Sodium Balance in Renal Failure
A Comparison of Patients with Normal Subjects Under Extremes of Sodium Intake

HEIN A. KOOMANS, JAN C. ROOS, EVERT J. DORHOUT MEES, AND IBRAHIM M.K. DELAWI

SUMMARY To gain insight into the factors involved in the maintenance of sodium balance in patients with chronic renal failure, we studied 10 patients with a creatinine clearance of 11.5 ± 4.0 ml/min after equilibrium on 20 and 120 mEq of sodium per day. The measurements included blood pressure, plasma volume, blood volume, extracellular fluid volume, plasma renin activity, plasma aldosterone, and plasma norepinephrine. For comparison, eight normal volunteers were studied after equilibration on 20, 200, and 1128 mEq of sodium per day. The latter intake was chosen to match the high sodium intake per residual renal function in the patients. In the patients, equilibrium after raised sodium intake was accompanied by a marked increase in blood pressure and blood volume, a moderate fall in plasma renin activity and levels of aldosterone and norepinephrine, and only little expansion of the interstitial space. The 24-hour creatinine clearance rose by 21.2 ± 7.2%. Fractional sodium excretion (× 100%) was 5.3 ± 0.8% during the 120 mEq sodium diet. In the normal volunteers, increasing the sodium intake from 20 to 1128 mEq/day evoked no consistent change in blood pressure but caused a comparable rise in blood volume, considerable suppression of plasma renin activity, aldosterone, and norepinephrine, and a much larger increase in interstitial volume. Their creatinine clearance had risen by 22.4 ± 6.5%, and their fractional sodium excretion during the 1128 mEq sodium intake was 3.9 ± 0.2%. These results suggest that in normal subjects the maintenance of sodium balance over a wide range of sodium intake is particularly dependent on variations of neurohumoral influences on the kidney, while in patients with renal failure relatively large variations in arterial pressure are necessary as well. The marked difference in amount and distribution of the retained volume may be explained by a vasoconstrictive reaction to sodium loading in the patient group. (Hypertension 7: 714-721, 1985)

KEY WORDS • sodium loading • hypertension • blood volume • extracellular fluid volume • renin • aldosterone • norepinephrine

In normotensive subjects, only very large increases in sodium intake will raise the blood pressure to some extent and it is almost impossible to obtain a hypertensive level.1 Contrarily, in humans with advanced renal failure, hypertension frequently occurs even during a normal sodium intake.2,3 Since the classical report of Ambard and Beaujard4 in 1904, it has been known that increases in sodium intake in patients with diminished renal function are accompanied by increases in arterial pressure. Indeed, in a previous study we found that, within a group of patients with varying degrees of renal failure, the salt sensitivity of the blood pressure increased with decreasing renal function.5

Although the mechanism underlying renal hypertension has not been completely elucidated, it is likely to be related to the relative inability of the diseased kidney to excrete sodium. Under such conditions increased sodium intake will more readily lead to volume retention, which sets in motion a sequence of changes leading to elevation of the arterial pressure.6,7 This event, and the concomitant suppression of sodium-retaining factors like angiotensin II, aldosterone, and adrenergic tone, promotes restoration of the sodium balance. Because normal subjects exhibit only minor changes in blood pressure during variation of sodium intake, it may be expected that the volume responses are also small in comparison to patients with renal failure, but that no difference would be found if comparable sodium loads relative to the glomerular filtration rate are administered.

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In the present study, we have investigated this issue by assessing blood pressure, fluid volumes, and hormonal factors in patients with advanced renal failure after equilibration on two levels of sodium intake. For comparison, a group of normal subjects was studied during three levels of sodium intake, two of which were in the same range as those in the renal patients. The third sodium intake level chosen was very high to match the high sodium loads per residual renal function in the patients.

Subjects and Methods

Studies were carried out in 11 patients with stable chronic renal failure and creatinine clearances of about 10 ml/min. None of these subjects had overt heart failure. No selection was made with respect to blood pressure level or nature of renal disease. Any antihypertensive medication, including diuretics, had been discontinued at least 2 weeks before the study. Patient data are given in Table 1. Additional studies were performed in eight healthy volunteers (aged 21–26 yr; 2 women and 6 men). None of these subjects had a family history of hypertension. The protocol was approved by the Utrecht University Hospital Ethical Committee, and informed consent was obtained from all subjects.

