EXPERIMENTAL AUGMENTATION OF CORONARY FLOW BY RETARDATION OF THE ARTERIAL PRESSURE PULSE*

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NUMEROUS surgical methods for increasing the blood supply to the myocardium of persons suffering from coronary insufficiency have been reported. Among these are the attempts to increase the extracoronary collateral supply to the muscle by the induction of pericardial adhesions[1] or the suturing of such vascular structures as the omentum,[2] muscle flaps,[3] or lung[1] to the surface of the heart. The efforts to stimulate the growth of collateral anastomoses to the coronary system by implanting one of the internal mammary arteries into the ventricular myocardium[4, 5] have yielded equivocal results. A new approach, used by Beck and associates,[6] perfuses the coronary capillary bed in a retrograde fashion by arterialization of the coronary sinus. This procedure is not yet fully developed, nor has it been finally evaluated. For this reason, an investigation was undertaken to determine whether the blood supply through narrowed coronary arteries could be improved by delaying the arterial pressure wave so that it arrives in the coronary arteries during diastole. This was accomplished by perfusing the coronary artery from one of the systemic arteries by interposing a suitable length of rubber tubing to delay the transmission of the pulse wave.

HEMODYNAMIC ANALYSIS

It has long been known that contraction of the left ventricle not only furnishes the pressure head for driving blood into the coronary arteries, but also offers resistance to coronary flow during systole. Since the pressure source for and the resistance to coronary flow have a common origin, the measurement of phasic flow is the only method that can permit evaluation of the determinants of coronary flow during successive phases of the cardiac cycle.[7]

The upper solid line curve (P_1) of Fig. 1 is the aortic pressure curve which represents the central coronary perfusion pressure. The lower solid line curve (Q_1) is the phasic flow pattern as obtained with an orifice meter.[7] It will be noted that during systole the coronary blood flow is less than during diastole, in spite of the fact that the pressure head is greater. This demonstrates that the peripheral coronary resistance is greatest during myocardial contraction. With subsequent ventricular relaxation and diminution of peripheral resistance, coronary flow rises sharply and reaches its maximum,

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even though the pressure perfusing the coronary arterial tree at this time is lower than at the previous systolic peak. It is during this diastolic period, and until the onset of the next systolic contraction, that the myocardium receives the major portion of its blood flow.

It would seem reasonable, then, to assume that if one were able to perfuse the coronary bed with higher pressures during diastole when resistance is lower, a greater flow could be obtained during this portion of the cardiac cycle. In addition, one would expect that a higher pressure applied during this period of time would dilate the coronary vessels to a greater degree. The dilated coronary bed would then be expected to carry more blood, and this would again increase the flow. It, therefore, would be desirable to perfuse the coronary bed with pulse pressures which are not only out of phase, but which also have a high peak.

