed to bleed. Although it has been pointed out that drainage channels from the occluded artery are present their functional capacity must be shown. There are three reasons for believing that true reversed capillary flow occurs when backflow is prevented.

1. When the circumflex artery and its venous system are isolated as above, the artery and accompanying vein retain their original color relations as long as the peripheral arterial pressure exceeds the arterialized venous pressure. At roughly identical pressures the artery remains red and the vein becomes red. When the arterial perfusion pressure is further reduced to lower peripheral artery pressure the artery changes color and appears like a vein. Such a situation exists also when the artery is completely clamped from its perfusion source. The same color relationship holds when backflows are being measured. In other words,
the veins serve as arteries, and the arteries as veins.

2. Studies of peripheral pressures show that elevation of sinus pressure produces increases of peripheral coronary pressure which acutely never attain the systolic or diastolic pressure levels of the sinus. (See tables 1 and 2.) If the measurements of the actual retrograde flow is thus far impossible. However, certain estimations have been made by four different methods.

1. The first method is based upon calculated flows due to pressure differences between the sinus and the peripheral coronary artery.

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Normal Backflow</th>
<th>Backflow with Sinus Arterialization cc./min.</th>
<th>Total Backflow Minus Normal Backflow cc./min.</th>
<th>Coronary Sinus Pressure mm. Hg</th>
<th>Circumflex Artery Pressure mm. Hg</th>
<th>Retrograde Flow into Ligated Vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>111 to 119</td>
<td>3.4</td>
<td>8.1</td>
<td>4.7</td>
<td>50</td>
<td>37/15</td>
<td></td>
</tr>
<tr>
<td>120 to 125</td>
<td>2.2</td>
<td>6.7</td>
<td>5.6</td>
<td>50</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>1.2</td>
<td>6.8</td>
<td>5.6</td>
<td>50</td>
<td>20</td>
<td>3.4</td>
</tr>
<tr>
<td>121</td>
<td>0.8</td>
<td>5.6</td>
<td>4.8</td>
<td>45</td>
<td>21</td>
<td>3.7</td>
</tr>
<tr>
<td>122</td>
<td>5.0</td>
<td>7.2</td>
<td>2.2</td>
<td>50</td>
<td>15</td>
<td>3.2</td>
</tr>
<tr>
<td>124</td>
<td>1.6</td>
<td>3.6</td>
<td>2.0</td>
<td>50</td>
<td>15</td>
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<td>125</td>
<td>2.8</td>
<td>10.4</td>
<td>7.6</td>
<td>50</td>
<td>15</td>
<td>4.2</td>
</tr>
</tbody>
</table>

B. Same for Anterior Descendens Artery

<table>
<thead>
<tr>
<th></th>
<th>Normal Backflow</th>
<th>Backflow with Sinus Arterialization cc./min.</th>
<th>Total Backflow Minus Normal Backflow cc./min.</th>
<th>Coronary Sinus Pressure mm. Hg</th>
<th>Circumflex Artery Pressure mm. Hg</th>
<th>Retrograde Flow into Ligated Vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>126</td>
<td>0.8</td>
<td>10.0</td>
<td>9.2</td>
<td>50</td>
<td>28</td>
<td>4.1</td>
</tr>
<tr>
<td>128</td>
<td>3.6</td>
<td>6.6</td>
<td>3.0</td>
<td>50</td>
<td>24</td>
<td>1.5</td>
</tr>
</tbody>
</table>

artery were a dead end system, both the sinus and peripheral coronary pressures should be equal. In order to test whether the elevation in peripheral coronary pressure resulting from sinus pressure elevation is due merely to a blocking of the escape of the normal interarterial flow the following experiment was done. Normal interarterial backflow was measured. The sinus pressure was elevated and blood withdrawn from the peripheral artery in amounts which exceeded the normal interarterial backflow. Although this reduced peripheral coronary artery pressure (P.C.P.) somewhat it remained above the normal level. It is felt, therefore, that the major increase in peripheral coronary artery pressure is due to true retrograde flow.

