Plasma Renin Activity in Acute Tubular Necrosis and Other Renal Diseases Associated with Hypertension

By W. H. Tu, M.D.

With the technical assistance of Margaret Dawson

In 1945 Goormaghtigh called attention to prominence of the juxtaglomerular apparatus in the crush syndrome. He speculated that the juxtaglomerular apparatus probably releases vasopressor substance, causing arteriolar spasm at the vascular pole of the glomerular tufts,1 and that this vasopressor substance was one of the main factors responsible for the rise of blood pressure in the crush syndrome.2

Recently Tobian3 has reviewed evidence which suggests that renin is secreted by the juxtaglomerular apparatus in conditions involving reduced stretch of the juxtaglomerular cells, and proposed that the juxtaglomerular apparatus probably is a volume receptor. It is generally recognized that acute tubular necrosis frequently develops in association with severe renal ischemia.4 Although arterial hypertension arises in a significant number of patients with acute tubular necrosis,5, 6 the importance of the renal pressor mechanism and of electrolyte-fluid metabolism relative to one another, and to arterial hypertension, has not been clearly defined.

The present study was undertaken to investigate plasma renin activity in various phases of acute tubular necrosis and other renal diseases accompanied by arterial hypertension. Preliminary studies in acute tubular necrosis have been reported previously.7, 8

Materials and Methods

Three groups of subjects were studied for plasma renin activity: 23 normal control subjects (eight women and 15 men ranging in age from 16 to 41 years), 18 patients with acute tubular necrosis, and 11 hypertensive patients with renal disease.

The clinical descriptions of the patients with acute tubular necrosis are shown in Table 1. The oliguric phase was defined as the period prior to the onset of the diuretic phase in which the daily urinary output exceeded 1,000 ml. with steady increase. Eleven patients survived the oliguric phase, and eight were available for follow-up during the diuretic phase. The patients were managed conservatively, with particular attention to the maintenance of fluid-electrolyte balance and to the provisions of nonprotein calories. They were, however, not force-fed. Hemodialysis, as required, was performed by means of the twin-coil kidney9 or a low-resistance pumpless system.10 The net fluid balance (Δweight) during oliguric phase was estimated retrospectively from change of body weight.*

Table 2 lists the clinical information on the patients with hypertension and renal disease. Three of the 11 patients had accelerated hypertension of less than six months’ duration: two had polyarteritis and one had systemic lupus erythematosus (SLE). The other 8 patients had long-standing hypertension and end-stage chronic renal disease; their survival depended upon repeated hemodialysis during periods varying from a few months to longer than one year; details of this program and the patients have been described.12, 13

*Wf = Wft - 0.5 (m - n) + net fluid balance
Net fluid balance = Wft - Wftm - 0.5 (m - n) where Wft in kilograms equals weight on day n from the onset of renal failure, Wftm in kilograms equals weight on the first day of plateau of decreasing weight during the diuretic phase (“dry weight”) on day m of disease, and 0.5 Kg. is the daily catabolic tissue loss.11

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Table 1

Clinical and Laboratory Findings in Eighteen Patients with Acute Tubular Necrosis during Oliguric Phase and Diuretic (Recovery) Phase

