Mesenteric Hemodynamics in Early Experimental Renal Hypertension in Dogs

By Geza Simon, Motilal B. Pamnani, John F. Dunkel, and Henry W. Overbeck

ABSTRACT

To investigate mesenteric hemodynamics in early perinephritic hypertension, we measured blood flows and intravascular pressures in innervated, collateral-free, naturally perfused loops of ileum in 50 male mongrel dogs anesthetized with sodium pentobarbital. In addition, we studied venous pressure-volume relationships in temporarily occluded segments of mesenteric veins in vivo and in excised segments of mesenteric veins in vitro. In 10 dogs (group H-1), one kidney was wrapped in silk 11 days before study; in 15 other dogs (group H-2), one kidney was wrapped 4 weeks before study and the other was removed 2 weeks before study. Twenty-five additional dogs were prepared as normotensive controls: in 10 one kidney was sham-wrapped (group C-1), and in 15 one kidney was sham-wrapped and the other was removed (group C-2). A significant rise in mean arterial blood pressure occurred in groups H-1 and H-2. Compared to controls, (1) ileal blood flow in the hypertensive dogs (H-1 plus H-2) was increased by 17% (P < 0.05), (2) calculated ileal vascular resistances (total and segmental) were unchanged (P > 0.05), and (3) in vivo and in vitro mesenteric vein pressure-volume curves of H-2 (but not of H-1) hypertensive dogs were shifted in the direction of the pressure axis (P < 0.05). These data suggest that in the early stages of perinephritic hypertension in dogs (1) ileal blood flow is increased, (2) ileal vascular resistance is not elevated, and (3) mesenteric venous compliance is reduced. Analysis of the venous pressure-volume curves suggests that the decreased venous compliance is attributable to factors other than smooth muscle contraction.

KEY WORDS perinephritic hypertension mesenteric blood flow arterial resistance small vessel resistance venous resistance vascular pathology autoregulation ileum venous compliance

Over the past few years several investigators have observed that cardiac output is increased in the early (less than 4 weeks) stage of experimental renal hypertension (1-4). Ferrario et al. (2) have found increased cardiac output in unanesthetized dogs during the first 4 weeks of perinephritic hypertension. Total peripheral vascular resistance decreases slightly during the first 2 weeks and then begins to rise gradually. After 4-6 weeks, the cardiac output returns to normal, and the hypertension is sustained by increased total peripheral resistance. More recently, Ferrario (4) has demonstrated similar hemodynamic changes in dogs with early one-kidney Goldblatt hypertension.

As a result of these observations, it has been suggested that the later rise in total peripheral resistance is a vascular autoregulatory response to increased blood flow through the peripheral vascular beds produced by the elevated cardiac output (2-8). It has also been suggested that the increase in cardiac output results from an increase in venous return to the heart due to peripheral venous constriction, decreased venous compliance, or both (1, 2, 9).

To test these hypotheses, Overbeck et al. (10) and Overbeck (11) investigated the hemodynamics of the limb vascular bed in both the early and the chronic (more than 4 weeks) stages of perinephritic hypertension in pentobarbital-anesthetized dogs. These authors found similar limb hemodynamics in the early and chronic stages, including normal blood flow and increased vascular resistance. In addition, Overbeck (11) has presented evidence to suggest decreased compliance of the femoral vein in dogs with early perinephritic hypertension.

Although the studies of Overbeck et al. (10) and
Overbeck (11) do not provide evidence that the increase in limb vascular resistance in perinephritic hypertension can be attributed to an autoregulatory response to increased limb blood flow, it is possible that autoregulation plays a role in other vascular beds. In the present study, we investigated the possibility of autoregulation in the mesenteric vascular bed. Because of the important blood reservoir function of the splanchnic vessels, we also measured pressure-volume relationships in mesenteric veins. Decreased compliance of these veins could contribute to the increase in cardiac output in early perinephritic hypertension.

