Epinephrine and the Carotid Sinus
Baroreceptor Reflex

Influence on Capacitive and Resistive Properties of the Total Systemic Vascular Bed of the Dog

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SUMMARY  To quantify the interaction between epinephrine infusion and carotid sinus baroreceptor reflex control of vascular capacity and resistance, we have simultaneously measured total systemic compliance, $C_t$, arterial compliance, $C_a$, changes in "unstressed vascular volume," $AV_0$, and resistance, $R$, in nine dogs whose carotid sinuses were isolated and cardiac output fixed by a perfusion pump. In response to intrasinus pressures (ISP) of 50, 125, and 200 mm Hg without epinephrine infusion, total systemic compliance ($C_t$) was 1.00, 1.10, and 1.22 ml/mm Hg per kg, whereas arterial compliance showed no change and averaged 0.0984 ml/mm Hg per kg for all ISP's. Resistance was 1.45, 0.88, and 0.57 mm Hg/(ml per min per kg) for intrasinus pressure of 50, 125, and 200 mm Hg. The change in unstressed vascular volume from ISP of 50 to 125 was 7.32 ml/kg and 5.03 ml/kg for an ISP change from 125 to 200 mm Hg. When epinephrine was infused at a constant rate of 1.3 μg/min per kg at a fixed ISP of 125 mm Hg, arterial pressure rose by 69.1 mm Hg, the change in unstressed vascular volume was 8.02 ml/kg, and resistance increased from 0.89 to 1.54 mm Hg/(ml per min per kg), an increase of 73% of control. At the same infusion rate and at each ISP of 50, 125, and 200 mm Hg, compliances, $C_t$ and $C_a$ and resistance were measured. In contrast to the control data, $C_t$ showed no increase with changes in ISP (0.92, 0.94, and 0.92 ml/mm Hg per kg), whereas $C_a$ measured 0.081 ml/mm Hg per kg. Resistance was 1.71, 1.46, and 1.19 mm Hg/min per kg for intrasinus pressures of 50, 125, and 200 mm Hg. The change in unstressed vascular volume caused by an ISP change of 50-125 mm Hg was 1.78 ml/kg and for an ISP change of 125-200 mm Hg was 1.30 ml/kg. The data indicate that epinephrine greatly attenuates the reflex control of the vascular properties by mechanisms other than the modification of the carotid sinus receptor characteristics.


THE pressor action of epinephrine is well documented in most textbooks of physiology. However, most of the studies on epinephrine have used isolated parts of the circulation. Difficulty arises when one attempts to quantify the contributions of these various parts to the overall pressor effect of epinephrine (Ahlquist, 1963).

Caldini et al. (1974) and Emerson (1966), using preparations in which venous return was diverted into a reservoir while keeping cardiac output constant, studied the effects of epinephrine in the overall systemic vascular bed. Although these studies dealt with the quantitative effects of epinephrine on the capacitive and resistive properties of the systemic vascular bed, the carotid sinus and aortic arch baroreceptor regions were not denervated, and the pressures in these receptor areas were not controlled. Thus, the apparent actions of epinephrine could have been buffered by the carotid sinus baroreceptor reflex which has been shown to change vascular resistance and capacity (Shoukas and Sagawa, 1973). Neither set of data separates the direct action of epinephrine from the buffering action of the reflex system.

The purpose of this investigation was to study the interaction between epinephrine infusion and carotid sinus baroreceptor reflex control of vascular capacity and resistance in the entire systemic vascular bed of the dog.

Methods

Baroreceptor Reflex Control of Capacity and Resistance

Nine mongrel dogs (22.5 ± 1.3 kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv). Heat cauterization and complete ligation of the cut tissue masses were used for every incision to minimize blood loss.

The left and right carotid sinuses were isolated (Shoukas and Sagawa, 1973) from the rest of the circulatory system. The internal and external carotid arteries and any small branches originating from the carotid bifurcation were completely ligated. A four-way glass connector was attached to the distal segment of each common carotid artery, the proximal end of the right common carotid ar-
tery, and a servocontrolled nonpulsatile pressure-generating system. The proximal end of the right common carotid artery was clamped when intrasinus pressure was to be controlled. When the clamp was removed, intrasinus pressure would equal arterial pressure. Mean intrasinus pressure was monitored via catheters placed in the left and right lingual arteries and connected to a pressure transducer (Statham P23AC). The cervical vagosympathetic trunks were exposed and cut to eliminate the buffering effect of the aortic arch baroreceptor reflex and the cardiopulmonary receptor reflexes.

