Modulation of vascular capacitance by angiotensin and nitroprusside: a mechanism of changes in pericardial pressure

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ABSTRACT The aim of the present study was to test the hypothesis that vasoactive drugs may modify left ventricular diastolic function by shifting blood between the systemic vascular bed and the heart, thereby changing pericardial and left ventricular pressure. The experiments were done in 10 open-chest, anesthetized, previously splenectomized dogs in which changes in pericardial surface pressure in response to intravenous sodium nitroprusside and angiotensin were related to changes in blood volume in the abdominal region. Blood volume was determined by blood pool scintigraphy ($^99m$Tc) and regions of interest were drawn in the liver and in the mesenteric area. Angiotensin was infused at rates that were adjusted to increase mean aortic pressure by 20 and 30 mm Hg, and nitroprusside was infused at rates to decrease mean aortic pressure by 30 and 50 mm Hg. Angiotensin increased pericardial pressure by 3 and 5 mm Hg at the respective doses and there were increments in left ventricular end-diastolic pressure (LVEDP) and left ventricular diameter (sonomicrometry). Angiotensin decreased blood volume in the mesenteric region by 14% and 17%, but did not significantly change blood volume in the liver region. Angiotensin increased portal venous pressure and decreased mesenteric blood volume, suggesting increased mesenteric venous compliance. Nitroprusside had opposite effects: pericardial pressure was decreased by 5.5 and 6.5 mm Hg by the respective doses. The doses of nitroprusside increased blood volume in the mesenteric region by 14% and 20%, but did not significantly change blood volume in the liver region. Nitroprusside decreased portal pressure and increased mesenteric blood volume, suggesting increased mesenteric venous compliance. Changes in pericardial pressure with the two drugs varied inversely with changes in blood volume in the mesenteric region. In conclusion, angiotensin and nitroprusside change LVEDP by changing pericardial pressure. The two drugs had opposite effects on venous capacitance in the abdominal region. Changes in pericardial pressure varied inversely with changes in mesenteric blood volume. Thus, we propose that the mechanism whereby vasoactive drugs alter pericardial pressure is by shifting blood between the systemic venous bed and the heart, thereby changing heart size and necessarily pericardial pressure.


RECENTLY THERE HAS BEEN increasing interest in the influence of the pericardium on left ventricular diastolic function. We have previously shown that the left ventricular diastolic pressure-volume relationship was shifted markedly downward and rightward after pericardectomy, indicating that the pericardium has an important constraining effect on the left ventricle during diastole. Shirato et al. found that blood volume expansion increased pericardial pressure (Pperic) and shifted the left ventricular diastolic pressure-dimension relationship upward and leftward, while sodium nitroprusside decreased Pperic and caused a downward and rightward shift. After removal of the pericardium, however, neither of these interventions caused a shift, all the pressure-dimension points falling along a single curve. Linderer et al. showed that in the absence of an effective atrial contraction left ventricular stroke volume and end-diastolic diameter decreased at a given end-diastolic pressure. This observation is best explained by the unemptied atria compromising the pericardial space, raising Pperic and thus diminishing left
ventricular transmural diastolic pressure. More recently we have shown that reduction of left ventricular filling pressure by intravenous nitroglycerin in the acutely failing dog heart is in part due to a decrease in *P*_{peric}. These experimental studies suggest that the pericardium has important effects on left ventricular diastolic function.

It has been proposed that acute shifts in the left ventricular diastolic pressure-volume curve in patients with heart failure after the administration of vasodilators such as sodium nitroprusside and nitroglycerin or a vasoconstrictor such as angiotensin are caused by changes in *P*_{peric}. In support of this hypothesis we have recently demonstrated in man that the downward shift of the left ventricular diastolic pressure-volume curve by nitroglycerin is due to decreased extraventricular constraint.

We propose that the mechanism whereby vasoactive drugs alter *P*_{peric} is by shifting blood between the systemic venous bed and the heart, thereby changing heart size and thereby *P*_{peric}. The present study was designed to test this hypothesis. The experiments were done in anesthetized dogs in which splanchic blood volume was measured by blood pool scintigraphy. The splanchic region was studied because it is the major blood reservoir. The effects of sodium nitroprusside and angiotensin on *P*_{peric} were related to changes in venous capacitance in the abdominal region.