Methods

Healthy conditioned male mongrel dogs weighing 18–27 kg were trained to lie quietly during femoral artery punctures for blood pressure measurements. A mean arterial blood pressure of less than 130 mm Hg was documented on at least two occasions in each dog. During the entire study period, the dogs were maintained on a diet of standard dog chow (Wayne Dog Food) and water ad libitum. A total of 50 dogs was used. They were divided into the following groups: H (hypertensive)-110 dogs, H-2 15 dogs, C (control)-110 dogs, and C-2 15 dogs. Prior to surgery, the dogs were given procaine penicillin (60,000 units) and streptomycin (0.5 g) intramuscularly. Following surgery, femoral arterial blood pressures and right kidney under sodium pentobarbital anesthesia. For these studies, the dogs, fasted for 24 hours, were anesthetized with sodium pentobarbital (35 mg/kg, iv) and mechanically ventilated to maintain measured systemic arterial blood pH at 7.39–7.43. Hematocrits were measured weekly until the time of the pressure-volume studies (Fig. 2). The mean arterial blood pressure was kept at 37–38°C by a heating lamp, and it was kept moist by covering it with Saran Wrap. A femoral artery was cannulated (PE 240) for monitoring large artery pressure (P LA). Intravascular pressures were measured by Statham P23Gb pressure transducers and recorded on a Sanborn oscillographic recording machine.

Beginning 90 minutes after the initial anesthesia in all dogs, repeated measurements of intravascular pressures and mesenteric venous outflow were obtained (by stop-watch and graduated cylinder) for 30 minutes. At the conclusion of these measurements, the ileal loop and its mesenteric vasculature were excised and weighed.

Steady-state measurements (defined as the average of two or more consecutive readings of blood flow, taken every 5 minutes, within ± 1 ml of each other) were used in our calculations. Blood flow was expressed as ml/min and ml/min 100 g−1 ileum. We divided intravascular pressure gradients by the blood flow to calculate steady-state total and segmental vascular resistances as follows.

Mesenteric total resistance (R T)

\[
R_T = \frac{(P_{LA} - P_{SA})}{blood\ flow\ 100\ g^{-1}\ ileum}
\]

Mesenteric large artery resistance (R LA)

\[
R_{LA} = \frac{(P_{LA} - P_{SA})}{blood\ flow\ 100\ g^{-1}\ ileum}
\]

Mesenteric small vessel resistance (R SV)

\[
R_{SV} = \frac{(P_{SA} - P_{SV})}{blood\ flow\ 100\ g^{-1}\ ileum}
\]

Mesenteric large vein resistance (R LV)

\[
R_{LV} = \frac{(P_{LV} - P_{SV})}{blood\ flow\ 100\ g^{-1}\ ileum}
\]

Flows, pressures, and calculated resistances in dogs of the hypertensive groups were compared with those of controls by Student's t-test, rejecting the null hypothesis at probability values less than 0.05.

We studied mesenteric hemodynamics in dogs of groups H-1 and C-1 11 days after surgery. We studied groups H-2 and C-2 2 weeks after nephrectomy. For these hemodynamic studies, the dogs, fasted for 24 hours, were anesthetized with sodium pentobarbital (35 mg/kg, iv). Supplemenal doses of sodium pentobarbital (50–100 mg, iv) were given later, as necessary, but not before the completion of mesenteric blood flow and pressure measurements. The dogs were intubated with a cuffed endotracheal tube and mechanically ventilated to maintain measured systemic arterial blood pH at 7.39–7.43. We obtained 5 ml of blood for the measurement of blood urea nitrogen and then gave heparin (12,000 USP units, iv) for systemic anticoagulation.
Small artery and its branches and the adjacent nerves were also clamped at points indicated by the solid bars in Figure 2. After clamping, the venous segment was drained of its blood content through the indwelling catheter until intrasegmental pressure, monitored through a T-tube arrangement, was atmospheric. Then, to produce step increases in intrasegmental pressure, we injected 0.05-ml samples of the dog's own blood at 37-38°C into the distal end of the indwelling catheter; 6-19 injections of blood were made, producing intrasegmental pressures up to 50 mm Hg. A 10-second pause after each injection was allowed to establish steady-state pressures. These steady-state intrasegmental pressures were measured with a Statham P23Gb pressure transducer and recorded. We then withdrew 0.05-ml samples of blood at similar intervals, again measuring the resulting pressures. The time required for each pressure-volume study was less than 5 minutes. Circulation through the venous segment was then restored by removing the clamps. Data were accepted if all of the injected blood was recovered from the segment, returning intrasegmental pressure to atmospheric level ± 2 mm Hg. This pressure-volume measurement was repeated after a waiting period of 25 minutes. Using the average of two or three series of measurements, a venous pressure-volume curve was constructed for each dog. Injection-phase volumes producing intrasegmental pressures of 5, 15, 25, and 35 mm Hg and calculated compliance (ΔV/ΔP) in the pressure range of 0 to 10 mm Hg in the hypertensive dogs were compared by Student's t-test with respective values in the control normotensive dogs. A similar analysis was done for values during the withdrawal phase. These data were also analyzed by methods developed by Gill and Hafs (13). This latter analysis, although more complex, takes into consideration the split-plot structure of the data, where data points are not independent and correlations of errors may be induced. In this latter analysis, we compared the pressure-volume curves as a whole of hypertensives with those of normotensives over the volume range of 0 to 0.45 ml. Several pressures in the higher volume ranges were derived by extrapolation from the individual pressure-volume curves.

