Cardiovascular and Humoral Responses to Extremes of Sodium Intake in Normal Black and White Men

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SUMMARY To examine possible racial differences in the relationship between urinary sodium excretion ($U_{Na}$) and blood pressure in whites and blacks, and to characterize cardiovascular, renal and humoral responses, we studied 14 normotensive men (seven white and seven black) at six levels of sodium intake from 10-1500 mEq/24 hrs. Systolic and diastolic pressure increased from $113 \pm 2/69 \pm 2$ mm Hg (SEM) at the 10 mEq/24 hr level of sodium intake to $131 \pm 4/85 \pm 3$ mm Hg at the 1500 mEq/24 hr level of sodium intake ($p < 0.001$). Cardiac index increased concomitantly from $2.6 \pm 0.1$ to $3.6 \pm 0.3$ l/min/m$^2$ ($p < 0.001$). Linear and quadratic regression analysis of the relationship of $U_{Na}$ and blood pressure revealed that blacks had higher blood pressures with sodium loading than whites. Sodium loading caused a significant kaliuresis that was greater in whites than blacks. Six subjects were restudied while receiving potassium replacement. Compared with initial responses, blood pressure was elevated to a lesser degree ($p < 0.02$) and a greater natriuresis appeared at a level of 1500 mEq/24 hr of sodium intake ($p < 0.02$). The data suggest that blacks have an intrinsic reduction in the ability to excrete sodium compared with whites. The increases in blood pressure with acute sodium loading can be attributed to an increase in cardiac index. Potassium balance appears to influence the responses in blood pressure that occur with sodium loading.

THE HYPOTHESIS that salt may be partially responsible for the development of arterial hypertension was first proposed in recorded medical history in the Nei Ching,1 "The Yellow Emperor's Classic of Internal Medicine" in 600 B.C. The Yellow Emperor said: "Hence if too much salt is used in food, the pulse hardens, tears make their appearance, and the complexion changes..." This idea has since been examined by numerous investigators; however, the evidence is mostly circumstantial.2 Increases in arterial blood pressure have been observed with increases in salt intake in subjects with diminished renal function since the report of Ambard and Beaujard in 1904.3 We recently reported that consistent increases in blood pressure occurred in normotensive human subjects when they were subjected to a sodium intake greater than 800 mEq per day.4 In the present report we have identified differences in response to sodium administration in black and white subjects that may be important in clarifying the increased prevalence of hypertension among blacks compared with whites. In addition, we have examined the cardiovascular responses associated with the blood pressure elevation. Finally, we have determined that the state of potassium balance may be an important factor in the development of the blood pressure elevation with increased salt loads.

Methods

Fourteen normotensive, healthy male volunteers (mean age 32 years, range 18-40 years) were recruited by advertisement and were studied at the Indiana University Clinical Research Center. The protocol was approved by the Indiana University Medical Center Human Use and Clinical Research Center Committees, and informed consent was obtained from each volunteer after detailed explanation of the procedures to be performed. Seven subjects were black and seven subjects were white. The black and white subjects were similar in age, and none had a family history of hypertension.

Observations were recorded at six levels of sodium intake — 10, 300, 600, 800, 1200, and 1500 mEq/24 hr. All 14 subjects were studied at the 10- and 300-mEq/24 hr levels. Eight subjects (four blacks and four whites) then received 800 and 1500 mEq/24 hr sodium, while six (three blacks and three whites) received 600 and 1200 mEq/24 hr sodium. The subjects were given a daily diet containing 10 mEq sodium, 80 mEq potassium, 65 g protein, 50 g fat, 270 g carbohydrate, 400 mg calcium, and 1000 mg phosphorus. The diet included standard items such as meat, eggs, vegetables, fruit and bread. Each subject consulted with the research dietician before the study. Personal food preferences were permitted as much as possible. All meals were eaten at the Clinical Research Center. Dietary sodium intake was maintained as 10 mEq/24 hr for 7 days. Two hundred ninety milliequivalents of sodium in the form of sodium...
chloride were added to the diet for 3 days (300-mEq sodium diet). Either an additional 590 or 790 mEq sodium (a diet of 600 and 800 mEq sodium) were added to the 10-mEq diet for the next 3 days. To achieve high sodium intakes, sodium was given with bouillon between meals and at bedtime. For the last 3 days, the subjects were hospitalized and received the 600-mEq or 800-mEq sodium diet. Through the night they received 600 or 700 mEq sodium, respectively (sodium intake of 1200 and 1500 mEq/24 hr) in the form of intravenous normal saline. Fluid intake (distilled water) was allowed as desired.