**Methods**

**Experimental preparation.** Experiments were carried out in 10 mongrel dogs weighing 18 to 25 kg. One week before the study each dog was splenectomized and a catheter was inserted into a main branch of the portal vein with the proximal end tunneled into a subcutaneous pouch. Dogs were splenectomized for two reasons: (1) to avoid the problem of a changing hematocrit that would render inappropriate the calculation of splenic volume by the radionuclide blood pool method, and (2) because the spleen in dogs is a large and important blood reservoir, while the human spleen is of minor hemodynamic importance. On the day of the experiment the dogs were anesthetized with a 25 mg/kg iv bolus of sodium pentobarbital followed by a continuous infusion of 3.5 mg/kg/hr. The dogs were placed in the supine position and were ventilated by a constant-volume respirator (Model 607, Harvard Apparatus Co., Inc; Millis, MA). Through a midline sternotomy the pericardium was incised and a 3 × 3 cm flat Silastic balloon was positioned on the anterolateral surface of the left ventricle at the mid left ventricular level for measurement of *P*_{peric}. This was loosely stitched to the epicardium. Ultrasonic crystals were sutured to the epicardium to allow measurement of the anteroposterior diameter of the left ventricle. The anterior crystal was placed 2 cm from the atrioventricular sulcus to the left of the left anterior descending coronary artery; the posterior crystal was placed 1 cm from the atrioventricular sulcus to the left of the posterior descending coronary artery. The pericardium was then loosely sutured, with care taken to avoid artificial constriction. An electrocardiogram was monitored from a limb lead and body temperature was maintained by a warming lamp. Left ventricular pressure was measured with a No. 8F micromanometer-tipped catheter with a reference lumen (Model PC-480, Millar Instruments, Houston, TX) that was introduced via a femoral artery. Aortic pressure and central venous pressure were recorded through catheters introduced via a femoral artery and vein, respectively. The fluid-filled catheters were connected to transducers (Model P231b, Statham-Gould, Oxnard, CA). Catheters for infusions and blood sampling were introduced into jugular and femoral veins. Pressures, diameters, and the electrocardiogram were recorded on a multichannel recorder (Model VR 16, Electronics for Medicine/Honeywell, White Plains, NY). Data were also recorded on analog tape (Model 3968A, Hewlett-Packard, Palo Alto, CA) for later playback and analysis.

**Radionuclide studies.** Equilibrium blood pool radionuclide angiography was used to quantitate the changes of regional blood volume in the abdomen. Labeling of the red blood cells was achieved by intravenous injection of 16 mg stannous pyrophosphate followed 20 to 30 min later by 20 mCi of 99mTc pertechnetate. Static 60 sec scintigrams of the entire abdomen were recorded (at intervals outlined below) with a gamma camera (Model DYNA-MO 4, Picker, Northford, CT) equipped with a diverging collimator and interfaced to a mobile nuclear medicine computer (Model DPS-2800, ADAC Laboratories, San Jose, CA). To minimize the amount of circulating free isotope, scintigrams were recorded at least 45 min after initial labeling. The interval from the first to the last recording was approximately 2 hr. Straight anterior views of the abdomen were used. Care was taken to maintain the same camera position throughout each experiment. To define the same anatomic segments when selecting the regions of interest in consecutive scintigrams, landmarks were sutured to the skin and liver. Since the dog-camera position was unchanged in successive recordings, regions of interest were drawn only on the first scintigram. The correct positions of the regions selected were confirmed in subsequent images by use of the analog pictures and the lead markers. The exact time of each scintigram was noted and for each measurement a 10 ml blood sample was drawn for determination of blood specific radioactivity.

The following regions were studied: a segment of the liver defined by a circle with a radius of 10 pixels around a lead marker, and a mesenteric segment given by the average count rate in two rectangular regions of interest (5 × 10 pixels) located in the lower abdominal quadrants. These mesenteric regions of interest were defined within areas that did not include large abdominal vessels or major abdominal organs. Each regional count rate was corrected for physical decay of 99mTc and for the specific activity of the radiotracer assessed from blood samples drawn at the time of each scan. Background was not taken into account in the calculations since the activity external to the dog was considered to remain constant and activity from organs other than mesentery or liver was assumed to be relatively small and to vary in parallel (i.e., as a function of central venous pressure). The results were expressed as percentages of the initial value measured in the given region of interest. This technique has been used successfully to measure regional mesenteric and limb blood volume changes and measured volume changes correlated well with standard strain-gauge plethysmographic measurements.

