Failure of Renin Suppression by Angiotensin II in Hypertension

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SUMMARY Angiotensin II was infused at rates varying from 0.1 to 10 ng/kg per minute into 49 subjects with hypertension and 26 normotensive subjects and changes in blood pressure, plasma angiotensin II, and plasma renin activity (PRA) were determined after 20 and 30 minutes at each dose. Similar dose-related increases in angiotensin II and blood pressure occurred with a threshold of 1 ng/kg per minute in the normotensive and hypertensive subjects. Whereas angiotensin II induced a significant, dose-related decrement in renin activity in the normotensive subjects, with a threshold of 1.0 ng/kg per minute, no significant change in renin activity occurred in either the normal-renin or high-renin hypertensive subjects. In a separate study, nine normotensive and six hypertensive sodium-restricted subjects were given a converting enzyme inhibitor, SQ 20881, 30 μg/kg. Despite a significantly greater fall in blood pressure (P < 0.006) and angiotensin II concentration (P < 0.045) in the hypertensive subjects, they did not have a greater rise in plasma renin activity. We conclude that angiotensin II reduces renin release in normal man at infusion rates that yield plasma angiotensin II levels within the physiological range but has a strikingly reduced influence on renin release in hypertension. In high-renin hypertension due to renal artery stenosis or nephrosclerosis, renin release is presumed to be relatively autonomous because of a dominant, intrarenal mechanism. The mechanism in normal-renin essential hypertension is not clear, but the abnormality could well be related to the pathogenesis of the hypertension.

RENNIN RELEASE is influenced by extracellular volume and sodium, sympathetic nervous system activity and catecholamines, potassium and angiotensin II concentrations.1 A number of reports have documented that angiotensin II inhibits renin secretion.6-7 Since inhibition was independent of changes in blood pressure, it has been suggested that angiotensin directly affects renin release via a short feedback loop. However, pharmacological concentrations of angiotensin II, i.e., infusion rates greater than 3 ng/kg per minute, usually were either used or required to suppress renin secretion.

The control of renin release is significantly altered in subjects with hypertension. The most common example is the subnormal rise in plasma renin activity in response to volume depletion in the 20–40% of hypertensive subjects with low-renin essential hypertension. Acute suppression of renin has been evaluated less extensively but, in many patients with normal-renin hypertension, renin activity is less responsive to the suppressive effect of sodium.6,8 The purpose of the present study was to define whether angiotensin II within the physiological range alters renin release in normal man and to compare its efficacy in subjects with hypertension.

Methods

Sixty-eight subjects with hypertension and 58 normotensive control subjects were studied in the Clinical Research Center of the Peter Bent Brigham Hospital. The age range for the hypertensive subjects was 19–66 and, for the normotensives, 18–64 years. None of the normotensive subjects was taking drugs, and there was no evidence of renal, cardiovascular, or endocrine abnormalities on a careful in-patient evaluation. All subjects with hypertension had a diastolic blood pressure greater than 90 mm of mercury on three different occasions and documented evidence of hypertension for at least 6 months prior to the study. In addition, the results of the following studies were normal: creatinine clearance, 24-hour urine vanillylmandelic acid (VMA), metanephrines, catecholamines, 17 hydroxy- and 17 ketosteroid excretions. In all subjects, stimulated levels of plasma renin activity were determined after balance had been achieved on a 10 mEq Na, 100 mEq K intake; measurement was made in the morning after the subject had been upright for 3 hours. The normal range under these conditions in our laboratory is between 2.4 and 15 ng/ml per hour. Normotensive and hypertensive subjects were studied under identical conditions of metabolic balance.

Twenty-four percent of the hypertensive subjects had high-renin hypertension. On the basis of an intravenous pyelogram, renogram, and (in 40% of the cases) angiography, 46% of the high-renin and 21% of the normal-renin hypertensive subjects had evidence of renal
disease—one-third unilateral renal artery stenosis, and two-thirds bilateral parenchymal or small-vessel disease.

