Total Circulatory Capacity in the Rat

Effects of Epinephrine and Vasopressin on Compliance and Unstressed Volume

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SUMMARY In thoracic-spinal-cord-transected rats, mean circulatory pressure (Pmc) was measured during brief circulatory arrest by inflating an indwelling balloon in the right atrium and total blood volume (Vb) was measured with 51Cr. The Pmc-Vb relationship was determined over the range ± 30% Vb by rapid blood infusion or withdrawal. An infusion of 1.8 μg/kg per min of epinephrine for 20–40 minutes caused the total circulatory compliance (Ctc) to decrease 18%, the extrapolated unstressed circulatory volume (VU) and Vb to decrease 8.8 and 7.3 ml/kg, respectively, and Pmc to increase 41% (2.8 mm Hg). Total circulatory capacity (circulatory volume at a Pmc of 8 mm Hg) was decreased 13.7 ml/kg by epinephrine at the above infusion rate. When vasopressin (20 ng/kg per min) and epinephrine (0.3 μg/kg per min) were infused together for 20–40 minutes, compared to a 0.3 μg/kg per min infusion of epinephrine alone, the net effect of vasopressin was a 4.8 ml per kg decrease in Vb and a 5.9 ml/kg decrease in total circulatory capacity, with insignificant decreases in Ctc and VU. The results indicate that in rats both epinephrine and vasopressin act to decrease blood volume via transcapillary fluid shifts, and that vasopressin has a relatively small overall venoconstricting action.


QUANTITATIVE assessment of changes in circulatory capacitance have been studied in dogs with various versions of the pump/bypass/reservoir technique or the mean circulatory pressure (Pmc)-blood volume (Vb) method (Hainsworth and Linden, 1979). In the former approach, total blood volume (circulating volume of the dog plus reservoir volume) usually is assumed to remain constant so that measurable changes in the reservoir volume represent corresponding changes in the circulating volume of the dog. In the Pmc-Vb approach, total circulatory compliance and the extrapolated unstressed circulatory volume are derived from the total circulatory pressure-volume relationship. However, whether the changes in capacitance are assessed by the changes in reservoir volume or by the changes in extrapolated unstressed volume and compliance, if the Vb changes by an unknown amount from loss or gain of fluid at the capillaries, the data could lead to quantitatively inaccurate conclusions. Since there is evidence that rapid and reversible changes in Vb can occur readily in humans (Fawcett and Wynn, 1960; Cohn, 1966; Tarazi et al., 1970; Bessa, 1975) and animals (Maddox et al., 1977; Green et al., 1978; Yamamoto et al., 1980) in response to a variety of stimuli, it seems important that in any study of circulatory capacitance, careful attention be given to possible changes in Vb.

One of the aims of this study was to utilize the Pmc-Vb method to determine the effects of epinephrine on circulatory capacitance in rats, taking into account possible changes in Vb. The drawbacks to this method are possible interferences from autonomic reflexes, transcapillary fluid shift, and vascular stress-relaxation/reverse stress-relaxation (SR/RSR) that might occur during the rapid Vb changes (Guyton et al., 1973; Green, 1975; Rothe, 1979). However, these problems were mitigated in the present study by transecting the spinal cord, which essentially eliminated any measurable effects of the autonomic reflexes on Pmc, and by making the changes in Vb rapidly enough that any changes in Pmc resulting from fluid shift were quantitatively insignificant and possible changes resulting from SR/RSR were minimized.

A second aim of this study was to determine whether a high blood level of vasopressin can change circulatory capacitance in rats. Cowley et al. (1980) recently reported the quantitative aspects of vasopressin’s control of arterial pressure during hemorrhage and questioned if part of the mechanism through which vasopressin helps restore arterial pressure toward control was mediated by venoconstriction. Although earlier reports have dealt with some aspects of the possible venoconstricting action of vasopressin (Emerson, 1966; Diana and Shadur, 1973; Richardson and Withring-
ton, 1978; Altura, 1978), the influence of vasopressin on the overall capacitance of the circulation is still not clearly understood.

