Pre- and Postcapillary Vascular Responses to Sympathetic Nerve Stimulation in DOCA-Hypertensive Dogs

TOMMY A. BROCK, PH.D., BERNARD P. FLEMING, PH.D., AND JOHN N. DIANA, PH.D.

SUMMARY Measurements of precapillary resistance ($R_p$), postcapillary resistance ($R_v$), and mean capillary hydrostatic pressure ($P_{ci}$) were made during sympathetic nerve stimulation (SNS) under constant-flow perfusion in isolated hindlimbs from deoxycorticosterone acetate (DOCA)-hypertensive dogs. We found that both pre- and postcapillary vascular responses to SNS were greater in the DOCA-hypertensive group when compared to the control group. Intraarterial injections of norepinephrine produced a dose-response curve for precapillary vessels in the hypertensive group that was asymmetrically shifted to the left (increased slope) and exhibited a significant decrease in vasoconstrictor threshold. These results, coupled with our earlier observations, suggest that the hyperresponsiveness of the precapillary segment in DOCA-hypertensive dogs could be attributed to both structural and intrinsic alterations of the resistance vessels. We present evidence that suggests, however, that the increased postcapillary resistance with SNS may be explained by a structural alteration causing a decrease in the diameter of existing postcapillary vessels, or may be due to a decrease in the actual number of postcapillary vessels, or both. It is concluded that in this model of hypertension, postcapillary vascular changes also contribute to the overall increase in total peripheral resistance.

(Hypertension 3: 471-478, 1981)

KEY WORDS • isogravimetric • sympathetic nerve stimulation

It has been previously reported that venous distensibility is decreased in experimental hypertension1-4 as well as in essential hypertension.5-8 The factors that contribute to this phenomenon remain unclear. In isolated hindlimbs from deoxycorticosterone acetate (DOCA)-hypertensive dogs, we previously demonstrated that the decreased venous distensibility was in part due to some form of structural alteration of the postcapillary segment.9 Hindlimbs from hypertensive dogs exhibited an increased venous resistance following maximal pharmacological vasodilation, as compared to control hindlimbs. The observed structural differences may be due to vascular hypertrophy,10 an increase in vascular tissue water and electrolyte content ("waterlogging"),11,12 or both.

There is additional evidence that the decreased venous distensibility in hypertension may also be due to increased venomotor tone. Takeshita and Mark9 reported that venous distensibility increased significantly (20%) in patients with borderline hypertension following phentolamine infusion, but did not increase in normotensive patients. Likewise, Walsh et al.9 found that hypertensive patients failed to demonstrate a decrease in venous distensibility after tilting, a phenomenon that occurred in normotensive patients. In experimental hypertension, venous responsiveness to norepinephrine2 and adrenergic nerve stimulation2 are enhanced.

The present experiments were designed to study pre- and postcapillary vascular responses to sympathetic nerve stimulation (SNS) in deoxycorticosterone acetate (DOCA)-salt-induced hypertension. Our results demonstrate that the increased responses of the postcapillary vascular bed in the isolated hindlimbs from dogs with DOCA-salt hypertension may be due to one or more structural factors: 1) a decrease in the initial resting caliber of the postcapillary vessels; 2) a decrease in the actual number of postcapillary vessels; 3) or both. The phenomenon may aid in decreasing venous distensibility in this form of hypertension.
Materials and Methods
Experiments were performed on the hindlimbs isolated from 14 male normotensive dogs and eight male hypertensive dogs (15 to 18 kg). Dogs in the normotensive control group were obtained at least 1 day prior to an experiment. The following procedure was used to induce hypertension: the dogs were given sodium pentobarbital anesthesia (30 mg/kg i.v.), and the right kidney was removed via a flank incision. A recovery period of 6 days followed; on the sixth day, each animal was given an initial subcutaneous injection of deoxycorticosterone acetate (DOCA, Sigma) suspension, 25 mg/kg. Subsequent injections of DOCA were given weekly until each animal was sacrificed. Each dog in the DOCA-treated group had access to 0.9% NaCl plus 5.0% dextrose drinking solution ad libitum. The dogs were maintained on a standard diet of Purina Laboratory Dog Chow.

