The Role of Sympathetic Activity in Normal Renin Essential Hypertension

FRANCISCO W. HONG TAI ENG, M.D., MARLA HUBER-SMITH, B.S., AND DAISY S. MCCANN, PH.D.

SUMMARY Understanding the connection between sympathetic activity and essential hypertension is still rudimentary. We studied interrelationships of plasma catecholamines, plasma renin activity (PRA), aldosterone, sodium intake, and therapeutic response of 20 normal renin hypertensives. Based on plasma norepinephrine (NE), this population fell into two distinct subsets. The 11 patients in the "normal" NE subset had a basal NE of 257 ± 49 pg/ml (vs 250 ± 62 pg/ml in normotensives), while nine patients in the "high" range NE group averaged 522 ± 125 pg/ml. Both NE subsets showed significant correlation between mean arterial pressure (MAP) and NE. Only the "normal" NE subset showed significant correlation between MAP and PRA, and MAP and aldosterone.

Correlations between changes in Na⁺ excretion and NE, PRA, and aldosterone were all negative and statistically significant. Blood pressure was controlled in eight of 11 "normal" NE patients but only in one of nine "high" NE patients by restriction of Na⁺ intake and/or use of a diuretic.

(Hypertension 2: 14-19, 1980)

KEY WORDS • essential hypertension • sympathetic nervous system • norepinephrine • renin activity • aldosterone • sodium intake

WETHER the sympathetic system plays a role in the pathogenesis and maintenance of some forms of essential hypertension is still debatable.1, 2 Excess sympathetic activity has been implicated in the pathogenesis of high renin essential hypertension,3-8 while suppression of sympathetic nerve function has been reported in subjects with low renin essential hypertension.6 A number of reports to the contrary can also be found in the literature.8-9

We have studied the interrelationships of plasma catecholamines, plasma renin activity (PRA), and plasma aldosterone, as well as their responses to restriction of sodium intake in a group of 20 normal renin hypertensives (normal renin as defined by Brunner et al.10). The study yields an insight into the potential role of plasma norepinephrine (NE) in the classification of essential hypertension.

Methods

This study (table 1) focused on 20 consecutive patients with normal renin essential hypertension (borderline to moderately severe), ages 29–74 years, who were seen for the first time by Dr. Eng. The population consisted of 11 men and nine women, 12 black and eight white. Criteria for admission to the study were: 1) confirmed diagnosis of hypertension based on arterial pressure greater than 140 mm Hg systolic and/or 90 mm Hg diastolic on prior clinic visits; 2) normal PRA levels; and 3) absence of antihypertensive medication. Mean arterial pressure (MAP) was calculated from the diastolic pressure plus one-third of the pulse pressure. Hypertension of renal origin was ruled out with the aid of blood urea nitrogen and serum creatinine measurements, and by intravenous pyelography. Informed consent was obtained from all patients in the study.

A 24-hour urine was collected by the patients for assay of sodium, potassium, creatinine, and aldosterone excretion rates. The collection was timed to begin 24 hours prior to a return appointment when baseline blood specimens were collected. Appointments were held between 9 a.m. and 11 a.m. so that all subjects had been up and active for at least 2 hours prior to blood sampling. A butterfly needle was inserted in the antecubital vein, and blood specimens were collected for PRA and plasma aldosterone. The needle was kept patent with heparin in saline (100 U/ml). The patient assumed a supine position and rested for 20 minutes; then blood was collected for plasma catecholamine assay. Arterial pressures were measured with the patient both seated and stand-
ing, the lowest of three successive readings being recorded in each instance. The patients were instructed to restrict sodium intake to 80 mEq/24 hours and to return 1 week later with another urine collected 24 hours immediately preceding the appointment, as before.

Each individual patient served as his or her own control; i.e., comparisons were made between hypertensive patients on an ad libitum diet and these same patients after restricted sodium intake. Patients were followed for 6-14 months. Diuretics and/or other chemotherapy was added when necessary.

