PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 175, 366–373 (1984)

Control of Hemodynamic Adjustments during Acute Volume Expansion in the Rabbit (41808)

ROBERT F. TAYLOR, JACQUE L. BERGMAN, AND D. FRED PETERSON

Department of Physiology, Oral Roberts University School of Medicine, Tulsa, Oklahoma 74171

Abstract. The influence of reflexes mediated by the carotid sinus, aortic, and vagus nerves on control of blood pressure were investigated in the pentobarbital-anesthetized rabbit during an acute intravascular volume expansion. Blood, kept at 37°C, was gradually infused at 2.5-min intervals until the blood volume of each animal was expanded to 10, 20, 30, and 40% above normal. Responses in sinoaortic–vagally denervated rabbits were compared to intact rabbits. Both intact and denervated animals showed a significant increase in central venous pressure with each 10% addition of blood. Heart rate did fall significantly in the intact group but not in the denervated group. No significant changes were identified in mean arterial pressure (MAP) in either group. In both groups changes in cardiac output were significantly greater than control for 20, 30, and 40% expansion and calculated total peripheral resistance fell in both groups at all levels of expansion when compared to control. The absence of significant changes in MAP within the intact and denervated groups suggests that sinoaortic–vagal reflexes are not affecting control of MAP in response to slow, acute volume expansion in the intact rabbit. On the other hand, since total peripheral resistance fell in both groups, a non-sinoaortic–vagal mechanism appears to be functional. This mechanism may assist in increasing vascular capacitance in order to prevent significant increases in blood pressure.

The nervous system regulates systemic blood pressure through the integration of several negative-feedback reflex mechanisms. Both high-pressure arterial baroreceptors and low-pressure cardiopulmonary receptors are reported to be involved in short-term blood pressure regulation (1, 2).

Numerous volume expansion studies have demonstrated that rapid infusion of saline, dextran, or whole blood produces immediate changes in atrial pressure, heart rate, and mean arterial pressure in the dog (3–6). These changes are said to be due, in part, to reflexes initiated by stimulation of stretch receptors located in both high- and low-pressure sites (7, 8). On the other hand, it has also been shown that activity from vagally mediated low-pressure receptors exerts a continuous inhibition on renal sympathetic activity as well as on ADH release. Excitation of these receptors due to volume expansion results in reflexly increased urine production and, thus, through control of blood volume, long-term blood pressure regulation (9, 10). Hence, during acute volume expansion the nervous system may be involved in blood pressure regulation, heart rate adjustments, and urine production.

Recent studies have suggested that under some conditions the nervous system may not contribute to the regulation of blood pressure during acute volume expansion in the rabbit (11–13). Chen *et al.* (12) and Faris *et al.* (13) indicated no change in mean arterial pressure in the face of an increased blood volume. This observation persisted in the presence or absence of the aortic and vagus nerves while carotid sinus pressure was maintained constant at 90 mm Hg (12). However, in this and other previous studies experimental conditions were not always clear. Infusion rate or total percentage of body weight infused was not always specified (8, 11, 12, 14). Urine production, blood gases, and hematocrit were usually not mentioned (5, 7, 8, 11, 15, 16), yet these variables could indicate changes in total body fluid, compartmental fluid shifts, and chemoreceptor stimulation. Clearly, unspecified differences in experimental conditions could account for differences in conclusions regarding the role of the nervous system in response to acute volume expansion.

The present study was designed to investigate the collective influence of the carotid sinus, aortic, and vagus nerve reflexes on the control of cardiovascular variables during an acute intravascular volume expansion under controlled conditions. By careful section of pathways involved in these reflexes, the com-

0037-9727/84 $1.50

bined influence of these neural mechanisms could be examined while controlling for other possible influences.