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, sex</th>
<th>Blood pressure mm. Hg</th>
<th>Net fluid balance, liters</th>
<th>Plasma vasoconstrictor activity Oliguric, μg./100 ml.</th>
<th>Diuretic, μg./100 ml.</th>
<th>Cause of renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.W.</td>
<td>39 M</td>
<td>180/120</td>
<td>0</td>
<td>15.4</td>
<td>20.0</td>
<td>Spontaneous rhabdomyolysis</td>
</tr>
<tr>
<td>C.He.</td>
<td>57 M</td>
<td>190/120</td>
<td>1.9</td>
<td>20.0</td>
<td>0</td>
<td>Crush injury</td>
</tr>
<tr>
<td>D.M.</td>
<td>34 M</td>
<td>160/110</td>
<td>3.0</td>
<td>2.0</td>
<td>1.4</td>
<td>Poisoning?; oligemic shock?</td>
</tr>
<tr>
<td>J.B.</td>
<td>35 M</td>
<td>150/80</td>
<td>0</td>
<td>0.4</td>
<td>0.3</td>
<td>Crush injury</td>
</tr>
<tr>
<td>S.S.</td>
<td>38 M</td>
<td>160/110</td>
<td>5.6</td>
<td>0.9</td>
<td>1.9</td>
<td>Severe fluid and electrolyte depletion; diabetic acidosis</td>
</tr>
<tr>
<td>A.B.</td>
<td>40 M</td>
<td>160/90</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>Oligemic shock following ligation of inferior vena cava</td>
</tr>
<tr>
<td>T.B.</td>
<td>55 M</td>
<td>120/80</td>
<td>0</td>
<td>1.0</td>
<td>0.5</td>
<td>Biliary tract surgery</td>
</tr>
<tr>
<td>R.M.</td>
<td>37 M</td>
<td>170/110</td>
<td>0</td>
<td>0.0</td>
<td>0.1</td>
<td>Crush injury, multiple fractures</td>
</tr>
<tr>
<td>C.H.</td>
<td>36 M</td>
<td>160/90</td>
<td>1.2</td>
<td>1.1</td>
<td>0</td>
<td>Upper respiratory infection? fluid and electrolyte depletion</td>
</tr>
<tr>
<td>B.H.</td>
<td>16 M</td>
<td>180/86</td>
<td>4.0</td>
<td>4.0</td>
<td>0</td>
<td>Crush injury</td>
</tr>
<tr>
<td>H.K.</td>
<td>53 M</td>
<td>160/90</td>
<td>2.0</td>
<td>3.3</td>
<td>0.6</td>
<td>Crush injury; multiple fractures</td>
</tr>
<tr>
<td>J.H.</td>
<td>32 F</td>
<td>180/110</td>
<td>0</td>
<td>3.0</td>
<td>3.0</td>
<td>Incomplete abortion (septic?); pre-existing hypertension</td>
</tr>
<tr>
<td>H.V.</td>
<td>62 M</td>
<td>210/130</td>
<td>0</td>
<td>2.7</td>
<td>0.6</td>
<td>Hemorrhage, aneurysm of abdominal aorta (resection); pre-existing hypertension</td>
</tr>
<tr>
<td>N.W.</td>
<td>43 F</td>
<td>180/100</td>
<td>0</td>
<td>0.0</td>
<td>1.8</td>
<td>Mushroom poisoning</td>
</tr>
<tr>
<td>G.K.</td>
<td>42 M</td>
<td>90/75</td>
<td>10.0</td>
<td>10.0</td>
<td>0</td>
<td>Fluid and electrolyte depletion</td>
</tr>
<tr>
<td>H.S.</td>
<td>65 M</td>
<td>110/80</td>
<td>2.0</td>
<td>2.0</td>
<td>0</td>
<td>Hemorrhage, aneurysm of abdominal aorta</td>
</tr>
<tr>
<td>T.E.</td>
<td>22 M</td>
<td>120/80</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>Postvalvulotomy</td>
</tr>
<tr>
<td>D.F.</td>
<td>52 F</td>
<td>120/84</td>
<td>1.0</td>
<td>1.8</td>
<td>0</td>
<td>Postvalvulotomy</td>
</tr>
</tbody>
</table>

