Renal Venous Renin Determinations in the Diagnosis of Surgically Correctable Hypertension

By Annette Fitz, M.D.

SUMMARY

Renin activity in renal vein plasma was measured in six normal subjects and 59 hypertensive patients. The average renin value in renal venous plasma in normal subjects was the same as that found in patients with essential hypertension and renal parenchymal hypertension. Renal venous renin levels were markedly elevated in patients with significant renal lesions who were improved by surgery but were normal in patients with insignificant renal artery stenosis. We defined an abnormal renal vein renin level as one which is higher than 4.1 ng/ml of plasma, the highest normal, and which is also more than twice as great as the level obtained from the opposite kidney. On 19 patients who were operated upon for renal hypertension, there were no "false positive tests," and two "false negative tests." One patient with essential hypertension had abnormal values by these standards. Since occasional "false positive" and "false negative" results occur, we presently recommend that this test be used with, but not to the exclusion of, other tests of renal function in preoperative evaluations. As experience with the test increases, and as more prospective studies are done, it may prove to be the single most useful device to predict surgical success in patients with renal artery and renal parenchymal hypertension.

Additional Indexing Words:
Blood pressure  Renal parenchymal disease  Renal artery stenosis
Renal vascular hypertension

RENAL LESIONS, particularly stenosis of the renal artery, often cause correctable human hypertension. The role of renal disease in hypertension has been confirmed experimentally in many animal species. Evidence indicates that such experimental hypertension is often accompanied in the early stages by increased formation and release of renin and angiotensin. This increase in renin and angiotensin is thought to occur secondary to decreased renal perfusion pressure or renal blood flow. These factors are often found in human renovascular hypertension.

Correctable renal hypertension is frequently associated with detectable increases in peripheral vein renin, and these determinations have been advocated for the screening of hypertensive patients. Peripheral vein renin levels, however, are altered by the posture of the patient, by sodium balance, by concomitant drug therapy, and by associated conditions such as congestive heart failure, cirrhosis of the liver, or accelerated hypertension. Furthermore, some patients with correctable renal hypertension have been reported to have normal peripheral vein levels.

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Table 1

Renal Venous Renin Activity* in Normal Men

<table>
<thead>
<tr>
<th>Normal subject no.</th>
<th>Renin (ng/ml)</th>
<th>Ratio, H/L</th>
<th>Difference, H — L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RRV†</td>
<td>LRV‡</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.4</td>
<td>3.7</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>4.1</td>
<td>3.5</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>5</td>
<td>3.3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>—</td>
<td>2.4</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>2.7</td>
<td>2.9</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*Pickens method.
†Right renal vein.
‡Left renal vein.

Since total body dilution of small increases in renin secretion might cause the peripheral renin activity to remain in the normal range, many investigators have proposed that the renal vein effluent be sampled and measured for renin or angiotensin as a diagnostic tool. Judson and Helmer reported that differential renal venin renin values were of value in selecting patients for surgery. Goorno and Kaplan and McPhaul and associates also have reported success in predicting the significance of a renal artery lesion by testing for a pressor substance found in the renal venous effluent. Nevertheless, information on the usefulness of the various tests of renal venous pressor activity in evaluating the hypertensive patient is limited, and we felt that further evaluation of this procedure was warranted. We measured the renal venous renin activity in six normal subjects and 59 completely evaluated hypertensive patients in order to understand better the usefulness of this observation in selecting patients for surgery.