Materials and Methods. Twenty male New Zealand white rabbits weighing between 1.85 and 2.95 kg were anesthetized with sodium pentobarbital (Abbott Laboratories) (30 mg/kg) via the marginal ear vein. Supplemental dosages of sodium pentobarbital were administered through a cannula inserted into the femoral vein in order to maintain a light level of surgical anesthesia (active corneal reflex) throughout the experiment.

A cannula connected to a Statham P23 dB transducer was placed in the descending aorta (via femoral artery) to record pulsatile and mean arterial pressure (MAP). The right jugular vein was cannulated with polyethylene tubing positioned just outside the right atrium to record central venous pressure using a Statham P23 dB transducer. ECG was obtained using sternal needle electrodes and heart rate (HR) was recorded from the electrocardiogram with a cardiotachometer coupler. Body temperature was maintained by placing the animal on a heating pad and recording rectal temperature with a YSI telethermister probe (model 43TD). Blood gases and pH were determined on an Instrumentation Laboratories 713 pH and blood gas analyzer.

Both aortic nerves and vagi were carefully isolated through a midline cervical incision and the carotid sinuses were exposed for later denervation in the sinoaortic–vagal denervated groups. A tracheostomy was performed and these animals breathed spontaneously throughout the experiment. The urinary bladder was reflected outside the body through a midline incision and drained completely via a 20-gauge needle. Urine produced after the start of the infusion was collected and, periodically, the volume which had accumulated was replaced by intravenous infusion with dextran or whole blood until termination of the experiment.

In 10 animals both carotid sinuses were located and denervated. Internal and external carotid arteries were left patent but all smaller vessels and associated tissues were ligated and cut. Subsequently, all vessels in the area were painted with 2-propanol using a cotton swab. The test for complete sinus denervation was the absence of the usual baroreflex rise in blood pressure due to clamping of both carotid arteries. Sectioning of both vagi and aortic nerves combined with carotid sinus denervation resulted in a sinoaortic–vagally denervated animal. The control group also consisted of 10 rabbits surgically prepared in the same manner as the denervated group, except that the nerves were not cut or treated with propanol.

A second group of eight rabbits were prepared as described above. Four of these had all nerves intact and four were sinoaortic–vagally denervated. Through a right thoracotomy between the third or fourth intercostal space, the aortic arch was isolated, and an electromagnetic flow probe (Carolina Instruments) attached. A continuous measurement of ascending aortic flow was obtained throughout the experiment. Each animal was artificially ventilated continuously (Harvard Apparatus, Model 665), and the chest was not closed. These animals were respirated with room air. The stroke volume and respiratory rate were set to prevent spontaneous respiratory movements and to maintain the blood gases as normal or slightly hypocapnic and hyperoxic. Total peripheral resistance (TPR) was obtained mathematically from mean arterial pressure, central venous pressure, and cardiac output (CO).

Each group was volume-expanded with donor rabbit blood through a cannulated femoral artery using a 50-ml glass syringe rinsed with heparin (200 units/ml). Ten percent of blood volume was infused with a Harvard syringe pump over 30 sec and a 2-min equilibration time was allowed between each successive infusion. Each animal received a 10, 20, 30, and 40% increase in intravascular volume. The theoretical blood volume for each animal was calculated using the factor of 56 ml/kg body weight (18) so that percentage volume expansion could be determined.

To monitor the red blood cell concentration, hematocrits were measured before and after infusion using heparinized capillary tubes and an IEC microhematocrit centrifuge. As volume was infused, the colloidal osmotic pressure of the animal was maintained by periodic infusions of up to 3 ml of 10% dextran (mol wt 173,000, Sigma Chemicals) in physiologic saline solution. Donor rabbits were bled in order to obtain 80–100 ml of whole blood. A 2.3% sodium citrate saline solution was

added in order to prevent the donor blood from clotting (0.1 ml citrate solution/ml blood). Because rabbits do not have natural isoagglutinins to red cells (17), there is little risk in infusing unmatched whole blood. The citrated blood was stored in a refrigerator at 5°C and used within 36 hr after it was collected. Prior to infusion, the dextran solution and donor rabbit blood were maintained at 37°C in a constant-temperature water bath.

