Session III. Salt Sensitivity

Salt Sensitivity

Definition, Conception, Methodology, and Long-term Issues

Jay M. Sullivan

Several laboratories have examined the relation between salt intake and blood pressure in both experimental animals and humans. The human studies have used widely varying methodologies and different criteria for sodium sensitivity. Nonetheless, these studies have produced convincing data that the blood pressure of some individuals is far more sensitive to the effects of sodium depletion or loading than that of others. Furthermore, a minority of the population appears to comprise acutely salt-sensitive individuals. Some studies have shown that sodium-sensitive individuals share several characteristics. They include increased forearm vascular resistance, decreased venous compliance, suppressed plasma renin activity, and lower circulating aldosterone concentration. These findings have also been described in the Dahl salt-sensitive rat, which suggest a genetic link in humans as well as the rat. Long-term follow-up of sodium-sensitive and sodium-resistant groups has shown that although blood pressure levels are approximately equal in the two groups during sodium depletion, resumption of a daily sodium intake of about 150 meq results in significantly higher levels of blood pressure and forearm vascular resistance in the sodium-sensitive group. This difference persists for at least 12 months. (Hypertension 1991;17[suppl I]:I-61-I-68)

Studies of the relation between sodium intake and blood pressure have led to several controversies. Among them is the question of whether the characteristic of sodium sensitivity actually exists or whether a high sodium diet minimally raises the average blood pressure of a population. If sodium sensitivity does exist, is it an all-or-none phenomenon, which is present in some individuals and totally absent in others, or is it a spectrum of sodium sensitivity?

Salt sensitivity can be loosely defined as an increase in blood pressure that results from a relatively high sodium intake. Questions arise when one attempts to define the boundaries of these various terms. How great a rise in blood pressure is necessary? How much sodium is required to elicit a hypertensive response? Are individuals salt-sensitive if their blood pressure fails to rise on a sodium intake that is in the high range of normal for a given population (e.g., 200–250 meq/day for North Americans) but rises on an atypically high sodium intake, such as 400–800 meq/day? How long must sodium loading continue to constitute an adequate trial of sodium sensitivity? How long must blood pressure elevation persist to indicate sodium sensitivity? Is an elevation of blood pressure to a level less than that representative of clinical hypertension an indication of sodium sensitivity? Is an individual sodium-sensitive if he or she never becomes clinically hypertensive? Does sodium sensitivity change with time or with age? Do such changes in lifestyle as weight reduction or regular aerobic exercise affect sodium sensitivity?

The concept of sodium sensitivity originated in population surveys conducted in various parts of the world, which demonstrated that the prevalence of hypertension rises with habitual dietary sodium intake or urinary sodium excretion.1 Hypertension is unknown in those societies in which no sodium is added to the diet. (Note that such population groups do not show an increase in blood pressure with age.) Yet, even in those populations consuming the highest amounts of sodium (e.g., the inhabitants of the northern Japanese islands, whose sodium intake averages 435 meq/day), fully 60% of the population remains normotensive and is probably not sodium-sensitive.2 However, is the increase in blood pressure resulting from the aging process a manifestation of sodium sensitivity that requires lifelong sodium ingestion to elicit? Can the physiological or biochemical properties characteristic of various animal models of sodium sensitivity be used as markers of sodium sensitivity in humans, or must we search for markers unique to humans?
Animal Studies

In laboratory animals, there is compelling evidence that sodium sensitivity is genetically transmitted. Dahl et al observed that rats varied in their response to increased dietary sodium intake. By selective inbreeding of animals showing a hypertensive response to sodium, they were able to produce a rat model that invariably developed hypertension when given a high sodium diet. They were able to produce a sodium-resistant strain by similar inbreeding. The Dahl rats have been extensively studied and several characteristics identified that might serve as markers of sodium sensitivity in humans, thus helping to define sodium sensitivity. In hemodynamic studies, the elevation of blood pressure in the salt-sensitive rat has been found to initially result from an increase of both cardiac output and total peripheral vascular resistance, subsequently evolving into a hemodynamic profile of elevated vascular resistance alone. The salt-sensitive animal also demonstrates increased responsiveness to a variety of pressor agents, increased blood volume, and increased cardiac microsomal Na,K-ATPase activity.