Plasma NE means were calculated both from linear and log transformed data. The significance of differences between means was tested using Student's t test. Linear regression coefficients were determined with a programmable Monroe 325 calculator, and the significance again determined using Student's t test, where

\[ t = r \sqrt{\frac{N-2}{1-r^2}}. \]

The 24-hour urines were analyzed for Na⁺ and K⁺ by flame photometry, and for creatinine by the Folin Wu method. Urinary aldosterone was measured by radioimmunoassay (RIA), using an antibody purchased from Diagnostic Products Corp. (Culver City, CA). Plasma NE and epinephrine were measured as in earlier studies\textsuperscript{15, 16} by the single isotope derivative radioenzymatic technique;\textsuperscript{14} PRA and aldosterone levels were ascertained by RIA using the Clinical Assays' kit (Cambridge, MA) for the former, and a Diagnostic Products' antibody for the latter. The "normal" averages quoted are those derived from a group of healthy normotensive persons drawn largely from our laboratory staff (10 men, seven women; ages 17-63, mean age 34 ± 14 years). Blood for this group was obtained under the same conditions as for the hypertensive patients.

**Results**

The average MAP of the hypertensive group was 114 ± 11 mm Hg seated, and 123 ± 12 mm Hg stand-

**Table 1. Characteristics of Hypertensive Study Group.**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, sex, race</th>
<th>Height (in)</th>
<th>Weight (lb)</th>
<th>Average BP before study (mm Hg)</th>
<th>Heart rate</th>
<th>NE (supine) (pg/ml)</th>
<th>Epi (supine) (pg/ml)</th>
<th>PRA (after 2 hr active) (ng/ml/hr)</th>
<th>Na⁺ (mEq/24 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>38/F/B</td>
<td>62</td>
<td>174</td>
<td>187/110</td>
<td>108</td>
<td>238</td>
<td>58</td>
<td>1.86 ± 0.85</td>
<td>137</td>
</tr>
<tr>
<td>2</td>
<td>59/F/B</td>
<td>62</td>
<td>190</td>
<td>165/99</td>
<td>64</td>
<td>284</td>
<td>44</td>
<td>1.76 ± 0.78</td>
<td>145</td>
</tr>
<tr>
<td>3</td>
<td>67/F/B</td>
<td>62</td>
<td>121</td>
<td>177/85</td>
<td>64</td>
<td>344</td>
<td>74</td>
<td>2.11 ± 1.02</td>
<td>153</td>
</tr>
<tr>
<td>4</td>
<td>50/F/W</td>
<td>59</td>
<td>113</td>
<td>166/90</td>
<td>112</td>
<td>167</td>
<td>27</td>
<td>1.11 ± 0.68</td>
<td>143</td>
</tr>
<tr>
<td>5</td>
<td>29/M/W</td>
<td>69</td>
<td>195</td>
<td>130/98</td>
<td>76</td>
<td>249</td>
<td>10</td>
<td>1.08 ± 0.75</td>
<td>143</td>
</tr>
<tr>
<td>6</td>
<td>34/M/B</td>
<td>72</td>
<td>211</td>
<td>159/111</td>
<td>84</td>
<td>243</td>
<td>48</td>
<td>2.0 ± 1.25</td>
<td>140</td>
</tr>
<tr>
<td>7</td>
<td>39/M/B</td>
<td>74</td>
<td>285</td>
<td>151/112</td>
<td>76</td>
<td>247</td>
<td>25</td>
<td>1.59 ± 1.06</td>
<td>145</td>
</tr>
<tr>
<td>8</td>
<td>68/M/B</td>
<td>69</td>
<td>165</td>
<td>206/112</td>
<td>76</td>
<td>285</td>
<td>83</td>
<td>2.05 ± 0.75</td>
<td>140</td>
</tr>
<tr>
<td>9</td>
<td>32/F/B</td>
<td>63</td>
<td>111</td>
<td>151/116</td>
<td>70</td>
<td>282</td>
<td>27</td>
<td>2.35 ± 1.25</td>
<td>176</td>
</tr>
<tr>
<td>10</td>
<td>41/F/W</td>
<td>65</td>
<td>126</td>
<td>165/101</td>
<td>86</td>
<td>191</td>
<td>23</td>
<td>1.31 ± 0.91</td>
<td>131</td>
</tr>
<tr>
<td>11</td>
<td>42/M/W</td>
<td>68</td>
<td>226</td>
<td>148/90</td>
<td>64</td>
<td>298</td>
<td>34</td>
<td>1.76 ± 0.94</td>
<td>114</td>
</tr>
</tbody>
</table>

