Impaired Renal Blood Flow and Cortical Pressure Autoregulation in Contralateral Kidneys of Goldblatt Hypertensive Rats

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SUMMARY Experiments were conducted on two-kidney, one clip renal vascular hypertensive rats to assess the ability of the kidney contralateral to renal vascular stenosis to autoregulate renal blood flow (RBF), glomerular filtration rate (GFR), and hydrostatic pressures in cortical structures during conditions of acutely reduced renal arterial blood pressure (BP). When observed at their respective, spontaneous BPs, RBF and GFR were not different in the contralateral kidneys of the hypertensive rats (n = 11) compared to normal animals (n = 7). However, the contralateral kidneys exhibited a significantly higher renal vascular resistance (RVR), 28.9 ± 2.8 mm Hg • min/ml than the control animals, 23.1 ± 1.5 mm Hg • min/ml. At spontaneous BP (169 ± 5 mm Hg), urine flow, absolute and fractional sodium excretion, and absolute and fractional potassium excretion were all significantly greater in the contralateral kidneys of hypertensive rats than in kidneys of normal rats. Hydrostatic pressures in cortical structures were similar in the two groups. When BP was reduced acutely, the kidney contralateral to the renal artery stenosis achieved only small decreases in RVR that failed to allow RBF, GFR, or cortical pressures to be maintained. In contrast, normal rats efficiently autoregulated RBF and GFR. In addition, hydrostatic pressures in proximal tubules, distal tubules, and first order peritubular capillaries were maintained during reductions in BP to as low as 100 mm Hg. Urine flow and electrolyte excretion decreased to a greater extent in the hypertensive kidneys, such that at comparable BP these indices of excretory function were not different in the two groups. These observations indicate that the capacity of the contralateral kidney to maintain hemodynamic and glomerular function at reduced BP is compromised severely and suggest the possibility that the impaired autoregulatory capability may contribute to the maintenance of hypertension observed in this model. (Hypertension 3: 67-74, 1981)

KEY WORDS - renal vascular hypertension - two-kidney, one clip Goldblatt hypertensive rat - glomerular filtration rate - renal vascular resistance - sodium excretion - potassium excretion

The precise role of altered renal function as a contributing factor to hypertension has been a topic of controversy for many years. Several investigators have supported the hypothesis that some derangement in renal function must be present in order for the hypertension to be maintained. Although renal function has been examined in several hypertensive models, variable results have been reported concerning the integrity of renal hemodynamic mechanisms that allow the maintenance of clearance and excretory function at hypertensive or normotensive BP. One model of hypertension of particular interest is the two-kidney, one clip model in the rat. This model allows evaluation of the function of the kidney opposite the stenosis (the contralateral kidney) as it responds to the systemic influences that result in elevated BP consequent to the renal arterial stenosis imposed on the other kidney.

Our earlier investigations suggested that autoregulatory mechanisms were altered in the kidney contralateral to renal artery stenosis since glomerular filtration rate was not maintained when BP was reduced acutely. However, these earlier studies focused on the activity of the distal tubule-glomerulus feedback system as it was related to the autoregulatory mechanism. The goal of the present study was to examine the efficiency of vascular resistance adjustments as reflected by renal blood flow (RBF) and renal cortical pressure autoregulation in the kidney contralateral to the renal artery stenosis. The specific questions we addressed were whether hemodynamic...
function in the contralateral kidney would be normal at hypertensive BPs and how efficiently hemodynamic function would be maintained during acute reductions in BP to normotensive levels. To evaluate the associated microvascular and tubular events following reductions in BP, peritubular capillary and free-flow proximal and distal intratubular hydrostatic pressures were examined at several levels of renal arterial BP. Further, excretory function of the contralateral kidney following reduction in renal BP was also evaluated. These hemodynamic, cortical pressure and excretory observations were compared to responses observed in normal animals examined contemporaneously with identical protocols.

Methods

Experiments were performed on Sprague-Dawley rats weighing 210 to 260 g. Animals were maintained on a complete rat chow diet (Wayne Lab Blox, Allied Mills, Inc., Chicago, Illinois) containing 0.15 mEq Na+/g, and allowed free access to food and water. Two groups of animals were examined with the protocols described below.