Various abnormalities of the autonomic nervous system have also been described: evidence for an increased neurogenic component to vascular resistance, an increased pressor response to intracerebral administration of angiotensin II or hypertonic saline, abnormal baroreceptor reflex control of heart rate, increased renal α2- and α3-adrenergic receptor density, and impaired sensitization of aortic baroreceptors. These animals also show substantial sensitivity to all forms of experimentally induced hypertension.

Several observations indicate renal involvement in the development of salt-sensitive hypertension. Dahl et al demonstrated, by a series of cross-transplantation experiments, that a kidney from a salt-sensitive rat causes blood pressure elevation when transplanted into a salt-resistant rat. Conversely, a kidney from a salt-resistant rat transplanted into a salt-sensitive rat causes a decrease in blood pressure. They also showed, by a series of parabiotic experiments, that a hypertensiogenic substance is released into the circulation of the salt-sensitive rat. The salt-sensitive rat also showed enhanced excretion of a saline load, a reduced number of glomeruli, abnormal renal vascular resistance, an abnormal pressure-natriuresis curve that requires a higher level of perfusion pressure for a given level of sodium excretion, decreased urinary kallikrein excretion, renal vascular lesions, decreased renal and plasma renin, a decreased number and granularity of renal medullary interstitial cells (which excrete a vasodepressor lipid), decreased renal Na,K-ATPase activity, and increased cell number but decreased renal cell size during salt loading. Sterzel et al found evidence of albuminuric glomerular disease before the development of hypertension, which accelerated as blood pressure rose. Rapp et al have recently made the important observation that the Dahl salt-sensitive rat has a restriction fragment length polymorphism in the renin gene.

These renal abnormalities are associated with several endocrine and metabolic changes. For example, the Dahl salt-sensitive rat is known to have decreased urinary prostaglandin E2 synthesis and excretion, increased adrenal synthesis of 18-hydroxydeoxycorticosterone, decreased plasma aldosterone levels, increased antidiuretic hormone release during high salt intake, increased prostaglandin I2 production, suppressed adrenal renin activity, and impaired release of eicosanoid precursors from phospholipid stores. Some of these observations have been made in humans who appear to be salt-sensitive; they are among the most promising markers of sodium sensitivity currently known.

Human Studies

Studies of sodium sensitivity in humans have brought up several additional problems regarding definition and methods. A lack of uniformity exists in both criteria and techniques used in the studies reported to date (Table 1). Approaches have varied. Rapid sodium loading and depletion, such as those reported by Luft et al, who used a protocol that consisted of the administration of 2 l saline i.v. over a 4-hour period that constituted the sodium loading period, and a 10 meq sodium diet plus 40 mg furosemide orally every 8 hours that constituted a period of sodium depletion. A contrasting approach is one by Rocchini et al, who used a 14-day period of sodium depletion during which the subjects received a 30 meq sodium diet preceded by a period of sodium loading consisting of 250 meq sodium daily for 14 days. The amount of the sodium load has varied from 180 meq/day in the studies of Sowers et al to 1,600 meq/day in the studies of Luft et al. Although the hemodynamic and hormonal changes accompanying extreme sodium intake are of interest, one can argue that changes in response to the upper range of usual sodium intake for a given population will probably identify those individuals sensitive to the amount of salt normally found in their particular living environment.

Likewise, no uniformity exists in the magnitude of blood pressure change required to identify an individual as salt-sensitive, although the reported prevalence of salt sensitivity is similar, especially among hypertensive patients (Table 1). Sparse information is available on the reproducibility of these studies. In 15 reported studies, the majority have not used a definition of salt sensitivity; they have simply viewed blood pressure changes as a continuous variable in relation to changes in other hemodynamic and hormonal mechanisms associated with blood pressure control. Arbitrarily established criteria have varied from an increase in mean arterial blood pressure of at least 5% in normotensive and borderline hypertensive individuals to an increase in mean arterial blood pressure exceeding 10% in hypertensive patients. Although several studies have assigned diets in
TABLE 1. Sodium Sensitivity: Methods and Criteria

