Mechanism of Renin Release during Acute Ureteral Constriction in Dogs

Ivar Eide, Einar Løvning, Øivind Langård, and Fredrik Kiil

SUMMARY The relationship between renal arterial pressure and renin release was examined in anesthetized dogs during complete or partial ureteral constriction. During complete ureteral occlusion ureteral pressure rose to 95 ± 4 mm Hg and renin release increased from 1.7 ± 0.7 to 22.3 ± 3.1 μg/min; renal blood flow (RBF) was not significantly changed. Renin release was not further increased during subsequent renal arterial constriction; RBF fell in proportion to perfusion pressure, indicating maximum autoregulated arteriolar dilation. During partial ureteral constriction to a ureteral pressure of 65 ± 6 mm Hg, renin release was moderately raised but release mechanisms became fully stimulated when renal arterial pressure was reduced to 104 ± 3 mm Hg. By further constriction of the renal artery, RBF fell in proportion to perfusion pressure and renin release remained high and constant. In control experiments without ureteral constriction, renal arterial pressure had to be reduced to below 65 ± 8 mm Hg to fully stimulate renin release (22.0 ± 3.8 μg/min which is not different from 22.3 ± 3.1 μg/min during ureteral occlusion). During partial ureteral constriction, saline infusion (0.9% NaCl at 40 ml/min) raised urine flow, sodium excretion, renal pelvic pressure, and renin release. Thus, the stimulatory effect on renin release of a rise in ureteral pressure exceeded the inhibitory effect of increased sodium excretion. This observation, together with maximum renin release coinciding with complete arteriolar dilation during various combinations of renal arterial and ureteral constriction, is compatible with the conclusion that arteriolar dilation is the predominating stimulus to renin release during ureteral constriction.

URETERAL constriction increases renin release by stimulating intrarenal mechanisms which either may be activated by reduced delivery of sodium to the distal nephron (macula densa mechanism) or by dilation of the afferent arterioles (autoregulation mechanism). Autoregulated dilation is probably mediated by a reduction in transmural pressure at the level of afferent arterioles and glomerular capillaries during a rise in intratubular pressures. The relationship between the paradoxical dilation of afferent arterioles during a rise in intrarenal pressure and renin release has not been examined previously in detail.

Most of the information about the autoregulation mechanism has been obtained by reducing renal arterial pressure. Studies on the intact kidney and on the nonfiltering kidney preparation have shown that renin release increases progressively during renal arterial constriction, concomitant with an autoregulated arteriolar dilation so that renal blood flow (RBF) is maintained. At a renal arterial pressure of 60–70 mm Hg, both renin release and afferent arteriolar dilation become maximal. With further reduction in perfusion pressure, arterioles remain maximally dilated and RBF falls in proportion to the perfusion pressure but maximal autoregulated dilation ensures high and constant renin release.

This pattern may be modified by ureteral constriction. By complete ureteral occlusion, such high intrarenal pressures may be generated that afferent arterioles already are maximally dilated at control renal arterial pressure. Hence, RBF would fall even with a small reduction in renal arterial pressure below control, whereas renin release would remain high and constant. During partial ureteral constriction, the lowest autoregulating pressure would be below control but higher than 60–70 mm Hg; again, according to the autoregulation hypothesis, renin release would be expected to remain high and constant within the pressure range over which RBF varies in proportion to perfusion pressure.

After having established these relationships, we examined the question of whether the autoregulation mechanism is more potent than the macula densa mechanism in regulating renin release during ureteral constriction. Isotonic saline was infused at high rates during partial ureteral constriction. Increased delivery of sodium to the macula densa region would inhibit renin release. On the other hand, a stimulatory effect would also be elicited because renal pelvic and intrarenal pressures would rise during constant ureteral constriction as urine flow increased. The net effect would be a rise in renin release only if the autoregulation mechanism predominated.