Six of the eight subjects (three black and three white) who received 1500 mEq/24 hr sodium at the highest level of sodium intake were restudied according to the same protocol, except that potassium deficits were avoided. The state of potassium balance was recalculated daily from the urinary potassium excretion of each subject. Potassium losses were replaced daily by oral potassium chloride elixir based on the previous day's potassium excretion.

The subjects were weighed every morning before breakfast after voiding. Blood pressures were taken daily before meals by the indirect auscultatory technique. The same mercury manometers (Baum, Inc., New York, New York) and cuffs were used throughout the study. The subjects rested supine in a darkened room for 5 minutes, and then blood pressure and measurements of heart rate were taken in the nondonnominant arm each minute for 5 minutes. The same observers were responsible for these measurements throughout the study.

Twenty-four-hour urine specimens were obtained daily for the determination of sodium, potassium and creatinine concentrations. At 8:00 a.m. on the morning of the final day at each level of sodium intake, blood specimens were obtained after 2 hours of ambulation for hematocrit, creatinine, sodium, potassium, plasma renin activity and plasma aldosterone concentrations.

Since invasive techniques were not acceptable, cardiac index, stroke index, end-systolic left ventricular volume, and end-diastolic left ventricular volume were measured noninvasively by echocardiography. These techniques have been extensively studied by cardiologists at Indiana University. Rasmussen et al. compared the echocardiographically determined mitral valve stroke volume to Fick stroke volumes in 16 patients with normal ventriculograms, and observed that the two techniques were highly correlated (r = 0.95). Our normal subjects were studied serially and therefore served as their own controls, permitting a careful assessment of relative changes.

Initially, left ventricular diastolic and systolic internal dimensions (LVIDd and LVIDs) were determined. The LVIDd was measured from the leading edge of the left septal surface to the leading edge of the posterior wall endocardium at the peak of the R wave. The LVIDs was measured from similar points at the peak of anterior position of the posterior left ventricular wall. End-systolic and diastolic volumes were determined by cubing the respective internal dimensions. The cube method was used because the subject group could be assumed to have symmetrically contracting, normally shaped left ventricles. Stroke index was estimated from the formula:

\[ \frac{(LVIDd)^3 - (LVIDs)^3}{BSA (m^2)} \]

and cardiac index was estimated using the formula:

\[ \frac{(LVIDd)^3 - (LVIDs)^3 \times HR}{BSA (m^2)} \]

where BSA = body surface area and HR = heart rate. All echocardiograms were recorded by the same technician and were evaluated independently by two observers. Electrocardiograms and chest roentgenograms were obtained on the final day of the 10-mEq diet and on the final day of the 1500-mEq diet.

**Subject Safeguards**

The tolerability of the protocol was examined in an initial pilot study. Two of the investigators and a medical student volunteer ingested first the 10-mEq/24 hr diet for 1 week, then the 800-mEq/24 hr diet for 1 week. We found that the diet was tolerable and that generous free water intake eliminated the tendency to develop diarrhea at the high sodium intake. After consulting a member of the Human Use Committee, approval was obtained to give additional sodium intravenously in the form of normal saline to these investigators. No ill effects were observed. Urinary sodium excretion approached the total sodium intake by 72 hours.

Four of the subjects (including the two investigators) are physicians, one teaches high school biology and the rest are Indiana University Hospital employees. All were aware of the nature and potential risks of the study. The subjects were examined by a physician investigator three times daily, except at the 1500-mEq/24 hr level of sodium intake, when they were examined four times daily.

