Effects of Splanchnic Nerve Stimulation on Cardiac Preload, Afterload, and Output in Cats

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SUMMARY  Splanchnic nerve stimulation (SNS) mobilizes up to 25% of the total blood volume from the splanchnic venous bed, constricts the splanchnic arterioles, and releases catecholamines and renin. This study examines the effects of these changes on cardiac preload, afterload, and output in cats anesthetized with chloralose. Before adrenalectomy, SNS caused increases in right atrial and arterial pressures and cardiac output, but total peripheral resistance did not change. After adrenalectomy, SNS increased right atrial pressure, arterial pressure, and peripheral resistance, but cardiac output did not change. It is concluded that adrenal catecholamines are necessary for an increased cardiac output during SNS. After adrenalectomy and elimination of the baroreceptor reflexes, SNS still caused no increase in cardiac output. When the increases in arterial pressure were prevented by nitroprusside infusions or by opening an arteriovenous (A-V) shunt, SNS caused an increase in cardiac output even though the increase in right atrial pressure was much smaller than before. The results are quantitatively described by the Frank-Starling relationship between stroke work and right atrial pressure and are interpreted as follows. Venoconstriction alone causes an increase in cardiac output with a minimal rise in cardiac preload (right atrial pressure). However, if afterload (systemic and pulmonary arterial pressures) increases, this reduces the increase in cardiac output causing a further rise in preload. The rise in preload tends to restore cardiac output but is limited by pooling of blood elsewhere in the venous system (about 4 ml/kg for each 1-mm rise in right atrial pressure). A new equilibrium is then reached between preload, afterload, and cardiac output. Thus, this study demonstrates the interaction between preload and afterload in the control of cardiac output. Circ Res 46:181-189, 1980

PREVIOUS studies have shown that the splanchnic venous bed is an important venous reservoir. It not only contains a significant portion of the cat's blood volume (36%), but a major part of this reservoir can be mobilized by activation of the sympathetic nerves (Greenway and Lister, 1974). The capacitance responses to sympathetic nerve stimulation have been studied in cat intestine (Folkow et al., 1963, 1964), colon (Hulten, 1969), liver (Greenway et al., 1969; Greenway, 1979a), and spleen (Greenway et al., 1968). The volumes of blood mobilized at different frequencies of nerve stimulation, calculated from these studies, are shown in Table 1. Data for the intestine and colon were pooled since the responses appeared to be similar, and they were changed from ml/100 g tissue to ml/kg body weight using the data of Greenway and Murthy (1972). The cat's total blood volume was taken as 52 ml/kg (Farnsworth et al., 1960; Groom et al., 1965; Greenway, 1979b). It can be seen that stimulation at frequencies of 1–8 Hz mobilizes up to 27% of the total blood volume. In dogs, the values are similar or higher in the intestine (Donald and Aarhus, 1974), liver (Greenway and Oshiro, 1972; Carneiro and Donald, 1977a), and entire splanchnic bed (Brooksby and Donald, 1971; Karim and Hainsworth, 1976). However, the total blood volume in the dog is larger (80 ml/kg).

Mobilization of volumes of blood of these magnitudes would be expected to increase cardiac output. However, stimulation of the splanchnic nerves also causes arteriolar vasoconstriction (Folkow et al., 1964; Greenway and Stark, 1971). Even though this is not well maintained in the intestine and liver (autoregulatory escape), some increase in arterial pressure and hence cardiac afterload would be expected. Although the effects of increases in cardiac preload and afterload have been studied extensively (Herndon and Sagawa, 1969; Ross, 1976; Parmley et al., 1977), their interaction in the intact circulation has not yet been clarified. Also, release of catecholamines from the adrenal medulla and renin from the kidney and the reflex consequences of all these direct effects complicate the picture and make prediction of the overall responses difficult.

In this study, we have examined the influence of some of these factors, particularly the roles of the adrenal glands, the baroreceptor reflexes, and afterload on right atrial pressure, stroke volume, and cardiac output.

