Intestinal Microvascular Adaptation During Maturation of Spontaneously Hypertensive Rats

H. Glenn Bohlen, Ph.D.

SUMMARY Adaptive microvascular changes to increased arterial pressure were investigated in the intestine of spontaneously hypertensive rats (SHR). In 4- to 5-week-old normal Wistar-Kyoto (WKY) and SHR rats, as well as in 18- to 21-week-old WKY rats, the number of arterioles of a given type per milligram of tissue were very similar. However, 18- to 21-week-old SHR had 30% to 35% fewer arterioles in the diameter range of 25–35 μm, as if intestinal vessels were lost or failed to grow during maturation. The largest and smallest arterioles in the intestine of adult SHR were constricted by 20% to 25%, but other vessels in the SHR had an equal or increased diameter relative to those in WKY rats. As a result of rarefaction and selective vasoconstriction in SHR, microvascular pressures in the intestinal muscle of SHR were near those in WKY rats, and those in villi of SHR were equal to those in WKY rats despite a 60% to 70% increase in mean arterial pressure in SHR. The percentage of small arterioles (<15 μm) that were intermittently closed to flow at rest was minimal, and the total number of small vessels per milligram of tissue was equal in WKY and SHR rats. These data indicate that the adaptive changes in the intestinal vasculature of SHR do not include the loss of small arterioles as occurs in skeletal muscle but that the vascular branching pattern is disturbed, and the largest and smallest arterioles are constricted in the intestine of SHR. (Hypertension 5: 739–745, 1983)

The majority of hemodynamic and microcirculatory studies of the Okamoto-Aoki spontaneously hypertensive rat (SHR) have dealt with the skeletal muscle vasculature. However, Ferrone et al. and Tobia et al. have shown that, during hypertension, the majority of organ vasculatures develop increased vascular resistance equal in proportion to that of skeletal muscle. In view of the diversity of microvascular functions and anatomical arrangements among the organs, it is difficult to extrapolate known characteristics of the hypertensive skeletal muscle vasculature to other organ systems. Therefore, it may not be warranted to assume that the skeletal muscle vascular characteristics of constriction to closure of arterioles as well as permanent loss of microvessels, or possibly vessel wall hypertrophy, occur throughout the body.

We investigated the format of intestinal microvascular adaptation to chronic hypertension in the SHR, and measured both the number and internal diameter of arterioles as well as the blood pressure within the microvessels. From these data, we analyzed the various modes of vascular adaptation and their relative importance to the increased intestinal vascular resistance during hypertension in the SHR.

Methods

We anesthetized 18- to 21-week-old and 4- to 5-week-old SHR and Wistar-Kyoto (WKY) rats (Taconic Farms) with Inactin (Byk Gulden, Kontanz, West Germany), in a dose of 10 mg/100 g body weight given intraperitoneally (1 mg/ml saline). Supplemental doses of 0.5 to 1 mg (subcutaneously) were given at approximately 2-hour intervals.

The animals were placed on a heating pad (36°C) as soon as they lost their ability to walk after the anesthetic was given. Upon surgical depth anesthesia, the right femoral artery was cannulated to measure mean arterial pressure and the trachea was cannulated. At all times, the body temperature was maintained between 37° and 38°C with a heating mat. In addition, the animal was tilted head up at a 30° incline; the rationale for this procedure is explained in Results.

A loop of jejunum was exposed through a midline incision. The bowel was prepared for observation using a previously reported technique. The muscle surface of the bowel was constantly bathed with a bicarbonate-buffered physiological solution. The P O2 and P CO2 of the solution over the tissue were both 40–45 mm Hg and the pH was 7.4 ± 0.05. These condi-
tions closely mimic intra-abdominal gas tensions and pH.10 The temperature of the tissue bath and support devices was maintained at 37°−38°C by circulating hot water through the support devices.