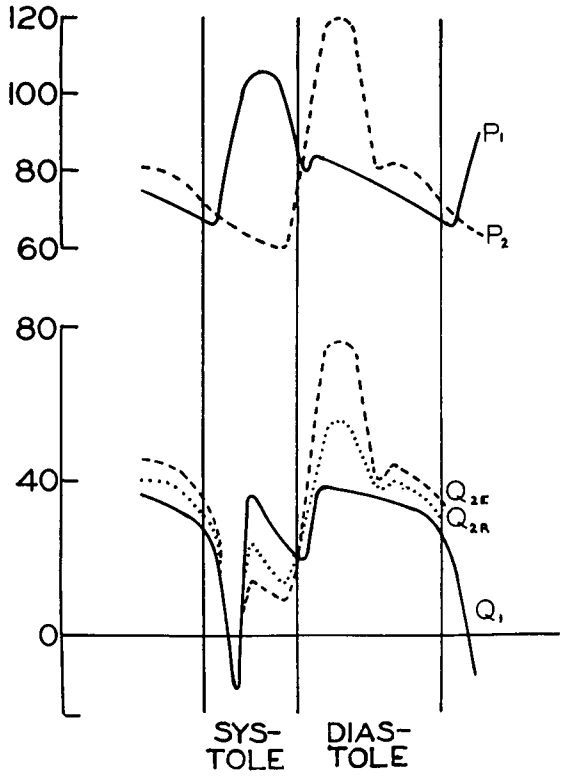

Fig. 1.—Heavy lines indicate normal aortic pressure (P_1) and phasic coronary flow (Q_1) after Gregg.[7] Dashed and dotted lines indicate predicted flows when the anterior descending coronary artery is perfused with pulse pressure out of phase with myocardial systole. P_2 represents proposed delayed coronary pressure; Q_{2R}, calculated flow in presumed rigid coronary system; Q_{2E}, calculated flow in presumed elastic coronary system.

The magnitude of the expected increase in coronary blood flow can be predicted on physical principles if we assume a delayed and peaked femoral pressure curve such as might be achieved experimentally. In Fig. 1, this curve (broken line, P_2) is superimposed over the normal curve. The systolic peak

is somewhat higher than that of the original aortic curve, but the mean pressure throughout the cardiac cycle is the same.

By applying Poiseuille's law, which defines the moment-to-moment relationships of pressure and flow, a first approximation to the expected increase in flow can be calculated. Poiseuille's law[8] is:

$$P = \frac{8Lv}{\pi r^4} \times Q, \tag{1}$$

where P equals the pressure head, Q the flow of blood, L the length of the vessel being perfused, y the viscosity of the blood, and r the radius of the vessel, all expressed in centimeter gram-second system units.

Let P_1 and Q_1, respectively, equal the pressure and flow at any instant in Fig. 1, and P_2 and Q_2 equal the projected pressure and the new flow, respectively. We can then solve for Q_2 from the following ratio of Poiseuille's law:

$$\frac{P_1}{P_2} = \frac{\frac{8Lv}{\pi r_1^4} \times Q_1}{\frac{8Lv}{\pi r_2^4} \times Q_2} \tag{2}$$

If we presume that L, the effective length of the coronary arterial tree, and v, the viscosity of the blood, do not change during a cardiac cycle, then the expression $\frac{8Lv}{\pi}$ is a constant and can be canceled to yield the expression

$$Q_2 = Q_1 \left(\frac{P_2}{P_1}\right) \times \frac{r_2^4}{r_1^4} \tag{3}$$

That is to say, if we want to know the flow at any instant during the cardiac cycle when a new pressure is being applied, we must know the previous pressure, the previous flow, the new pressure at that instant, and the effective radius of the coronary bed under the new pressure, as well as what it was under the original pressure.

The first three variables of this equation are immediately available from Fig. 1. The effective radius of the coronary bed, however, is information which we do not have. We can, however, attempt to calculate the limits between which the new flow curve must fall. The lower limit would be the flow, in a system in which the elasticity is zero, such that there would be no change in radius when an increased pressure was applied. This would mean, then, that the ratio $\frac{r_2^4}{r_1^4} = 1$, and therefore $Q_{2r} = Q_1 \left(\frac{P_2}{P_1}\right)$ where Q_{2r} is the flow through an assumed rigid coronary bed (plotted in Fig. 1 as a dotted line). We can calculate the upper limit if we assume that the coronary bed is as elastic as the most elastic artery that we know in the body, that is, the arch of the aorta, since information about the elasticity of this structure is available. Numerous studies[9, 10] have shown that when a closed section of the arch of the aorta is filled with fluid and the pressure is raised from 0 to 100 mm. Hg, then the volume is roughly doubled. Green, Gregg, and Wiggers[11] have shown that the change in volume of the anterior descending branch of the left coro-

nary artery is directly proportional to the change in pressure over the range from 20 to 140 mm. of mercury. Combining these two observations, we can write as an upper limit to the distention due to pressure.

$$V_2 - V_1 = V_1 \left(\frac{P_2 - P_1}{100}\right) \tag{4}$$

where V_2 is the volume of the coronary bed at pressure P_2, and V_1 is the volume at a lower pressure, P_1. Dividing Equation (4) by V_1 and squaring both sides we obtain

$$\left(\frac{V_2}{V_1}\right)^2 = \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{5}$$