Methods

Fifty-nine carefully studied hypertensive patients were obtained from the wards and clinics at the University of Iowa Hospitals and the Iowa City Veterans Administration Hospital. Both men and women, ranging in age from 17 to 69 years, were included. Six normal male prisoner volunteers with blood pressures below 130/85

Table 2

Renal Venous Renin Activity in Patients with Essential Hypertension

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Renin (ng/ml)*</th>
<th>Ratio, H/L</th>
<th>Difference, H — L</th>
<th>Thiazides or &lt; 800 mg Na in diet</th>
<th>Blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.6</td>
<td>6.6</td>
<td>0</td>
<td>0</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>1.3</td>
<td>0</td>
<td>—</td>
<td>1.3</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>3.7</td>
<td>3.2</td>
<td>1.2</td>
<td>0.5</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>1.6</td>
<td>1.3</td>
<td>1.2</td>
<td>0.3</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>2.8</td>
<td>1.3</td>
<td>2.2</td>
<td>1.5</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>4.2</td>
<td>—</td>
<td>—</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>0.7</td>
<td>1.1</td>
<td>1.6</td>
<td>0.4</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>1.3</td>
<td>1.7</td>
<td>1.3</td>
<td>0.4</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>4.1</td>
<td>3.8</td>
<td>1.1</td>
<td>0.3</td>
<td>Yes</td>
</tr>
<tr>
<td>11</td>
<td>5.0</td>
<td>1.4</td>
<td>3.6</td>
<td>3.6</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>1.4</td>
<td>1.3</td>
<td>1.1</td>
<td>0.1</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>3.5</td>
<td>3.9</td>
<td>1.1</td>
<td>0.4</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>1.3</td>
<td>1.1</td>
<td>1.2</td>
<td>0.2</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>1.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>6.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>1.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>No</td>
</tr>
<tr>
<td>18</td>
<td>1.4</td>
<td>1.3</td>
<td>1.1</td>
<td>0.1</td>
<td>No</td>
</tr>
<tr>
<td>19</td>
<td>14.0†</td>
<td>18.0†</td>
<td>1.3</td>
<td>4.0</td>
<td>No</td>
</tr>
<tr>
<td>Mean</td>
<td>2.7</td>
<td>2.3</td>
<td>1.4</td>
<td>0.7</td>
<td></td>
</tr>
</tbody>
</table>

Key: No sample = —.

*Mean & se: RRV + LRV = 2.5 ± 0.3, Pickens method.
†Helmer method: patient had accelerated hypertension.

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### Table 3

Renal Venous Renin Activity in Patients with Renal Parenchymal Disease (No Operation)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Renin (ng/ml)</th>
<th>Ratio, D/L or D/N</th>
<th>Difference, H — L or D — N</th>
<th>Disease</th>
<th>Blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>3.3</td>
<td>2.9</td>
<td>1.1</td>
<td>0.4</td>
<td>130/85</td>
</tr>
<tr>
<td>21</td>
<td>1.7</td>
<td>0.7</td>
<td>2.4</td>
<td>1.0</td>
<td>160/120</td>
</tr>
<tr>
<td>22</td>
<td>3.9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>230/125</td>
</tr>
<tr>
<td>23</td>
<td>2.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>175/122</td>
</tr>
<tr>
<td>24</td>
<td>3.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>150/105</td>
</tr>
<tr>
<td>25</td>
<td>2.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>150/110</td>
</tr>
<tr>
<td>26</td>
<td>1.1</td>
<td>1.4</td>
<td>0.8</td>
<td>— 0.3</td>
<td>140/90</td>
</tr>
<tr>
<td>27</td>
<td>2.4</td>
<td>—</td>
<td>1.1</td>
<td>0.2</td>
<td>140/90</td>
</tr>
<tr>
<td>28</td>
<td>3.8</td>
<td>—</td>
<td>1.1</td>
<td>0.3</td>
<td>180/120</td>
</tr>
<tr>
<td>29 (Helmer method)</td>
<td>3.8</td>
<td>—</td>
<td>1.2</td>
<td>0.7</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Mean &amp; se</td>
<td>2.8 ± 0.3</td>
<td>1.3</td>
<td>+ 0.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4

Renal Venous Renin Activity in Patients with Hypertension Improved by Surgery: Significant Renal and Renovascular Lesions

