Interrelationships Between Blood Pressure, Sodium, Potassium, Serum Cholesterol, and Protein Intake in Japanese

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SUMMARY Interrelationships among blood pressure (BP), sodium (Na), potassium (K), dietary protein, and serum cholesterol level (Choi) were examined in 62% (1120) of 1818 Japanese inhabitants of both sexes aged over 30 years who lived in a rural village in Japan. Fasting single-spot urine specimens were collected in the morning to measure Na, K, urea nitrogen (UN), inorganic sulfate (SO\(_4\)), and creatinine (Cr). The Cr ratios of Na, K, UN, SO\(_4\), Na/K, and SO\(_4\)/UN were analyzed by multiple regression analysis to determine independent associations with BP together with age, obesity index, hematocrit (Hct), Choi, triglyceride (TG), and fasting serum glucose level (Glu). Except for Na/Cr in men, Na/Cr and Na/K were found to be independently and positively related to BP, particularly to systolic BP (SBP). In contrast, K/Cr and SO\(_4\)/UN (an index related to the dietary score of sulphur-containing amino acids derived mainly from animal protein) were both negatively associated with SBP, and UN/Cr (an index of total protein intake) was positively associated with SBP in men. Choi was linked to BP negatively in men but positively in women. Age, obesity index, TG, and Hct were generally positively and significantly related to BP in both sexes. The results confirmed on epidemiological grounds the positive link of Na and the negative link of K to BP within a single population in Japan. They further suggest, although only in men, that there is a negative relationship of Choi and dietary animal protein with BP. (Hypertension 6: 736-742, 1984)

KEY WORDS • sodium • potassium • animal protein • cholesterol • hypertension • multivariate analysis

HYPERTENSION and its sequelae greatly contribute to morbidity and mortality in middle-aged populations, especially in industrial societies, and multiple genetic or environmental factors influence blood pressure (BP) levels. Clinical and experimental evidence suggests a role for dietary salt in the genesis of hypertension.\(^1\)\(^-\)\(^3\) Yet, despite a considerable number of epidemiological surveys, conclusive results are lacking in Western societies\(^4\) that prove a positive correlation between dietary salt intake and BP within one population, as critically reviewed by Simpson\(^3\) in 1979. Except for the results reported by Kesteloot et al.\(^6\) convincing evidence is also lacking even in high-risk societies with a high salt consumption.

We have now extended our studies on the relationship between salt and BP in a rural Japanese population that consumes large amounts of salt. Our present study was performed in 1978 as a part of a comparison of farming and fishing villages with different death rates from stroke.\(^7\) To determine if there was an independent association between urinary Na output and BP within one population, we reanalyzed the data from the farming population. We used multiple regression analysis, as previously described.\(^8\)

We were particularly interested to see if there was a link between BP and dietary protein intake or serum cholesterol, as we previously found\(^9\) that a diet rich in protein (particularly animal protein) or in cholesterol attenuates the development of severe hypertension and prevents cerebral apoplexy in the stroke-prone spontaneously hypertensive rat (SP-SHR).

Materials and Methods

The study was carried out in the summer of 1978 in Daiwa Village, a small rural village with a population of 2700 that is secluded in the mountain area of Shimane Prefecture where the traditional Japanese life style and dietary habits have been well preserved for many years. The inhabitants are mostly farmers of a low socioeconomic class who rarely dine out.
All inhabitants aged over 30 years were encouraged to undergo general medical examinations conducted by the Shimane Institute of Health Science with the cooperation of the medical staff of Shimane Medical University. Participants were not informed of our particular interest in salt or protein intake in order to avoid deliberate changes in their usual dietary customs. Single-spot urine specimens after the first voiding, up to lunch time, were collected from all participants who had been fasting overnight, and the samples were stored at —20°C until assayed. Concentrations of Na and K were determined by flame photometry (Hitachi 205, Tokyo), urea nitrogen (UN) by the urease method, creatinine (Cr) by Jaffe’s procedure, and inorganic sulfate (SO₄) by the turbidimetric method described by Dodgson.¹⁰