D. Quantitative Estimation of Retrograde Flow into the Occluded Artery

Although the above observations and a prior reasoning indicate that retrograde flow does occur into the occluded artery, direct These calculations are expressed by the formula

\[ R.F. = B.F. \times \frac{S.P. - P.C.P.}{S.P.} \]

where \( R. F. \) = retrograde flow into the occluded artery.

\( B.F. \) = total backflow minus normal interarterial backflow from the open peripheral artery.

\( S. P. \) = mean sinus pressure.

\( P. C. P. \) = mean peripheral coronary pressure with elevation of sinus pressures.

These values are listed in table 3 under the column “Calculation Method”.

2. The second method is based on the premise that at equal mean sinus and arterial pressure there is no capillary flow between the veins and artery. The values were obtained in this way. The mean coronary sinus pressure was elevated (usually to 50 mm. Hg) and the resulting peripheral coronary pressure was measured. Then both the sinus and coronary
artery were perfused at the previously measured peripheral coronary pressure. The amount of blood flowing into the artery under these circumstances was measured. The normal interarterial backflow was subtracted from the metered arterial inflow. The results are shown in table 3 (Arterial Inflow Method).

3. This is a reverse of method 2. A rotameter was placed between the subclavian artery and the coronary sinus so as to meter sinus inflow in the venous isolation preparation. The circumflex artery was perfused from the aorta. Mean sinus and peripheral circumflex pressures were set at identical levels of 50 mm. Hg. Sinus inflow was noted. The artery was clamped and mean sinus pressure was maintained at 50 mm. Hg. The increase in sinus inflow was measured and listed in table 3 (Sinus Flow Method).

4. It was noted in the venous isolation preparations that with the sinus pressure elevated and sinus inflow being measured with the peripheral artery bleeding, sinus inflow always decreased when the peripheral coronary artery was closed, that is, when backbleeding was prevented. It, therefore, appeared reasonable that if the decrease in sinus inflow were subtracted from the backflow contributed by the sinus (that is, total backflow minus normal interarterial backflow) the result should be true retrograde flow. These results are listed in table 3 (Backflow Minus Sinus Inflow).

A study of these calculated and measured flows reveal that there is wide variation and even some impossibilities since in experiments R 120 and R 124 some values exceed the amount contributed by the sinus even when operating against atmospheric pressure. However, the accurate measurement of such low flows with a rotameter is difficult. Of more importance, however, is the fact that by all methods there is evidence of retrograde flow into an occluded vessel. Since these flows can never exceed the amounts shown in the fourth column, table 3, the conclusion that their magnitude is indeed small is inevitable.