**Sodium-Restricted Study**

In order to stimulate renin secretion prior to administration of angiotensin II, 26 normotensive control subjects and 48 subjects with hypertension were studied when in balance on a 10 mEq sodium, 100 mEq potassium intake. After an overnight fast with the subjects supine, control blood samples were obtained for blood urea nitrogen, sodium, potassium, supine renin activity, angiotensin II, and cortisol. Angiotensin II (Hypertensin; Ciba) then was administered according to two different protocols. In 14 normotensive subjects and in all 48 subjects with hypertension, a dose-response relationship was obtained by infusing angiotensin II at 0.1, 0.3, 1, and 3, in some cases 10 ng/kg per minute, with each dose given for 30 minutes. Samples were obtained at 20 and 30 minutes after initiating each dose. In 12 additional normotensive subjects, a single dose (1, 3, or 10 ng/kg per minute) was infused and the responses were compared with those resulting from multiple-dose infusions.

**High-Sodium Study**

Because of the renin responses to angiotensin II observed in the low-sodium studies, a second group of subjects was studied on a 200 mEq sodium, 100 mEq potassium intake. In all subjects, 5 days were allowed to achieve metabolic balance prior to the infusion of angiotensin II. In 14 normotensive and 16 hypertensive subjects, angiotensin was infused at rates of 1 and 3 and, in some cases, 0.1, 0.3, and 10 ng/kg per minute, with each dose given for 30 minutes. Samples were obtained at 20 and 30 minutes after initiating each dose. In 12 additional normotensive subjects, a single dose (1, 3, or 10 ng/kg per minute) was infused and the responses were compared with those resulting from multiple-dose infusions.

**Converting Enzyme Inhibition**

Nine normotensive subjects and six subjects with essential hypertension (one with high renin) were given SQ 20881, 30 μg/kg (a nonapeptide peptidyl-dipeptide hydro-lase inhibitor) over a 3-minute period and the plasma levels of renin activity and angiotensin II were determined 20 minutes later. Some data were reported previously.10

During all three protocols, blood pressure was monitored at intervals of 2 minutes for 30 minutes prior to and throughout the angiotensin II infusion. Mean blood pressure was calculated as the sum of diastolic plus one-third of the pulse pressure.

**Laboratory Procedures**

Daily weights were recorded and 24-hour urine specimens were collected from 7 a.m. to 7 a.m. for measurement of sodium and potassium. Accuracy of the urine collections was checked by creatinine determinations. Urine sodium and potassium were measured by flame photometry using lithium as an internal standard. Plasma angiotensin II and renin activity were measured by a double antibody radioimmunoassay procedure previously described.11

**Statistical Evaluation**

Group means have been presented with the standard error of the mean as the index of dispersion. Evaluation of statistical probability was carried out where appropriate with Student's t-test corrected by Dunnett's convention.12 Otherwise, the Wilcoxon rank sum (WRST) or Fisher direct probability test (FDPT) for nonparametric data was used. The null hypothesis was rejected when the P values were less than 0.05.

The protocol was approved by the Human Subjects Committee of the Peter Bent Brigham Hospital, and written consent was obtained from each subject after a detailed explanation of the protocol.

**Table 1**  Biochemical and Physiological Characteristics of the Normotensive, Normal-Renin Hypertensive and High-Renin Hypertensive Subjects*