Dietary Na and K ingestion relative to body size was then assessed by Na/Cr and K/Cr ratios, respectively, and protein intake by SO₄/Cr (a possible index of the amount of dietary-salt-containing amino acid derived mainly from animal protein”), UN/Cr (a possible index of total protein intake¹²), and SO₄/UN (an index reportedly related to the “net dietary protein calorie per cent” or sulfur amino acid score in diets³). Although whole-day urine specimens are more desirable for estimating sodium intake than single-spot urine samples, we used the latter because of the magnitude of the study. Also, we had previously shown both in a volunteer study with controlled diets¹³ and under field conditions” that partial urine samples could validly be used instead of 24-hour urine specimens.

Blood pressure was measured by well-trained medical staff with the use of a standard mercury sphygmomanometer. The subjects sat quietly for at least 5 minutes before BP measurement. Disappearance of the Korotkoff sounds (phase V) was used to determine the diastolic blood pressure (DBP). Obesity index was calculated (%) as the excess weight relative to the standard weight for height and sex determined from Minowa’s Chart¹⁶ (the standard reference chart in Japan). Blood specimens were collected while the subjects were fasting in the morning; they were analyzed for hemoglobin (Hb), hematocrit (Hct), cholesterol (Choi), triglycerides (TG), and glucose (Glu), by standard techniques.

Of 1818 subjects invited, 1180 (64.9%) agreed to participate; subjects without detectable diseases and without antihypertensive treatment, according to World Health Organization (WHO) criteria. The subjects taking antihypertensive drugs were excluded from analysis, which left 1120 inhabitants (503 men, 617 women) or 61.7% of the population aged over 30 years for study. Table 1 lists the participation rates of subjects by age and sex; rates ranges from 45% to 65% for men and 50% to 73% for women.

Basic Statistics of the Variables
Mean values ±1 SD of all variables in men and women are listed in Table 2. Height, weight, systolic

### TABLE 1. Participation Rates of Subjects According to Age

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Men No.</th>
<th>%</th>
<th>Women No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>48/103</td>
<td>46.6</td>
<td>69/119</td>
<td>58.0</td>
</tr>
<tr>
<td>40-49</td>
<td>118/201</td>
<td>58.7</td>
<td>147/212</td>
<td>69.3</td>
</tr>
<tr>
<td>50-59</td>
<td>129/211</td>
<td>61.1</td>
<td>172/255</td>
<td>67.5</td>
</tr>
<tr>
<td>60-69</td>
<td>114/176</td>
<td>64.8</td>
<td>136/194</td>
<td>70.1</td>
</tr>
<tr>
<td>70+</td>
<td>94/163</td>
<td>57.7</td>
<td>93/184</td>
<td>50.5</td>
</tr>
<tr>
<td>Total</td>
<td>503/854</td>
<td>58.9</td>
<td>617/964</td>
<td>64.0</td>
</tr>
</tbody>
</table>

The number in the study population is presented as participated number/invited number.

