Control of glomerular filtration rate by renin–angiotensin system

JOHN E. HALL, ARTHUR C. GUYTON, THOMAS E. JACKSON, THOMAS G. COLEMAN, THOMAS E. LOHMEIER, AND NICK C. TRIPPODO

Department of Physiology and Biophysics, University of Mississippi
School of Medicine, Jackson, Mississippi 39216

HALL, JOHN E., ARTHUR C. GUYTON, THOMAS E. JACKSON, THOMAS G. COLEMAN, THOMAS E. LOHMEIER, AND NICK C. TRIPPODO. Control of glomerular filtration rate by renin–angiotensin system. Am. J. Physiol. 233(5): F366-F372, 1977. -The role of the renin–angiotensin system (RAS) in autoregulating renal blood flow (RBF) and glomerular filtration rate (GFR) during reductions in renal artery pressure (RAP) was examined in the following groups of anesthetized dogs: group I, normal controls, n = 10; group II, normal dogs after intrarenal infusion of angiotensin II antagonist (AIIA), n = 7; group III, sodium-depleted controls, n = 7; group IV, sodium-depleted dogs after intrarenal infusion of AIIA, n = 10. In groups I and III, RBF and GFR did not change significantly between RAP's of 85-127 mmHg, and decreased only 5-14% below control values at an RAP of approx. 70 mmHg. After AIIA in normal dogs (group II), RBF increased above control values when RAP was lowered; GFR remained relatively constant in group II as RAP was reduced to 85 mmHg, but decreased to 71 ± 5% of the control value at 70 mmHg. After AIIA in sodium-depleted dogs (group IV), RBF autoregulation was well maintained, but GFR decreased progressively to 43 ± 6% of the control value when RAP was reduced to 70 mmHg. Although filtration fraction (FF) and calculated efferent arteriolar resistance in groups I and III remained relatively constant when RAP was reduced, in groups II and IV (in which the RAS was nonfunctional because of angiotensin II blockade) FF and efferent arteriolar resistance decreased progressively at all RAP's below control. These observations are consistent with the hypothesis that the RAS plays an important role in controlling GFR through an efferent arteriolar constrictor mechanism, especially during high renin states such as sodium depletion.

sodium depletion; angiotensin II antagonist; renal blood flow; renal autoregulation; efferent arterioles

THE ROLE OF THE RENIN–ANGIOTENSIN system in regulating renal hemodynamics has been extensively studied but is still poorly understood. Several investigators have suggested that angiotensin may participate via an intrarenal feedback system in autoregulating renal blood flow (RBF) and glomerular filtration rate (GFR) during changes in renal artery pressure (8, 24-26). According to one hypothesis, a decrease in renal artery pressure reduces the intrarenal formation of angiotensin II, which in turn decreases afferent arteriolar resistance and helps to return renal blood flow and GFR toward normal (24-26). An apparent contradiction to this hypothesis is the finding that infusion of angiotensin II antagonists or chronic renin depletion does not impair autoregulation of renal blood flow (1, 2, 15, 18). However, recent micropuncture studies in which superficial nephron GFR regulation was studied after infusion of angiotensin II antagonists or converting enzyme inhibitor, or after renin depletion, support the hypothesis that an intact renin–angiotensin system is necessary for normal control of superficial nephron GFR (21, 22).

Recently we reported that chronic renin depletion in dogs, caused by a high sodium diet and injections of deoxycorticosterone acetate (DOCA) for several weeks, dissociated autoregulation of renal blood flow and GFR during reduced renal artery pressure. Although renal blood flow autoregulation was well maintained after renin depletion, GFR, filtration fraction, and efferent arteriolar resistance (calculated by indirect methods) decreased progressively when renal artery pressure (RAP) was reduced (15). In normal dogs, autoregulation of renal blood flow and GFR were closely coupled and filtration fraction as well as efferent arteriolar resistance remained relatively constant during changes in renal perfusion pressure (15). These data are consistent with the hypothesis that the renin–angiotensin system may participate in regulating GFR via an efferent arteriolar constrictor mechanism rather than through changes in afferent arteriolar resistance, as previously assumed (24-26). An increased intrarenal formation of angiotensin II during reductions in renal artery pressure could help maintain efferent arteriolar tone, and, consequently, the effective filtration pressure, despite the activation of vasodilator mechanisms (e.g., myogenic or distal tubular feedback) which would tend to dilate efferent as well as afferent arterioles.

