ABSTRACT

In anesthetized vagotomized cats with both carotid arteries occluded, stretch of the walls of the thoracic aorta performed without obstructing aortic blood flow induced reflex increases in arterial blood pressure (systolic: 136 ± 4 [SE] to 170 ± 7 mm Hg), heart rate (230 ± 10 to 236 ± 11 beats/min), and maximum rate of rise of left ventricular pressure (dP/dt max) (2,337 ± 256 to 3,155 ± 302 mm Hg/sec). In cats with spinal transection (C7), similar increases were observed. These responses were abolished by infilrating the walls of the thoracic aorta with xylocaine. In adrenalectomized cats with intact central nervous systems, reflex responses were reduced but were still statistically significant. Phenoxybenzamine abolished the pressor response but not the increases in heart rate and dP/dt max. Propranolol drastically reduced the increases in heart rate and dP/dt max but not the pressor response. It is concluded that stretch of the thoracic aorta induced an increase in sympathetic activity affecting the heart, the peripheral vessels, and, probably, the adrenal glands through a spinal reflex.

KEY WORDS
dP/dt max
spinal sympathetic cardiovascular reflexes
adrenal glands
vagotomy

Methods

Nineteen cats were anesthetized with chloralose and urethane (60 and 250 mg/kg, respectively, ip). In two cats sodium pentobarbital (35 mg/kg, ip) was used. The cervical vagi were cut, and then a carotid artery and a femoral artery were cannulated with short, wide-bore polyethylene catheters. After injection of a paralyzing dose of gallamine triethiodide, positive-pressure respiration was initiated using a Harvard respirator connected to a tracheal cannula. The respirator was adjusted to maintain arterial gases and pH (measured on an Astrup model RM 1304 blood acid-base analyzer) within physiological limits. The guidelines of the American Physiological Society regarding anesthetized, curarized animals were observed.

In five cats the spinal cord was sectioned at C7. In another five cats hydrocortisone (20 mg, iv) was administered, and the adrenal glands were removed through an abdominal midline laparotomy. Additional hydrocortisone (30 mg/hour) was then administered during the experiment by slow intravenous infusion.
Hemodynamic Responses to Aortic Stretch

All cats were placed on their right side, and the left hemithorax was widely opened from the fourth to the tenth rib. A special cannula was used to stretch the walls of the thoracic aorta without obstructing aortic blood flow. It consisted of a stainless steel tube surrounded by a thin rubber cylinder which could be inflated via a metal tube mounted perpendicular to the catheter. The vessel was completely divided and the cannula inserted. Cannulas of different dimensions (5-7 cm long, 3-5 mm, i.d.) were selected according to the size of the aorta. The cannula was heparinized and a thin rubber tube close to one end of the cannula. The cat was heparinized 7 days before the experiment. The cannula measured by comparing the carotid and femoral pressures. It consisted of a stainless steel tube surrounded by a thin rubber cylinder which could be inflated via a metal tube mounted perpendicular to the catheter. The vessel was completely divided and the cannula inserted. Cannulas of different dimensions (5-7 cm long, 3-5 mm, i.d.) were selected according to the size of the aorta. The cannula was heparinized and a thin rubber tube close to one end of the cannula. The cat was heparinized 7 days before the experiment. The cannula measured by comparing the carotid and femoral pressures.

