Reflex Effects of Left Ventricular Distention

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Regulatory functions were attributed to reflexes from the left heart as early as 100 years ago. An adequate stimulus and a potential physiologic role for the drug-induced reflexes which were found have not been evident until recently. The earlier literature has been adequately reviewed.1-3 In 1959, Aviado and Schmidt4 and Doutheil and Kramer5 published observations from which it would appear that acute distention of the left ventricle is the "physiologic" stimulus for the reflex circulatory changes which had been observed by so many earlier investigators after subjecting the left ventricle and its vasculature to unphysiologic stimuli. The data reported here confirm these observations4,5 and describe the previously unknown reflex dilation of systemic veins elicited by distention of the left ventricle.

Methods

A modified heart-lung bypass method was used in open-chest dogs under pentobarbital sodium (25 mg./Kg. 3 dogs) or chloralose (80 mg./Kg. 9 dogs) anesthesia. The entire peripheral venous return and the blood from the right ventricle and the left atrium (entered via the atrial appendages) was collected in the graduated "venous" reservoir of the heart-lung machine by gravity drainage;6 blood was then oxygenated and returned into a femoral artery by a calibrated, variable-speed, occlusive pump. A rubber balloon was inserted into the left ventricle through a purse-string controlled stab wound at the apex.7 When the balloon was positioned in the outflow tract of the left ventricle, the balloon's distention by a syringe did not cause incompetence of the mitral or aortic valves unless very extreme conditions were reached. Incompetence of the valves was recognized by characteristic changes of the systemic and left ventricular pressure tracings; observations from experiments during valvular incompetence are not reported here.

In some experiments, the pulmonary artery was ligated, but in others there was no dissection in the region of the pulmonary artery in order to avoid destruction of nervous pathways. In all experiments, pressures were measured in the aortic arch or a femoral artery (Statham strain gage P23A, 3 mm. o.d. polyethylene tube) and in the left ventricle (Statham strain gage P23G, 12 cm. long and 1 mm. o.d. cardiac catheterization tube) and recorded in curvilinear coordinates at paper speeds of 1 and 50 mm./sec. There was no evidence for changes of ventricular function caused by mechanical irritation of the endocardium by the pressure registration cannula, as suggested by Doutheil and Kramer.5 In 3 experiments, the vagi were isolated in the neck for purposes of vagotomy.

Results

When all other experimental conditions were constant and when increasing volumes of air were injected into the balloon, the left ventricle became progressively more distended and the left ventricular diastolic pressure more positive. There was evidence of peripheral vasodilation whenever the left ventricular diastolic pressure exceeded 10 to 15 mm. Hg. At such diastolic pressures, the left ventricle appeared maximally distended to the observer, but its volume was not measured. At constant systemic (machine) flow, vasodilation was apparent from the reduction of the systemic arterial pressure (fig. 1) and from the increase of the intracorporeal and decrease of the extracorporeal blood volumes, which were observable by the decreased level of the "venous" reservoir. Bradycardia was con-
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sistently observed under these conditions. In many of our experiments, sudden distention of the left ventricle caused not only bradycardia but also pulsus alternans. Vagotomy abolished these effects produced by left ventricular distention.

The changes of systemic arterial pressure varied among individual dogs; the maximum decrease of systemic arterial pressure after left ventricular distention was 35 mm. Hg. The systolic or pulse pressure in the left ventricle did not influence the systemic arterial pressure in our experiments. When air was injected into the balloon rapidly, and in amounts sufficient to produce overdistention, the systemic arterial pressure fell in each instance; after left ventricular pressures became stabilized, the systemic arterial pressure would usually rise somewhat and would stabilize 5 to 15 mm. Hg below the control levels (fig. 1). For the sake of accuracy, instances are reported in table 1, section A, where the systemic arterial pressure stabilized at or above the control level. Such observations were made only after the preparation had deteriorated or when additional air was injected into a ventricle which was already distended. When distention of the left ventricle was relieved by decreasing the air content of the balloon, the systemic arterial pressure usually returned to the control level (systemic flow constant) after the invariable initial “overshoot.”