Right Renal Artery Stenosis, Two-Kidney Goldblatt Hypertensive Rats

Experiments were carried out on two-kidney Goldblatt hypertensive rats obtained by constricting the right renal artery with a siler clip of 0.2 mm throat opening 3 to 4 weeks prior to study. Except for those few animals that develop renal infarction following placement of the clip, nearly all (approximately 80%) of the rats became severely hypertensive. We examined the effect of changes in BP on the left kidney (contralateral) exposed to high BP. The same micropuncture and clearance observations were made in these animals as described below for the control rats, except that the higher spontaneous BP allowed a larger BP range to be evaluated.

Control Rats

The control animals were normal Sprague-Dawley rats. Experiments were done only when BP was in the 130 to 140 mm Hg range following surgical preparation of the animal. The incidence of occurrence of stable, spontaneous BP in this high range of normal following the surgical procedures was about 5% to 10%. This restricted these studies to a relatively small number of successful experiments. On the other hand, a large enough pressure change could be produced in these rats without further interventions such as carotid clamping or vagotomy. Following surgical preparation, animals from each of the groups described above were evaluated for efficiency of autoregulation of RBF, GFR, and pressures in cortical microstructures in response to acute reductions in BP imposed by an aortic clamp.

Anesthesia was induced with pentobarbital sodium (Nembutal, 50 mg/kg i.p.), and maintained with small doses given intravenously. Animals were prepared for micropuncture on a thermostatically controlled, heated table surface. A tracheostomy was performed, and three small polyethylene catheters were inserted into one external jugular vein for administration of anesthetic and infusion of solutions. An arterial cannula inserted into the femoral artery allowed continuous measurement of arterial BP with a transducer (Model P-23 DC, Statham Medical Instruments, Hato Rey, Puerto Rico) which was recorded on a Grass Polygraph Recorder (Model 5, Grass Instruments, Quincy, Massachusetts). The left kidney was exposed through a transverse, subcostal incision, and placed in a small lucite cup. The ureter was catheterized with thin-walled tubing (i.d., 0.45-0.50 mm), and a small adjustable clamp was placed around the aorta between the renal arteries. An electromagnetic flow probe (Model EP 401.5, Carolina Medical Electronics, King, NC, 1.5 mm circumference) was placed on the renal artery to allow continuous measurement of renal blood flow (RBF). The technique for calibration of the flow meter has been described previously. Mechanical zero flow was checked by momentarily occluding the renal artery in every experiment. The kidney surface was superfused continuously with warm (38°C) isotonic saline from the tip of a quartz rod light conductor. An inulin solution (7.5 g/dl) in 150 mM NaCl (Polyfructosan, Laevosan Gesellschaft, Linz, Austria) was administered as a priming dose of 1 ml followed by an infusion at 20 μl/min (1.2 ml/hr). Measurements were initiated 20 min later. Each period consisted of one 30-minute or two 20-minute urine collections. Femoral arterial blood samples were taken at the midpoint of, or between, the urine collections.

In some experiments micropuncture protocols were conducted simultaneously with clearance collection periods. Following the initial observations, BP was reduced by constricting the aortic clamp. An additional 10 minutes were allowed to achieve a steady-state condition, and the protocol as described for the control period was repeated. This sequence was repeated at several levels of renal perfusion pressure in each experiment. Although recovery spontaneous BP was not always as high as the initial value, we attempted to obtain control, spontaneous BP observations at the end of each study in order to assess the effects of time-dependent changes in the preparation. Most animals had recovery arterial BPs within 10 mm Hg of the initial BP value.

Hydrostatic pressures of superficial cortical structures were measured with a servo-nulling pressure device (Model 900, W-P Instruments, New Haven, Connecticut) as described previously. Pipette tip sizes were 4-6 μm diameter, and tip resistances were 0.8 to 1.2 meg ohms. Pressures were continuously recorded on the Grass recorder.