A right thoracotomy was performed at the 5th intercostal space under positive pressure ventilation with 95% O₂ and 5% CO₂. Figure 1 illustrates the surgical preparation and the perfusion circuit necessary to measure total systemic vascular compliance, arterial compliance, and blood volume shifts in the dog. The right atrial appendage was cannulated first and connected to the outflow side of a perfusion pump (Sarns Model 5M6002) primed with whole blood from another dog. The superior vena cava then was cannulated and blood drained into a reservoir. Perfusion was started immediately with an initial flow of 35 ml/min per kg. The inferior vena cava then was cannulated, and the pump flow was readjusted so that arterial pressure approached the level that existed before atrial cannulation and maintained constant throughout the experiment. Perfusion flow rate averaged 111.7 ± 3.9 (SD) ml/min per kg for the nine dogs tested. Ligation of the azygos vein completed the surgery.

Central mean arterial and venous pressures were measured through catheters placed in the thoracic aorta and the inferior vena cava via the right femoral artery and vein, respectively, and connected to pressure transducers (Statham P23AC and P23BB). Zero pressure was referenced at the junction of the inferior vena cava and the right heart under direct inspection. Blood volume in the reservoir was monitored continuously by recording the hydrostatic pressure of the column of blood with a pressure transducer (Beckman model 807, 215071). The system was calibrated by changing the reservoir blood volume by a known amount and recording the corresponding pressure change. The resolution of the blood volume change was 5.0 ml. All pressure, flow, and volume signals were smoothed by a filter with a time constant of 1 second and recorded on an ink recorder (Brush model Mark 200). All data presented were normalized to individual body weights to allow comparison among the dogs.

Intrasinus pressure initially was fixed at 125 mm Hg. The height of the opening of the tube draining venous return into the reservoir was adjusted such that mean central venous pressure measured 5 mm Hg. It previously was found that, at central venous pressures below 3.0 mm Hg, there was a pressure-dependent nonlinearity of compliance (Shoukas and Sagawa, 1971). We therefore chose a value of 5 mm Hg to minimize the nonlinearity in the compliance measurements. Only after arterial and venous pressures and reservoir volume reached steady state were measurements of total systemic and lumped arterial vascular compliances begun.

To determine the total vascular compliance, the height of the outflow tube was raised quickly, increasing central venous pressure by approximately 2 mm Hg. The blood volume in the reservoir decreased concomitantly with the venous pressure increase and reached a new steady value after 2-3 minutes. This change in steady state volume divided by the change in steady state venous pressure results in the total systemic vascular compliance. The outflow tube then was lowered to its previous control level of 5 mm Hg; this then caused a concomitant increase in steady state reservoir volume. Total systemic compliance again was calculated from the steady state changes in volume and venous pressure. The measurement of total compliance was

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repeated again to check the reproducibility of the data. This resulted in four measurements of total compliance between a central venous pressure of 5–7 mm Hg and an intrasinus pressure of 125 mm Hg.

A measure of the lumped arterial compliance was determined while intrasinus pressure was fixed at 125 mm Hg and after reservoir volume, mean arterial pressure, and venous pressure had reached steady state levels. Mean arterial pressure was decreased by approximately 25–50 mm Hg by transferring blood from the arteries to the reservoir through the auxiliary pump (Fig. 1) while venous pressure was maintained constant. This decrease in mean arterial pressure caused a steady state increase in reservoir blood volume. The ratio of this blood volume change to the change in mean arterial blood pressure was calculated as a measure of lumped arterial compliance. The pump was stopped and mean arterial pressure rose to its original level while steady state reservoir volume decreased. This change gave another value of arterial compliance. Mean arterial pressure then was raised by infusion of blood from the reservoir into the arteries. After a steady state had been reached the pump was stopped; this resulted in a decrease in arterial pressure back to control and the return of reservoir blood volume to its initial level.

Changes in total vascular capacity caused by the carotid sinus baroreceptor reflex were determined by measuring shifts of blood between the systemic vascular bed and the reservoir. With venous pressure controlled at 5 mm Hg and systemic flow maintained constant, the pressure in the isolated sinuses was changed from 125 to 50 mm Hg. Four minutes later, the resultant change in steady state reservoir blood volume was determined as a measure of the decrease in total vascular capacity.