<table>
<thead>
<tr>
<th>Author</th>
<th>Protocol</th>
<th>Subjects</th>
<th>Criteria</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luft, 1977</td>
<td>210 mg Na, 40 mg furosemide t.i.d.</td>
<td>NT</td>
<td>ΔMean BP*</td>
<td>NT, HT</td>
</tr>
<tr>
<td>Kawasaki, 1978</td>
<td>109 mg Na (7 days), 9 meq Na (7 days), 240 mg Na (7 days)</td>
<td>HT</td>
<td>ΔMean BP &gt;10%</td>
<td>50%</td>
</tr>
<tr>
<td>Sullivan, 1980</td>
<td>Ad libitum (1 day), 10 mg Na (4 days), ad libitum (2 days), 200 mg Na (4 days)</td>
<td>NT and BHT</td>
<td>ΔMean BP &gt;5%</td>
<td>29%</td>
</tr>
<tr>
<td>Fujita, 1980</td>
<td>9 mg Na (7 days), 249 mg Na (7 days), 9 mg Na (4 days), 40 mg furosemide t.i.d. (1 day)</td>
<td>HT</td>
<td>ΔMean BP &gt;10%</td>
<td>50%</td>
</tr>
<tr>
<td>Takeshita, 1982</td>
<td>70 mg Na (7 days), 345 mg Na (7 days)</td>
<td>HT</td>
<td>ΔMean BP &gt;10%</td>
<td>47%</td>
</tr>
<tr>
<td>Koornans, 1982</td>
<td>20 mg Na, 500 mg/100 ml Cr (until in balance)</td>
<td>CRF</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Campcse, 1982</td>
<td>10 mg Na (7 days), 100 mg Na (7 days), 200 mg Na (7 days); random order</td>
<td>HT</td>
<td>ΔMean BP &gt;10%</td>
<td>60%</td>
</tr>
<tr>
<td>Ishii, 1983</td>
<td>6 g NaCl (2 days), 15 g NaCl (5 days)</td>
<td>NT and HT</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Koornans, 1983</td>
<td>50 mg Na (14 days), 300 mg Na (14 days); random order</td>
<td>NT and HT</td>
<td>ΔMean BP &gt;5% or systolic BP &gt;10%</td>
<td></td>
</tr>
<tr>
<td>Fujita, 1984</td>
<td>Ad libitum, furosemide 25 mg/day (7 days), 180 mg Na (7 days)</td>
<td>NT and BHT</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Weinberger, 1986</td>
<td>210 mg Na (4 hr), 10 mg Na, 40 mg furosemide t.i.d.</td>
<td>NT and HT</td>
<td>ΔMean BP &gt;10%</td>
<td>51%</td>
</tr>
<tr>
<td>Dustan and Kirk, 1988</td>
<td>I: 150 mg Na (3 days), 9 mg Na, 1 mg/kg NaCl (4 days), 25 ml/kg NS (3 days)</td>
<td>NT and HT</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Sowers, 1988</td>
<td>40 mg Na (14 days), 180 mg Na (14 days)</td>
<td>NT and HT</td>
<td>ΔMean BP &gt;5% or systolic BP &gt;10%</td>
<td></td>
</tr>
<tr>
<td>Rocchini, 1984</td>
<td>250 mg Na (14 days), 30 mg Na (14 days)</td>
<td>NT and HT</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Oshima, 1987</td>
<td>3 g NaCl (7 days), 20 g NaCl (7 days)</td>
<td>Mild and moderate HT</td>
<td>ΔMean BP*</td>
<td></td>
</tr>
<tr>
<td>Sharma, 1989</td>
<td>220 mg Na (7 days), 20 mg Na (7 days)</td>
<td>NT</td>
<td>ΔMean BP &gt;3 mm Hg</td>
<td>46%</td>
</tr>
<tr>
<td>Umeda, 1989</td>
<td>34 mg Na (8 days), 340 mg Na (8 days)</td>
<td>HT</td>
<td>ΔMean BP &gt;10%</td>
<td></td>
</tr>
</tbody>
</table>

BP, blood pressure; NS, normal saline; NT, normotensive; HT, hypertensive; BHT, borderline hypertensive; CRF, chronic renal failure.

*No numerical cutoff was used.

random order, few studies have been conducted involving the same subjects studied first on a high salt diet and then on a low salt diet, after which a repeat study was done in reverse order. One such study is that of Dustan and Kirk,44 who found that a period of sodium loading after an ad libitum diet revealed more sodium-sensitive normotensive individuals than did salt loading after a period of sodium depletion. This study suggests the need for additional information on the influence of baseline diet on response to changes in dietary sodium intake. Several reported studies clearly indicate that, in addition to the amount of sodium, the amount of chloride contained in the diet has a profound influence on the response to sodium.51 Similarly, there are data to suggest that a high potassium diet ameliorates the hypertensive response to sodium administration in salt-sensitive subjects.42 The many published studies also indicate that we still do not know the time period during which an individual has to consume a high salt diet before sodium sensitivity is apparent. If individuals followed one of the reported protocols for 1 month, 6 months, or 1 year, would more salt sensitivity be evident?

