Differences have been noted between normotensive and hypertensive individuals in salt intake, intracellular electrolytes, total body electrolytes, serum electrolytes, and the renal excretion of sodium and water. If changes in serum sodium concentration reflected intracellular or metabolic alterations in electrolyte balance, an easily determined factor would be available for study of electrolyte abnormalities in relation to the development of hypertension. Three investigators have reported a slight increase in serum sodium concentration in patients with essential hypertension, whereas two other studies report no difference. The purpose of this study was to define more accurately the associations between serum sodium, serum potassium, and blood pressure level by standardizing to the greatest degree possible all methods and measurements, and by assessing the importance of such variables as age, sex, and body build. An additional purpose was to evaluate further the relationship of stated salt intake to blood pressure level and serum electrolyte concentrations.

Methods
Selection of Subjects
Male and female normotensive and hypertensive inpatients and outpatients, free from any disease other than essential hypertension that might affect blood pressure or serum sodium level, were selected. Evident renal, cardiac, and adrenal disease, as well as diabetes mellitus, were causes for exclusion. Hypertensive patients with renal, cerebral, or cardiac complications, or who were on antihypertensive medication, were also excluded. Within these limitations unselected normotensive patients and consecutive clinic patients with hypertension were studied. Information was collected on each about age, sex, race, height, weight, personal and family history of hypertension, and previous and present salt intake (by use of questions outlined by Dahl). All inpatient blood pressures were taken upon awakening of the subject in the morning. All outpatient pressure readings were taken after the patients had rested for 15 minutes. In every case the patient was recumbent and the cuff was placed on the right arm. The level when Korotkoff's sounds first appeared was recorded as the systolic pressure and the level of complete disappearance as the diastolic pressure. Hypertension was defined as either a systolic blood pressure reading above 140 or a diastolic reading above 90 mm. Hg. Mean blood pressure was calculated as the diastolic pressure plus one third of the pulse pressure. Venous blood was collected from patients who were fasting or were more than 3 hours postprandial. It was centrifuged within 2 hours of collection and the serum was frozen. To reduce day-to-day variations in methodology, data were recorded and groups of sera from both normotensive and hypertensive patients were analyzed by flame photometry for sodium and potassium during the same period.

Data were obtained on 118 patients (69 normotensive and 49 hypertensive) but were complete for 50 normotensive and 43 hypertensive patients. Patients were between ages 20 and 60. Sixteen of the 118 values of serum sodium were outside the range of 130 to 155 mEq. per liter and six serum potassium levels were outside 3.5 to 5.5 mEq. per liter. These were considered to be evidence of unknown disease or laboratory error and were rejected. The distribution of these discarded values showed no relation to blood pressure.

Statistical Analysis
Statistical analyses were completed to evaluate many relationships as shown in tables 1, 2, and 3. As a preliminary step in the analysis of the difference in serum sodium and potassium levels in the hypertensive versus the normotensive group, a Chi-square test of the difference between the sex composition of the two groups was completed. This shows a significantly higher proportion of women in the hypertensive group than in the normotensive group (Chi-square = 5.13, 0.01 < p < 0.025). Furthermore, the two groups are of
Table 1

Serum Sodium and Hypertension

<table>
<thead>
<tr>
<th>Group of subject's</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>t</th>
<th>Degrees of freedom</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>Mean serum sodium (mEq./L.)</td>
<td>Number of patients</td>
<td>Mean serum sodium (mEq./L.)</td>
<td></td>
</tr>
<tr>
<td>Men under 40 years of age</td>
<td>24</td>
<td>141.9</td>
<td>7</td>
<td>142.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Men 40 to 49 years of age</td>
<td>9</td>
<td>142.0</td>
<td>8</td>
<td>140.8</td>
<td>-0.53</td>
</tr>
<tr>
<td>Men over 49 years of age</td>
<td>8</td>
<td>145.1</td>
<td>8</td>
<td>139.9</td>
<td>-2.82</td>
</tr>
<tr>
<td>Women under 40 years of age</td>
<td>8</td>
<td>142.2</td>
<td>2</td>
<td>143.2</td>
<td>0.20</td>
</tr>
<tr>
<td>Women 40 to 49 years of age</td>
<td>8</td>
<td>140.5</td>
<td>13</td>
<td>141.7</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Table 2