This hypothesis was further investigated in the present study by use of a competitive inhibitor of angiotensin II, since it is possible that some unknown effect of a high salt diet and DOCA loading, which was unrelated to renin depletion, was responsible for the impairment of GFR autoregulation observed in our previous study. Although several other investigators have studied the effects of angiotensin II blockade on renal blood flow autoregulation, in some cases little attention has been paid to the control of GFR (1, 3). In studies in which GFR was measured, the results have been complicated by the use of isolated kidney preparations (18) or...
because the studies were conducted under conditions of marked diuresis (2) instead of in the normal hydropenic state. To our knowledge, there have been no previous attempts to investigate the effects of angiotensin II blockade on GFR autoregulation in animals which are in varying states of sodium balance. Since the activity of the renin–angiotensin system is closely related to the sodium status of the animal, it seems likely that the quantitative importance of angiotensin II in regulating GFR could vary considerably, depending on sodium balance.

In the present study the effects of angiotensin II blockade on the control of GFR, renal blood flow, and urinary electrolyte excretion during changes in renal artery pressure were studied in normal as well as in sodium-depleted dogs.

**METHODS**

Thirty-four male mongrel dogs weighing 17–28 kg were studied in four groups. Dogs in groups I (n, 10) and II (n, 7) were fed a standard kennel ration (Purina high protein dog meal), while those in groups III (n, 7) and IV (n, 10) were maintained for 3 wk on a sodium-deficient diet (h/d dietary animal food, Riviana Foods, Inc.) which provided approx. 5 meq sodium/day. Dogs in groups III and IV were also injected intramuscularly with 20 mg furosemide at the end of the 1st and 2nd wk of sodium depletion.

At the time of the experiment, the dogs were anesthetized with sodium pentobarbital (25–30 mg/kg i.v.), and rectal temperature was maintained constant by warming the table on which the dog rested. The left ureter and spermatic vein were exposed via a retroperitoneal flank incision and cannulated. Urine was directed through a photoelectric drop counter and collected, and renal venous blood samples were obtained through the spermatic vein cannula. Renal blood flow was measured with an electromagnetic flow transducer connected to a square-wave flowmeter (Carolina Medical Electronics). Distal to the flow transducer, a 23-gauge, curved needle was inserted into the renal artery for infusion of angiotensin II antagonist (AIIA) and was maintained patent by infusion of 0.1 ml/min of isotonic saline. To lower the renal artery pressure, an adjustable clamp was placed on the abdominal aorta just above the left renal artery. Renal artery pressure was measured and systemic arterial blood samples were collected from a catheter inserted into a femoral artery and advanced into the abdominal aorta to a level just below the left renal artery. Mean arterial pressure was measured from another femoral catheter advanced into the aorta to a level above the adjustable clamp. Mean arterial pressure, renal artery pressure, renal blood flow, and urine flow were recorded continuously on a Grass polygraph. Glomerular filtration rate was determined from the renal arteriovenous extraction of 125I[iothalamate] (Glofil, Abbott Laboratories). A priming dose of 0.45 μCi/kg of iothalamate was administered, followed by a sustaining intravenous infusion of 0.003 μCi/kg per min in 1.0 ml/min of isotonic saline in groups I and II. In order to maintain sodium depletion in groups III and IV, the sustaining infusion was administered in only 0.2 ml/min of isotonic saline. Glomerular filtration rate was calculated as

\[
GFR = \frac{(1 - Hct) \times RBF \times [(A - V)/A]}{A} 
\]

where Hct is the systemic arterial hematocrit measured by the microcapillary method, while A and V are the systemic arterial and renal venous 125I radioactivities, respectively. Duplicate 1.0-ml arterial and renal venous plasma samples were collected for measurement of A and V for determination of plasma electrolytes and protein concentration. The arteriovenous extraction method for estimating GFR was used because of the oliguria which accompanied reductions in renal artery pressure in the normal hydropenic dogs or the sodium-depleted dogs. In preliminary studies in our laboratory, GFR’s obtained from the arteriovenous extraction of 125I[iothalamate averaged 0.99 ± 0.01 (r = 0.99, n, 22) of inulin clearance. Plasma and urine sodium and potassium concentrations were determined by flame photometry, and the plasma protein concentrations were measured with a refractometer (American Optical). Plasma renin activity was determined by radioimmunoassay of angiotensin I and expressed as nanograms angiotensin I/ml per h (13).