E. Drainage Pathways from Occluded Arteries

Although the previous studies indicate a small retrograde capillary flow based on indirect measurements, certain direct metered values have been obtained. The role of the large posterior veins emptying directly into the right auricle and not sharing in elevation of venous pressure have been investigated. A
second cannula was placed in the circumflex artery and directed peripherally at X in figure 1. In some cases a rotameter was connected between the two cannulas. In other cases a calibrated inverted glass U tube was used. The ascending limb of this tube was filled with saline to give a sharp blood-saline junction. Clamping of the artery between the two cannulas usually resulted in no flow in either direction in the presence of normal sinus pressure. However, elevation of sinus pressure gives a prompt flow of from 1.6 to 7 cc. per minute of highly unsaturated blood passing from the central to the peripheral circumflex artery. Flow is first detected at sinus pressures of approximately 30 mm. Hg and steadily increases with the creation of higher sinus pressures. Measurement of the pressures in the central and distal branches reveals adequate pressure differences to explain the direction of flow. For example, in experiment R 181 (not shown) a mean sinus pressure of 60 mm. Hg produced a forward circumflex flow of 1.6 cc. per minute with a total peripheral circumflex pressure of 30 mm. Hg. Mean central circumflex pressure was 38 mm of mercury in contrast to 24 mm. of mercury found in the distal segment. In the same experiment the normal backflow from the central segment was only 0.6 cc. per minute which increased to 3.6 cc. per minute at a sinus pressure of 60 mm. Hg. Backflows from the distal segment were 1.2 and 3.8 cc., respectively. Subtraction of the normal backflow of 0.6 cc. from the metered forward flow of 1.6 cc. leaves a retrograde flow of at least 1 cc. arising from the central circumflex artery. This is indeed small when compared with the normal inflow of 9 cc. per minute in this branch. However, the fact that the central circumflex pressure was but 38 mm. Hg in the face of a sinus pressure of 60 probably indicates other small routes of exit in addition to the distal circumflex artery. That such extra drainage was also venous is likely since venous anastomoses were visible at the apex. Furthermore, at the conclusion of this experiment fluid injected into the central branch of the circumflex flowed both from sinus and posterior veins. In experiment R 180, figure 2, in which the central circumflex branch was very large there was a normal backflow of 1.4 cc. per minute from the central branch which increased to 12.4 cc. per minute with the sinus pressurized at 70 mm. Hg. The flow from central to distal circumflex was approximately 6 cc. per minute while the total circumflex pressure was 35 mm. Hg. When this flow was prevented the pressure in the central branch reached 60 mm. Hg which again probably indicates small additional escape routes.

These experiments are of interest from two standpoints. In the first place the metered flows check closely with the calculated retrograde flows based on differences between the sinus and peripheral coronary pressures. Of more interest, however, are the measurements of the amount and direction of retrograde flows which indicate the importance of the non-pressurized veins.

A consideration of the myocardial area supplied by the entire left coronary serves to demonstrate the magnitude of these accessory veins. It has been clearly shown by Gregg that they are sufficient to drain the left coronary flow which does not appear in the sinus. It has been observed in these experiments that normal left coronary inflow can by no means be abolished even though coronary sinus pressure exceeds coronary perfusion pressure. Such a situation requires a considerable drainage system in addition to the sinus. That the large posterior nonpressurized veins serves in that capacity was shown by its direct cannulation. For example, in experiment R 179 (not shown) there was a flow from the cannulated posterior vein of 8 cc. per minute which decreased to 5.2 cc. per minute when the circumflex artery was occluded. Elevation of sinus pressure augmented the flow to 15.2 cc. per minute. Release of the circumflex artery resulted in a venous outflow of 16.4 cc. per minute. However, even though the peripheral circumflex was allowed to bleed, thereby removing all retrograde and collateral flow, sinus pressure elevation resulted in a flow of 14.8 cc. per minute from the vein. This experiment demonstrates not only the importance of this vein for circumflex drainage, but also shows that a considerable amount of blood introduced into the sinus may escape without passing through capillaries.
Measurement of sinus inflow therefore cannot critically demonstrate retrograde capillary flow.

Finally, when dilute India ink was injected into the sinus it was found that the injected area comprised but from 62 to 82 per cent of the area supplied by the left coronary. The noninjected area included the anterior left border of the right ventricle, an area along the posterior veins and the entire interventricular septum. It is, therefore, believed that these areas contain sizeable accessory veins or possibly thebesian veins in the case of the septum.