Microvascular pressures were measured with a servo-null pressure system manufactured by Instrumentation for Physiology and Medicine, Inc. (San Diego, California). Micropipettes were sharpened to a tip diameter of 1−2 μm and filled with 2 m NaCl. In an in vitro calibration, the relationship of an applied test pressure to that recorded with the servo-null system was linear over the range of 0−150 mm Hg.

Red cell velocity in arterioles was measured with a dual-slit velocity tracking system (Instrumentation for Physiology and Medicine, Inc.) based on the dual slit approach developed by Johnson and Wayland.11 The velocity system was calibrated using whole blood (Hct = 35%−43%) in vitro and in vivo conditions as described by Harper and Bohlen.12 Blood flow was calculated from the lumenal cross sectional area and the corrected velocity. Recorded velocities were divided by 1.6, which is an empirically derived correction factor to calculate the average red cell velocity for measurements made during transillumination.12,13 In all cases, red cell velocity was measured in first order arterioles, which had internal diameters in the same range as the glass tubing used in calibration of the velocity system.

Internal and external diameters of microvessels were determined with a digital video image splitting system developed by the Indianapolis Center for Advanced Research (Indianapolis, Indiana). The output of the system was processed with an Apple II Plus microcomputer. Changes in dimension of slightly less than 1 μm could be detected at magnifications of × 600 to 1200. All vessel images were recorded using a closed circuit Sony video system so that measurements could be made after the experiment.

The protocol for studies on the microvasculature of the intestinal muscle and mucosal layers was to record the diameter of each vessel for a minimum of 3 minutes followed by abolishing all active vascular smooth muscle tone with externally applied adenosine solution (10−4M). When adenosine was present, no additional vasodilation occurred if the tissue was exposed to sodium nitroprusside (1 mg/ml of bathing solution). Therefore, the concentration of adenosine used caused maximum dilation. Use of adenosine on the intestine had no effect on arterial blood pressure; sodium nitroprusside, however, caused a dose-dependent fall in mean arterial pressure after 10 to 15 minutes of exposure. Red cell velocity was measured in first order arterioles during resting and passive conditions. Outer and inner diameters of the first-, second-, and third-order arterioles, the only arterioles with a continuous muscle coat,17 were used to calculate the vessel wall thickness and the vessel wall cross-sectional area. The total number of first-, second-, and third-order arterioles were counted during resting and passive conditions. The third-order arterioles' very small size required counting the vessels along each parent second-order arteriole during

resting and passive conditions at a magnification of × 250. The number of vessels in total and as a function of tissue surface area and weight was determined in a section of tissue 19 mm long and 7 mm wide.

When microvascular pressures were to be measured, the diameter of the vessel was measured before and after micropipette penetration. If penetration caused a sustained change in diameter, the pressure measurement was not used. All diameter data to be presented were obtained prior to pipette penetration.

During each experiment, isoproterenol (Sigma Chemical Company, St. Louis, Missouri) was added to the bathing solution until spontaneous intestinal motility was sufficiently suppressed to allow observation. If the isoproterenol concentration exceeded 10−6 g/ml, the preparation was discarded because slight vasodilation would occasionally develop slowly. Isoproterenol rarely caused a measurable change in diameter of vessels in SHR and WKY rats at the concentrations used.

The anatomical arrangement of the intestinal microvasculature is displayed in figure 1. This schematic pattern was identical in normal and hypertensive rats except for minor differences described in Results.

The data are presented as the means plus standard error of the mean; a p < 0.05 or less, as computed with Duncan's new multiple range test,14 indicated a significant difference in means. A total of 15 SHR and 17 WKY adult rats and eight young WKY and 6 young SHR were successfully used to obtain these data.

