Effects of Subpressor Doses of Angiotensin II on Renal Hemodynamics in Relation to Blood Pressure

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SUMMARY The renal hemodynamic response to subpressor doses of angiotensin II (AII; 0.1 and 0.5 ng/min/kg) was investigated in untreated 49-year-old men (n = 50) representing a wide blood pressure range. Renal blood flow, renal vascular resistance (RVR), glomerular filtration rate (GFR), filtration fraction (FF), plasma renin activity (PRA), plasma AII, plasma aldosterone, and the urinary excretion of sodium and norepinephrine were studied. The higher the initial blood pressure the greater was the increase in RVR in response to AII infusion (p < 0.002), indicating an increased renal vascular reactivity with increase in initial blood pressure. The AII infusion gave a significant rise in RVR in both the borderline and hypertensive group, but gave no increase in RVR in the normotensive group, implying an enhanced sensitivity of the renal vasculature in the borderline and hypertensive group. The increase in RVR was greater in the hypertensive than in the borderline group, i.e., the hypertensives had a steeper dose-response curve than the borderline group, which points to the presence of structural vascular changes in the renal vessels in the hypertensives. The increase in RVR in response to AII was positively correlated to sodium intake and plasma aldosterone concentration, indicating that these two factors might modulate the renal vascular reactivity. These factors could, however, only partly explain that RVR increased more the higher the initial blood pressure.

Thus, the results indicate that there is an increased reactivity of the renal vascular bed to AII in essential hypertension. The increased reactivity seems to be mediated through an increased sensitivity of the renal vasculature to AII in mild essential hypertension and also through the presence of structural vascular changes in established hypertension. These factors may lead to a reduced excretion of sodium and water and may therefore be of importance in the development and progression of essential hypertension. (Hypertension 5: 368-374, 1983)

KEY WORDS essential hypertension • renal blood flow • renal vascular resistance • angiotensin II • vascular reactivity • epidemiology

DURING the development of essential hypertension renal blood flow declines and renal vascular resistance increases, while the glomerular filtration rate remains normal in mild to moderate essential hypertension.1-4

Two principal pathophysiological mechanisms have been discussed, namely, increased myogenic tone in the renal resistance vessels and structural renal vascular changes in response to the blood pressure increase. Increased myogenic tone might be due either to an increased vasoconstrictor activity in the renal vascular bed or to an increased sensitivity (lowered threshold dose needed) to vasoconstrictor stimuli such as AII, sympathetic nervous activity, or circulating catecholamines. Structural vascular changes increasing the wall/lumen ratio will lead to an increased steepness of the dose-response curve.5-6

Both these mechanisms, increased myogenic tone and structural vascular changes, would give rise to an enhanced vascular reactivity to vasoconstrictor stimuli. These factors have been ascribed a decisive role in the salt and water excretion by the kidney in hypertension.2-7

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The aim of this study was to determine whether signs of an increased reactivity of the renal vascular bed to All could be demonstrated in borderline and essential hypertension and, if so, at what blood pressure levels it was detectable. For this purpose, subpressor doses of All were infused in randomly selected men of the same age representing a wide blood pressure range.

Methods

Subjects Studied

A detailed presentation of the study population and the selection procedure has previously been given. In brief, 60% of the two age groups of 49-year-old men living in Göteborg were invited to a blood pressure screening in 1975 and 1976. Of the 3205 subjects invited, 2375 (74%) attended. Based on diastolic blood pressure (DBP), 120 subjects representing the entire blood pressure range were randomly selected. Higher proportions of subjects in the upper than in the lower part of the blood pressure range were included in order to increase the validity of the description of variables in the borderline and definitely hypertensive part of the blood pressure distribution. Of those fulfilling the selection criteria, subjects on antihypertensive treatment were excluded since we wished to study only untreated subjects. Of the 93 subjects who were given All infusion, 19 were excluded because of increase of blood pressure (see below) and another 24 were excluded due to voiding difficulties. The results from the remaining 50 subjects are reported.

