Effect of an Intravenous Sodium Chloride Load on Renal Hemodynamics and Electrolyte Excretion in Essential Hypertension

By Paul T. Cottie, M.D., John M. Weller, M.D., and Sibley W. Hoehler, M.D.

Excretion of infused sodium, chloride, and water increased proportionately in patients with progressively more severe grades of hypertension and of increased renal vascular resistance. These relationships held so long as renal plasma flow and glomerular filtration rate were not greatly impaired. The abnormality was characterized by increased renal tubular rejection of sodium, chloride and water.

That most hypertensive patients excrete more water, sodium, and chloride than do normotensive patients when given sodium chloride has been well established since the studies of Farnsworth and Barker.1-3 They pointed out that during diuresis a higher percentage of filtered chloride is excreted by hypertensive individuals. Green, Wedell, Wald, and Learned4 found water and sodium excretion to be directly related to blood pressure when water and sodium were administered. Using osmotic loading, Brodsky and Graubarth5 demonstrated a 2 to 2 ½ times greater sodium chloride excretion in hypertensive than in normotensive patients. Birchall, Tuthill, Jacobs, Trautman, and Findley6 found a lack of antidiuretic response following hypertonic sodium chloride administration during water diuresis in hypertensive patients which they concluded was not due to a reduction in the release of antidiuretic hormone. Thompson, Silva, Kinsey, and Smithwick7 showed that hypertensive patients reject a higher proportion of infused sodium than do normotensive patients and that sodium excretion roughly correlates with the mean arterial blood pressure. Studies by Green and Ellis8 also revealed that sodium output correlated with blood pressure. Both basal sodium excretion and excretion under sodium chloride load were higher in hypertensive than in normotensive individuals. Green, Johnson, Bridges, and Lehmann9 classified hypertensive patients as "high salt-excretors" and "normal salt-excretors." High salt-excretors had an elevated output of salt and water, both under basal conditions and under load, an increased salt appetite, nearly normal glomerular filtration rate maintained in the face of reduced renal plasma flow, and a normal cardiac output. Normal salt-excretors had a normal output of salt and water, both under basal conditions and under load, a normal salt appetite, a marked decrease in glomerular filtration rate and renal plasma flow, and a normal cardiac output. It was suggested that sodium output correlated with the filtration fraction. These findings were interpreted as an indication that "high salt-excretors" represent an earlier stage of hypertensive disease, whereas "normal salt-excretors" represent a later stage.

The present investigation was undertaken to determine: (1) if these abnormalities of water and electrolyte excretion are present in mild hypertension before there is impairment of renal plasma flow or whether they are secondary to hemodynamic dysfunction of the kidneys; (2) if the increased water and sodium chloride excretion found in hypertensive individuals under load is related to an in-

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EFFECT OF SODIUM CHLORIDE LOAD

TABLE 1.—Blood Pressure, Age and Sex of Subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Arterial blood pressure (mm. Hg)</th>
<th>Age</th>
<th>Number of males</th>
<th>Number of females</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Normal</td>
<td></td>
<td></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Mean</td>
<td>110/70</td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>102/66 to 119/80</td>
<td>25 to 56</td>
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<tr>
<td>II. Mildly hypertensive</td>
<td></td>
<td></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Mean</td>
<td>156/97</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>142/86 to 180/108</td>
<td>31 to 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III. Moderately severely hypertensive</td>
<td></td>
<td>36</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Mean</td>
<td>174/118</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>160/111 to 185/121</td>
<td>27 to 50</td>
<td></td>
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</tr>
<tr>
<td>IV. Severe hypertensive</td>
<td></td>
<td></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Mean</td>
<td>213/137</td>
<td>43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>190/125 to 232/159</td>
<td>29 to 52</td>
<td></td>
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</tr>
</tbody>
</table>

crease in glomerular filtration rate or filtration fraction or is a consequence of augmented tubular rejection; and (3) if it is adequate to group patients with varying degrees of hypertension into "high salt-excretors" and "normal salt-excretors."