Methods

Cats (2.3–3.8 kg, mean 3.0 kg) were anesthetized by intramuscular injection of ketamine HCl (Keta-
lar, Parke-Davis, 20 mg/kg) followed, after insertion of a cannula into a forelimb vein, by intravenous infusion of α-chloralose (Sigma Chemical Co., 50 mg/kg as a 1% solution in 0.9% NaCl, dissolved at 90°C and cooled to 37°C). Arterial pressure was recorded from a cannula in the right femoral artery by a Statham P23Dc transducer, and heart rate was recorded from the arterial pressure pulsations. All recordings were made on a Beckman 8-channel dynograph. The trachea was cannulated, and artificial ventilation was instituted to maintain peak expired CO₂ levels in the range of 4-5% (Beckman Medical Gas Analyser LB-2). A cannula was inserted through the right jugular vein with its tip in the superior vena cava 1 cm above the heart. This cannula was used to record right atrial pressure and to inject Ringer-Locke’s solution for cardiac output measurements.

The chest was opened through the 5th right intercostal space, and the pulmonary artery was punctured with an 18-gauge hypodermic needle. A 2F thermal dilution catheter was passed through the needle into the pulmonary artery, and the needle was withdrawn. The catheter was held in place by a suture through the fibrous tissue between the pulmonary artery and the aorta, and the chest was closed. The catheter was connected to a cardiac output system (IL 701, Instrumentation Laboratory Inc.). Cardiac output was determined by injecting 1 ml Ringer-Locke’s solution at room temperature over 4 seconds into the right atrial catheter using a Harvard infusion pump. In three cats, a different arrangement was used to allow simultaneous recording of pulmonary arterial pressure and cardiac output. The pulmonary artery was punctured using a short length of 18-gauge hypodermic needle. This needle was connected to a polyethylene tube connected to a P23Dc Statham pressure transducer. The needle was tied in place, and the 2F thermal dilution catheter was passed down it into the pulmonary artery.

The abdomen was opened by a midline incision, and portal pressure was recorded from a catheter inserted via the small vein from the appendix. The left splanchnic nerve was ligated and cut, and the peripheral end was tied into a Perspex ring containing two platinum electrodes. The nerves were stimulated with rectangular pulses of 15 V, and 1 msec in duration (Grass S44 stimulator), at frequencies of 1, 2, 4, and 8 Hz. The reproducibility of these responses has been analyzed previously (Greenway, 1979a). The usual duration of stimulation was 3-4 minutes, but 8-minute periods were examined for each frequency in different cats to confirm that the responses were well maintained for this period. The right splanchnic nerve was cut. The abdomen then was closed with sutures. In all experiments, the positions of the cannulas and thermistor and the completeness of section of the splanchnic nerves were verified postmortem.

The following procedures were carried out as required in the various series of experiments. Adrenalectomy was performed. The vagi were ligated and cut. For experiments in which it was desired to prevent alterations in the reflex discharge from the baroreceptors, the vagi were cut to eliminate the aortic baroreceptors, but we did not section the sinus nerves since this produced an unwanted hypertension. Also it was not possible to perfuse isolated carotid sinus pouches since occlusion of the carotid arteries in cats causes substantial CNS depression due to the dependence of cerebral blood flow on these vessels. We therefore administered 2000 IU heparin, intravenously, and long-circuited both carotid arteries through a single piece of polyethylene tubing. By controlled partial occlusion of this tube with recording of pressure downstream from the clamp, it was possible to hold carotid sinus pressure approximately constant when systemic arterial pressure increased during splanchnic nerve stimulation. Sodium nitroprusside (Nipride, Roche, 2-20 μg/kg per min) was infused intravenously when required using a syringe driven by a continuously variable speed motor. The infusions were begun and ended 30 seconds before nerve stimulation was begun and ended, respectively, and the dose was adjusted to maintain arterial pressure at the prestimulation level for the duration of the stimulation period.