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Renin (ng/ml)</th>
<th>Ratio, D/L or D/N</th>
<th>Difference, H — L or D — N</th>
<th>Preoperative blood pressure (mm Hg)</th>
<th>Lesion</th>
<th>Thiazides or &lt; 800 mg Na in diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>9.0</td>
<td>1.0</td>
<td>9.0</td>
<td>8.0</td>
<td>210/115</td>
<td>Vascular</td>
</tr>
<tr>
<td>31</td>
<td>25.0</td>
<td>6.6</td>
<td>3.8</td>
<td>18.4</td>
<td>190/120</td>
<td>Vascular</td>
</tr>
<tr>
<td>32</td>
<td>1.3</td>
<td>1.5</td>
<td>0.9</td>
<td>— 0.2</td>
<td>150/110</td>
<td>Traumatic rupture of kidney</td>
</tr>
<tr>
<td>33</td>
<td>4.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>190/120</td>
<td>Bilateral vascular lesions</td>
</tr>
<tr>
<td>34</td>
<td>4.4</td>
<td>0.9</td>
<td>4.9</td>
<td>3.5</td>
<td>200/120</td>
<td>Vascular</td>
</tr>
<tr>
<td>35</td>
<td>2.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>185/110</td>
<td>Vascular</td>
</tr>
<tr>
<td>36</td>
<td>5.9</td>
<td>3.0</td>
<td>2.0</td>
<td>2.9</td>
<td>160/105</td>
<td>Vascular stenosis &amp; pheochromocytoma</td>
</tr>
<tr>
<td>37</td>
<td>8.1</td>
<td>3.8</td>
<td>2.1</td>
<td>4.3</td>
<td>180/120</td>
<td>Hydro-nephrosis</td>
</tr>
<tr>
<td>38</td>
<td>6.2</td>
<td>1.4</td>
<td>4.4</td>
<td>4.8</td>
<td>185/110</td>
<td>Vascular</td>
</tr>
<tr>
<td>39</td>
<td>560.0*</td>
<td>127.0*</td>
<td>4.4</td>
<td>433.0</td>
<td>188/110</td>
<td>Vascular</td>
</tr>
<tr>
<td>40</td>
<td>212.0*</td>
<td>40.0*</td>
<td>5.3</td>
<td>172.0</td>
<td>160/105</td>
<td>Vascular</td>
</tr>
<tr>
<td>41</td>
<td>800.0*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>160/110</td>
<td>Vascular</td>
</tr>
</tbody>
</table>

Mean & se renin (Pickens) 7.2 ± 2.1 2.6 ± 0.8 4.1 6.0

*Renin levels, method of Helmer.
Table 5

Renal Venous Renin Activity in Patients with Insignificant Stenosis of Renal Artery Not Improved by Operation

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Renin (ng/ml)</th>
<th>Ratio, D/N</th>
<th>Difference, D - N</th>
<th>Preoperative blood pressure (mm Hg)</th>
<th>Lesion</th>
<th>Thiazides or &lt;800 mg Na in diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>1.0</td>
<td>1.0</td>
<td>0</td>
<td>180/100</td>
<td>Vascular</td>
<td>No</td>
</tr>
<tr>
<td>43</td>
<td>2.0</td>
<td>1.0</td>
<td>0</td>
<td>170/120</td>
<td>Vascular</td>
<td>Yes</td>
</tr>
<tr>
<td>44</td>
<td>1.6</td>
<td>1.4</td>
<td>1.1</td>
<td>170/120</td>
<td>Vascular</td>
<td>No</td>
</tr>
<tr>
<td>45</td>
<td>2.7</td>
<td>1.0</td>
<td>2.7</td>
<td>150/100</td>
<td>Vascular</td>
<td>No</td>
</tr>
<tr>
<td>46</td>
<td>4.2</td>
<td>2.6</td>
<td>1.6</td>
<td>170/125</td>
<td>Vascular</td>
<td>No</td>
</tr>
<tr>
<td>47</td>
<td>3.4</td>
<td>—</td>
<td>—</td>
<td>180/120</td>
<td>Vascular</td>
<td>No</td>
</tr>
<tr>
<td>48</td>
<td>6.6</td>
<td>6.6</td>
<td>0</td>
<td>170/120</td>
<td>Vascular</td>
<td>No</td>
</tr>
</tbody>
</table>