Blood pressure of the dogs in the DOCA/NaCl-treated groups was monitored weekly via a direct femoral artery puncture with the dogs under light sodium thiopental anesthesia. On the day of an experiment, the mean aortic pressure (MAP) was measured in the anesthetized dog (sodium thiopental, 30 mg/kg i.v.) by advancing a pressure catheter into the dorsal aorta via the right common carotid artery. Blood samples were drawn from a central venous catheter and hematocrits determined. Plasma samples were analyzed for sodium, potassium, and chloride. Blood-urea nitrogen and creatinine levels were analyzed to serve as indicators of renal function.

Isogravimetric Experiment
The experimental procedures used for isolating and perfusing the dog hindlimb have been described in detail previously. Pre- and postcapillary resistances were determined by the isogravimetric method originally developed by Pappenheimer and Soto-Rivera. Whole blood collected from a normotensive donor dog was used to perfuse all hindlimbs to minimize possible differences in blood chemistry between the groups. Briefly, several isogravimetric states were obtained for each hindlimb by reducing arterial pressure and increasing venous pressure to maintain hindlimb weight constant. Mean isogravimetric capillary hydrostatic pressure \((P_{al})\) was then determined by extrapolating the linear relationship between the isogravimetric venous pressure \((P_{vl})\) and isogravimetric flow \((Q_i)\) to zero flow. Postcapillary resistance \((R_p)\) and \(P_{al}\) were determined using least-squares linear regression analysis. Precapillary resistance \((R_n)\) was calculated using the relation: \(R_n = (P_{al} - P_{vl})/Q_i\) where \(P_{al}\) equals isogravimetric arterial pressure.

During isolation of the hindlimb, both femoral and sciatic nerves (which contain the sympathetic efferents to the hindlimb) were isolated. The above isogravimetric procedure was then duplicated during sympathetic nerve stimulation. The cut ends of the nerves were supramaximally stimulated \((3-12\ Hz, 60\ V, 10\ msec)\) using a Grass S5 stimulator. Before stimulation, 40 mg of gallamine triethiodide (Flaxedil, Davis and Geck) was administered to the perfusion system. This dose of gallamine was sufficient to prevent any visible signs of skeletal muscle contraction to electrical stimulation throughout the study period. Precapillary postcapillary resistance and isogravimetric capillary hydrostatic pressure were then determined. The vascular bed was allowed to recover for several minutes between each period of stimulation, during which time the hindlimb perfusion pressure returned to baseline.

Exogenous Norepinephrine and Vascular Reactivity
Vascular reactivity of the hindlimb to norepinephrine was determined in the following manner. Blood flow to the limb was set at 5.8 ml/min kg-i. The dose-response relationship of each hindlimb was determined by injecting constant volumes (100 \(\mu\)l) of norepinephrine bitartrate (Sigma, 0.01–100 \(\mu\)g) into the perfusion tubing connected to the femoral artery. Bolus injections of a similar volume of saline produced no detectable hemodynamic response. The maximum response to each dose of norepinephrine was measured as the peak change in perfusion pressure. Enough time was allowed between doses for perfusion pressure to return to its prestimulus baseline.

Data Analysis
Data were analyzed using the following statistical procedures. Precapillary responses to SNS were analyzed using a three-way analysis of covariance on an IBM computer. Least-squares linear regression analysis was used to obtain the best fit for lines describing data points and slopes of the regression lines. Student's unpaired t test was used throughout the study when comparing differences between group means. The minimum level of significance in all cases was considered to be \(p < 0.05\).