**Experimental protocol.** The following variables were recorded: pressures in the left ventricle, the aorta, the portal vein, and the inferior vena cava, pericardial surface pressure, anteroposterior diameter of the left ventricle, and vascular volumes in mesenteric and hepatic regions.

Animals were transfused (using blood from a donor dog) until the left ventricular end-diastolic pressure (LVEDP) was approximately 10 mm Hg. Angiotensin was then infused at two dif-
different rates adjusted to increase mean aortic pressure by 20 mm Hg and then 30 mm Hg. This required average infusion rates of 0.09 and 0.26 μg/kg/min, respectively. During these infusions, a 5 to 10 min stabilization period was allowed before recordings were made. Another recording was taken 15 min after discontinuation of the angiotensin infusion, when aortic pressure had declined. The dogs were then given transfusions until LVEDP of approximately 15 mm Hg was reached and recordings were obtained before intravenous administration of sodium nitroprusside. The infusion rates of sodium nitroprusside were adjusted to lower mean aortic pressure by 30 and 50 mm Hg (average doses of 12 and 24 μg/kg/min, respectively). A final recording was made 30 min after termination of the nitroprusside infusion.

In the two additional dogs the effects of angiotensin and sodium nitroprusside were studied under conditions of markedly elevated LVEDP. Sodium nitroprusside was infused intravenously after LVEDP had been increased to 30 mm Hg by transfusion. The nitroprusside infusion was then discontinued for 15 min. LVEDP was adjusted to approximately 20 mm Hg before angiotensin was infused. The infusion rates of sodium nitroprusside and angiotensin were adjusted to achieve the same changes in mean aortic pressure described above.

To compare the effects of an increase in afterload produced by an alternate means, a pneumatic occluder on the descending thoracic aorta was used. In each of two dogs, three repeated aortic partial occlusions were performed to increase mean aortic pressure to a value similar to that obtained with the high dose of angiotensin, i.e., approximately 30 mm Hg. Recordings were obtained over the first few beats after onset of the occlusions.

Statistics. A two-way analysis of variance was used for group comparison between control measurements and those during each intervention. When the F ratio indicated a significant effect of an intervention, Student’s t test for paired observations was performed to determine the level of statistical significance of the difference between the control and the intervention values. Because multiple (n = 3) t tests were done on the data in tables 1 and 2, the probability value was adjusted according to the Bonferroni rule; an adjusted probability of less than .01 was considered to indicate statistical significance. Data are reported as mean ± SE.

Results

Left ventricular pressure-dimension relationships and pericardial pressure. The baseline LVEDP and Pperic before volume loading were 7 ± 1 (mean ± SE) and 2 ± 1 mm Hg, respectively. Before administration of angiotensin LVEDP was increased to 10 ± 0 mm Hg by transfusion; the corresponding Pperic was 5 ± 0 mm Hg (table 1). Angiotensin at the low and the high dose increased LVEDP by 4 (p < .005) and 8 mm Hg (p < .005) and increased Pperic by 3 (p < .05) and 5 mm Hg (p < .005), respectively. Therefore, the elevation of LVEDP secondary to angiotensin was primarily a reflection of increased Pperic; there was only modest increase in transmural LVEDP (i.e., LVEDP minus Pperic). In accord with this, angiotensin caused only moderate increments in left ventricular anteroposterior diameter (table 1). Figure 1 shows left ventricular diastolic pressure-diameter loops from a representative experiment; angiotensin displaced the pressure-diameter loop upward and rightward. Figure 2 shows the effect of angiotensin on left ventricular diastolic pressure-diameter relationships in a dog with markedly elevated LVEDP after blood transfusion. Angiotensin caused a marked upward shift of the left ventricular intracavitary pressure diameter relationship. However, there was no apparent change in the left ventricular transmural pressure-diameter relationship, indicating that the upward shift was almost entirely due to increased Pperic.