--- = Not done because of death or discharge.
### Table 2

**Clinical and Laboratory Findings in Eleven Patients with Hypertension and Renal Disease**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, sex</th>
<th>Blood pressure, mm. Hg</th>
<th>Optic fundi*</th>
<th>Blood urea nitrogen, mg./100 ml</th>
<th>Plasma vasoconstrictor activity, µg./100 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated hypertension Polyarteritis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R.T.</td>
<td>21</td>
<td>250/160</td>
<td>IV</td>
<td>(2.4) †</td>
<td>30.0</td>
</tr>
<tr>
<td>M.M.</td>
<td>17</td>
<td>150/130</td>
<td>III</td>
<td>150</td>
<td>7.5</td>
</tr>
<tr>
<td>Systemic lupus erythematosus:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.B.</td>
<td>20</td>
<td>200/128</td>
<td>IV</td>
<td>125</td>
<td>3.3</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic glomerulonephritis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P.F.</td>
<td>35</td>
<td>180/110</td>
<td>IV</td>
<td>25-80</td>
<td>0</td>
</tr>
<tr>
<td>R.H.</td>
<td>30</td>
<td>160/100</td>
<td>Normal</td>
<td>15-90</td>
<td>0.6</td>
</tr>
<tr>
<td>F.S.</td>
<td>40</td>
<td>190/110</td>
<td>II</td>
<td>30-90</td>
<td>0.4</td>
</tr>
<tr>
<td>J.C.</td>
<td>19</td>
<td>250/95</td>
<td>IV</td>
<td>45-160</td>
<td>0.3-0.8</td>
</tr>
<tr>
<td>H.G.</td>
<td>23</td>
<td>190/120</td>
<td>Normal</td>
<td>30-80</td>
<td>0.9</td>
</tr>
<tr>
<td>C.S.</td>
<td>41</td>
<td>150/100</td>
<td>Normal</td>
<td>30-90</td>
<td>0</td>
</tr>
<tr>
<td>Polycystic renal disease:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.A.</td>
<td>27</td>
<td>160/90</td>
<td>Normal</td>
<td>30-70</td>
<td>0</td>
</tr>
<tr>
<td>Subacute glomerulonephritis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K.S.</td>
<td>13</td>
<td>120/80</td>
<td>Normal</td>
<td>60</td>
<td>0</td>
</tr>
</tbody>
</table>

*Graded according to Keith-Wagener classification.
† Figure in parentheses = serum creatinine, mg. per 100 ml.

Blood obtained from a peripheral vein, the inferior vena cava, or a radial artery was centrifuged and prepared as described by Helmer and Judson;¹⁴ the treated plasma (without correction to pH 7.4) was assayed for vasoconstrictor and vasopressor activity, with use of synthetic asp¹-val⁵-angiotensin II* as standard. Plasma activity was expressed as µg. of synthetic angiotensin II per 100 ml. of plasma.

**Bioassay Methods**

**Vasoconstrictor Activity Assay**

The method of Helmer and Judson¹⁴ was used. Strips of rabbit aorta, 40 mm. by 3 mm., were prepared as described by Furchgott and Bhadrikom,¹⁵ and mounted in a muscle chamber. A tension of 1.84 Gm. was applied to the strip. The contraction of the strip in response to standard angiotensin or plasma was recorded on either a kymograph or by a displacement transducer† and a Sanborn recorder with a minimum paper speed of 1.25 mm. per minute. A satisfactory strip preparation for assay responded to a standard dose of 25 to 50 µg. (100 µg. per ml.) of synthetic asp¹-val⁵-angiotensin II by a contraction of at least 10 mm. or by a recorded pressure of 5 mm. Hg. The standard used in each test was freshly prepared from a stock solution containing 500

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*Hypertensin, Ciba Pharmaceutical Company, Summit, New Jersey; supplied through the courtesy of Anthony E. Abramo, M.D.

† Force displacement transducer FT038, Grass Instrument Company, Quincy, Massachusetts.
Linear dose-response relationship for angiotensin and for plasma.

µg. of angiotensin II per ml. of saline. The aortic strip did not contract on injection of 1 to 10 u. of vasopressin.*

As an approximate measure of quantitation, the response of the strip to plasma (plasma response = PR) was bracketed by its response to the standard doses of angiotensin II (angiotensin response = AR) before and after the unknown sample was tested. When the PR differed from the AR by less than 10 per cent, it was assumed that the vasoconstrictor activity of the plasma was equal to the standard dose of angiotensin times PR/AR. A zero level was assigned when 2 to 3 ml. of plasma caused no contraction of a satisfactory strip. Replicate determinations were performed four times on the same plasma sample, giving a coefficient of variation of 15.6 per cent.

Vasopressor Assay

The vasopressor activity of treated plasma was assayed in rats weighing 200 to 300 Gm., 24 hours after nephrectomy. Ten to 30 µg. of synthetic asp¹-val⁵-angiotensin II or up to 1.0 ml. of treated plasma was injected into the rat via the left jugular vein. Blood pressure was recorded with a Statham transducer via the left carotid artery.

Characteristics of the Bioassay System

Within the dose ranges tested, the steep or linear part of the logarithmic relationship between dose and response obtained (figs. 1 and 2).

