Exaggerated Natriuretic Response to Atrial Natriuretic Factor in Rats Developing Spontaneous Hypertension

David M. Pollock and William J. Arendshorst

The present study was designed to evaluate the renal response to atrial natriuretic factor (ANF) in young rats developing spontaneous hypertension (SHR) and compare this response to age-matched, normotensive controls (WKY) and adult animals. At 6 weeks of age, intravenous infusion of ANF (0.25 μg/kg min) in anesthetized, euvoletic rats produced a significantly larger natriuresis and diuresis in SHR compared with WKY rats; this strain difference was not observed in rats 11 weeks of age. SHR showed no age-related change in the natriuretic response to ANF, whereas adult WKY rats exhibited a greater response than young WKY rats. To determine the effect of renal perfusion pressure on the magnitude of the renal response to ANF, additional groups of 6- and 11-week-old SHR were studied while renal perfusion pressure was lowered acutely by aortic constriction (SHR-AC) to values similar to age-matched WKY rats. In young rats, the diuretic and natriuretic response to ANF was greatest in SHR, intermediate in SHR-AC, and lowest in WKY rats. In adult animals, the natriuretic and diuretic response was similar in SHR and WKY rats and tended to be less in SHR-AC. These results in both 6- and 11-week-old SHR are consistent with previous reports that the magnitude of the response to ANF is directly related to acute changes in renal perfusion pressure. Furthermore, we conclude that 1) the kidney of young SHR is hyperresponsive to ANF, 2) WKY rats, but not SHR, exhibit age-related increases in responsiveness to ANF, 3) increased renal perfusion pressure cannot completely account for the exaggerated renal response in young SHR, and 4) the relation between pressure and the response to ANF is not observed with chronic elevations in renal perfusion pressure in hypertensive rats. (Hypertension 1990;16:72–79)

There is considerable evidence of impaired renal function during the development of genetic hypertension that suggests that the kidney plays a pivotal role in the pathogenesis of this disease. Our laboratory has reported abnormalities, relative to the genetic normotensive control Wistar-Kyoto (WKY) rats, concerning sodium and water balance, glomerular dynamics, tubuloglomerular feedback activity, and denervation diuresis in young rats developing spontaneous hypertension (SHR). Because the atrial natriuretic factor (ANF) is thought to be involved in the control of renal function and body fluid homeostasis, it is possible that ANF may affect kidney function differently in SHR versus normotensive rats.

Several investigators have reported elevated plasma levels of ANF in adult SHR (more than 12 weeks old) compared with WKY rats. Increased release of ANF is often associated with elevated atrial pressure and thus could explain the difference in plasma concentrations in established hypertension. Similar changes in plasma ANF have been reported for other models of hypertension despite differences in the pathogenic mechanisms. High ANF levels in adult SHR suggest that this hormone may not be responsible for producing the relative salt and water retention that occurs in young SHR but rather is released as a compensatory mechanism to another intrinsic disorder. It is possible, however, that the kidneys of young rats have an abnormal sensitivity to ANF that may contribute to an inability to excrete appropriate amounts of sodium and water during the development of spontaneous hypertension.

The effects of ANF on renal function in young SHR are not known. In addition, there is no concen-
sus concerning the renal response to ANF in adult SHR and WKY rats. Some reports suggest that ANF produces an exaggerated natriuretic response in SHR, whereas other studies show similar responses in the hypertensive and normotensive strains. It is not clear whether the variable results of different laboratories is due to differences in fluid-volume status, dose of ANF administered, source of animals, age, degree of hypertension, experimental preparations, or other factors. Furthermore, exaggerated natriuretic responses are not always observed in nonsprontaneous models of hypertension compared with the appropriate normotensive control.

Renal perfusion pressure may account for some of the differences in the renal response to ANF between hypertensive SHR and normotensive WKY rats reported in some studies. Recent studies suggest that the magnitude of the natriuretic response to ANF is a direct function of renal perfusion pressure and that ANF augments pressure-induced changes in sodium excretion in normotensive animals. However, the influence of perfusion pressure on the renal response to ANF in SHR or other models for hypertension has not been examined. Although several investigators have reported no difference in the excretory responsiveness between adult SHR and WKY rats, the kidneys per se may be hyporesponsive to ANF if the animals were not hypertensive.