The general protocol was to allow an interval of 20-30 minutes after completion of the surgery for the variables to stabilize. Then, three measurements of cardiac output were made at 2- to 3-minute intervals before each period of nerve stimulation. The means of all the measurements at the times the cardiac outputs were determined were taken as the control values for that period of nerve stimulation. During nerve stimulation, cardiac output determinations were made at 1-minute intervals. The means of all the values at these times were taken as the experimental value. No consistent changes with time occurred during the periods of stimulation. Intervals of at least 20 minutes at the lower frequencies and 30 minutes at the higher frequencies were allowed for recovery after cessation of stimulation before the next control values were taken. This time is necessary due to the slow refilling of the spleen (Greenway, 1979b).

To verify the validity and reproducibility of the cardiac output measurements and the suitability of

<table>
<thead>
<tr>
<th>Stimulation frequency (Hz)</th>
<th>Volume mobilized (ml/kg)</th>
<th>% Total blood volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intestine</td>
<td>Liver</td>
</tr>
<tr>
<td>1</td>
<td>0.46</td>
<td>1.09</td>
</tr>
<tr>
<td>2</td>
<td>0.76</td>
<td>2.62</td>
</tr>
<tr>
<td>4</td>
<td>1.22</td>
<td>3.58</td>
</tr>
<tr>
<td>8</td>
<td>1.52</td>
<td>4.37</td>
</tr>
</tbody>
</table>
the calibration factor (K = 88) recommended by the manufacturers, the following additional experiments were done. Four anesthetized cats were bled to death. Large cannulas were placed in the superior and inferior venae cavae and in the pulmonary artery as far from the heart as possible. Blood was circulated through the right side of the heart at 37°C from a reservoir using a Sigmamotor pump at rates of 100–300 ml/min. Flow was determined by timing the collection of blood. A small cannula was introduced into the superior vena cava 1 cm above the heart to allow infusion of 0.9% NaCl at room temperature, and the 2F thermal dilution catheter was placed in the pulmonary artery. With the calibration factor K = 88, the thermodilution measurement was equal to 0.997 times the direct measurement, and the coefficients of variation for multiple readings at various flows ranged from 3 to 7%. In intact anesthetized cats, the least variability between multiple determinations was observed when the infusions lasted 4 seconds. Rapid infusions (1–2 seconds) gave greater variations which could be associated with phases of the respiratory cycle. When 1 ml of Ringer-Locke’s solution at room temperature was given over 4 seconds, the coefficients of variation for multiple measurements were 5–10%. Although each cat received some 100 ml of Ringer-Locke’s solution over about 5 hours, arterial hematocrits did not decrease by more than 2% over this period, and most cats produced more than 50 ml of urine. The hematocrit at the end of the experiments was 36 ± 1.1% (mean and SE; n = 23) for all the cats.

All data were analyzed by randomized complete-block analysis of variance with multiple comparisons by Duncan’s multiple range test (Steel and Torrie, 1960).

**Results**

Twenty three cats were studied. To assess the possible effects of surgery, control cardiac outputs were compared at various stages in the experiments. Before opening the abdomen, the cardiac output was 141 ± 5.5 (mean ± se) ml/min per kg body weight. After opening the abdomen, cardiac output was 145 ± 5.4 ml/min per kg, and after preparation and section of the splanchnic nerves and adrenalectomy, it was 152 ± 7 ml/min per kg. These values were not significantly different. The control values of the other measured variables also showed little change during the course of the experiments (see figures), except for heart rate which tended to increase somewhat.

**Responses in Cats with Intact Adrenals**

In nine cats, the responses to stimulation of the left splanchnic nerve at frequencies of 1, 2, 4, and 8 Hz were examined before the adrenals were removed. The results are shown in Figure 1. Right atrial pressure increased markedly, and portal pressure showed increases similar to those reported previously (Greenway et al., 1969; Greenway, 1979a). Stroke volume increased markedly, and this resulted in an increased cardiac output even though heart rate decreased. Arterial pressure increased, but calculated peripheral resistance (arterial minus right atrial pressure divided by cardiac output) was unchanged except at the highest frequency of stimulation.