### TABLE 2. Age, Anthropometric Data, Blood Pressure, Urinary Factors, and Blood Tests

<table>
<thead>
<tr>
<th>Factor</th>
<th>Men (n = 503)</th>
<th>Women (n = 617)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>54.6±14.1</td>
<td>53.9±13.1</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.59±0.061</td>
<td>1.47±0.07</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>54.8±8.5</td>
<td>48.1±8.5</td>
</tr>
<tr>
<td>Quetelet index (wt/ht²)</td>
<td>21.8±2.8</td>
<td>22.2±3.2</td>
</tr>
<tr>
<td>Obesity index (%)</td>
<td>+2.5±12.2</td>
<td>+3.2±14.5</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>131.7±21.4*</td>
<td>129.1±21.4</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>78.5±12.9</td>
<td>75.6±12.0</td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na/Cr (mol/mol)</td>
<td>19.0±12.0</td>
<td>25.9±13.3</td>
</tr>
<tr>
<td>K/Cr (mol/mol)</td>
<td>4.52±2.28S</td>
<td>6.06±2.85</td>
</tr>
<tr>
<td>Na/K (mol/mol)</td>
<td>4.54±2.84</td>
<td>4.71±2.64</td>
</tr>
<tr>
<td>SCr/Cr (mol/mol)</td>
<td>0.949±0.400$</td>
<td>1.15±0.50</td>
</tr>
<tr>
<td>UN/Cr (mol/mol)</td>
<td>53.5±18.6*</td>
<td>56.4±20.4</td>
</tr>
<tr>
<td>SO₄/UN (mol/mol)</td>
<td>0.0195±0.0200</td>
<td>0.0210±0.0066</td>
</tr>
<tr>
<td>Blood test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>14.2±2.0t</td>
<td>12.4±1.3</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>43.4±4.4U</td>
<td>41.9±3.1</td>
</tr>
<tr>
<td>Total Choi (mg/dl)</td>
<td>162.2±32.3t</td>
<td>174.2±33.3</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>125.6±103.1t</td>
<td>110.5±62.3</td>
</tr>
<tr>
<td>Fasting Glu (mg/dl)</td>
<td>110.2±28.6</td>
<td>107.4±24.4</td>
</tr>
</tbody>
</table>

Values are means ± SD. Obesity index is (actual body weight — standard weight) x 100/standard weight. Quetelet = Quetelet index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Cr = creatinine; SO₄ = inorganic sulfate; UN = urea nitrogen; Hb = hemoglobin; Hct = hematocrit; Choi = cholesterol; TG = triglyceride; Glu = blood glucose.

*p < 0.05, statistical significance vs females. ip < 0.01, statistical significance vs females. Xp < 0.001, statistical significance vs females.
BP (SBP), DBP, Hb, Hct, and TG were significantly higher in men, while Cr ratios of urinary electrolytes and protein derivatives and Choi were higher in women. Differences between men and women with regard to age, Quetelet index, obesity index, fasting serum Glu, Na/K, and SO₄/UN were not significant. These results suggest that dietary compositions with regard to electrolytes and proteins are the same in both sexes.

Simple Regression Analysis

Matrices of simple correlation coefficients are shown in Table 3. For SBP, the highest correlation was with age in both men (r = 0.31) and women (r = 0.48), and the second highest correlation was with obesity index in men but with serum lipids in women. For DBP, on the other hand, the closest association was with obesity index (r = 0.27), followed by Hct and serum lipids in men, but with Hct (r = 0.29) followed by serum lipids and obesity index in women.

Urinary factors were found to be weakly related to BP. In women, Na/Cr was positively related to SBP (r = 0.09), K/Cr negatively (r = -0.10), and Na/K