After a latent period longer than that in AR of comparable magnitude, the aortic strip responded to plasma by a slow contraction (fig. 3).

As shown in figure 4, the latent periods were inversely related to the magnitude of AR (r = 0.849, p < 0.001) or PR (r = 0.408, p < 0.0025). Since AR and PR are a linear function of the dose, the latent period is an inverse function of the concentration of active plasma substance or of synthetic angiotensin II. The latent period in response to a mixture of angiotensin II and inactive treated human plasma was the same as that in response to a mixture of angiotensin II and

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*Pitressin, Parke-Davis & Company, Detroit, Michigan.

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saline (fig. 3), suggesting that the different latent period in response to plasma and angiotensin probably is not due to the physical characteristics of plasma per se.

The observation by Helmer and Judson\textsuperscript{14} that the vasoconstrictor activity of plasma is lost or markedly decreased by heat at pH 5.5 was confirmed in 27 observations by boiling the plasma for 10 minutes.

Plasma from three patients was assayed for pressor activity. As shown in table 3, the vasoconstrictor activity paralleled the vasopressor activity in all instances, but the former was consistently greater than the latter by ratios of 5.3, and 2.8 in each plasma sample from these patients.

**Results**

**Plasma Renin Activity in Normal Subjects**

The mean average vasoconstrictor activity of plasma in 23 normal subjects was comparable to that of 0.5 μg per 100 ml. (S.D.M. 0.13) of angiotensin II, with a range of 0 to 1.7 μg.

**Plasma Renin Activity in Acute Tubular Necrosis (Tables 1 and 4)**

1. **Oliguric phase.** The mean plasma activity for the 18 patients during the oliguric phase of ATN was comparable to that of 3.7 μg. (S.D.M. 1.0) of angiotensin II per 100 ml., with a range of 0 to 20 μg. The incidence of increased plasma renin activity exceeding 3 μg per 100 ml. was greater among patients with crush injuries or rhabdomyolysis (five of six patients, or 83 per cent) than among those whose renal failure was due to other causes (three of 12 patients, or 25 per cent). The difference was significant at a 3-per cent level. The increased plasma renin activity of the individual patient tended to diminish as the urinary output increased.

2. **Diuretic (recovery) phase.** During the diuretic phase, the mean value for plasma renin activity in eight patients was comparable to that of 0.5 μg (S.D.M. 0.2) per 100

ml. of angiotensin II, with a range of 0 to 2.0 μg. Only one value (patient D.W.) exceeded the upper limit of normal.

Thus, in the group with ATN, the plasma renin activity increased during the oliguric phase \( p < 0.005 \) and returned to normal during the recovery phase \( p > 0.1 \). The plasma renin activity in the entire group was inversely related to the daily urinary output \( r = -0.525, p < 0.001 \), as shown in figure 5.

Among the patients who had no history of pre-existing arterial hypertension or excessive fluid and sodium retention, the incidence of arterial hypertension (systolic > 160 or diastolic > 100 mm. Hg) was greater when plasma renin activity exceeded 3 μg. per 100 ml. (eight of 10) than when plasma renin activity did not exceed 3 μg. per 100 ml. (two of 20) \( p = 0.02 \) per cent)

**Hypertension and Renal Disease (Table 2)**

1. **Acute tubular necrosis**. The plasma renin activity was increased in each of these three patients, ranging from 3.3 to 30 μg. per 100 ml., with a mean of 13.5 μg. (S.D.M. 8.38, \( p < 0.5 \)). Patient R.T., whose plasma exhibited the highest renin activity of all human subjects studied, showed no evidence of heart failure until she succumbed to infarction and acute perforation of the small bowel; it is thus highly improbable that plasma activity in these subjects was related to circulatory failure.\(^{16}\)

2. **Chronic (terminal) renal failure.** In none of the patients in this group did the plasma renin activity exceed the normal range, despite various degrees of hypertensive cardiovascular disease and heart failure: the mean value was 0.2 μg. per 100 ml. (S.D.M. 0.07, \( p > 0.1 \)) of angiotensin with a range of 0 to 0.9 μg.

Results of assays in all groups studied are summarized in table 4 and figure 6.