Results
DOCA/NaCl-treated hypertensive dogs were sacrificed 34 ± 8 days following initiation of treatment. Both control and hypertensive dogs were free of heartworms and outwardly healthy. Mean arterial pressure appeared to be increased following 1 week of treatment, and continued to rise throughout the test period (fig. 1). Mean aortic pressure of the hypertensive group measured at the time of sacrifice was increased by 29% over that recorded for the control group (160 ± 10 vs 124 ± 5 mm Hg, \(p < 0.001\)). Hypertensive dogs demonstrated a significant increase in hematocrit at the time of sacrifice (45.3 ± 1.8 vs 37.7 ± 1.1%, \(p < 0.001\)) as compared to control dogs. Plasma sodium was also significantly increased in the hypertensive group (155.0 ± 3.8 vs 146 ± 1.6 mEq/l \(p < 0.05\)) while plasma potassium was slightly reduced (2.9 ± 0.3 vs 3.9 ± 0.1 mEq/l, \(p < 0.05\)). Blood-urea nitrogen (control = 14.0 ± 0.9; DOCA = 12.7 ± 1.1 mg/100 ml) and creatinine (control = 0.9 ± 0.1; DOCA = 0.9 ± 0.1 mg/100 ml) were not different between groups of dogs.
FIGURE 1. Increase in mean arterial pressure during administration of deoxycorticosterone acetate and saline to nephrectomized dogs. Arrow denotes time of unilateral nephrectomy. Data are expressed as mean values ± SEM for five to eight dogs. Level of significance: *p ≤ 0.05.

Pressure vs Flow Measurements

The mean isogravimetric capillary pressure (Pci) was used to establish the pressure difference between the effective midpoint of the capillary and the points where arterial (Pai) and venous (Pvi) pressures were measured. Figure 2 illustrates the pressure-flow curve obtained for the precapillary vascular bed. For any given flow, the perfusion pressure was greater in the hindlimbs from hypertensive dogs. Likewise, the slope of the pressure-flow relationship was significantly greater in the hypertensive group, and the 95% confidence intervals did not overlap. Presented in figure 3 are mean values for the pressure-flow points obtained for the postcapillary vascular segment. Again, the postcapillary pressure difference at any given flow was significantly increased in the hindlimbs from hypertensive dogs. The slope of the pressure-flow curve was significantly greater in the hypertensive group, and the 95% confidence intervals did not overlap. The Pci of the isolated hindlimbs was not different between groups (control = 13.6 ± 0.7; DOCA = 15.0 ± 0.9 mm Hg).

Sympathetic Nerve Stimulation

For any given flow, sympathetic nerve stimulation (SNS) resulted in greater precapillary pressure differences in the hypertensive group when compared with precapillary pressure differences at similar flows in the control group. The effect of SNS on the actual change in precapillary resistance (ΔRc) is presented in table 1. Since the relationship between flow and precapillary responses to nerve stimulation was complex, we analyzed the data using an analysis of variance. The dependent variable was change in precapillary resistance. The independent variable was the group consisting of either control or hypertensive hindlimbs using the two metric covariates, frequency and hindlimb flow. There were no significant two-way or three-way interaction effects. After adjusting for the covariates, the deviation from the grand mean, 6.67, was 0.79 for the control and 1.31 for the hypertensive groups, a difference of 2.10. The observed significance was p = 0.002. Postcapillary vascular responses to SNS are presented in figure 4. At each stimulation frequency, ΔRc (Rc is constant over a
consistently evoked greater pressor responses in hindlimbs from DOCA/NaCl hypertensive dogs; the average threshold dose was approximately four times less in the DOCA/NaCl group (9.0 ± 1.0 vs 35.0 ± 7.0 ng, p < 0.005).

Discussion

The role of the sympathetic nervous system in decreasing venous distensibility in hypertension has not yet been fully defined. The present study was designed to examine the effect of adrenergic nerve stimulation on pre- and postcapillary vascular responses and capillary permeability in isolated hindlimbs from DOCA-hypertensive dogs. Both pre- and postcapillary vessels of DOCA-hypertensive dogs exhibited increased responses to SNS, but SNS had no detectable effect on capillary permeability to plasma proteins.