Before administration of sodium nitroprusside, a blood transfusion was given that increased LVEDP to 15 ± 1 mm Hg and Pperic to 8 ± 1 mm Hg (table 2). Nitroprusside at the low and the high dose decreased LVEDP by 8 (p < .005) and 10 (p < .005) mm Hg and decreased Pperic by 6 mm Hg (p < .005) in each case. Thus, in parallel to the observations with angiotensin, nitroprusside decreased LVEDP primarily by decreasing Pperic; there were only moderate reductions in transmural LVEDP and in left ventricular anteroposterior diameter (table 2). Figure 1 shows a representative

| TABLE 1 |
| Effects of angiotensin (mean ± SE) |

<table>
<thead>
<tr>
<th></th>
<th>Before drug</th>
<th>Low dose angiotensin</th>
<th>High-dose angiotensin</th>
<th>After angiotensin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean aortic (mm Hg)</td>
<td>130 ± 3</td>
<td>151 ± 4^b</td>
<td>161 ± 4^b</td>
<td>112 ± 7</td>
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<tr>
<td>LV systolic (mm Hg)</td>
<td>142 ± 8</td>
<td>155 ± 3</td>
<td>168 ± 5</td>
<td>127 ± 6</td>
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<td>LVEDP (mm Hg)</td>
<td>10.4 ± 0.5</td>
<td>14.9 ± 1.5^b</td>
<td>18.0 ± 2.0^b</td>
<td>8.8 ± 1.5</td>
</tr>
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<td>Transmural LVEDP (mm Hg)</td>
<td>5.2 ± 0.5</td>
<td>6.7 ± 1.0</td>
<td>7.8 ± 0.7</td>
<td>5.1 ± 0.8</td>
</tr>
<tr>
<td>Peric (mm Hg)</td>
<td>5.2 ± 0.2</td>
<td>8.2 ± 0.8^a</td>
<td>10.2 ± 1.2^a</td>
<td>3.8 ± 0.8</td>
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<tr>
<td>Central venous (mm Hg)</td>
<td>4.3 ± 0.4</td>
<td>5.3 ± 0.9^a</td>
<td>6.3 ± 1.2</td>
<td>4.0 ± 0.9</td>
</tr>
<tr>
<td>Portal pressure (mm Hg)</td>
<td>9.0 ± 1.0</td>
<td>10.3 ± 1.0^a</td>
<td>12.6 ± 1.2^a</td>
<td>8.1 ± 1.1</td>
</tr>
<tr>
<td>LV A-P diameter (mm)</td>
<td>55.1 ± 2.2</td>
<td>55.9 ± 2.2^b</td>
<td>56.0 ± 2.2^b</td>
<td>54.6 ± 2.3</td>
</tr>
<tr>
<td>Liver blood (%)</td>
<td>100</td>
<td>97 ± 3</td>
<td>95 ± 5</td>
<td>102 ± 6</td>
</tr>
<tr>
<td>Mesenteric blood (%)</td>
<td>100</td>
<td>87 ± 4^a</td>
<td>83 ± 3^b</td>
<td>88 ± 7</td>
</tr>
</tbody>
</table>

^a p < .05; ^b p < .005.

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Nitroprusside

Control

Angiotensin

\[ P_{LV} - P_{Peric} \]

![Graph](image)

**Figure 1.** Effects of nitroprusside and angiotensin on the left ventricular diastolic pressure-diameter relationship in a dog with slightly elevated LVEDP. Sodium nitroprusside caused a shift in the pressure-diameter relationship leftward and downward, whereas angiotensin caused a shift upward and to the right. P_peric represents the difference between the left ventricular intracavitary pressure (solid line) and the left ventricular transmural pressure (dotted line). Note that the two agents had opposite effects on P_peric. LV = left ventricular; \( P_{LV} \) = left ventricular pressure; A-P = anteroposterior.

experiment that demonstrates that nitroprusside displaced the left ventricular diastolic pressure-diameter loop leftward and downward. In the two dogs in which LVEDP was increased to 30 mm Hg before administration of nitroprusside there was a marked downward shift of the left ventricular diastolic pressure-diameter relationship (figure 2). This downward shift was accounted for by a decrease in P_peric.

**Venous pressures and regional blood volumes.** Angiotensin and nitroprusside had opposite effects on blood volume in the mesenteric region (tables 1 and 2 and figures 3 and 4). Angiotensin at the low dose caused a decrease in mesenteric blood volume of 13% (\( p < .005 \)) and the high dose caused a 17% decrease (\( p < .005 \)) when compared with predrug values. This was accompanied by increments in portal vein pressure from 9 ± 1 to 10 ± 1 (\( p < .05 \)) and to 13 ± 1 mm Hg (\( p < .005 \)), respectively, after the 0.09 and 0.26 \( \mu \)g/kg/min doses of angiotensin. Nitroprusside, on the other hand, increased mesenteric blood volume by 15% (\( p < .05 \)) and 20% (\( p < .005 \)), respectively, at the low and high doses of the drug. Nitroprusside decreased portal vein pressure from 11 ± 2 to 9 ± 1 (\( p < .005 \)) at the low dose and to 7 ± 1 mm Hg (\( p < .005 \)) at the high dose.