Patients with chronic renal failure were admitted to a metabolic ward and received a diet containing 20 mEq of sodium and 70 mEq of potassium. To advance sodium balance on this low intake level, they were encouraged to use a salt-poor diet a week before admission. When, as judged from body weight and sodium excretion, balance had been achieved, we measured plasma volume (PV), extracellular fluid volume (ECFV), plasma renin activity (PRA), plasma aldosterone (PA), and plasma norepinephrine (PNE) during recumbency. Blood pressure was recorded with a sphygmomanometer four times daily after 10 minutes of supine rest in a quiet room. From these measurements, the mean arterial pressure (MAP = diastolic pressure + 1/3 pulse pressure) was calculated.

After completion of these measurements, the sodium intake was raised to 120 mEq/day by adding sodium chloride. Again, after sodium balance had been achieved, which generally occurred within 1 week, the aforementioned measurements were repeated. Twenty-four-hour urine collections were made throughout the study.

The normal subjects first received a diet containing 20 mEq of sodium (low sodium) for 5 days as outpatients. They returned to the metabolic ward daily at noon for the measurement of body weight and blood pressure. The latter was taken by hand after the subject had rested supine for 10 minutes in a quiet room. The subjects spent the morning of Day 5 recumbent in a quiet laboratory room for collection of the same data as collected in the patient group. Blood pressure was recorded for 2 hours with an Arteriosonde (model 1217; Hoffman-La Roche Inc., Cranbury, NJ, USA). The arterial pressure was calculated as a mean from these measurements and those taken by hand. After an interval of 2 days of free diet, a diet containing 200 mEq of sodium (normal sodium diet) was started and the measurements (except the volume measurements) were repeated on the fifth day of this period. After another 2 days, the subjects were hospitalized and received 300 mEq of sodium chloride orally, supplemented by a daily infusion of 4 to 6 L of isotonic sodium chloride solution divided equally from 0700 hours until 2400 hours. The amount infused was adjusted individually to provide a total load of about 12 mEq of sodium per milliliter per minute of (estimated) glomerular filtration rate. Five subjects received 1224 mEq, one subject 1070 mEq, and two subjects 916 mEq of sodium daily (mean 1128 ± 141 mEq; high sodium diet. On the morning of the fourth day, the same measurements as during the low salt diet were done. During this period the subjects were screened regularly for symptoms of overhydration. During each study period 24-hour urine collections were made. Potassium intake was kept constant at 80 mEq/day.

The ECFV and PV measured as 82Br- and 131I-labeled albumin distribution volumes, as described elsewhere. Blood volume was calculated from PV and whole body hematocrit. The 82Br space was corrected for Donnan’s equilibrium and erythrocyte 82Br content. The PRA (pmol/L/sec) was measured by radioimmunoassay according to a modification of the method described by Haber et al. Undiluted plasma was incubated for 1 hour at 37 °C at pH 5.6 in the presence of phenylmethylsulfonyl fluoride and 8-hydroxyquinoline as inhibitors, followed by deproteinization with acetone/4 N ammonia (9:1), dried with an air stream and dissolved in PRA buffer. The PA (pmol/L) was assayed by radioimmunoassay after extraction from 2 ml of plasma with dichloromethane. The PNE (pmol/L) was measured by the radioenzymatic technique described by Peuler and Johnson with minor modifications in the composition of the incubation mixture. Rat liver catechol-O-methyltransferase was isolated by ammonium sulfate protein fractionation. Sodium, potassium, and creatinine were determined by autoanalyzer (Technicon, Tarrytown, NJ, USA).
Changes within groups and differences between groups were evaluated by Wilcoxon’s test for paired and unpaired data. Correlations were analyzed with Spearman’s ranking correlation test. All data are presented as means ± SEM.

Results
Electrolyte Excretion and Renal Function
One patient (Patient 11) did not achieve sodium balance during the high sodium diet. Her findings are given separately. The remaining patients reached sodium balance within the period of the study. Their mean daily sodium excretion is given in Figure 1. During the high sodium intake the estimated cumulative sodium balance was +254 mEq. Creatinine clearance (C) and fractional sodium excretion \(\text{C}_{\text{Na}}/\text{C}_{\text{creatinine}} \times 100\%\) increased in all patients, while potassium excretion remained unaltered. The mean values are presented in Table 2. The percent increase in creatinine clearance was 21.2 ± 7.2%.