**TABLE 1**

Effects of Stretching the Walls of the Thoracic Aorta in Vagotomized Cats

<table>
<thead>
<tr>
<th>Group</th>
<th>No. cats</th>
<th>No. trials</th>
<th>Carotid artery systolic pressure (mm Hg)</th>
<th>Carotid artery diastolic pressure (mm Hg)</th>
<th>Left ventricular end-diastolic pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Left ventricular dP/dt max (mm Hg/sec)</th>
</tr>
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<tbody>
<tr>
<td>Intact CNS</td>
<td>8</td>
<td>33</td>
<td>136 ± 4</td>
<td>105 ± 3</td>
<td>2.9 ± 0.8</td>
<td>230 ± 10</td>
<td>2337 ± 256</td>
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<tr>
<td>Spinal cord section</td>
<td>6</td>
<td>26</td>
<td>113 ± 6</td>
<td>74 ± 5</td>
<td>3.5 ± 0.3</td>
<td>172 ± 17</td>
<td>2108 ± 260</td>
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<tr>
<td>Adrenalectomized</td>
<td>5</td>
<td>16</td>
<td>131 ± 7</td>
<td>92 ± 9</td>
<td>4.8 ± 1.1</td>
<td>221 ± 13</td>
<td>2052 ± 548</td>
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<tr>
<td>(intact CNS)</td>
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</table>

Both common carotid arteries were occluded and the vagi cut in all cats. All values are means ± SE. P values were determined using a paired t-test. NS = not significant.

CNS = central nervous system.
Results

Cats with Intact Central Nervous Systems.—In eight vagotomized cats with both their common carotid arteries occluded, stretch of the walls of the thoracic aorta induced marked increases in systolic, diastolic, and pulse arterial pressures, left ventricular systolic pressure, and dP/dt max. Heart rate increased only a few beats per minute, and left ventricular end-diastolic pressure increased by less than 1 mm Hg. All these changes were statistically significant (Table 1). Figure 1A shows one of these experiments: blood pressures, left ventricular dP/dt max, and heart rate rose soon after inflation of the balloon and remained elevated throughout the period of stimulation. These hemodynamic effects were not due to obstruction of the thoracic aortic blood flow caused by the experimental maneuver, since a parallel pressure increase was observed both above and below the cannula. In several experiments, as in the one presented in Figure 1A, a second late increase in blood pressure was recorded after the initial rise. When the balloon was deflated, all variables decreased toward control levels, which were reached after different periods of time (30-230 seconds).

These cardiovascular responses were much less evident if one common carotid artery was not occluded, thus allowing the full operation of that baroreceptive area.

Cats with Spinal Section.—In six vagotomized cats with their spinal cord sectioned at C1, the aortic stretch produced similar circulatory responses (Table 1). Figure 2 shows one of these experiments. All variables returned to control 30–120 seconds after cessation of the stimulus.

Reflex Nature of the Response.—In four cats with intact central nervous systems and in one with spinal section, 1% xylocaine was infiltrated under the adventitia of that portion of the thoracic aorta which was stretched by the balloon. Table 2 shows the very significant reduction or abolition of all of the responses to aortic stretch induced by this procedure. The small decrease in dP/dt max shown in Table 2 was not due to the stimulus; it probably resulted from some absorption of the anesthetic into the bloodstream. After administration of xylocaine, however, the cat's reactivity was still perfectly preserved, as shown by the cardiovascular responses to a strong nociceptive stimulus (clamping of the paw). Light nociceptive stimuli did not elicit cardiovascular responses because of the level of anesthesia. These experiments showed that the effects of aortic stretch were initiated from receptors located in the aortic walls.

Peripheral Mechanisms of the Reflex Responses.—To assess the contributions of cardiac and peripheral vascular mechanisms to the responses elicited by aortic stretch, adrenergic blockade and cardiac denervation were carried out in some cats.

Propranolol (1 mg/kg, iv) was injected over a period of 30 minutes in four cats with intact central nervous systems. Left ventricular dP/dt max and
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After slow intravenous injection of phenoxybenzamine hydrochloride (5 mg/kg) in four spinal cats, the increase in systolic pressure induced by aortic stretch was drastically reduced; arterial diastolic pressure was somewhat decreased, and pulse pressure was increased. There were slight decreases in left ventricular end-diastolic pressure. The response of dP/dt max was not significantly altered, but heart rate increased much more than it did in the control period (Table 2). The cardiac effects (heart rate, dP/dt max) of the aortic stretch were prolonged and continued after cessation of the stimulus (Fig. 2B).

Sympathetic denervation of the heart was performed in some cats by cutting the cardiac nerves or by bilateral stellectomy. Although the cardiac effects of aortic stretch were reduced, they could not be abolished by denervation. Since the residual effects could have been mediated by a reflex increase in catecholamine output from the adrenal glands, the experiments were repeated in a group of adrenalectomized cats.