Study Protocol

The study was carried out within 1 month of screening. The subjects were on unrestricted diets and remained outpatients during the study. After a 3-day urine collection for determination of urinary sodium and norepinephrine, renal function and hormonal variables were studied. A diagnostic examination for exclusion of secondary hypertension, including repeated blood pressure measurements then followed at the outpatient Hypertension Clinic, as previously described.

The protocol was approved by the Ethical Committee of the University of Göteborg, and the participants’ informed consent was obtained before the start of the study.

Blood Pressure

The DBP was recorded when the Korotkoff sounds disappeared (phase 5). Mean arterial pressure (MAP) was calculated as DBP plus one-third of the pulse pressure. In situations when several blood pressures were recorded, the arithmetic mean was used. At screening, blood pressure was measured in the supine position after a few minutes’ rest. During the clearance procedure blood pressure was measured to the nearest 1 mm Hg using an automatic device for cuff inflation and deflation with simultaneous registration of cuff pressure, Korotkoff sounds, and ECG. Blood pressure was registered twice every 10 minutes during the 40-minute clearance periods and twice every 15 minutes during the 30-minute periods. The variation in MAP during the three basal clearance periods was 0.7 ± 3.8 mm Hg (mean ± SD) in the whole group. This variation in MAP was of the same order in the normotensive, borderline, and hypertensive group and was regarded as a measure of the normal blood pressure variation. The upper normal limit for increase in MAP was thus 8.3 mm Hg (mean plus 2 SD) in the whole group. We therefore considered the dose of All to be subpressor if it did not increase MAP by more than 8 mm Hg. Subjects who had an increase in MAP of more than 8 mm Hg during All infusion were excluded from the analyses.

Blood pressure at the Hypertension Clinic was measured on three different occasions within one month of the clearance measurements. Blood pressure was measured supine after 5 minutes’ rest, using the same method as at screening.

Clearance

Glomerular filtration rate (GFR) was measured as inulin clearance (CIn) and renal plasma flow as p-aminohippurate clearance (CpAH) using the continuous infusion technique. Details of methods and analyses have been given previously. After an equilibration period of 45 minutes, three basal 40-minute clearance periods were performed, followed by two 30-minute clearance periods during which All was given (angiotensin periods). The subjects were hydrated with 10 ml of water per kg body weight before clearance measurements, and water was then given to compensate for diuresis. In addition, 200 ml of water was given after the third clearance period. Urine was collected without catheterization.

A constant intravenous infusion of All (Hypertensin, Ciba) dissolved in 0.9% saline (50 ng/ml) was given during the angiotensin periods, 0.1 and 0.5 ng/min/kg, respectively, by means of a calibrated motor-driven syringe. A plastic cannula had been inserted into a cubital vein in each arm. The infusions were given in the left arm and blood samples were taken from the right arm in the middle of each clearance period. The values of CIn and CpAH were corrected to 1.73 m² body surface area. Filtration fraction (FF) was calculated as the CIn/CpAH ratio (%). Hematocrit was measured using a hematocrit centrifuge. Renal blood flow was calculated as CpAH/1 – hematocrit. Renal vascular resistance was calculated as MAP at clearance/RBF (mm Hg·min/liter). The individual change in RVR during All infusion was estimated using the linear regression coefficient as a measure of the slope of the regression line for the relationship between RVR and the All dose as illustrated in figure 1.

Renin-Angiotensin-Aldosterone

Venous blood for analysis of plasma renin activity (PRA), plasma All, plasma aldosterone, sodium, and potassium concentration was sampled during the second clearance period at 10 a.m., when the subjects had been resting semirecumbent for 2 hours.
I

\[ y = \beta x + \alpha \]

\[ \begin{align*}
\text{Renal vascular resistance (mm Hg \cdot \text{min}^{-1} \cdot \text{kg}^{-1})} \\
\text{Dose of angiotensin II (ng \cdot \text{min}^{-1} \cdot \text{kg}^{-1})}
\end{align*} \]

**Figure 1.** Response of renal vascular resistance (RVR) to All infusion was calculated by linear regression using the three observations obtained initially and during infusion of the two doses of All (0, 0.1, and 0.5 ng/min/kg). Increase in the regression coefficient (beta) indicates increase in the RVR response to All.