In the normal volunteers the sodium excretion closely approached the intake at all three levels of sodium intake (Figure 2). In the last period, the mean intake was 1128 mEq/day and the estimated cumulative sodium balance was +689 mEq. Creatinine clearance rose in all subjects but one when sodium intake was increased (see Table 2). The overall increase from low to high sodium intake was 22.4 ± 6.5%. Fractional sodium excretion increased in each subject when sodium intake was increased. Potassium excretion increased only when sodium intake was raised from normal to high levels.

Blood Pressure
Individual changes in mean arterial pressure are given in Figure 3. In most patients the blood pressure was elevated even during low sodium intake. Increase of sodium supply raised blood pressure further in all patients; the mean increase was 12.2 ± 1.4 mm Hg. In the normal subjects no consistent changes in blood pressure were observed. In only two subjects was the blood pressure substantially higher during the high sodium intake compared with that during the low sodium intake; two others even showed some reduction in blood pressure.

Body Fluid Volumes
Body weight, ECFV, blood volume, and PV are given in Table 2. The increase of sodium intake caused a mean rise in body weight and ECFV amounting to

![Figure 1. Mean daily sodium excretion (± SEM) in 10 patients with chronic renal failure. The broken lines represent the sodium intake, which amounts to 20 and 120 mEq/day respectively.](http://hyper.ahajournals.org/content/7/5/716/F1)

**Table 2. Renal Performance, Blood Pressure, Body Fluids, and Humoral Factors at Different Sodium Intakes**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chronic renal failure</th>
<th>Normal subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{U}_{\text{Na}}) (mEq/24 hr)</td>
<td>21 ± 3†</td>
<td>22 ± 4†</td>
</tr>
<tr>
<td>(\text{U}_{\text{Na}}) (mEq/24 hr)</td>
<td>42 ± 4</td>
<td>45 ± 19</td>
</tr>
<tr>
<td>(\text{C}_{\text{cr}}) (ml/min)</td>
<td>10.4 ± 1.3‡</td>
<td>12.3 ± 1.4</td>
</tr>
<tr>
<td>(\text{FENa}) (%)</td>
<td>1.2 ± 0.2†</td>
<td>5.3 ± 0.8</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>117 ± 4†</td>
<td>129 ± 5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.5 ± 1.7†</td>
<td>63.0 ± 1.7</td>
</tr>
<tr>
<td>ECFV (L)</td>
<td>13.0 ± 0.6‡</td>
<td>14.6 ± 0.5</td>
</tr>
<tr>
<td>Blood volume (L)</td>
<td>4.01 ± 0.26†</td>
<td>4.44 ± 0.29</td>
</tr>
<tr>
<td>Plasma volume (L)</td>
<td>2.84 ± 0.18†</td>
<td>3.24 ± 0.21</td>
</tr>
<tr>
<td>PRA (fmol ANG I/L/sec)</td>
<td>580 ± 89†</td>
<td>734 ± 143‡</td>
</tr>
<tr>
<td>PA (pmol/L)</td>
<td>542 ± 258§</td>
<td>518 ± 197‡</td>
</tr>
<tr>
<td>PNE (nmol/L)</td>
<td>2.82 ± 0.22†</td>
<td>3.72 ± 0.45</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
The right-hand column refers to differences within the normal group from 20 to 1128 mEq of sodium intake.

\(\text{U}_{\text{Na}}\) = sodium excretion rate; \(\text{U}_{\text{Na}}\) = potassium excretion rate; \(\text{C}_{\text{cr}}\) = creatinine clearance; \(\text{FENa}\) = fractional sodium excretion; MAP = mean arterial pressure; ECFV = extracellular fluid volume; PRA = plasma renin activity; ANG I = angiotensin I; PA = plasma aldosterone; PNE = plasma norepinephrine.

* Sodium intake (mEq/24 hr).
† p < 0.01.  ‡ 0.01 < p < 0.05.
§ Geometrical mean
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1.46 ± 0.22 kg and 1.61 ± 0.18 L respectively in the patients, which corresponded with the estimated cumulative sodium balance. No edema was detected. More substantial changes were observed in the normal subjects, in whom, from low to high sodium intake, the increments in body weight and in ECFV were 4.04 ± 0.61 kg and 3.65 ± 0.63 L respectively, which are both significantly larger than that observed in the patients (p < 0.01). Some vesperal edema was a common finding. Even from normal to high sodium intake level, the increase in body weight (2.69 ± 0.40 kg) was larger than the one noticed in the patients (p < 0.05).