Methods

Experiments were performed on mongrel dogs of both sexes averaging 18.6 ± 0.7 kg in body weight. Food was withheld for 24 hours but the dogs had free access to water. Anesthesia was induced by sodium pentobarbital (Nembutal), 25 mg/kg, iv, and maintained with additional doses of 1–3 mg/kg as required. Polyethylene catheters were inserted into the aorta to record systemic blood pressure and for blood sampling, and through the femoral vein into the left renal vein for blood sampling. The left artery was exposed through a flank incision, all visible nerves were cut, and an electromagnetic flow probe was positioned on the artery close to the aorta for continuous
measurement of RBF. The flowmeter (Nycotron, Oslo) had been calibrated on renal and femoral arteries of the same caliber. A polyvinyl catheter was inserted into the renal artery peripheral to the flow probe with its tip directed upstream. Aortic and renal arterial pressures were measured continuously with a Statham transducer (P23Gb) and a Sanborn recorder. A plastic clamp, adjustable from the outside, was placed between the flow probe and the polyvinyl catheter to constrict the renal artery. The ureter was cannulated with a polyethylene catheter for collection of urine; ureteral pressure was raised by gradual clamping of the catheter and measured through a three-way stopcock interposed in the catheter near its proximal end. Most dogs received 5.5% mannitol in hypotonic saline (0.3-0.45% NaCl) at a rate of 6-10 ml/min throughout the last hour preceding the experimental procedure, but in four dogs isotonic saline (0.9% NaCl) was infused at a similar rate.

Blood samples for measurement of glomerular filtration rate (GFR) and renin release were obtained under conditions of steady state at least 10 minutes after arterial or ureteral constriction and under control conditions about 30 minutes after release of constrictions. The number of dogs participating in the various experiments and the sequence of the different procedures are apparent from the Results.

Arterial and renal venous blood specimens were sampled simultaneously for determination of renin release, GFR, and hematocrit (Hct). Plasma renin in aortic and renal venous blood was determined by radioimmunoassay according to Haber et al., as previously described, following incubation of the buffered plasma samples with an excess of exogenous renin substrate while angiotensinases were inhibited by ethylenediaminetetraacetic acid (EDTA), dimercaprol (BAL) and 8-hydroxyquinoline. Renin release was calculated as the product of the renal extraction of $^{51}$Cr-EDTA by renal plasma flow: $(v - a) \cdot RBF \cdot (1 - Hct)$. The measurements of renin release were referred with measurements of GFR, which was estimated as the plasma clearance of $^{51}$Cr-EDTA by renal plasma flow. Sodium concentrations in urine and plasma were measured with a flame photometer (Evans Electrosemelenium).

Each dog served as its own control and the statistical probabilities of differences were calculated using Wilcoxon’s test for paired comparison. A difference was regarded as statistically significant at $P < 0.05$.

**Results**

**EFFECTS OF URETERAL AND RENAL ARTERIAL CONSTRICITION ON RENIN RELEASE**

Table 1 summarizes experiments on eight dogs which were first subjected to renal arterial constriction to produce a perfusion pressure well below the range of autoregulation, and then to ureteral occlusion. During both procedures, renin release rose to high levels which were not significantly different. During ureteral occlusion, ureteral pressure rose to 95 ± 4 mm Hg, whereas RBF did not change significantly from the value recorded during control periods before ureteral occlusion.

The effects of raising ureteral pressure in steps were examined in six dogs and the results are summarized in Figure 1. Up to a ureteral pressure of 75 ± 3 mm Hg, RBF increased ($P < 0.001$). With further elevation of perfusion pressure, up to 96 ± 6 mm Hg, RBF remained constant or fell slightly. Renin release increased significantly at each of the four steps of ureteral constriction shown in Figure 1; more than half of the total increase in renin release took place during the final step which raised ureteral pressure from 75 ± 3 to 96 ± 6 mm Hg. These examinations were performed during mannitol diuresis but renin release and RBF also rose in four dogs infused with saline (0.9% NaCl at 8-10 ml/min).

Figure 2 shows the results of constriction of the renal artery during complete ureteral occlusion which raised ureteral pressure to an average of 95 ± 5 mm Hg. Afferent arterioles were completely dilated during ureteral occlusion since RBF fell in proportion to the reduction in renal arterial pressure. Ureteral occlusion raised renin release to 18.7 ± 2.3 μg/min in these six dogs and subsequent renal arterial constriction had no significant effect on renin release. However, ureteral pressure fell during

