3. Renal Pressor System in Hypertensive Patients†

**HIDEO UEDA, YOSHIHIRO KANEKO AND TADANAO TAKEDA**

[2nd Department of Internal Medicine (Director: Prof. H. Ueda), Faculty of Medicine, University of Tokyo, Tokyo]

I. In order to evaluate the significance of determination of renin activity of renal vein plasma in hypertensive patients, renal (with venous catheterization method) and systemic vein blood were taken at the same time in normotensive and hypertensive patients, and the renin activity of the isolated plasma was measured as follows: the plasma was incubated at pH 5.5 for 24 hrs. and was boiled for 10 min., 0.1–0.2 ml of the supernatant was injected into a rat treated with sodium pentobarbital and pentolinium, and the pressor response was compared with that to standard synthetic angiotensin. Pressor activity of the incubated plasma was accepted as indicating renin activity when the following criteria were satisfied: pressor response to the supernatant should be similar in form to that to synthetic angiotensin, should increase with incubation and should be destroyed by chymotrypsin, and pressor response of renal vein plasma should be greater than that of systemic vein plasma. Renin activity thus measured was expressed as nanograms (ng = 10⁻⁹ µg) angiotensin formed per ml plasma. Fig. 1 illustrates one example of bioassay.

Table I summarizes renin activity measured in normotensive and hypertensive patients. The subjects tested were taking 3–10 gm NaCl daily and had no specific medication. Renin activity of renal and systemic vein plasma of 16 normotensive subjects averaged 2.1 and 1.3 ng/ml respectively. Fifteen patients with essential hypertension and 7 patients with chronic glomerulonephritis showed no significant increase in renin activity as shown in Table I. However, renin activity of the involved renal vein plasma of 9 renovascular hypertensive patients showed a marked increase which was highly significant. Two hypertensive patients with coarctation of the aorta showed no increase in renin activity.

Bilateral renal vein plasma was taken at the same time with two KIFA catheters introduced into the bilateral renal veins through the femoral veins under fluoroscopic control and their renin activities were compared in 16 hypertensive patients. There was a marked difference in renin activity between the affected and unaffected kidneys in 6 renovascular hypertensive patients, while left and right renal vein plasma showed no significant difference in 10 patients with es-

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sential hypertension. The finding suggests that comparison of renin activities of bilateral renal vein plasma could be very useful in diagnosis of renovascular hypertension and in determination of indication for surgery.

In 2 hypertensive patients with renal artery stenosis renin activity of renal vein plasma was measured before and after the stenosis was repaired by surgery. Markedly elevated renin activity measured before the surgery decreased to the normal range in parallel with blood pressure after the successful surgery. These findings suggest that renal pressor system is playing an important role in mechanism of human renovascular hypertension.

II. Recently Skinner, McCubbin and Page showed in dogs that reduction in renal perfusion pressure increased renin secretion from the kidney. In an attempt to examine this phenomenon in man, arterial pressure was lowered by i. v. infusion of sodium nitroprusside (50–150 µg/min.) in normotensive and hypertensive patients and the effect on renin activity of renal vein plasma was studied.

Fig. 2 shows effect of reduction in arterial pressure in one normotensive subject. Reduction of mean arterial pressure (MAP) from 93 to 79 mmHg did not cause significant change in renin activity. However, when pressure was lowered further to 69 mmHg, there occurred a marked increase in renin activity of renal vein plasma. The increase almost disappeared 20 min. after cessation of the infusion. The finding indicates reduction in pressure caused increased release of renin from the kidney.

In 13 normotensive subjects, renin activity increased from 1.4±0.8 to 14.4±3.1 ng/ml

<table>
<thead>
<tr>
<th>Renin Activity Measured in Hypertensive Patients</th>
<th>No. of Cases</th>
<th>BP Average mmHg</th>
<th>Systemic Vein Plasma Range</th>
<th>Renin Activity (ng/ml)</th>
<th>Renal Vein Plasma Range</th>
<th>Mean±SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>16</td>
<td>129/77</td>
<td>0.6–2.4</td>
<td>1.3±0.2</td>
<td>0.7–4.5</td>
<td>2.1±0.6</td>
</tr>
<tr>
<td>Essential Hypertension</td>
<td>15</td>
<td>179/106</td>
<td>0.4–2.8</td>
<td>1.5±0.2 (n.s.)</td>
<td>0.5–2.9 (n.s.)</td>
<td>1.8±0.2</td>
</tr>
<tr>
<td>Chronic Glomerulonephritis</td>
<td>7</td>
<td>172/97</td>
<td>0.8–2.5</td>
<td>1.3±0.2 (n.s.)</td>
<td>1.3–4.7 (n.s.)</td>
<td>2.6±0.3</td>
</tr>
<tr>
<td>Renovascular Hypertension</td>
<td>9</td>
<td>195/121</td>
<td>1.2–19</td>
<td>6.7±1.0 (p&lt;0.001)</td>
<td>7.0–45 (p&lt;0.001)</td>
<td>18.6±3.8</td>
</tr>
</tbody>
</table>

EFFECT OF REDUCTION OF ARTERIAL PRESSURE ON RELEASE OF RENIN IN NORMOTENSIVE SUBJECT

![Graph showing the effect of reduction of arterial pressure on renin activity](image)

Fig. 2.