**Discussion**

According to Helmer and Judson, and Davis and his co-workers, the treated plasma

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*Table 4*

**Summary of Plasma Renin Activity in Human Subjects Studied**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of subjects</th>
<th>No. of determinations</th>
<th>Range, μg./100 ml.</th>
<th>Mean, μg./100 ml.</th>
<th>S.D.M.*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>23</td>
<td>23</td>
<td>0-1.7</td>
<td>0.5</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Acute tubular necrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in oliguria</td>
<td>18</td>
<td>30</td>
<td>0-20</td>
<td>3.7</td>
<td>1.0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>in diuresis</td>
<td>8</td>
<td>13</td>
<td>0-2</td>
<td>0.2</td>
<td>0.2</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accelerated phase</td>
<td>3</td>
<td>3</td>
<td>3-30</td>
<td>13.5</td>
<td>8.38</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Chronic (terminal) renal failure</td>
<td>8</td>
<td>18</td>
<td>0-0.9</td>
<td>0.2</td>
<td>0.07</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

*Standard deviation of mean.

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contains renin or renin-like substance. In the context of the current concept, angiotensin I is formed from renin substrate in the presence of the enzyme renin. The inactive angiotensin I is converted into active angiotensin II by converting enzyme present in plasma. The treated plasma contains all of these components necessary for formation of active angiotensin II. In addition, it contains angiotensinase. Since the converting enzyme is present in sufficient amount in the treated plasma, this enzyme is probably not a limiting factor for formation of angiotensin II. Accordingly, the assay method used in the present study measures the net activity of plasma components for formation of angiotensin II.

The prolonged latency of response to treated plasma (fig. 4) may reflect conversion of inactive angiotensin I into angiotensin II by the converting enzyme, which is inactive at the pH of 5.5 of treated plasma, but active at the pH (7.4) of Krebs buffer solution. Helmer observed that the vasopressor activity of natural asp1-leu5-angiotensin II equals that of synthetic asp1-val5-angiotensin II on cat preparation; whereas the vasodepressor activity of synthetic angiotensin II on the rabbit aortic strip is only one fourth that of the natural asp1-leu5-angiotensin II. If such a difference in the specific activity also holds between rat and rabbit aortic strip, then the difference between these two preparations, expressed as the equivalent of synthetic angiotensin II, which was observed in the present study, is probably more apparent than real.

The results of the present study and the histologic evidence of hyperfunction of the juxtaglomerular apparatus described by Goormaghtigh suggest continuing operation of the renin secretory mechanism in the oliguric phase of acute tubular necrosis. Although the exact mechanism regulating renin secretion defied long-continued search by many investigators, a sensing device—a volume or stretch receptor in the juxtaglomerular apparatus as proposed by Tobian—seems to provide an attractive explanation. The present study does not provide data concerning the renin secretory mechanism. Some features inherent in the diseases studied, however, seem to deserve comment. Panarteritis and fibrinoid degeneration of arterial walls in polyarteritis, and edema of renal tissue in acute tubular necrosis, which may conceivably involve the afferent arterioles, may encroach upon the lumen in a manner analogous to partial occlusion of a renal artery. The edema of the kidney may decrease the distensibility or the stretch of the juxtaglomerular apparatus. These phenomena appear to be the critical stimulus for hypersecretion of renin.

The persistent reduction of renal blood flow during the oliguric phase of acute tubular necrosis, while the general circulation has been restored to normal also deserves attention, although a causal relationship with renin secretion cannot be determined at present.

The arterial pressure is dynamically determined by cardiac output and by flow resistance. A change in total blood volume only indirectly entails changes in arterial blood volume and pressure. The causal relationship between renin and arterial hypertensive disease has not been clearly elucidated. There is little doubt that occlusion of a renal artery initiates acute arterial hypertension, and the affected kidney may release an increased amount of renin. Renal participation, how-
ever, in primary hypertension and in long-standing renovascular hypertension not necessarily reversible by removal of an abnormal kidney or by relief of the renal artery lesion, is obscure.