### Table 3. Matrices of First-Order Correlation Coefficients (r) in Both Sexes

<table>
<thead>
<tr>
<th></th>
<th>SBP</th>
<th>DBP</th>
<th>Age</th>
<th>01</th>
<th>Hct</th>
<th>Choi</th>
<th>TG</th>
<th>Glucose</th>
<th>Na/Cr</th>
<th>K/Cr</th>
<th>SO4Cr</th>
<th>UN/Cr</th>
<th>Na/K</th>
<th>SO4/UN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>SBP</td>
<td>0.71</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td>0.31</td>
<td>0.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Age</td>
<td>0.31</td>
<td>0.14</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>OI</td>
<td>0.24</td>
<td>0.27</td>
<td>-0.18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hct</td>
<td>0.19</td>
<td>0.19</td>
<td>-0.31</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choi</td>
<td>0.10</td>
<td>0.10</td>
<td>0.05</td>
<td>0.24</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>0.19</td>
<td>0.19</td>
<td>-0.09</td>
<td>0.27</td>
<td>0.20</td>
<td>0.33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Glu</td>
<td>0.09</td>
<td>0.09</td>
<td>0.03</td>
<td>0.12</td>
<td>0.04</td>
<td>0.05</td>
<td>0.08</td>
<td>0.16</td>
<td>0.12</td>
<td>0.12</td>
<td>0.25</td>
<td>0.13</td>
<td>0.19</td>
<td>-0.12</td>
</tr>
<tr>
<td>Na/Cr</td>
<td>-0.02</td>
<td>-0.07</td>
<td>-0.09</td>
<td>-0.01</td>
<td>-0.02</td>
<td>-0.06</td>
<td>-0.04</td>
<td>-0.08</td>
<td>-0.02</td>
<td>-0.02</td>
<td>0.55</td>
<td>0.54</td>
<td>0.56</td>
<td>0.72</td>
</tr>
<tr>
<td>K/Cr</td>
<td>-0.10</td>
<td>-0.08</td>
<td>-0.06</td>
<td>-0.02</td>
<td>-0.03</td>
<td>-0.05</td>
<td>-1.2</td>
<td>0.28</td>
<td>0.25</td>
<td>0.25</td>
<td>0.30</td>
<td>0.16</td>
<td>0.23</td>
<td>0.23</td>
</tr>
<tr>
<td>SCyCr</td>
<td>-0.04</td>
<td>-0.07</td>
<td>-0.05</td>
<td>-0.02</td>
<td>0.00</td>
<td>-0.04</td>
<td>-0.04</td>
<td>0.72</td>
<td>0.21</td>
<td>0.21</td>
<td>0.24</td>
<td>0.18</td>
<td>0.23</td>
<td>0.43</td>
</tr>
<tr>
<td>UN/Cr</td>
<td>-0.01</td>
<td>-0.06</td>
<td>-0.01</td>
<td>-0.07</td>
<td>-0.04</td>
<td>0.01</td>
<td>-0.10</td>
<td>0.54</td>
<td>0.56</td>
<td>0.56</td>
<td>0.72</td>
<td>0.13</td>
<td>0.19</td>
<td>-0.12</td>
</tr>
<tr>
<td>Na/K</td>
<td>0.09</td>
<td>0.01</td>
<td>-0.16</td>
<td>0.06</td>
<td>0.01</td>
<td>-0.10</td>
<td>0.66</td>
<td>-0.08</td>
<td>0.39</td>
<td>0.25</td>
<td>0.28</td>
<td>0.30</td>
<td>0.16</td>
<td>0.23</td>
</tr>
<tr>
<td>SO4/UN</td>
<td>-0.12</td>
<td>-0.09</td>
<td>-0.04</td>
<td>-0.04</td>
<td>0.02</td>
<td>-0.02</td>
<td>-0.01</td>
<td>0.58</td>
<td>0.51</td>
<td>0.71</td>
<td>0.58</td>
<td>0.58</td>
<td>0.33</td>
<td>0.33</td>
</tr>
</tbody>
</table>

0.078 ≤ r ≤ 0.114 (p ≤ 0.05); 0.114 ≤ r ≤ 0.145 (p < 0.01); r ≥ 0.145 (p ≤ 0.001).

Correlation coefficients without statistical significance are shown in parentheses. See Table 2 for abbreviations.
positively \( r = 0.09 \). In men, these three factors were also similarly related to SBP, but \( SO_4/UN \) was negatively related to both SBP \( r = -0.12 \) and DBP \( r = -0.09 \). Urinary factors were closely interrelated in general, except for the correlations of \( SO_4/UN \) with other urinary components in men, where the links were fairly weak \( r < 0.2 \) compared to those in women \( r = 0.21 \) to 0.70).

The Association of certain variables with age was different by sex; Hct was negatively related \( r = -0.31 \) in men but nil in women, and serum lipids were positively related in women but negatively or nil in men. However, the obesity index and Na/K were decreased with advancing age in both sexes.