Data collected in studies conducted by my colleagues and I over the past several years exemplify some of the problems encountered in the study of sodium sensitivity. The methods used in these studies have been reported in detail elsewhere.34,35 We have now studied 183 volunteers, 111 normal subjects and 72 patients with labile, borderline hypertension. Analysis of the blood pressure change with sodium loading yielded a normal distribution of responses (Figure 1). We elected to arbitrarily designate as sodium-sensitive only that small portion of the study group who showed an increase of mean blood pressure exceeding 5% when progressing from low to high sodium intake. With this criterion, we found that 15% of the white normotensive subjects and 29% of the white borderline hypertensive patients were sodium-sensitive, but 27% of the normotensive black subjects and 50% of the borderline hypertensive black patients were sodium-sensitive. We have reexamined our data to determine whether a shorter period of sodium depletion or repletion might serve as a more expedient way to screen populations for sodium sensitivity. We found that the decrement in blood pressure during sodium depletion usually occurred gradually over a 3–4-day period. However, the increase in blood pressure to a level exceeding 5% required sodium repletion for a period of at least 5 days (Figure 2). At this point, the increase in blood
pressure became statistically significant \((p=0.0078)\). Examining the response to salt, we found that the transition from a low to high salt diet invariably resulted in a significant increase in cardiac dimensions.\(^5\) In both the salt-sensitive and salt-resistant volunteers, the cardiac index increased 7-8%. The difference in blood pressure response was accounted largely by differences in vascular resistance. Those who were salt-resistant had an average decrease in total peripheral vascular resistance of 10.8%, whereas those who were salt-sensitive fell an average of 5.3%.\(^2\) Within the latter group, there were some individuals who actually vasoconstricted.

Information is scarce on the reproducibility of sodium-sensitivity testing. We have addressed this problem in studies of 19 subjects. One sodium-resistant and 10 sodium-sensitive volunteers underwent a repeat study during which time their high sodium diet was supplemented with 200 meq potassium. Nine of the 10 sodium-sensitive subjects were still sodium-sensitive on retesting, and the one sodium-resistant subject remained sodium-resistant. Sharma et al\(^4\) restudied seven sodium-sensitive and sodium-resistant subjects with a randomized, crossover, single-blind protocol, observing that 14 of 15 displayed the same response. We also retested two sodium-sensitive and two sodium-resistant subjects with protocols omitting supplemental potassium at intervals that varied from 1 to 10 years. Three of these four volunteers had the same results when subjected to sodium depletion and repletion a second time. The only subject who showed no signs of sodium sensitivity was one who had lost 20 pounds and joined an aerobic exercise program for the 5 intervening years between the two studies. Rocchini et al\(^6\) have similarly found that obese adolescents who lost weight displayed less reduction in blood pressure with sodium restriction than they initially did. These observations suggest that weight reduction might be a way to modify salt sensitivity. The effect of age on sodium sensitivity has received limited study. Weinberger et al\(^4\) observed that their sodium-sensitive subjects were significantly older than sodium-resistant subjects. However, Palmer et al\(^3\) reported that only 57% of a group that averaged 85 years of age were sodium-sensitive, a frequency approximating that reported in younger subjects, and Umeda et al\(^9\) found no increase in their sodium sensitivity index with age.