**Table 1** Comparison of Effects of Renal Arterial Constriction and Ureteral Occlusion on Renin Release and Renal Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>RAP (mm Hg)</th>
<th>UP (mm Hg)</th>
<th>RBF (ml/min)</th>
<th>Hct (%)</th>
<th>GFR (ml/min)</th>
<th>AP (mm Hg)</th>
<th>Renin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>109±16</td>
<td>0±0</td>
<td>166±18</td>
<td>38±1</td>
<td>23±3</td>
<td>131±6</td>
<td>27±8</td>
</tr>
<tr>
<td>Arterial constriction</td>
<td>148±3</td>
<td>0±0</td>
<td>110±16</td>
<td>37±2</td>
<td>12±2</td>
<td>138±7</td>
<td>109±24</td>
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<tr>
<td>Control</td>
<td>126±7</td>
<td>0±0</td>
<td>164±24</td>
<td>37±2</td>
<td>19±3</td>
<td>129±7</td>
<td>27±7</td>
</tr>
<tr>
<td>Ureteral occlusion</td>
<td>131±16</td>
<td>95±4</td>
<td>181±21</td>
<td>36±2</td>
<td>4±1</td>
<td>138±5</td>
<td>98±14</td>
</tr>
<tr>
<td>Control</td>
<td>128±6</td>
<td>0±0</td>
<td>163±19</td>
<td>36±2</td>
<td>20±2</td>
<td>132±6</td>
<td>52±13</td>
</tr>
</tbody>
</table>

RAP = renal arterial pressure; UP = ureteral pressure; RBF = renal blood flow; Hct = hematocrit; GFR = glomerular filtration rate; AP = aortic pressure; RR = renin release; $(v - a) / (100 - Hct)/100$, where $v$ and $a$ are renal venous and arterial renin concentrations.

Results are expressed as mean ± s of experiments in eight dogs weighing 18.5 ± 0.8 kg.

The experiments were performed during intravenous infusion of 5.5% mannitol in 0.3% NaCl at 6-8 ml/min. Arterial constriction: renal artery was constricted for 10-20 minutes before samples were obtained. Renal arterial pressure was reduced below the autoregulation range. Control samples were obtained 30-40 minutes after release of constriction. Ureteral occlusion: samples were obtained after 12-18 minutes of ureteral occlusion. Final control samples were obtained after 30-35 minutes.
renal arterial constriction. It might therefore be argued that the stimulus to renin release, caused by ureteral constriction, was reduced.

To examine this possibility, the experiment was repeated with the addition that the ureteral pressure was kept constant by connecting the end of the ureteral catheter to a reservoir of isotonic saline. The results of experiments in six dogs are summarized in Table 2. During reduction of the renal arterial pressure, there was a retrograde flow from the reservoir into the kidney; GFR was zero, or negative, and RBF was markedly reduced. Renal venous renin concentrations were greatly increased but renin release was not, in any experiment, higher during the combined procedure than during ureteral occlusion alone.

Figure 3 summarizes the effects of constricting the renal artery during partial ureteral constriction. At a renal arterial pressure of 126 ± 5 mm Hg, ureteral pressure was raised to 65 ± 5 mm Hg. Renal arterial pressure was reduced to 104 ± 3 mm Hg before ureteral pressure and RBF fell significantly. According to this criterion, maximal arteriolar dilation was obtained at renal arterial pressure of 104 ± 3 mm Hg when the ureteral pressure was 65 ± 8 mm Hg. This shift in the range of autoregulation of RBF was associated with the predicted change in the pattern of renin release. Renin release was maximal at the perfusion pressure of 104 ± 3 mm Hg in the sense that renin release could not be increased by further reduction of renal arterial pressure.

In control experiments without ureteral constriction, the renal arterial pressure was reduced to 65 ± 8 mm Hg in these six dogs before RBF fell significantly. Confirming previous observations, we found that the renal artery had to be constricted at least to this pressure to reach maximal renin release when ureteral pressure was not raised.