The purpose of the present study was to evaluate the renal response to ANF in young rats developing spontaneous hypertension (6-week-old) and compare this response with that of age-matched normotensive WKY controls. We also examined the effect of ANF during a more established phase of hypertension by comparing the renal response to ANF in 11-week-old SHR and WKY rats. To elucidate the influence of perfusion pressure in determining the magnitude of the renal response, additional groups of 6- and 11-week-old SHR were studied while renal perfusion pressure was lowered to values similar to age-matched WKY rats.

Methods

Experiments were conducted on 6- and 11-week-old SHR and WKY rats from our breeding colony in Chapel Hill originally obtained from the National Institutes of Health stock. Animals were fasted but allowed free access to water the night before the experiment. After inducing anesthesia with pentobarbital sodium (50 mg/kg i.p.), rats were placed on a heating table with body temperature servo-controlled at 37° C. The trachea was cannulated (PE-205) to facilitate free breathing. A femoral artery was cannulated (PE-50) for blood sampling and continuous measurement of arterial pressure. A femoral venous cannula (PE-10) was placed in the jugular vein for infusion of 0.85% NaCl (0.8 ml/hr), [3H]inulin (4 μCi/hr•100 g-1), and p-aminohippurate (PAH) (6 mg • hr-1 • 100 g-1). A second cannula (PE-10) was placed in the jugular vein for infusion of 0.85% NaCl (0.8 ml/hr). Both ureters were cannulated (PE-10) for urine collection. After surgery, the rats were allowed to stabilize for 60–90 minutes before starting control measurements.

In groups of 6- and 11-week-old SHR with aortic constriction (SHR-AC), a silk ligature (5-0) was placed around the abdominal aorta just proximal to both renal arteries, threaded through PE-50 tubing and attached to a screw-type constrictor. The constrictor was adjusted to maintain femoral artery pressure at a level similar to WKY rats beginning 30 minutes after the completion of surgery and 30–60 minutes before starting control measurements. A minimum of four rats of each strain and age group served as sham controls by having the ligature loosely placed around the aorta without any constriction. Results from the sham rats were not different from those without the constrictor and thus the data were combined.

The protocol for urine collection was identical in all experiments. Two 30-minute control periods were followed by continuous intravenous infusion of ANF (0.25 μg • kg-1 • min-1, 1-28; Bachem, Inc., Torrance, Calif.). After a 10–15-minute equilibration period, two 30-minute experimental periods were obtained. Femoral arterial blood samples were taken periodically with a terminal blood sample taken from the left renal vein to determine the extraction of PAH.

Urine and plasma sodium and potassium concentrations were determined by flame photometry (model SICa, Perkin-Elmer, Norwalk, Conn.) and urine osmolality by vapor pressure depression (Wescor, Logan, Utah). Activity of [3H]inulin was determined using a liquid scintillation spectrophotometer (Packard Instrument Co., Meriden, Conn.). Glomerular filtration rate (GFR) was evaluated as the clearance of inulin. The concentration of PAH in urine and plasma was determined using a colorimetric method. Renal plasma flow (RPF) and renal blood flow (RBF) were evaluated as the clearance/extraction of PAH and RPF/(I–hematocrit), respectively. Renal vascular resistance (RVR) was calculated as an arterial pressure–3 mm Hg/RBF; 3 mm Hg was used as an estimate of renal venous pressure.

Values reported (mean±SEM) for the control and experimental periods are derived from the average of the two consecutive observation periods as there were no significant differences for any variable. Clearance data were calculated as the average of both kidneys or normalized to kidney weight as indicated. Analysis of variance based on a multivariate general linear model was used to determine significance when evaluating data from multiple groups (WKY rats, SHR, and SHR-AC) and included post hoc individual group comparisons (SYSTAT, Inc., Evanston, Ill.). Student's t test for paired data was used to determine significance between
TABLE 1. Age, Body Weight, and Total Kidney Weight of Wistar-Kyoto Rats, Spontaneously Hypertensive Rats, and Spontaneously Hypertensive Rats With Aortic Constriction