Urine samples were collected under oil in tared containers, and urine volumes were determined gravimetrically. Inulin concentration in plasma (P, mg/ml) and urine (U, mg/ml) was measured with a semimicroanthrone technique. Urine and plasma
sodium and potassium concentrations (\(U_{Na}\) and \(U_K\) and \(P_{Na}\) and \(P_K\), mEq/liter) were determined by flame photometry. Kidney GFR (ml/min) was computed from urine and plasma inulin concentrations ([U/P]_in) and urine flow rate (\(\mu l/min\)). Sodium and potassium concentrations in urine (\(U_{Na}\) or \(U_K\)) and urine flow rate (\(V\)) gave sodium or potassium excretion rates (\(U_{Na}V\) or \(U_KV\), nEq/min). Renal vascular resistance (RVR) was calculated as the quotient of renal BP and RBF, expressed in peripheral resistance units (mm Hg/ml/min).

Values for each BP for each animal were averaged, and overall mean values were derived from mean values for each experiment. Observations were analyzed with standard statistical techniques for paired or unpaired data. Analysis of variance was accomplished with a general linear models procedure-regression program (Wilk's criterion) on a computer (I.B.M., Model 370). Significance was accepted as a \(p\) value of < 0.05. Some of the observations were subjected to least-squares curve-fitting procedures on a Tektronics 4051 computer (Tektronics, Inc., Beaverton, Oregon) with a general procedure regression program (Plot 50 Statics Series, Tektronics Computer Library).

Results

The RBF/BP relationships for 16 control kidneys and for 15 nonclipped kidneys of Goldblatt hypertensive rats are shown in figure 1. The initial RBFs at the respective, spontaneous BPs, 140 ± 2 mm Hg (X ± SEM) and 170 ± 5 mm Hg, were not different in the two groups, 6.4 ± 0.4 ml/min in controls and 6.3 ± 0.5 ml/min in contralateral kidneys (\(p > 0.50\)). When corrected for kidney weight, RBF in the hypertensive kidneys, 4.4 ± 0.5 ml/min/g, was significantly less than in the control kidneys, 5.8 ± 0.2 ml/min/g (\(p < 0.001\)). Contralateral kidneys of Goldblatt hypertensive rats failed to exhibit efficient autoregulatory adjustments in renal vascular resistance over the entire pressure range examined from 200 (170 ± 5) to 90 mm Hg. The RBF was 6.3 ± 0.5 ml/min at the average spontaneous BP of 170 mm Hg and fell to 5.5 ± 0.3 ml/min when BP was reduced to 150 mm Hg, to 5.2 ± 0.3 ml/min at 135 mm Hg, to 5.0 ± 0.3 ml/min when BP was changed to 120 mm Hg, and to 4.1 ± 0.3 ml/min when BP was lowered to 90 mm Hg, the lowest pressure examined. The RBF of normal rats did not change significantly when BP was decreased from 140 to as low as 95 mm Hg, but was reduced significantly when BP was altered to levels below 95 mm Hg (analysis of variance).

When assessed at spontaneous BP, the RVRs (fig. 1, bottom panel) of the two groups were significantly different, 23.1 ± 1.5 mm Hg-min/ml at a BP of 140 mm Hg in the control rats compared to 28.9 ± 2.8 mm Hg-min/ml at a BP of 168 ± 2 mm Hg in the kidneys of Goldblatt rats (\(p < 0.001\)). The elevated RVR in the contralateral kidneys was present not only at the spontaneous pressure levels but was also observed at every comparable BP level examined (all \(p < 0.05\)). Average RVR was 28.9 ± 2.8 at 168 mm Hg, 28.7 ± 1.9 at 150 mm Hg, 27.2 ± 1.8 at 135 mm Hg, 25.8 ± 1.9 at 120 mm Hg, and 24.2 ± 2 mm Hg-min/ml at a BP of 90 mm Hg. In contrast, RVR in the control animals decreased from 23.1 ± 1.5 at 140 mm Hg, to 20.4 ± 0.9 at 130 mm Hg, to 18.8 ± 0.8 at 118 mm Hg, and to 17.9 ± 0.8 mm Hg-min/ml at 108 mm Hg (all \(p < 0.05\)). The RVR failed to decrease further with reductions in BP to 95 mm Hg or below. Hematocrit was 50 ± 1 vol% in both groups of animals at the beginning of the experiment. With repetitive blood sampling during the course of the experiments, hematocrits fell to 43 ± 1 vol% for the controls and 46 ± 1 vol% for the Goldblatt animals.