**Responses in Adrenalectomized Cats**

In nine cats, the adrenals were removed after the first series of stimulations, and in an additional 14 cats, the adrenals were removed initially. The nerves were stimulated as before and the results are shown in Figure 2. After adrenalectomy, left splanchnic nerve stimulation failed to cause a significant rise in cardiac output. The changes in right atrial pressure and portal pressure were not significantly different from those in cats with intact adrenals. Although the control heart rate was somewhat greater, the decreases during stimulation were similar to those in the previous series. In this series, although stroke volume did increase, the increase...
FIGURE 2 Effects of left splanchnic nerve stimulation in 23 adrenalectomized cats.

was much smaller than in the first series and was sufficient only to compensate for the decreased heart rate; hence, cardiac output did not increase. Examination of the responses in individual cats showed that, in some, cardiac output increased slightly, whereas in others, it decreased to below the prestimulation control level. In these latter cats, the increases in calculated peripheral resistance were substantial.

It seemed possible that the absence of an increased cardiac output in this series was due to inhibition of the positive inotropic effect of the sympathetic nerves, through the baroreceptor reflex. Such an effect might have been overcome in the cats with intact adrenals by the direct action of medullary catecholamines on the heart. To test this hypothesis, we examined the responses after elimination of the baroreceptor reflexes.

Responses after Adrenalectomy and Elimination of the Baroreceptor Reflex

In four cats, the responses to splanchnic nerve stimulation were recorded after bilateral vagotomy with the carotid arteries intact, whereas in two cats, the responses were recorded during constant carotid arterial pressure but with the vagi intact. There were no obvious differences between these cats and those in the adrenalectomized series. This suggested that neither bilateral vagotomy nor constant carotid arterial pressure alone caused a change in the responses to nerve stimulation.

In six cats, the responses were examined after both bilateral vagotomy and constant carotid arterial perfusion. As arterial pressure rose during nerve stimulation, the clamp on the carotid arterial long-circuit was closed to maintain distal carotid arterial pressure at the prestimulation level. The results in this series are shown in Figure 3. The decreases in heart rate were abolished, and the increases in arterial pressure and calculated peripheral resistance were greater than in the previous series. Although the rise in right atrial pressure was slightly smaller, it was still highly significant, and the rise in portal pressure was as large as before, suggesting that nerve stimulation was mobilizing blood from the splanchnic reservoir. However, stroke volume and cardiac output still failed to increase. The control values of cardiac output tended to decrease...
during these series; the reason for this was not clear. Thus, removal of the influence of the baroreceptor reflex prevented a decrease in heart rate but did not allow cardiac output to increase in response to the rise in right atrial pressure. We therefore formulated the new hypothesis that the effects of the increase in afterload (arterial pressure) balanced the effects of the increase in preload. We therefore examined the effects of preventing the increase in afterload.

Responses in Adrenalectomized Cats Given Nitroprusside during Stimulation

In 10 cats, sodium nitroprusside was infused intravenously beginning 30 seconds before the onset of nerve stimulation, in doses which, as closely as possible, held arterial pressure at the prestimulation level. The doses required ranged from 2 to 20 μg/min per kg. By themselves, these doses caused a fall in arterial pressure and a decrease in cardiac output in all the cats. The responses to nerve stimulation are shown in Figure 4. It can be seen clearly that, when the arterial pressure was held constant during splanchnic nerve stimulation, there was a marked increase in cardiac output and stroke volume and that this was achieved in spite of a very much smaller rise in preload (right atrial pressure). Since we have shown previously that sodium nitroprusside infusions do not reduce the hepatic venous responses to sympathetic nerve stimulation (Greenway, 1979a), it appeared likely that the smaller increase in right atrial pressure was due to the ability of the heart to pump the mobilized blood out of the central veins.