**F. Studies upon the Degree of Persistence of Backflow**

These experiments were done as before except that when the preparation had been completed the sinus was arterialized and at 15 minute intervals the peripheral pressure and the backflow were measured. As shown in table 4, experiment 176, the favorable pressure gradient between coronary veins and peripheral artery, even when allowed to operate over considerable time, failed to induce vascular expansion with increased retrograde flow. Instead the backflows decreased and the peripheral coronary pressure increased slightly to reduce the effective pressure gradient. During these experiments the areas of the heart drained by the pressurized veins became firm to the touch and filled with gross hemorrhage. Similar results were obtained when the artery was permanently clamped or when perfused from the aorta. Evidences of hemorrhage appeared early while the right ventricle and interventricular septum remained normal. Hemorrhage was first seen as small areas in the perivascular fat which enlarged and multiplied to include the entire area. Microscopic examination showed the hemorrhage to be extravascular and to be more pronounced in the subepicardial regions. Also, valves were regularly found even in small veins. It is suggested that the flow and pressure changes are the result of extravascular compression from hemorrhage and possibly edema which not only limits the vascular bed concerned with backflow, but also, with arterial drainage. There is a possibility that the hemorrhage has its origin in the rupture of the attachment of the venous valves.

**G. The Effect of Sinus Pressure Elevation on Left Ventricular Output**

These studies were done by methods previously described and can be divided into two groups. In the first group sinus pressure was elevated by partial or complete sinus occlusion so as to escape the effects of an arteriovenous fistula. Figure 3A and B, shows a typical experiment. There is a slow but definite decrease in left ventricular output of 180 cc. per minute. This exceeds the reduction in total venous return due to sinus occlusion. Figure 3C shows that sinus arterIALIZATION in the presence of complete sinus occlusion likewise results in a decreased output. Eight observations in four experiments reveal an average reduction in output of 207 cc. per minute. It is believed this observed fall in output is of cardiac origin.

In the second group the sinus was open or partially occluded and was arterialized so as to produce an arteriovenous fistula. As indicated in figure 3D, the sudden elevation of sinus pressure results in a prompt rise in ventricular output from 920 to 1150 cc. per minute. In
five measurements on four dogs there was an average increase in output of 194 cc. per minute. In each case, however, as the sinus was progressively occluded so as to elevate sinus pressure, there was a reduction in output as described above and shown in figure 3C.
H. Effects of Elevation of Sinus Pressure on Normal Coronary Artery Inflow

Since elevation of sinus pressure by sinus occlusion or by partial occlusion and arterialization is frequently accompanied by changes in aortic pressure, it is necessary to measure coronary flow under constant perfusion pressure in order to critically evaluate the true mechanism of flow changes. Such flow measurements were made in both the circumflex and common left coronary arteries. Figure 4A, B, C, and D, shows a typical result in the latter with arterialization of the sinus. This record shows a decrease in flow with sinus pressure elevation with recovery to near normal within a few minutes. Upon sudden release of sinus pressure the coronary flow quickly increases to even above normal and then more slowly returns to the normal. It is noteworthy that this sudden increase in flow with subsequent return to normal is identical with the coronary artery response to any temporary slight restriction of coronary flow (fig. 4E, F, and G). This response is due to an expansion of the coronary vascular bed as a result of some degree of myocardial ischemia.

I. Electrocardiographic Effects of Elevation of Sinus Pressure

These effects which have been recorded in lead aVR may be divided into three groups.

1. The first group consists of the effects of elevation of sinus pressure in the presence of normal coronary artery flow. These changes have been previously described and consist merely of slight to moderate flattening of the T wave with or without minor S-T segment depression. (See fig. 5, top.)

2. This second group consists of the changes produced by elevation of sinus pressure when coronary inflow is restricted. Figure 5, middle, shows that restriction of coronary inflow to reduce the mean peripheral coronary pressure to 50 mm. Hg produces no electrocardiographic...
change. However, the elevation of mean coronary sinus pressure to 50 mm. Hg results in marked S-T segment depression and T-wave inversion. The electrocardiogram returns to normal when the sinus pressure is reduced to its normal level. Many similar experiments indicate that even more severe changes occur with further reductions in peripheral coronary pressure.

3. This group consisted of studies as to the electrocardiographic effects of sinus pressure elevation after complete occlusion of a coronary artery. Figure 5, bottom, shows the typical results. The record displays the usual features produced by circumflex occlusion. Elevation of coronary sinus pressure produces unquestionable evidence of improved oxygenation of the myocardium.