**Baseline laboratory data**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, sex, race</th>
<th>Height (in)</th>
<th>Weight (lb)</th>
<th>Average BP before study (mm Hg)</th>
<th>Heart rate</th>
<th>NE (supine) (pg/ml)</th>
<th>Epi (supine) (pg/ml)</th>
<th>PRA (after 2 hr active) (ng/ml/hr)</th>
<th>Na⁺ (mEq/24 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±sd</td>
<td>45 ±14</td>
<td>66 ±5</td>
<td>174 ±55</td>
<td>164 ±21/102 ±10</td>
<td>80 ±17</td>
<td>257 ±49</td>
<td>41 ±22</td>
<td>1.72 ± 0.41</td>
<td>142 ±15</td>
</tr>
<tr>
<td>Mean ±sd</td>
<td>49 ±16</td>
<td>68 ±5</td>
<td>168 ±48</td>
<td>161 ±14/99 ±11</td>
<td>90 ±10</td>
<td>552 ±125</td>
<td>62 ±24</td>
<td>1.99 ± 0.65</td>
<td>144 ±23</td>
</tr>
</tbody>
</table>

B = black; W = white; M = male; F = female; NE = norepinephrine; Epi = epinephrine; PRA = plasma renin activity; BP = blood pressure.

*Normal NE group.

†High NE group.

Patient 1 was off medication for 2 weeks, Patient 20 for 1 week. All others had either never been on treatment (n = 14) or had been off for 1 month or more.
ing (mean ± SD). The MAP figures are derived from systolic pressures of 151 ± 26 mm Hg (seated), 156 ± 23 (standing); and diastolic pressures of 95 ± 11 (seated), 106 ± 11 (standing) (table 2). There were no statistically significant differences between the measured biochemical parameters of the study group as compared to those of normal controls with the exception of the catecholamine levels. Urinary creatinine ranged from 750-2000 mg/24 hr. The potassium excretion rate was within the normal range. The plasma NE of the supine hypertensive subjects averaged 390 ± 175 pg/ml as compared to 250 ± 62 pg/ml for normal controls, and 654 ± 282 pg/ml for standing hypertensives as compared to 405 ± 110 pg/ml for normal controls. (The means obtained from log transformation of the supine data are 355 and 242 pg/ml respectively.)

Peripheral epinephrine levels were also significantly higher for the supine hypertensive patients (50 ± 26 pg/ml) as compared to those of normal controls (30 ± 18 pg/ml). This difference was lost upon standing: for the hypertensive group the mean was 65 ± 32 pg/ml as compared to 55 ± 22 pg/ml for normal controls. The mean NE increase on standing was a substantial 66%; that for epinephrine was 28% and not statistically significant. (The interassay coefficient of variation for NE in our hands is 0.09%, while that for epinephrine is 0.32. The difference is due to the fact that normal epinephrine levels, in the range of 28-35 pg/ml, are near the limit of assay sensitivity,14 at an order of magnitude lower than that of NE.)

Significant correlation for baseline levels was found between supine NE and both sitting and standing MAP, (r = 0.49, n = 20, p < 0.025). A consideration of plots of supine NE versus PRA and plasma aldosterone (the latter is shown in figure 1 and is similar to the former) led us to conclude that we are dealing with two different populations: 1) the "normal" NE group with NE levels in the range of 257 ± 49 pg/ml, and 2) the "high" NE group with

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**Table 2. Effect of Sodium Restriction on Blood Pressure, Catecholamines, Plasma Renin Activity, Plasma, and Urinary Aldosterone of Hypertensive Patients**