Methods

Surgical Procedures

Male Wistar rats, weighing 366–434 g, were anesthetized with ether for the placement of intravascular catheters in the following areas: left femoral artery for measuring arterial pressure, left femoral vein advanced to the thoracic inferior vena cava for measuring venous pressure, left common carotid artery for infusing and withdrawing blood, and two catheters in the right external jugular vein, one for drug infusion and the other (having a balloon at its tip and advanced to the right atrium) for arresting the circulation during measurement of mean circulatory pressure (PMC) (Yamamoto et al., 1980). After placement of catheters, 1% lidocaine was applied to all surgical wounds and the source of ether was removed. Approximately 2–3 hours later, the rat was reanesthetized with a carefully titrated dosage of sodium pentobarbital (approximately 30 mg/kg), administered through the jugular vein catheter. Additional injections of pentobarbital were given during the experiment. A tracheotomy was performed for insertion of a tracheal tube. To eliminate possible interference due to autonomic reflexes during blood volume (V_B) alterations which were to be performed later during the experiment, the spinal cord was transected by aspiration between the first and second thoracic vertebrae, leaving neural control of respiration intact. During this surgical procedure, a small amount of ether was used in some rats for additional anesthesia. Bleeding was controlled by use of a cautery and application of absorbable gelatin. A catheter then was temporarily inserted into the spinal canal and its tip advanced 1–2 cm caudad the second thoracic vertebra for injection of 0.05 ml 1% lidocaine. The wound was then packed with gauze and closed with suture. Completeness of spinal transection was assessed after each experiment as described below. Two rats were eliminated from the study due to incomplete spinal cord transection, three rats were eliminated due to bleeding during the experiment, and three rats required blood transfusion from donor rats to replace excessive blood loss during surgery (1–3 ml).

Experimental Procedures

Rectal temperature was monitored throughout the experiment and the rats were kept warm with a lamp. In rats that were to receive drugs, infusion through the jugular vein catheter was begun approximately 5–15 minutes after completion of surgery. After starting the drug infusion, 20–30 minutes were allowed for stabilization; during this period ²⁹Cr-tagged red cells were injected through the inferior vena cava catheter and allowed to mix for a minimum of 15 minutes before the first blood sample was taken for V_B measurement.

Arterial and venous pressures were measured with Statham transducers and a Grass recorder. The transducer-recorder channel used for measuring venous pressure was calibrated with a water manometer (Trippodo et al., 1981).

Groups

Four different levels of vascular constriction were induced in four different groups of randomly assigned spinal-cord-transected rats (n = 12 per group). Group 0 did not receive drug infusion and was considered as having a relatively low level of vascular constriction due to blunting of normal vascular tone by spinal transection. Group 0.3 received epinephrine infused at 0.3 μg/kg per min; preliminary results suggested that this dosage would restore vascular tone to approximately normal (see Discussion). Group 1.5 received epinephrine infused at 1.5 μg/kg per min and was considered as having a relatively high level of vascular constriction. Group 0.9V received epinephrine infused at 0.3 μg/kg per min plus arginine vasopressin (367 IU/mg) infused at 20 mg/kg per min. Thus, the effects of vasopressin on circulatory capacitance could be assessed in animals devoid of most cardiovascular reflexes but having an initial approximate normal level of circulatory capacitance.

PMC-V_B Curve

PMC and V_B were measured as described previously (Yamamoto et al., 1980; Trippodo et al., 1981). Briefly, PMC was measured from the arterial and venous pressures during circulatory arrest brought about by inflating an indwelling balloon in the right atrium. V_B was measured with ⁵¹Cr-tagged red cells and the F_ratio (described below). Previous studies have shown that repeated measurements of PMC and V_B using these methods can be performed in rats without causing significant physiological changes in hemodynamics or V_B (Yamamoto et al., 1981). To obtain the PMC-V_B curve for each rat, PMC was measured at the "control" state (approximately 20–30 minutes after the start of drug infusion) and immediately after infusing or withdrawing a known volume of blood through the carotid artery. V_B was changed initially by ±15 and ±30% of the rat’s estimated V_B, but in most experiments V_B was changed by ±25%, using fresh blood from donor rats for infusion and a 10-minute recovery period between changes. V_B was measured immediately before V_B changes, correcting for loss of ⁵¹Cr radioactivity due to previous sampling or blood removal, and the amount of blood infused or withdrawn was added or subtracted to the prevailing V_B to obtain the V_B during each PMC measurement. Immediately after each V_B change, V_B was restored to its pre-existing level. PMC and V_B were also measured during a second "control" period at the end of each
experiment. The $P_{MC} - V_B$ curve was then determined from a minimum of four data points (two at "control" $V_B$ and two at $+25\%$ $V_B$) for each rat by linear regression analysis, using the method of least squares. In most cases, the regression coefficient for this relationship was greater than 0.96.