After a 60- to 90-min stabilization period, the renal arterial infusion of isotonic saline was replaced by an infusion of the competitive inhibitor [Sar1, Ile8]angiotensin II (Bachem Inc.) at a rate of 0.25 μg/kg body wt per min in 0.1 ml/min of isotonic saline in groups II (normal sodium intake) and IV (sodium-depleted). After an additional 90 min, during which saline or angiotensin II antagonist was infused into the renal artery, renal artery pressure was reduced in steps to approx. 100, 85, and 70 mmHg, and renal function was permitted to stabilize for 15–20 min after each step reduction in pressure before data were collected. After the last step decrease in renal artery pressure, the clamp was released and post-control data were obtained for 60 min.

In preliminary studies, intrarenal infusion of [Sar1, Ile8]angiotensin II for 90 min completely blocked the renal hemodynamic effects of 10 ng of angiotensin II injected directly into the renal artery in both normal and sodium-depleted dogs.

Control data were compared with experimental data within each group by Dunnett’s (11) paired t test for multiple comparisons. Statistical significance was considered to be P < 0.05. All data in text, tables, and figures are expressed as means ±SE.

**RESULTS**

**Normal Dogs**

**Group I:** controls; **group II:** renal artery infusion of AIIA. Arterial pressure, renal blood flow, GFR, and filtration fraction before reduction of renal artery pressure in groups I (normal, controls) and II (normal, infused with angiotensin II antagonist) are shown in Table 1. There were no substantial differences in renal function between the two groups except for potassium excretion (Fig. 1), which was significantly higher in...
group II, possibly because of the reported agonistic effects of [Sar^1,Ile^8]angiotensin II on the adrenal cortex, causing an increased secretion of aldosterone (5, 6).

The changes in urinary sodium and potassium excretion during reductions in renal artery pressure are shown in Fig. 1. Urinary sodium excretion decreased markedly in both groups as pressure was lowered, while potassium excretion was relatively constant until renal artery pressure was reduced to 70–80 mmHg.

The effects of lowering renal artery pressure on renal hemodynamics are illustrated in Fig. 2. Renal blood flow did not change significantly in group I between renal artery pressures of approx. 85 and 125 mmHg. In dogs infused with AIIA, renal blood flow increased 9–20% above the control level when renal artery pressure was reduced to 100, 85, and 70 mmHg. Glomerular filtration rate was relatively constant in both groups between renal artery pressures of 85 and 125 mmHg. At a renal artery pressure of 70 mmHg, GFR decreased only to 90 ± 4% of the control level in group I, but at this same pressure GFR decreased to 71 ± 5% of the control level in dogs infused with AIIA. Filtration fraction decreased progressively in group II at renal artery pressures of 100 mmHg and below, falling to 63 ± 4% of the control value at a pressure of approximately 70 mmHg. In normal control dogs, filtration fraction either increased slightly or did not change when renal artery pressure was reduced in steps.

**Sodium-Depleted Dogs**

Group III: controls; group IV: renal artery infusion of AIIA. Renal arterial infusion of [Sar^1,Ile^8]angiotensin II caused marked changes in renal function in sodium-depleted dogs. Renal blood flow and GFR were approximately 38 and 20% greater, respectively, in sodium-depleted dogs after infusion of AIIA than in the control sodium-depleted dogs (Table 1). Urinary sodium and potassium excretion, as well as fractional sodium and potassium excretion, were also significantly greater in sodium-depleted dogs infused with AIIA than in control sodium-depleted dogs (Fig. 3). Sodium excretion was more than 4 times as great in group IV as in group III during the control period. When renal artery pressure was lowered, urinary sodium and potassium excretion decreased significantly in both groups, although the absolute changes were much greater in group IV than in group III (Fig. 3).

