Effect of Cardiac Contraction on Coronary Blood Flow

By David C. Sabiston, Jr., M.D. and Donald E. Gregg, Ph.D., M.D.

In the experimental animal the basic and controversial problem was studied of the influence of cardiac contraction on coronary blood flow. Normally beating hearts were perfused at a constant pressure, and coronary inflow and outflow were determined. In order to assess the role of systole, prolonged periods of ventricular asystole and fibrillation were induced and observations were made of the changes in coronary flow. With the cessation of cardiac contraction blood flow in the coronary arteries and coronary sinus rose appreciably. The results of these studies support the concept that contraction of the heart muscle, by compression of the myocardial vascular bed, behaves as a throttling mechanism and impedes coronary flow. The method employed permits a separation and quantitation of the effects on coronary flow resulting from cardiac contraction and the vasomotor state of the coronary vessels.

The effect of organized cardiac contraction on flow through the capillary bed of the myocardium remains unsettled despite much work that has been done to elucidate this basic problem. Evidence has accumulated in support of 2 opposing viewpoints. One concept is that the shortening of the muscle fibers during systole compresses the vascular bed in the myocardium and acts as a "throttling" mechanism. The opposing view is that cardiac contraction "massages" or "kneads" the blood through the vascular bed and increases coronary flow. The primary objective in this study has been an evaluation of the effect of organized myocardial contraction on coronary flow in the intact animal. This problem has been attacked by the elimination of this factor by the induction of ventricular asystole or ventricular fibrillation. Comparisons have been made of coronary flow in the beating heart perfused at a constant pressure with those in the nonbeating heart under the same conditions.

Methods

Twenty-seven adult mongrel dogs were anesthetized with intravenous pentobarbital (25 mg./Kg.). Respiration was maintained through an endotracheal tube connected to a demand-valve apparatus supplied with oxygen. The left chest was entered through the fourth intercostal space and the pericardium was opened. The appropriate coronary vessels were then cannulated. The left coronary artery was dissected at its origin from the aorta and a specially designed brass cannula was inserted into it via the left subclavian artery and tied securely in place by means of a ligature. For study of the right, circumflex, or descending branches of the coronary arteries, the vessel was dissected and ligated close to its origin. A small glass or polyethylene cannula was inserted into the distal end for perfusion. For flow measurement in the coronary sinus a flexible polyvinyl catheter was introduced through the right atrial appendage into the sinus and maintained in place at its orifice by a suture ligature. A rotameter was placed in the circuit, and blood was returned to the superior vena cava via the external jugular vein. In some experiments blood was allowed to drain from the coronary sinus catheter to the atmosphere. Mean coronary arterial pressure was determined by use of a Statham strain gage. A diagrammatic illustration of the experimental preparation is shown in figure 1.

Blood entering the coronary artery was first passed through a recording rotameter connected to a carotid artery and between experimental observations this vessel supplied the coronary perfusion. For a short time prior to induction of asystole and during this period, blood was perfused from a reservoir at or near the prevailing mean aortic pressure. Heparin was used as an anticoagulant (200 mg. initially and 100 mg. each 30 min.). In some instances this was supplemented by pontamine-fast pink (150 mg./Kg. initially and each hour thereafter) or Treburon (35 mg./Kg. and 125 mg. each hour thereafter). Asystole was produced by direct stimulation of both vagus nerves in the neck with an Electrodyne stimulator† delivering 250 volts at a

* Manufactured by Statham Instruments, Inc.,
Hato Rey, Puerto Rico.
† Manufactured by Electrodyne Co., Endicott St.,
Norwood, Mass.

From the Department of Cardiorespiratory Diseases, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D.C.

Circulation, Volume XV, January 1957
frequency of 30/sec. This stimulus resulted in a period of asystole of 4 to 26 sec. Ventricular fibrillation was induced by direct stimulation of the left ventricle with an inductorium. A continuous recording of aortic and coronary perfusion pressure and coronary arterial and venous flow was obtained with an oscillograph.