Although it seemed most likely that the responses in this series were consequences of the control of arterial pressure, it remained possible that nitroprusside had other unknown actions. We therefore reexamined this question in another series.

Responses in Adrenalectomized Cats with an Arteriovenous (A-V) Shunt

In five cats, after administration of 2000 IU heparin, intravenously, the lower abdominal aorta and inferior vena cava were cannulated with 4-cm long Teflon cannulas (i.d. 5 mm) connected by a 12-cm length of Silastic tubing (i.d. 8 mm). The long-circuit was clamped during the control periods and opened sufficiently during nerve stimulation to prevent any increase in arterial pressure. The results are shown in Figure 5. It can be seen that increases in stroke volume and cardiac output occurred, but these were somewhat smaller than during the nitroprusside infusions even though the increases in preload (right atrial pressure) were again larger. The control values for cardiac output and stroke volume were smaller than in previous series due to occlusion of the circulation to the hindquarters. It seemed possible that the differences between the responses during nitroprusside infusions and during A-V shunt control of arterial pressure might reflect differences in the pulmonary arterial pressure since nitroprusside might be expected to relax the pulmonary vessels as well as the systemic arterioles.

Changes in Pulmonary Arterial Pressure during Splanchnic Nerve Stimulation

In three cats, pulmonary arterial pressure was recorded at the same time that the other measurements were made. The cats were adrenalectomized, and a series of nerve stimulations was carried out. A second series was then done with nitroprusside infusions to control arterial pressure. The cats were then heparinized, and a third series was carried out with an A-V shunt to control arterial pressure. The responses were similar to those previously described, and the pulmonary arterial pressure responses are shown in Figure 6. It can be seen that splanchnic nerve stimulation caused increases in pulmonary arterial pressure in the adrenalectomized series where there were no changes in cardiac output and in the A-V shunt series where arterial pressure was controlled and cardiac output in-
Discussion

The primary objective of these experiments was to examine the relationships between splanchnic vasoconstriction and cardiac output and the effects of the simultaneous increase in afterload caused by splanchnic arteriolar vasoconstriction. We were unable to measure all the variables required for a complete analysis. We could not simultaneously measure the volumes of blood mobilized from the intestine, liver, and spleen, and we had to rely on the extensive data in the literature (Table 1). However, the responses we have obtained have remained consistent over 10 years, and we have seen no consistent differences in the responses to stimulation of the splanchnic nerves and the post-ganglionic fibers to the individual organs. Thus, the adrenal medullary secretions do not modify the direct venous responses to any marked degree. We were unable to study the pulmonary circulation adequately in all the experiments, we measured mean right atrial pressure rather than right ventricular end-diastolic pressure, and we did not record left ventricular end-diastolic pressure. Thus we have to analyze the data in terms of overall cardiac function and accept the problems of using mean atrial instead of end-diastolic ventricular pressure (Sarnoff et al., 1965). Within these limitations, we are able to report the effects of splanchnic nerve stimulation on cardiac preload, afterload, and output.

Splanchnic vasoconstriction mobilizes blood from the splanchnic venous reservoir and in turn raises right atrial pressure. The extent of this rise in right atrial pressure depends on two factors which come into balance—the ability of the heart to increase cardiac output and the extent to which the rise in right atrial pressure causes pooling of blood in other venous beds, that is, the overall compliance of the venous system. In the adrenalectomized series, cardiac output did not increase, and the entire volume of blood expelled from the splanchnic venous bed must have pooled elsewhere in the venous system. From the total volumes of blood mobilized (Table 1) and the increments in right atrial pressure (Fig. 2), the overall venous compliance is 4.03 ± 0.15 (mean ± SE) ml/kg per mm Hg. This value is somewhat higher than values reported in the literature for dogs (Shoukas and Sagawa, 1973; Drees and Rothe, 1974; Mitzner and Goldberg, 1975). This value for venous compliance can then be applied in the nitroprusside series. In this series, a part of the blood volume mobilized was pooled due to the increase in right atrial pressure. The remainder resulted in a sustained increase in cardiac output (Fig. 4) of 3.10 ± 0.37 ml/min per kg for each 1 ml/kg of blood that was mobilized but not pooled in the systemic venous bed as a consequence of the rise in right atrial pressure.