At this new level of intrasinus pressure of 50 mm Hg, the total systemic vascular compliance and arterial compliance were again determined. Intrasinus pressure was elevated back to 125 mm Hg and the shifts of blood volume between the animal and reservoir were remeasured. Intrasinus pressure was then elevated to 200 mm Hg at a constant venous pressure of 5 mm Hg, and shifts of blood between the animal and reservoir were measured, as well as total systemic and arterial compliance.

After completing the control runs, we set intrasinus pressure at 125 mm Hg and venous pressure at 5 mm Hg. Arterial pressure and reservoir volume were allowed to reach steady state values. While intrasinus pressure and venous pressure were maintained at these values, epinephrine was injected at a constant rate (1.19 ± 0.03 μg/min per kg) into the reservoir. Reservoir blood volume and arterial pressure then were measured. The entire experimental procedure then was repeated as in the control runs. Arterial and total systemic compliance, blood volume shifts, and resistance changes were determined with the carotid sinus pressure set at 50, 125, and 200 mm Hg with epinephrine infusion at a rate of about 1 μg/min per kg.

Open Loop Analysis of Overall Baroreceptor Reflex

In a separate series of experiments, the effect of changing isolated carotid sinus pressure on mean systemic arterial pressure was determined before and during epinephrine infusion. Seven mongrel dogs weighing between 15.9 and 17.7 kg (mean weight of 17.2 ± 0.57 kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv). The carotid sinuses were isolated as previously described. Intrasinus and arterial pressures were monitored via catheters in the lingual artery and femoral artery. The dogs were allowed to breathe room air without the aid of a respirator. The vagus nerves were cut to eliminate any buffering effect of the aortic arch baroreceptors and cardiopulmonary receptors.

During a control run, intrasinus pressure was increased from 50 to 200 mm Hg, in steps of 25 mm Hg. Intrasinus pressure was then decreased from 200 to 50 mm Hg in steps of 25 mm Hg. An interval of at least 3 minutes was allowed between each step change in intrasinus pressure to allow arterial pressure to reach a steady state level. After this control run, intrasinus pressure was maintained at 125 mm Hg. After arterial pressure had reached a steady level, epinephrine was infused into the dog at a constant rate that ranged between 3.25 μg/min and 5.00 μg/min.

For each dog, the dose was classified low, medium, or high, depending on the increase in arterial pressure. A low dose produced a 5–20% increase in arterial pressure, a medium dose produced a 20–40% increase in arterial pressure, and a high dose produced a 40–60% increase in arterial pressure. The mean values ± se for low, medium, and high doses for seven dogs were 0.65 ± 0.13, 1.24 ± 0.22, and 1.85 ± 0.33 μg/min per kg. The order of infusion of low, medium, and high doses of epinephrine was random. At each level of constant-rate epinephrine infusion, intrasinus pressure was varied in a manner similar to that for the control runs. After the infusion of the three different doses of epinephrine, infusion was stopped and, after 10 minutes, a second control run was performed. The data from this control run and the control run prior to epinephrine infusion were combined and used in the analysis.

All data are reported as the mean value ± se of the mean. In series I experiments, nine dogs were tested, and in series II experiments seven dogs were tested. A P value less than 0.05 was considered to be significant, by paired t-test.

Results

Baroreceptor Reflex Control of Vascular Capacity and Resistance

In response to epinephrine infusion at a fixed intrasinus pressure of 125 mm Hg, the arterial pressure rose by 69.1 ± 11.13 mm Hg and reservoir
volume increased by 8.02 ± 1.21 ml/kg. The total systemic vascular resistance also increased from 0.89 ± 0.09 to 1.54 ± 0.21; this change was statistically significant (P < 0.001).