For purposes of statistical analysis, comparisons between animals were made at 10, 20, 30, and 40% increase in intravascular volume. Values were taken when recorded variables were stable just prior to each addition of volume. A two-way analysis of variance (ANOVA) with repeated measurements was used to determine whether or not there were changes in HR, CVP, CO, TPR, and MAP as a result of progressive blood volume expansion and denervation. When significance was determined by ANOVA, the Newman–Keuls test was employed to pinpoint the areas of significance. The independent t test was used to determine any differences in total urine output between the intact and the denervated animals.

Results. *Volume expansion with nerves intact, chest closed.* Heart rate underwent a significant fall due to 10% volume expansion. All values thereafter were significantly different from control (Table I). The mean HR decreased from 260.0 ± 33.7 to 228.2 ± 22.6 beats/min after 30% expansion. This value was significantly lower than after 10% infusion. Figure 1 illustrates the changes in HR from control for each rabbit.

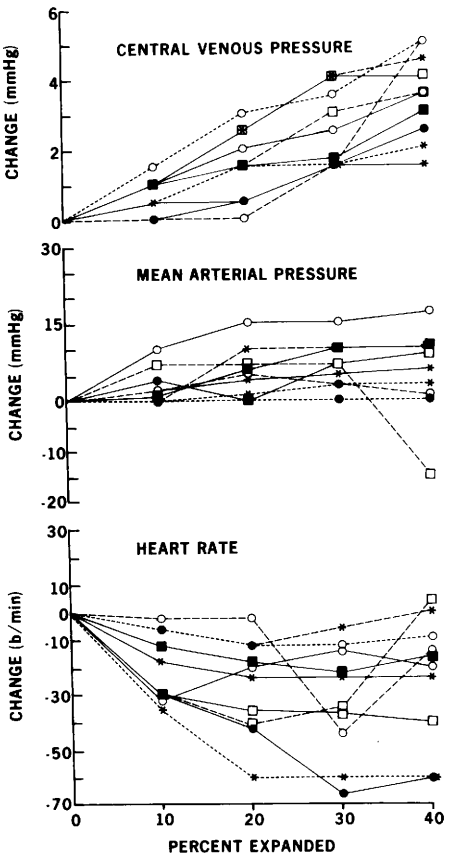

FIG. 1. The effects of gradual expansion in blood volume on changes in heart rate, central venous pressure, and mean arterial pressure in 10 intact rabbits. Each line represents results obtained in one rabbit.

TABLE I. HEMODYNAMIC VARIABLES FOLLOWING EXPANSION

Percentage expansion	Mean arterial pressure (mm Hg)	Central venous pressure (mm Hg)	Heart rate (b/min)
	Intact animals		
0	92.7 ± 6.3	−0.6 ± 1.4	260 ± 34
10	95.7 ± 7.1	−0.0 ± 1.4*	238 ± 30*
20	97.7 ± 6.7	1.0 ± 1.3*	231 ± 26*
30	98.7 ± 6.1	2.0 ± 1.3*	228 ± 23*
40	96.8 ± 4.8	2.8 ± 1.7*	236 ± 23*
	Denervated animals		
0	128.0 ± 13.1	1.0 ± 2.4	298 ± 46
10	130.2 ± 11.7	2.6 ± 2.3*	296 ± 52
20	132.7 ± 12.9	3.7 ± 1.9*	293 ± 56
30	132.4 ± 12.7	4.3 ± 1.9*	286 ± 50
40	131.0 ± 10.7	5.4 ± 1.9*	289 ± 48

Note. Values are means ± the standard deviations of 10 animals.
* Difference from control is statistically significant $P < 0.05$.