<table>
<thead>
<tr>
<th>Variables</th>
<th>WKY</th>
<th>SHR</th>
<th>SHR-AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (wk)</td>
<td>6.4±0.1</td>
<td>6.3±0.2</td>
<td>6.2±0.2</td>
</tr>
<tr>
<td>Body wt (g)</td>
<td>107±3</td>
<td>92±6</td>
<td>97±8</td>
</tr>
<tr>
<td>Kidney wt (g)</td>
<td>1.21±0.04</td>
<td>1.05±0.08</td>
<td>1.13±0.08</td>
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<td>Rats (n)</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

11-week-old rats

<table>
<thead>
<tr>
<th>Variables</th>
<th>WKY</th>
<th>SHR</th>
<th>SHR-AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (wk)</td>
<td>10.7±0.2</td>
<td>11.1±0.4</td>
<td>10.7±0.3</td>
</tr>
<tr>
<td>Body wt (g)</td>
<td>239±8</td>
<td>239±7</td>
<td>244±8</td>
</tr>
<tr>
<td>Kidney wt (g)</td>
<td>2.09±0.07</td>
<td>2.08±0.05</td>
<td>2.28±0.14</td>
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<tr>
<td>Rats (n)</td>
<td>8</td>
<td>10</td>
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</tr>
</tbody>
</table>

Values are mean±SEM. WKY, Wistar-Kyoto rats; SHR, spontaneously hypertensive rats; SHR-AC, spontaneously hypertensive rats with aortic constriction.

control and ANF periods within a given rat strain. Results with p<0.05 were considered significant.

TABLE 2. Renal Function and Hemodynamic Data in 6-Week-Old Rats Before and During Infusion of Atrial Natriuretic Factor

<table>
<thead>
<tr>
<th>Variables</th>
<th>Period</th>
<th>WKY</th>
<th>SHR</th>
<th>SHR-AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal perfusion pressure (mm Hg)</td>
<td>control</td>
<td>109±3</td>
<td>119±5</td>
<td>106±1*</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>107±5</td>
<td>110±5</td>
<td>105±1</td>
</tr>
<tr>
<td>p (ANF vs. control)</td>
<td></td>
<td></td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Renal blood flow (ml/g weight)</td>
<td>control</td>
<td>6.9±0.5</td>
<td>7.2±0.4</td>
<td>6.0±0.5</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>6.2±0.4</td>
<td>6.8±0.4</td>
<td>6.0±0.5</td>
</tr>
<tr>
<td>Renal vascular resistance [mm Hg/(ml/min−1•g weight)]</td>
<td>control</td>
<td>15.7±1.2</td>
<td>16.4±1.8</td>
<td>19.1±2.0</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>16.9±1.0</td>
<td>16.5±2.4</td>
<td>17.9±1.5</td>
</tr>
<tr>
<td>Glomerular filtration rate (ml/min−1•g weight)</td>
<td>control</td>
<td>1.31±0.12</td>
<td>1.32±0.10</td>
<td>1.04±0.06</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>1.22±0.11</td>
<td>1.33±0.11</td>
<td>1.07±0.06</td>
</tr>
<tr>
<td>Filtration fraction</td>
<td>control</td>
<td>0.33±0.04</td>
<td>0.29±0.03</td>
<td>0.32±0.02</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>0.33±0.03</td>
<td>0.34±0.06</td>
<td>0.31±0.02</td>
</tr>
<tr>
<td>Urine flow rate (g/l•min−1•kidney wt)</td>
<td>control</td>
<td>3.37±0.74</td>
<td>3.89±0.71</td>
<td>2.70±0.26</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>4.36±0.84</td>
<td>7.34±1.25</td>
<td>4.23±0.49</td>
</tr>
<tr>
<td>Sodium excretion (µeq/min−1•kidney wt)</td>
<td>control</td>
<td>1.03±0.22</td>
<td>1.10±0.25</td>
<td>0.55±0.13</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>1.36±0.25</td>
<td>2.21±0.38</td>
<td>1.29±0.29</td>
</tr>
<tr>
<td>Potassium excretion (µeq/min−1•kidney wt)</td>
<td>control</td>
<td>0.56±0.08</td>
<td>0.49±0.05</td>
<td>0.50±0.05</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>0.51±0.05</td>
<td>0.50±0.05</td>
<td>0.54±0.06</td>
</tr>
<tr>
<td>Fractional excretion (%)</td>
<td>control</td>
<td>0.44±0.06</td>
<td>0.57±0.09</td>
<td>0.49±0.05</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>0.63±0.07</td>
<td>1.05±0.16</td>
<td>0.74±0.08</td>
</tr>
<tr>
<td>Sodium</td>
<td>control</td>
<td>0.75±0.11</td>
<td>1.07±0.19</td>
<td>0.62±0.15</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>1.06±0.14</td>
<td>2.21±0.32</td>
<td>1.26±0.21</td>
</tr>
<tr>
<td>Potassium</td>
<td>control</td>
<td>14.4±0.7</td>
<td>16.0±1.31</td>
<td>19.2±2.1†</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>14.7±1.2</td>
<td>16.7±1.82</td>
<td>20.8±2.6</td>
</tr>
<tr>
<td>Urine osmolality [mOsm (kg H2O)−1]</td>
<td>control</td>
<td>1591±114</td>
<td>1464±120</td>
<td>1532±101</td>
</tr>
<tr>
<td></td>
<td>ANF</td>
<td>1354±117</td>
<td>1130±102</td>
<td>1459±130</td>
</tr>
<tr>
<td>Rats (n)</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SEM. WKY, Wistar-Kyoto rats; SHR, spontaneously hypertensive rats; SHR-AC, spontaneously hypertensive rats with aortic constriction.