At the conclusion of these in vivo hemodynamic studies, a 5-cm segment of the superior mesenteric vein, the caudal pancreatic-duodenal vein serving as a midpoint, was removed. With the collaterals tied off and cut near their origin, this mesentric vein segment was transferred immediately to a chamber containing Krebs-Ringer's bicarbonate solution (NaCl 118.3 mM, KCl 4.7 mM, MgSO4 1.2 mM, KH2PO4 1.2 mM, Ca gluconate 2.5 mM, NaHCO3 25.0 mM, and glucose 11.1 mM) kept at 37-38°C and aerated with a 95% O2-5% CO2 gas mixture. The pH of the tissue bath was adjusted to 7.40-7.43, if necessary, by the addition of 0.1-0.5 ml of 0.1N HCl. We secured each end of the cut venous segment to the tip of a thin-walled glass cannula with an outside diameter similar to the inside diameter of the vein. The in vitro length of the venous segment was adjusted to 4 cm in each experiment. The vein was perfused in the direction of flow in the intact dog at constant flow (25 ml/min) with the same Krebs-Ringer's solution used in the chamber. To produce step increases in intrasegmental pressure, we stopped perfusion, drained the vein to atmospheric pressure, and then injected 0.2-ml samples of Krebs-Ringer's solution. Pressure-volume measurements were repeated at 25-minute intervals. At the end of the experiment, the venous segment was weighed to within ±0.001 g. The in vitro data were analyzed in the same way as the in vivo
pressure-volume data. Pressure-volume curves as a whole were compared by the method of Gill and Hafs (13) over the volume range of 0 to 2.0 ml.

We also studied superior mesenteric vein pressure-volume relationships by rapid constant infusion of Krebs-Ringer's solution at 9.88 ml/min (infusion-withdrawal pump, Harvard Apparatus), reaching a maximum intrasegmental pressure of 40-50 mm Hg within 5-15 seconds. In three H-2 and three C-2 dogs, we repeated these rapid infusions after we had relaxed the venous segment by perfusion with NaCN in saline (500 mg/liter) at 37°C for 20 minutes.

Finally, in four H-2 and four C-2 dogs, an intact mesenteric vascular arcade was removed and placed in 10% buffered Formalin for histopathologic examination. Transverse sections of veins were taken from the mesentry and examined using the following stains: hematoxylin and eosin, Lillie's allochrome, Alcian Blue PAS, Verhoff's elastica, Wilder's reticulin, and Gomori's tri-chrome. Venous morphology was studied with a light microscope by one author (J. F. D.) who did not know the source of the tissue. At autopsy, we examined the kidney(s).