PRA, plasma All, and plasma aldosterone were determined by radioimmunoassay as previously described.\(^1\) All was measured in only 27 subjects.

**Urinary Excretion of Sodium and Norepinephrine**

Urine was collected during the 3 days preceding the clearance procedure and the mean value was used.\(^5\) Sodium and potassium in plasma were determined by flame photometry. Urinary norepinephrine excretion was determined in urine collected during the 24-hour period preceding the clearance measurements. Urine was acidified and free norepinephrine was analysed using a modification of the method described by von Euler and Lishajko.\(^11\)

**Characteristics of the Study Group**

None of the subjects had a history of, or showed signs of, myocardial infarction, angina pectoris, cardiac decompensation, intermittent claudication or stroke. All fundoscopic changes were of Grade I or II according to the Keith-Wagener classification. None of the subjects in the study group had secondary hypertension and all had normal serum creatinine and serum electrolytes.

Three groups were defined, to permit comparisons with more clinically oriented studies. The subjects having a DBP of < 95 mm Hg at screening and a DBP of \(\leq 90\) mm Hg (mean of three recordings) at the Hypertension Clinic constituted the normotensive group \((n = 7)\), and the remaining subjects were allocated to the borderline group \((n = 33)\). Blood pressure and heart rate in different situations are given in Table 1 and background data of hormones and electrolytes in the three groups are given in Table 2.

**Statistical Methods**

Standard methods were used for calculation of means, standard deviations (sd), standard error of the mean (sem), and for linear and multiple regression analysis. The response of a variable to All infusion was estimated for each subject using linear regression analysis for the relationship between the doses of All \((0, 0.1\) and 0.5 ng/min/kg) and the corresponding three

**Table 1.** Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and Heart Rate (HR) in Different Situations in the Three Groups (Mean ± SD)

<table>
<thead>
<tr>
<th>Situation</th>
<th>Normotensive group ((n = 7))</th>
<th>Borderline group ((n = 33))</th>
<th>Hypertensive group ((n = 10))</th>
</tr>
</thead>
<tbody>
<tr>
<td>At screening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>124 ± 9</td>
<td>159 ± 12</td>
<td>184 ± 13</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>84 ± 9</td>
<td>111 ± 9</td>
<td>124 ± 10</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>96 ± 8</td>
<td>127 ± 9</td>
<td>144 ± 10</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>83 ± 14</td>
<td>81 ± 12</td>
<td>88 ± 9</td>
</tr>
<tr>
<td>At the Hypertension Clinic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>122 ± 5</td>
<td>145 ± 12</td>
<td>172 ± 12</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>74 ± 6</td>
<td>92 ± 7</td>
<td>112 ± 7</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>90 ± 5</td>
<td>110 ± 8</td>
<td>132 ± 6</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>73 ± 11</td>
<td>71 ± 8</td>
<td>77 ± 9</td>
</tr>
<tr>
<td>During basal clearance</td>
<td></td>
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<td></td>
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<tr>
<td>periods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>109 ± 11</td>
<td>131 ± 13</td>
<td>155 ± 16</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>68 ± 6</td>
<td>84 ± 9</td>
<td>98 ± 13</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>82 ± 6</td>
<td>100 ± 10</td>
<td>117 ± 13</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>67 ± 7</td>
<td>69 ± 10</td>
<td>76 ± 12</td>
</tr>
<tr>
<td>During infusion of All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1 ng/min/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>110 ± 13</td>
<td>132 ± 15</td>
<td>155 ± 18</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>67 ± 6</td>
<td>85 ± 10</td>
<td>99 ± 15</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>81 ± 8</td>
<td>101 ± 10</td>
<td>118 ± 15</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>64 ± 7</td>
<td>65 ± 10</td>
<td>72 ± 12</td>
</tr>
<tr>
<td>During infusion of All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 ng/min/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>113 ± 11</td>
<td>135 ± 14</td>
<td>163 ± 18</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>69 ± 6</td>
<td>86 ± 10</td>
<td>101 ± 12</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>83 ± 7</td>
<td>102 ± 10</td>
<td>122 ± 13</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>63 ± 8</td>
<td>64 ± 10</td>
<td>70 ± 10</td>
</tr>
</tbody>
</table>