**Blood Volume**

Red blood cells were labeled on each day of the experiment by incubating 1 ml of fresh blood (containing heparin) from donor rats with $50 \mu Ci$ of $^{51}$Cr at room temperature for 30 minutes (Nelson and Swan, 1971). The red cells were washed three times in isotonic saline and resuspended in saline to a hematocrit of about 40. Approximately $36 \mu Ci$/kg of $^{51}$Cr-labeled red cells in 0.2 ml were injected through the venous catheter, flushed with 0.5 ml of saline, and allowed to mix for at least 15 minutes. For each $V_B$ measurement, blood was collected directly from the cleared arterial catheter into two capillary tubes precalibrated to 0.023 ml each. After centrifugation of the capillary tubes and the recording of the hematocrits, the tubes, along with three similarly prepared samples of $^{51}$Cr-red cell solution, were placed in a $y$ scintillation spectrometer. Radioactivity of the blood samples and red cell solution were recorded for 10 and 1 minutes, respectively; all total counts after subtracting background counts were greater than 7000. $V_B$ was calculated with a programmable calculator which summed and stored accumulated radioactivity lost through sampling and blood removal. $V_B = (\text{net radioactivity}/\text{blood radioactivity concentration}) + 0.8$, where net radioactivity was the difference between the amount injected and the amount lost and 0.8 was the $F_{cells}$ ratio (Gregersen and Rawson, 1959; Wang, 1959).

Previous studies from this laboratory in normotensive and hypertensive rats (Trippodo et al., 1981; Yamamoto et al., 1981) and unpublished data in dozens of rats that received infusions of drugs, red blood cells, plasma and various solutions showed that the $F_{cells}$ ratio of rats in various physiological states ranges from 0.75 to 0.88 and averages approximately 0.8.

**Completeness of Spinal Cord Transection**

In lightly anesthetized rats with intact autonomic reflexes, a secondary rise in venous pressure, which marks the onset of reflex venous constriction, starts about 11 seconds after initiation of circulatory arrest; in rats with complete spinal cord transection this secondary rise in venous pressure does not occur (Yamamoto et al., 1980). To assess the completeness of spinal cord transection in the present study, at the end of each experiment circulatory arrest was induced by right atrial balloon inflation and maintained for about 45 seconds. In two rats, obvious technical problems were encountered during surgical transection of the spinal cord, and it was not surprising that a secondary rise in venous pressure occurred during this test procedure, indicating incomplete transection of the spinal cord; they were therefore eliminated from the study. All other rats exhibited a relatively flat venous plateau pressure during prolonged circulatory arrest as described previously, i.e., venous pressure did not increase more than 0.5 mm Hg during the 45-second test period; indeed, in most cases it decreased slightly (less than 0.5 mm Hg).

**Definition of Terms**

The following variables were derived from the equation of the $P_{MC} - V_B$ curve for each rat: total circulatory compliance ($C_{TC}$, reciprocal of the slope); extrapolated unstressed circulatory volume ($V_0$, volume-axis intercept); and total circulatory capacity ($V_B$ at a specific $P_{MC}$ in this study groups were compared at 8 mm Hg, a normal value of $P_{MC}$ for conscious rats under resting conditions (Samar and Coleman, 1978; Yamamoto et al., 1980)). These terms have been defined previously in relation to the systemic circulation by Shoukas and Sagawa (1971, 1973).