Neither angiotensin nor nitroprusside caused significant changes in regional blood volume in the liver (tables 1 and 2). Angiotensin, however, increased central venous pressure from 4 ± 0 to 5 ± 1 (\( p < .05 \)) and 6 ± 1 mm Hg (\( p > .05 \)), respectively, at the low and high doses of the drug. Nitroprusside decreased central venous pressure from 6 ± 1 to 4 ± 0 (\( p < .005 \)) and 3 ± 0 mm Hg (\( p < .005 \)) at the low and the high doses, respectively.

**Change in P_peric vs change in regional blood volume with angiotensin and nitroprusside.** Figure 5 shows changes in P_peric vs changes in blood volume in the mesenteric region. With one exception, all infusions of angiotensin both decreased mesenteric blood volume and increased P_peric. Similarly, with a single exception, all nitroprusside interventions both increased mesenteric blood volume and decreased P_peric. Least squares linear regression indicated a significant negative correlation (\( \Delta P_{Peric} = -0.22 \Delta \text{mesenteric blood volume} - 0.54; r = -0.68, p < .00005 \)). In contrast, figure 6 shows no relationship between the change in P_peric and the change in liver blood volume.

**Responses to partial occlusions of descending thoracic aorta.** The change in P_peric secondary to sudden partial occlusion of the descending aorta was compared with
LABORATORY INVESTIGATION—PHYSIOLOGY

Nitroprusside  Control  Angiotensin

PLV  PLV-Peric

FIGURE 2. Effects of nitroprusside and angiotensin on the left ventricular diastolic pressure-diameter relationship in a dog with markedly elevated LVEDP. Sodium nitroprusside shifted the left ventricular diastolic pressure-diameter relationship downward, whereas angiotensin caused an upward shift. The left ventricular transmural pressure-diameter relationship (dotted lines) showed only minor changes. Therefore, the pressure-diameter shifts with these agents were due to changes in Pperic. Abbreviations are as in figure 1.

that produced by infusion of angiotensin. As shown in figure 7, similar increases in mean aortic pressure by acute constriction caused significantly (p < .01) smaller changes in Pperic than those that occurred with angiotensin infusion. Both partial aortic occlusion and angiotensin infusion caused LVEDP to increase, from 9 ± 0 to 16 ± 1 mm Hg (p < .01), and from 10 ± 0 to 18 ± 2 mm Hg (p < .01), respectively. Pperic was

TABLE 2
Effects of sodium nitroprusside (mean ± SE)

<table>
<thead>
<tr>
<th></th>
<th>Before drug</th>
<th>Low dose nitroprusside</th>
<th>High-dose nitroprusside</th>
<th>After nitroprusside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
<td>130 ± 4</td>
<td>102 ± 2B</td>
<td>82 ± 3B</td>
<td>116 ± 3B</td>
</tr>
<tr>
<td>LV systolic pressure (mm Hg)</td>
<td>139 ± 5</td>
<td>114 ± 3</td>
<td>97 ± 4</td>
<td>123 ± 3</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>14.7 ± 1.1</td>
<td>6.7 ± 0.8B</td>
<td>4.9 ± 1.1B</td>
<td>9.3 ± 1.5B</td>
</tr>
<tr>
<td>Transmural LVEDP (mm Hg)</td>
<td>6.7 ± 0.4</td>
<td>4.2 ± 0.5</td>
<td>3.5 ± 0.8</td>
<td>4.7 ± 0.9</td>
</tr>
<tr>
<td>Peric (mm Hg)</td>
<td>8.0 ± 1.0</td>
<td>2.5 ± 0.8B</td>
<td>1.5 ± 0.6B</td>
<td>4.6 ± 0.9B</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>6.4 ± 0.7</td>
<td>4.0 ± 0.3B</td>
<td>2.6 ± 0.5B</td>
<td>4.1 ± 0.7B</td>
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<tr>
<td>Portal pressure (mm Hg)</td>
<td>11.4 ± 1.5</td>
<td>9.2 ± 1.1B</td>
<td>7.4 ± 0.8B</td>
<td>8.7 ± 1.0A</td>
</tr>
<tr>
<td>LV A-P diameter (mm)</td>
<td>56.0 ± 2.1</td>
<td>54.6 ± 2.5A</td>
<td>54.1 ± 2.2B</td>
<td>55.1 ± 2.3</td>
</tr>
<tr>
<td>Liver blood volume (%)</td>
<td>100</td>
<td>98 ± 4</td>
<td>99 ± 3</td>
<td>96 ± 1B</td>
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<tr>
<td>Mesenteric blood volume (%)</td>
<td>100</td>
<td>115 ± 6B</td>
<td>120 ± 5B</td>
<td>94 ± 4</td>
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</table>