In most of the observations where the left ventricular diastolic pressure rose above 10 to 15 mm. Hg after inflation of the balloon, the volume of blood of the animal increased while that in the extracorporeal circuit decreased (table 1, section B). Changes of the venous reservoir levels which indicated this redistribution of blood appeared within seconds after distention of the left ventricle. In many of the experiments described here, the pulmonary artery was ligated and the right atrium drained into the reservoir; therefore, the increased blood volume of the dog during periods of ventricular distention could not be attributed to retention of blood in the thoracic viscera, but must be explained by systemic vasodilation. The maximal decrease of the extracorporeal blood volume observed here amounted to 40 ml./Kg. (about ½ of the 10.4 Kg. dog’s estimated blood volume). In this animal, there had been no dissection around or ligation of the pulmonary artery; the right heart and the left atrium were drained and a balloon in the pulmonary artery prevented coronary venous blood flow into the lungs. Decreases of the extracorporeal blood volume after left ventricular distention were observed at some time in every experiment, but their magnitude varied. When the left ventricle was distended for brief periods (10 to 20 minutes) these volume changes were usually fully reversible. After prolonged experimentation and multiple insults to the heart, the intracorporeal blood volume gradually increased; the “blood volume response” to left ventricular distention decreased in intensity and the extracorporeal blood volume did not return to the control levels after deflation of the balloon. The transitory increase of the intracorporeal blood volume with distention of the left ventricle was abolished after vagotomy (6 observations, 3 experiments).

From table 1, section C, it appears that the heart rate usually slowed when the left ventricular diastolic pressure was increased. A "response" in this table is indicated by a
**Table 1**

Response of Systemic Arterial Pressure, Intracorporeal Blood Volume, and Heart Rate to Variations of Left Ventricular Diastolic Pressure*

<table>
<thead>
<tr>
<th>Left ventricular diastolic pressure</th>
<th>&gt;10 mm. Hg increase</th>
<th>&gt;10 mm. Hg decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Systemic arterial pressure:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Decrease</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>No change</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>B. Intracorporeal blood volume:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Decrease</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>No change</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>C. Heart rate:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Decrease</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>No change</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

*Left ventricular distention changed by varying the air content of the balloon; systemic flow constant.

Discussion

Distention of the left ventricle as an adequate cause of circulatory reflexes was originally suggested by Daly and Vernet in 1927. Jarisch and Zotterman observed discharges in afferent cardiac nerve fibers after "pinching" the left ventricle of cats and suggested that "pressure" was the adequate stimulus for reflexes from the left ventricle. The mass of data concerning drug-induced reflexes from the left heart has been adequately reviewed. Reports concerning reflexes from the coronary arteries to the circulation have been reviewed by Aviado and Schmidt and by Schmier. After studying the conflicting results in the literature, we agree with the reviewers that the existence of circulatory reflexes resulting from changes of pressure or flow in the coronary vessels has not been proven and that the physiologic role and the significance of the drug-induced reflexes from the left heart are not clear. In retrospect, it appears likely that the inconsistent positive findings supporting the existence of reflexes from the coronary to the systemic circulation were caused by unobserved, acute distention of the left ventricle rather than by changes of pressure or of flow in the coronary vessels.

Several years after preliminary publications, Aviado and Schmidt, and also Douthat and Kramer, reported observations of bradycardia and of dilation of systemic arteries occurring after distention of the left ventricle and which were abolished by interrupting conduction in the vagus nerves. These reflex effects of left ventricular distention simulated drug-induced reflexes from the left ventricle, and therefore suggested that the "Bezold-Jarisch" family of reflexes from the left ventricle are referable to pressoreceptors.