<table>
<thead>
<tr>
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<th>Normotensive subjects</th>
<th>Hypertensive subjects</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Female (%)</td>
<td>Weight (kg)</td>
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<tr>
<td></td>
<td>26</td>
<td>38</td>
<td>70.8 ± 2.5</td>
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<tr>
<td></td>
<td>35</td>
<td>37</td>
<td>74.8 ± 3.8</td>
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<td></td>
<td>11</td>
<td>45</td>
<td>77.2 ± 3.7</td>
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<tr>
<td></td>
<td>Age (yr)</td>
<td></td>
<td>38 ± 3</td>
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<tr>
<td></td>
<td>35</td>
<td></td>
<td>42 ± 2</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td></td>
<td>35 ± 4</td>
</tr>
<tr>
<td></td>
<td>Serum sodium (mEq/liter)</td>
<td>142 ± 1</td>
<td>138 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.3 ± 0.1</td>
<td>4.0 ± 0.1</td>
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<td></td>
<td></td>
<td>1.1 ± 0.1</td>
<td>0.9 ± 0.1</td>
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<tr>
<td></td>
<td>Urine sodium (mEq/24 hr)</td>
<td>12 ± 3</td>
<td>10 ± 1</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>9 ± 2</td>
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<tr>
<td></td>
<td>Mean blood pressure (mm Hg)</td>
<td>76 ± 4</td>
<td>103 ± 3†</td>
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<td></td>
<td></td>
<td></td>
<td>92 ± 4†</td>
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<tr>
<td></td>
<td>Serum creatinine (mg/dl)</td>
<td>1.1 ± 0.1</td>
<td>1.1 ± 0.1</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.9 ± 0.1</td>
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<tr>
<td></td>
<td>Serum potassium (mEq/liter)</td>
<td>4.3 ± 0.1</td>
<td>4.0 ± 0.1</td>
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<td></td>
<td></td>
<td></td>
<td>4.0 ± 0.1</td>
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<tr>
<td></td>
<td>Supine plasma angiotensin II (pg/ml)</td>
<td>51 ± 5</td>
<td>38 ± 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>71 ± 5</td>
</tr>
<tr>
<td></td>
<td>Supine plasma renin activity (ng/ml per hour)</td>
<td>3.8 ± 0.5</td>
<td>3.4 ± 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7.8 ± 1.1†</td>
</tr>
</tbody>
</table>

* When balance had been achieved on a 10 mEq sodium, 100 mEq potassium intake (mean ± SEM).
† P < 0.01 different from normotensive.
Results

Response of Sodium-Restricted Subjects to Angiotensin Infusion

The characteristics of the subjects studied on the 10 mEq sodium, 100 mEq potassium intake are summarized in Table 1. There were no differences between the three groups with respect to age, weight, sex distribution, serum creatinine, or urine sodium and potassium levels at the time of the study. As would be anticipated, the blood pressure was significantly greater \((P < 0.01; \text{FDPT})\) in both hypertensive groups than in normotensive controls. Plasma angiotensin II concentrations and renin activity prior to the angiotensin infusion were similar in the normal-renin and normotensive subjects but greater, as anticipated, in the high-renin hypertension subgroup.

In the normotensive subjects, all data for a given dose have been pooled. There were no significant differences in the absolute or incremental changes in blood pressure, angiotensin II, or renin levels whether a single or graded infusion of angiotensin was given. Specifically, in the subjects receiving multiple doses, the decrement in renin activity with an infusion rate of 1 ng/kg per minute was 14 ± 4% and was 34 ± 6% with a rate of 3 ng/kg per minute. In five subjects receiving an infusion of only 1 ng/kg per minute, the decrement was 19 ± 5%, and in the four subjects given 3 ng/kg per minute, it was 35 ± 8%. The normal subjects infused with graded doses had received angiotensin II for 120 minutes at the completion of the infusion of 3 ng/kg per minute, in contrast to 30 minutes with the single-dose studies.

Angiotensin II infusion induced a dose-related increase in plasma concentration of angiotensin II that reached significance \((P < 0.05; \text{Student's } t\)-test) at an infusion rate of 1 ng/kg per minute in all subjects studied (Fig. 1). There were no significant differences in the increments in plasma angiotensin II concentration between normotensive and either subgroup of hypertensive subjects. Blood pressure responses to angiotensin II also were similar in the three groups of subjects. However, many of the hypertensive subjects had a normal blood pressure at the time of the study because there had been significant decreases in mean blood pressure from admission levels of 128 ± 6 (normal renin) and 122 ± 6 (high renin) mm Hg. Threshold sensitivity was at an infusion rate of 1 ng/kg per minute, and there were no significant differences in the incremental responses in blood pressure at any infusion rate (Fig. 1).

In contrast to the similarity of the vascular response in the three groups of subjects, there were significant differences in the response of renin activity to angiotensin II. A significant \((P < 0.05; \text{Dunnett's test})\) dose-related...
reduction in renin activity in the normotensive group was observed with a threshold sensitivity of 1.0 ng/kg per minute (Fig. 1). In contrast, in both hypertensive subgroups even an infusion rate of 3 ng/kg per minute did not produce a significant change in renin activity (Fig. 1).