Mean & se 3.1 ± 0.7 2.3 ± 0.9 1.2 0.8

mm Hg were studied while on the clinical research ward at the University of Iowa Hospitals (table 1). These normal subjects and all hypertensive patients had a complete history and physical examination as well as intravenous urography, radioactive renography, and aortography. Blood pressures in hypertensive subjects averaged more than 140/90 while hospitalized. Samples of renal venous blood were obtained from patients who were to undergo aortography for evaluation of their hypertension. All but eight of the 30 patients with renal artery lesions had split function tests12 as well. Serum sodium determinations were done by flame photometer with an internal standard. The serum sodium values were obtained on admission, prior to therapy, and prior to renal vein sampling.

Nineteen patients were classified as having essential hypertension after an extensive work-up revealed no cause for hypertension (table 2). Ten patients with renal parenchymal disease were so classified on the basis of a renal biopsy or because of unequivocal evidence of parenchymal diseases on intravenous pyelograms and arteriograms (table 3). Twelve patients were placed in the group with "significant" renal artery stenosis or renal disease if surgery resulted in a sustained (>12 months, 11 patients; >6 months, one patient) fall in mean blood pressure of greater than 25 mm Hg without additional drug therapy (table 4).

In seven patients, blood pressure did not improve following adequate surgery. These were classified as insignificant renal artery stenosis (table 5). An additional 11 patients were thought to have insignificant stenosis when intravenous pyelograms, radioactive renograms, split renal function tests and indocyanine-green renal blood flows indicated equal renal function despite presence of a renovascular lesion demonstrated by aortography (table 6).

The normal subjects and the majority of patients were not restricted in sodium intake and were not receiving drugs. Exceptions, noted in the tables, occurred in those patients who were severely hypertensive and in whom it was felt discontinuing treatment would influence adversely their clinical course. Various maneuvers, such as sodium restriction, Valsalva maneuvers and postural changes, have been advocated as useful stimuli to increase the accuracy of the test. We wished to evaluate the patients, insofar as possible, in the basal state, and, therefore, avoided the use of such stimuli.

The method of Pickens and associates13 for measurement of renin activity in human plasma with 4-hour incubation was used with slight modification in all but the five determinations for which the Helmer assay (1-hour incubation) was utilized.14 Samples of blood were obtained while the patient was recumbent prior to aortography. Correct catheter placement was determined by injection of 1 ml of contrast material into the renal vein and by determination of the renal venous oxygen saturation. Results are recorded as nanograms (ng) of angiotensin produced by incubation per milliliter of plasma. Statistical significance of the difference between group means was determined by Student's t test.15 The mean and standard error of the mean difference were calculated for all groups.

Results were evaluated on the basis of two factors: (1) the absolute level of renin obtained from a kidney; (2) a comparison of the level of renin obtained from the diseased or stenotic kidney with that from its normal mate. The latter comparison was made in two ways: (a) A ratio was obtained by dividing the renin from the diseased kidney by the renin from the normal kidney (D/N). In normals and patients with essential hypertension this ratio was obtained by dividing the higher by the lower value (H/L). A comparison was also made by subtracting the "normal" value from the value obtained from the
Table 6

Renal Venous Renin Activity in Patients with Insignificant Renal Artery Stenosis; No Operation