Pressure vs Flow Relationships

The interpretation of the isogravimetric pressure-flow relationships shown in figures 2 and 3 needs to be clarified. Of possible importance, although not explicitly referred to in these figures, is the prevailing level of the mean transmural pressure and its influence on overall vascular resistance. As isogravimetric flow (Qi) is increased, the mean precapillary transmural pressure, \((P_{ai} + P_{ci})/2\) will increase, and if this vascular segment behaves passively, its effective diameter will increase, thereby reducing \(R_a\). On the postcapillary side, as Qi is increased the mean transmural pressure there, \((P_{ci} + P_{vi})/2\), will decrease, and passive venous collapse may take place. Thus, as Qi is altered, opposite changes take place in pre- and postcapillary transmural pressures; these forces may passively alter vascular caliber, making interpretation of resistance changes from these isogravimetric

Table 1. Change in Precapillary Resistance Following Sympathetic Stimulation of the Isolated Hindlimb in Control and DOCA/NaCl Hypertensive Dogs

<table>
<thead>
<tr>
<th>Dog group</th>
<th>Frequency (Hz)</th>
<th>Hindlimb flow (ml/min • 100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2.0</td>
</tr>
<tr>
<td>Control (n = 12)</td>
<td>3</td>
<td>3.8 ± 1.0</td>
</tr>
<tr>
<td>DOCA/NaCl (n = 8)</td>
<td>4.6 ± 1.3</td>
<td>3.6 ± 0.8</td>
</tr>
<tr>
<td>Control (n = 12)</td>
<td>6</td>
<td>6.8 ± 2.1</td>
</tr>
<tr>
<td>DOCA/NaCl (n = 8)</td>
<td>12.7 ± 1.5</td>
<td>6.9 ± 1.3</td>
</tr>
<tr>
<td>Control (n = 12)</td>
<td>9</td>
<td>10.6 ± 1.7</td>
</tr>
<tr>
<td>DOCA/NaCl (n = 8)</td>
<td>11.6 ± 2.5</td>
<td>8.9 ± 1.2</td>
</tr>
<tr>
<td>Control (n = 12)</td>
<td>12</td>
<td>11.4 ± 2.9</td>
</tr>
<tr>
<td>DOCA/NaCl (n = 8)</td>
<td>15.0 ± 2.6</td>
<td>10.5 ± 1.5</td>
</tr>
</tbody>
</table>

Precapillary resistance is expressed in units of mm Hg/ml/min • 100g (tissue). Results are expressed as the mean ± SE.
pressure-flow curves difficult. To eliminate this problem, we examined the relationship between the mean transmural pressures and $R_a$ and $R_v$ for the same data shown in figures 2 and 3. The result is that both pre- and postcapillary resistances in the DOCA/NaCl dog hindlimb were elevated above the values for the control limbs at all values of mean pre- and postcapillary transmural pressure. This result confirms previous results found in DOCA/NaCl hypertensive dogs by Brock et al.\(^1\) Therefore, opposite passive changes in vascular caliber occurring in the pre- and postcapillary segments as flow is altered do not alter the conclusions reached from the data in figures 2 and 3, namely, that both $R_a$ and $R_v$ in DOCA/NaCl dog hindlimbs are elevated above those values found in the control limbs.

**Precapillary Vascular Responses**

It has been previously demonstrated that mesenteric\(^{17}\) and hindquarter\(^{18}\) vascular responses to SNS are enhanced in DOCA/NaCl hypertensive rats. This phenomenon was confirmed for the DOCA-hypertensive dogs in this study. Both structural changes in the resistance vessels and functional alterations of vascular smooth muscle may be responsible. We\(^{12}\) as others\(^{19,20}\) have shown that resting precapillary (arterial) resistance, following maximal pharmacological vasodilatation, is increased in DOCA-hypertensive animals above that of control preparations. Since all active tone is presumed to be removed, it is thought that this phenomenon reflects hypertrophy of the elements in the vascular wall with subsequent narrowing of the vessel lumen. Folkow and associates\(^{21,22}\) have presented evidence that medial hypertrophy contributes to the hyperresponsiveness of hypertensive vascular tissue. This was indicated in the present experiments by an increase in the steepness of the log dose-response curves to norepinephrine injection were greater and the dose-response relationship steeper. Both results are a reflection of an enhanced vascular hyperreactivity in DOCA/NaCl dog hindlimbs.