Before epinephrine infusion, when intrasinus pressure was either increased or decreased between 50 and 125 mm Hg, the change in reservoir volume was 7.32 ml/kg (fig. 2). This value is statistically different P < 0.001 by paired *t*-test from the value of 1.78 ml/kg obtained for the same change in intrasinus pressure during epinephrine infusion. Reservoir volume change was 5.03 ml/kg before the epinephrine infusion and decreased to 1.30 ml/kg during epinephrine infusion (P < .005) when intrasinus pressure was increased or decreased between 125 and 200 mm Hg. The total blood volume change before epinephrine infusion amounted to 12.35 ml/kg for an intrasinus pressure change from 50 to 200 mm Hg whereas, during epinephrine infusion, the value dropped to 3.08 ml/kg. The difference between these values (12.35 - 3.08), namely, 9.27 ml/kg, is very close to the change in reservoir volume of 8.02 ml/kg caused by the epinephrine infusion while intrasinus pressure was maintained at 125 mm Hg. Before epinephrine infusion, the reflex changes in reservoir volumes were significantly different (P < 0.02 paired *t*-test) for intrasinus pressure between 50 and 125 mm Hg (7.32 ml/kg) compared with 5.03 ml/kg for intrasinus pressure between 125 and 200 mm Hg. During epinephrine infusion, the reflex changes in reservoir volume were not significantly different between the two ranges of intrasinus pressure by paired *t*-test.

Shown in Figure 3 are the total systemic vascular compliances before and during epinephrine infusion for the three intrasinus pressures. Before epinephrine infusion, the compliance did increase significantly with increases in intrasinus pressure (P < 0.05). There was a 22% increase in the compliance for an intrasinus pressure increase from 50 to 200 before epinephrine infusion. However, no reflex increase in total systemic vascular compliance was seen during epinephrine infusion. Moreover, the compliance values were smaller than control at any intrasinus pressure, and the difference was significant at the P < 0.01 level for all intrasinus pressures.

Arterial compliance measured before and during epinephrine infusion and at each intrasinus pressure showed no statistically significant differences. The average value of arterial compliance at each intrasinus pressure both before and during epinephrine infusion averaged 0.083 ± 0.011 ml/mm Hg per kg.

Vascular resistance, calculated as the mean arterial pressure minus venous pressure divided by flow, showed highly significant (P < 0.005) decreases when intrasinus pressure was increased. Plotted in Figure 4 are the resistances as a function of intrasinus pressure. Epinephrine infusion caused the resistance to increase at each intrasinus pressure. These increases in resistance were significant at the P < 0.005 level by paired *t*-test. During the epinephrine infusion, the resistance still decreased significantly (P < 0.005) when intrasinus pressure was elevated from 50 to 125 and to 200 mm Hg. This finding is clearly different from the result for total systemic vascular compliance in which there were no changes with changes in intrasinus pressure after epinephrine infusion.

Before epinephrine infusion, the average change in arterial resistance for intrasinus pressures between 50 and 125 mm Hg was 0.57 ± 0.09 mm Hg/(ml per min per kg) and 0.317 ± 0.057 units between 125 and 200 mm Hg. The difference was significant (P < 0.005) between the two intrasinus pressure ranges. During epinephrine infusion, the average change in resistance was 0.22 ± 0.06 mm Hg/(ml per min per kg) for intrasinus pressure between 50 and 125 mm Hg and 0.28 ± 0.06 mm Hg/(ml per min per kg) for intrasinus pressure between 125 and 200 mm Hg. There was no statistically significant difference between these values.

**Open Loop Analysis of Baroreceptor Reflex**

As intrasinus pressure was decreased, mean arterial pressure increased in a sigmoidal manner. The mean value of the arterial pressure observed during decreasing intrasinus pressure is shown in the upper left panel of Figure 5. With infusion of epinephrine, mean arterial pressure was consistently higher at any given intrasinus pressure than the control. In addition, as the dose was increased, the intrasinus pressure vs. arterial pressure curves become successively flatter and less sigmoidal in shape. The difference in arterial pressures between
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1.50
0.50
0.00

CONTROL
EPINEPHRINE

TOTAL COMPLIANCE ml·mmHg⁻¹

INTRASINUS PRESSURE mmHg

FIGURE 3 Total systemic vascular compliances vs. intrasinus pressure before and after epinephrine infusion (1.19 mg/min per kg). See text for details.

the control curve and high-dose epinephrine curve at an intrasinus pressure of 50 mm Hg was smaller than the difference between the control curve and the high-dose epinephrine curve at an intrasinus pressure of 200 mm Hg.

Shown in the upper right panel of Figure 5 are the control runs and epinephrine curves when intrasinus pressure was increased. Again, a similar sigmoidal curve was obtained for all the curves. There was a consistent difference, \( P < 0.05 \), in arterial pressure between the control runs of decreasing and increasing intrasinus pressure at any given intrasinus pressure. This hysteresis was also seen during infusion of epinephrine.