Results

Arterial Blood Pressure

One of the recurring problems with the SHR is an often unexplained and abrupt drop in mean arterial pressure to near normal pressures when anesthetized. De Lano and Zweifach15 have recently described this problem in some detail. In our present study, we used a variation of a technique developed by Willis16 which minimized problems with inappropriately low arterial pressures that occurred in approximately one-third of the anesthetized adult SHR. In brief, elevation of the thorax and head of the SHR stabilized the arterial pressure, and this effect seemed to be mediated by improved depth of ventilation. At an incline of 30°−35°, the systolic arterial pressure recorded during Inactin (10 mg/100 g, i.p.) or 2% choralose-10% urethane (0.6 ml/100 g) anesthesia was very similar (± 5 mm Hg) to the tail-cuff systolic pressure in the conscious SHR. Elevation of the head and thorax had no appreciable influence on WKY or standard Wistar rats, but all the WKY and SHR were elevated during this study. If the elevation procedure was stopped, the mean arterial blood pressure decreased 20−50 mm Hg within 30 minutes in those SHR that were for some reason susceptible to a drop in arterial pressure when anesthetized. Restoration of tilt increased the blood pressure to the original pressure (± 5 mm Hg) within approximately 30 minutes. As a precautionary measure, all rats were placed in the tilt position as soon as surgical depth anesthesia was reached. Tilt angles of...
20°–40° were equally effective, but tilt angles less than 10° had no appreciable benefit. In 4 to 5-week-old animals, the arterial blood pressure remained stable for about 1 hour after surgery and thereafter decreased in both WKY and SHR. The fall in blood pressure was directly related to opening the abdominal cavity because the blood pressure remained stable so long as the abdominal cavity was not opened. However, since an abdominal incision was necessary, I elected to only study vascular morphology in young rats due to the problems with maintenance of a stable cardiovascular system.

**Numbers of Arterioles**

The number of first-, second-, and third-order arterioles in young and adult WKY and SHR as a function of tissue weight and the ratio of 2A to 1A and 3A to 2A are presented in table 1. All vessels in the tissue over a 19 × 7 mm plastic plate could be seen and counted. At the end of the experiment, the tissue over the plastic plate was excised, blotted, and immediately weighed. In all cases, the number of vessels per milligram of tissue refers to the wet weight of tissue. In 4- to 5-week-old SHR and WKY rats, the number of 1A, 2A, and 3A per milligram of tissue was not statistically

<table>
<thead>
<tr>
<th>Vessel</th>
<th>4-5 weeks old</th>
<th>18-21 weeks old</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WKY (n = 8)</td>
<td>SHR (n = 6)</td>
</tr>
<tr>
<td>1A/mg tissue</td>
<td>0.131±0.006</td>
<td>0.129±0.006</td>
</tr>
<tr>
<td>2A/mg tissue</td>
<td>1.54±0.11</td>
<td>1.46±0.13</td>
</tr>
<tr>
<td>3A/mg tissue intact</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3A/mg tissue passive</td>
<td>13.6±0.3</td>
<td>12.8±0.4</td>
</tr>
<tr>
<td>2A per 1A</td>
<td>11.6±0.4</td>
<td>11.4±1.1</td>
</tr>
<tr>
<td>3A per 2A</td>
<td>9.0±0.5</td>
<td>9.1±0.4</td>
</tr>
<tr>
<td>Tissue weight</td>
<td>57.4±2.0</td>
<td>58.5±2.9</td>
</tr>
</tbody>
</table>

*Significant difference (p < 0.05) between equal age SHR and WKY.
†Significant difference between different aged animals of same type.
different \( (p > 0.05) \), and the ratio of the number of 2A branches per 1A as well as 3A per 2A was identical. These measurements were made in totally passive preparations.

In 18- to 21-week-old WKY and SHR, the number of 1A/mg tissue was not different. The number of 2A/mg tissue was significantly decreased \( (p < 0.05) \) by about 31% in adult SHR rats. There was a slight but significant \( (p < 0.05) \) decrease in the number of 3A open to flow in adult SHR relative to WKY rats during resting conditions. Upon making the tissue passive, the number of 3A in either young or adult SHR and WKY rats was not different \( (p > 0.05) \). In adult WKY rats, 6% ± 1% of the total number of 3A were closed during resting conditions whereas 12% ± 2% of the 3A were closed in adult SHR based on vessel counts in each animal. Upon adding adenosine \( (10^{-4} \text{M}) \) to open all arterioles, no additional first- or second-order arterioles opened, and sodium nitroprusside \( (1 \text{ mg/ml}) \) also failed to open any additional 1A or 2A. The number of 4A, 5A, MA, and DA vessels was not counted because in both WKY and hypertensive animals there was one 4A, four to five 5A, one main arteriole (MA) in each villus, and two DA for each third-order arteriole (fig. 1). Therefore, the maximum number of these vessels was essentially identical in WKY and SHR because these animals had statistically equal total numbers of 3A.