Since the volume of a cylindrical vessel is

$$V = \pi r^2 L \tag{6}$$

and, if the length remains constant during a volume change, then the radius ratio can be found by dividing two equations of this form, thus:

$$\frac{V_2}{V_1} = \frac{r_2^2 L}{r_1^2 L} = \frac{r_2^2}{r_1^2} \tag{7}$$

Squaring both sides of Equation (7) we get

$$\frac{V_2^2}{V_1^2} = \frac{r_2^4}{r_1^4} \tag{8}$$

Substituting this value of the volume ratio in Equation (5)

$$\frac{r_2^4}{r_1^4} = \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{9}$$

Then Equation (3) becomes

$$Q_2 = Q_1 \left(\frac{P_2}{P_1}\right) \times \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{10}$$

We can now solve this equation for Q_2 for a series of points, and draw the upper limit of the flow curve Q_{2E} on Fig. 1, which would represent the flow through this arterial bed if this system were the most elastic possible. The expected flow curve then must fall somewhere between these two limits. Obviously, flow is somewhat diminished during the latter part of systole, but definitely increased during diastole. By measuring the areas under these flow curves, it was found that we could expect an increase in flow somewhere between 20 and 40 per cent.

EXPERIMENTAL METHODS

Since the increase in flow realized depends on the elasticity of those portions of the coronary bed which offer the largest flow resistance, and since this cannot be evaluated mathematically, a method was devised for determining the gain in flow experimentally on anesthetized dogs. The thorax was opened under proper artificial respiration. The experimental setup is diagrammatically illustrated in Fig. 2. A large metal cannula was inserted through the bracheocephalic artery into the arch of the aorta of the dog. This led through a Y-tube to the orifice meter and from the orifice meter to the left circumflex coronary artery which we cannulated at a point 2 or 3 mm. beyond where it arose from the left common coronary artery. It thus was possible to perfuse the left circumflex coronary artery with aortic pressures

similar to those normally prevailing. The blood circuit from the aorta to the cannula in the left circumflex coronary artery is a rigid system and the blood is an incompressible fluid; therefore, the time delay in the arrival of the pulse to the left circumflex coronary artery is negligible. Since the central coronary pressure normally supplying the coronary bed is the same as aortic pressure, this enabled us to study, as others[12, 13] have done, the normal flow through the left circumflex coronary artery.

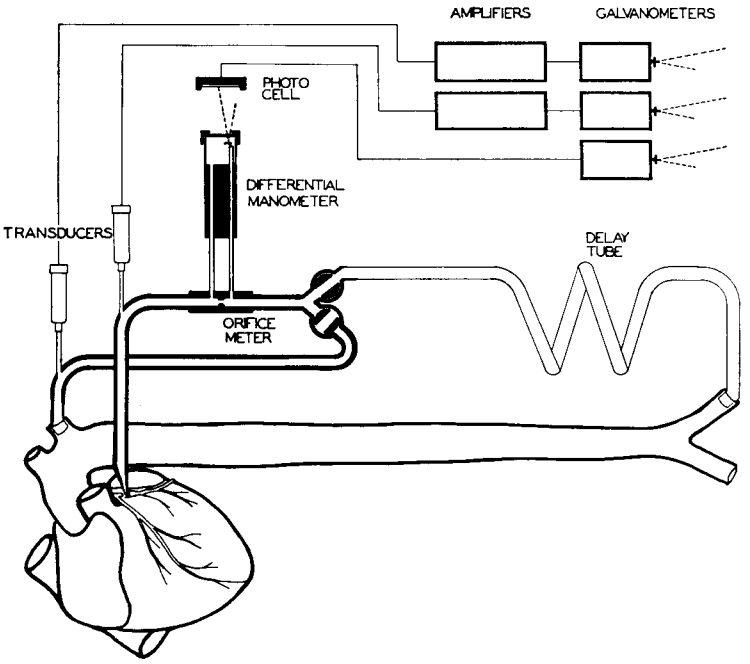

Fig. 2.—Schematic diagram of experimental setup. (Discussion in text.)