METHODS

Renal plasma flow, glomerular filtration rate, sodium, chloride, and potassium clearance and water excretion were studied following sodium chloride loading in normotensive patients and in patients having varying degrees of essential hypertension. None had cardiac failure or edema. Venous pressures and arm-to-tongue circulation times were determined on all severely hypertensive patients and these values were normal. None of the patients had primary renal disease or azotemia, nor had they been sympathectomized. Table 1 shows the arterial blood pressure, sex, and age distribution of the subjects. There were 5 individuals in each group. All were instructed to add no salt to a regular diet, either in its preparation or at the table, but to distribute over their food the contents of one packet containing 2 Gm. of sodium chloride per day. This diet was instituted and all medication was stopped 3 weeks before the study, except for 3 severely hypertensive patients who had treatment with ganglionic blocking agents discontinued 2 weeks before. All were instructed to collect a 12-hour urine the night before the test, which was performed the following morning in the fasting ambulant state. Three pre-loading collection periods were followed by 6 load periods, all of 15 minutes' length. An indwelling bladder catheter was used and the patients remained recumbent during the test. The glomerular filtration rate was measured by inulin and renal plasma flow by para-aminohippurate clearance. Prior to the pre-loading periods, a priming infusion of 43 ml. of 10 per cent inulin and 2 ml. of 20 per cent sodium para-aminohippurate diluted with 0.9 per cent sodium chloride to 150 ml.; given at a rate of 8 ml. per minute per 1.73 M.² body surface, was followed by a sustaining infusion containing 75 ml. of inulin solution and 4.0 ml. of sodium para-aminohippurate solution diluted with 0.9 per cent sodium chloride to 1,000 ml., given at a rate of 8 ml. per minute per 1.73 M.² body surface. Bladder rinsing was started 20 minutes after beginning the sustaining infusion. The load infusion was started at the end of the third preloading period and was given during 4 or 5 periods. One or 2 recovery periods with isotonic saline infusion followed the load. The load infusion contained 500 ml. of 2.5 per cent sodium chloride per 1.73 M.² body surface and inulin and sodium para-aminohippurate equivalent in concentration to that in the sustaining infusion. It was given at a rate of 8 ml. per minute per 1.73 M.² body surface. The resorcienol method of Roe as modified by Schreiner" was used for determination of inulin. Para-aminohippurate was determined by the method of Smith, Finkelstein, Aliminoss, Crawford, and Graber.¹¹ The para-aminohippurate plasma concentration was usually between 1 and 2 mg. per 100 ml. Sodium and potassium were analyzed by flame photometry. Chlorides were determined by the method of Schales and Schales.¹² The hematocrit was checked at regular intervals and arterial blood pressure and pulse rate were taken during each period.

RESULTS

In figure 1, it can be seen that the mean
TABLE 2.—Determined and Calculated Values for the Overnight (0), Pre-load (1-3), and Load (4-9) Periods

<table>
<thead>
<tr>
<th>Patient and groups</th>
<th>Periods</th>
<th>Mean arterial blood pressure (mm. Hg)</th>
<th>Ctn (ml/min.)</th>
<th>CPAH (ml/min.)</th>
<th>Filtration fraction</th>
<th>Renal resistance (dynes-sec.-cm.⁻¹)</th>
<th>Urine volume (ml/min.)</th>
<th>CNa (ml/min.)</th>
<th>CCl (ml/min.)</th>
<th>CK (ml/min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Normal</td>
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<tr>
<td>W.A.</td>
<td>0</td>
<td>1-3 88 79 496 0.160 7,399 2.53 1.94 1.89 11.0</td>
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<td></td>
<td></td>
<td>4-9 87 108 643 0.169 2.04 3.29 3.24 8.56</td>
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<tr>
<td>J.G.</td>
<td>0</td>
<td>1-3 89 82 462 0.177 7,626 1.11 1.82 2.03 13.7</td>
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<td>4-9 84 82 465 0.176 1.42 2.45 3.83 15.2</td>
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<tr>
<td>I.S.</td>
<td>0</td>
<td>1-3 94 127 842 0.152 4,137 1.63 1.56 2.00 13.7</td>
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<td>4-9 98 110 714 0.155 1.67 2.35 3.06 25.4</td>
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<td>S.F.</td>
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<td>1-3 81 92 587 0.157 6,033 0.59 1.40 1.18 9.06</td>
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<td>4-9 86 119 708 0.169 1.62 3.18 3.20 11.7</td>
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<tr>
<td>R.G.</td>
<td>0</td>
<td>1-3 93 92 496 0.185 7,253 1.07 1.43 1.60 19.0</td>
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<td>4-9 95 88 471 0.187 1.48 2.08 2.18 17.1</td>
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<tr>
<td>Mean</td>
<td></td>
<td>1-3 89 94 577 0.166 6,490 1.39 1.63 1.70 16.3</td>
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<tr>
<td>S.D.</td>
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<td>5.1 18.5 61.7 0.040 2,906 0.74 0.24 0.36 7.84</td>
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<td>4-9 144 106 524 0.183 2.93 3.69 5.16 7.34</td>
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<tr>
<td>Mean</td>
<td></td>
<td>1-3 118 96 518 0.168 9,384 3.44 1.98 1.41 17.6</td>
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<tr>
<td>S.D.</td>
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<td>124 93 571 0.164 2.24 2.80 2.90 18.4</td>
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<tr>
<td>Mean</td>
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<tr>
<td>S.D.</td>
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<td>130 101 570 0.179 2.87 3.79 6.03 18.2</td>
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<tr>
<td>Mean</td>
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<td>1-3 122 166 744 0.219 6,051 4.74 3.67 3.00 30.6</td>
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<tr>
<td>S.D.</td>
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<td>119 164 875 0.182 3.88 5.53 6.85 39.3</td>
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<tr>
<td>Mean</td>
<td></td>
<td>1-3 109 118 725 0.165 6,151 1.48 1.60 1.50 22.2</td>
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<tr>
<td>S.D.</td>
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<td>108 112 667 0.167 2.16 3.48 3.80 33.4</td>
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<tr>
<td>Mean</td>
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<td>1-3 126 111 602 0.188 8,416 3.17 2.60 2.83 19.2</td>
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<td>S.D.</td>
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<td>14.8 32.8 117 0.071 4,492 1.17 0.427 0.95 8.58</td>
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<tr>
<td>Mean</td>
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<td>4-9 125 115 641 0.175 2.82 3.80 4.80 24.5</td>
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<tr>
<td>S.D.</td>
<td></td>
<td>13.3 27.6 140 0.019 0.69 1.011 0.29 12.9</td>
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</tbody>
</table>