The third-order arterioles that were closed to flow at rest in both WKY and SHR resumed their closure as soon as the adenosine was washed away. The 3A that were closed did allow very brief periods of red cell flow during passive conditions. Upon adding adenosine \( (10^{-4} \text{M}) \) to open all arterioles, no additional first- or second-order arterioles opened, and sodium nitroprusside \( (1 \text{ mg/ml}) \) also failed to open any additional 1A or 2A. The number of 4A, 5A, MA, and DA vessels was not counted because in both WKY and hypertensive animals there was one 4A, four to five 5A, one main arteriole (MA) in each villus, and two DA for each third-order arteriole (fig. 1). Therefore, the maximum number of these vessels was essentially identical in WKY and SHR because these animals had statistically equal total numbers of 3A.

The third-order arterioles that were closed to flow at rest in both WKY and SHR resumed their closure as soon as the adenosine was washed away. The 3A that were closed did allow very brief periods of red cell flow for 3–10 seconds, two to three times each minute. However, these brief periods of flow did not follow any particular behavior pattern in the context of duration of the flow period or number of flow periods per minute. When the flow periods did occur, the vessels that were typically closed only dilated enough to allow passage of red cells in single file.

**Vessel Dimensions**

The diameter and vessel wall thickness, wall thickness-to-lumen ratio, and vessel wall cross-sectional area at rest are presented for adult rats in table 2 for those vessels that have a continuous smooth muscle coat. The resting and passive diameters as well as the percent of control (resting) diameter during the passive state are listed for each vessel in table 3. The resting diameters of 1A and 5A in SHR were significantly \( (p < 0.05) \) smaller than comparable types of vessels in WKY rats. The resting diameters of the 3A in SHR were not significantly \( (p > 0.05) \) different from those in WKY rats, but the 2A were dilated (table 2). The only vessels in SHR to have significantly \( (p < 0.05) \) different diameters when passive were the 1A, which were smaller than normal, and 2A, which were larger than normal (table 3). The 2A in adult SHR dilated proportionately more and 3A dilated proportionately less than normal (table 3), as judged by the percent of control diameters during passive conditions.

The major differences in vessel wall characteristics at rest in adult animals were an increased \( (p < 0.05) \) wall-to-lumen ratio, vessel wall thickness, and cross-sectional area for 3A in SHR, increased \( (p < 0.05) \) wall thickness and area for 2A, but decreased cross-sectional area for 1A of SHR (table 2).

The percent of control flow during adenosine exposure was 303% ± 57% in adult WKY rats compared to 305% ± 33% for adult SHR. The same maximum flow changes encountered in adult WKY or SHR occurred whether adenosine or sodium nitroprusside was used to cause vasodilation. Sodium nitroprusside \( (1 \text{ mg/ml}) \) was not used routinely in the study because occasionally topical application caused systemic hypotension in preliminary studies.

**Microvascular Pressures**

Microvascular pressures throughout the intestinal vasculature of adult WKY and SHR are presented in figure 2. Measurements of capillary pressure in the muscle layer were not possible because vasodilation occurred if sufficient isoproterenol was used to fully suppress motility in the large animals. This was not a problem in the mucosa because the micropipette stabilized the villus.