Adrenalectomized Cats.—After removal of the adrenal glands, the aortic stretch still induced all the described cardiovascular effects in five cats with intact central nervous systems (Table 1). The magnitude of the responses was smaller than it was in the cats with adrenal glands, although the difference was statistically significant only for the arterial pressure effects. The maximum changes were observed soon after the onset of the stimulus, and the late rise in blood pressure was never seen in this group of cats (Fig. 3). Moreover, when the balloon was deflated, all variables returned to control levels after short periods of time (4–15 seconds).

In two of these cats, section of the left inferior cardiac nerve and the pericoronary nerve completely abolished the cardiac effects of the stimulation. It is therefore very likely that in cats with adrenal glands the residual cardiac effects of aortic stretch after cardiac denervation are due to a reflex increase in the adrenal output of catecholamines.

Effect of an Afterload Increase on Left Ventricular dP/dt max.—In six cats, an increase in systolic arterial pressure comparable to that elicited by aortic wall distention was induced by

heart rate were decreased by the drug. Aortic stretch induced a smaller but clear increase in arterial and left ventricular pressures; heart rate remained constant, and left ventricular dP/dt max increased only very slightly and slowly during the period of stimulation (Fig. 1B).

The changes in hemodynamic responses are shown in Table 2.

<table>
<thead>
<tr>
<th>Effect of Phenoxybenzamine and Propranolol on the Reflex Responses Elicited by Aortic Stretch</th>
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</table>

All values are means ± P values were determined by a paired Student’s t-test. ns = not significant. Δ = maximum changes induced by aortic wall distention. Xylocaine was injected intravenously after anesthesia (1 mg/kg), and propranolol (5 mg/kg) and phenoxybenzamine (5 mg/kg) were administered intravenously.
Effects of stretching the thoracic aorta in an adrenalectomized vagotomized cat with an intact central nervous system and both common carotid arteries occluded. Abbreviations are the same as they are in Figure 1.

partially obstructing the aorta with a tourniquet. The average percent rise in $dP/dt$ max obtained in this way (+12%) was much smaller than that induced by aortic stretch (+32%). This difference was statistically significant ($P < 0.05$).

**Effect of Different Anesthetics.**—The reflex effects obtained in two cats anesthetized with sodium pentobarbital (one with an intact central nervous system and one with spinal cord section) were similar to those obtained in the other cats anesthetized with the chloralose-urethane mixture.

**Adequacy of the Stimulus.**—All the cardiovascular responses that have been described were clearly evident with stretches that increased aortic diameter, measured with a precision caliper at the point of maximum distention, only 10%. This change in aortic radius was of the same magnitude as that observed when the mean pressure of the thoracic aorta was mechanically increased (aortic stenosis) 50–60 mm Hg. A similar distensibility of the aortic walls has been reported in the dog (17). The stimulus we used was therefore comparable to changes that can be observed in physiological situations.

**Discussion**

A mechanical stretch of the walls of the thoracic aorta induced significant increases in systemic arterial blood pressure, heart rate, and left ventricular $dP/dt$ max. These cardiovascular responses were not due to some direct interference with aortic blood flow caused by the experimental maneuver; they represented neurally mediated phenomena, since they all disappeared after infiltration of the aortic walls with a local anesthetic. The same responses were present in spinal preparations, and, therefore, the integration of the reflex appears to take place in the spinal cord. It is probable that supraspinal baroreceptive mechanisms exert an inhibitory influence on these reflex responses, because the effects of aortic stretch were greatly attenuated unless both common carotid arteries were occluded in vagotomized cats with intact brains.

Gruhzit et al. (18) have observed that a rise in aortic pressure, produced in dogs by intravenous injection of epinephrine, induces a reflex hind-limb vasodilatation initiated by receptors which are probably located in the thoracic aorta and mediated by spinal afferent pathways. It is difficult to compare their results with ours because of the differences in the stimuli and the preparations. Furthermore, the fact that we always observed a rise in arterial blood pressure does not rule out the possibility that some vasodilatation occurred in some vascular territories.