In Figure 4 the individual changes in blood pressure are plotted against the individual changes in ECFV. For this evaluation ECFV was expressed as milliliters
per kilogram of lean body mass, as reported earlier. Relative to the change in blood pressure, the change in ECFV was much larger in the normal subjects ($p < 0.005$).

The increases in blood volume and PV in the patients ($0.43 \pm 0.07$ L and $0.40 \pm 0.07$ L respectively) were similar to those observed in the normal subjects from low to high sodium diet ($0.46 \pm 0.08$ L and $0.43 \pm 0.08$ L respectively). The ratio between blood volume and interstitial fluid volume remained unchanged in the patients: $0.396 \pm 0.018$ during 20 mEq of sodium diet and $0.393 \pm 0.017$ during 120 mEq of sodium diet. For the ratio between plasma volume and interstitial fluid volume these values were $0.282 \pm 0.013$ and $0.284 \pm 0.012$. In the normal subjects, both ratios decreased significantly ($p < 0.02$) after switching from the low to the high sodium diet: blood volume/interstitial fluid volume from $0.398 \pm 0.019$ to $0.347 \pm 0.010$ and PV/interstitial fluid volume from $0.246 \pm 0.010$ to $0.224 \pm 0.08$. Neither in the patients nor in the normal subjects did we find correlations between changes in any of these fluid volumes and changes in blood pressure.

### Plasma Renin Activity and Aldosterone and Norepinephrine Levels

During low sodium intake the PRA and PA levels were not different between the normal and patient group (see Table 2). The values always decreased when sodium intake was increased. In the patients, PRA fell by $59 \pm 4\%$ and PA levels by $42 \pm 7\%$. In the normal subjects, PRA decreased by $72 \pm 3\%$ and PA level by $69 \pm 8\%$ after changing from low to normal sodium intake. During this intake level their PRA and PA levels were still similar to those measured in the normal subjects consuming 200 mEq of sodium. The PRA levels tended to be lower in the normal subjects during the 1128 mEq of sodium intake than in the patients on the 120 mEq intake, but the difference was not significant ($p = 0.09$). In the normal subjects the drop in PNE levels from the low to the very high sodium intake was significantly larger than the one in the patients ($p < 0.005$). There were no correlations between these hormonal changes and changes in blood pressure or the amount of fluid retention in either the patients or the normal volunteers.

#### Subject Not Attaining Sodium Balance

Patient 11, who had polycystic kidney disease, continued to retain sodium during the diet containing 120 mEq of sodium, which led to a large gain in weight and ECFV (Table 3). Her PRA and PA level were markedly stimulated during the low sodium diet but became suppressed very effectively after the sodium intake was raised, while no change in blood pressure was noticed.

### Discussion

These results confirm a previous report that the sensitivity of the blood pressure to changes in sodium intake is greatly increased in patients with advanced renal failure. Small increments in sodium intake were invariably followed by a large increase in blood pressure caused a further decrease of PRA by $78 \pm 4\%$ and of PA by $48 \pm 10\%$ to values much below the levels observed in the patients ($p < 0.001$).

The mean values of PNE are also presented in Table 2. During the diet containing 20 mEq of sodium, the PNE levels were slightly but not significantly ($p = 0.09$) lower in the patients than in the normal subjects. When on the 120 mEq of sodium diet, the patients displayed a similar mean concentration as that measured in the normal subjects consuming 200 mEq of sodium. The PNE levels tended to be lower in the normal subjects during the 1128 mEq of sodium intake than in the patients on the 120 mEq intake, but the difference was not significant ($p = 0.09$). In the normal subjects the drop in PNE levels from the low to the very high sodium intake was significantly larger than the one in the patients ($p < 0.005$). There were no correlations between these hormonal changes and changes in blood pressure or the amount of fluid retention in either the patients or the normal volunteers.