**Laboratory Methods**

Sodium and potassium concentrations in plasma and urine were measured by a flame photometer (Instrumentation Laboratories, Boston, Massachusetts). Creatinine was measured by an automated technique (Technicon, Chauncey, New York). Plasma renin activity and plasma aldosterone were measured by previously reported radioimmunoassay methods. The data were analyzed statistically by analysis of variance (repeated measures when indicated), t test, regression analysis, and nonparametric tests, when appropriate. The relationship between urinary sodium excretion and blood pressure was also subject to quadratic regression analysis. The 95% limits of probability were considered significant.
Results

Blood Pressure Responses

Table 1 shows the systolic and diastolic blood pressure of each subject on the balance days at each level of sodium intake, and the probabilities by repeated measures analysis of variance. These probabilities indicate whether or not there was a significant interaction between blood pressure and sodium intake. There was considerable variability in the response within individual subjects. Although most developed a significant increase in both systolic and diastolic pressure with a high sodium intake, a few failed to increase either systolic or diastolic pressure. The whites developed a significant mean elevation (p < 0.05) in systolic and diastolic pressure at the 1200- mEq/24 hr sodium intake compared with the 10- mEq/24 hr sodium intake. The blacks developed significant increases by 800 mEq (p < 0.05), and again at 1500 mEq/24 hr (p < 0.05). When the data from all subjects were combined, systolic pressure increased significantly between the 10-800-mEq/24 hr levels and between the 1200-1500-mEq/24 hr levels of sodium intake (p < 0.05). Mean diastolic pressure increased, with significant increments at the 800- and the 1500-mEq/24 hr levels of sodium intake (p < 0.05).

The relationship between urinary sodium excretion and systolic blood pressure in white and black subjects is shown in figure 1. For the white subjects, linear regression analysis resulted in a significant relationship (r = 0.48, p < 0.001), defined by the expression: y = 111.5 + 0.0083x. Quadratic regression yielded a relationship (y = 112.4 + 0.000706x + 0.00000655x²) with a coefficient of correlation of 0.50 (p < 0.01). This relationship approached, but did not quite achieve, an improvement over the linear expression (0.1 > p > 0.05). In the black subjects, linear regression also yielded a significant relationship (r = 0.73, p < 0.001), defined by the expression: y = 113 + 0.0139x. However, the quadratic regression resulted in an improvement (p < 0.001) over linear regression.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Race</th>
<th>Blood pressure</th>
<th>Sodium intake (mEq/24 hr)</th>
<th>Probability</th>
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<td></td>
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<td>Diastolic</td>
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<td>70 ± 2</td>
<td>115 ± 2</td>
</tr>
<tr>
<td>All whites</td>
<td>Diastolic</td>
<td>69 ± 2</td>
<td>69 ± 2</td>
<td>71 ± 3</td>
</tr>
<tr>
<td>All blacks</td>
<td>Systolic</td>
<td>113 ± 2</td>
<td>68 ± 3</td>
<td>119 ± 2</td>
</tr>
<tr>
<td>All blacks</td>
<td>Diastolic</td>
<td>71 ± 3</td>
<td>71 ± 3</td>
<td>71 ± 3</td>
</tr>
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<td>All subjects</td>
<td>Systolic</td>
<td>113 ± 2</td>
<td>69 ± 2</td>
<td>117 ± 2</td>
</tr>
<tr>
<td>All subjects</td>
<td>Diastolic</td>
<td>70 ± 2</td>
<td>70 ± 2</td>
<td>71 ± 3</td>
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</table>
FIGURE 1. Relationship between urinary sodium excretion \( (U_{NaV}) \) and systolic pressure in whites and blacks. In whites the quadratic expression is convex downward; in blacks it is convex upward \( (p < 0.005) \).

\( r = 0.75, p < 0.001 \). The relationship is defined by: 
\[ y = 112 + 0.0233x - 0.000077x^2 \]
Comparison of the regression analysis on urinary sodium excretion and systolic blood pressure in the black and white subjects revealed significant differences in the linear \( (p < 0.01) \) and the quadratic regressions \( (p < 0.005) \). Moreover, the quadratic regression of the white subjects yielded a curve convex downward, while that of the blacks yielded a curve convex upward.

Similar analyses were performed on diastolic blood pressure (fig. 2). For the white subjects, the linear regression \( y = 70.1 + 0.0041x \) was significant \( (r = 0.26, p < 0.01) \); however, the quadratic expression \( y = 71.5 - 0.008x + 0.00001x^2 \) was an improvement over the linear expression \( (p < 0.01) \) and provided a correlation coefficient of 0.36 \( (p < 0.001) \). The curve of the quadratic expression was convex downward. In the black subjects, the linear regression yielded a highly significant correlation \( (r = 0.50, p < 0.001) \) defined by: 
\[ y = 69.8 + 0.0104x \]
The quadratic regression afforded no improvement \( (p < 0.5) \). The linear regressions of whites and blacks were significantly different \( (p < 0.01) \).