To accomplish the perfusion of the coronary artery with a delayed pressure pulse, one or both femoral arteries were cannulated. This blood was led through a rubber tube, acting as a delay tube, to the other limb of the Y and through the orifice meter to the same cannula in the left circumflex coronary artery. Since normally the transmission time of the pulse down the elastic aorta to the femoral arteries is from .05 to .07 second, and since a further delay of any desired length of time could be obtained by using appropriate lengths of rubber tubing to connect the femoral arteries with the Y-tube, it was possible to perfuse the coronary artery with pulsatile pressures out of phase with myocardial systole. In some experiments an adjustable orifice meter and differential manometer were used in order to measure phasic left circumflex coronary inflow.

In other experiments, aortic pressures were recorded from a transducer in the cannula from the aorta, and coronary pressures were recorded from a

transducer in the cannula to the coronary artery. A Hathaway Recording System[14] was used. In order to correct for the inherent nonlinearity of the orifice meter and differential manometer, a selenium photoelectric cell was introduced into the optical circuit of the flowmeter and the output of this photoelectric cell was led to one of the optical galvanometers of the Hathaway Recording System. By empirically adjusting the intensity and angle of the incident beam on the photoelectric cell, it was possible to correct the output of the flowmeter automatically so that the record would be a linear recording of the phasic flow through the system.

In four other experiments, precisely the same setup was used except that a rotameter was employed to measure mean flows through the left circumflex coronary artery.

In an attempt to design a satisfactory delay line, the use of various types of tubing was explored. It was found that latex rubber surgical tubing, 3 mm. inside and 5 mm. outside diameters, transmitted the pulse wave at a velocity of about 20 M. per second and permitted use of comparatively short lengths of the tubing from 80 to 120 centimeters. To maintain the peaked form of the pulse wave in the delay line, it was important that the junctions be constructed so as to minimize wave reflections.

RESULTS

Seven dogs were used to explore the mean flows by using a photoelectric bubble flowmeter[15] in a circuit similar to that shown in Fig. 2. A great deal of difficulty was encountered in obtaining pulse forms that resembled what we desired; because of the comparatively long lengths of external rigid tubing, the effective mass of the experimental circuit was too high. Nevertheless, in some of the experiments it was found that, when the left circumflex coronary artery was perfused with delayed pulses, some small increase in flow (up to 11 per cent) was occasionally observed.

In nine animals good pulse contours were obtained by reducing the effective mass of the external rigid circuit. This was done by reducing the length to about 30 cm. and increasing the diameter to about 1 centimeter. In each of fifty-six separate observations, blood flow through the left circumflex coronary artery was increased when this artery was perfused with a pulse pressure out of phase with the aortic pressure, as compared with the control perfusion when the pulse pressure was in phase with the aortic pressure. The increase in all of these observations varied between 22 and 53 per cent. Precautions were observed to rule out consequences such as changes in temperature of the blood perfusing the coronary artery and the dilating effect of temporary myocardial anoxia immediately preceding the observed coronary flow. Sections of a typical record of one of these experiments using the setup illustrated in Fig. 2 are shown in Fig. 3. In segment *A*, the coronary pressure is in phase with the aortic pressure, but it is slightly distorted due to its transmission through the meter. The flow rapidly drops to below zero in the early part of systole. After this, forward flow is re-established and there is some flow into the coronary artery during the

latter part of systole. At the onset of diastole, however, the flow rises rapidly and the major portion of the coronary blood flow occurs during this period. In segment *B*, Fig. 3, the coronary pressure is out of phase with the aortic pressure, the peak occurring during myocardial diastole. The phasic flow again rapidly drops to below zero in the early part of systole, but remains low throughout this entire period. At the onset of diastole the curve rises rapidly and reaches a peak which is almost double that seen in segment *A*. Obviously, the diastolic gain in flow exceeds the loss during systole. The phasic flow curves are distorted by the natural frequency of the differential manometer, which can be seen to be about 20 cycles per second. Unfortunately, the frequency response and the