The results of the studies examining the efficiency of GFR autoregulation in the nonclipped kidneys of 11 hypertensive animals and the left kidneys of seven control rats during acute reductions in renal arterial pressure were summarized in tables 1 and 2. At a spontaneous BP of 170 ± 5 mm Hg, GFR was 1.349 ±

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**Figure 1.** Renal blood flow autoregulation and renal vascular resistance. Upper graph: Renal blood flow (RBF, ml/min) is shown as a function of renal blood pressure (BP, mm Hg). Significantly different behavior of RBF in the two groups was confirmed with analysis of variance. Center graph: Computed renal vascular resistance (RVR) is shown as a function of renal blood pressure for the same animals. Asterisks denote statistically significant interval changes compared to values at the next higher BP (\(p < 0.05\)). Renal vascular resistance is presented in units (mm Hg/min/ml). Observations from normal animals are represented by open symbols (\(X ± SEM\)) and observations from the contralateral kidneys of two-kidney, one clip Goldblatt hypertensive animals are represented by closed symbols in both panels.
TABLE 1. Clearance and Excretory Observations During Acute Alterations in Renal Blood Pressure in Contralateral Kidneys of Two-Kidney, One Clip Goldblatt Hypertensive Rats

<table>
<thead>
<tr>
<th>BP (mm Hg)</th>
<th>Kidney weight (g)</th>
<th>V (μl/min)</th>
<th>GFR (ml/min)</th>
<th>GFR/g (ml/min/g)</th>
<th>UNaV (μEq/min)</th>
<th>FRNa (%)</th>
<th>UNaV (μEq/min)</th>
<th>FRK (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>170 ± 5</td>
<td>1.23 ± 0.08</td>
<td>21.6 ± 5.6</td>
<td>1.349 ± 0.075</td>
<td>1.083 ± 0.083</td>
<td>1.600 ± 0.660</td>
<td>98.94 ± 0.57</td>
<td>2.59 ± 0.48</td>
<td>52 ± 7</td>
</tr>
<tr>
<td>156 ± 2</td>
<td>9.8 ± 1.4</td>
<td>1.160 ± 0.090</td>
<td>0.941 ± 0.093</td>
<td>0.335 ± 0.075</td>
<td>97.72 ± 0.26</td>
<td>1.60 ± 0.21</td>
<td>71 ± 5</td>
<td></td>
</tr>
<tr>
<td>137 ± 2</td>
<td>7.7 ± 1.8</td>
<td>1.069 ± 0.149</td>
<td>0.849 ± 0.099</td>
<td>0.205 ± 0.139</td>
<td>98.86 ± 0.09</td>
<td>0.72 ± 0.13</td>
<td>76 ± 7</td>
<td></td>
</tr>
<tr>
<td>120 ± 1</td>
<td>4.8 ± 0.8</td>
<td>0.781 ± 0.073</td>
<td>0.609 ± 0.057</td>
<td>0.072 ± 0.021</td>
<td>99.93 ± 0.02</td>
<td>0.49 ± 0.02</td>
<td>85 ± 3</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BP = renal blood pressure; V = urine flow; GFR/g = glomerular filtration rate/gram kidney weight; UNaV = sodium excretion rate; FRNa = fractional reabsorption of sodium; UNaV = potassium excretion rate; and FRK = fractional reabsorption of potassium.

TABLE 2. Clearance and Excretory Observations During Acute Alterations in Renal Blood Pressure in Left Kidneys of Normal Rats