**Multiple Regression Analysis**

Multiple regression analysis (MRA) equations were determined for SBP and DBP for each sex in two different ways (MRA-I and -II) according to the set of the urinary factors put into calculation. In MRA-I equations, Na/Cr, K/Cr, \( SO_4/Cr \), and UN/Cr factors related to the "quantity" of electrolytes or protein. In MRA-II equations, Na/K and \( SO_4/UN \) factors related to the "quality" of the dietary intake of electrolytes and protein, respectively, were collectively computed together with other variables. Table 4 shows the MRA-I results, which indicate that SBP was strongly and DBP weakly related to Na/K in women but not in men. The SBP was negatively related to K/Cr in men but not in women; DBP was not related to K/Cr in either sex. Table 5 shows the MRA-II results, which indicate that SBP was positively related to Na/K in both sexes, while DBP was not. Some urinary protein derivatives were also found to be independently related to SBP, although only in men; UN/Cr was positively related to SBP in MRA-I equations and \( SO_4/UN \) negatively in MRA-II. \( SO_4/Cr \) was unrelated to blood pressure.

Cholesterol was the only variable that correlated differently with BP by sex; in MRA-I it was inversely related in men but positively in women. The same tendency was consistent in MRA-II, but F value remained significant only in relation to DBP in women.

According to the F value for each variable, age was the greatest determinant for SBP in both sexes, and for DBP in men. Particularly, the relative importance of age as a determinant of SBP was incomparably higher \( F = 163.6 \) than other variables in women. Obesity index had the second closest correlation with both SBP and DBP in men, but Hct related more closely to BP than obesity index in women. Triglyceride was found to be weakly but positively linked to DBP in men in both MRA-I and II, while the significance detected between TG and SBP in women in MRA-II was not consistent in MRA-I. Fasting blood Glu was unrelated to BP.

The MRA-I equations were highly significant \( p < 0.001 \) and explained about 21% and 31% of the variation in SBP in men and women, respectively, and 15% and 20% in DBP in terms of coefficients of determination. Similar results were obtained with MRA-II equations.

**TABLE 4. Partial Regression Coefficients Between Blood Pressure and Variables in Multiple Regression Analysis (MRA-I)**

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Dependent variables</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SBP</td>
<td>DBP</td>
</tr>
<tr>
<td>Age</td>
<td>(0.40)</td>
<td>0.611</td>
<td>(0.25)</td>
</tr>
<tr>
<td>Obesity</td>
<td>(0.29)</td>
<td>0.497</td>
<td>(0.24)</td>
</tr>
<tr>
<td>Hct</td>
<td>(0.07)</td>
<td>0.361</td>
<td>(0.18)</td>
</tr>
<tr>
<td>Choi</td>
<td>-0.0539 (-0.08)</td>
<td>3.9*</td>
<td>-0.0115 (-0.03)</td>
</tr>
<tr>
<td>TG</td>
<td>0.0115 (0.06)</td>
<td>1.6</td>
<td>0.0156 (0.12)</td>
</tr>
<tr>
<td>Fasting Glu</td>
<td>0.0150 (0.03)</td>
<td>0.4</td>
<td>-0.0105 (-0.03)</td>
</tr>
<tr>
<td>Na/Cr</td>
<td>0.149 (0.09)</td>
<td>2.2</td>
<td>-0.009 (-0.01)</td>
</tr>
<tr>
<td>K/Cr</td>
<td>-1.67 (-0.19)</td>
<td>13.6§</td>
<td>-0.44 (-0.08)</td>
</tr>
<tr>
<td>SCVCr</td>
<td>-2.15 (-0.04)</td>
<td>0.4</td>
<td>-$</td>
</tr>
<tr>
<td>UN/Cr</td>
<td>0.125 (0.13)</td>
<td>4.6*</td>
<td>0.019 (0.03)</td>
</tr>
</tbody>
</table>

| Regression constant   | 87.1                | 43.0 |       |
| Multiple regr. coeff. (R) | 0.47 | 0.40 | 0.56   |
| Coeff. of determination (R²) | 0.22 | 0.16 | 0.31   |
| se                    | 19.0                | 12.0 | 18.4   |
| F value               | 14.48               | 10.7§ | 29.1§ |

Standard partial regression coefficients are presented in parentheses. See Table 2 for abbreviations.