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Renin (ng/ml)</th>
<th>Ratio, D/N</th>
<th>Difference, D — S</th>
<th>Blood pressure (mm Hg)</th>
<th>Thiazides or &lt;800 mg Na in diet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diseased</td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>kidney</td>
<td>kidney</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>1.0</td>
<td>1.2</td>
<td>0.8</td>
<td>— 0.2</td>
<td>184/98</td>
</tr>
<tr>
<td>50</td>
<td>3.3</td>
<td>3.8</td>
<td>0.9</td>
<td>— 0.5</td>
<td>160/105</td>
</tr>
<tr>
<td>51</td>
<td>2.5</td>
<td>3.8</td>
<td>0.7</td>
<td>— 1.3</td>
<td>200/105</td>
</tr>
<tr>
<td>52</td>
<td>4.3</td>
<td>1.2</td>
<td>3.6</td>
<td>3.1</td>
<td>170/110</td>
</tr>
<tr>
<td>53</td>
<td>4.3</td>
<td>1.9</td>
<td>2.3</td>
<td>2.4</td>
<td>180/110</td>
</tr>
<tr>
<td>54</td>
<td>2.2</td>
<td>2.3</td>
<td>1.0</td>
<td>— 0.1</td>
<td>170/120</td>
</tr>
<tr>
<td>55</td>
<td>3.3</td>
<td>4.8</td>
<td>0.7</td>
<td>— 1.5</td>
<td>150/110</td>
</tr>
<tr>
<td>56</td>
<td>0.8</td>
<td>0.7</td>
<td>1.1</td>
<td>0.1</td>
<td>160/100</td>
</tr>
<tr>
<td>57</td>
<td>4.5</td>
<td>2.8</td>
<td>1.6</td>
<td>1.7</td>
<td>190/115</td>
</tr>
<tr>
<td>58</td>
<td>1.8</td>
<td>1.6</td>
<td>1.1</td>
<td>0.2</td>
<td>200/130</td>
</tr>
<tr>
<td>59</td>
<td>5.0</td>
<td>4.0</td>
<td>1.2</td>
<td>1.0</td>
<td>180/120</td>
</tr>
</tbody>
</table>

Mean & se 3.0 ± 0.4 2.6 ± 0.4 1.4 ± 0.4

steno tic or diseased kidney (D — N). In normals and in the patients with essential hypertension the lower renin was subtracted from the higher renin value (H — L).

Results

In the normals the average renin content from the right kidney was 2.7 ng/ml, slightly lower than the value of 2.9 ng/ml obtained from the left. The average value of renin from nine normal kidneys was 2.8 ± 0.32 ng/ml of plasma. The H/L ratio was over 2.2 in one patient, but the actual difference was small (H — L = 1.2). The highest individual normal value for renin obtained was 4.1 ng/ml of plasma.

Samples were obtained from 33 kidneys in 19 men and women with essential hypertension (table 2). Bilateral samples were obtained in 14 patients. The mean value for renin of 2.5 ± 0.3 ng/ml of plasma was not significantly different from the normal. The range of renin values in these patients was greater than that found in the normals; the lowest value (Pickens' method) was 0, the highest value was 6.6 ng/ml of plasma in a patient with labile blood pressure. When the comparison between kidneys was made, two patients (nos. 6 and 11, table 2) had an H/L ratio greater than 2.0. Only patient 11 had a marked difference between kidneys when both proportion (H/L) and absolute differences (H — L) are considered.

Three patients (nos. 1, 11, and 16, table 2) had renal renin values greater than 4.1 ng/ml, the highest value noted in normals.

Ten patients (cases 20 to 29) had renal parenchymal disease and were not operated upon (table 3). Bilateral samples were obtained in six of these patients. Ratios are recorded as D/N or D — N when unilateral disease was present, or as H/L and H — L when patients had bilateral disease. In one patient (no. 21, table 3) the ratio was over 2, but the difference between kidneys was only 1.0 ng, a normal value. The mean renin for this group was 2.8 ± 0.3 ng/ml, not different from normal.