Results

From an average preoperative value of 118 mm Hg, mean arterial blood pressure in unanesthetized dogs rose 11 mm Hg (P < 0.001, N = 23) during the first 2 weeks after one kidney was wrapped in silk. Following removal of the opposite kidney, the mean arterial blood pressure rose on the average by an additional 40 mm Hg (P < 0.001, N = 12). In the control groups, the preoperative mean arterial blood pressure was 118 mm Hg, and there was no significant (P > 0.05) change in blood pressure following sham surgery (N = 24) or nephrectomy (N = 13). There was no statistically significant difference between the hypertensive and the control groups in body weight (Table 1) or hematocrit at the time of the hemodynamic studies. The mean blood urea nitrogen of H-1 and H-2 hypertensive dogs, 13.1 (N = 9) and 19.4 (N = 12) mg/100 ml, respectively, was not significantly different (P > 0.05) from that of C-1 and C-2 dogs, 14.1 (N = 8) and 15.2 (N = 13) mg/100 ml, respectively. The general health of all dogs whose hemodynamic studies were included in the results remained good.

Table 1 shows group means ± se of blood flows, pressures, and calculated resistances at 90-120 minutes following the induction of sodium pentobarbital anesthesia in the early two-kidney hypertensive (H-1), and the early one-kidney hypertensive (H-2), and the appropriate control (C-1 and C-2) dogs. Table 1 also shows the combined data from groups H-1 plus H-2 and groups C-1 plus C-2. Ileal blood flow and pressure data were rejected from one H-2 hypertensive dog because of malignant hypertension, manifested by blindness, an awake mean arterial blood pressure of 225 mm Hg, and a hematocrit of 31%, and from one C-2 control dog because of atrial fibrillation in the course of the hemodynamic studies. The ileal blood flow of these dogs was 18.0 and 25.2 ml/min 100 g−1, respectively.

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>C-1 (N = 10)</th>
<th>C-1 (N = 14)</th>
<th>C-1 + C-2 (N = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow (ml/min)</td>
<td>18.8 ± 0.9</td>
<td>21.0 ± 1.8</td>
<td>20.5 ± 1.7</td>
</tr>
<tr>
<td>Blood flow (ml/min 100 g−1)</td>
<td>48.2 ± 3.6</td>
<td>53.9 ± 5.0</td>
<td>46.7 ± 3.2</td>
</tr>
<tr>
<td>Pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large artery (PLa)</td>
<td>156.5 ± 3.2</td>
<td>163.4 ± 4.1</td>
<td>145.9 ± 3.4</td>
</tr>
<tr>
<td>Small artery (Psa)</td>
<td>122.5 ± 3.9</td>
<td>114.4 ± 4.9</td>
<td>106.8 ± 3.7</td>
</tr>
<tr>
<td>Small vein (Psv)</td>
<td>12.7 ± 0.8</td>
<td>12.9 ± 1.0</td>
<td>11.6 ± 0.5</td>
</tr>
<tr>
<td>Large vein (Plv)</td>
<td>7 ± 0.6</td>
<td>7 ± 0.6</td>
<td>7 ± 0.6</td>
</tr>
<tr>
<td>Resistance (mm Hg/ml min−1 100 g−1)</td>
<td>3.24 ± 0.23</td>
<td>3.20 ± 0.31</td>
<td>3.22 ± 0.32</td>
</tr>
</tbody>
</table>

* P < 0.05 for comparison of hypertensive group with appropriate control group.
† P < 0.001 for comparison of hypertensive group with appropriate control group.
‡ Held constant at 7 mm Hg.
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Table 2 presents the in vivo and Table 3 the in vitro mesenteric vein pressure-volume data during the injection phase. The means ± SE of total volumes (ml) which produced intravenous pressures of 5, 15, 25, and 35 mm Hg and the means ± SE of calculated compliance, ΔV/ΔP, in the pressure range of 0 to 10 mm Hg are tabulated. Pressure-volume relationships and calculated compliances in veins from dogs of group H-1 were not significantly different from values in the control group (C-1). Split-plot analysis confirmed this finding (P > 0.05). In contrast, in dogs of group H-2, the total volumes producing intravenous pressures of 5, 15, 25, and 35 mm Hg were significantly lower by Student’s t-test (P < 0.05) in H-2 hypertensives than they were in C-2 controls. These conclusions were again corroborated by split-plot analysis (P < 0.005 in vivo and in vitro).