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Normal controls (unrestricted sodium)</th>
<th>Hypertensive patients: unrestricted sodium diet</th>
<th>Hypertensive patients: 80 mEq Na⁺ diet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total group</td>
<td>Normal NE subset</td>
<td>High NE subset</td>
</tr>
<tr>
<td>Systolic BP sitting</td>
<td>121 ± 10</td>
<td>151 ± 26</td>
<td>150 ± 22</td>
</tr>
<tr>
<td>Diastolic BP sitting</td>
<td>74 ± 8</td>
<td>95 ± 11</td>
<td>93 ± 13</td>
</tr>
<tr>
<td>Systolic BP standing</td>
<td>127 ± 12</td>
<td>156 ± 23</td>
<td>150 ± 13</td>
</tr>
<tr>
<td>Diastolic BP standing</td>
<td>89 ± 11</td>
<td>106 ± 11</td>
<td>103 ± 11</td>
</tr>
<tr>
<td>NE supine (pg/ml)</td>
<td>250 ± 62</td>
<td>390 ± 175*</td>
<td>257 ± 49</td>
</tr>
<tr>
<td>NE standing (pg/ml)</td>
<td>405 ± 110</td>
<td>654 ± 282*</td>
<td>450 ± 92</td>
</tr>
<tr>
<td>Epi supine (pg/ml)</td>
<td>30 ± 18</td>
<td>50 ± 26*</td>
<td>41 ± 22</td>
</tr>
<tr>
<td>Epi standing (pg/ml)</td>
<td>55 ± 22</td>
<td>65 ± 32</td>
<td>56 ± 24</td>
</tr>
<tr>
<td>PRA (mg/ml/hr)</td>
<td>2.0 ± 0.9</td>
<td>1.84 ± 0.53</td>
<td>1.72 ± 0.41</td>
</tr>
<tr>
<td>p aldosterone (pg/ml)</td>
<td>70 ± 45</td>
<td>77 ± 23</td>
<td>70 ± 19</td>
</tr>
<tr>
<td>u aldosterone (ng/24 hr)</td>
<td>12 ± 5</td>
<td>11 ± 4</td>
<td>10 ± 4</td>
</tr>
<tr>
<td>u sodium (mEq/24 hr)</td>
<td>120 ± 50</td>
<td>143 ± 18</td>
<td>142 ± 15</td>
</tr>
<tr>
<td>u potassium (mEq/24 hr)</td>
<td>55 ± 39</td>
<td>67 ± 17</td>
<td>66 ± 17</td>
</tr>
<tr>
<td>u creatinine (g/24 hr)</td>
<td>1.2 ± 0.4</td>
<td>1.21 ± 0.36</td>
<td>1.3 ± 0.41</td>
</tr>
</tbody>
</table>

* Differences between normotensive and hypertensive patients significant at p < 0.05 confidence level.
† Differences between hypertensive patients on an ad libitum diet and a restricted sodium intake significant at p < 0.05 confidence level. Hypertensive pretreatment levels are for 20 patients except for two standing catecholamines where n = 18. The 80 mEq diet figures are based on n = 17 for urinary measures and n = 18 for plasma measures.

Abbreviations: BP = blood pressure; NE = norepinephrine; Epi = epinephrine; PRA = plasma renin activity; p = plasma; u = urine.
plasma NE levels at 522 ± 125 pg/ml. All of the data were considered both for the total group and for the two NE subsets. Correlations between the baseline parameters on an ad libitum sodium diet are shown in table 3 for each of the two hypertensive subsets.

Among the biochemical parameters of the normal NE subset, significant positive correlations were observed between seated MAP and supine NE, and PRA and aldosterone. Significant positive correlations were also obtained between supine NE and PRA and aldosterone. On the other hand, in the high NE subset, the only significant correlation with seated MAP was the supine NE. In this group significant negative correlations were obtained between supine NE and urinary sodium and between standing NE and urinary aldosterone and sodium.

PRA and aldosterone interrelationships were high, as were those of plasma and urinary aldosterone.

Three patients returned to the unit after 1 week of salt restriction without 24-hour urines: two with blood pressure in the normal range (< 140/90 mm Hg), one with unchanged MAP. Compliance with the salt restriction for the remaining 17 subjects was estimated by the decrease in sodium excretion: the mean Na⁺ excretion for 17 subjects fell to 67 ± 30 mEq/24 hr. Concurrently, mean plasma NE, PRA, and aldosterone each rose, while epinephrine values remained unchanged (table 2). Based on linear regression curves, correlations for these increases with the change in Na⁺ excretions were all negative and statistically significant (table 4). Overall MAP fell in 12 of 20 patients placed on the low sodium diet. The mean decrease in MAP for the normal NE subset was 10.8 ± 10.6 mm Hg, while for the high NE subset it was 6.8 ± 9.1 mm Hg (p = not significant). Removal from the normal NE subset of the single subject whose MAP did not drop on salt restriction alters the average MAP of this group from 10.8 ± 10.6 to 13.3 ± 7.6 mm Hg. Correlation of change in MAP with the change in sodium excretion was statistically not significant, either for the total group (r = 0.30, n = 17) or for the subsets. There was no significant change in mean heart rate for either group.