The efficacy of angiotensin in suppressing renin release in the normotensive subjects was in part dependent on the control renin level. At infusion rates of both 1 and 3 ng/kg per minute, the decrement was correlated significantly \( P < 0.001 \) with the control renin level \( r = 0.78 \) and 0.93, respectively; Fig. 2). In contrast, there was no correlation between control renin level and decrement in plasma renin activity in either of the hypertensive subgroups even when angiotensin II was infused at a rate of 3 ng/kg per minute (Fig. 2). The points representing the hypertensive subjects fall above the line representing the normal response over the entire range of basal renin activities. For both the normal-renin \( P < 0.0006 \); FDPT) and high-renin \( P < 0.02 \); FDPT) subgroups, distribution was significantly asymmetrical compared to that for the normotensive subjects. Thus, differences in control renin levels cannot explain the failure of angiotensin II to suppress renin release in the hypertensive subjects. Furthermore, these differences could not be explained by differences in either absolute or incremental peak angiotensin II levels between the normotensive and hypertensive subjects.

**Response of Sodium-Loaded Subjects to Angiotensin II Infusion**

The characteristics of the subjects studied on the 200 mEq sodium intake are summarized in Table 2. There were no differences in respect to age, weight, sex distribution, serum, or urine sodium and potassium levels on the day prior to the angiotensin II infusion. As anticipated, the blood pressure was significantly greater \( P < 0.01 \) (FDPT) in both hypertensive subgroups. Statistical analysis of the high-renin subgroup is limited in view of the small number of subjects studied.

Incremental angiotensin II levels were similar in the three groups of subjects studied and not significantly different from those observed on the low-sodium intake. A dose-response relationship was noted in all cases with a significant increment \( P < 0.05 \); Student’s \( t \)-test) occurring with an infusion rate of 1 ng/kg per minute in all three groups of subjects (Fig. 3).

Vascular responses in all three groups of subjects were greater than that noted in the sodium-restricted state. A significant \( P < 0.01 \); Student’s \( t \)-test) dose-related increase in mean blood pressure occurred with a threshold sensitivity of 0.3 ng/kg per minute, i.e., an infusion rate which did not produce a measurable increase in plasma angiotensin II levels. Although threshold sensitivity was not different in the three groups, the subjects with hypertension had a greater \( P < 0.01 \); FDPT) incremental rise [17 ± 1.5 and 24 (one subject) mm Hg] at the highest level of angiotensin II infused, 3 ng/kg per minute, compared to the normotensive subjects (11 ± 1 mm Hg).

Vascular responses were enhanced in all three groups of subjects studied on the high-sodium intake when compared with the appropriate sodium-restricted group. However, the efficacy of angiotensin II in suppressing renin activity was diminished (Fig. 3). In none of the groups was there a significant dose-related effect of angiotensin II on renin suppression even at infusion rates as high as 10 ng/kg per minute.

Six of the normotensive subjects were studied on both high- and low-sodium intakes. Their renin and blood pressure responses to angiotensin II infusion were also significantly different on the two diets \( P < 0.01 \).

**Response to Administration of SQ 20881**

In the normotensive subjects, 3 minutes after administering 30 \( \mu \)g of SQ 20881/kg, mean blood pressure fell significantly (−5 ± 1 mm Hg; \( P < 0.05 \)). However, 20 minutes later, mean blood pressure had returned to control in most subjects (Fig. 4). At the same time, plasma renin activity (PRA) had increased significantly \( P < 0.01 \) by 2.2 ± 0.6 ng/ml per hour and angiotensin II levels had declined (11 ± 3 pg/ml; \( P < 0.01 \)). In the subjects with hypertension, the decrements in blood pressure (−8 ± 2 mm Hg) and angiotensin II levels (−29 ±
HIGH SALT DIET

PLASMA RENIN ACTIVITY

PLASMA ANGIOTENSIN-II

MEAN BLOOD PRESSURE

FIGURE 3 Responses of mean blood pressure, plasma angiotensin II, and plasma renin activity to graded infusions of angiotensin II in normotensive, normal-renin hypertensive, and high-renin hypertensive subjects. Infusions were given after balance had been achieved on a 200 mEq Na, 100 mEq K intake (mean ± SEM). There were no significant differences between the groups except for blood pressure responses. The hypertensive subjects had significantly greater increments when given angiotensin II.