For the purpose of illustration, three hypothetical examples will be considered: 1) a normotensive (N) postcapillary segment consisting of six vessels in parallel with an effective lumenal radius ($r_i$) of 1.0 (arbitrary units); 2) a hypertensive (H1) segment consisting of 6 vessels with a reduced radius of 0.9; and 3) another hypertensive (H2) segment consisting now of only four vessels but with the same effective radius as the normotensive segment. The postcapillary resistance is computed utilizing the following formula for a parallel-coupled network:\(^{23}\) $R_v = C/n\cdot r_i^4$ where $C$ is a constant determined by the length of the vessels in the segment and by the effective blood viscosity. Both of these factors are assumed to be identical in all three hypothetical situations.

A wall/lumen ratio of 1/12 (= 0.083) was assumed for the normotensive postcapillary vessel.\(^{24}\) The cross-sectional area of these vessels was assumed to remain unchanged in hypertension so that a wall thickness ($w$) and $w/r_i$ could be computed for HI. The baseline hypothetical postcapillary resistances can now be computed (table 2). The ratio of the baseline hypertensive $R_v$ to normotensive $R_v$ is about 1.50 in the examples; because of the appropriate choice of numbers for the example, the ratio compares with the experimentally determined baseline $R_v$ ratio of 1.51.

### Table 2. Parameters for the Normotensive (N) and Hypertensive (H1 and H2) Postcapillary Circulation Models

<table>
<thead>
<tr>
<th>Model</th>
<th>$r_i$</th>
<th>$n$</th>
<th>$w/r_i$</th>
<th>$R_v$</th>
<th>$R_v/R_v^N$</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1.0</td>
<td>6</td>
<td>0.083</td>
<td>0.167C</td>
<td>—</td>
</tr>
<tr>
<td>H1</td>
<td>0.9</td>
<td>6</td>
<td>0.091</td>
<td>0.254C</td>
<td>1.52</td>
</tr>
<tr>
<td>H2</td>
<td>1.0</td>
<td>4</td>
<td>0.083</td>
<td>0.250C</td>
<td>1.50</td>
</tr>
</tbody>
</table>

$r_i$ = assumed baseline internal vascular radius arbitrary units; $n$ = number of parallel coupled postcapillary vessels; $w/r_i$ = wall to lumen ratio. $R_v$ = postcapillary resistance. $C$ = constant which reflects effective blood viscosity and vascular length. $R_v^N/R_v =$ ratio of predicted postcapillary resistances for hypertensive (H) and normotensive (N) changes.

**Figure 6.** Log-dose response curves to norepinephrine of isolated hindlimbs of DOCA-salt hypertensive and control animals. Data are expressed as mean increases in perfusion pressure (± SEM). Significant difference from control value: *$p \leq 0.025$; **$p \leq 0.01$.**
Another contributing factor to the vascular hyper-responsiveness may have been an increased sensitivity of the arterial smooth muscle to norepinephrine. Bohr and coworkers\textsuperscript{16, 26} have demonstrated that vascular smooth muscle from DOCA-hypertensive rats and pigs exhibits an increased sensitivity to norepinephrine that is independent of changes in wall stress. Likewise, Ekas and Lokhandwala\textsuperscript{17} have demonstrated an increased sensitivity of the mesenteric vascular bed to exogenous norepinephrine. This increase in vascular norepinephrine sensitivity was also observed in the present study in the perfused hindlimb vasculature of DOCA-hypertensive dogs.