Abbreviations are as in table 1.

*p < .05; **p < .005.
increased from 3 ± 0 to 5 ± 1 mm Hg (p < .05) by portal aortic occlusion and from 5 ± 0 to 10 ± 1 mm Hg (p < .05) by angiotensin.

Discussion

In the present investigation the two vasoactive drugs angiotensin and sodium nitroprusside were used to study the interaction between the capacitance vessels and the left ventricle. Our hypothesis was that changes in Pperic with vasoactive drugs such as angiotensin and nitroprusside are due to shifts of blood between the venous vascular bed and the central circulation, including the heart. In support of this hypothesis we found an inverse relationship between changes in Pperic and changes in blood volume in the mesenteric region. The finding that angiotensin increased portal vein pressure and decreased mesenteric blood volume indicates vеноconstriction. Previous studies are conflicting as to whether or not angiotensin has vеноconstrictor properties.18–21 These studies, however, have been limited to the vascular bed of the extremities, which represents a quantitatively relatively unimportant part of the capacitance vasculature.11 The present study, which focuses on the more important blood reservoir, the splanchnic region, shows that angiotensin has important effects on regional blood volume distribution through marked vеноconstriction in the mesenteric region. Previous studies on isolated venous strips have shown vеноconstriction by angiotensin in mesenteric and portal veins, but not in somatic veins.21

Although liver blood volume remained unchanged with angiotensin, there was a significant rise in portal vein pressure, and central venous pressure tended to increase, suggesting some degree of vеноconstriction in the liver also. The reason that liver blood volume did not decrease might be related to the existence of different venous compartments within the liver, including veins with smooth muscle in the vessel walls as well as entirely passive segments. If there are venous segments downstream from the sinusoids that dilate passively due to increased central venous pressure, it is possible that this increase in volume could negate a decrease in vascular volume elsewhere.

FIGURE 3. Portal venous pressure (Pport) and mesenteric blood volume (expressed as percent of control volume) data from individual dogs. The results of angiotensin administration are shown by open symbols; those of nitroprusside administration are shown by closed symbols. Control observations are indicated by circles, low-dose drug administration by squares, and high-dose drug administration by triangles. Note that angiotensin consistently increased pressure and decreased volume (i.e., increased venomotor tone) while nitroprusside decreased pressure and increased volume (i.e., decreased venomotor tone).

FIGURE 4. Summary of changes in portal venous pressure (Pport) and mesenteric blood volume (mean ± SE). Symbols are the same as in figure 3.
Sodium nitroprusside has effects opposite to those of angiotensin; there was a decrease in portal vein pressure and an increase in the mesenteric regional blood volume, indicating venodilation, after nitroprusside. Regional blood volume in the liver remained unchanged, but the decrease in central venous pressure suggests venodilation in the liver as well. (It is not clear what pressure would best be used to characterize the capacitance of the liver. We also plotted liver blood volume against portal venous pressure and found qualitatively identical results.)