Serum Potassium and Hypertension

<table>
<thead>
<tr>
<th>Group of subject's</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>t</th>
<th>Degrees of freedom</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>Mean serum potassium (mEq./L.)</td>
<td>Number of patients</td>
<td>Mean serum potassium (mEq./L.)</td>
<td></td>
</tr>
<tr>
<td>Men under 40 years of age</td>
<td>25</td>
<td>4.98</td>
<td>7</td>
<td>4.97</td>
<td>-0.07</td>
</tr>
<tr>
<td>Men 40 to 49 years of age</td>
<td>8</td>
<td>4.93</td>
<td>9</td>
<td>4.96</td>
<td>0.34</td>
</tr>
<tr>
<td>Men over 49 years of age</td>
<td>7</td>
<td>4.95</td>
<td>9</td>
<td>4.84</td>
<td>-0.97</td>
</tr>
<tr>
<td>Women under 40 years of age</td>
<td>7</td>
<td>4.69</td>
<td>1</td>
<td>4.69</td>
<td>0.00</td>
</tr>
<tr>
<td>Women 40 to 49 years of age</td>
<td>8</td>
<td>4.98</td>
<td>13</td>
<td>4.85</td>
<td>-0.71</td>
</tr>
</tbody>
</table>

significantly different age, the average age of the normotensive subjects being 38.6 years and that of the hypertensive patients 45.9 years (t = 4.26, p < 0.005). Since the factors of age and sex are associated in the two groups, the significance of the difference between the average serum sodium and serum potassium was tested, age-sex specified, by the t test. An initial examination of the assumptions of normality of distribution and equality of variance showed that they were sufficiently well satisfied to permit the valid application of the t test.

Results

Serum Electrolytes

There was no significant difference between the mean serum sodium of the hypertensive group and that of the normotensive group (table 1). A similar statement applies to mean serum-potassium (table 2). These comparisons also were made separately in each age-sex subgroup. The only exception was that normotensive men over the age of 50 tended to have a somewhat higher serum sodium than their hypertensive counterparts. It should be noted that there were no normotensive women age 50 or over in the study. In the normotensive group and in the hypertensive group, there was no association between systolic, diastolic, or mean blood pressure and the serum sodium, serum potassium, or sodium to potassium ratio (table 3A).