Our experimental preparation differed from others in many technical aspects and in the preservation of an innervated carotid sinus and aortic arch. Our data confirm the occurrence of the previously described systemic arterial dilation and bradycardia which appear after distention of the left ventricle. The effects described and discussed here cannot be attributed to changes of coronary flow because this parameter (which was measured in many experiments) changed independently. The disappearance of the effects after section of the vagi attest their reflex nature. The reflexes were observed even when the left atrium was decompressed, the right heart drained, and the pulmonary artery obstructed, making these areas unlikely as the origin of the reflexes. It appears clear from the above that receptors in the left ventricle and not elsewhere elicited these reflex circulatory effects.

The marked increase of the intracorporeal blood volume, occurring with the other hemodynamic effects during overdistention of the left ventricle, has not been reported before. The magnitude of this increase in blood volume during relatively modest decreases of the arterial pressure identify the systemic veins as the site for the retained blood. Veins and arteries are known to contract and dilate together in response to drugs and other physiologic stimuli; simultaneous dilation of peripheral arteries and veins after left ventricu-
lar distention is therefore not unexpected. However, when the systemic arterial pressure falls as a result of changes in cardiac output, reflexes from the carotid sinus usually cause venoconstriction.\textsuperscript{10-18} It appears that the reflexes described here which dilate systemic arteries and veins after overdistention of the left ventricle must overcome opposing baroreceptors. This could be one of the reasons why the effect of reflexes from the left ventricle can be observed only when its distention is extreme.

The significance of the phenomena described here cannot be assessed at this time. All investigators who have studied patients with cardiogenic shock and failure after myocardial infarction agree that this condition is characterized by reduced cardiac output and normal or elevated, but not depressed, peripheral resistance.\textsuperscript{12, 19} However, these patients were not in extremis; for this reason the reflex phenomena observed here may have been masked or absent. Furthermore, the heart in an anesthesized, open-chest dog is usually deprived of its pericardial restraint and its function is therefore disturbed. When acute failure occurs in an intact organism, the dilating left ventricle encroaches upon the right ventricle, limiting diastolic filling of the right ventricle, cardiac output, and reducing systemic arterial pressure, thus ultimately controlling and reducing its own size.\textsuperscript{20, 21}

**Summary**

In open-chest dogs, the peripheral circulation was carried on a heart-lung machine. The pulmonary artery was obstructed and the left atrium and the right ventricle were drained into the venous reservoir of the machine. A balloon in the bloodless left ventricle permitted its distention. Pressures were recorded in the left ventricle and the aortic arch or a femoral artery. After distention of the left ventricle, the left ventricular diastolic pressure rose, the systemic arterial pressure fell, and bradycardia occurred. Distention of the left ventricle also caused reflex dilation of systemic veins. These effects were reversible and were abolished by section of the vagi. They are attributed to receptors in the myocardium of the left ventricle. It is considered likely that these reflex effects of left ventricular distention contribute to the mechanism of cardiogenic shock.

**Summario in Interlingua**

In cases a thorax aperte, la circulation peripheric esses transferite a un machina cardo-pulmo. Le arteria pulmone esses obstruita, e le atrio sinistre e le ventriculo dextere esses connectite con le reservoir venose del machina. Un ballon in le extramaine ventriculo sinistre permittuva su distension. Essa registrata le pression in le ventriculo sinistre e le areo aortic e un arteria femoral. Post distension del ventriculo sinistre, le tension diastolico sinistro-ventricular cresceva, le tension sistemic-arterial descendeva, e bradycardia se declarava. Distension del ventriculo sinistre etiam causava le dilation reflexe del vena systemica. Iste effectos esses revertibile. Illos esses abolite per section vagal. Illos es attribuite a re-ceptores in le myocardio del ventriculo sinistre. Es considerate como probabile che iste effectos reflexe de distension sinistro-ventricular contribue al mechinismo de choc cardiogene.

**References**

8. **Daly, I. de B., and Verney, E. B.: Localization of receptors involved in the reflex regulation of the heart rate. J. Physiol. 62: 330, 1927.**

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