<table>
<thead>
<tr>
<th>BP (mm Hg)</th>
<th>Kidney weight (g)</th>
<th>V (μl/min)</th>
<th>GFR (ml/min)</th>
<th>GFR/g (ml/min/g)</th>
<th>UNaV (μEq/min)</th>
<th>FRNa (%)</th>
<th>UNaV (μEq/min)</th>
<th>FRK (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>129 ± 1</td>
<td>1.11 ± 0.05</td>
<td>3.7 ± 0.4</td>
<td>1.172 ± 0.134</td>
<td>1.051 ± 0.082</td>
<td>0.043 ± 0.010</td>
<td>99.978 ± 0.008</td>
<td>1.04 ± 0.20</td>
<td>79 ± 5</td>
</tr>
<tr>
<td>115 ± 0</td>
<td>3.6 ± 0.3</td>
<td>1.133 ± 0.099</td>
<td>1.023 ± 0.069</td>
<td>0.034 ± 0.006</td>
<td>99.976 ± 0.005</td>
<td>0.837 ± 0.131</td>
<td>83 ± 3</td>
<td></td>
</tr>
<tr>
<td>95 ± 0</td>
<td>2.6 ± 0.2</td>
<td>0.815 ± 0.053</td>
<td>0.735 ± 0.024</td>
<td>0.031 ± 0.001</td>
<td>99.977 ± 0.009</td>
<td>0.512 ± 0.010</td>
<td>87 ± 3</td>
<td></td>
</tr>
<tr>
<td>70 ± 0</td>
<td>1.8 ± 0.3</td>
<td>0.444 ± 0.049</td>
<td>0.404 ± 0.045</td>
<td>0.014 ± 0.002</td>
<td>99.983 ± 0.003</td>
<td>0.118 ± 0.031</td>
<td>96 ± 4</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: see footnote to table 1.

0.074 ml/min in the contralateral kidneys of the Goldblatt animals, a value not significantly different from that of the control animals, 1.172 ± 0.134 ml/min, observed at a spontaneous BP of 129 ± 1 mm Hg (p > 0.10). When corrected for the larger kidney weight of the contralateral kidneys (1.23 ± 0.06 g) compared to control kidneys (1.11 ± 0.05 g), the GFR/g was nearly identical in the two groups (1.083 ± 0.083 ml/min/g, Goldblatt; 1.051 ± 0.082 ml/min/g control). In contrast to the behavior of normal kidneys, efficient autoregulation of GFR was not evident in the contralateral kidneys of the Goldblatt hypertensive animals during conditions of acutely reduced BP (tables 1 and 2).

Pressure observations were made in cortical structures at spontaneous BP and following acute reductions in BP in seven contralateral kidneys of Goldblatt rats and in 15 control animals. Pressures in peritubular capillaries were not different in contralateral kidneys, 11.7 ± 0.6, compared to normal kidneys, 12.0 ± 0.6 mm Hg, at their respective spontaneous BP levels (fig. 2). Pressures in proximal tubules, 16.0 ± 0.7, were slightly but insignificantly higher in the contralateral kidneys than in the control animal kidneys, 14.6 ± 0.6 mm Hg, at the respective spontaneous BP levels. In contrast, pressures in distal tubules of the Goldblatt animals, 11.4 ± 1.6, were greater than in the control animals, 8.7 ± 0.8 mm Hg (fig. 2). The hydrostatic pressures in the contralateral kidneys of hypertensive rats decreased progressively with each step change in renal BP from the spontaneous BP of 169 ± 1 mm Hg. In the control animals, the pressures in all of the structures observed were not altered significantly when BP was reduced to as low as 93 ± 1 mm Hg.

Urine flow and sodium excretion data from the contralateral kidneys of the hypertensive rats are shown as a function of BP in figures 3 and 4 and tables 1 and 2. At an average BP of 170 ± 5 mm Hg, urine flow was 21.6 ± 6 μl/min compared to 3.7 ± 0.4 μl/min in the control kidneys at the lower, spontaneous BP of 129 ± 1 mm Hg observed in this group (p < 0.01). Urine flow from the contralateral kidneys changed from 21.6 ± 5.6 μl/min at spontaneous BP to 9.8 ± 1.4 μl/min at 156 mm Hg, to 7.7 ± 1.8 μl/min at 137 mm Hg, and to 4.8 ± 0.8 μl/min at a BP of 120 mm Hg. As shown in figure 3, urine flow from contralateral and normal kidneys was disproportionately increased at the higher BP levels examined, giving rise to the nonlinear relationship evident for those data. These observations were not extended into the lower BP ranges examined in the RBF studies because of the marked prolongation of the requisite clearance periods.