Twelve patients had significant stenosis or renal parenchymal disease and were improved by operation (table 4). Samples in three of the patients (nos. 39, 40, and 41) were obtained at operation; the Helmer assay was used. This technique gives higher renin levels, and these values probably are further elevated because they were obtained at operation. The renin levels from the diseased kidney in this group of patients are much higher than levels noted in normals and essential hypertensives. The mean renin value from the stenotic or diseased kidney using the Pickens method was 7.2 ± 2.1 ng/ml of
plasma, significantly higher than the mean of 2.5 ng/ml in essential hypertensives ($P < 0.001$). In addition, the average D/N ratio of 4.1 in these patients is significantly higher than the ratio of 1.3 in essential hypertensives ($P < 0.001$). One patient (no. 32) in this group with a ruptured kidney had a ratio of less than 2, and also had a value from the diseased kidney of less than 4.1 ng/ml. One additional patient had a normal renin concentration in venous blood obtained from the diseased kidney. One patient (no. 33) had severe bilateral stenosis; both values were high. One patient (no. 37) with severe unilateral hydronephrosis and accelerated hypertension also had a high renin level.

Seven patients were considered to have insignificant renal artery stenosis, since their hypertension was not measurably improved after operation (table 5). In these patients the renin obtained from the stenotic kidney (3.1 ± 0.7 ng/ml) was not different from the value obtained from the opposite kidney (2.3 ± 0.9 ng/ml), nor was it different from levels found in normals or patients with essential hypertension.

After extensive evaluation including intravenous pyelography, radio-opaque renography, aortography, and split renal function tests or tests of renal blood flows by Cardio-Green dilution technique,16 11 patients were classified as having insignificant renal artery stenosis (table 6). The mean renin level of 3.0 ng/ml from the stenotic kidney is not different from the level found in normal patients or patients with essential hypertension. The differences between the stenotic and nonstenotic kidney were minimal, except in two patients (nos. 52 and 53) for whom the values from the stenotic side were two to three times that of the nonstenotic side. Four patients (nos. 52, 53, and 59) had values from the stenotic kidney which exceeded those values found in normals. In two of these patients (nos. 57 and 59), however, the D/N ratio was below 2.0, and the difference between kidneys (D – N) was not large.

Patients 31 and 37 (table 4) had accelerated hypertension. In these patients values from both renal veins were high; despite this a marked difference was noted between kidneys. One patient (no. 48, table 5), not improved by operation, had accelerated hypertension. In this instance renin levels were high, but equal.

Two negative split renal function tests by Stamey criteria12 were found in the patients (nos. 32 and 37) who were improved by surgery. One patient (no. 43) in the unimproved group (table 5) had a split function test indicative of significant renal artery stenosis.

Serum sodium and bilateral renal vein renin levels were available in 15 normals and patients with essential hypertension. When total renal vein renin (from both kidneys) was correlated with sodium an insignificant r value of -0.193 was obtained. A correlation value was also calculated for serum sodium and renin in patients with renal artery lesions. An r value of -0.373 was obtained which was also insignificant at the 5% level.

**Discussion**

The exact role of the renin-angiotensin system in the genesis of human renal hypertension is uncertain. In animals with hypertension secondary to renal artery stenosis the increase of renin and angiotensin is transient unless malignant hypertension is produced. Despite this, studies in humans show that peripheral arterial or venous renin or angiotensin levels are often elevated in the presence of significant renal artery stenosis. This suggests that man, unlike the dog, may maintain high renin levels in chronic renal or renal vascular hypertension. Since some patients with significant renal artery lesions have undeniably normal peripheral venous renin levels, even when standing, it seemed desirable to develop a test with more discriminatory power. Under these circumstances renal vein renin activity levels might be helpful in making the diagnosis of surgically correctable renal disease, regardless of the role renin and angiotensin play in the etiology of hypertension. It is also important to determine whether renin determinations

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are a good predictive index without additional measures such as manipulation of posture, reduction of sodium intake and hypotension, or simultaneous determinations of renal blood flow.