Central venous pressure (CVP) increased significantly ($P < 0.05$) in a stepwise fashion from control in all animals with each increase in blood volume. Table I shows the mean values of CVP for 10 rabbits at each stage of expansion. Volume expansion caused CVP to increase from an average of −0.60 ± 1.4 mm Hg at control to 2.80 ± 1.7 mm Hg expansion in the intact group. The responses for each individual animal are shown in Fig. 1. The maximum change in CVP always occurred during the 40% expansion level.

Average mean arterial pressure rose slightly due to volume expansion. The mean value ranged from 92.7 ± 6.3 mm Hg at control to

TABLE II. BLOOD PARAMETERS—VOLUME EXPANSION

	pH	PCO_2	PO_2	Hematocrit
Intact before infusion	7.46 ± 0.1	28.0 ± 7.2	91.2 ± 6.7	35.3 ± 2.7
Intact after 40% expansion	7.49 ± 0.1	26.6 ± 6.4	92.9 ± 11.5	38.9 ± 1.5
Denervated before infusion	7.43 ± 0.1	31.9 ± 9.8	81.6 ± 9.8	35.9 ± 6.8
Denervated after 40% expansion	7.43 ± 0.1	27.2 ± 6.2	89.6 ± 19.7	37.2 ± 5.6

Note. Values are mean ± SD.

98.7 ± 6.1 mm Hg at 30% expansion (Table I). These changes did not prove to be significant even though a slight, consistent increase or no change in arterial pressures was observed in all except two animals (Fig. 1).

Throughout the experiments, the pH, PO_2, PCO_2, and hematocrit remained within normal limits. Table II shows values before infusion and after 40% volume expansion. There were no significant changes in any of these parameters. The mean value of urine output for the intact group was 3.90 ± 2.96 ml which represented the total volume accumulated at the end of the experiment.

Nerves intact, chest open. In the four artificially ventilated rabbits instrumented with aortic flow probes, cardiac output (CO) rose in response to volume expansion (Fig. 2). Average CO values ranged from 96.5 ± 20.3 ml/min/kg for control to 153.3 ± 37.0 ml/min/kg at 40% expansion. Cardiac output was significantly different from control at all levels of volume expansion. CO at 30 and 40% expansion was significantly greater than that at 10%. Stroke volume changes paralleled cardiac output (control, 0.62 ± 0.12 ml; 40%, 1.15 ± 0.27 ml). Total peripheral resistance fell from control (29.4 ± 3.0 PRU) in all animals. The fall was significantly different from control at 20, 30, and 40% and was 31% below control (20.4 ± 2.4 PRU) at 30% expansion. Changes in other measured variables were similar to those seen in closed chest animals. Mean arterial pressure did not change significantly. The range of values was 102 ± 8 mm Hg control to 108 ± 5 mm Hg at 40% expansion. Heart rate underwent a significant decline; 339 ± 47 beats/min, control to 281 ± 40 beats/min at 30% expansion. The open-chested rabbit had a higher resting central venous pressure which rose gradually due to volume expansion (3.8 ± 2.3 mm Hg control to 5.8 ± 2.0 mm Hg, 40%).

Volume expansion with sinoaortic/vagal denervation, chest closed. Acute volume expansion did not significantly affect average HR, and there was a great deal of variability in the responses of the 10 denervated animals (Fig. 3). Responses ranged from a maximum increase of 29 beats/minute to a maximum decrease of 55 beats/minute (Fig. 3).

Individual changes in CVP in the 10 denervated rabbits were also more variable than in intact animals but as a group showed significant increases during volume expansion (Fig. 3).