The open loop gains for individual dogs were calculated for the control and epinephrine curves for either decreasing or increasing intrasinus pressure. The gain curves are shown in the lower panels of Figure 5. For decreasing intrasinus pressure (lower left panel of Figure 5), the maximum gain of 1.09 ± 0.05 occurred at a mean intrasinus pressure of 137.5 mm Hg for the control curves. This value diminished significantly \( (P < 0.05) \) to 0.91 ± 0.11, 0.82 ± 0.12, and 0.58 ± 0.13 with low, medium, and high rates of epinephrine infusion, respectively. The gain values between the control and epinephrine curves were not significantly different at other intrasinus pressures. The gain curves for increasing intrasinus pressure (lower right panel of Figure 5) showed similar results. The maximum gain was 0.77 ± 0.08, 0.62 ± 0.09, 0.56 ± 0.12, and 0.49 ± 0.10 for control low, medium, and high-dose epinephrine curves. Again, there was no significant differences between control and epinephrine curves except at the maximum gain which occurred at 137.5 mm Hg.

The maximum gain in individual dogs occurred either in the intrasinus pressure range from 100 to 125 or from 125 to 150 mm Hg. After epinephrine infusions at the maximum gain value still occurred in the same ranges as in the control runs for individual dogs. Since it was observed that, in individual dogs, the maximum gain occurred at different absolute values of intrasinus pressure, the simple averaging of arterial pressure and gain data from individual dogs at each intrasinus pressure tended to flatten the curves, as seen in Figure 5. It is desirable to know the arterial pressure and gain curves when flattening by averaging is avoided. For this purpose, the data were replotted by shifting the curves obtained from each dog so that the intrasinus pressures at which the peak gain occurred, ISPo, would superimpose on each other. This ISPo value was 123.2 ± 5.0 mm Hg for all seven dogs. Figure 6 shows the same data as Figure 5, except that in Figure 6 they were replotted after the curves were shifted.

Results similar to those in Figure 5 were obtained for the arterial pressure vs. ISPo curve (Fig. 6, upper panel). There was a consistent difference \( (P < 0.05) \) in arterial pressure between the control runs of decreasing and increasing intrasinus pressure after shifting ISPo. The difference was also present when epinephrine was infused.

The open-loop gains for individual dogs were recalculated for either decreasing or increasing intrasinus pressure and are shown in the lower panel of Figure 6. For decreasing intrasinus pressure (lower left panel of Figure 6), the maximum gain was 1.46 ± 0.12 for the control run. This value diminished significantly \( (P < .05) \) to 1.10 ± 0.11, 0.97 ± 0.10 and 0.81 ± 0.12 with low, medium, and high rates of epinephrine infusion, respectively. In

FIGURE 4 Total peripheral resistance vs. intrasinus pressure before and after epinephrine infusion. See text for explanation.
contrast to the data shown in Figure 5, the gain values between control and epinephrine curves were also significantly different at ISP₀ + 25 mm Hg and ISP₀ – 25 mm Hg. The gain curves for increasing intrasinus pressure showed very similar results. The maximum gain was 0.79 ± 0.09, 0.71 ± 0.11, 0.63 ± 0.09 and 0.49 ± 0.07 for control, low, medium, and high-dose epinephrine curves. The gain values were significantly different between control and epinephrine curves at ISP₀ – 25, ISP₀, and ISP₀ + 25.
Discussion

Our study demonstrates that pressure changes resulting from epinephrine infusion can be modified by the carotid sinus baroreceptor reflex. This result is opposite to the results of Brown and Hilton (1954, 1955) and Hilton and Brown (1956) from studies in which they infused bolus injections of epinephrine before and after denervation of the carotid sinus. They concluded that the carotid sinus baroreceptor reflex is ineffective in modifying the arterial pressure response to epinephrine. Kendrick (1959), using a preparation nearly identical to that used by Brown and Hilton (1954, 1955), concluded that the arterial pressure responses caused by bolus injections of epinephrine, depend on the existing sympathetic activity. Guyton and Gillespie (1951) studied the effects of epinephrine on arterial blood pressure in normal and areflexic dogs. In the normal dogs, epinephrine had no effect on arterial blood pressure until the rate of injection of epinephrine was above 1.0 μg/min per kg. In the areflexic dog, epinephrine caused significant increases in arterial pressure at infusion rates well below this value. These authors concluded that the reason for the lack of change in arterial pressure below a rate of 1.00 μg/min per kg in normal dogs was that the baroreceptors were controlling and maintaining the arterial blood pressure. The difference in the results may well stem from the fact that the studies of Brown and Hilton (1954, 1955) and Hilton and Brown (1956) looked only at the transient peak responses in arterial pressure to bolus injections of epinephrine, whereas we report steady state changes in arterial pressure caused by constant infusion of epinephrine.