**Postcapillary Vascular Responses**

Previous studies have suggested that venous distensibility is decreased in hypertension.\textsuperscript{1-10} There is evidence that the sympathetic nervous system may produce excessive venoconstriction, and thus play a role in decreasing venous distensibility. Takeshita and Mark\textsuperscript{8} showed that phentolamine significantly increased venous distensibility in subjects with borderline hypertension, but not in normotensive subjects. Likewise, Walsh et al.\textsuperscript{4} demonstrated that essential hypertensive patients failed to show a change in venous distensibility after being tilted, whereas distensibility decreased 27% in normotensive patients. This suggested that venous smooth muscle tone was already maximal. In experimental hypertension, Bevan et al.\textsuperscript{10} demonstrated increased venous responsiveness to SNS in rabbits with aortic-coarctation-induced hypertension, while Greenberg and Bohr\textsuperscript{4} demonstrated increased venous responsiveness to norepinephrine in spontaneously hypertensive rats.

Examination at the postcapillary resistance changes to SNS indicates that the changes in $R_v$ that occur at any level of stimulation are increased in DOCA-salt hypertension. The results in figure 4 indicate that, although the change in $R_v$ in response to SNS is increased in DOCA-salt hypertension, no potentiation of this response is seen as the rate of SNS increases. This type of response is to be contrasted with that occurring in total peripheral resistance (TPR) after splanchnic nerve stimulation in spontaneously hypertensive rats (SHR).\textsuperscript{23} These authors found that the frequency-response relationship for neurogenic control in SHR was steeper than in normotensive control rats (NCR). In this study the accentuated TPR change upon SNS was attributed to an increased wall/lumen ratio of the hypertensive resistance vessels. The responses observed in figure 4 in the DOCA-hypertensive postcapillary segment may be explained by either a decreased effective postcapillary diameter of existing vessels and/or a decreased number of patent postcapillary vessels.

For the purpose of illustration, three hypothetical examples will be considered: 1) a normotensive (N) postcapillary segment consisting of six vessels in parallel with an effective luminal radius ($r_l$) of 1.0 (arbitrary units); 2) a hypertensive (HI) segment consist-
ing of 6 vessels with a reduced radius of 0.9; and 3) another hypertensive (H2) segment consisting now of only four vessels but with the same effective radius as the normotensive segment. The postcapillary resistance is computed utilizing the following formula for a parallel-coupled network:

$$RV = C/n_r$$

where C is a constant determined by the length of the vessels in the segment and by the effective blood viscosity. Both of these factors are assumed to be identical in all three hypothetical situations.

A wall/lumen ratio of 1/12 (≈ 0.083) was assumed for the normotensive postcapillary vessel. The cross-sectional area of these vessels was assumed to remain unchanged in hypertension so that a wall thickness (w) and w/r could be computed for HI. The baseline hypothetical postcapillary resistances can now be computed (table 2). The ratio of the baseline hypertensive Rv to normotensive Rv is about 1.50 in the examples; because of the appropriate choice of numbers for the example, the ratio compares with the experimentally determined baseline Rv ratio of 1.51.

To compute the effects of SNS upon Rv in this example, we adopted assumptions very similar to those used by Folkow et al. in their construction of the hypothetical norepinephrine-vascular resistance dose-response curve for SHR and NCR. Figure 7 indicates the changes in postcapillary resistance that occur in these hypothetical situations; note that the abscissa is the percent decrease in smooth muscle length.

To make figures 4 and 7 compatible, one would need to know the extent of muscle shortening that would occur at any level of SNS in the postcapillary segment. This exact information is not available, but the values chosen for figure 7 are thought to be reasonably representative and thus allow the following points to be made. First, comparison of figures 5 and 7 shows there is a reasonable similarity between the experimental resistance changes observed and those predicted by the simple models of the postcapillary segment. Second, the models do not predict a potentiated response to SNS. For a thin-walled venous vessel with a small wall/lumen ratio, the potentiating effect of wall thickness on resistance changes is quite small. Thus, even in Case HI with a slightly increased w/r, no structurally related potentiation is predicted. This is to be contrasted with the potentiation of the TPR changes observed in SHR splanchic nerve stimulation. The TPR potentiation observed in this study was attributed to the increased w/r, in precapillary vessels. Furthermore, simply decreasing the number of patent postcapillary vessels would not give rise to a potentiated resistance response. This has been experimentally observed by Hallback et al. in studies where the rat hindlimb vasculature was artificially "rarefied" by graded microplugging, and norepinephrine-resistance dose-response curves were compared with those obtained in SHR hindlimbs.