having a DBP of \(< 95\) mm Hg at screening and a DBP of \(\leq 90\) mm Hg (mean of three recordings) at the Hypertension Clinic were assigned to the hypertensive group \((n = 10)\). Subjects
observations for the studied variable. The regression coefficient was used as a measure of the slope of the regression line. This is illustrated for RVR in figure 1. The response of MAP, Cln, CPAH and FF to All was calculated in the same way. When calculating the regression coefficients the log dose should ideally be used. This was, however, not possible in this study since the first of the three doses was zero. Since the observations were linearly oriented as in the example in figure 1 in almost all of the subjects it seems justified to use an arithmetic dose scale.

Since there was an enrichment of subjects in the higher blood-pressure range, the blood-pressure frequency distribution was skewed to the right. In correlation analyses of blood pressure versus other variables a non-parametric test has therefore been used and the correlation coefficients are given as Spearman’s coefficients of rank correlation (R). In correlation analyses between other variables, which were about normally distributed, the correlation coefficient of Pearson (r) was used. The hypothesis of no difference in means between two groups was tested using Student’s t test. The hypothesis of no difference in means between other variables, which were about normally distributed, the correlation coefficient of Pearson (r) was used. Values of p < 0.05 were regarded as statistically significant.

### Results

#### Blood Pressure

As demonstrated in table 1, blood pressure and heart rate were considerably lower during basal clearance periods than at screening and at the Hypertension Clinic. At the lowest dose level of All, MAP did not change more than 1 mm Hg in any of the three groups. At the highest dose level, MAP tended to increase slightly in all three groups. There was no significant correlation between initial MAP and the response of MAP to All, measured as the regression coefficient, in the whole study group (R = 0.008), i.e., MAP did not increase more in response to All infusion in subjects with high initial MAP than in subjects with low initial MAP.

#### Renal Hemodynamics and Renal Function

The response of CPAH and renal blood flow to All, measured as the regression coefficient, was negatively correlated to initial MAP (R = −0.30; p < 0.05) and R = −0.30; p < 0.05, respectively. Thus, the higher the initial blood pressure the greater was the decline in CPAH and RBF during All infusion.

The response of RVR to All was positively correlated to initial MAP (R = 0.48; p < 0.002), i.e., the higher the initial blood pressure the greater was the increase in RVR. The individual responses of RVR to All in relation to initial MAP are plotted in figure 2.
The mean RVR values during basal clearance periods and at the two dose levels of All for the normotensive, borderline, and hypertensive groups are shown in figure 3 and table 3.

The lowest All dose increased the mean RVR by 6.2%, 6.7%, and 8.2%, respectively, in the normotensive, borderline, and hypertensive groups. This RVR increase was significant in the borderline group (n = 33) but not in the normotensive and hypertensive groups, which were considerably smaller (n = 7 and 10, respectively). At the highest All dose, the mean RVR increased from the initial value by 3.4% in the normotensive group, 13.9% in the borderline group, and 25.3% in the hypertensive group. This increase in RVR was significant in the hypertensive and borderline groups but not in the normotensive group, indicating a higher sensitivity to All in the two former groups than in the latter.

Figure 4 shows the percentage increase in RVR at the two dose levels of All in relation to log dose All in the three groups. The percentage increase in RVR from the initial value was significantly greater in the hypertensive than in the borderline group at the highest dose level of All, indicating a steeper slope of the dose-response curve in the hypertensives. The question whether the slope of the dose-response curve in the borderline group was steeper than that in the normotensive group could not be determined in this study since RVR did not change in the normotensive group and no dose-response curve could therefore be constructed in this group.