Alpha-receptor blockade suppressed the rise in blood pressures induced by the aortic stretch but not the increase in heart rate and left ventricular $dP/dt$ max. Actually a much larger increase in heart rate was observed after administration of phenoxybenzamine. This increase probably resulted from inhibition of norepinephrine reuptake or interference with catecholamine metabolism by the drug (19), which would result in greater availability of adrenergic transmitter for beta-stimulating effects. The decrease in arterial diastolic pressure observed under these conditions was presumably due to some beta-adrenergic (20) or sympathetic cholinergic (21) vasodilatation induced by the stimulus. Thus, the experiments with alpha-receptor blockade showed that the blood pressure increase was mainly due to peripheral vasoconstriction and that the rise in $dP/dt$ max was largely independent of the increase in afterload and could actually occur even when aortic diastolic pressure decreased during stimulation (Fig. 2B). The modest influence of increases in afterload on $dP/dt$ max was further proven by comparing the effects of similar rises in aortic pressure during...
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reflex responses and during mechanical constriction of the aorta (see Results).

The administration of a beta-receptor blocking agent did not affect the increases in blood pressure but completely abolished the tachycardia and drastically reduced the increase in dP/dt max. The very small residual effect on dP/dt max probably depended mostly, if not exclusively, on the rise in afterload (22, 23).

The validity of left ventricular dP/dt max as an index of myocardial contractility was supported in these experiments by the fact that its maximum value was always attained before the opening of the semilunar valves (23). However, before assuming that the increase in dP/dt max was the result of an increase in sympathetic discharge to the heart, other factors should be ruled out, i.e., changes in afterload, preload, heart rate, and circulating catecholamines (13, 22, 23). The role of afterload has already been discussed. The influence of changes in preload on dP/dt max (23) must have been minimum, since left ventricular end-diastolic pressure remained practically constant during aortic stretch. It also seems unlikely that the rise in dP/dt max resulted primarily from a staircase phenomenon (23) caused by the simultaneously elicited tachycardia, because heart rate only increased a few beats per minute even though dP/dt max increased much more substantially (in average 30% over control values).

Another point that should be discussed is the contribution of the adrenal glands to the observed cardiovascular responses. On purely theoretical grounds, an increase in afferent nervous activity involving several spinal segments (T7-T10) in part corresponding to those from which the splanchnic nerves originate should reflexly stimulate adrenal secretion. This supposition was supported by the fact that the cardiac effects of aortic stretch could not be completely suppressed by cardiac denervation. This last observation contrasts with results found when cardiovascular responses are elicited through afferent cardiac sympathetic fibers projecting to higher segments of the spinal cord (13, 14). However, the persistence of all the reflex responses in adrenalectomized cats proved that they were only partly due to increased catecholamine output from the adrenal glands. As predicted, in these cats cardiac denervation completely abolished the reflex increases in heart rate and dP/dt max.

In conclusion, our experiments indicate the existence of spinal cardiovascular reflexes initiated by mechanical stimuli acting on vascular sensory endings. We are not suggesting that the thoracic aorta represents another reflexogenic area in the classical sense: on the contrary, it is likely that nervous control of circulation is obtained through a variety of neural circuits (1, 3, 4) and that spinal reflexes represent diffuse, elementary mechanisms. The spinal reflex discussed in the present paper appears to operate by a positive feedback mechanism: a stimulus likely to duplicate the effects of an increase in aortic blood pressure produces a further increase in blood pressure, heart rate, and dP/dt max. Thus, the conception that nervous control of the circulation is exerted exclusively through negative feedback mechanisms seems to be in conflict with some of the experimental evidence.

References


Reflex Hemodynamic Responses Initiated from the Thoracic Aorta
FRANCO LIOY, ALBERTO MALLIANI, MASSIMO PAGANI, GIORGIO RECORDATI and
PETER J. SCHWARTZ

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