Results

A total of 248 observations of coronary flow with the heart in either asystole or ventricular fibrillation was made as follows:

Left Coronary Artery Inflow in Ventricular Asystole. There were 4 animals in which flow through the left coronary artery was studied and 40 inductions of prolonged asystole were performed. In each instance there was a rise in coronary flow after the onset of asystole. The average control flow was 93 ml./min. and following asystole it rose to 141 ml./min., representing an increase of 59 per cent (table 1). Maximal flow was reached in 1 to 4 sec. and remained elevated, although there was usually a slight fall with time. (In 2 later experiments in an unrelated study, coronary flow rose with asystole but fell later to a value below that of the control. Such a response was thought to be abnormal and probably the result of partial obstruction of the coronary sinus.)

Flow in a Left Coronary Artery Branch and in the Right Coronary Artery During Ventricular Asystole. The possibility was investigated of a difference in response of the coronary bed supplied by the right coronary artery or a major branch of the left coronary artery from that of the main left coronary artery. Two experiments were done with cannulation of both the right and left coronary arteries. Typical results during 1 of these experiments is shown in figure 2. Both right and left coronary arterial flows rose simultaneously, indicating that the beds supplied by these vessels respond in a similar manner during asystole.

A total of 171 determinations in 13 animals were made of coronary flow in the circumflex branch of the left coronary artery during ventricular asystole. In every instance flow rose
in the vessel as it was perfused at the preasystolic mean aortic pressure level. The average flow before asystole was 42 ml./min. and following asystole the value rose to 61 ml./min., representing an increase of 50 per cent (table 1). A typical record of the rise in circumflex flow during asystole is shown in figure 3.

Left Coronary Artery Inflow and Coronary Sinus Drainage in Asystole. In 3 animals, 6 determinations of both the left coronary arterial inflow and coronary sinus drainage were recorded during asystole while coronary perfusion was maintained at a constant pressure. Coronary arterial flow was always increased during asystole (31 to 77 per cent), with an average increase of 50 per cent. In each instance except 1, coronary sinus flow was also increased (table 2). Typically, there was an initial fall in coronary sinus drainage for 2 to 3 sec. and then it rose to exceed control values (fig. 4).

Coronary Arterial Inflow and Coronary Sinus Drainage in Ventricular Fibrillation. In 5 animals, a total of 8 simultaneous determinations of flow through the left coronary artery and the coronary sinus were made before and after the onset of ventricular fibrillation (table 3). The coronary inflow rose from 11 to 72 per cent, with an average increase of 26 per cent. The rise of flow in the coronary sinus varied from 16 to 76 per cent, with an average of 37 per cent. A typical record illustrating the increase in both arterial inflow and venous drainage is shown in figure 5. A rise in arterial flow in both the circumflex and descendens branches of the left coronary artery is also shown to occur with ventricular fibrillation.

The possibility must be considered that a portion of the augmentation of coronary inflow...
TABLE 2.—Left Coronary Artery and Coronary Sinus Flow in Ventricular Asystole

<table>
<thead>
<tr>
<th>No.</th>
<th>Control (ml/min)</th>
<th>In asystole (ml/min)</th>
<th>Per cent increase</th>
<th>Control (ml/min)</th>
<th>In asystole (ml/min)</th>
<th>Per cent increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>119</td>
<td>156</td>
<td>31</td>
<td>72</td>
<td>86</td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td>111</td>
<td>151</td>
<td>36</td>
<td>68</td>
<td>80</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>94</td>
<td>166</td>
<td>77</td>
<td>38</td>
<td>59</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>105</td>
<td>168</td>
<td>60</td>
<td>62</td>
<td>52</td>
<td>-16</td>
</tr>
<tr>
<td>5</td>
<td>95</td>
<td>142</td>
<td>49</td>
<td>34</td>
<td>48</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>142</td>
<td>209</td>
<td>47</td>
<td>94</td>
<td>108</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Average</td>
<td></td>
<td>50</td>
</tr>
</tbody>
</table>

Average

with removal of coordinated ventricular contraction is related to events other than prolongation of the period of diastole. During asystole the central pressure and flow in a coronary artery or branch not perfused from the constant pressure reservoir decrease during induced asystole. In most dog hearts collateral channels exist between the coronary arteries and their branches. Accordingly, experiments were performed to test whether a portion of the increase of coronary inflow in the perfused coronary artery with vagal stimulation or with ventricular fibrillation arises from passage of blood to the nonperfused vessel by these channels. A total of 23 determinations on 3 animals were performed in which flow in the circumflex and descendens branches was determined following clamping of one or the other after the induction of asystole (fig. 3). As the descendens artery was clamped and its flow fell to 0, no appreciable rise occurred in the circumflex flow. The reverse was also true, that is, when the circumflex was clamped there was no appreciable rise in flow through the descendens coronary bed. Similarly, clamping of either the right coronary artery or a branch of the left coronary artery during asystole did not affect flow through the other coronary artery. Fi-
nally, occlusion of the circumflex branch following fibrillation did not significantly alter flow in the descendens branch.