When epinephrine was given at 1.0 μg/min per kg, the reflex change in reservoir blood volume was greatly attenuated, whereas the changes in total vascular compliance were totally abolished. A higher dose of epinephrine, 2.1 μg/min per kg, totally abolished the changes in reservoir blood volume. The reflex changes in resistance responses were greatly attenuated but were not abolished even at this high dose. The baroreceptor reflex seems to have a much greater effect on precapillary vessels than on postcapillary vessels. Other studies on isolated vascular beds also support this idea (Hadjiminas and Öberg, 1968; Folkow and Mellander 1960; Mellander, 1964).

The changes in reservoir blood volumes caused by epinephrine at constant intrasinus pressure amounted to 8.02 ml/kg. This value is slightly lower than the average value of 9.75 ml/kg found by Caldini et al. (1974), who used an epinephrine dose nearly five times that which we had given. Emerson (1966), using very similar techniques, obtained a value of nearly 20 ml/kg, which is nearly three times the value obtained in this study or in that by Caldini et al. (1974). Unfortunately, venous pressure was not controlled carefully in the Emerson study, and part of the volume change could have been caused by changes in venous pressure.

Although we did not specifically test whether the pressure-volume relationship was linear in this study, our previous results showed the total systemic compliance did not change between venous pressures of 3–10 mm Hg. (Shoukas and Sagawa, 1971). A linear pressure-volume relationship has also been confirmed by Drees and Rothe (1974) and Caldini et al. (1974), who used very different techniques.

The absolute value of the compliance in this study was 1.10 ml/mm Hg per kg which is nearly one half the value reported previously by us (Shoukas and Sagawa, 1971, 1973), as well as by others (Numao, 1977; Drees and Rothe, 1974). In the present experiments, we did not control dogs' body temperatures as critically as we had done in our other studies. In a separate study, we found that the difference in compliance values was caused to a major extent by the difference in body temperature. This finding also has been confirmed by Green and Jackman (1979). In our experiments, a decrease in body temperature of 6°C was found to decrease total systemic vascular compliance by nearly 42%. We therefore consider hypothermia to be the primary cause for the smaller compliance found in the present experiment. Despite this fact, the baroreceptor reflex was shown to affect the compliance of the systemic vascular bed to a mild but statistically significant degree. As shown in Figure 3, the total systemic vascular compliance before and during epinephrine infusion at any given intrasinus pressure also decreased. This decrease amounted to approximately 15% of the control. Mitzner and Goldberg (1975) and Caldini et al. (1974) also found very similar decreases in total systemic vascular compliance.

The lumped arterial compliance was found to be insensitive to both the baroreceptor reflex system and epinephrine infusion. The mean value for all intrasinus pressures was 0.081 ± 0.010 ml/mm Hg per kg. This value was not significantly different by t-test of mean from the value previously obtained of 0.0777 ± 0.025 ml/mm Hg per kg (Shoukas and Sagawa, 1973). Arterial compliance measured by our technique is an overestimate of the true lumped arterial compliance. Since flow through the systemic vascular bed was changed, there would be pressure changes in small veins despite the constancy of central venous pressure. Therefore, some venous volume is included in the volume change used to measure the lumped arterial compliance.

The total blood volume shifts in the reservoir amounted to 12.35 ml/kg for an intrasinus pressure change from 50 to 200 mm Hg. This value is nearly 5 ml/kg greater than the value of 7.5 ml/kg obtained previously (Shoukas and Sagawa, 1973). Part of the difference can be explained by the fact that the previous study covered only the range of intrasinus pressure from 75 to 175 mm Hg. The remainder may well be accounted for by the differences in body temperature between the two studies.
The blood volume shifts seen with the baroreceptor reflex can be, in part, caused by changes in unstressed vascular volume, as well as by changes in vascular compliance. For example, the 20% decrease in compliance value we measured at a venous pressure of 5 mm Hg can cause a 1.0 ml/kg shift of blood. This value is nearly 12% of the total shift in blood volume we observed. Caldini et al. (1974) hypothesized that epinephrine caused blood flow to redistribute from one region of small time constant to another region of large time constant, and this caused a passive volume shift from the dog to the reservoir, which amounts to 70% of the values we obtained. However, in another recent study by Connolly et al. (1979), it was shown that passive redistribution of blood flow from one region to another cannot account for the reflex volume shifts.