In other control experiments, we examined whether ischemia or reduction in GFR might increase renin release during ureteral constriction. Ureteral pressure was raised after constricting the renal artery to a pressure below the range of autoregulation. Figure 4, summarizing experiments in 18 dogs, shows that renin release was as high during renal arterial constriction alone as during combined

\[ \text{RENIN RELEASE (per cent)} \]

\[ \text{RAP (mm Hg)} \]

\[ \text{RBF (ml/min)} \]

\[ \text{GFR (ml/min)} \]

\[ \text{RENIN RELEASE (\mu g/min)} \]

\[ \text{UP (mm Hg)} \]

\[ \text{UO+AC} \]
TABLE 2  Comparison of the Effects of Arterial Constriction and Ureteral Occlusion on Renin Release and Renal Hemodynamics when Ureteral Pressure was Artificially Maintained at Maximum Levels by Connecting the Ureteral Catheter to a Reservoir

<table>
<thead>
<tr>
<th></th>
<th>Renin</th>
<th>RAP (mm Hg)</th>
<th>UP (mm Hg)</th>
<th>RBF (ml/min)</th>
<th>Hct (%)</th>
<th>GFR (ml/min)</th>
<th>AP (mm Hg)</th>
<th>Renin</th>
<th>a (ng/ml)</th>
<th>v (ng/ml)</th>
<th>RR (µg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>117±7</td>
<td>0±0</td>
<td>183±31</td>
<td>36±4</td>
<td>18±4</td>
<td>126±8</td>
<td>52±15</td>
<td>80±21</td>
<td>3.6±1.7</td>
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</tr>
<tr>
<td>Ureteral occlusion</td>
<td></td>
<td>126±10</td>
<td>86±8</td>
<td>216±28</td>
<td>35±4</td>
<td>6±2</td>
<td>135±10</td>
<td>106±30</td>
<td>322±88</td>
<td>31.5±12.2</td>
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</tr>
<tr>
<td>Ureteral occlusion and arterial constriction</td>
<td></td>
<td>52±2</td>
<td>87±9</td>
<td>39±9</td>
<td>34±4</td>
<td>0±0</td>
<td>97±26</td>
<td>87±21</td>
<td>893±294</td>
<td>18.0±7.9</td>
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<tr>
<td>Control</td>
<td></td>
<td>119±11</td>
<td>0±0</td>
<td>153±18</td>
<td>36±4</td>
<td>20±5</td>
<td>126±11</td>
<td>61±21</td>
<td>83±25</td>
<td>2.0±0.7</td>
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<tr>
<td>Arterial constriction</td>
<td></td>
<td>51±2</td>
<td>0±0</td>
<td>95±16</td>
<td>36±4</td>
<td>9±3</td>
<td>128±19</td>
<td>141±35</td>
<td>639±266</td>
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</tr>
<tr>
<td>Control</td>
<td></td>
<td>121±9</td>
<td>0±0</td>
<td>124±30</td>
<td>36±4</td>
<td>22±5</td>
<td>129±10</td>
<td>38±9</td>
<td>61±18</td>
<td>2.3±1.1</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1. 
Results are expressed as mean ± se of experiments in five dogs weighing 19.3 ± 1.6 kg.

renal arterial and ureteral constriction. Both RBF and GFR were significantly reduced when ureteral constriction was superimposed.

EFFECTS ON RENIN RELEASE OF RAISING SODIUM EXCRETION DURING URETERAL CONSTRUCTION

Saline infusion inhibits renin release at control blood pressure\(^2\) and during vasodilation induced by renal arterial constriction\(^6\) or infusion of ethacrynic acid.\(^7,8\) A similar effect would be expected during ureteral constriction. By infusing saline at a rate of 40 ml/min during partial ureteral constriction, both this inhibitory effect and the stimulatory effect associated with further autoregulated vasodilation would be elicited. The results of experiments on six dogs are summarized in Table 3. As urine flow increased, sodium excretion exceeded control; renal pelvic pressure rose from 49 ± 5 to 77 ± 3 mm Hg concomitantly with a marked increase in RBF. Renin release rose significantly \((P < 0.01)\), indicating that the stimulatory effect of arteriolar dilation exceeded the inhibitory effect related to increased sodium excretion.

Discussion

The renal hemodynamic effects of variations in renal arterial and ureteral pressure are indicated in the schematic drawing shown in Figure 5. The solid curved lines indicate the increase in arteriolar diameter when renal arterial pressure is reduced.\(^2\) As shown in the bottom panel, arteriolar dilation would be complete at the perfusion pressure of about 60 mm Hg under conditions of no ureteral constriction. At a ureteral pressure of 90-100 mm Hg, arterioles would be maximally dilated already at control renal arterial pressure (top panel). The columns in Figure 5 indicate the renin release expected according to the autoregulation hypothesis. Not all experimental situations depicted in Figure 5 were examined in the present study but the results obtained are consistent with the autoregulation hypothesis.