The effects of intrarenal infusion of AIIA on autoregulation of renal blood flow and GFR in sodium-depleted dogs are illustrated in Fig. 4. Angiotensin II blockade did not substantially alter the renal blood flow response

---

**TABLE 1. Renal function in normal and sodium-depleted control dogs and in normal and sodium-depleted dogs treated with intrarenal infusion of [Sar^1,Ile^8]angiotensin II**

<table>
<thead>
<tr>
<th>Group</th>
<th>Condition</th>
<th>n</th>
<th>Before aortic constriction</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>normal, controls</td>
<td>10</td>
<td>RAP (mmHg)</td>
<td>FF (%)</td>
</tr>
<tr>
<td></td>
<td>124.3</td>
<td>4.76</td>
<td>31.4</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>±3.8</td>
<td>±0.36</td>
<td>±2.0</td>
<td>±0.05</td>
</tr>
<tr>
<td>II</td>
<td>sodium-depleted, controls</td>
<td>7</td>
<td>126.1</td>
<td>4.86</td>
</tr>
<tr>
<td></td>
<td>±3.0</td>
<td>±0.52</td>
<td>±1.1</td>
<td>±0.11</td>
</tr>
<tr>
<td>III</td>
<td>sodium-depleted, AII antagonist</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Before aortic constriction</td>
<td>115.0</td>
<td>5.53</td>
<td>29.2</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>126.4</td>
<td>6.18</td>
<td>32.7</td>
</tr>
<tr>
<td></td>
<td>±2.4</td>
<td>±0.18</td>
<td>±1.3</td>
<td>±0.04</td>
</tr>
<tr>
<td>IV</td>
<td>sodium-depleted, AII antagonist</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Before aortic constriction</td>
<td>115.0</td>
<td>6.18</td>
<td>29.2</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>126.4</td>
<td>6.18</td>
<td>32.7</td>
</tr>
<tr>
<td></td>
<td>±2.4</td>
<td>±0.18</td>
<td>±1.3</td>
<td>±0.04</td>
</tr>
</tbody>
</table>

**Notes:** Values represent means ± SE obtained during a control period before reduction of renal artery pressure by aortic constriction and a recovery period 60 min after reductions in renal artery pressure. Abbreviations: RAP, renal artery pressure; RBF, renal blood flow; FF, filtration fraction; GFR, glomerular filtration rate; PCOP, plasma colloid osmotic pressure; PRA, plasma renin activity.

---

**FIG. 1. Effect of reducing renal artery pressure (RAP) on urinary sodium (U_\text{Na}, \mu\text{eq/min per g kidney wt}) and potassium (U_\text{K}, \mu\text{eq/min per g kidney wt}) excretion in dogs fed a normal sodium diet. Solid lines represent responses of control dogs (n, 10) and dashed lines represent responses of dogs which received intrarenal infusion of angiotensin II antagonist (n, 7). Values represent means ± SE.**
to reductions in renal artery pressure: blood flow decreased only about 3 and 10%, respectively, in groups III and IV, as renal artery pressure was decreased from control values of 115–127 mmHg to approx. 70 mmHg. Glomerular filtration rate was also regulated effectively in control sodium-depleted dogs, remaining relatively constant as renal artery pressure was reduced to 100 and 85 mmHg, and decreasing only to 86 ± 4% of the control value at a pressure of approx. 70 mmHg. However, in sodium-depleted dogs infused with AIIA, GFR decreased progressively when renal artery pressure was reduced below control levels. At a pressure of 69 mmHg, GFR averaged only 43 ± 6% of the control value. Filtration fraction in group IV also decreased markedly as renal artery pressure was reduced to 100 mmHg and below, averaging only 48 ± 6% of the control value at a pressure of 69 mmHg. In contrast, filtration fraction in the control sodium-depleted dogs was relatively constant within the range of renal perfusion pressures studied.

DISCUSSION

In the present study, the role of the renin–angiotensin system in controlling renal blood flow, GFR, and electrolyte excretion was examined in normal and sodium-depleted dogs. Renal arterial infusion of the competitive inhibitor [Sar1,11e8]angiotensin II (0.25 μg/kg per min) for 90 min in normal dogs did not substantially alter renal function, although marked agonistic effects (i.e., reduced renal blood flow and urine flow) of AIIA were observed immediately after the infusion was begun. However, in sodium-depleted dogs antagonist infusion caused large increases in renal blood flow and urine flow, as well as sodium and potassium excretion, small increases in GFR, and small decreases in filtration fraction and mean arterial pressure. In previous studies in our laboratories, intrarenal infusion of angiotensin II antagonists also caused significant increases in renal blood flow and GFR and a marked natriuresis and diuresis in sodium-depleted and dehydrated dogs (16, 19, 23). These findings support the hypothesis that during high renin states such as sodium depletion the renin–angiotensin system may play an important intrarenal role in regulating electrolyte excretion. This is probably due, at least in part, to angiotensin’s effects on renal hemodynamics. However, these studies do not
rule out the possibility that angiotensin II may also directly enhance renal tubular reabsorption of electrolytes during sodium depletion.