It is considered unlikely that in these experiments vagal stimulation per se affected coronary inflow in any way other than by mechanical removal of myocardial contractions because, within 1 sec. or less from the onset of stimulation, coronary flow reached its new level where it was maintained during asystole. Similarly, application of electrodes to the ventricle to induce fibrillation did not appear in itself to affect coronary flow, since repeated ventricular stimulation by this means during ventricular fibrillation did not alter coronary flow.

**Discussion**

For nearly 3 centuries physiologists have debated the question of the direction and magnitude of the effect of ventricular systole on coronary blood flow. In 1689 Scaramucci expressed the view that the coronary vessels filled during ventricular relaxation and emptied during ventricular contraction. The names of Thebesius, Vieussens, and Morgagni are associated with those who maintained that the coronary arteries are prevented from filling during systole due to closure of their orifices by the aortic valves. While now all agree that the latter mechanism is untenable, there is much less certainty regarding the net effect of organized contraction of cardiac muscle fibers on coronary blood flow. With skeletal muscle the analogous situation is more clearly understood and the experimental results have been in closer agreement. Many observers have reported increased venous outflow during the contraction of this type of muscle. Blalock first made simultaneous observations of arterial inflow and venous drainage in the gastrocnemius before, during, and after contraction. These studies clearly demonstrated a reduction in flow in the artery during contraction with a corresponding increase in venous flow. By use of the technic of direct transillumination Knisely and associates have observed flow in the capillary bed of the frog and its relationship to muscular contraction. It was observed that the striated muscle fibers became wider and compressed the capillaries enough to stop flow at the beginning of a powerful contraction. As individual fibers began to relax flow began again. Studies on the myocardial vascular bed with this technic have shown compression of the capillaries by ventricular contraction to the point of erythrocyte standstill.

The importance of ventricular systole in the control of coronary flow is illustrated in a number of studies. In the left coronary artery perfused during systole at a pressure approximately equal to the prevailing mean aortic pressure, arterial inflow approaches 0. Other studies have shown that for an equivalent time period, left coronary artery systolic inflow is less than diastolic inflow. These observations lend support to the concept that organized ventricular contraction results in diminished coronary flow. However, in other studies the systolic flow in the coronary sinus has been observed to be much greater than the diastolic flow, which might suggest that ventricular systole augments coronary flow, and coronary sinus drainage has been noted to decrease during ventricular fibrillation. From the available data there is evident a lack of agreement as to the net effect of systolic contraction on flow in the coronary bed.

It is a difficult task to assess the factor of the extravascular myocardial support, and several groups of investigators have made attempts to evaluate its role in the regulation of flow in the heart-lung preparation. Various methods have been employed in an effort to clarify this problem. Hilton and Eichholtz, Hammouda and Kinosita, and Anrep and Hauser have employed ventricular fibrillation to remove, at least in part, the effect of cardiac contraction and have determined the changes that occur in coronary flow. These investigators found that in this preparation coronary arterial inflow increased during fibrillation. In contradistinction to this, Osher in studying the pressure-coronary sinus flow relationships of perfused hearts both beating and fibrillating found a decreased flow during ventricular fibrillation. Garcia Ramos also noted less flow during ventricular fibrillation in the isolated mammalian heart perfused by the circulating blood of another animal. Recently Wiggers has presented an evaluation of the effect of ventric-
ular contraction on coronary flow by integrating phasic flow curves recorded from the coronary sinus. Measurements were made of instantaneous flow in the coronary sinus in late diastole when the effects of myocardial compression and volume elasticity were minimal. From these data it was concluded that systole results in an augmentation in coronary flow. The validity of an analysis based upon phasic flow data rests upon the assumption that flow in the epicardial arteries and veins represents actual flow in the myocardial capillary bed. This point remains to be proved.