\* \( p < 0.05 \), statistically significant.

\( t/F < 0.01 \), statistically significant.

\( t/F < 0.001 \), statistically significant.

\( §SCVCr \) was not included because of the insufficient level of tolerance.
Sodium and Blood Pressure

Although the bulk of experimental or clinical data implicates excessive Na intake in the genesis of hypertension, there is no conclusive epidemiological evidence in Western populations with relatively low Na intake that higher Na intake is associated with a greater prevalence of hypertension. Some investigators claim to have demonstrated a link between Na and BP within a population, but those studies were not designed with a view to homogeneity of the survey populations nor was there any attempt to correlate factors such as age or body weight, as critically reviewed by Simpson in 1979.

Although there are data suggestive of an association between higher Na intake and hypertension in some Japanese populations, the study by Kesteloot et al. of a Korean population (with a daily consumption of about 16 g salt) may be the only one at present with an independent association between Na and BP within a homogeneous population. Moreover, this study allowed for age and body mass index. Our analyses confirmed that urinary indices related to dietary Na intake, namely, Na/Cr and Na/K, are associated independently and positively with BP, in particular with SBP except for Na/Cr in men. This is further epidemiological evidence for the pathogenic role of salt in hypertension. It is possible that the relationships of Na/Cr and Na/K to BP were enhanced in multivariate analysis, because these variables were simultaneously related in a negative fashion to age, and age was correlated positively with BP.

The reason why it is easier to detect a link between Na and BP in Japan and Korea than in Western societies is not clear. Potassium is known to counteract the effect of Na on BP, but K/Cr can be calculated from published mean values to be lower in Western populations (New Zealand = 4.4 mol/mol<sup>13</sup>; Belgium = 4J<sup>23</sup>) than in Korea (5.7 mol/mol<sup>4</sup>) or Japan (5.4 mol/mol, this study). It may be that Na intake in Western populations is too small to bring out the relationship between Na and BP, or that some other confounding factors are involved in making a link between Na and BP elusive. Inadequate measures of Na intake might also be implicated, as discussed later.

Potassium and Blood Pressure

Meneely and associates were the first to suggest that Na may have an adverse effect on BP and life expectancy, which can be ameliorated by increasing...
the K intake. Similar experimental observations were made by others.\textsuperscript{34-36} Epidemiological evidence, on the contrary, remains scarce since Sasaki’s preliminary observation\textsuperscript{37} on the low incidence of stroke in a Northern district of Japan where the inhabitants ingest high levels of K from apples. Recently, Kesteloot et al.\textsuperscript{38} and Staessen et al.\textsuperscript{37} independently confirmed the negative relationship between K and BP in Belgian and Korean populations after they corrected for other variables. Our results also show urinary K excretion to be negatively linked to BP in men.

**Protein and Blood Pressure**

The first experimental observation on the possible beneficial effect of dietary protein was reported by Yamori et al.\textsuperscript{28} in 1976. In this study, a diet rich in animal protein (fish meat) was found to attenuate the development of severe hypertension and to prevent cerebral apoplexy in stroke-prone SHR. The natriuretic effects of a diet rich in animal proteins and the depressor effects of some sulfur amino acids (a central effect was confirmed in the case of taurine\textsuperscript{39}) may be involved in triggering a depressor mechanism. Recently, Dehaven et al.\textsuperscript{40} found that net urinary Na loss and a concomitant decrease in SBP were significantly greater with a low caloric and pure animal-protein diet than with an isocaloric mixed diet used for the treatment of obesity. Degoulet et al.\textsuperscript{41} similarly described a negative, significant correlation between mortality from stroke and animal-protein consumption. This analysis was based on statistical data collected in 21 developed countries.