Stated Salt Intake

As shown in table 3B, relationships were sought between salt intake (determined by Dahl's questions) and the other major variables measured. No association was found between the stated salt intake and, (a) the mean blood pressure, (b) a past history of increased blood pressure, (c) the serum sodium level, or (d) the potassium level.
### Analysis of Factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>Group of subjects</th>
<th>Chi-Square</th>
<th>Degrees of freedom</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Serum electrolytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean blood pressure level and serum sodium concentration</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>1.431</td>
<td>1</td>
<td>0.20 &lt; p &lt; 0.30</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure level and serum sodium concentration</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.420</td>
<td>1</td>
<td>0.50 &lt; p &lt; 0.75</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure level and serum sodium concentration</td>
<td>Normotensive</td>
<td>0.039</td>
<td>1</td>
<td>0.75 &lt; p &lt; 0.90</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.424</td>
<td>1</td>
<td>0.50 &lt; p &lt; 0.75</td>
<td></td>
</tr>
<tr>
<td>Mean blood pressure level and serum potassium concentration</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.003</td>
<td>1</td>
<td>0.950 &lt; p &lt; 0.975</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure level and serum potassium concentration</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>1.284</td>
<td>1</td>
<td>0.25 &lt; p &lt; 0.50</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure level and serum potassium concentration</td>
<td>Normotensive</td>
<td>0.644</td>
<td>1</td>
<td>0.25 &lt; p &lt; 0.50</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.593</td>
<td>1</td>
<td>0.25 &lt; p &lt; 0.50</td>
<td></td>
</tr>
<tr>
<td>Mean blood pressure level and serum sodium-potassium concentration ratio</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.000+</td>
<td>1</td>
<td>0.975 &lt; p &lt; 0.990</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure level and serum sodium-potassium concentration ratio</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.048</td>
<td>1</td>
<td>0.75 &lt; p &lt; 0.90</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure level and serum sodium-potassium concentration ratio</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.074</td>
<td>1</td>
<td>0.75 &lt; p &lt; 0.90</td>
<td></td>
</tr>
<tr>
<td>B. Stated Salt Intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stated salt intake and mean blood pressure level</td>
<td>Normotensive</td>
<td>(Exact test)</td>
<td>1</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.224</td>
<td>1</td>
<td>0.60 &lt; p &lt; 0.70</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>1.166</td>
<td>2</td>
<td>0.50 &lt; p &lt; 0.60</td>
<td></td>
</tr>
<tr>
<td>Stated salt intake and a past history of high blood pressure</td>
<td>All</td>
<td>0.668</td>
<td>2</td>
<td>0.70 &lt; p &lt; 0.80</td>
</tr>
<tr>
<td>Stated salt intake and serum sodium concentration</td>
<td>All</td>
<td>9.477</td>
<td>8</td>
<td>0.30 &lt; p &lt; 0.40</td>
</tr>
<tr>
<td>Stated salt intake and serum potassiam concentration</td>
<td>All</td>
<td>2.377</td>
<td>2</td>
<td>0.30 &lt; p &lt; 0.40</td>
</tr>
<tr>
<td>Stated salt intake and a family history of hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
p Indicates the probability of observing a Chi-square as large as or larger than that actually observed when there is no association in the population from which these measurements were drawn.

The "exact test" is used whenever frequencies are too small to permit the valid application of Chi-square. (See Biometrika Tables for Statisticians: Eds., E. S. Pearson and H. O. Hartley, Vol. I. Cambridge University Press, 1956, p. 65). The words "not significant" used in connection with this test indicate that the corresponding association fails to approach the 5 per cent significance level.

### Other Factors

Chi-square tests for associations between various factors were generally done separately for the normotensive and hypertensive groups. There was no association between sex and serum sodium in either group. Age also was not related to serum sodium or to systolic blood pressure in the two groups. There was a slight tendency toward an association of systolic blood pressure and age within the hypertensive group, but this failed to reach statistical significance. Diastolic blood pres-
sure and age were unrelated in the normoten-

sive group, but a significant association was

present in the hypertensive group. Neither

serum sodium nor systolic or diastolic blood

pressure was related to height-weight index

in either group.

Discussion

A change in electrolyte balance across the

cell wall could influence arteriolar resistance

either by causing swelling of the cells (in-

creased sodium within the cells), or by altering

the membrane potential (a change in

K⁺/K⁺o ratio) and increasing sensitivity to

neurogenic or vasopressor stimuli. Many stud-
i

es have been carried out to evaluate the path-

ogenetic role of abnormal electrolyte metab-

olism in essential hypertension, but the results

have not been consistent. This is reflected in

previous evaluations of the serum sodium and

potassium, which are summarized in table 4.

Some showed a significant difference in serum

sodium and potassium between normal and

hypertensive individuals. It was thought that

this type of study should be repeated to be

sure that such differences were due to the

presence of high blood pressure alone and not

to the numerous variables. Therefore, as com-

plete data as possible were collected on each

patient. Normal and hypertensive subjects

were studied simultaneously, and sera from

both groups were analyzed at the same time

in our own laboratory. Moreover, the serum

electrolyte levels were studied in relation to

actual blood pressure values, rather than to

merely the presence or absence of hyperten-

sion.