The mean microvascular pressure in 1A, the largest of the arterioles, of SHR was significantly \( (p < 0.05) \) greater than the mean systemic arterial pressure in

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**Table 2. Vessel Wall Characteristics of Intestinal Arterioles in 18- to 21-Week-Old WKY and SHR**

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter (µ)</th>
<th>Wall thickness (µ)</th>
<th>Wall area (µ²)</th>
<th>Wall/lumen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A-WKY</td>
<td>87.8 ± 7.5</td>
<td>15.8 ± 1.1</td>
<td>4745 ± 509</td>
<td>0.21 ± 0.02</td>
</tr>
<tr>
<td>1A-SHR</td>
<td>70.9 ± 4.1*</td>
<td>14.0 ± 1.0</td>
<td>3677 ± 372*</td>
<td>0.22 ± 0.02</td>
</tr>
<tr>
<td>2A-WKY</td>
<td>26.8 ± 1.4</td>
<td>9.3 ± 0.9</td>
<td>1136 ± 181</td>
<td>0.34 ± 0.03</td>
</tr>
<tr>
<td>2A-SHR</td>
<td>31.9 ± 2.7*</td>
<td>10.9 ± 1.1</td>
<td>1651 ± 325*</td>
<td>0.36 ± 0.02</td>
</tr>
<tr>
<td>3A-WKY</td>
<td>11.6 ± 0.7</td>
<td>5.2 ± 0.4</td>
<td>281 ± 35</td>
<td>0.48 ± 0.02</td>
</tr>
<tr>
<td>3A-SHR</td>
<td>12.7 ± 1.2</td>
<td>6.5 ± 0.3*</td>
<td>384 ± 20*</td>
<td>0.56 ± 0.07*</td>
</tr>
</tbody>
</table>

*p < 0.05.

**Table 3. Resting and Passive Internal Diameter of Intestinal Arterioles of 18- to 21-Week-Old WKY and SHR**

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Resting diameter (µ)</th>
<th>Passive diameter (µ)</th>
<th>% Control diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A-WKY</td>
<td>87.8 ± 7.5</td>
<td>94.5 ± 11</td>
<td>117.1 ± 3.0</td>
</tr>
<tr>
<td>1A-SHR</td>
<td>70.9 ± 4.1*</td>
<td>80.5 ± 2.5*</td>
<td>120.0 ± 2.5</td>
</tr>
<tr>
<td>2A-WKY</td>
<td>26.8 ± 1.4</td>
<td>38.0 ± 2.5</td>
<td>143.0 ± 7.6</td>
</tr>
<tr>
<td>2A-SHR</td>
<td>31.9 ± 2.7*</td>
<td>47.7 ± 3.7*</td>
<td>166.0 ± 9.4*</td>
</tr>
<tr>
<td>3A-WKY</td>
<td>11.6 ± 0.7</td>
<td>17.9 ± 1.1</td>
<td>161.0 ± 7.7</td>
</tr>
<tr>
<td>3A-SHR</td>
<td>12.7 ± 1.2</td>
<td>16.5 ± 3.8</td>
<td>140.0 ± 14.0*</td>
</tr>
<tr>
<td>5A-WKY</td>
<td>14.0 ± 1.2</td>
<td>25.5 ± 5.0</td>
<td>185.0 ± 7.7</td>
</tr>
<tr>
<td>5A-SHR</td>
<td>10.4 ± 0.7*</td>
<td>21.5 ± 6.1</td>
<td>198.0 ± 17.0</td>
</tr>
</tbody>
</table>

Values are means ± SEM. *p < 0.05.
FIGURE 2. Microvascular pressures in 18- to 21-week-old WKY and SHR during resting conditions. Note that the pressure in the largest arterioles, 1A, of SHR is higher than the mean arterial pressure in WKY rats. The lower segment of each major curve represents pressures in mucosal distributing arterioles, DA, and capillaries. The line connecting the 5A and 4V represents the possible range of muscle layer capillary pressures. Asterisks denote a significantly (p < 0.05) higher pressure in SHR than WKY rats.