### Table 3. Data of One Patient (Patient 11) Not Attaining Sodium Balance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sodium intake (mEq/24 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN,V (mEq/24 hr)</td>
<td>20</td>
</tr>
<tr>
<td>Uk,V (mEq/24 hr)</td>
<td>11</td>
</tr>
<tr>
<td>Ccr (ml/min)</td>
<td>57</td>
</tr>
<tr>
<td>FEoo (%)</td>
<td>12.3</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>0.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>102</td>
</tr>
<tr>
<td>ECFV (L)</td>
<td>53.1</td>
</tr>
<tr>
<td>Blood volume (L)</td>
<td>11.0</td>
</tr>
<tr>
<td>Plasma volume (L)</td>
<td>3.2</td>
</tr>
<tr>
<td>PRA (fmol ANG I/L/sec)</td>
<td>2.1</td>
</tr>
<tr>
<td>PA (pmol/L)</td>
<td>2230</td>
</tr>
<tr>
<td>PNE (nmol/L)</td>
<td>1210</td>
</tr>
</tbody>
</table>

Abbreviations as for Table 2.
sure, while, in normal subjects, increments about 10 times as large could produce only a small, and not consistently present, blood pressure rise. The rise in blood pressure in normal subjects was less obvious than the one observed by Luft et al., who administered equally high salt loads to healthy human beings. Differences in study protocol do not give a ready explanation, and no other reference studies in which similar sodium loads were supplied are available, as far as we know.

Our observations are in accordance with the concept developed by Guyton et al., who proposed that the kidney's ability to excrete sodium and water is the overriding mechanism of blood pressure regulation. In patients with renal failure this ability is obviously reduced consequent to the fall in the number of functioning nephrons or glomerular filtration. Thus, if the glomerular filtration rate were the main determinant of the hemodynamic sequelae of sodium loading, similar sodium loads relative to the glomerular filtration rate in subjects with and without renal impairment should evoke similar hemodynamic responses.

However, this supposition did not appear to hold true in our study; when given a comparable sodium load per nephron, the patients reacted with a much larger rise in blood pressure, less suppression of PRA, PA, and PNE, and less total volume retention but a similar rise in blood volume. Therefore, the question is raised whether the increase in sodium excretion needed to restore sodium balance was mediated differently in these patients.

In the normal subjects the change from a low to a very high sodium intake caused a rise in creatinine clearance of 22.4%, which is similar to that seen in the study by Luft et al. Almost the same relative increase was observed in the patients with chronic renal failure, which indicates some reserve renal function even in these subjects. More substantial changes were observed in fractional sodium excretion, which rose about fourfold in the patients and was similar to the rise in the normal subjects from normal to high sodium intake. In the latter group, fractional sodium excretion increased about 40-fold from low to high sodium intake to a value that approached the fractional sodium excretion in the patients. Thus, in both groups the changes in sodium excretion were, for the most part, accomplished by adjustments of the tubular sodium reabsorption.

As outlined above, the tremendous increase in fractional sodium excretion in the normal volunteers occurred without a consistent change in blood pressure and was apparently dependent on other factors; in particular, their renin-angiotensin-aldosterone system was very effectively suppressed during the high sodium intake. The PNE concentration, which may be taken with some reserve as a measure of sympathetic tone, was also significantly suppressed. These humoral changes were similar to those observed by Luft et al. and suggest that they played a major role in the achievement of the high fractional sodium excretion. In addition, the large increase in extracellular volume may have reduced tubular reabsorption by a change in peritubular physical factors caused by simple dilution.

When compared for the same range of absolute sodium excretion — from 20 to 120 mEq in the patients and from 20 to 200 mEq in the normal subjects — neither the PRA and PA levels nor their degree of suppression were different in the patients (see Figure 5). Therefore, when taken as a function of sodium excretion rate, a reduced flexibility of the PRA, as reported by others, was not a characteristic of the patients under study. At the same time, however, the fractional excretions were much higher in the patients: 5.3% against only 0.8% in the normal subjects. That is, during similar suppression of renin and aldosterone, individual nephrons in the patients with renal failure augmented their sodium excretion much more than did the nephrons in the normal subjects. Moreover, at comparably high fractional sodium excretion rates (i.e., when the normal subjects consumed 1128 mEq and the patients consumed 120 mEq of sodium), PRA and PA were suppressed to considerably lower values in the normal subjects. The same holds true for the observed changes in PNE levels, although the ultimately attained concentrations were not significantly different between the two populations. The concomitant increment of extracellular fluid was much less in the patients.

Therefore, how the large rise in fractional sodium excretion rate was mediated in the patients with diminished renal function remains to be explained. It is attractive to hypothesize that their substantial rise in blood pressure played an important role, which was complementary to the suppression of neurohumoral sodium-retaining influences. The observation that the one patient who did not attain balance on the diet containing 120 mEq of sodium (see Table 3) showed no increase in blood pressure, fits this notion, but further direct proof is not offered by the current study. Such proof may follow from experiments in which the effects of blood pressure changes on the kidney are abolished, for example, through the animal model recently used by Hall et al. Their experiments demonstrated that uninephrectomized dogs did not escape from the sodium-retaining effects of aldosterone or angiotensin II when the renal perfusion pressure was kept constant with a servocontrolled system.