An analysis of the baseline characteristics of our volunteers revealed that the main differences between the salt-sensitive and salt-resistant groups were greater proportions of sodium-sensitive borderline hypertensive and black patients (Table 2). In 1975, Mark et al\(^4\) observed a rise in forearm vascular resistance in borderline hypertensive subjects given a 400 meq sodium diet. We examined the peripheral hemodynamic response to sodium loading and found that both normotensive and hypertensive sodium-sensitive subjects had relatively high forearm vascular resistance when compared with the salt-resistant subjects; in addition, forearm vascular resistance tended to rise with sodium loading in the salt-sensitive subjects, whereas it fell or changed very little in those who were salt-resistant\(^2\) (Figure 3). This abnormality did not appear to be based on permanent structural changes because we discovered that the level of minimum vascular resistance during reactive hyperemia was approximately the same in the two groups.\(^2\) Thus, the salt-sensitive person has high vascular resistance, but this high resistance can be overcome by metabolic stimuli. We found that the venous system is abnormal in the sodium-sensitive subject (Table 2). Venous capacitance is relatively low; thus, their vascular tree appears to be stiff compared with the sodium-resistant individual. We examined endocrine parameters and found that plasma renin activity and aldosterone concentration during the stimulus of sodium depletion was lower in the sodium-sensitive than the sodium-resistant subject, a finding reported by other laboratories as well.\(^4,4\) The abnormalities of vascular resistance, plasma renin activity, and aldosterone concentration resemble those reported in the Dahl salt-sensitive rat.\(^5,19\)
TABLE 2. Subject Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normotensive</th>
<th>Hypertensive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sodium-resistant</td>
<td>Sodium-sensitive</td>
</tr>
<tr>
<td></td>
<td>(n=94)</td>
<td>(n=17)</td>
</tr>
<tr>
<td>Men (%)</td>
<td>58.5</td>
<td>64.7</td>
</tr>
<tr>
<td>Women (%)</td>
<td>41.5</td>
<td>35.3</td>
</tr>
<tr>
<td>White (%)</td>
<td>87.2</td>
<td>76.5</td>
</tr>
<tr>
<td>Black (%)</td>
<td>12.8</td>
<td>23.5</td>
</tr>
<tr>
<td>Family history of hypertension (%)</td>
<td>66.0</td>
<td>52.9</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>26.5</td>
<td>25.9</td>
</tr>
<tr>
<td>Venous capacitance (ml/100 g)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.75±0.15</td>
<td>1.30±0.24†</td>
</tr>
<tr>
<td></td>
<td>4.24±0.29</td>
<td>2.39±0.40‡</td>
</tr>
<tr>
<td></td>
<td>28.62±2.07†</td>
<td>7.10±1.80‡</td>
</tr>
</tbody>
</table>

*Values are mean±SEM.

tp<0.0020; †p<0.0007; and ‡p<0.0080 compared with respective sodium-resistant values.

One might hope that measurement of either forearm vascular resistance, venous capacitance, plasma renin activity, or aldosterone concentration as a marker of sodium sensitivity is possible, thus avoiding the inconvenience of sodium loading, sodium depletion, or both for several days to determine salt sensitivity. However, data distribution shows a substantial overlap of results between salt-sensitive and salt-resistant patients in terms of all these parameters. Thus, their measurement does not appear to be an adequate method of identifying an individual as salt-sensitive. Intracellular ions and several ion transport systems have been examined in hypertensive patients, producing variable results. Abnormal sodium-lithium countertransport, a genetically determined trait, has been the most consistent finding\textsuperscript{55} and has also been described in non-modulating hypertensive individuals who are sodium-sensitive\textsuperscript{56,57}; thus, it might serve as a marker of sodium sensitivity.

Evidence has emerged that an abnormality of catecholamine regulation is involved in sodium sensitivity. Plasma norepinephrine ordinarily rises in response to sodium restriction because of a reduction in intravascular volume. During sodium repletion, plasma norepinephrine levels decline in normal individuals. Conversely, Campese et al\textsuperscript{39} have observed that plasma norepinephrine levels fail to suppress normally in salt-sensitive patients. In our sodium-sensitive normotensive and hypertensive subjects, plasma norepinephrine levels responded normally to sodium repletion. It has been reported that urinary dopamine levels do not rise appropriately with increases in sodium intake in salt-sensitive subjects. Additionally, certain sodium-sensitive hypertensive individuals have impaired ability to modulate their renovascular and adrenal responsiveness to angiotensin II.\textsuperscript{56}

Although there has been a great deal of interest in the response of individuals to short-term changes in sodium intake, little attention has been directed toward the long-term implications of these findings. We have followed a group of seven salt-sensitive and 24 salt-resistant individuals who have undergone repeated measurements of blood pressure, weight, urinary sodium and potassium excretion, echocardiographic estimation of cardiac output and total peripheral resistance, and plethysmographic measurements of forearm blood flow and forearm vascular resistance. These measurements have been repeated every 6 months, and 31 subjects have now completed at least 1 year of follow-up. We found that mean arterial blood pressure, which was approximately equal in the two groups during sodium depletion, remains higher in the sodium-sensitive group than the sodium-resistant group over 1 year of follow-up. We have also discovered that urinary sodium excretion, which was identical in the two groups at the beginning of the study, tends to fall in salt-sensitive individuals with time. One possible explanation for
this finding is the fact that these individuals learn that they are salt-sensitive while taking part in the short-term studies and, either consciously or unconsciously, reduce their daily sodium intake (Figure 4).