WKY rats. All arteriolar pressures from 1A through the 5A of the muscle layer and DA of the villus were significantly (p < 0.05) higher than normal. In addition, all venular pressures in SHR were on the average 3-5 mm Hg higher than normal; however, venular pressures in WKY and SHR were very variable from vessel to vessel of a given type. The only vessel type in WKY and SHR to have statistically equal (p < 0.05) pressures were the mucosal capillaries. All mucosal capillary pressures were measured in the upper half of the villus, and these capillaries were exclusively perfused by the distributing arterioles that originated near the villus apex. The villus outflow enters the submucosal venous plexus at the level of 2V (fig. 1). The mucosal capillary pressures in both WKY and SHR were lower than those recorded in the 2V because pressures in 2V were recorded upstream from the point where mucosal venules entered the 2V. This procedure for pressure measurement in 2V was necessary because the gradually enlarging 2V were very reactive to mechanical stimulation and vigorously constricted when the pipette entered the vessel wall.

The diameters of intestinal venules were measured prior to penetration with servo-null micropipettes. The diameters of 4V and 2V in hypertensive rats were 16.1 ± 1.9 µ and 73.9 ± 1.6 µ compared to 13.2 ± 1.3 µ and 75.6 ± 4 µ in WKY rats. The IV of SHR (119.6 ± 7.2 µ) were significantly smaller (p < 0.05) than normal (151.9 ± 6.9 µ). However, the first- and second-order venules were very highly tapered in both WKY and SHR, even as the first-order vessels exited the intestine. Therefore, direct comparison of the diameters of 1A, in particular, was difficult, and the difference of 1A diameters between WKY and hypertensive rats may not be valid.

In figure 3, the ratio of the microvascular pressure to mean arterial pressure for each vessel type is displayed. This analysis was used to determine the fraction of the mean arterial pressure that reached a given section of the microvasculature. Beginning with the second-order arterioles and all subsequent microvessels in SHR, the pressure fraction was equal to, or significantly (p < 0.05) smaller than, that in WKY rats.

Lymphatic Vessels

In normal adult animals, the lymphatics of the submucosa and muscle layer were nearly collapsed and rarely exhibited any spontaneous changes in diameter. In the adult SHR rat, the lymphatics of the muscle layer were slightly distented, and continuous flow of fluid, as marked by lymphocytes, was present; occasionally, slow changes in diameter occurred. The lymphatics of the submucosa in the SHR were only slightly more distended than in WKY rats, but very slow flow (movement of lymphocytes) was observed.
Discussion

The elevation of the systemic arterial pressure in the SHR presents all organ vasculatures with a common problem of possible overperfusion and elevated microvascular pressures. Studies such as those by Ferrone et al. and Toiba et al. have demonstrated that virtually all organ systems experience an increase in vascular resistance that contributes to hypertension while possibly protecting the smallest vessels of the microvasculature from high pressure. As will be subsequently discussed, the microvascular characteristics in the skeletal muscle and intestine are sufficiently different in the SHR to conclude that a common form of microvascular adaptation in the various organs of spontaneously hypertensive rats may not exist.

The permanent and temporary closure or rarefaction of arterioles with a resting diameter of about 30 μm and smaller has been recognized as a major change in the skeletal muscle vasculature during hypertension in SHR. As shown in table 1, a permanent loss of about 30%–35% of the second-order arterioles and a minor active closure of third-order and smaller arterioles were the only evidence of rarefaction in the intestinal vasculature of SHR. As shown in figures 2 and 3, the loss of second-order arterioles in SHR did not dissipate the arterial pressure proportionately more in SHR than in WKY rats. The approximately 6% difference in the total number of third-order arterioles that were open to flow during intact conditions in adult WKY and SHR was inconsequential compared to differences of 40%–60% that have been reported between WKY and SHR for similar vessels in skeletal muscle. In skeletal muscle, the decreased number of small arterioles open to flow during resting conditions has been attributed both to a permanent loss of vessels as well as to an accentuated active closure of those vessels that remain. A permanent loss of small arterioles (3A) did not occur in the intestine of SHR because the number of vessels per milligram of tissue open to flow during passive conditions was normal (table 1). Exactly why one tissue should experience permanent and temporary closure of small arterioles, and why another tissue should be virtually unaffected in the SHR is not known.