Figure 4 illustrates the in vivo and Figure 5 the in vitro mesenteric vein hysteresis loops (means) of H-2 and C-2 dogs. Both the injection and the withdrawal curves of H-2 dogs were shifted in the

### Table 2

**In Vivo Mesenteric Vein Pressure-Volume Relationships (Injection Phase)**

<table>
<thead>
<tr>
<th>Intravenous pressures (mm Hg)</th>
<th>C-1 (N = 10)</th>
<th>H-1 (N = 10)</th>
<th>C-2 (N = 15)</th>
<th>H-2 (N = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.174 ± 0.021</td>
<td>0.185 ± 0.021</td>
<td>0.238 ± 0.029</td>
<td>0.157 ± 0.017*</td>
</tr>
<tr>
<td>15</td>
<td>0.370 ± 0.040</td>
<td>0.340 ± 0.024</td>
<td>0.426 ± 0.038</td>
<td>0.305 ± 0.031*</td>
</tr>
<tr>
<td>25</td>
<td>0.484 ± 0.042</td>
<td>0.443 ± 0.032</td>
<td>0.534 ± 0.038</td>
<td>0.393 ± 0.036*</td>
</tr>
<tr>
<td>35</td>
<td>0.532 ± 0.045</td>
<td>0.495 ± 0.041</td>
<td>0.584 ± 0.040</td>
<td>0.431 ± 0.036*</td>
</tr>
<tr>
<td>0–10</td>
<td>0.0288 ± 0.0032</td>
<td>0.0276 ± 0.0027</td>
<td>0.0332 ± 0.0038</td>
<td>0.0240 ± 0.0024*</td>
</tr>
</tbody>
</table>

All values are means ± SE.

* P < 0.05 for comparison of hypertensive group with appropriate control group.

### Table 3

**In Vitro Superior Mesenteric Vein Pressure-Volume Relationships (Injection Phase)**

<table>
<thead>
<tr>
<th>Intravenous pressures (mm Hg)</th>
<th>C-1 (N = 9)</th>
<th>H-1 (N = 9)</th>
<th>C-2 (N = 11)</th>
<th>H-2 (N = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.211 ± 0.138</td>
<td>0.960 ± 0.123</td>
<td>1.009 ± 0.145</td>
<td>0.513 ± 0.086*</td>
</tr>
<tr>
<td>15</td>
<td>2.014 ± 0.168</td>
<td>1.632 ± 0.123</td>
<td>1.815 ± 0.200</td>
<td>1.160 ± 0.106*</td>
</tr>
<tr>
<td>25</td>
<td>2.281 ± 0.175</td>
<td>1.872 ± 0.125</td>
<td>2.073 ± 0.202</td>
<td>1.444 ± 0.095†</td>
</tr>
<tr>
<td>35</td>
<td>2.449 ± 0.184</td>
<td>2.020 ± 0.135</td>
<td>2.233 ± 0.201</td>
<td>1.645 ± 0.083†</td>
</tr>
<tr>
<td>0–10</td>
<td>0.1757 ± 0.0151</td>
<td>0.1400 ± 0.0123</td>
<td>0.1564 ± 0.0193</td>
<td>0.0928 ± 0.0101*</td>
</tr>
</tbody>
</table>

All values are means ± SE.

* P < 0.05 for comparison of hypertensive group with appropriate control group.

† P < 0.01 for comparison of hypertensive group with appropriate control group.
In vivo mesenteric vein pressure-volume curves (means of groups). The solid and broken lines indicate the injection-phase pressure-volume curve of group C-2 (N = 15) and group H-2 (N = 15), respectively. Horizontal bars represent ± SE. Withdrawal curves (dot-dash lines) for control (N = 15) and hypertensive (N = 15) groups are also shown. A single asterisk = P < 0.05, and two asterisks = P < 0.01 for comparisons of the injection curves from the control and hypertensive groups.

direction of the pressure axis. (In contrast, even during the withdrawal phase, pressure-volume curves for groups H-1 and C-1 did not significantly differ [data not shown].) The injection curves of both H-2 and C-2 dogs were convex to the volume axis, but the injection curves of hypertensive dogs appeared to be steeper over the low pressure range (0 to 15 mm Hg).