Visual inspection of the data suggested that stroke volume was determined by the balance between cardiac preload approximated by right atrial pressure.
pressure and cardiac afterload approximated by arterial pressure. There has been considerable discussion on which parameter is the best measure of afterload, and if mean arterial pressure is used, on what is the best expression of the relationship between stroke volume and arterial pressure (Ross, 1976; Parmley et al., 1977). With the data available to us, we calculated an approximation to stroke work (stroke volume times arterial minus right atrial pressures), and the relationship between these calculated values and right atrial pressure is shown in Figure 7. It can be seen that four of the six groups of data appear to fall on a single curve. The values during stimulation of the nerves in cats with intact adrenals were much greater than in the other series. The values during nerve stimulation in the A-V shunt series tend to fall below the curve. These exceptions are discussed later. The curve formed by the rest of the data (excluding the cats with intact adrenals and those with an A-V shunt) is not linear or logarithmic, and an equation to describe it was therefore obtained using a polynomial regression program. Stroke work equalled 4.6(RAP)² - 9.4/(Arterial pressure - RAP), where RAP is right atrial pressure. For right atrial pressures above 6 mm Hg, the value of cardiac output for a right atrial pressure of 6 mm Hg must be used since the equation does not model the flat part of the curve. The role of contractility is discussed later.

These results in adrenalectomized cats with an intact venous system suggest that afterload is an important determinant of cardiac output. This conclusion is somewhat at variance with results obtained in preparations where right atrial pressure and aortic pressure were controlled independently (Sonnenblick and Downing, 1963; Herndon and Sagawa, 1969). Under these conditions, stroke volume was relatively independent of arterial pressure up to about 180 mm Hg at any given atrial pressure, and markedly different stroke work-end-diastolic pressure curves were obtained at different arterial pressures. We are unable to account for these differences.

Our calculations of stroke work do not involve right ventricular afterload (approximated by pulmonary arterial pressure), and the experiments reported here on pulmonary arterial pressure must be regarded as a preliminary study. In the series in which pulmonary arterial pressure and systemic arterial pressure either changed together (adrenalectomized series) or both remained constant (nitroprusside series), the data fitted the analysis in Figure 7. However in the A-V shunt series, systemic arterial pressure remained constant, whereas pulmonary arterial pressure increased during nerve stimulation (Fig. 6). The points for stroke work fell below those for the other series (Fig. 7). It seems possible that, if changes in pulmonary pressure were incorporated into the calculation of stroke work, this series might also lie on the same curve, but we do not have sufficient data for a quantitative analysis. Nevertheless, it seems clear that it is important to consider pulmonary arterial pressure as well as systemic arterial pressure as a component of afterload when attempting to predict cardiac output.

In some ways, the responses during splanchnic nerve stimulation in the absence of the adrenals resemble the situation in clinical heart failure. In both cases, increases in venous and right atrial pressures fail to increase cardiac output. If afterload

<table>
<thead>
<tr>
<th>Group</th>
<th>Protocol</th>
<th>Portal pressure</th>
<th>Right atrial pressure</th>
<th>Pulmonary artery pressure</th>
<th>Stroke volume x Heart rate</th>
<th>Cardiac output</th>
<th>Peripheral resistance</th>
<th>Arterial pressure</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Adrenals intact</td>
<td>+</td>
<td>++</td>
<td>NM</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Adrenex</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Adrenex + reflex block</td>
<td>+</td>
<td>+</td>
<td>NM</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>4</td>
<td>Adrenex + nitropr.</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>0</td>
<td>++</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Adrenex + A-V shunt</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>?</td>
</tr>
</tbody>
</table>

* increase; 0 no change; — decrease; NM not measured; ? small change not significant at all frequencies; adrenex = adrenalectomized cats, nitropr = nitroprusside.