The primary physical cause of increased vascular resistance in the small intestine of our SHR was vasoconstriction of the largest and smallest arterioles (table 3). By comparison, the arterioles of adult SHR have been shown to have an inner diameter equal to or slightly larger than comparable vessel types in WKY rats for the cremasteric, gracilis, and spinotrapezius muscles. These data for the absence of vasoconstriction in three different muscle groups may indicate that vasoconstriction of those vessels open to flow is not a characteristic of the overall skeletal muscle vasculature in SHR. In contrast, the presence of intestinal vasoconstriction with minimal rarefaction and the absence of constriction but substantial rarefaction in skeletal muscles raises two distinct possibilities relative to the cause of hypertension. If a common mechanism caused the microvascular changes in both tissues, the expression of this mechanism is influenced by the host tissue or the unique properties of each vasculature. Alternatively, two or more different mechanisms may cause the observed differences in the characteristics of the intestinal and skeletal muscle microvasculatures in adult SHR.

One of the central issues related to hypertension in the SHR is whether vessel wall hypertrophy and an increased vessel wall-to-lumen ratio influences vascular caliber and reactivity. Folkow proposed that hypertrophy of the vascular smooth muscle was a compensatory response to elevated microvascular pressures and gradually caused a mechanical vasoconstriction. In vivo measurement of comparable arteriole branch orders in the skeletal muscle of adult SHR has not supported either an increased wall-to-lumen ratio or increase in vessel wall cross-sectional area. However, both the second- and third-order arterioles in the intestine of adult SHR had a significantly (p < 0.05) increased vessel wall area. Only the third-order vessels in the intestine exhibited a significantly (p < 0.05) increased wall thickness-to-lumen ratio during intact conditions, but neither the 2A or 3A were constricted in the intestine of SHR during resting conditions.

There is a paradox in that there was a significant decrease in vessel wall area for 1A of adult SHR (table 2) even though the pressure in this vessel is grossly elevated (fig. 2). Furthermore, the 1A of SHR have a normal wall thickness-to-lumen ratio at rest, which would not protect the vessel wall from having a substantially increased vessel wall stress due to the increased intravascular pressure (fig. 2). The data from the intestinal vasculature and those reported previously for the skeletal muscle vasculature indicate that arterial wall hypertrophy can occur, but that hypertrophy is not necessarily an obligatory response to hypertension. There is no question, however, that the vessel wall is in some way altered during hypertension. As shown in table 3, the passive diameters of the 1A, 3A, and 4A arterioles in SHR are either smaller or equal to those in normal animals. Similar circumstances have also been reported for skeletal muscle.

An explanation for the normal passive diameters in the intestinal and skeletal muscle vasculature of SHR despite the higher than normal microvascular pressures would be increased passive vessel wall stiffness.

The changes or adaptations of the intestinal vasculature appear to have a beneficial effect in the SHR. The muscle layer capillary pressures in the SHR were elevated only 10%–20% and the mucosal capillary pressures were equal to those in WKY rats, as shown in figure 2, despite a 60%–70% increase in mean arterial blood pressure in SHR. Much of this protection against high intestinal capillary pressure was provided by a major dissipation of arterial pressure across the smallest arterioles (3A, 5A, DA) (figs. 1 and 3). Zweifach et al. has previously reported that the smallest arterioles in spinotrapezius muscle were predominately responsible for maintaining a near normal capillary pressure in young and mature WKY and SHR. Bohlen et al. reported that young SHR have a significantly increased...
capillary pressure compared to WKY rats, although the average difference is only about 4 mm Hg. The dependence of nearly normalized intestinal and skeletal muscle\textsuperscript{18, 19} capillary pressures on changes in the smallest arterioles in SHR may indicate the presence of a common mechanism in various vasculatures to protect the exchange vessels from high pressure.

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References

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