MAP in the denervated rabbits did not undergo any significant changes from control (Table I). The individual responses of 10 rab-

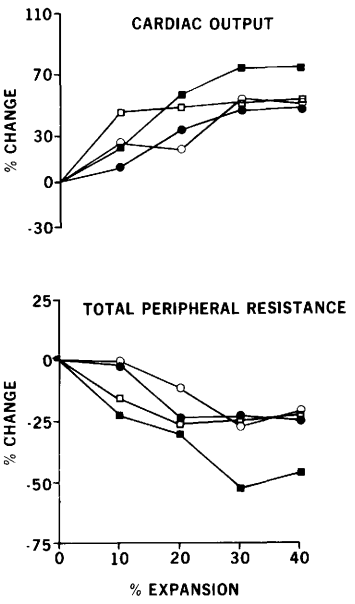

FIG. 2. The effects of gradual expansion in blood volume on changes in cardiac output and total peripheral resistance in four intact rabbits. Each line represents results obtained in one rabbit.

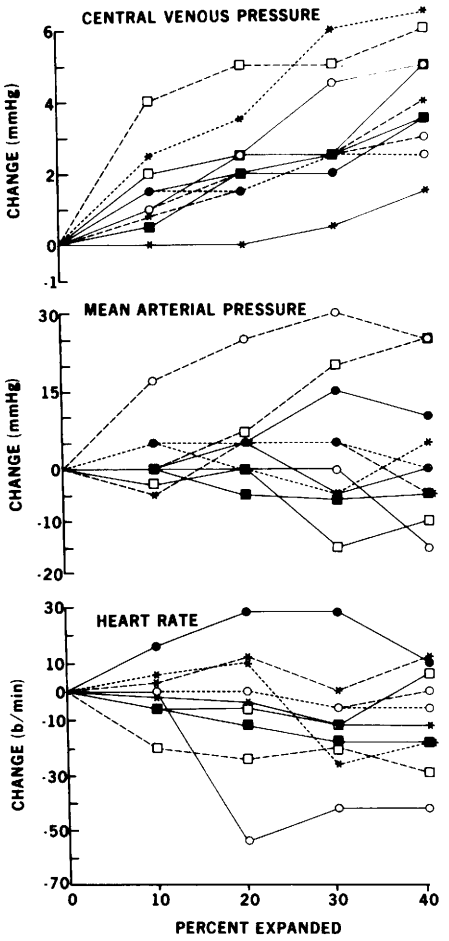

FIG. 3. The effects of gradual expansion in blood volume on changes in heart rate, central venous pressure, and mean arterial pressure in 10 denervated rabbits. Each line represents results obtained in one rabbit.

bits in Fig. 3 shows a wide range of responses due to 40% expansion (+25 mm Hg to −15 mm Hg). Two individuals stand out as having an elevation of MAP above 15 mm Hg while most of the remaining animals did not change much from control at any time during volume infusion.

Table II shows that pH, PO_2, PCO_2, and hematocrit in the denervated group after 40% expansion were unchanged from the control values collected before infusion. The mean value of urine output for the denervated group was 11.20 ± 8.26 ml which was significantly greater than the urine loss seen in the intact group ($P < 0.02$).

Nerves cut, chest open. Cardiac output and stroke volume rose due to volume expansion in this group of four rabbits. Average control value for CO was 104.8 ml/min/kg and the highest average value was 144.0 ± 10.0 ml/min/kg at 30% expansion (Fig. 4). Stroke volume again paralleled CO rising from 0.78 ± 0.11 ml control to 1.31 ± 0.09 ml at 40% expansion. All levels of expansion resulted in CO and SV significantly above control. Total peripheral resistance fell from 27.6 ± 3.6 to 20.4 ± 1.2 PRUs at 20% expansion. Values at 20, 30, and 40% expansion were significantly less than control. Other measured variables indicated the same responses as in the closed-chested animals. No significant changes were found in blood pressure (109 ± 11 to 127 ± 5 mm Hg at 40% expansion) or heart rate (270 ± 17 beats/min to 279 ± 17 beats/min at 40% expansion). Resting CVP was high, 2.8 ± 1.2 mm Hg, and rose significantly to 5.6 ± 0.6 mm Hg at 40% expansion.