*p<0.05 vs. SHR.
†p<0.05 vs. WKY rats.

Results

Average age, body weight, and total kidney weight were similar within the young and adult groups of rats (Table 1).

Six-Week-Old Rats

Results of renal hemodynamic and excretory determinations in 6-week-old rats are presented in Table 2. During the control period, SHR had a 10—13 mm Hg higher arterial pressure than WKY rats (Figure 1). By design, SHR-AC had a renal perfusion pressure that was nearly identical to WKY rats. Despite these differences in perfusion pressure during the control period, renal hemodynamic and urinary excretory variables were similar in the three groups of 6-week-old rats.

Infusion of ANF in young rats produced a significant hypotensive response only in SHR (Figure 1). Renal perfusion pressure decreased −9±2 mm Hg in SHR, −2±2 in WKY rats, and −1±1 mm Hg in SHR-AC. No changes in RBF, RVR, GFR, or filtra-
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Renal Response to ANF in Hypertensive Rats

a.

160
150
140
130
120
110
100
90

6 wk
11 wk

SHR
WKY
SHR-AC

CONTROL ANF CONTROL ANF

FIGURE 1. Plots showing mean arterial pressure during control and atrial natriuretic factor (ANF) infusion periods (0.25 μg·kg⁻¹·min⁻¹) in 6- and 11-week (wk)-old Wistar-Kyoto (WKY) rats, spontaneously hypertensive rats (SHR), and SHR with aortic constriction (SHR-AC). *Represents p<0.05 vs. control within a given group. Values represent mean±SEM.

a.

120
110
100
90
80

6 wk
11 wk

WKY (9) SHR (9) SHR-AC (9)
WKY (10) SHR (10) SHR-AC (8)

FIGURE 2. Bar graphs showing changes in urine flow and sodium excretion produced by infusion of atrial natriuretic factor (ANF) (0.25 μg·kg⁻¹·min⁻¹) in 6- and 11-week (wk)-old Wistar-Kyoto (WKY) rats, spontaneously hypertensive rats (SHR), and SHR with aortic constriction (SHR-AC). Number of rats in each group are indicated in parentheses. Values represent mean±SEM.