(P<0.001) when MAP reduced from 92 (127/75) to 67 (94/53) mmHg. The increase usually became manifest 15 to 20 min. after reduction in pressure, continued during the hypotensive period, and disappeared when pressure returned to the control level after cessation of the infusion. In 3 cases bilateral renal vein plasma was tested and showed essentially the same increase in renin activity during reduction in arterial pressure.

Fig. 3 shows relationships between MAP level and renin activity of renal vein plasma in % of the control value when pressure was lowered by sodium nitroprusside.

When MAP was lowered below 75 (about 100/60) mmHg in normotensive subjects, signi-
significant increase in renin activity occurred in almost all cases tested. Above this level, no significant increase was seen as shown in Fig. 3. The findings suggest that there exists a threshold for increased secretion of renin in normotensive subjects. When pressure decreases below the threshold, the kidney releases increased amount of renin, counteracting the decrease in pressure. In other words, the kidney may act as a baroreceptor, and thus renal pressor system could play a role in maintaining normal arterial pressure in man. This renal baroreceptor mechanism seems to be sensitive to mean arterial pressure. It is still unknown what final mechanism initiates increased secretion of renin when arterial pressure is decreased. However, it is noteworthy that the threshold of 75 mmHg is near the level under which renal autoregulation is destroyed.

If one kind of hypertension be caused by increased secretion of renin from the kidney, the threshold of arterial pressure for renin secretion in the hypertension should be shifted to higher than normal level. If the threshold is within the normal range, it is likely that renal pressor system is not involved in mechanism of the hypertension, though it may play a role in maintaining normal arterial pressure. This point was studied further in patients with essential and renal hypertension.

Effect of reduction in arterial pressure was observed in 12 patients with essential hypertension. As shown in Fig. 3, increased release of renin was not observed above 75 mmHg when pressure was lowered by sodium nitroprusside. When pressure was lowered further, it caused a significant increase like in normotensives. The finding indicates that the threshold for increased

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secretion of renin is within the normal range in essential hypertension, and suggests that increased secretion of renin may not be involved in mechanism of this disease. However, the finding does not prove this, since changes in minute amount of renin can not be detected by the present method and since possible actions of this minute renin are still unknown.

In 6 hypertensive patients with chronic glomerulonephritis tested, the threshold for increased secretion of renin was found to be within the normal range like in essential hypertension, which suggests that renal pressor system may not be associated with renal hypertension of this type. The mechanism of hypertension in chronic glomerulonephritis is still unknown.

Fig. 4 shows the results obtained in a patient with renovascular hypertension. Vein plasma from the affected kidney showed significantly increased renin activity before reduction of pressure, which is characteristic in this disease. When MAP was lowered from 122 to 85 mm Hg, renin activity increased from 7 to 52 ng/ml. When pressure recovered, renin activity returned almost to the control level. In 5 patients with renovascular hypertension, renin activity increased from 10.7 ± 3.3 to 36.6 ± 12.6 ng/ml when MAP was lowered from 153 (208/126) to 102 (138/84) mmHg.

As shown in Fig. 3, an increase in renin secretion occurred at the level far above 75 mm Hg in patients with renovascular hypertension; the threshold of pressure for increased renin secretion was clearly elevated. This upward shift of the threshold to higher level seems to indicate that renal pressor system plays a role not only in initiating but also in maintaining high arterial pressure in renovascular hypertension. However, it should be noted that this upward shift of the threshold of pressure observed in this disease dose not imply resetting of the threshold of the renal baroreceptor mechanism at higher level, since pressure distal to the stenosis of the renal artery could be much lower than pressure measured proximal to the stenosis.

In conclusion, renin activity of renal vein plasma was markedly elevated in renovascular hypertension while it was in the normal range in essential hypertension or in chronic glomerulonephritis. Determination of renin activity of bilateral renal vein plasma was found to be useful in functional diagnosis of renovascular hypertension. Reduction in mean arterial pressure below 75 mmHg caused increased secretion of renin from the kidney in normotensive subjects while reduction in pressure above 75 mmHg did not, suggesting that there exists a threshold of pressure for increased secretion of renin. The kidney may act as a baroreceptor by this mechanism and renal pressor system may be playing a role in maintaining normal arterial pressure in man. The threshold for secretion of renin was shifted to much higher level in renovascular hypertension while it was in the normal range in essential hypertension or in chronic glomerulonephritis. This upward shift of the threshold for secretion of renin seems to indicate that renin-angiotensin system plays a role in maintaining high arterial pressure in renovascular hypertension.

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REFERENCE