Angiotensin II also appears to participate in the regulation of GFR when renal artery pressure is reduced. In control sodium-depleted and normal dogs which were not infused with AIIA, regulation of renal blood flow and GFR were closely coupled between renal perfusion pressure and GFR. When these indirect methods were used to calculate renal segmental vascular resistances in the present study, the distributions of blood flow and glomerular filtration in the kidney were assumed to be relatively constant. Although we did not measure renal blood flow distribution, other investigators have reported that intrarenal infusion of competitive inhibitors of angiotensin II did not alter renal blood flow distribution at normal or reduced renal artery pressures (1, 18). In addition, estimates of superficial nephron filtration fraction suggest that it is only slightly lower than the whole kidney filtration fraction even though outer cortical nephrons are believed to have lower filtration fractions than inner cortical nephrons (10). Because of these considerations it seems unlikely that changes in blood flow distribution could have played a major role in causing the marked dissociation of renal blood flow and GFR observed in angiotensin II-alone dogs during reductions in renal artery pressure.

The changes in renal segmental vascular resistances calculated by these two indirect methods are shown in Figs. 5 and 6. In normal as well as in sodium-depleted dogs calculated afferent arteriolar resistances decreased markedly when renal artery pressure was reduced, and this response was not substantially altered by AIIA. These studies provide no evidence, therefore, that the renin–angiotensin system participates directly in causing vasodilation of afferent arterioles and autoregulation of renal blood flow during reductions in arterial pressure, as proposed by Thurau and his colleagues (24-26). In the present study, in normal dogs infused with AIIA, renal blood flow actually increased above control levels as renal artery pressure was reduced to 100, 85, and 70 mmHg, probably because of a normal dilation of afferent arterioles combined with excessive dilation of efferent arterioles. Several other investigators have also reported that renal blood flow autoregulation is well maintained in normal dogs after AIIA (1-3, 18).

The primary effect of AIIA in both groups was to alter the efferent arteriolar response to pressure reductions. In both normal and sodium-depleted dogs not infused with AIIA, efferent arteriolar resistance either increased slightly or remained relatively constant when renal perfusion pressure was reduced. After angiotensin calculated from the systemic arterial oncotic pressure and the filtration fraction, and $P_e$ is the proximal tubular hydrostatic pressure calculated by assuming the linear relationship between GFR and $P_e$ proposed by Huss et al. (17). Peritubular capillary hydrostatic pressure ($P_s$) was assumed to bear a constant relationship to $P_e$, as suggested by several investigators (12, 17). With the second method, nonequilibrium of filtration pressure was assumed and $P_s$ as calculated as $P_s = (GFR/K) + \pi_a + P_e$, where $\pi_a$ is the average glomerular capillary oncotic pressure calculated as $(\pi_a + \pi_e)/2$, $\pi_a$ is the systemic arterial oncotic pressure, and $K$ is the glomerular capillary filtration coefficient, which has been reported to remain constant during reductions in renal artery pressure (4, 20). Afferent (AR) and efferent (ER) arteriolar resistances were calculated as $AR = (RAP - P_e)/RBF$, and $ER = (P_s - P_e)/(RBF - GFR)$. When these indirect methods were used to calculate renal segmental vascular resistances in the present study, the distributions of blood flow and glomerular filtration in the kidney were assumed to be relatively constant. Although we did not measure renal blood flow distribution, other investigators have reported that intrarenal infusion of competitive inhibitors of angiotensin II did not alter renal blood flow distribution at normal or reduced renal artery pressures (1, 18). In addition, estimates of superficial nephron filtration fraction suggest that it is only slightly lower than the whole kidney filtration fraction even though outer cortical nephrons are believed to have lower filtration fractions than inner cortical nephrons (10). Because of these considerations it seems unlikely that changes in blood flow distribution could have played a major role in causing the marked dissociation of renal blood flow and GFR observed in angiotensin II-alone dogs during reductions in renal artery pressure.