![Graph showing response of renal vascular resistance to All infusion](image)

**Figure 2.** Response of renal vascular resistance to All infusion (i.e., beta RVR; see text to figure 1) in relation to initial mean arterial pressure in all the subjects studied.

![Graph showing means ± SEM for renal vascular resistance (RVR) in the three groups, initially and during infusion of All, 0.1 and 0.5 ng/min/kg, respectively. The RVR during All infusions is compared with the basal RVR within each group. **p < 0.01).](image)

**Figure 3.** Means ± SEM for renal vascular resistance (RVR) in the three groups, initially and during infusion of All, 0.1 and 0.5 ng/min/kg, respectively. The RVR during All infusions is compared with the basal RVR within each group. **p < 0.01).

![Graph showing change in renal vascular resistance from basal value in relation to the logarithm of the All dose given in the three groups. **p < 0.01](image)

**Figure 4.** Means ± SEM for the percentage increase in renal vascular resistance from the initial value, in relation to the logarithm of the All dose given in the three groups. **p < 0.01.)
The response of C\textsubscript{r} and FF to All, measured as the regression coefficients, did not change significantly with increase in initial MAP (R = -0.21 and 0.13, respectively). C\textsubscript{r} decreased in all three groups and FF rose slightly in the borderline and hypertensive groups, but these changes were not significant (table 3).

**Interrelation Between the RVR Response to All Infusion and Sodium Excretion, Sympathetic Nervous Activity, and Renin-Angiotensin-Aldosterone**

The response of RVR to the All infusions, measured as the regression coefficient, was positively correlated to the 24-hour urinary sodium excretion (r = 0.26; p < 0.05) and plasma aldosterone (r = 0.26; p < 0.05) but was not correlated to the 24-hour norepinephrine excretion, heart rates during basal clearance periods, initial PRA, or initial plasma All concentration.

To elucidate the relative influence of sodium intake and plasma aldosterone on the RVR response to All-infusion, a multiple regression analysis was performed. When sodium intake or plasma aldosterone, or both of these variables, were taken into account, the response of RVR to All was still positively correlated to initial MAP (p < 0.006).

**Discussion**

The effect of subpressor doses of All on renal hemodynamics and renal function was studied in a population sample of untreated 49-year-old men, who represented a wide blood-pressure range. The results are therefore, not influenced by variations due to age, sex, or antihypertensive treatment, factors known to influence the studied variables.\textsuperscript{12-14}

In most earlier investigations of the renal response to All, pressor doses have been used, which makes it difficult to separate renal vascular changes induced by All from those induced by autoregulation in response to increase in the systemic blood pressure. In this study, All was given in lower doses (0.1 and 0.5 ng/min/kg) than those reported to be subpressor in earlier studies of normal subjects. Intravenous All doses of less than 2 ng/min/kg are reported to give no or minimal blood pressure increase in humans.\textsuperscript{15} Nevertheless, a tendency toward an increase in MAP and a fall in heart rate on the higher of the two All doses was observed, but these changes were within the normal variation during the basal clearance periods.

There were no significant changes in GFR or FF during All infusion, indicating that All in this low dosage did not affect the resistance of the efferent arteriole significantly more than the resistance of the afferent arteriole. An increase of FF has often been reported in studies using higher All doses.\textsuperscript{17, 18}

The main finding of this study was that the higher the initial blood pressure the greater the increase in RVR in response to All infusion, i.e., the greater was the reactivity to All infusion. All induced a significant rise in RVR in both the borderline and hypertensive group but not in the normotensive group, indicating that the threshold All dose for renal vascular response

was not reached in the normotensive group. The sensitivity of the renal vessels to All therefore appeared to be enhanced in the borderline and hypertensive groups.