12 ng/ml) were significantly greater (P < 0.006, P < 0.045, respectively). In contrast, the increment in renin activity (3.1 ± 1.7 ng/ml per hour) was similar to that observed in the normotensive subjects and not significant (Fig. 4). Additionally, the ratio of increment in renin-decrement in blood pressure with SQ 20881 was significantly less (P < 0.017; FDPT) in the hypertensive subjects (0.5 ± 0.3 vs. 11.4 ± 5.8 ng/ml per hour per mm Hg); i.e., equivalent falls in blood pressure produced smaller increments in PRA in the hypertensive subjects. Although a similar trend was present between the increment in PRA and decrement in angiotensin II (0.3 ± 0.2 in hypertensive and 6.4 ± 5.8 ng/ml/hr/pg/ml in the normotensive subjects) it did not reach statistical significance (P < 0.078; FDPT).

Discussion

A decade ago, de Champlain and his colleagues3 infused angiotensin at rates of 15-35 ng/kg per minute into four sodium-restricted normotensive subjects and reported a significant decrement in renin activity 30-180 minutes after the beginning of the infusion. Michelakis and Horton,6 using both pressor (100 ng/kg per minute) and nonpressor (1.5-3 ng/kg per minute) doses of angiotensin II, reported decrements in renin activity; however, the changes did not reach statistical significance.6 Their subjects were studied on an ad libitum sodium intake. Recently, Mendelsohn et al.7 reported significant decrements in renin activity in sodium-restricted normotensive subjects with angiotensin II infusions that produced a mean increment in plasma angiotensin II of 31.6 pg/ml.7 The present study confirms and extends these previous findings by documenting that angiotensin II can suppress renin activity with little or no demonstrable change in the plasma levels of angiotensin II or blood pressure in sodium-restricted normotensive subjects. The present data also suggest that the entire dose-response relationship occurs over the range of plasma angiotensin II concentrations observed under physiological conditions that are reproduced by infusion rates from 0.3-3 ng/kg per minute.

Two previous studies have reported the responses of renin activity to angiotensin infusion in hypertensive subjects. De Champlain et al.3 reported the responses of six hypertensive subjects to infusions of angiotensin II at rates from 6.4 to 15 ng/kg per minute. They documented a decrement in renin activity in most. Mendelsohn et al.7 also studied renin responsiveness in 17 subjects with

FIGURE 4 The individual changes in plasma renin activity, mean blood pressure, and angiotensin II concentration 20 minutes after the administration of SQ 20881 (30 μg/kg) in nine normotensive and six hypertensive subjects. All subjects were studied supine, in balance on a 10 mEq Na, 100 mEq K diet.
hypertension and reported significant decrements in renin activity. Several differences in the design of the earlier studies and the present one may explain the differing results. In the earlier reports, a limited number of individuals were studied, the angiotensin dose administered was considerably higher, and a significantly longer time period was allowed between control and response values during which other factors including diurnal rhythm may also influence renin release.

The mechanism responsible for the difference in efficacy of angiotensin II in suppressing renin activity in the normotensive and hypertensive subjects is not known. It could not be accounted for by a change in a number of other factors regulating its secretion, e.g., volume, blood pressure, sodium, or potassium. The differences also could not be ascribed to differences in control renin or angiotensin II levels or peak increments in angiotensin during its infusion since they were similar in normotensive and hypertensive subjects.

The failure of angiotensin to alter renin release in the subjects with documented renal disease might have been anticipated. In all probability, the dominant factor modulating renin release in these subjects (27% of the total) is the structural alteration in the kidney, i.e., nephrosclerosis, renal artery stenosis, etc. Angiotensin II may produce little if any effect in subjects in whom a significant anatomical change in the kidney has occurred.

It has been documented amply that vascular responses to exogenous angiotensin II are decreased in the presence of high circulating levels of angiotensin or renin. Thus, the failure of physiological angiotensin infusions to suppress renin activity in subjects with high-renin hypertension could be due to a decreased sensitivity of the receptors mediating this effect if they act in a manner similar to vascular receptors. Although this is certainly a plausible explanation in the high-renin hypertensive subjects, it is less likely to be true in the normal-renin subgroup.