Alternatively, the large rise in sodium excretion per nephron in the patients may have resulted from increased concentrations of a natriuretic substance that has been found in the blood of patients with far advanced renal failure or from enhanced end-organ sensitivity to efferent mediators within the volume control system. The latter possibility is one of the mechanisms proposed by Epstein et al., who noticed a far greater increase in fractional sodium excretion in renal patients undergoing head-out immersion compared with similarly treated healthy controls. The present study does not provide evidence for or against these possibilities.

In both groups increased sodium intake was accompanied by a positive sodium balance and a rise in body
fluids, but there were differences in total retention and distribution of fluid. The increase in blood volume was considerable and of similar magnitude in the patients and in the normal subjects. However, the increase in total extracellular fluid, judged from body weight, \(^{25}\)Br distribution volume, and cumulative sodium balance, was much more substantial in the normal subjects and in the same range as found in the study by Luft et al.\(^{1,13}\) The total retention was much larger in the normal subjects, which contrasts with their minute blood pressure response. It seems as if they endure the volume expansion rather indolently, while the patients try to resist it (see Figure 4). This dissimilarity also is expressed in the reduction of the ratio between blood volume and interstitial fluid volume that occurred in the normal subjects but not in the patients. We observed an equally different pattern of volume distribution when we studied the effects of sodium loading in patients with severe and moderate renal failure.\(^5\)

These different patterns of volume response may be related to different hemodynamic reactions. Increased sodium intake is believed to be followed by a rise in blood volume, cardiac filling pressure, cardiac output, and arterial pressure; the latter is needed to raise sodium excretion to the level of intake.\(^5\)\(^7\) In extension, it has been postulated that a sustained elevation of cardiac output eventually leads to arteriolar vasoconstriction because of whole body autoregulation,\(^20\)\(^21\) which down-regulates cardiac output, maintains the elevated blood pressure, and simultaneously reduces interstitial expansion by decreasing capillary hydrostatic pressure.\(^25\)\(^25\) Although speculative, the larger rise in interstitial volume in the normal volunteers may be explained by a lack of this autoregulatory vasoconstriction at the time of our measurements. In fact, the finding of an increased blood volume and unaltered blood pressure suggests that at the time of measurements even some vasodilatation was present to which the marked suppression of neurohumoral factors may have contributed. Contrarily, the marked elevation of blood pressure, the preservation of the ratio between blood volume and interstitial volume, and the relatively moderate suppression of these neurohumoral factors observed in the patients suggest that in these subjects some degree of vasoconstriction had occurred. However, the one patient who did not achieve sodium balance and in whom the blood pressure did not increase (see Table 3) demonstrated that this tendency is not a rule. We cannot exclude that a time factor is responsible for these differences, because in animals subjected to sodium loading, the autoregulatory adjustments may be postponed to 1 to 3 weeks after the start of the loading.\(^22\)\(^25\)\(^26\)

Increased salt sensitivity was also observed in about half the patients with essential hypertension, where it has been attributed to reduced suppressibility or enhanced sensitivity to sympathetic tone or parts of the renin-angiotensin-aldosterone system.\(^25\)\(^29\) Therefore, a parallel exists with our observations in patients with renal failure, and it is plausible that the presumed vasoconstriction may have been due to the persistent influence of these neurohumoral factors on the arterioles, and the salt sensitivity to their effect on the kidneys, as well as to a reduced glomerular filtration rate.

In sum, these studies demonstrate that the blood pressure was very salt sensitive in patients with renal failure, whereas in normal subjects it was not. In the latter, restoration of the sodium balance during salt loading most likely depended on suppression of the renin-angiotensin-aldosterone system and sympathetic tone and occurred at the cost of a relatively large interstitial fluid expansion. Contrarily, in patients with renal failure both suppression of salt-retaining factors and a rise in blood pressure were probably important; in these subjects the restoration of sodium balance was accompanied by relatively little interstitial fluid expansion but a blood volume expansion equivalent to that in the normal subjects. These different patterns can be explained by a more vigorous vasoconstrictive reaction to sodium loading in patients with renal failure.

References

Sodium balance in renal failure. A comparison of patients with normal subjects under extremes of sodium intake.
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