**Possible Blood Shift between Thoracic and Systemic Circuits**

To evaluate the effect of a possible shift of blood from the thoracic to the systemic circuit on $P_{MC}$ (see Discussion), $P_{MC}$ was measured as described above in eight rats weighing 320–390 g and compared to the mean systemic pressure ($P_{MS}$) measured by simultaneously occluding the right atrium and aorta. Appropriate catheters and a right atrial balloon-tipped catheter were placed while the rat was anesthetized with ether. In addition, a second, but much smaller balloon-tipped catheter (constructed of PE 10 tubing and latex rubber) was placed in the aortic arch via the right common carotid artery. The proper position of the aortic balloon was accomplished by observing the decrease in arterial pressure to 10–15 mm Hg during brief (5–7 seconds) inflation of the balloon. The position of the balloon was also verified in several rats at postmortem examination. The ether then was removed and sodium pentobarbital was administered to maintain anesthesia. $P_{MC}$ was measured as before by inflating the right atrial balloon (0.3 to 0.4 ml). $P_{MS}$ was measured by inflating the atrial and aortic (0.1 ml) balloons simultaneously. Eight pairs of measurements of $P_{MC}$ and $P_{MS}$ in alternating order were made during each of three conditions: no drug infusion; epinephrine infusion at 1.5 $\mu g$/kg per min; and vasopressin infusion at 20 ng/kg per min.

$V_B$ **Effects of Epinephrine in Anephric Rats**

To determine the effects of epinephrine on $V_B$ mediated through mechanisms other than through possible changes in urinary excretion, five male Wistar rats (350–600 g) were prepared with femoral
arterial and venous catheters while the rats were anesthetized with ether. The source of ether was then removed and sodium pentobarbital was administered intravenously to maintain a light surgical plane of anesthesia. Nephrectomy was performed through a midline laparotomy, the wound was closed, and the rat was allowed to stabilize for 20–30 minutes. During this period, $^{51}$Cr-tagged red cells were injected intravenously and allowed to mix for a minimum of 15 minutes. After collecting the control data (Fig. 4) epinephrine was infused intravenously (1.5 $\mu$g/kg per min) for 20 minutes. Data were collected again after 20 minutes of epinephrine infusion and 20 minutes after the infusion was stopped. Mean arterial pressure, hematocrit, and $V_B$ were measured as described above. Red cell volume was determined as hematocrit X $V_B$ and plasma volume was determined as $V_B$ minus red cell volume.

**Statistical Analyses**

Significances of differences among groups were assessed with the one-way analysis of variance. When significant differences were found among all groups with the analysis of variance, the differences between groups 0.3 and 0.3V were analyzed further with Dunnett's test (Dunnett, 1964). The differences in values before and after epinephrine infusion shown on Figure 4 and the measurements of $P_{MC}$ vs. $P_{MC}$ were analyzed with the paired $t$-test. A $P$ value of < 0.05 was considered statistically significant. All values given are means ± SE unless indicated otherwise.

**Results**

The results of one experiment are shown in Figure 1 to illustrate how the various data were derived in each rat. The closed circle on the graph designates blood volume ($V_B$) and mean circulatory pressure ($P_{MC}$) measured during the first "control" period (52.5 ml/kg and 9.0 mm Hg, respectively). The two extreme open circles indicate $P_{MC}$ measured during the $V_B$ changes, and the open circle in between indicates $P_{MC}$ and $V_B$ measured during the second "control" period. The equation for the straight-line relationship between $V_B$ and $P_{MC}$, which was determined by linear regression analysis, was then used to derive total circulatory compliance ($C_{TC}$), reciprocal of the slope, defined as total circulatory compliance was 3.3 ml/kg per mm Hg and the volume-axis intercept, defined as extrapolated unstressed circulatory volume was 23.6 ml/kg.

The mean values for $V_B$ and total circulatory capacity are illustrated graphically in Figure 2 by the solid circles indicating volumes at $P_{MC}$ of zero and 8 mm Hg, respectively. As expected, increasing levels of drug infusion from none in group 0 to the relatively high level in group 1.5 resulted in decreasing magnitudes of total circulatory capacity. Hence, $V_B$, $C_{TC}$, $V_B$, and total circulatory capacity were greatest in group 0, next to greatest in group 0.3, next to least in group 0.3V, least in group 1.5 (Table 1, Fig. 2). $P_{MC}$ showed the exact opposite relative pattern among the four groups; the highest value
CIRCULATORY CAPACITY/Trippodo