**Figure 7** Relationship between stroke work calculated as stroke volume times arterial minus right atrial pressures and mean right atrial pressure for all the experiments. The solid line was calculated from the data excluding the responses during nerve stimulation in cats with intact adrenals and with A-V shunts.
is decreased, cardiac output will tend to increase, and this in turn will result in a decrease in preload. This decrease in preload will normally tend to limit the change in cardiac output but, if right atrial pressure is greater than 6 mm Hg (where the curve becomes flat in Fig. 7), a decrease in preload will not have this limiting effect. Hence, the patient in heart failure should show a larger change in cardiac output in response to arteriolar vasodilators. In addition, a more complete equation would also include right ventricular afterload and, if sodium nitroprusside reduced right ventricular afterload, as occurred in our cats, this could explain the puzzling observation that, in some patients, nitroprusside increases cardiac output with no change in left ventricular afterload (arterial pressure) (Parnley et al., 1977).

So far, we have taken no account of changes in contractility. The data in Figure 7 fall on a single Frank-Starling curve suggesting contractility was approximately constant in these experiments. The stroke work during nerve stimulation in cats with intact adrenal glands was clearly much greater, as would be expected from the known effects of catecholamines on contractility (Innes and Nickerson, 1975). It was surprising, however, that stroke work during nerve stimulation in the adrenalectomized cats was not reduced below the curve since heart rate fell substantially. This suggests that the negative chronotropic effects of the baroreceptor reflex were not accompanied by negative inotropic effects.

The role of renin in these responses has not been investigated. It may play a significant role. It is well known that the intestinal and hepatic arterial vascular constriction produced by splanchnic nerve stimulation is not well maintained in cats (autoregulatory escape—Folkow et al., 1963; Greenway and Stark, 1971), and yet the increase in arterial pressure was well maintained during up to 8 minutes of nerve stimulation. Also, the increases in arterial pressure were often greater than those obtained by complete mechanical occlusion of the celiac and mesenteric arteries (unpublished observations). This suggests that splanchnic nerve stimulation produced a more generalized vasoconstriction, and this could have been mediated by angiotensin. Further studies on this aspect are required.

Finally, the effects of splanchnic nerve stimulation in this paper have important implications in regard to CNS control of cardiac output by modulation of venous reservoirs. It is clearly important to know whether the CNS can selectively activate the splanchnic venoconstrictor fibers or whether vasoconstriction is always accompanied by arteriolar vasoconstriction and medullary catecholamine secretion. It seems clear that activation of the sympathetic nerves to the liver, spleen, and intestine is not necessarily accompanied by adrenal medullary secretion in the dog. Hemorrhage causes sympathetic effects on the hepatic venous bed (Brooksby and Donald, 1972; Carneiro and Donald, 1977b) but may not always release catecholamines (Hall and Hodge, 1971). In cats, hemorrhage causes splanchnic vascular responses (Greenway and Lister, 1974), and adrenal medullary secretion increases if the hemorrhage is rapid but not if it is slow (Hall and Hodge, 1971). In cats, inhibition of the carotid baroreceptors causes hepatic arteriolar vasoconstriction without hepatic venoconstriction (Lautt and Greenway, 1972) but, in dogs, both sections of the hepatic vascular bed appear to be constricted (Brooksby and Donald, 1971; Karim and Hainsworth, 1976; Carneiro and Donald, 1977a, 1977b). Thus, differentiated CNS control of splanchnic arteriolar and splanchnic venous reservoir function and its implications for control of cardiac output require further study.

Acknowledgments

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