The sensitivity of the renal vascular bed to All can be modified by several factors. Thus, sodium loading potentiates and sodium depletion decreases the vasoconstrictor response in both normal and hypertensive man.\textsuperscript{15, 16, 19} An increased vascular response to All infusion has been found in other situations with low plasma levels of All, as in primary aldosteronism, "low renin hypertension," and following inhibition of converting enzyme.\textsuperscript{19-22} This has been attributed to a diminished prior occupancy of vascular All receptor sites,\textsuperscript{23} an increase in receptor number,\textsuperscript{24} or increased receptor affinity.\textsuperscript{20}

In this study the response of RVR to All infusion was positively correlated both to the sodium intake (measured as the sodium excretion) and to the plasma aldosterone concentration but was not significantly correlated to the initial PRA or initial plasma All concentration. In the latter case, however, data were available for only 27 of the studied subjects, which reduced the possibility of detecting a correlation. A multiple regression analysis showed that sodium intake and plasma aldosterone could only partly explain that RVR rose more during All infusion the higher the initial blood pressure. Since central and peripheral adrenergic facilitation by All has been demonstrated,\textsuperscript{25} it is possible that the initial sympathetic nervous activity was of importance for the renal response to All. Emotional stress may also induce a significant increase in RVR.\textsuperscript{26} In this study the response of RVR to All was not correlated to indices of sympathetic activity, like initial heart rate or the 24-hour urinary excretion of norepinephrine.

In addition to increased sensitivity of the renal vasculature to All, which will shift the dose-response curve to the left in a parallel manner, increased renal vascular reactivity to All may result from structural vascular changes in the form of an increased bulk of contractile tissue in the vessel wall.\textsuperscript{27, 28} The latter changes will increase the wall/lumen ratio and thereby increase the steepness of the dose-response curve in response to a vasoconstrictor.\textsuperscript{27, 28} In this study, using only subpressor doses of All, it was not possible to get a complete dose-response curve for the effect of All on RVR, but the first important part of the dose-response curve could be defined in the borderline and hypertensive group (fig. 4). The finding that the hypertensive group had a steeper slope of the dose-response curve than the borderline group points to the presence of structural renal vascular changes in the hypertensives. The question whether structural vascular changes were present also in the borderline group could not be answered in this study (see Results).

Folkow et al.\textsuperscript{6, 27} and Göthberg et al.\textsuperscript{28} have made extensive studies of the renal vascular bed in spontaneously hypertensive rats and have shown that structural changes are present early in the development of hypertension. Folkow's group has found that spontaneously
Hypertensive rats showed an exaggerated increase in RVR in response to graded doses of norepinephrine, i.e., a steeper dose response curve, than normotensive control rats, although the sensitivity to threshold doses of norepinephrine was the same in the two types of rats. This response could be completely due to an increased wall/lumen ratio in the renal resistance vessels of the spontaneously hypertensive rats.

Earlier studies on the renal vascular response to supressor doses of All in man have all been performed in normal subjects as far as we are aware, except for a study reported in a review by Hollenberg and Adams, in which potential kidney donors with normotension or essential hypertension were given infusions of All into the renal artery in connection with renal arteriography. Although no details were presented, it was claimed that the hypertensive subjects required a lower dose of All to elicit a renal vascular response and had a steeper slope of the dose-response curve than the normal subjects. That study, like ours, may thus indicate that the increased vascular reponsiveness to All in essential hypertension depends on both increased sensitivity to All and structural vascular changes.

The infussion of All into the renal artery in the study presented by Hollenberg and Adams is likely to have raised the intrarenal All concentration well above the physiological level. The intravenous All infussion in our study should have raised the plasma All concentration by about 5 pg/ml, which means that the plasma concentration should have remained within or near the normal range for the subjects studied (2–30 pg/ml). The results might therefore indicate that All in physiological doses can induce significant changes in RVR in hypertension.

In conclusion, the present study has demonstrated that the RVR increase in response to supressor doses of All is greater the higher the initial blood pressure. The increased reactivity of the renal vascular bed to All in essential hypertension seems to be mediated through an increased sensitivity of the renal vasculature to All in mild essential hypertension and also through the presence of structural renal vascular changes in established hypertension. Increased renal vascular resistance may lead to reduced renal excretion of sodium and water and may therefore be of importance in the development and progression of essential hypertension.

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