Table 1  Circulatory Volume and Capacity in Spinal-Cord Transected Rats

<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>0.3</th>
<th>0.3V</th>
<th>1.5</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>396 ± 4</td>
<td>389 ± 3</td>
<td>405 ± 6</td>
<td>402 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Blood volume (ml/kg)</td>
<td>57.1 ± 1.4</td>
<td>56.0 ± 1.4</td>
<td>51.2 ± 1.7</td>
<td>49.8 ± 1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>46.5 ± 0.6</td>
<td>46.6 ± 0.9</td>
<td>49.6 ± 0.7</td>
<td>49.4 ± 0.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean circulatory pressure (mm Hg)</td>
<td>6.4 ± 0.3</td>
<td>7.8 ± 0.2</td>
<td>8.1 ± 0.4</td>
<td>9.0 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.96 ± 0.01</td>
<td>0.96 ± 0.01</td>
<td>0.97 ± 0.01</td>
<td>0.98 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Total circulatory compliance (ml/kg per mm Hg)</td>
<td>3.3 ± 0.1</td>
<td>3.1 ± 0.2</td>
<td>2.8 ± 0.1</td>
<td>2.7 ± 0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Extrapolated unstressed circulatory volume (V'o) (ml/kg)</td>
<td>35.2 ± 1.7</td>
<td>31.9 ± 1.7</td>
<td>28.5 ± 1.6</td>
<td>26.6 ± 1.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total circulatory capacity (ml/kg)</td>
<td>61.7 ± 1.4</td>
<td>56.9 ± 1.4</td>
<td>51.0 ± 1.6</td>
<td>48.0 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 12 per group.

* Group 0 received no drug infusion, group 0.3 received epinephrine (0.3 μg/kg per min); group 0.3V received epinephrine (0.3 μg/kg per min) and vasopressin (20 ng/kg per min); group 1.5 received epinephrine (1.5 μg/kg per min).

† Probability by analysis of variance, NS = not significant (P > 0.05).
‡ P < 0.05 for comparisons between groups 0.3 and 0.3V by Dunnett's test.

was observed in group 1.5, and the lowest in group 0.

Comparing group 0.3V with group 0.3 revealed significant decreases in VB and total circulatory capacity in group 0.3V, but the differences in PMC, CT, and V0 were not found to be significant (Table 1), suggesting that vasopressin infusion resulted in only a small degree of venoconstriction. In contrast to vasopressin's relatively mild effect on total circulatory capacity, it caused a large increase in mean arterial pressure (Fig. 3), suggesting a marked effect on the arterioles.

In eight rats, PMC and mean systemic pressure (PMS) were measured in alternating order during no drug infusion, epinephrine infusion, and vasopressin infusion. The mean ± SE for PMC and PMS, respectively, were 6.1 ± 0.2 and 6.0 ± 0.2 mm Hg during no drug infusion; 8.8 ± 0.2 and 8.9 ± 0.2 mm Hg during epinephrine infusion, and 6.6 ± 0.2 and 6.2 ± 0.2 mm Hg during vasopressin infusion. There were no significant differences between PMC and PMS.

In the anephric rats, epinephrine infusion caused a significant decrease in VB and plasma volume with only a slight insignificant change in red cell volume (Fig. 4). Since urinary excretion could not occur in these rats, the VB change must have been mediated mostly through increased whole-body
FIGURE 3 Mean arterial pressure and blood volume in four groups of spinal cord-transected rats during the first and second "control" periods (C1 and C2) and at two periods immediately before changing blood volume (Vb1 and Vb2). The four groups are represented as follows: solid line—group 1.5; broken line with dots—group 0.3; broken line—group 0.3V; and dotted line—group 0. The means ± SE's are indicated. Mean arterial pressure and blood volume were not significantly different in C1 and C2 in any group.