The changes in renal segmental vascular resistances calculated by these two indirect methods are shown in Figs. 5 and 6. In normal as well as in sodium-depleted dogs calculated afferent arteriolar resistances decreased markedly when renal artery pressure was reduced, and this response was not substantially altered by AIIA. These studies provide no evidence, therefore, that the renin–angiotensin system participates directly in causing vasodilation of afferent arterioles and autoregulation of renal blood flow during reductions in arterial pressure, as proposed by Thurau and his colleagues (24-26). In the present study, in normal dogs infused with AIIA, renal blood flow actually increased above control levels as renal artery pressure was reduced to 100, 85, and 70 mmHg, probably because of a normal dilation of afferent arterioles combined with excessive dilation of efferent arterioles. Several other investigators have also reported that renal blood flow autoregulation is well maintained in normal dogs after AIIA (1-3, 18).

The primary effect of AIIA in both groups was to alter the efferent arteriolar response to pressure reductions. In both normal and sodium-depleted dogs not infused with AIIA, efferent arteriolar resistance either increased slightly or remained relatively constant when renal perfusion pressure was reduced. After angiotensin

FIG. 4. Effect of reducing renal artery pressure (RAP) on renal blood flow (RBF), glomerular filtration rate (GFR), and filtration fraction (FF), expressed as percentage of control values, in sodium-depleted dogs. Solid lines represent responses of control sodium-depleted dogs (n = 7) and dashed lines represent responses of sodium-depleted dogs which received intrarenal infusion of angiotensin II antagonist (n = 10). Values represent means ± SE.
II blockade, efferent arteriolar resistance (calculated using either method) decreased progressively during reductions in renal artery pressure in normal as well as in sodium-depleted dogs. Similar changes in calculated efferent arteriolar resistance were noted in a previous study with renin-depleted dogs (15). These findings provide further support for the hypothesis that an intact renin–angiotensin system is essential for maintaining efferent arteriolar tone when renal artery pressure is reduced. Apparently a decrease in renal artery pressure activates a vasodilator mechanism, possibly by reducing flow rate or electrolyte delivery to the distal tubule (21, 22). The vasodilator mechanism tends to decrease efferent as well as afferent arteriolar resistance. When the renin–angiotensin system is intact, the tendency toward vasodilation of efferent arterioles is counteracted by the vasoconstrictor effect of angiotensin II, and efferent resistance is either increased slightly or maintained at normal levels. The maintenance of efferent arteriolar resistance along with efferent arteriolar vasodilation (which was not substantially modified by AIIA in the present study) allows GFR to be effectively regulated during reductions in arterial pressure. With a nonfunctional renin–angiotensin system, vasodilation of efferent as well as afferent arterioles occurs when renal artery pressure is lowered and the dilation of efferent arterioles hinders autoregulation of GFR.

The quantitative importance of efferent versus afferent arteriolar resistance changes in controlling GFR seems to vary considerably depending on sodium balance and the existing state of the renin–angiotensin system. In dogs maintained on a normal sodium intake, autoregulation of GFR is only slightly impaired by angiotensin II blockade even though marked decreases in efferent arteriolar resistance occur when pressure is lowered. Apparently the fall in efferent arteriolar resistance is compensated for by an increase in renal blood flow above control levels, and GFR is regulated effectively over most of the normal autoregulatory pressure range. However, in sodium-depleted dogs, the
vasoconstrictor effect of angiotensin II on efferent arterioles is much more important in maintaining GFR during reductions in renal artery pressure. After intrarenal infusion of AIIA, GFR, filtration fraction, and calculated efferent arteriolar resistance decreased progressively as renal artery pressure was reduced to 100 mmHg and below in sodium-depleted dogs. At a renal artery pressure of approx. 70 mmHg, GFR and filtration fraction were only about 43 and 48%, respectively, of the control levels even though renal blood flow was reduced by less than 10%.

In summary, the results from the present study provide support for the hypothesis that autoregulation of GFR results from a complex composite of afferent and efferent arteriolar resistance changes and that the renin–angiotensin system participates in controlling GFR via an efferent arteriolar constrictor mechanism rather than through changes in afferent arteriolar tone as other investigators have suggested (24-26).

This work was supported by National Institutes of Health Grant HL-11678, and a grant from the Mississippi Heart Association. J. E. Hall is a National Institutes of Health Postdoctoral Fellow (F32 HL-06060).

REFERENCES