Third, as can be observed, either a decreased baseline postcapillary diameter (HI) or a decreased number of patent vessels (H2) in the DOCA-salt hypertensive hindlimb may be responsible for the enhanced postcapillary resistance changes observed with SNS. As previously discussed, in DOCA-salt hypertensive hindlimbs the higher Rv observed with maximal vasodilatation would imply a decreased baseline diameter, and the lower filtration coefficient would be consistent with a decreased number of patent postcapillary vessels. Therefore, a reasonable conclusion based on these two experimental results and the model predictions might be that both a decreased effective postcapillary diameter and a decreased number of patent postcapillary vessels are responsible for the observed changes occurring in the venous segment of the DOCA-salt hypertensive hindlimb. It has been demonstrated that the number of patent precapillary arterioles is actually decreased in skeletal muscle of SHR. Therefore, one might expect the number of patent postcapillary vessels to decrease to maintain tissue homeostasis. Hutchins and Darnell, however, found that there are approximately twice as many fourth-order venules (20 μm) in the cremaster muscle of the SHR. Consistent with this observation are the results of Folkow et al. and Bohlen et al. that Rv is reduced in SHR hindparts and cremaster muscle, respectively. We find, however, that Rv is increased in our DOCA/NaCl dog hindlimbs. This elevated Rv in our hypertension model may, as we stated above, be due to a decreased number of functional, parallel-coupled postcapillary vessels. The different behavior of the postcapillary segment in the SHR and DOCA/NaCl muscular circulation only indicates that care must be taken when comparing the two different experimental models.

The functional significance of the sympathetic component to decreased postcapillary vascular distensibility remains to be determined. Simon et al. could not establish any correlation between decreased venous distensibility and systemic hemodynamic parameters in patients with established hypertension. Several reports indicate that there is a redistribution of blood volume from the peripheral circulation to the cardiovascular circulation in borderline hypertensive patients. Since plasma volume is reported to be reduced in several forms of experimental hypertension, increased venous responses to sympathetic activation may increase postcapillary resistance and decrease venous distensibility, thus helping to maintain normal cardiac output in established hypertension. However, in patients with borderline hypertension, these same phenomena may serve to intermittently elevate cardiac output, a feature characteristic of this form of hypertension.

It is important to note that alterations occurring in precapillary vessels are also occurring in postcapillary vessels not exposed to the high arterial pressure in DOCA/NaCl hypertensive dogs. Similarly, other investigators have shown that abnormalities can occur in arteries protected from the increased pressure in hypertensive animals. Berecek and Bohr have demonstrated that the hindlimb vascular bed, protected from the increased pressure load, exhibits an increased sensitivity to norepinephrine, as did the nonprotected vascular bed in DOCA-hypertensive pigs.
Bell and Overbeck found that, in rats with aortic coarctation hypertension, the normotensive vascular beds distal to the coarctation exhibited increased resistance and impaired maximal vasodilatation. These observations suggested that abnormalities seen in vascular smooth muscle in hypertension are not secondary to increased intravascular pressure. Instead, humoral and neural factors must be considered in finding an explanation for the abnormalities seen in postcapillary vessels.

References

27. Hutchins PM, Darnell AE: Observations of a decreased number of small arterioles in spontaneously hypertensive rats. Circ Res 34 and 35 (suppl 1): I-161, 1975
33. Bell DR, Overbeck HW: Increased resistance and impaired maximal vasodilatation in normotensive vascular beds of rats with coarctation hypertension. Hypertension 1: 78, 1979
Pre- and postcapillary vascular responses to sympathetic nerve stimulation in DOCA-hypertensive dogs.
T A Brock, B P Fleming and J N Diana

doi: 10.1161/01.HYP.3.4.471
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/3/4/471

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/