S.D. = Standard deviation of the mean.

Mean arterial pressures calculated as one-half of the sum of the mean systolic and diastolic pressures.

\[ Pm - Pe \]

Renal resistance calculated from the formula \[ R = \frac{Pm - Pe}{Q} \times 1328 \] where \( Pm \) equals the mean arterial
### Table 2—Continued

| Patient and groups | Periods | Mean arterial blood pressure (mm. Hg) | $C_{IN}$ (ml./min.) | $CP_{AH}$ (ml./min.) | Filtration fraction | Renal resistance (dynes-sec.-cm$^{-2}$) | Urine volume (ml./min.) | $C_{Na}$ (ml./min.) | $C_{Cl}$ (ml./min.) | $C_{K}$ (ml./min.) |
|--------------------|---------|--------------------------------------|---------------------|----------------------|---------------------|----------------------------------------|-------------------------|---------------------|---------------------|---------------------|---------------------|
| **III. Moderately severely hypertensive** |         |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
| D.A.               | 0       | 149                                  | 111                 | 444                  | 0.250               | 14,101                   | 0.96                     | 0.97                | 0.97                | 0.97                | 0.97                |
|                    | 4-9     | 148                                  | 112                 | 470                  | 0.239               | 4.49                     | 4.16                     | 5.68                | 5.68                | 34.9                | 30.3                |
| J.M.               | 0       | 146                                  | 97                  | 507                  | 0.190               | 11,183                   | 6.17                     | 4.57                | 4.57                | 4.60                | 18.4                |
|                    | 4-9     | 153                                  | 89                  | 511                  | 0.177               | 4.57                     | 5.03                     | 6.11                | 9.31                | 24.7                |                     |
| T.L.               | 0       | 146                                  | 117                 | 558                  | 0.209               | 9,917                    | 4.20                     | 3.44                | 3.82                | 45.0                |                     |
|                    | 4-9     | 149                                  | 105                 | 567                  | 0.186               | 10.65                    | 7.70                     | 9.31                | 52.7                |                     |                     |
| W.L.               | 0       | 146                                  | 117                 | 558                  | 0.209               | 9,917                    | 4.20                     | 3.44                | 3.82                | 45.0                |                     |
|                    | 4-9     | 149                                  | 105                 | 567                  | 0.186               | 10.65                    | 7.70                     | 9.31                | 52.7                |                     |                     |
| S.D.               | 0       | 147                                  | 75                  | 367                  | 0.205               | 15,268                   | 5.45                     | 6.23                | 7.00                | 33.1                |                     |
|                    | 4-9     | 144                                  | 71                  | 369                  | 0.193               | 7.50                     | 9.78                     | 10.6                | 30.3                |                     |                     |
| Mean S.D.          | 0.4     |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
| Mean S.D.          | 4-9     | 147                                  | 108                 | 490                  | 0.219               | 12,617                   | 4.81                     | 4.67                | 5.30                | 30.3                |                     |
| W.B.               | 0       |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
|                    | 4-9     | 151                                  | 65                  | 366                  | 0.245               | 26,775                   | 2.93                     | 2.37                | 2.20                | 20.0                |                     |
| S.W.               | 0       | 147                                  | 85                  | 359                  | 0.239               | 18,120                   | 4.75                     | 4.27                | 9.70                | 20.5                |                     |
|                    | 4-9     | 141                                  | 86                  | 381                  | 0.228               | 7.21                     | 7.40                     | 15.05               | 22.4                |                     |                     |
| R.E.               | 0       |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
|                    | 4-9     | 158                                  | 45                  | 220                  | 0.206               | 35,460                   | 1.49                     | 0.62                | 4.00                | 14.0                |                     |
| C.A.               | 0       |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
|                    | 4-9     | 168                                  | 92                  | 389                  | 0.236               | 18,935                   | 5.80                     | 4.67                | 5.20                | 37.3                |                     |
| Mean S.D.          | 15.9    |                                      |                     |                      |                     |                                        |                         |                     |                     |                     |                     |
| Mean S.D.          | 4-9     | 176                                  | 69                  | 287                  | 0.241               | 26,154                   | 3.20                     | 2.60                | 4.50                | 19.2                |                     |
| Mean S.D.          | 11.2    | 70                                  | 304                  | 0.232               | 4.36                     | 4.50                     | 6.90                     | 19.5                |                     |                     |