During sodium depletion, mean arterial blood pressure fell an average of 7.4% in the sodium-sensitive group. With sodium repletion, blood pressure rose 3.4% and was 4.0% above sodium-depleted levels 1 year later. Conversely, sodium depletion resulted in a fall in blood pressure of only 0.2% in the sodium-sensitive group, an additional 2.3% during sodium repletion, and at 1 year was only 1.1% above sodium-depleted levels. The blood pressure of the sodium-sensitive subjects was significantly higher than that of the sodium-resistant ones ($p<0.009$) at all times except during sodium depletion, when pressures were approximately equal. However, the 24-hour urinary sodium excretion of the sodium-sensitive and sodium-resistant groups did not significantly differ between the two groups, although a trend toward lower sodium excretion with time was noted among those who were sodium-sensitive. The periods of sodium depletion and repletion were performed in a clinical research center. Blood pressure and sodium excretion did not significantly differ during sodium depletion, but during sodium repletion, sodium excretion was slightly lower and blood pressure significantly higher in the sodium-sensitive group. These observations are consistent with an abnormal pressure-natriuresis relation in the sodium-sensitive group, which is similar to observations in the Dahl salt-sensitive rat.

As in our larger group of subjects who underwent short-term testing for sodium sensitivity, forearm vascular resistance was significantly higher in the sodium-sensitive group during high, low, and ad libitum sodium diets ($p<0.009$). After 12 months of follow-up, average forearm vascular resistance was 59% higher in the sodium-sensitive group. Forearm vascular resistance climbed steeply by 40% during sodium repletion but at 6 and 12 months was approximately the same as levels obtained during the baseline ad libitum diet.

The cardiac index did not significantly differ between the sodium-sensitive and sodium-resistant groups during short-term sodium depletion and repletion. However, by 12 months the cardiac index was 21.3% higher than during sodium depletion in the sodium-resistant group ($p=0.0005$) but only 4.8% higher in the sodium-sensitive group (NS). Thus, the sodium-resistant group demonstrated the capacity of adapting to a significant increase in cardiac output without a significant increase in blood pressure because of an appropriate decrease in total peripheral vascular resistance.

In addition, we have contacted our volunteers once a year to determine their current blood pressure and diet status. This long-term study has been designed to determine if those individuals who appear to be sodium-sensitive by short-term manipulation of dietary sodium intake eventually become hypertensive if they continue to follow the usual North American diet. We have performed a preliminary life-table analysis of normotensive and borderline hypertensive salt-sensitive and salt-resistant subgroups. The end point for this portion of the study is the institution of antihypertensive therapy or the development of average diastolic blood pressure exceeding 90 mm Hg. As expected, we found that the probability of developing chronic hypertension was greater for those in the borderline hypertensive group than in the normotensive volunteers. For the borderline hypertensive group, clinical hypertension developed more frequently in those who were sodium-resistant during the early years of follow-up. However, with time the incidence of hypertension in the sodium-sensitive group rose to levels approximately the same as in the sodium-resistant group. For the normotensive group,
the incidence of hypertension was higher in the sodium-sensitive subjects. Thus, at least for the normotensive subjects, the presence of sodium sensitivity suggested that the individual was more likely to become hypertensive with time than one who manifested sodium resistance. We acknowledge the importance of the continual addition of patients to this long-term study and the follow-up of larger groups, as it is only through such a long-term follow-up that the true clinical implications of sodium sensitivity will become established.

In summary, we have found that the blood pressure of a minority of our population responds to changes in dietary sodium intake within the range of "normal" with much greater changes than are seen in the majority of individuals. These sodium-sensitive persons share several physiological characteristics with the Dahl salt-sensitive rat, a genetic model of sodium responsiveness. These characteristics are: 1) an enhanced blood pressure response to sodium depletion or repletion; 2) higher baseline blood pressure; 3) higher forearm vascular resistance, particularly with sodium loading; 4) suppressed renin release during sodium depletion; 5) reduced circulating aldosterone levels; and 6) a shift in the blood pressure--natriuresis relation. These observations support the conclusion that sodium sensitivity is genetically linked in humans as well as in Dahl salt-sensitive rats.

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References


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