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ANF infusion in adult rats produced a significant decrease in arterial pressure in SHR and WKY rats (Figure 1). In SHR-AC, renal perfusion pressure was maintained stable at normotensive values during control and experimental periods (Figure 1). The average decrease in renal perfusion pressure produced by ANF was $-19\pm3$ mm Hg in SHR, $-8\pm4$ in WKY rats, and $0\pm1$ mm Hg in SHR-AC. ANF did not affect mean RBF, RVR, GFR, or filtration fraction in WKY rats and SHR (Table 3). Unlike young SHR-AC, adult SHR-AC respond to ANF with increases in RBF and GFR, whereas RVR was decreased. Despite these responses, there were no significant differences among groups in terms of the ANF-induced changes in renal hemodynamic variables. ANF produced consistent changes in urinary excretion. Absolute and fractional water and sodium excretion increased in all three groups; the increase in fractional water excretion in SHR-AC was of borderline significance ($0.1<p<0.05$). In contrast to the strain differences noted earlier for 6-week-old rats, ANF produced similar increases in water and sodium excretion in each group of adult rats (Figure 2). The increases observed in SHR-AC tended to be less (25 and 40% less on the average) than SHR and WKY rats. ANF-induced increases in fractional excretion of water and sodium exhibited a similar pattern to absolute changes (Figure 3). Absolute potassium excretion increased only in SHR-AC; fractional potassium excretion was not affected by ANF in any group. ANF decreased urine osmolality only in WKY rats. Small decreases in hematocrit were observed in SHR and SHR-AC although the changes were not different from WKY rats.

**Discussion**

The present investigation provides interesting observations that WKY rats and SHR exhibit age-
and pressure-related differences in the renal response to ANF. A more pronounced diuretic and natriuretic response was observed in 6-week-old SHR than in age-matched normotensive WKY rats. This new finding indicates that the kidneys of young SHR are hyperresponsive to ANF during the development of hypertension. This strain difference was no longer discernible at 11 weeks of age when SHR are in an established phase of hypertension. An alternative explanation for our results is that WKY rats are hypersensitive to ANF at a young age. However, comparisons within a strain revealed an age-related increase in the natriuretic and diuretic response to ANF in WKY rats similar to other nonnormotensive strains,\(^\text{27}\) whereas the excretory responses in 6- and 11-week-old SHR were not different. Chevalier et al.\(^\text{27}\) reported evidence that metabolic clearance of ANF decreases with age. Thus, it is possible that the exaggerated natriuretic response to ANF in young SHR compared with age-matched WKY rats is due to a relatively lower clearance of exogenously administered ANF. These observations suggest a more rapid development or maturity in the hypertensive strain or that ANF release may be enhanced as hypertension develops.

Previous work examining the effect of ANF on renal function in adult SHR and WKY rats have produced mixed results. Gellai et al.\(^\text{16}\) and Marsh et al.\(^\text{17}\) found similar natriuretic responses to ANF in conscious SHR and WKY rats. In anesthetized rats, however, several laboratories reported exaggerated responses in SHR.\(^\text{13-15}\) Taken together, these observations might suggest that anesthesia has an influence on the response to ANF in one or either of these strains of rats. However, Pollock and Banks\(^\text{28}\) previously demonstrated that the natriuretic response to ANF is not affected by pentobarbital anesthesia in normotensive Sprague-Dawley rats. In the present study, pentobarbital was the anesthetic and donor plasma was infused to maintain euvolesma similar to conscious animals.\(^\text{29}\) Thus the fluid-volume state may be an important factor in determining the magnitude of the excretory response when comparing SHR and WKY rats. It is possible, however, that anesthesia may influence the clearance of ANF differently in hypertensive and normotensive animals. In addition, it is not known whether SHR and WKY rats obtained from different sources have the same rate of development of hypertension so that direct comparison of data for age-related phenomenon obtained from different laboratories and sources of rats should be viewed with caution. In this regard, the present study provides information on renal responsiveness in SHR and WKY rats from single colonies and using identical protocols.

Our results indicate small decreases in the diuretic and natriuretic response to ANF in SHR when renal perfusion pressure was acutely reduced to normotensive levels similar to WKY rats at both 6 and 11 weeks of age. These findings extend previous studies indicating a pressure-dependency of the excretory response in dogs\(^\text{23}\) and normotensive strains of rats.\(^\text{22,24,25}\) We cannot exclude the possibility that the larger degree of ANF-induced hypotension may have blunted an otherwise exaggerated response in adult SHR. The mechanisms responsible for the larger reduction in arterial pressure produced by ANF in SHR is not clear but could be because of different factors such as the number of ANF receptors, effects on total peripheral resistance or cardiac output, or antagonism of vasoconstrictor systems. In young SHR-AC, the excretory response to ANF was still greater than in WKY rats. We conclude that most of the exaggerated response in young SHR can be attributed to increased renal perfusion pressure, but there remains some other determinant of the renal response to ANF that is different between SHR-AC and WKY rats. Limited evidence supports several possible explanations including a decreased clearance of ANF from plasma or increased receptor number or sensitivity in young SHR.\(^\text{27,30}\) Changes in arterial pressure proximal to the aortic constriction site could potentially influence release of endogenous ANF, which in turn could influence end-organ responsiveness.