Discussion. Our results demonstrate that the short-term neurally mediated regulating systems do not play an important collective role in the control of blood pressure during

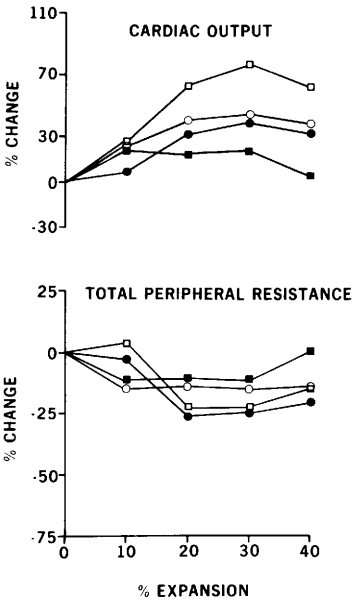

FIG. 4. The effects of gradual expansion in blood volume on changes in cardiac output and total peripheral resistance in four denervated rabbits. Each line represents results obtained in one rabbit.

slow volume expansion in the anesthetized rabbit. Responses measured in the intact group support previous findings that MAP did not significantly change following a substantial volume expansion (11, 13, 14). Our results do indicate a heart rate decrease after 10% expansion. Kumade and Sagawa (8) volume-expanded rabbits by 20% and showed a significant decrease in HR by 5% as well as a 6% increase in MAP. Our data support the fall in heart rate, but not the rise in arterial pressure.

The absence of significant change in MAP within the intact group might have at first been attributed to regulation by sinoaortic–vagal reflexes. Kumada and Sagawa recorded an increased level of aortic nerve activity during a 20% volume expansion (8). This suggests that the aortic arch reflex senses very small pressure changes or, indirectly, senses a change in blood volume. Indeed, this could possibly explain the small but significant fall in heart rates we observed. Our results, however, show that blood pressure was regulated as well after denervation as it was before the nerves were cut. Holding carotid sinus pressure constant, Chen (11) demonstrated that after the aortic nerves and the vagi were sectioned, volume expansion did not cause a significant change in MAP or HR. Chen did not report hematocrit, blood gases, urine production or the rate of infusion, yet the results are similar to the present findings. Measurements in our study ruled out significant problems associated with large blood infusions such as hemodilution or blood gas changes. Although urine production was not studied, urine collection allowed accurate compensation for total volume loss. Hematocrit measurements assured us that there was not substantial volume shift from the intravascular space into the interstitium.

The obvious resting differences in MAP between the denervated group and the intact group (Table I) can be explained as a direct result of the denervation. After sinoaortic and vagal nerve interruption in the rabbit, arterial pressure is elevated (19). A rise in the CVP baseline after denervation would be expected concomitant with the overall increase in systemic arterial pressure. Hence our results confirm that the arterial baroreceptors and vagi are playing a role in maintaining blood pressure at the normotensive level in rabbits prior to denervation. Also, as would be expected, in the open-chested experiments, resting central venous pressure was elevated.

Bainbridge (3) observed tachycardia during volume expansion in the anesthetized dog. This has been observed in conscious dogs as well (5, 20). Tachycardia has been observed when initial heart rate is slow and bradycardia when the initial heart rate is fast in the dog (15). Since the initial HR in the rabbit is high and the amount of tonic cardiac vagal restraint has been shown to be minimal (14), this may account for the fall in HR seen in our intact rabbits. The bradycardia was abolished after sinoaortic–vagal denervation.

In this study a significant, stepwise increase in CVP was seen with gradual expansion of the blood volume. Cevesse and Guyton (21) reported a consistent elevation in CVP above control directly after infusion in dogs which showed evidence of persistent overdistention of the circulatory system. Gupta *et al.* (7) saw an increase in atrial receptor nerve activity in vagal afferents due to a 20% expansion of the initial blood volume. However, in the present study, even though this consistent, significant rise in CVP was observed, no identifiable change in the mechanisms controlling MAP were observed due to denervation. This does not support the findings of Gupta *et al.* (7). Even though cardiac receptors do not seem to be affecting control of MAP in the intact animal, they are presumably being stimulated under the conditions of this present investigation and may be reflexly responsible for the observed bradycardia.