Dilation of the afferent arterioles during ureteral constriction was first proposed because elevation of ureteral pressure to 50-60 mm Hg did not reduce GFR, whereas RBF increased.\(^3,4\) Despite arteriolar dilation, total renal vascular resistance may remain unaltered or even increase during progressive ureteral constriction. The reason is that the rise in ureteral pressure results not only in arteriolar dilation but also in an increase in peritubular capillary pressure. The pressure drop between peritubular capillar-
ies and the renal vein increases accordingly during ureteral constriction and accounts for the increase in total renal vascular resistance. This increase in resistance is probably not caused by constriction of the muscles in the wall of the venules and intrarenal veins but by a waterfall mechanism (Starling resistance). Because of this double effect, arterioles may continue to dilate up to the ureteral pressure of 95–100 mm Hg, which far exceeds the ureteral pressure at which the highest RBF was recorded.

The maximal renin release obtained by constricting the renal artery and ureter does not reflect the maximum renal capacity for renin secretion; the high renin release during renal arterial constriction to a pressure below the range of autoregulation can be raised by more than 50% by isoproterenol infusion, we have recently observed (unpublished studies) the same stimulatory effect of isoproterenol on renin release during ureteral constriction.

In several previous studies, the increase in renin release during ureteral constriction has been attributed to a stimulation of the macula densa mechanism. Delivery of sodium to the distal convoluted nephron is probably reduced already before a reduction in GFR occurs and is progressively reduced as GFR falls toward zero. On the other hand, saline infusion increases GFR and inhibits proximal sodium reabsorption. Intravenous saline infusion at rates which increase sodium excretion will, therefore, raise the delivery to the macula densa region and inhibit renin release. Two observations in our study indicate that the macula densa mechanism for renin release was not the predominating one during ureteral constriction. First, a reduction in GFR to almost zero, as when ureteral constriction was superimposed on renal arterial constriction, did not result in a further increase in renin release (Fig. 4). Second, infusion of saline during partial ureteral constriction increased sodium excretion above control concomitantly with a rise in renin release (Table 3). This rise in renin release is readily explained in terms of the autoregulation hypothesis as renal pelvic pressure rose concomitantly with the increase in urine flow.

Our study therefore provides additional evidence for

### Table 3: Renin Release and Renal Hemodynamics during Ureteral Constriction and Saline Infusion

<table>
<thead>
<tr>
<th></th>
<th>AP (mm Hg)</th>
<th>UP (mm Hg)</th>
<th>RBF (ml/min)</th>
<th>Hct (%)</th>
<th>GFR (ml/min)</th>
<th>Ua (mmol/liter)</th>
<th>UaV (mol/min)</th>
<th>Renin a (ng/ml)</th>
<th>V (ng/ml)</th>
<th>RR (µg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>122±5</td>
<td>0±0</td>
<td>113±11</td>
<td>39±1</td>
<td>24±4</td>
<td>18±5</td>
<td>17±5</td>
<td>48±13</td>
<td>113±37</td>
<td>4.6±2.4</td>
</tr>
<tr>
<td>Ureteral constriction</td>
<td>122±4</td>
<td>49±5</td>
<td>155±29</td>
<td>37±1</td>
<td>22±5</td>
<td>10±6</td>
<td>8±5</td>
<td>65±9</td>
<td>178±49</td>
<td>12.1±5.4</td>
</tr>
<tr>
<td>Ureteral constriction</td>
<td>129±6</td>
<td>77±3</td>
<td>221±38</td>
<td>25±2</td>
<td>21±6</td>
<td>22±5</td>
<td>29±6</td>
<td>59±12</td>
<td>212±50</td>
<td>25.9±8.7</td>
</tr>
<tr>
<td>Control</td>
<td>121±5</td>
<td>0±0</td>
<td>179±30</td>
<td>31±2</td>
<td>27±5</td>
<td>65±6</td>
<td>211±69</td>
<td>49±18</td>
<td>94±43</td>
<td>4.7±2.6</td>
</tr>
</tbody>
</table>

**Ua =** urinary sodium concentration; **UaV =** urinary sodium excretion; other abbreviations as in Table 1.

Results are expressed as mean ± SE of experiments in six dogs weighing 17.5 ± 2.4 kg.