On the basis of these electrocardiographic studies it is apparent that acute elevation of sinus pressure is not only ineffective, but is actually anoxating* to the myocardium in all cases except in the presence of complete coronary occlusion or drastic reduction in coronary flow.

J. Myocardial Oxygen Consumption

Although arterialization of the sinus results in retrograde capillary flow the real benefit to the myocardium must depend upon the amount of oxygen consumed by the heart. Accordingly, experiments were done to measure retrograde flow from the total left coronary with arteriovenous oxygen differences between the arterial blood entering the sinus and the venous blood escaping from the artery. The retrograde flow when back bleeding was prevented was calculated as in method 1 above. The weight of myocardium supplied by the left coronary was considered to be 85 per cent of the total heart weight. In three experiments the oxygen consumptions resulting from arterialization of the sinus were 14, 24 and 25 per cent of the normal, respectively. Declining aortic pressure and cardiac dilatation during the brief periods required for collection of data showed the complete cardiac intolerance to such drastic reductions in blood supply to such a large myocardial area.

DISCUSSION

The results of these experiments serve to clarify several unanswered questions. The demonstration of a small retrograde flow with elevation of sinus pressure in the presence of complete arterial occlusion probably provides the explanation of the modification of the mortality following acute arterial occlusion previously reported.1-2 It is believed that although this small flow is insufficient to maintain myocardial contraction it does prevent ventricular fibrillation. Although elevation of sinus pressure increased both backflow and peripheral coronary pressure when the entire left coronary was occluded, this has never been sufficient to maintain left ventricular contraction since rapidly falling aortic pressure required the admission of blood into the left coronary artery within about one minute. The fact that retrograde flow increases with augmentation of sinus pressure and is particularly related to sinus diastolic pressure supplies the explanation to the superior benefit provided by arterialization of the sinus in contrast to the benefit resulting from complete or partial sinus occlusion. The continuous perfusion of the sinus from an artery simply provides the sinus with a higher diastolic pressure which is more favorable for retrograde flow. In accord with the findings of Heimbeker39 on the mesentery, these experiments demonstrate that blood passing in a retrograde manner through myocardial capillaries also gives up its oxygen to the myocardium.

The question of possible benefit to the septum from elevation of sinus pressure has been investigated by injection studies. The injection of dilute India ink into the coronary sinus is well distributed throughout the entire left ventricle. In no case, however, has the central septal area showed any injection. In an effort to test further whether the septal drainage was via the coronary sinus, the septal artery was injected. In each case the central portion of the septum was injected and the injection material never appeared in the coronary sinus. It is reasoned, therefore, that in the dog the

* The word 'anoxating' is used loosely to express the effects of a reduction in the blood supply to the myocardium.
septum could not possibly be retroperfused from the coronary sinus.

It is believed that elevation of the sinus pressure in the presence of normal coronary inflow renders the myocardium mildly anoxic. This view is supported by these observations: that coronary flow is restricted, that aortic output is reduced, that the electrocardiogram reveals a mild ischemic pattern and that there is an expansion of the coronary bed. The increase in coronary flow to above normal which occurs with reduction in sinus pressure immediately following prior elevation is by far the more sensitive indicator of myocardial anoxia or ischemia. The mechanism of such ischemia is theoretic, but is probably a result of a reduction in the normal capillary flow produced by an augmentation of pressure at the venous ends of capillaries. Under such a situation there is a loss in the pressure differential. That such capillary blockade probably occurs is evidenced by the marked electrocardiographic changes produced when identical mean pressures are applied to the coronary sinus and the coronary artery.