The present study clearly shows that when one attempts to describe the direct action of a humoral substance on the vascular system parameters, capacitance and resistance, the baroreceptor system must be prevented from being forced by the same substance, because the reflex exerts an important control on these vascular system parameters. Furthermore, to quantify hormonal and reflex changes in venous vascular capacity, one must give careful attention to arterial capacitance. Although this capacitance may be small, the reflex or hormonal change in arterial pressure is usually quite large and, therefore, the volume shifts into or out of the arterial segment are significant. Shown in Figure 7 is the effect of lowering intrasinus pressure from 200 to 50 mm Hg. Initially, the reflex increase in arterial pressure was prevented by draining blood from the artery to the reservoir by an auxiliary pump. Under this condition, reservoir blood volume increased by as much as 200 ml, indicating a decrease in venous capacity. In the center of the record, the arterial pressure control was removed, thereby allowing arterial pressure to increase. This increase in arterial pressure caused reservoir blood volume to decrease markedly as blood entered the arterial segment.

This supports the above contention that, although the arterial capacitance is small, there are large volume changes in the arterial segment. When arterial pressure was returned to the initial level, the reservoir volume returned to the original steady state value. In the same dog, a similar experiment was performed. Intrasinus pressure was controlled at 125 mm Hg, and epinephrine was given at a rate of 2.0 μg/min per kg, as indicated by the vertical arrows in Figure 8. Epinephrine caused a large volume shift out of the dog, as indicated by the large increase in reservoir blood volume seen in Figure 8. Again, when arterial pressure was allowed to rise under the influence of epinephrine (the part labeled “uncontrolled” in Fig. 8), the volume response became much smaller than when arterial pressure was controlled. This result is similar to the baroreceptor reflex responses. It can be concluded from these experiments that both epinephrine and the baroreceptor reflex system do change vascular capacity. One question that does remain is the following. If intrasinus pressure were allowed to follow arterial pressure, as in the normal circulation, would the reflex system attenuate the volume shift caused by the epinephrine? Shown in Figure 9 is a record of that experiment. Intrasinus pressure was allowed to follow arterial pressure while epinephrine was given to the animal. Notice that the blood volume shift from the dog into the reservoir was attenuated considerably.

One question that arises is, does the epinephrine act at the carotid sinus baroreceptor site to modify the reflex or at some other site? In our present experiments, the carotid sinuses were isolated completely from the rest of the circulation. No exogenous epinephrine could have reached the carotid sinus baroreceptor site. Therefore, the attenuating effects of epinephrine on reflex control of vascular parameters could not have been mediated by its direct action on the baroreceptor themselves. Two alternative sites of interaction are the reflex center in the central nervous system and in the peripheral vasculature. The present study does not distinguish between the two. The peripheral vasoconstrictor action of epinephrine is well known, and this can easily explain the parallel shift of the intrasinus pressure-arterial pressure relation curve with the dose-dependent attenuation of the maximum depressor range shown in Figure 5. On the other hand, if the attenuation occurs in the central nervous system, more complex changes might result. The current findings do not exclude the central nervous system interaction at all.

FIGURE 7 Recording of reservoir volume, venous pressure, intrasinus pressure, and mean arterial pressure.
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MAP CONTROLLED UNCONTROLLED CONTROLLED

FIGURE 8 Recording of reservoir volume, venous pressure, intrasinus pressure, and mean arterial pressure. Arrows indicate beginning and end of epinephrine infusion.

MAP CONTROLLED UNCONTROLLED CONTROLLED

FIGURE 9 Recording of reservoir volume, venous pressure, intrasinus pressure, and mean arterial pressure. Arrows indicate beginning and end of epinephrine infusion. Intrasinus pressure was allowed to follow arterial pressure.

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References


Folkow B, Mellander S (1964) Veins and venous tone. Am Heart J 68: 397-408
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