In general, the incidence of arterial hypertension appeared to be increased during the oliguric phase, in patients whose plasma renin activity exceeded 3 μg per 100 ml., but without pre-existing arterial hypertension or excessive salt and water retention. Particularly in two patients (D.W., C.H.e.), in whom the plasma renin activity was markedly elevated, the hypertension seems to have paralleled the plasma renin activity. These findings may suggest that significant elevation of blood pressure in some patients with acute tubular necrosis may be associated, at least in part, with increased plasma renin activity. It is interesting to note that while a fluid excess, estimated to be less than 1 liter, occurred in these patients, in another patient (S.S., table 1) arterial hypertension developed concurrently with a fluid excess estimated at 7.8 liters, but with no demonstrable elevation of plasma renin activity. The absence of demonstrable elevation in plasma renin activity resembles that in patients with practically nonexistent excretory renal function during the terminal stage of chronic renal disease.

The results of studies by others on renin in patients with accelerated (“malignant”) hypertension have varied; no increase or some degree of increase have been observed.

The data from the present study suggest that the nature and the duration of underlying disease processes may be an important consideration in studying renin in hypertension and renal disease. Thus, the patients with polyarteritis and systemic lupus erythematosus had clearly elevated plasma renin activity; whereas those in the terminal stage of chronic renal disease consistently had no elevation of activity. In patients of the latter group, the renin secretory mechanism in the kidney may be obliterated (by fibrosis and hyalinization) as suggested by the histologic study of juxtaglomerular cells by Turgeon et al.; a more credible explanation is that arterial hypertension is related to water and salt retention and to an extrarenal neurogenic mechanism (resetting of baroreceptor) rather than to the renin-angiotensin system.

Summary

By in vitro and in vivo bioassay methods, activity of plasma renin was studied in patients with acute tubular necrosis, polyarteritis, systemic lupus erythematosus, or the terminal stage of chronic renal disease.

Plasma renin activity was increased during the oliguric phase of acute tubular necrosis, polyarteritis, or systemic lupus erythematosus; it was not increased during the diuretic phase of acute tubular necrosis and in the terminal stage of chronic renal disease.

Acute reversible hypertension, observed in some patients during the oliguric phase of acute tubular necrosis, was associated with a marked increase in plasma renin. A similar association was observed in hypertensive patients with polyarteritis or systemic lupus erythematosus, but not in hypertensive patients with the terminal stage of chronic renal disease. These data suggest that the renin mechanism may participate in the acute hypertension of acute tubular necrosis, polyarteritis, and systemic lupus erythematosus, but not in chronic hypertension in the present study.

Acknowledgment

Appreciation is expressed to Dr. James Hopper for his constant encouragement; and to Drs. O. M. Helmer, R. E. Bolinger, and E. Grey Dimond for their support and guidance during the initial phase of this study and to Dr. Belding H. Scribner, for permission to include some of the patients in this study.

Addendum

Since this article was submitted for publication, Vander and Miller (Am. J. Physiol. 207:537, 1964) reported that during mannitol diuresis in the anesthetized dog the renal secretion of renin was inversely related to the rate of urinary sodium excretion. Furthermore, renin secretion rose when the ureter was clamped. Since the composition of the urine remains constant during mannitol diuresis, the rate of urinary sodium excretion appears to be a function of urine volume.

The inverse correlation between plasma renin activ-
ity and daily urine output observed in the present study (fig. 5) appears to be in accord with the experimental work of Vander and Miller. The following situations may conceivably influence the renal secretion of renin in acute tubular necrosis: (1) alteration of composition or flow rate of tubular fluid by increased nonselective back-diffusion; (2) obstruction of the tubular lumen by casts, creating a situation in the obstructed nephron similar to that produced by clamping of the ureter as was done by Vander and Miller.

References
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Lord Joseph Lister

Lord Joseph Lister (1827-1912), the first medical man ever to be elevated to the English peerage, opened the door to modern surgery through his discovery of antiseptic procedures. Until the 1860's surgery had proceeded slowly—despite the earlier discovery of anesthesia—because of the gangrene and blood poisoning that usually accompanied even the setting of a compound fracture. Lister's history-making and successful operation was performed while an assistant pumped a spray of carbolic acid throughout the operating room, an innovation based on Lister's theory of airborne infection. The success of this technique enabled Lister, and other surgeons, to perform operations that had been unthought of until then. His revolutionary procedure paved the way to modern heart and brain surgery.
Plasma Renin Activity in Acute Tubular Necrosis and Other Renal Diseases Associated with Hypertension
W. H. TU and Margaret Dawson

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