Samples were obtained after 13–17 minutes of ureteral occlusion and after 35–45 minutes of combined ureteral constriction and saline/mannitol infusion.

Final control samples were obtained 35–40 minutes after release of ureteral constriction. Control renin release at the end of the experiment was mean ± SE of experiments in five dogs.
the view that the macula densa mechanism for renin release becomes less sensitive under conditions of afferent arteriolar dilation. In two previous studies, arterioles were dilated either by reducing renal arterial perfusion pressure or by infusing ethacrynic acid; under both experimental conditions, to reduce renin release sodium excretion had to be raised by saline infusion far in excess of control.

It is conceivable that other intrarenal mechanisms might influence renin release during ureteral constriction, but, as shown in this study, great reductions in GFR and RBF do not seem to be of significance. Churchill et al. proposed that renal arterial and ureteral constriction stimulated renin release by different mechanisms. They measured the renin activity in arterial plasma of dogs and found that renin release became less sensitive under conditions of afferent arteriolar dilation. In two previous studies, arterioles were dilated either by reducing renal arterial perfusion pressure or by infusing ethacrynic acid; under both experimental conditions, to reduce renin release sodium excretion had to be raised by saline infusion far in excess of control.

As shown in Table 2, there was actually a reduction in renin release when intrarenal pressures were artificially raised in the already vasodilated kidney. This reduction in renin release probably reflects uneven perfusion of the renal parenchyma by low RBF.

A diversion of blood flow from the outer cortical layers where most of the renin is formed, might act as an intrinsic renal mechanism for renin release. However, both an inward distribution of blood flow toward the medulla and inner cortical zones and an outward redistribution of blood flow have been found during ureteral constriction, but in all these studies both cortical and outer medullary blood flow measured in absolute terms rose or remained unchanged. Constant or increased RBF could, in the face of increasing peritubular capillary pressure, indicate arteriolar dilation. Actually, Carlson and Sparks found in four dogs that renal venous renin activity increased concomitantly with a rise in cortical blood flow during elevation of ureteral pressure.

The results of some previous examinations of renin release during ureteral constriction may be reinterpreted in terms of the autoregulation hypothesis. Freeman et al. found that ethacrynic acid increased renin release and that ureteral occlusion had no further effect on renin release. However, ethacrynic acid dilates afferent arterioles almost completely. For this reason, renin release should be high and remain unaltered during added ureteral or renal arterial constriction. Kaloyanides et al. reported that renin release, raised by ureteral constriction, could be reduced toward control by raising renal arterial pressure. Their observations are consistent with the scheme in Figure 5; a rise in renal arterial pressure exerts a progressive vasoconstrictive effect by the autoregulation mechanism and would thus counteract the stimulatory effect on renin release at high and constant ureteral pressure.

**Acknowledgments**

The skilled assistance of Ellen Dahl and Mildred Lewis is gratefully acknowledged.

**References**

We found that the specific activities of certain enzymes of a plasma membrane enriched fraction isolated from mesenteric arteries of spontaneously hypertensive rats (SHR) were greater than those of Ontario normotensive Wistar rats (NWRo). Furthermore, maximum ATP-dependent calcium accumulation under certain conditions was greater for this fraction from SHR than from NWRo. There is no ideal control for SHR and therefore more than one strain of normotensive rat should be used in studies of this type. In the present investigation we have studied enzymatic and calcium accumulation parameters in a second strain, California Wistar normotensive rats (NWRc). Levy has reported that this strain exhibits a vascular response to pressor agents that is identical to that of the Kyoto normotensive rats from which the SHR was developed. Therefore, one aim of this study was to evaluate whether the differences previously reported between 5- to 6-month-old SHR and NWRc were due to strain differences unrelated to hypertension.

Two other types of experiments also were carried out in the present investigation to further characterize the relationship between hypertension and the alterations in the abovementioned membrane parameters. First, three age groups of SHR and NWRc were compared to determine whether enzymatic activities or calcium accumulation were abnormal in the early as well as in the late stages of hypertension. Second, these same parameters were studied in mesenteric arteries from rats treated with the antihypertensive agent, hydralazine, to determine whether the prevention of hypertension would also prevent the development of differences between SHR and normotensive rats.
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Circ Res. 1977;40:293-299
doi: 10.1161/01.RES.40.3.293

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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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