The decrease in backflow and the markedly hemorrhagic myocardium resulting from but a few hours of sinus pressure elevation is indeed disappointing, especially in view of the fact that mean sinus pressure was carefully limited to 50 mm. Hg. The use of large amounts of heparin may have contributed significantly. Such vascular trauma may be minimized in the more chronic dogs of Beck by virtue of the fact that the operation is done in two stages thereby producing a more gradual increase in sinus pressure. By such a technic the vessels may develop a resistance to rupture.

In conclusion it appears evident that acute arterialization of the coronary sinus renders the myocardium mildly ischemic in the presence of normal coronary circulation, but following complete and nearly complete coronary occlusion it provides a few cubic centimeters of retrograde capillary flow which serves to prevent ventricular fibrillation for at least a few hours.

Although it is tempting to make predictions based upon these studies as to the effect of chronic arterialization of the sinus as is produced in the Beck operation, it is felt that actual study of the Beck dogs is necessary. It is very questionable whether the remarkable protection described by Beck can be ascribed to the rather meager retrograde flows as found in these experiments. Three possibilities suggest themselves. Chronic sinus arterialization may: (1) produce augmentation of retrograde flow; (2) stimulate the growth of capillaries from the coronary venous system, or (3) stimulate the growth of new or pre-existing interarterial or extra coronary collaterals. Studies are now in progress to determine which if any of these possibilities are in operation.

Summary

The acute effects of elevation of coronary sinus pressure have been studied on dogs. It has been shown that the perfusion of the sinus from a systemic artery produces larger retrograde flows than those resulting from simple sinus occlusion, probably because of the higher sinus diastolic pressure. Evidence is presented which indicates that retrograde flow declines within three hours.

The studies reveal that a small retrograde flow occurs even into an occluded artery since sizeable escape routes from the artery exist. (Anterior and posterior cardiac veins.)

Elevation of coronary sinus pressure reduces left ventricular output mildly in the absence of an arteriovenous fistula and elevates output when an arteriovenous fistula is created simultaneously.

Electrocardiographic evidence shows that elevation of coronary sinus pressure results in mild myocardial anoxia in the presence of normal arterial inflow, marked myocardial ischemia when arterial inflow is reduced, and mild alleviation of the ischemia due to complete arterial occlusion.

Observations of changes in coronary flow show that elevation of sinus pressure produces a mild reduction in coronary inflow with resulting expansion of the vascular bed due to a degree of myocardial anoxia.

Studies on the amount of oxygen uptake by the myocardium resulting from arterializa-
tion of the sinus is approximately from 14 to 25 per cent of normal.

The conclusion is reached that arterIALIZación of the coronary sinus provides acute benefit to the myocardium following coronary ligation, but it is insufficient to maintain normal con-
traction. However, in the presence of normal or reduced coronary inflow acute elevation of sinus pressure results in myocardial anoxia probably due to restriction of capillary flow.

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SUMARIO ESPAÑOL
Los efectos fisiológicos agudos de un anastomosis de Beck de la aorta al seno coronario han sido estudiados. La evidencia presentada muestra que la arterialización del seno coronario resulta en una pequeña circulación retrogradada del seno por los capilares a la arteria oclusa y que dicha circulación retrogradada supone un 14 a 25 por ciento de la demanda normal de oxígeno del miocardio. Se sugiere que esto es insuficiente para mantener la contracción miocárdica, pero probablemente evita la fibrilación ventricular. Sin embargo, cuando se arterializa el seno en presencia de circulación coronaria normal o reducida datos electrocardiográficos y de circulación coronaria muestran anoxia del miocardio. Esto probablemente se debe a la restricción en circulación capilar y resulta en una expansión del cauce vascular coronario.

REFERENCES
9 Robertson, H. F.: Physiology, pathology and clinical significance to experimental coronary sinus obstruction; its relation to cardiac surgery, coronary thrombosis and nutrition of heart by thebesian vessel or coronary sinus backflow. Surgery 9: 1, 1941.
20 Heinbecker, R., Vivien, T., and Blalock, A.:


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