Sodium and Potassium Balance

The cumulative sodium data are depicted in figure 3. The net increase in total body sodium for the subjects who received 800 and 1500 mEq/24 hr was 1402 mEq, while those who received 600 and 1200 mEq/24 hr developed an 851-mEq increase in total body sodium. The cumulative potassium balance (fig. 4) became negative on day 10 in subjects receiving 800 and 1500 mEq/24 hr sodium, and on day 11 in those receiving 600 and 1200 mEq/24 hr. The subjects who received the higher sodium load developed a net potassium deficit of \(-263\) mEq, while those who received the smaller sodium load developed a net deficit of \(-163\) mEq.

The cumulative sodium retention for white subjects was 1100 mEq, which was not different from the 1162 mEq recorded for black subjects. However, the white subjects developed a net potassium deficit of \(-334\) mEq, while the black subjects developed a deficit of only \(-45\) mEq \( (p < 0.001) \). The difference in the state of potassium balance for white and black subjects on each study day is given in figure 5. Data from the sub-
subjects who received 600 and 1200 mEq/24 hr sodium at the higher levels were pooled with those who received 800 and 1500 mEq/24 hr, respectively. During the initial period of the study, when sodium intake was very low, the black subjects retained potassium to a greater degree than the whites. During the period of sodium loading, the whites excreted more potassium than the blacks.

Renal, Humoral and Cardiac Responses

Table 2 shows the changes in weight, plasma and urinary electrolytes, PAH and creatinine clearance, plasma renin activity, and plasma aldosterone concentrations as sodium balance was approached at each level of sodium intake. A significant interaction (repeated measures analysis of variance) was observed between sodium intake and weight, urinary sodium

![Cumulative Sodium Balance](image1)

**Figure 3.** Cumulative sodium data. Subjects who received 800 and 1500 mEq/24 hr (solid line after day 9) gained 1402 mEq sodium, and those who received 600 and 1200 mEq/24 hr (dashed line after day 9) gained 851 mEq sodium.

![Cumulative Potassium Balance](image2)

**Figure 4.** Cumulative potassium data. Sodium loading caused a loss of potassium at the higher levels of sodium intake.
and potassium excretion, creatinine clearance, plasma renin activity and plasma aldosterone concentration. Weight is expressed as the change in weight with progressive sodium intake greater than 10 mEq/24 hr. Weight increased with each increase in sodium intake (p < 0.05). The urinary sodium excretion approached balance at each level of sodium intake. Urinary potassium excretion increased between the 10-600- and 1200-1500-mEq/24 hr levels of sodium intake. No consistent changes in plasma sodium and potassium concentrations were observed. Increases in creatinine clearance were observed between the sodium intake levels of 10–600 and 1200–1500 mEq/24 hr. The clearance of PAH, however, was not affected. Plasma renin activity decreased until the 600-mEq/24 hr level of sodium intake, after which no further differences were discernible. Plasma aldosterone concentration decreased at the 300-, 800- and 1500-mEq/24 hr levels of sodium intake (p < 0.05).

Table 3 is a list of the cardiovascular responses after balance at each level of sodium intake. No consistent changes in pulse rate occurred. Cardiac and stroke indexes increased between the 10–800, and 800–1500-mEq/24 hr levels of sodium intake (p < 0.05). No changes in left ventricular end-systolic volume occurred; however, left ventricular end-diastolic volume increased at the highest level of sodium intake (p < 0.05).

No differences were identified when the white and black subjects were compared with respect to differences in weight, plasma electrolytes, tests of renal function, humoral responses of cardiac and stroke indexes.

**Effect of Potassium Replacement**

Data from the six subjects who were restudied with maintenance of potassium balance are displayed in table 4. In the initial study, repeated measures analysis of variance on the measurements revealed a significant interaction between sodium intake and both systolic and diastolic pressure. Under the conditions of the second study, no such interaction was apparent between sodium intake and diastolic pressure. Moreover, systolic and diastolic pressure were significantly lower at the 1500-mEq/24 hr level of sodium intake than in the first study (p < 0.02). Significant differences were also apparent in sodium excretion. In the second study, urinary sodium excretion at the 1500-mEq/24 hr level of sodium intake exceeded that of the first study (p < 0.02). However, the