The relative pattern of change in UNaV was similar to those for V. All of the observations for UNaV from contralateral and normal kidneys are plotted as a function of their respective BP in figure 4. The nonlinear responses of sodium excretion to reductions of BP are demonstrated by the line representing the best fit equation for the observations shown. The large values for UNaV at the extreme elevations of BP explain the increased average for sodium excretion at spontaneous BP, shown in table 1. Generally, potas-
sium excretion and fractional cation excretions demonstrated the same pattern of change during acute reductions in BP as V and U_{NaV}. At comparable BP, the contralateral kidneys demonstrated urine flow rates and absolute and fractional electrolyte excretions that were not different from the control kidneys (all p > 0.05). Following changes in BP to 115 mm Hg in the control kidneys, urine flow was not significantly reduced from 3.7 ± 0.4 μl/min. However, when BP was reduced further in the normal animals, urine flow decreased significantly. The pattern of the change in absolute potassium excretion (UKV), or fractional potassium absorption (FRK), was similar to that for urine flow in the normal kidneys.

Discussion

The results of the present experiments demonstrate that the kidney contralateral to the vascular clip in a two-kidney, one clip renal vascular hypertensive model has alterations in its renal hemodynamic status that do not allow it to maintain normal BF and GFR except at the elevated arterial BP. At spontaneous BP, the RVR was greater in the contralateral kidneys of the hypertensive animals than in the normal kidneys, as suggested previously. In addition to the greater baseline RVR in the kidneys of hypertensive rats, the ability to adjust RVR efficiently during acute changes in BP was impaired. Although vascular resistance decreased during conditions of acutely reduced BP, these small RVR changes were inadequate to maintain RBF and GFR. Thus, RVR remained inappropriately high at all arterial pressures.

The loss of autoregulatory efficiency of hydrostatic pressure in superficial structures of contralateral kidneys is consistent with the whole kidney blood flow and GFR data as well as our earlier observations on
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FIGURE 4. Log sodium excretion rate at spontaneous and reduced BP. The log of the observed sodium excretion rate (nEq/min) at spontaneous BP (crossed symbols) and during conditions of acutely reduced BP (black circles) are shown for all observations for contralateral kidneys as a function of renal perfusion pressure (abscissa, mm Hg). These data were subjected to computer curve-fitting procedures. Analysis of the observations at spontaneous BP (n = 11) gave the best fit equation, \( y = 0.0058x + 0.46 \) (r = 0.79). When the observations at spontaneous BP were pooled with those obtained during conditions of acutely reduced BP (total, n = 34) the equation \( y = 0.088x + 0.52 \) (r = 0.69) was the best fit for the data; the line in the figure represents this equation. Observations from normal animals are represented as open circles.

single nephron GFR.\(^{19}\) In contrast, normal kidneys efficiently autoregulated RBF, GFR, peritubular capillary pressure, and pressures in proximal and distal tubules. Taken together, these data indicate that the augmented vascular resistance in contralateral kidneys of hypertensive rats is not simply the consequence of autoregulatory responses to the elevated systemic arterial pressure. These observations support the concept that the "normal RBF" observed in the contralateral kidneys can be maintained only at the greatly increased systemic arterial pressures that are generated in this hypertensive model.

Although previous studies have not reported the evaluation of the renal autoregulatory capability of the contralateral kidney, several investigators have reported observations of renal plasma flow (RPF) measured by PAH clearance\(^{20}\) or extraction\(^{21}\) or \(^{82}Rb\) uptake techniques\(^{20}\) at spontaneous BP. Based on these techniques, estimates of RPF to the unclipped kidney were within the range for normal animals\(^{20}\) or slightly elevated.\(^{21}\) In the present experiments, we observed RBFs that were similar in contralateral kidneys and in normal kidneys with an electromagnetic flowmeter that obviated possible errors of estimating RPF from PAH clearance or extraction data.\(^{20,21}\)

The nonlinear relationship between urine flow rate or Na excretion from the contralateral kidney following changes of arterial BP was also observed by Stumpe et al.\(^{26}\) when they examined renal function at spontaneous BP in each of a number of different animals.\(^{23}\) Our data confirm this observation in animals that were subjected to reductions in BP from the spontaneous BP values. Therefore, the exaggerated sodium and water excretion seen at extraordinarily high pressures are reflections of reduced fractional and absolute tubular reabsorption of salt and water. The observations of Lowitz and coworkers\(^{24}\) suggest that the diuresis and natriuresis seen at hypertensive BPs were, at least in part, the result of decreased loop of Henle reabsorption.\(^{24}\) The mechanism of these absorptive alterations remains to be elucidated but seems to be related to the magnitude of the BP elevation since, with reduction in BP, fractional reabsorption of sodium increased to the range observed in the control animals.