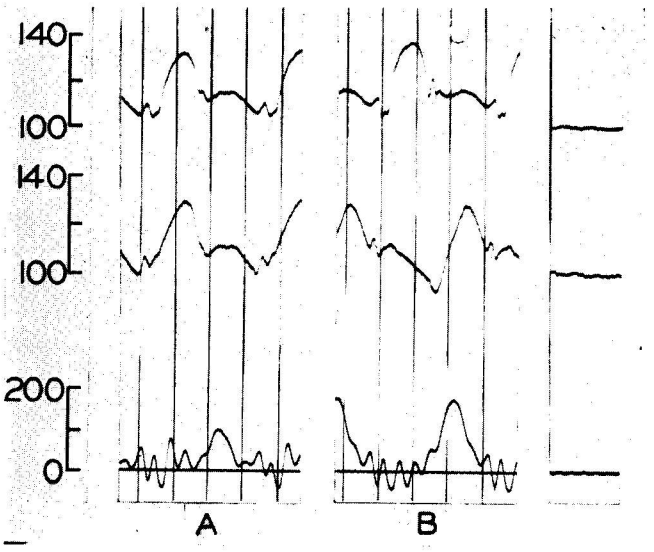

Fig. 3.—Segments of record from Dog 20. Upper curves represent aortic pressures in millimeters of mercury; middle curves, coronary perfusion pressures in millimeters of mercury; lower curves, phasic flow as recorded with an orifice meter in cubic centimeters per minute.
Segment *A* shows coronary perfusion pressure in phase with aortic pressure; segment *B* shows coronary perfusion pressure out of phase with aortic pressure. Time lines represent 0.1 second. Mean flow is 53 per cent greater with delayed pulse.

damping of the differential manometer was inadequate to record faithfully the phasic flows. This inadequacy, however, would not affect the recorded mean flow and still would give a qualitative indication of the actual phasic flow. The mean coronary pressures in segments *A* and *B* of Fig. 3 are, respectively, 109 and 105 mm. of mercury. The mean flow in segment *A* is 36 c.c. per minute, and in segment *B* it is 55 c.c. per minute, an increase of 53 per cent over the control.

Sections of a record from an experiment in which a commercially available rotameter was used to measure blood flows are shown in Fig. 4. As can be seen from the record, the rotameter records, not absolute mean flows, but rather a sine curve from which the mean flow can be read by drawing a line through the middle of the curve. In segment *A*, the coronary pressures are in phase with the aortic pressures and are only slightly distorted by passage

through the flowmeter. In segment *B*, the coronary pressures are out of phase with the aortic pressures, their peaks falling just after closure of the aortic valves. Although the peak is somewhat higher than that seen in segment *B* of Fig. 3, it is not delayed as much. In segment *A* the mean coronary pressure is 112 mm. Hg and the mean flow is 35 c.c. per minute. In segment *B* the mean coronary pressure is 110 mm. Hg and the mean flow is 44 c.c. per minute, an increase of 26 per cent.