Since angiotensin and nitroprusside affect arteriolar as well as venous motor tone, it might be argued that changes in Pperic with these agents are due primarily to alterations of left ventricular afterload. In response to this possible criticism, the change in Pperic induced by angiotensin was compared with that caused by constriction of the descending aorta sufficient to cause a similar increase in mean aortic blood pressure. Aortic constriction, however, caused only a small increase in Pperic. This is consistent with the observations and interpretation of Stokland et al.\textsuperscript{22} In their studies occlusion of the descending aorta produced an increase in left ventricular systolic pressure and an increase in left ventricular end-diastolic dimensions. When they produced the same increase in left ventricular systolic pressure by constriction of the ascending aorta, the increase in left ventricular end-diastolic dimensions was negligible. They concluded that substantial amounts of blood drain passively from the splanchnic bed and posterior caval circulation when arterial pressure drops to venous levels. In our study the difference between the increase in pericardial pressure after administration of angiotensin and the increase after descending aortic occlusion may have been due to a greater amount of blood mobilized by a leftward shift in the splanchnic (and perhaps systemic) vascular pressure-volume relationship(s) than by passive draining of the vasculature perfused by the descending aorta. Our observations are also consistent with the study of angiotensin by Stokland et al.\textsuperscript{23} They concluded that only half the rise in systemic pressure after angiotensin infusion is due to increased arteriolar resistance; the other half is due to an increase in preload caused by displacement of blood from the venous circulation, two-thirds of which comes from the splanchnic bed. According to their estimates of liver volume based on measurements of hepatic dimensions (sonomicroscopy), most of the blood comes from the liver. We cannot explain this difference between our results and theirs.

In the present study pericardial surface pressure was

\textbf{FIGURE 5.} The relationship between changes in Pperic and changes in mesenteric blood volume. With angiotensin (open circles) and nitroprusside (closed circles) there is an inverse relationship between changes in Pperic and those in mesenteric blood volume. With only two exceptions angiotensin decreased mesenteric blood volume and increased Pperic, while nitroprusside increased mesenteric blood volume and decreased Pperic.
recorded by a flat, liquid-containing balloon. We have previously shown that this device correctly measures pericardial constraint. To measure blood volume we used blood pool scintigraphy, a technique that has been shown to accurately measure changes in regional blood volume. To detect changes in the characteristics of the capacitance circulation, vascular regional blood volume was related to venous pressure for the mesenteric region (portal venous pressure) and for the hepatic region (central venous pressure). This procedure is, of course, not entirely correct, but seems justified since most of the blood is located in the venules and veins and venous pressure is a reasonable approximation of the average distending pressure of this compartment of the circulation. For the mesenteric regions portal venous pressure was used because the radioactivity measured in this region is assumed to originate predominantly from blood in the splanchnic vascular bed. In the present study left ventricular anteroposterior diameter was used as a variable of left ventricular volume. This single diameter does not truly reflect left ventricular volume when there are significant changes in left ventricular shape seen during displacements of the interventricular septum. However, the position of the septum during diastole is determined by the transseptal pressure gradient and major changes in left ventricular shape occur when there are discordant changes in left ventricular and right ventricular diastolic pressures. However, in the present study the interventions caused directionally similar changes in left- and right-sided pressures. Furthermore, while the imperfect estimate of left ventricular volume may slightly obscure the interpretation of shifts in the left ventricular diastolic pressure-diameter relationship, in this study pericardial pressure was measured directly. Although our results might be extrapolated with caution to patients with acute congestive heart failure, they cannot be extended without further verification to chronic states of heart failure, hypertrophy, or pericardial dilation.

FIGURE 6. The relationship between changes in Pperic and changes in liver blood volume. There was no consistent relationship between the two variables. (Symbols the same as in figure 5.)

FIGURE 7. Comparison of changes in Pperic after angiotensin with those induced by partial occlusion of the descending thoracic aorta. Although by design the two procedures produced similar increases in mean aortic blood pressure (PAo), the increase in Pperic with partial aortic occlusion was significantly smaller than that after angiotensin.
In summary, we have confirmed the study of Alderman and Glantz, which showed that nitroprusside shifts the diastolic pressure dimension relationship downward while angiotensin produces an upward shift. We have shown that these changes in intracavitary pressure can be accounted for by changes in Pperic. We observed that nitroprusside increases and angiotensin decreases the capacity of the systemic (mesenteric) vasculature. The changes in splanchnic vascular volume produced correlated inversely with the change in pericardial pressure. Therefore, we conclude that nitroprusside primarily increases the capacity of the systemic vascular bed, allowing blood to pool peripherally and cardiac volume to decrease. A smaller cardiac volume induces a decrease of Pperic, which in turn increases apparent left ventricular diastolic compliance (i.e., shifts the diastolic pressure-volume relation downward). The opposite mechanisms are in effect with infusion of angiotensin.

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