Our studies indicate that determination of bilateral renal venous renin activity is often a good index of surgical success. In the 12 patients who have achieved good results from surgery, high levels were noted from the stenotic kidney in 10. The average D/N ratio in these patients was usually, but not always, over 2. We eventually defined a "positive" renal vein renin test as one in which the renin from the diseased kidney was greater than normal (> 4.1 ng/ml) and which was more than twice the level in the opposite kidney (D/N > 2.0). Using these criteria the test gave no false positive results in the seven patients who had unsuccessful renal surgery. Two of the 12 patients who improved after surgery had false negative tests. These two patients are of special interest. Patient 32 (table 4), in addition to mild renal artery stenosis, had a nearly functionless kidney as a result of trauma which had occurred years earlier. It is conceivable that there was insufficient functioning tissue to produce a significant amount of renin. The other patient (no. 35, table 4) had severe nephrosclerosis in the nonstenotic kidney, and is unusual in that a good operative result was achieved despite a renal blood flow of 180 ml/min in the "normal" kidney. The results also suggest that differential renal vein renins might be especially useful when accelerated hypertension is present, since this condition itself, regardless of cause, usually is associated with high renin levels in peripheral veins. In those patients who had accelerated hypertension and were improved by surgery, there was a clear difference in renal venous renin levels. On the other hand, one unimproved patient (no. 48, table 5) with accelerated hypertension had equal, but elevated, renal venous renin levels.

Our observations in patients with essential hypertension and renal parenchymal disease indicate that an occasional abnormal value and abnormal ratio may occur. This is not surprising since Baldwin and co-workers and other workers have demonstrated inequalities in excretory and secretory function of kidneys in some patients with essential hypertension. Minor inequalities in renal venous renin activity represented only by an H/L ratio of 2.0 may occur on occasion. Except in the presence of a surgically significant renal arterial or renal parenchymal lesion, a high renin level, coupled with a ratio of 2.0 or greater, is unusual. Such a combination did occur in two patients, now classed as having insignificant lesions, and may represent a real limitation to the procedure. On the other hand, this may be a very early index of significant stenosis, not indicated by other standard tests. Further observation of these patients will be needed to clarify this point.

The normal levels of renal venous renin activity in patients with various renal diseases is in accord with previous work. Only one patient with a parenchymal lesion, patient 37 (table 4) had an elevated renin level. This young man with severe hydronephrosis and accelerated hypertension was improved by surgery. This supports the idea that an occasional patient with a parenchymal lesion may have hypertension on the basis of the renin-angiotensin system. Further study in a larger group of patients with hypertension and unilateral hydronephrosis and with pyelonephritis is needed to evaluate this possibility.

Brown and co-workers have noted a significant correlation between peripheral venous renin and serum sodium concentrations. We were unable to establish a good correlation between renal venous renin and sodium in our normals and patients with essential hypertension. When patients with renal artery stenosis were considered, the values obtained suggest that such a relationship may exist, although at a low level of significance.

The fact that high peripheral renin levels are obtained in most patients with significant renal artery hypertension suggests that renin secretion is also high. It is possible that high
peripheral levels might occur because of alterations in metabolism, rather than overproduction. The present study confirms the fact that the concentration of renin in renal vein blood from diseased kidneys of patients with renal artery hypertension is increased. It does not indicate whether total secretion is increased, since secretion is also related to renal blood flow, a measurement often reduced in the kidney behind a renal artery lesion. In addition, the possibility that renin excretion in the urine may be increased in patients with significant renal artery lesions must be further investigated before this problem can be settled.

Many factors, including the degree of nephrosclerosis,21 the type of medication,4 5, 22 diet,4 posture,3 glomerulonephritis,21 tubular sodium concentration,23 changes in renal perfusion pressure and renal blood flow,24 25 and neurogenic stimuli26 27 have been shown to alter juxtaglomerular activity or renin secretion. In view of this it is perhaps surprising that any pattern in renal vein renin activity can be discerned in these groups of patients. Despite these variables the only patients who consistently differed from the normals and essential hypertensives were the patients with significant renal artery stenosis. It is apparent, however, that occasional “false positive” and “false negative” tests occur. For this reason we recommend presently using bilateral renal venous renin levels in conjunction with other established methods of evaluating patients for surgery.

References


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