In the present study, a qualitative index of dietary animal-protein intake, SO\textsubscript{4}/UN, was found to be negatively correlated with SBP in men. This might favor the concept of a negative causal relationship between animal protein intake and BP. However, its potential was weak, with only a 2 mm Hg decrease of SBP for an increase of 1 SD of SO\textsubscript{4}/UN. SO\textsubscript{4}/Cr, a possible quantitative index of dietary sulfur amino acids, was unrelated, and UN/Cr, a possible index of total protein, was weakly but positively related to BP. The relative content of animal protein in the total protein ingested might have a greater effect on BP than the absolute intake.

**Cholesterol and Blood Pressure**

The relationship between Choi and BP is unclear. Although higher Choi levels have been demonstrated to result in enhanced sensitivity to circulating catecholamines in acute experiments,\textsuperscript{42} the development of hypertension in SHR or SP-SHR and the incidence of stroke in the latter have been repeatedly shown to be attenuated by chronic administration of a high-fat-cholesterol diet.\textsuperscript{9}

Epidemiological findings have been also equivocal with regard to the correlation between Choi and BP. The Framingham study\textsuperscript{33} showed that BP rises with an increase in Choi levels. The same was found in a cross-sectional, prospective epidemiologic study in Chicago\textsuperscript{34} for white males, but not for white females and black people. Univariate analysis by Komachi et al.\textsuperscript{35} found no link between Choi and BP in a survey of Japanese populations. Although the associations between BP and Choi were different in MRA-I and II, our results may be the first to show the possible sex difference in the link of Choi to BP; namely, Choi was found in MRA-I to be negatively associated in men and positively in women. The reason why the link in men, which tends to be positive in univariate analysis, turned into a negative relationship in multivariate analyses might be that the obesity index, which was positively related to both SBP and Choi in a simple regression analysis, blunted the link between Choi to BP. The reason of such a sex difference is unclear at the present time, but the sex difference in the Choi levels (higher in women) could account for a part of it.

**Other Variables**

Age was found to be closely related to BP, particularly SBP. This result is consistent with findings in Western populations\textsuperscript{34} and may mean that SBP is determined by the cumulative effects of many factors over a long period of time. With DBP, on the other hand, the correlation of age was smaller, and obesity was found to be as potent a determinant for DBP as age. Such a tendency was apparent in Western populations,\textsuperscript{34} where no positive association emerged in multivariate analyses between age and DBP and where relative weight was the strongest determinant of DBP. The link between obesity and BP appears more pronounced in Western populations,\textsuperscript{34} where obesity is much more common.

Hematocrit was also found to be closely related to BP, especially DBP, and the relationship appeared closer in women than in men. The Framingham results\textsuperscript{33} were consistent with this finding in that Hct was significantly related to BP in women but not in men. Although markedly increased Hct is known to be a primary cause of elevated BP in cases of polycythemia vera, the mild increase in Hct associated with higher levels of BP\textsuperscript{40} is regarded to be due to hemoconcentration secondary to the elevated BP.\textsuperscript{37}

There was a positive correlation of TG with both SBP and DBP. Similar findings were reported in the Stockholm prospective study\textsuperscript{36} where the log concentration of TG was significantly correlated with BP after adjustment for age. Finally, fasting blood Glu, although it was positively but weakly linked to BP in the MRA-I analysis, did not correlate with BP after adjustment for other variables. This finding is in agreement with the results of Stamler et al.\textsuperscript{38} and Berglund et al.\textsuperscript{39} Since blood Glu (after loading with 50 g orally) was observed to be positively related with BP by Stamler et al.\textsuperscript{34} higher BP might be associated with impaired Glu tolerance rather than an increased fasting Glu level. A similar relationship between Glu and BP was observed in SHR.\textsuperscript{40}

**Urine Collection**

Although single-spot urine samples were used in the present study, it is recognized that even a 24-hour
collection may be inadequate for characterizing an individual's dietary Na and K intake, because of the large day-to-day intradividual variability in urinary output. In spite of this, significant associations were detected between urinary outputs of Na and K and BP. The constancy of the life style of the study population and the wide interindividual variation of the measurements may have contributed to the detection of these associations.

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