Consistent with the idea that SHR have decreased clearance or renal sensitivity to ANF with age are plasma measurements of ANF levels in SHR and WKY rats. As hypertension develops, there is presumably an increase in release of ANF resulting in a decrease in atrial tissue concentrations in response to elevated arterial pressure. Under control conditions, SHR and WKY rats have similar plasma concentrations of endogenous ANF at 3–6 weeks of age.\(^\text{6,7}\) As the animals mature, plasma levels of both strains increase. SHR exhibit a more rapid rate of increase so that adults have significantly higher plasma levels of ANF than WKY rats.\(^\text{6,7}\) We now report that WKY rats, but not SHR, have age-related increases in renal responsiveness to exogenous ANF while the difference in arterial pressure between strains becomes more pronounced. These results are of particular interest because the relation between chronic changes in arterial pressure and the renal response to ANF in SHR contrasts with acute observations. Therefore, pressure-related modulation of the natriuretic and diuretic response to ANF is reset as SHR get older. In this regard, adult SHR are not different from several other models of hypertension.\(^\text{12,18,19,30}\) Renal responsiveness in chronically hypertensive animals is probably dampened by other control systems working to decrease sodium excretion.

We provide evidence that, at least in part because of the elevated arterial pressure, young SHR are more sensitive to ANF than WKY rats. As the hypertension becomes more established, the relation between pressure-natriuresis and the renal response to ANF appears to be reset. It is not clear why adult SHR with an elevated spontaneous arterial pressure do not have an exaggerated renal response to ANF. These observations agree with results for other forms of chronic hypertension. For example, similar
responses to ANF have been observed in Dahl salt-sensitive,19 deoxycorticosterone acetate-salt,18 and one-kidney, one clip31 hypertensive rats and their normotensive controls.

In further agreement with results from other laboratories, our results are consistent with the idea that the natriuretic response to ANF is independent of normotensive controls. Furthermore, ANF produced smaller increases in absolute and fractional excretion of water and sodium in adult SHR-AC despite having a significant increase in GFR not observed in nonconstricted rats. Our results for hypertensive rats extend previous studies showing that the slope of the relation between renal perfusion pressure and natriuresis within the autoregulatory range is increased by ANF without changes in GFR or RBF.24,25 These findings suggest a direct inhibition of tubular reabsorption independent of increases in GFR. In addition, strain differences in the diuretic and natriuretic responses cannot be attributed to differential effects of ANF on GFR.

The effect of renal perfusion pressure on the natriuretic response to ANF may be related to basal sodium excretion and changes in sodium delivery to the ANF-sensitive parts of the nephron. It is well recognized that pressure-natriuresis occurs by decreasing sodium and water reabsorption at several nephron segments possibly related to changes in Starling forces.33 ANF has recently been shown to inhibit sodium reabsorption in the medullary collecting duct, and therefore, a pressure-mediated increase in sodium delivery to this nephron segment would allow for a larger increase in fractional sodium excretion.34 In addition, Mendez et al35 have recently shown that changes in peritubular Starling forces can account for some, but not all, of the increased responsiveness in young SHR. In adult SHR, an attenuated renal response to ANF was observed given that an exaggerated natriuretic response would be expected at the higher renal perfusion pressure and thus providing additional evidence of abnormal function during established hypertension. Because the kidneys of young SHR are clearly capable of responding to the natriuretic and hypertensive effects of circulating ANF, these results are not consistent with a role for ANF in producing renal vasoconstriction and salt and water retention previously observed in this strain of rats during development of hypertension.1,2 On the other hand, the hypersensitivity to ANF in young SHR may represent an attempt at compensation for the factors responsible for elevated arterial pressure.

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References


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**KEY WORDS** • age • kidney • renal perfusion pressure • atrial natriuretic factor • genetic hypertension • diuresis • spontaneously hypertensive rat • Wistar-Kyoto rat
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