Discussion

When using the mean circulatory pressure-blood volume (PMC-VB) approach to study circulatory capacitance there are possible interferences from autonomic reflexes, transcapillary fluid shift, and stress relaxation/reverse stress relaxation (SR/RSR). However, in the present study, possible interference from autonomic reflexes was eliminated by transection of the spinal cord, and lack of reflex venoconstriction was verified at the end of each experiment by maintaining circulatory arrest for about 45 seconds. During this procedure, venous pressure increased to a plateau within 4–5 seconds and remained at or very close to that level. Thus, there was no secondary rise in venous pressure, which usually occurs in intact animals (Yamamoto et al., 1980), indicating abolishment of measurable reflex venoconstriction. To minimize the possible influence from fluid shift, VB changes were made rapidly followed immediately by measurement of PMC. Hence, the time required to infuse or withdraw blood and measure PMC was less than 15 seconds. The largest average change in PMC resulting from a VB change was 6.3 mm Hg in group 1.5. Assuming capillary filtration pressure changed by this amount and a whole-body capillary filtration coefficient of 0.135 ml/min per kg per mm Hg (Wolf, 1975), the amount of fluid filtered in 15 seconds would be only 0.2 ml/kg. Even in the group with the least total circulatory compliance (group 1.5), this volume change would alter PMC by less than 0.1 mm Hg. These considerations, therefore, clearly illustrate that the PMC-VB curve was obtained without quantitatively significant influences from reflexes and fluid shifts.

Regarding SR/RSR, only a general qualitative

FIGURE 4 Changes in mean arterial pressure, red cell volume (RCV), plasma volume, blood volume, and hematocrit during and after epinephrine infusion (1.5 μg/kg per min) in five anephric rats. Means ± SE's are indicated. *P < 0.05 for 20 minutes vs. preinfusion.
assessment can be made since there is no quantitative information available on this phenomenon in rats. SR/RSR opposes the effect of $V_B$ change on $P_{MC}$ and, hence, tends to decrease $P_{MC}$ after $V_B$ is increased (Prather et al., 1969) and increase $P_{MC}$ after $V_B$ is decreased. The net effect would be a clockwise rotation of the $P_{MC}$-$V_B$ curve. Thus, if enough SR/RSR occurred to affect the results, the measured values of total circulatory compliance ($C_{TC}$) in this study would be overestimates of the "true" compliance values, whereas the measured values of extrapolated unstressed circulatory volume ($V_0$) would be underestimates. To what extent, if any, SR/RSR affected the results cannot be determined, but since the $V_B$ changes were made rapidly it is believed that the effects were minimized.

In this study, the heart continued to beat during measurement of $P_{MC}$, and this may have caused variable amounts of blood to shift from the cardio-pulmonary to the systemic circuit. To evaluate the possible effect this may have had on the results, $P_{MC}$ measured by right atrial balloon inflation was compared to mean systemic pressure ($P_{MS}$) measured by simultaneous occlusion of the right atrium and aorta. Therefore, during measurement of $P_{MS}$, possible blood shifts between the thoracic and systemic circuits were prevented. There was no significant difference between $P_{MC}$ and $P_{MS}$ during no drug infusion, which confirmed the observations of Samar and Coleman (1978); neither were there significant differences between these two measurements during epinephrine and vasopressin infusions. These results suggest that the beating heart did not greatly affect the $P_{MC}$ as measured in this study.

One aim of this study was to determine the effects of epinephrine on $V_B$ and $C_{TC}$; or, in other words, to determine whether the line describing the $P_{MC}$-$V_B$ curve shifts in a parallel fashion (altered $V_B$), through a change in slope (altered $C_{TC}$), or by both mechanisms. Particular attention was given to possible changes in $V_B$ so that the effects on $V_B$ and $C_{TC}$ might be estimated more accurately. The results indicated that epinephrine shifted the $P_{MC}$-$V_B$ curve toward the pressure axis by both mechanisms, i.e., decreased $V_B$ and $C_{TC}$ and thus agree with the findings of Caldini et al. (1974) and Shoukas and Brunner (1980) in dogs. It was also found that there was a significant reduction in $V_B$ following epinephrine infusion which was similar in magnitude to the decrease in $V_0$. If $V_B$ has any relation to the true unstressed volume, the results would suggest that epinephrine infusion had little effect on stressed volume (the difference between $V_B$ and unstressed volume) and that the increased $P_{MC}$ was due mostly to decreased compliance. However, although the $P_{MC}$-$V_B$ curve is linear over a fairly wide physiological range (Guyton et al., 1973; Drees and Rothe, 1974; Caldini et al., 1974; Samar and Coleman, 1978; Yamamoto et al., 1980) it does not seem to be linear to zero pressure (Drees and Rothe, 1974), and the true unstressed and stressed volumes cannot be measured by this method.