The hypertension of eight of 11 subjects in the normal NE subset (NE < 374 pg/ml) normalized (< 140/90 mm Hg) in response to restriction of the Na⁺ intake and/or a diuretic. This was true of only one of the high NE subset; the remaining eight of the nine subjects required further chemotherapy.

Follow-up of these subjects for periods ranging from 6 to 14 months has confirmed the persistence of the difference in the responses of the two subsets of
TABLE 3. Correlations Between Baseline Parameters of the Hypertensive Groups Measured Pretreatment on an ad libitum Sodium Diet.

<table>
<thead>
<tr>
<th>MAP sit.</th>
<th>MAP STG.</th>
<th>NE sup.</th>
<th>NE STG.</th>
<th>E sup.</th>
<th>E STG.</th>
<th>PRA</th>
<th>p Aldo</th>
<th>u Aldo</th>
<th>u Na⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP sit.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>88</td>
<td>59</td>
<td>59</td>
<td>57</td>
<td>55</td>
<td>0.25</td>
<td>0.65</td>
<td>0.59</td>
<td>0.37</td>
<td>0.72</td>
</tr>
<tr>
<td>MAP STG.</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>0.01</td>
<td>0.09</td>
<td>0.19</td>
<td>0.18</td>
<td>0.05</td>
<td>0.07</td>
<td>0.38</td>
<td>0.30</td>
<td>0.16</td>
</tr>
<tr>
<td>NE sup.</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>0.33</td>
<td>0.24</td>
<td>0.32</td>
<td>0.44</td>
<td>0.15</td>
<td>0.08</td>
<td>0.76</td>
<td>0.52</td>
<td>0.87</td>
</tr>
<tr>
<td>NE STG.</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>79</td>
<td>0.25</td>
<td>0.25</td>
<td>0.35</td>
<td>0.41</td>
<td>0.58</td>
<td>0.09</td>
<td>0.64</td>
<td>0.08</td>
<td>0.64</td>
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<tr>
<td>E sup.</td>
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<tr>
<td>50</td>
<td>0.39</td>
<td>0.01</td>
<td>0.03</td>
<td>0.69</td>
<td>0.44</td>
<td>0.02</td>
<td>0.58</td>
<td>0.12</td>
<td>0.33</td>
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<tr>
<td>E STG.</td>
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<tr>
<td>48</td>
<td>0.78</td>
<td>0.84</td>
<td>0.80</td>
<td>0.41</td>
<td>0.66</td>
<td>0.03</td>
<td>0.41</td>
<td>0.09</td>
<td>0.66</td>
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<tr>
<td>PRA</td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
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<td>49</td>
<td>0.76</td>
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<td>0.66</td>
<td>0.03</td>
<td>0.41</td>
<td>0.09</td>
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</tr>
<tr>
<td>p Aldo</td>
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<tr>
<td>u Aldo</td>
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<tr>
<td>u Na⁺</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

MAP = mean arterial pressure, NE = norepinephrine, E = epinephrine, PRA = plasma renin activity, pAldo = plasma aldosterone, uAldo = urinary aldosterone, uNa⁺ = urinary sodium; sit = sitting, stg = standing, sup = supine; n = 9 refers to the high NE group, n = 11 to the low NE subset. Statistically significant correlations (p < 0.05) are shown in heavy type.

patients to therapy. Three patients were able to maintain normal blood pressure throughout the period of the study without intervention other than compliance with a low sodium diet.

Discussion

At present, evaluation of the sympathetic system appears to be best achieved by measuring circulating catecholamines. Such plasma assays, especially that of NE, have come of age and can be performed with considerable confidence. It does remain important with this assay, as with the measurement of other stress-related hormones such as cortisol, that precautions be observed in the specimen collection. Comparable data require comparable situations, i.e., control of position (supine or upright), unstimulated (or equally stressed) subjects, etc. Lake et al. have reported a direct correlation between age and plasma catecholamine levels. Like De Champlain and colleagues, we have not been able to discern such a relationship in our limited normotensive population.