A method has been devised in the present studies that is thought to measure separately the magnitude and direction of the effect of mechanical ventricular activity on flow through the coronary bed and that also permits simultaneous quantitation of the vasomotor state of the coronary vessels. This method consists essentially of the simultaneous recording of blood flow in the left coronary artery and coronary sinus together with the mean coronary perfusion pressure and mean aortic pressure. The coronary system was perfused at a constant pressure approximating the prevailing mean aortic pressure and measurements were made in the normally beating heart and then during ventricular asystole induced by vagal stimulation. The possible effect of vagal stimulation per se on the coronary vessels is a factor deserving comment. Anrep has shown that section of the vagi leads to an increase in coronary flow even when the heart rate is kept constant. Stimulation of the peripheral end of the vagus with rhythmically interrupted faradic current resulted in a slower heart rate with little change in coronary flow during the first 30 sec. Flow then began to diminish, reaching a minimum in 1 to 1\(\frac{1}{2}\) min. The important point relative to the studies reported here is that vagal stimulation would not be expected to have a direct intrinsic effect on the vessel wall that would result in an increase in coronary flow. A flow change, if any, would presumably be opposite in direction from that following the reduction or removal of the extravascular support. For comparison, similar determinations were made before and after ventricular fibrillation and it was demonstrated that coronary flow was increased under the latter circumstances.

The induction of ventricular asystole invariably has been associated with a marked rise in coronary arterial inflow and coronary sinus drainage. The level of coronary flow reached during ventricular asystole is thought to represent that due to the vasomotor state of the coronary bed alone at the prevailing aortic pressure, and the increase in flow that occurs during asystole to indicate the magnitude and direction of the effect of myocardial contraction on blood flow through the myocardial wall. Trends of the same direction but of smaller magnitude occurred when the ventricle was in a state of fibrillation.

**Summary**

Coronary arterial inflow and coronary sinus drainage have been determined in the perfused heart in both the beating state and after withdrawal of the extravascular support by the induction of asystole or ventricular fibrillation. The removal of the extravascular support by this means invariably resulted in an increase in flow in the coronary arterial bed and in the venous drainage from the coronary sinus. Evidence is presented to advance the concept that the net effect of ventricular contraction is to impede coronary flow. Contrariwise, the removal of this factor results in an increase in flow through the myocardial vascular bed. It is believed that this approach supplies a method for the separation and quantitation of the effects on the left coronary flow of myocardial contraction and of the smooth muscle in the walls of the coronary vessels.

**Summario in Interlingua**

Le influxo del arteria coronari e le drainage del sino coronari eseva determinate in le corde perfundite, tanto in le stato de pulsation como etiam post le elimination del supporto extravascular per le induction de asystole o fibrillation ventricular. Le elimination del supporto extravascular per iste medio resultava invariabilmente in un augmento del fluxo in le vasculatura del arteria coronari e in le drainage venose ab le sino coronari. Es presentate datos que supporta le concepto que
le efecto nette del contraction ventricular es un impedimento del flujo coronario. Inversemente, la eliminación de este factor resulta en un aumento del flujo en la vasculatura myocardial. Nos opina que este punto de vista permite el disefloppamiento de un metodo pro le separation e quantitation del efectos existe super el flujo coronario sinistre per le contraction myocardial e per le musculo lisie in le parietes del vasos coronario.

REFERENCES
2 Anrep, G. V.: The circulation in striated and plain muscles in relation to their activity. The Harvey Lectures, XXX. Baltimore, The Williams & Wilkins Company, 1936, p. 146.
8 —, and Green, H. D.: Registration and interpretation of normal phasic inflow into a left coronary artery by an improved differential manometric method. Am. J. Physiol. 130: 114, 1940.

The earliest writings of men who later became prominent are always of great interest to those who concern themselves with the development of genius. One thinks of Osler's "Christmas and the Microscope," Lister's "Observations on the Contractile Tissue of the Iris," of Humphry Davy's "Nitrous Oxide," published when he was twenty-two, and of many others.

Effect of Cardiac Contraction on Coronary Blood Flow
DAVID C. SABISTON, JR. and DONALD E. GREGG

_Circulation_. 1957;15:14-20
doi: 10.1161/01.CIR.15.1.14
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1957 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/15/1/14

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/