![Figure 5. Comparison of the cumulative potassium data between blacks and whites. The blacks retained more potassium on a low sodium intake and lost less potassium on a high sodium intake than the whites.](image-url)
Table 3. Cardiovascular Responses Following Balance at Each Level of Sodium Intake (mean ± SEM)

<table>
<thead>
<tr>
<th>Sodium intake (mEq/24 hr)</th>
<th>10</th>
<th>300</th>
<th>600</th>
<th>800</th>
<th>1200</th>
<th>1500</th>
</tr>
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<tbody>
<tr>
<td>Subjects (n)</td>
<td>14</td>
<td>14</td>
<td>6</td>
<td>8</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Pulse (beats/min)</td>
<td>70 ± 3</td>
<td>65 ± 3</td>
<td>70 ± 3</td>
<td>62 ± 5</td>
<td>69 ± 3</td>
<td>55 ± 4</td>
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<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.6 ± 0.1</td>
<td>2.8 ± 0.2</td>
<td>2.6 ± 0.2</td>
<td>2.9 ± 0.1</td>
<td>3.0 ± 0.2</td>
<td>3.6 ± 0.3</td>
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<tr>
<td>Stroke index (ml/bent/m²)</td>
<td>41.8 ± 1.9</td>
<td>44.3 ± 2.4</td>
<td>40.4 ± 4.6</td>
<td>50.5 ± 2.4</td>
<td>45.7 ± 5.4</td>
<td>58.2 ± 3.0</td>
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<tr>
<td>Left ventricular end-systolic volume (ml)</td>
<td>40 ± 3</td>
<td>42 ± 3</td>
<td>37 ± 5</td>
<td>39 ± 2</td>
<td>33 ± 4</td>
<td>35 ± 4</td>
</tr>
<tr>
<td>Left ventricular end-diastolic volume (ml)</td>
<td>118 ± 4</td>
<td>127 ± 5</td>
<td>110 ± 9</td>
<td>142 ± 7</td>
<td>128 ± 9</td>
<td>153 ± 5</td>
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</table>

The remaining variables in table 4 were not significantly altered by potassium repletion during sodium loading.

Protocol Tolerance

The protocol was well tolerated by all participants, and none withdrew from the study. Chest roentgenograms regularly revealed a mild increase in heart size. Blunted costophrenic angles were detectable in four subjects at the end of the study. No electrocardiographic changes were observed. No subject developed dyspnea, orthopnea, rales or abnormal cardiac findings, although trace pedal edema was regularly detected at the 1500-mEq/24 hr level of sodium intake. No subject felt weakness; however, fatigue was a common complaint, ostensibly because of nocturia at the high sodium intakes. The subjects were monitored after the study. Within 3 days their blood pressure returned to baseline values, as did their sense of well-being.

Discussion

In these studies we intended to: 1) delineate the relationship between sodium intake and arterial blood pressure in normotensive man; 2) compare responses to sodium in whites and blacks; 3) elucidate the mechanism of any observed increases in blood pressure; 4) clarify the normal kidney’s maximal abilities to conduct sodium regulation; and 5) examine any role for potassium in the responses of blood pressure to large intakes of sodium. Early reports suggested that massive quantities of sodium were necessary to raise blood pressure. This conclusion was supported by the recent report of Lowder and Brown, who described a hypertensive man whose blood pressure returned to normal when the 1200 mEq/24 hr sodium bicarbonate he had been taking surreptitiously was withdrawn. Kirkendall et al. observed no increase in

Table 4. Comparison of Data (mean ± SEM) from Six Subjects Restudied with Maintenance of Net Zero Potassium Balance