The denervated rabbits showed a significantly greater urine output during volume expansion than did those in the intact group. If it is assumed that cardiac receptors are being stimulated during volume expansion, then the decrease in renal sympathetic nerve activity and an inhibition of ADH demonstrated by Clement *et al.* (22) and Gilmore and Weisfeldt (9) suggests that a greater urine output would be observed in the intact group. However, the increase in the MAP baseline after denervation would presumably increase the renal filtration pressure which could account for the greater volume of urine output seen in the denervated group.

It was presumed that volume expansion would initially increase venous return with a

subsequent increase in stroke volume and cardiac output (23). Increased cardiac output with no change in total peripheral resistance would result in elevated blood pressure. Combined filling pressure and arterial pressure rises in the intact animals would stimulate reflex depression of heart rate and blood pressure; hence, blood pressure would be maintained near normal. In fact, stroke volume and cardiac output underwent similar increases due to volume expansion in both intact and denervated groups. This, combined with an increase in filling pressure and very little change in arterial pressure, resulted in a decrease in calculated total peripheral resistance. This fall in TPR was present in both groups; hence, it cannot be explained by sinoaortic or vagally mediated reflexes.

In light of the absence of a change in MAP during volume expansion within the denervated group in this study, it appears that a significant portion of the regulation of MAP during volume expansion in the rabbit must be due to non-sinoaortic–vagal factors. Renal clearance can be eliminated as a factor since total urine production was low and fluid lost through urine production was regularly replaced intravenously. Large volume shifts into the interstitium could not account for significant reduction in blood volume since such changes would have been reflected in the hematocrit. Afferent nerves arising in the thorax and traveling with the cardiac sympathetic nerves remained intact in our experiments. In the cat these afferents are known to increase peripheral resistance when excited (24). Thus, if they are functional in the rabbit, their excitation due to volume (7) should have led to increase rather than decrease in peripheral resistance. It is also possible that afferents arise from the peripheral vasculature itself which could signal volume expansion since viscerovisceral reflexes have been reported in responses to hepatic venous congestion (16). Venous pressures in those experiments were much higher than pressures measured in our study, although the possibility of splanchnic baroreceptors cannot be ignored.

It has been shown that an increase in blood volume will cause a transient rise of mean circulatory pressure and then a return back to normal after 90–120 min (23). Such a recovery in mean circulatory pressure without a corresponding fall in blood volume would indicate that there must have been a further dilation or relaxation of the venous system. This increase in venous capacitance or "stress–relaxation" has been described by Prather *et al.* (23). After 90–120 min stress relaxation reduces venous return and, hence, reduces cardiac output and filling pressure (23). Furthermore, this decrease in filling pressure would withdraw the stimulus for reflex regulation through the sinoaortic and vagal pathways. In our experiments compensation for each 10% increase in blood volume was accomplished within 2.5 min. Since our results indicate that the classic sinoaortic–vagal reflexes play no major role in blood pressure regulation under these experimental conditions and other possible factors seem unlikely, stress–relaxation appears to be occurring. Nevertheless, the stress–relaxation phenomenon must occur much more rapidly in the rabbit than previously estimated for the dog (23). This phenomenon appears to be responsible for continuous maintenance of a normotensive state throughout the course of the gradual volume expansion in the present study.