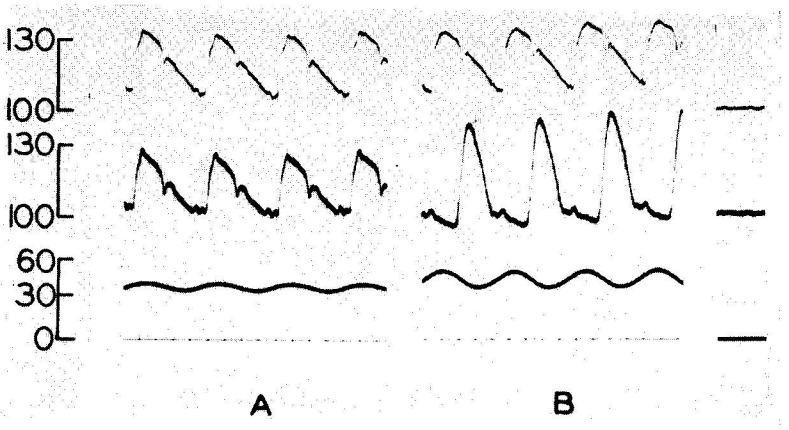

Fig. 4.—Section of record in Dog 23. Upper curves represent aortic pressures in millimeters of mercury; middle curves, coronary perfusion pressures in millimeters of mercury; lower curves, mean flow as recorded with a rotameter in cubic centimeters per minute.
Section *A* shows coronary perfusion pressure in phase with aortic pressure; section *B* shows coronary perfusion pressure out of phase with aortic pressure. Mean flow is 26 per cent greater with delayed pulse. Note that rotameter does not follow phasic flow changes.

DISCUSSION

The results of our experiments show that if it were possible to perfuse the coronary bed with peak systolic pressures during myocardial diastole an increase of flow through the coronary bed could be expected. This demonstration warrants the consideration of the possible development of a surgical procedure for improving coronary flow in persons suffering from coronary insufficiency. The pathologic changes of coronary sclerosis are such that it is entirely within the realm of possibility that this would have application in the surgical treatment of human arteriosclerotic heart disease. The atheromatous plaques in the coronary vessels are almost invariably restricted to the main-stems of the coronary arteries or to their immediate large branches. Over 50 per cent of the occlusions may be found within 3 cm., and 80 per cent within 6 cm., of the coronary ostia.[16, 17] About 66 per cent of all occlusions occur in the left anterior descendens.[17, 18] The distal portion of the coronary arterial tree, that portion imbedded in the myocardium, exhibits only minimal disease process. Further, the sclerotic process rarely occurs in a diffuse fashion throughout the epicardial arteries, but rather as more or less discrete plaques with areas in between available for anastomosis. The results of the pathologic process in the proximal portion of the coronary bed are a decrease in the mean perfusion pressure available to the coronary bed by the increased resistance of this seg-

ment and, thus a reduction of the coronary blood flow. Several arteries could be used to effect a direct anastomosis to the left coronary artery, such as the internal mammary, the splenic, the inferior epigastric, or one of several left intercostals. Any of these or a combination could be long enough to effect some delay in the arrival of the pulse wave to the coronary artery. Further, such an anastomosis, with the coronary arteries between the coronary ostia and the point where epicardial vessels descend into the myocardium, should effect a significant improvement in flow, because it would be possible to by-pass a portion of the diseased vessel and thus decrease the over-all resistance of the diseased coronary circuit. The improvement resulting from the direct anastomosis would have to be multiplied by the improvement resulting from the phase shift, so that the final improvement would be even greater.

SUMMARY

1. The phasic extravascular compression of the intramyocardial branches of the coronary artery causes increased resistance to flow during systole and decreased resistance during diastole.

2. It appeared that if it were possible to perfuse the coronary bed with systolic pressures during myocardial diastole, so as to be able to take advantage of the markedly decreased peripheral resistance during this period, an increase in coronary flow could be expected. This could be accomplished, for example, by delaying the arterial pressure peak long enough so that it would occur during diastole.

3. A theoretical analysis of the problem on the basis of Poiseuille's law led to the prediction that 20 to 40 per cent increase in flow through the left coronary artery might occur.

4. A delay of the pressure pulse so that the systolic peak was held back until diastole was achieved in twenty-six dogs by connecting the femoral artery by a proper length of tubing to the cannulated left circumflex artery.

5. Left coronary artery flows were studied with an orifice meter in order to record phasic flows and with a rotameter to record mean flows. It was found that the experimental data confirmed the theoretical analysis and that augmentation of flow was quantitatively and qualitatively as predicted by this theory.

6. It is suggested that this principle may prove surgically feasible as a means of improving coronary blood flow in arteriosclerotic heart disease.

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