It should be noted that the hypertensive

patients included in the present investigation

were rigidly screened, and no patient with

any cardiac, renal, or cerebral complication

was included. There were no cases of mali-

gnant hypertension. Perhaps the patients stud-

ied here had less severe hypertensive disease

than those reported by some investigators.

The range of systolic blood pressure up to 220

mm. mercury and diastolic up to 140 mm.

mercury would seem to be sufficient, however,

to show association to serum electrolyte levels

if one did exist. Statistical analysis of our

data disclosed no significant relationships be-

tween blood pressure and these electrolyte

concentrations. The small Chi-square values

found in many of our analyses do not indicate

absolutely no association in the larger popu-

lation of individuals from which subjects are

selected, but in conjunction with large p val-

ues, they suggest that true associations must

be small.

Each patient in this study was asked: "Do

you salt your food (a) before tasting, (b)
after tasting, or (c) not at all." These were

the same questions used by Dahl, who found

a direct relationship between elevation of the

blood pressure and the level of salt intake.1

The study presented here shows no such re-

lationship. It has been suggested that ques-

tions concerning stated salt intake may not

lead to accurate appraisal of actual salt in-
take, and other methods of estimating salt

intake have given conflicting results.12-14 Ev-

deence for an etiologic role of excessive salt in-
gestion in hypertensive states is cited in a

Table 4

Results of Present and Prior Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Serum sodium (mEq./L.)</th>
<th>Serum potassium (mEq./L.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotensive</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>Present study</td>
<td>142.2 ± 4.73 (57)</td>
<td>141.0 ± 4.05 (47)</td>
</tr>
<tr>
<td>Holly, Elliot, Holland¹</td>
<td>144.8 ± 3.81 (400)</td>
<td>147.3 ± 4.07 (75)</td>
</tr>
<tr>
<td>Albert, Morita, Isari⁰</td>
<td>142 ± 3.0 (43)</td>
<td>147 ± 5.0 (26)</td>
</tr>
<tr>
<td>Mathur &amp; Wadhawan¹</td>
<td>139.2 ± 7.6 (50)</td>
<td>144.4 ± 9.9 (30)</td>
</tr>
<tr>
<td>Weller⁰</td>
<td>143 ± 4.05 (11)</td>
<td>142 ± 6.08 (26)</td>
</tr>
<tr>
<td>Winer, Kirkendall et al.¹</td>
<td>No difference noted</td>
<td></td>
</tr>
<tr>
<td>Hilden &amp; Krogsgaard¹</td>
<td>Lowered in severe</td>
<td></td>
</tr>
</tbody>
</table>

Electrolyte values given as the mean ± standard deviation with number of subjects studied in parentheses.
recent review of ion metabolism in hypertension. Certain population groups appear to have more hypertension and higher salt intakes. Laboratory investigations indicate that high-salt diets will produce hypertension and also will aggravate various forms of experimental hypertension. Complicating this is the observation that high-potassium intake will protect against these effects. If a relationship between salt intake and hypertension exists, it is a highly complex one.

Summary

This study was undertaken to determine if an association exists between blood pressure level and serum sodium or potassium concentration. All methods and measurements were standardized, and variables possibly influencing these factors were analyzed. Since increased salt intake has been postulated as an etiologic factor in essential hypertension, each patient was questioned in this regard.

Fifty normotensive and 43 hypertensive patients were studied. No significant associations were found between the height of the blood pressure, the serum sodium or potassium level, and the stated salt intake.

References


For I have learned from much experience that diseases of the worst description may exist within the chest unmarked by any symptoms, and undiscoverable by any other means than percussion alone.—From On Percussion of the Chest. Published in 1761. Translated by John Forbes, M.D. In: Classics of Medicine and Surgery. New York, Dover Publications, Inc., 1959, p. 127.
Serum Sodium and Potassium in Essential Hypertension
BERNARD E. LEVINE, JOHN M. WELLER and RICHARD D. REMINGTON

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