The literature relating plasma catecholamines with hypertension is by no means uniform. Christensen and Christensen reported normal total plasma catecholamine levels in 16 patients with renal and essential hypertension. A lack of correlation between plasma NE levels and blood pressure has also been reported by other groups. Louis et al. reported a highly significant relationship between resting diastolic pressure and basal plasma NE concentrations of 31 patients with essential hypertension. De Champlain et al. found that 13 of 22 patients with essential hypertension had plasma catecholamine levels above the range encountered in their normotensive control population. The two hypertensive groups in this study were not characterized further. DeQuattro and various co-workers argue for a neurogenic origin of high renin hypertension based on a prevalence of high total plasma catecholamine levels.

Our study group was comprised of normal renin hypertensives. Based on plasma NE concentration, this population fell into two fairly distinct subsets that showed differences beyond the plasma catecholamine concentration although their MAP was similar. The two groups were designated as a normal NE subset with plasma NE levels below 374 pg/ml and high NE subset with NE levels above 374 pg/ml. The high NE subset is in the high normal rather than abnormal range characteristic of pheochromocytoma patients. Both NE subsets showed significant correlation between MAP and plasma NE concentrations. While the coefficient of correlation decreased (r = 0.49), it remained significant for the total group, a finding that agrees with data by Weidmann et al., who reported that urinary excretion of NE (but not epinephrine) correlated significantly with blood pressure in their population of benign essential hypertensives. The lower r value obtained for the total group, as com-
pared to the coefficient of correlation obtained for either of the subsets, supports the division of the hypertensive population into two subsets. Only the normal NE subset showed significant correlation between MAP and PRA as well as between MAP and the two aldosterone measurements. The normal NE group also showed the best correlation of supine NE with PRA and plasma aldosterone. Finally, this group had hypertension that was most responsive to Na+ restriction and/or diuretics. Since for a given blood pressure level in the high NE subset, only the NE level of the parameters measured differs from that in the normal NE subset, it appears that blood pressure in the high NE subset is more influenced by sympathetic nerve activity than by the renin-angiotensin-aldosterone axis.

The problems raised by the non-uniform response of both blood pressure and the renin-angiotensin system to severe levels of Na+ depletion, even within a given renin category, were recently discussed by Gavras et al. These authors concluded that "sufficient" sodium depletion would cause a fall in blood pressure in all hypertensive subjects and therefore correct the lack of uniform response. The crux of the problem becomes one both of theoretical definition and practical attainment of "sufficient" sodium depletion. Our data suggest that the influence of sympathetic activity on the cardiovascular system rather than on the renin-angiotensin system may provide the missing parameter. Our data therefore suggest that measures aimed at blocking the effects of the renin-angiotensin-aldosterone axis can be expected to have less effect on the blood pressure of the high NE subset than of the normal NE subset.

Sever et al. proposed that the demonstration of a role for plasma NE in essential hypertension required a postural challenge. Our data did not gain substantially by inclusion of these measures. On the whole, interrelationships between the various parameters became poorer when standing catecholamine values were considered rather than supine ones.

Restriction of sodium intake led to inversely proportional increases in NE, PRA, and plasma aldosterone but not epinephrine. In as yet unpublished studies we have seen substantial epinephrine increases in emotionally stressed patients. Romoff et al. reported increases in plasma epinephrine concentrations in patients on severely restricted sodium intake. The restriction to 80 mEq Na+/24 hr is a very moderate one, and the unchanged epinephrine suggests that little or no stress was experienced by our patients. In any event, the sodium restriction played no role in the adrenal epinephrine secretion, whereas it did affect sympathetic NE secretion. The highest correlation among the changes measured with sodium restriction was obtained between changes in sodium excretion and changes in plasma NE concentration. In his review of the sympathetic system in hypertension, De Champlain suggested not only a bimodal distribution of the hypertensive population on the basis of the sympathetic output, but also that studies undertaken from this point of view might lead to the development of more rational and efficient therapeutic approaches to this ill-defined, chronic disease. Our data support these concepts.

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