Pressure-volume relationships during rapid infusion into the superior mesenteric vein segments in vitro appeared to corroborate the step injection studies. Perfusing the in vitro vein with NaCN for 20 minutes failed to shift these pressure-volume curves away from the pressure axis. The average weight of superior mesenteric veins from hypertensive (H-2) dogs, 0.266 g, was not significantly different (P > 0.5) from that from control (C-2) dogs, 0.284 g. Histologic examination of stained sections of the mesenteric vascular arcade of four H-2 hypertensive and four C-2 control dogs provided no evidence for abnormalities in the morphology of small veins from hypertensive dogs. Specifically, there was no evidence for smooth muscle hypertrophy or proliferation, alteration in the size, shape, or position of smooth muscle nuclei, increased adventitial collagen, reticulin, or fibrous fibers, accumulation of neutral or acid polysaccharides, and endothelial cell hyperplasia or swelling.

Gross examination of the excised kidney(s) revealed no abnormality of the sham-wrapped kidney of normotensive control dogs. The capsule of the silk-wrapped kidney of hypertensive dogs was thickened, but the parenchyma appeared normal. The intact kidney of control and hypertensive dogs appeared normal.

Discussion

There have been numerous studies of hemodynamics in the chronic stage of experimental renal hypertension. These studies indicate that the cardiac output is normal and that the hypertension is attributable to an increase in peripheral vascular resistance, fairly uniformly distributed in the various regional vascular beds (15). Blood flow to the limbs (10), the heart (16), the brain (17), and the nonstenotic kidney (18, 19) is reported to be normal.

In contrast to the hemodynamics of the chronic stage, there is now evidence that in the early stage (less than 4 weeks) of experimental renal hypertension cardiac output is elevated (1-4). For example, in dogs in the early stage of perinephritic and one-kidney Goldblatt hypertension, the cardiac output is elevated and total peripheral vascular resistance is normal or decreased (2, 4). The transition in systemic hemodynamics occurring between the early and chronic stages of renal hypertension has been attributed to peripheral vascular autoregulatory responses to the early increase in cardiac output (2-8).

Consequently, there has been recent interest in studying regional hemodynamics during the early stages of experimental renal hypertension (11, 20). Overbeck (11), for example, investigated blood flow and pressures in the forelimb vascular beds of dogs with early two- and one-kidney perinephritic hypertension under sodium pentobarbital anesthesia. He found no evidence for increases in blood flow even in the very early (less than 2 weeks) stage of development of hypertension. There were instead...
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significant elevations of limb vascular resistance in these early hypertensive dogs similar to those in the chronic stage of one-kidney perinephritic hypertension (10). Without evidence for increased blood flow through the forelimb vascular beds, he concluded that it was unlikely that the increase in forelimb vascular resistance could be attributed to an autoregulatory response.

It was, therefore, of great interest to us to study the hemodynamics of other vascular beds during the developmental stage of perinephritic hypertension. Specifically, we were interested in determining whether the mesenteric vascular bed receives excess blood flow and whether an autoregulatory response is a plausible explanation for arteriolar constriction in this bed. We used experimental techniques and anesthesia similar to those used by Overbeck (11) to allow comparisons of his study and ours.

Our results indicate that in the early stage of perinephritic hypertension the regional hemodynamics of the mesenteric vascular bed appear to be substantially different from those of the forelimb. In contrast to the forelimb, where resistance is elevated, ileal resistance to flow is unchanged from normal and ileal blood flow is increased, at least if data from the two hypertensive groups are pooled. We feel it is valid to pool these flow data, because cardiac output, according to Ferrario et al. (2), is elevated in both groups of dogs. Total ileal blood flow on a per weight basis in our hypertensive dogs was increased 17% above normal. The maximum increase in cardiac output reported by Ferrario et al. (2) in dogs with early one-kidney perinephritic hypertension is 18%. It appears, then, that a portion of the elevated cardiac output in early experimental perinephritic hypertension increases the blood flow through the mesenteric vascular bed.