1. Heymans C, Ladon A. Research on dog head isolated and heated. Compt Rend (Belge) **92**:455–456, 1925.
2. Paintal AS. Vagal sensory receptors and their reflex effects. Physiol Rev **53**:159–227, 1973.
3. Bainbridge FA. Influence of venous filling upon the rate of the heart. J Physiol (London) **50**:65–84, 1915.
4. Bishop VS, Peterson DF. Pathways regulating cardiovascular changes during volume loading in awake dogs. Amer J Physiol **231**:854–859, 1976.
5. Horwitz LD, Bishop VS. Effect of acute volume loading on heart rate in the conscious dog. Circ Res **30**:316–321, 1972.
6. Mancia G, Shepherd JT, Donald, DE. Interplay among carotid sinus, cardiopulmonary and carotid body reflexes in dogs. Amer J Physiol **230**:19–24, 1976.
7. Gupta PD, Henry JP, Sinclair R, von Baumgarten R. Responses of atrial and aortic baroreceptors to nonhypotensive hemorrhage and to transfusion. Amer J Physiol **211**:1429–1437, 1966.
8. Kumada M, Sagawa K. Aortic nerve activity during blood volume changes. Amer J Physiol **218**:961–965, 1970.
9. Gilmore JP, Weisfeldt ML. Contribution of intravascular receptors to the renal responses following intravascular volume expansion. Circ Res **17**:144–154, 1965.

10. Henry JP, Pearce JW. The possible role of cardiac atrial stretch receptors in the induction of changes in urine flow. J Physiol (London) **131**:572–582, 1956.
11. Chen HI. Mechanism of alteration in baroreflex cardiovascular response due to volume loading. Japan J Physiol **28**:749–756, 1978.
12. Chen HI, Chai CY, Tung CS, Chen HC. Modulation of the carotid baroreflex function during volume expansion. Amer J Physiol **237**:H153–H158, 1979.
13. Faris IB, Iannos J, Jamieson GG, Ludbrook J. The circulatory effects of acute hypervolemia and hemodilution in conscious rabbits. Circ Res **48**:825–834, 1981.
14. Stinnett HO, Bishop VS, Peterson DF. Reduction in baroreflex cardiovascular responses due to venous infusion in the rabbit. Circ Res **39**:766–772, 1976.
15. Coleridge JCG, Linden RJ. The effect of intravenous infusions upon the heart rate of the anesthetized dog. J Physiol (London) **128**:310–319, 1955.
16. Kostreva DR, Castaner A, Kampine JP. Reflex effects of hepatic baroreceptors on renal and cardiac sympathetic nerve activity. Amer J Physiol **238**:R390–R394, 1980.
17. Cohen C, Tissot RG. Specialized research applications. II. Serological genetics. In: Weisbroth SH, Flatt RE, Kraus AL, eds. The Biology of the Laboratory Rabbit. New York, Academic Press, pp167–177, 1974.
18. Altman PL, Dittmer DS. Respiration and Circulation. Maryland, Fed Amer Soc Exp Biol, p381, 1971.
19. Pillsbury HRC III, Guazzi M, Freis ED. Vagal afferent depressor nerves in the rabbit. Amer J Physiol **217**:768–770, 1969.
20. Vatner SF, Boettcher DH, Heyndrickx GR, McRitchie RJ. Reduced baroreflex sensitivity with volume loading in conscious dogs. Circ Res **37**:236–242, 1975.
21. Cevesse A, Guyton AC. Isohemic blood volume expansion in normal and areflexive dogs. Amer J Physiol **231**:104–111, 1976.
22. Clement DL, Pelletier CL, Shepherd JT. Role of vagal afferents in the control of renal sympathetic nerve activity in the rabbit. Circ Res **31**:824–830, 1972.
23. Prather JW, Taylor AE, Guyton AC. Effect of blood volume, mean circulatory pressure, and stress relaxation on cardiac output. Amer J Physiol **216**:467–472, 1969.
24. Peterson DF, Brown AM. Pressor reflexes produced by stimulation of afferent fibers in the cardiac sympathetic nerves of the cat. Circ Res **28**:605–610, 1971.

Received April 11, 1983. P.S.E.B.M. 1984, Vol. 175.
Accepted November 28, 1983.