<table>
<thead>
<tr>
<th>Sodium intake (mEq/24 hr)</th>
<th>10</th>
<th>300</th>
<th>800</th>
<th>1500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure (mm Hg)</td>
<td>111 ± 2</td>
<td>116 ± 2</td>
<td>121 ± 3</td>
<td>131 ± 4</td>
</tr>
<tr>
<td>Diastolic pressure (mm Hg)</td>
<td>114 ± 2</td>
<td>115 ± 3</td>
<td>122 ± 4</td>
<td>124 ± 4</td>
</tr>
<tr>
<td>Urinary sodium excretion (mEq/24 hr)</td>
<td>12 ± 1</td>
<td>282 ± 22</td>
<td>706 ± 24</td>
<td>1442 ± 36</td>
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<td>Weight (kg)</td>
<td>1.2 ± 0.2</td>
<td>2.3 ± 0.4</td>
<td>5.5 ± 0.6</td>
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<tr>
<td>Creatinine clearance (ml/week)</td>
<td>112 ± 6</td>
<td>128 ± 6</td>
<td>130 ± 6</td>
<td>142 ± 7</td>
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<tr>
<td>PAH clearance (ml/min)</td>
<td>495 ± 45</td>
<td>519 ± 16</td>
<td>543 ± 36</td>
<td>524 ± 39</td>
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<td>Plasma renin activity (ng AI/ml/3 hr)</td>
<td>13.5 ± 3.0</td>
<td>3.0 ± 0.7</td>
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<td>0.7 ± 0.1</td>
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<td>Plasma aldosterone (ng/100 ml)</td>
<td>14.8 ± 4.0</td>
<td>8.2 ± 1.1</td>
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<tr>
<td>Cardiac index (l/min/m²)</td>
<td>39.6 ± 9.1</td>
<td>10.8 ± 3.0</td>
<td>4.6 ± 1.6</td>
<td>1.5 ± 0.2</td>
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<td>Stroke index (ml/beat/m²)</td>
<td>26.3 ± 8.1</td>
<td>8.2 ± 1.1</td>
<td>4.5 ± 0.4</td>
<td>2.5 ± 0.2</td>
</tr>
</tbody>
</table>

Data from second study appear below those of the first.
blood pressure in normal subjects given 410 mEq sodium/24 hr for 1 month. We concluded that in an acute study, a sodium intake in excess of 800 mEq/24 hr would be necessary to increase blood pressure, and still higher sodium intakes would be necessary to verify the increases in blood pressure. Our pilot study demonstrated that young, healthy subjects could tolerate massive intakes for short periods without difficulty. Therefore, we selected six levels of sodium intake, four of which were relatively massive, and designed a protocol that would address our experimental questions with as few subjects as possible.

The data confirm that blood pressure can be raised acutely in normotensive man by increasing sodium intake to very high levels. The relevance of these acute studies to blood pressure regulation in essential hypertension cannot be ascertained from the present data; however, the recent demonstration by Kawasaki et al., who showed that the blood pressure of certain hypertensives was quite sensitive to dietary increases of sodium to 249 mEq/24 hr, emphasizes the importance of sodium intake to blood pressure regulation in some hypertensives. In addition, the inhabitants of northern Japan regularly ingest a diet containing in excess of 400 mEq sodium/24 hr and also have a prevalence of hypertensives among their population of 40%.15

Although none of the subjects in the present study had a family history of hypertension, they displayed considerable variability in their response to the salt loads. Tobian16 recently emphasized the hereditary aspects of susceptibility to sodium. Dahl17 clearly established this principle in experimental animals when he bred from a single strain a race of rats highly susceptible to salt hypertension and a second race highly resistant to hypertension. When fed a diet containing 8% sodium chloride, the susceptible rats regularly develop severe hypertension. Such a sodium intake is massive even in comparison to the quantity of sodium given our subjects. Michell18 has calculated that an 8% salt diet for a 330-g rat eating 20 g/day is equivalent to 5600 mEq per day in human terms.

The differences in blood pressure responses of white and black subjects support the concept of a genetic predisposition to salt sensitivity of blood pressure. These observations are of interest, since American blacks have a higher incidence of hypertension than American whites,19 even though whites and blacks consume similar quantities of dietary sodium.20 The findings suggest that blacks are more susceptible to the hypertensinogenic effects of sodium than whites. Previous observations from our laboratory21 indicated that blacks do not excrete an intravenous salt load as well as whites over a 24-hour period, and their plasma renin activity remains more suppressed. These differences cannot be explained by creatinine or PAH clearances. The recent work of Levy et al.22 suggested that differences in kallikrein excretion may be the cause.

Tobian et al.23 have recently described their observations on the reduced capacities of Dahl hypertension-prone rats to excrete salt. They found that kidneys from hypertensive animals, when perfused at a normal pressure, excreted subnormal amounts of salt and water compared with kidneys from salt-resistant animals. The kidneys of black subjects may differ from those of white subjects in the ability to excrete salt and water at a given perfusion pressure over a wide range of pressures.