The apparently normal mesenteric vascular resistances (total and segmental) that we observed in our one-kidney hypertensive dogs suggest that passive vasodilation does not occur despite elevated intravascular distending pressures. This finding suggests decreased vascular distensibility in the hypertensive dogs, not only on the arterial but also on the venous side of the circulation. Because plasma volume is reportedly normal in early one- and two-kidney perinephritic hypertension (2), decreased venous distensibility may be the mechanism responsible for the increased cardiac output (1, 2, 9). Increases in mean circulatory pressure have been reported in dogs with one-kidney perinephritic and Goldblatt hypertension (2, 21). Direct evidence that venous compliance is decreased in perinephritic hypertension comes from the work of Overbeck (11), who observed that the pressure-volume curve of the femoral vein in early perinephritic hypertensive dogs is shifted in the direction of the pressure axis. The findings of the present study extend this previous observation by indicating that mesenteric vein compliance is decreased in early one-kidney perinephritic hypertension in dogs. Considering the important blood reservoir function of the mesenteric venous bed, this new finding has special significance. If the compliance of all mesenteric veins is similarly reduced in the early stage of perinephritic hypertension, venous return to the heart would be substantially elevated. Thus, this finding may well help to explain the mechanism of the increased cardiac output in one-kidney perinephritic hypertension.

Vascular wall stretch over lower pressure ranges is opposed by the elastic properties of vascular smooth muscle (22). Thus, the reduced venous compliance that we observed in hypertensive dogs over the low pressure range implies smooth muscle participation in the form of contraction or structural changes, or both. However, our data suggest that contraction of vascular smooth muscle is not responsible for the decreased venous compliance. Both the in vivo and the in vitro pressure-volume curves in hypertensives and normotensives were similar in shape and generally convex to the volume axis; however, vascular smooth muscle contraction characteristically changes the pressure-volume curve to a sigmoid configuration (22). We studied delayed compliance: following each injection, we allowed 10 seconds for equilibration of intravenuous pressure. Delayed compliance measurements are relatively insensitive to vascular smooth muscle contraction (22). We also studied venous compliance by rapid intravenous infusion (immediate compliance) but found no difference in the results obtained by the two techniques. The shift of the hypertensive pressure-volume curves in the direction of the pressure axis persisted during withdrawal, when venous smooth muscle is considered to be relaxed (22). Finally, NaCN, which ablates smooth muscle tone, did not change the shape of the pressure-volume curves.

These data suggest to us that structural changes in the venous walls involving the vascular smooth muscle are primarily responsible for the decreased venous compliance. Regarding the nature of these structural changes, histologic studies did not demonstrate any alteration in the physical dimensions
or the appearance of the hypertensive veins. This fact suggests subtle structural changes, such as those due to edema or an increase in the cellular or paracellular matrix (23, 24). In this regard, we have unpublished observations indicating that the water and sodium content of femoral veins from early and chronic stages of one-kidney perinephritic hypertension in dogs is increased. We suggest that such "waterlogging" of veins in hypertension may account for the reduced venous compliance.

Regarding the pathogenesis of these structural changes, our finding of reduced venous compliance in vitro, using an artificial solution, effectively eliminates the possibility that extrinsic humoral or neural factors are immediately responsible. However, we cannot rule out the possibility that the decreased venous distensibility may be a residual effect of humoral or neural factors.

The flow-resistance data from these studies indicate that in early perinephritic hypertension the compliance of resistance vessels may also be reduced. Although we feel it is likely that such changes may be attributable to increases in the salt and water content of arteries (23, 25), it is possible that the reduced arterial compliance is an early manifestation of long-term autoregulation (8) in response to the increased mesenteric blood flow. Continuing studies of the hemodynamics of the mesenteric vascular bed in the chronic stage of experimental renal hypertension will probably help to further define the role of autoregulation.

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