The same group of investigators reported earlier that they observed efficient autoregulatory behavior of superficial nephron GFR but not juxtamedullary nephron GFR when comparisons were made between observations from different animals each at spontaneous hypertensive BP.\(^{26}\) The failure to observe autoregulatory behavior in the present experiments is compatible with the apparent failure of juxtamedullary nephron GFR to autoregulate in the experiments of Stumpe et al.\(^{26}\) However, the suggestion of efficient autoregulatory behavior in superficial nephrons is difficult to reconcile with our present results or our earlier observations\(^{23}\) where we did not observe efficient autoregulatory behavior of superficial nephron GFR. Although Stumpe et al. reported GFR constancy of the superficial cortical nephrons, they did not evaluate the dynamic autoregulatory behavior of individual kidneys contralateral to the renal artery clip. It should be noted that the observation of GFR values in the normal range in animals having different spontaneous arterial BPs is not an adequate index to assess intrinsic autoregulatory capability of a kidney.

In a recent series of experiments, Schweitzer and Gertz\(^{26}\) reported that, in spite of significantly increased single nephron blood flow, resistance of the afferent arteriolo was increased 51% in kidneys contralateral to the renal artery clip in a similar model. These observations coincide with our whole kidney data, which also documented an elevated total RVR in the contralateral kidney. Further, our present observations indicate that this elevated RVR persists during conditions of reduced renal perfusion pressure as
reflected in the inefficient autoregulation of RBF.

The mechanism responsible for the altered hemodynamic status of the contralateral kidney is not evident. It is possible that adrenergic influences, reduced prostaglandin activity, altered kinin activity, and alterations in the renin-angiotensin system may play significant roles in maintaining the elevated RVR of the unclipped kidney early in the development of hypertension. Several observations suggest that renin-angiotensin influences may play a significant role in our rat model in this time frame. First the development of hypertension can be prevented by chronic blockade of renin-angiotensin. In addition, we have recently observed that GFR and water and electrolyte excretions of the hypertensive contralateral kidney are augmented during acute renin-angiotensin blockade with several agents. Whether altered activity of the renin-angiotensin system or other mechanisms might reduce the ability of the renal vasculature to adjust to conditions of acutely reduced BP, remains to be defined.

The observations that both RBF and GFR autoregulation are markedly impaired suggests that the predominant site of impaired vascular reactivity following acute reductions in BP is the preglomerular vasculature. Although possible shifts in afferent arteriolar to efferent arteriolar resistance ratios are suggested by our observations, the present data do not allow us to quantitate the effects of reduced BP on each resistance segment.

We have observed previously that tubuloglomerular feedback activity in this model is attenuated. Since it has been hypothesized that the distal tubuloglomerular feedback system plays a role in effecting autoregulatory adjustments in RVR, it seems possible that the impaired autoregulatory behavior of GFR and RBF of the contralateral kidney may be the direct result of the attenuated feedback responsiveness. It is possible that the impaired feedback activity could be the direct result of structural changes in the renal vasculature, altered Na⁺ -K⁺ ATPase activity in the vascular wall, or the greatly reduced renin content of the juxtaglomerular apparatus. Alternatively, as outlined above, some of these mechanisms could attenuate vascular responsiveness directly.

In summary, we have observed that the kidney contralateral to the renal artery stenosis in a two-kidney model of renal vascular hypertension fails to maintain hemodynamic, clearance, or excretory function efficiently during conditions of acutely reduced BP. Kidney GFR and RBF were not different from those of normal animals at their respective spontaneous BPs. However, at spontaneous BP, the hypertensive kidney exhibits an elevated RVR. Although RVR was decreased during conditions of acutely reduced renal BP in the contralateral kidneys, the changes in RVR were insufficient to maintain hemodynamic and clearance function. The failure of the contralateral kidney to appropriately adjust RVR in order to maintain hemodynamic function indicates that this perturbation may be of pathophysiologic importance in the maintenance of hypertension in this model.

References

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