An unanticipated finding was a similar reduced efficacy of angiotensin II in subjects with normal-renin hypertension who had no evidence of structural renal vascular changes, i.e., normal intravenous pyelogram, renogram, and arteriogram (15% of the total). The mechanism(s) responsible for this are unclear. Potassium balance and serum potassium concentrations were normal in this group. While elevated arterial blood pressure could be a factor, responsiveness was blunted in subjects whose arterial pressure had fallen into the normal range at the time of study. Circulating catecholamines and sympathetic nervous system activity were not assessed directly in this study and could provide an alternative mechanism. In the subjects with renal vascular hypertension, an intrarenal mechanism presumably becomes dominant, with increased vascular resistance proximal to the juxtaglomerular apparatus becoming the major determinant of renin release.

By analogy, a similar mechanism could be playing a role in the normal-renin essential hypertensive subjects. A functional abnormality involving the renal arterioles has been documented in such subjects and could be the mechanism for the blunted short feedback loop in a manner analogous to that postulated for the subjects with renal disease.

The renin response of the hypertensive subjects to SQ 20881 also supports the hypothesis that efficacy of angiotensin II in altering renin release is diminished in subjects with hypertension. The significantly greater decrements in angiotensin II and mean blood pressure in the hypertensive subjects should have produced a greater rise in PRA. Yet, not only were the increments in PRA observed not significantly different in the normotensive and hypertensive subjects, in the hypertensive subjects, the increment itself also was not significant.

In the normotensive subjects on a high-sodium intake, angiotensin II did not alter plasma renin activity significantly. Since plasma renin activity was already suppressed by the high-sodium intake, these findings may simply reflect a physiological floor below which renin activity cannot be further lowered by angiotensin II because of other factors regulating its secretion. On the other hand, since it has been well established that sodium intake has a striking influence on the responses of at least two other target tissues to angiotensin II, the reduced efficacy of angiotensin II may be part of the general change in the response of target tissues to this polypeptide that results from alterations in sodium intake. Previous studies have documented that sodium intake exerts a reciprocal influence on vascular and adrenal responses to angiotensin II; sodium restriction enhances adrenal and reducing vascular responses. Thus, if a similar phenomenon occurs with the short feedback loop, then the juxtaglomerular cell is affected by sodium intake in a manner similar to adrenal rather than vascular tissue.

Normotensive and hypertensive subjects on a high-sodium intake showed similar renin responses to angiotensin II but different vascular responses. In agreement with results of a number of previous studies, sodium loading enhanced vascular responses to angiotensin II in both the normotensive and hypertensive subjects. However, its effect in the subjects with hypertension was significantly greater than in the normotensives. Thus, while normotensive and hypertensive subjects had similar blood pressure responses to angiotensin II when sodium-restricted, when sodium-loaded the hypertensive subjects were significantly more responsive.

This study has revealed a decreased effectiveness of angiotensin II in physiological concentrations to modulate renin release in subjects with hypertension; this was observed when angiotensin II concentrations were either acutely decreased (thereby promoting PRA release) or increased (thereby suppressing PRA release). Furthermore, this decreased responsiveness was present in all forms of hypertension even though the underlying pathophysiological mechanisms may be different, i.e., renal parenchymal or renal vascular disease, high renin per se, or normal renin and functional changes in the renal arterioles. This disorder in renin release could be a cause of or a factor contributing to the hypertensive process, but is unlikely to reflect simply an elevated blood pressure per se, since many subjects had normal pressures at the time of study. Thus, whether the hypertensive subject was normotensive or hypertensive at the time of study made no difference; angiotensin II did not suppress renin activity in either group. It is not difficult to construct a
model in which an alteration in renin release could result in hypertension, but a primary derangement in the kidney which produces both an elevated blood pressure and a change in the control of renin release is equally plausible. Finally, this study adds further support to a growing body of data suggesting that the regulation of renin release is substantially altered in subjects with hypertension.

References

Failure of renin suppression by angiotensin II in hypertension.
G H Williams, N K Hollenberg, T J Moore, R G Dluhy, S Z Bavli, H S Solomon and J H Mersey

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