Although whites and blacks developed similar degrees of sodium retention after sodium loading, blacks differed from whites in potassium excretion. During the 10-mEq/24 hr level of sodium intake the blacks accumulated more potassium than the whites, while with sodium loading, the whites excreted more potassium than the blacks. The kaliuretic response after sodium loading in both groups may be attributed to increased sodium delivery to the distal nephron,24 or physical displacement of potassium from intracellular stores by sodium.13 The differences cannot be explained by natriuresis, plasma renin activity, or plasma aldosterone concentration. Racial differences in potassium excretion have been observed by Langford and Watson.25 Their observations suggested that blacks ingest less potassium than whites; however, blacks have not been found to have a lower total body potassium content than whites.26,27

The increase in blood pressure in response to sodium loading may be the result of an increased cardiac index. While total peripheral resistance was not measured directly, calculated peripheral vascular resistance decreased. These observations are consistent with those of Kirkendall et al.,28 who found that forearm vascular resistance decreased in normotensive subjects given 410 mEq sodium/24 hr. Mark and associates, however, found that forearm vascular resistance increased in hypertensives when they were exposed to a similar sodium intake.29 Since cardiac index was not different in blacks and whites in the present study, the differences in blood pressure must be attributed to differing responses in peripheral vascular resistance. Since these studies were short-term, we could not examine the possibility of subsequent "whole body" autoregulation as postulated by Guyton and associates.30

The data from the present study suggest that normal kidneys have a profound capacity to excrete excess sodium. Our subjects readily excreted the highest level of sodium intake within 72 hours, and it was not until this level was administered that clinical signs of total body sodium excess such as trace edema became evident. Creatinine clearance increased in our subjects, an observation consistent with the increases in inulin clearance observed by Kirkendall et al. The clearance of PAH, on the other hand, did not increase, suggesting that the filtration fraction increased. Plasma renin activity and plasma aldosterone concentrations were suppressed to low values by the 300-mEq/24 hr level of sodium intake. Unless an altered sensitivity to these humoral substances occurred with...
sodium loading, it is unlikely that their suppression after further increases in sodium intake facilitated the excretion of the huge sodium load. The increase in glomerular filtration rate may account in part for the ability of our subjects to excrete the sodium load; however, the increased filtration fraction would be expected to counterbalance this effect. Although the elevated blood pressure was no doubt contributory, the mechanisms responsible for the natriuresis in our subjects are unknown.

In the first series of experiments, increases in blood pressure with sodium loading were accompanied by significant urinary losses of potassium, particularly in the white subjects. Six subjects agreed to be restudied under conditions in which losses of potassium were prevented. Their blood pressures did not increase to the same degree as in the first study. Their natriuretic responses to 1500 mEq/24 hr of sodium intake were greater than in the first study, suggesting that the potassium chloride may have caused natriuresis. How this effect was mediated is not clear, since no differences in renal function, plasma renin activity, or plasma aldosterone concentration were observed. The effect may have been nonspecific and might have occurred with any non-sodium-containing chloride salt. In addition, since no differences in body weight change or cardiac and stroke indexes appeared, an effect on peripheral vascular resistance was possible.

While sodium intake has been implicated in human hypertension and clearly shown to be hypertensogenic in the rat by Dahl, evidence suggests that potassium is protective. Meneely et al. demonstrated that salt-sensitive rats given extra potassium lived longer than control rats, even though their pressures were not lower. Dahl et al. found that when salt-sensitive rats were given diets containing the same amount of sodium chloride, but different potassium chloride concentrations, mean blood pressure was greater in the rats that received less dietary potassium. Langford and Watson expressed the relationship between the states of urinary sodium and potassium balance as the sodium/potassium ratio, and analyzed the blood pressure measurements of 600 persons. They identified a significant correlation with diastolic blood pressure that was not apparent when sodium excretion alone was used. Although our data were from a short-term study in which vast quantities of sodium were administered, they support the concept that the level of potassium intake modulates the effects of sodium intake on blood pressure.

In summary, we have demonstrated that a massive intake of sodium caused an increase in blood pressure in normotensive subjects, and that the increase in blood pressure could be attributed to an increased cardiac index. Blacks, who had a greater increase in blood pressure at the higher sodium intakes than whites, excreted less potassium. Potassium repletion had an ameliorative effect on the increase in blood pressure, which may have been related to more effective sodium excretion.

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