The decrease in $V_B$ induced by epinephrine was partly, if not completely, due to increase whole-body transcapillary filtration and transfer of plasma fluid to extravascular compartments, since a similar and reversible decrease in $V_B$ was also induced in anephric rats (Fig. 4). However, increased urinary excretion might have contributed some to the plasma fluid loss in the rats with kidneys intact.

A second aim of this study was to determine whether a high blood level of vasopressin could alter total circulatory capacity in rats. Pullan et al. (1980) reported a greater than 100-fold increase in plasma vasopressin concentration in dogs in response to 30% hemorrhage. Hence, assuming a basal plasma level of 1-2 pg/ml of vasopressin in rats (Mohring et al., 1977, 1978), 100-200 pg/ml might be considered as a high physiological plasma level. Thus, the infusion rate of vasopressin used in this study (20 ng/kg per min), which has been found to produce a plasma level of 500 pg/ml in rats (A.W. Cowley, Jr., personal communication), was assumed to produce greater than maximum physiological effects of vasopressin.

The effects of vasopressin were tested in a group of anesthetized, spinal-cord transected rats (group 0.3V) receiving epinephrine at 0.3 µg/kg per min in order to restore total circulatory capacity to a relatively "normal" level. Comparison was made to a similar group of rats (group 0.3) that was treated in an identical manner except no vasopressin was infused. In group 0.3 mean arterial pressure, $P_{MC}$ and $C_{TC}$ were 98 ± 3 mm Hg, 7.8 ± 0.2 mm Hg, and 3.1 ± 0.2 ml/kg per mm Hg, respectively. These results compare favorably with values of 110 ± 3 mm Hg, 7.9 ± 0.2 mm Hg, and 3.2 ± 0.1 ml/kg per mm Hg, respectively, reported earlier in conscious intact rats (Yamamoto et al., 1980) indicating that in the present study the effects of vasopressin were assessed in rats having near "normal" initial total circulatory capacity but devoid of most cardiovascular reflexes. ($V_B$ values were different between the two studies since tagged albumin was used without correcting for the $F_{\text{rela}}$ ratio in the earlier study, whereas tagged red cells with the $F_{\text{rela}}$ ratio was used to measure $V_B$ in the present study.)

Vasopressin caused a small, but statistically significant decrease in total circulatory capacity (Table 1). $P_{MC}$ tended to be increased in the vasopressin group, but was not significantly different from that in group 0.3, probably because of the decreased $V_B$ in the vasopressin group. These results suggest that vasopressin can increase whole-body venous tone to some extent. However, since the arterial pressure rise in the vasopressin group
was much greater than the circulatory capacity decrease as compared with group 1.5, it can be reasoned that the whole-body arteriolar response to vasopressin was markedly greater than the whole-body venular response. The contention that vasopressin constricts mainly the resistance vessels and has only a minor effect on the capacitance vessels is supported by the finding that vasopressin decreases cardiac output (Montani et al., 1980). On the other hand, in certain specific vascular beds, vasopressin may have a greater effect on venules (Altura, 1978).

The results of the present study were obtained in rats without completely functioning autonomic reflexes, a condition that might enhance the venoconstrictor response to vasopressin (Cowley et al., 1974; Hoffman, 1980). Thus, it is possible that, in intact animals, the whole-body venoconstrictor response to vasopressin might be even less than the response observed here. Furthermore, it is likely that, in most circumstances associated with large increases of endogenous vasopressin, such as during hemorrhage and water deprivation, there also would be intense activation of the adrenergic nervous system, which has marked venoconstrictor properties. Under these conditions, although the intense arteriolar constrictor activity of vasopressin may be important (Cowley et al., 1980; Andrews and Brenner, 1981), its weak venoconstrictor activity would probably be of only small importance. On the other hand, in chronic pathological situations, such as in certain forms of experimental hypertension which have been shown to be associated with elevated levels of vasopressin, and/or increased cardiovascular sensitivity to vasopressin (Crofton et al., 1979; Mohring et al., 1980), the venoconstrictor properties of this hormone might prove to have a greater impact on arterial pressure.

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