Blood pressure of periods 1-3, $P_r$ arbitrarily equals 10 mm. Hg, and $Q$ (the renal blood flow) equals the mean $CP_{AH}$ of periods 1-3 (expressed as ml./sec.) divided by 1 minus the mean hematocrit values of periods 1-3. $EP_{AH}$ arbitrarily taken to be unity.

$C_{Na}$ of overnight periods calculated from the 12 hour urine volume and sodium concentration and the plasma sodium concentration just prior to the clearance infusion.
renal plasma flow of the normotensive and the mildly hypertensive groups was normal; in the moderately severely hypertensive group it was at the lower limit of normality; in the severely hypertensive group it was reduced by 50 per cent. The mean glomerular filtration rate of the latter group was decreased to 60 per cent of normal. Other groups had normal filtration rates. There was no change in blood pressure or renal hemodynamics under load except in one normotensive indivi-

dual (W.A.) who responded with an increase of renal plasma flow and glomerular filtration rate from the subnormal to the normal range (table 2).

The rate of urine flow in the pre-load period as well as the flow under load paralleled the mean arterial blood pressure in those groups with normal renal plasma flow and glomerular filtration rate. The mean urine flow during the pre-load period of the moderately severely hypertensive group was 3 times as high as that of the normotensive group. It should be noted that the pre-load period followed a priming infusion and was concurrent with a sustaining infusion containing inulin and para-aminohippurate in 0.9 per cent sodium chloride solution.

Despite scattering of individual values, differences in sodium clearance between normotensive, mildly, and moderately severely hypertensive individuals were quite apparent in the pre-load and load periods (fig. 2). The sodium clearance values of severely hypertensive patients exhibited a marked dissociation. Under loading conditions, 3 individuals followed the pattern of the moderately severely hypertensive group and 2 were slightly below the normal range.

Figure 3, summarizing the relationship be-
EFFECT OF SODIUM CHLORIDE LOAD

Table 3.—Analysis of Variance in Periods 4 to 9 of Groups I to IV

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Degrees of freedom</th>
<th>Variable</th>
<th>Urine volume</th>
<th>CNa</th>
<th>CK</th>
<th>CCl</th>
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</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>4</td>
<td></td>
<td>128.71*</td>
<td>53.65*</td>
<td>46.92*</td>
<td>46.43*</td>
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<tr>
<td>Between individuals within groups</td>
<td>16</td>
<td></td>
<td>25.75*</td>
<td>12.65*</td>
<td>26.28*</td>
<td>16.36*</td>
</tr>
<tr>
<td>Between individuals</td>
<td>20</td>
<td></td>
<td>46.34*</td>
<td>20.85*</td>
<td>30.47*</td>
<td>22.38*</td>
</tr>
<tr>
<td>Within individuals</td>
<td>92</td>
<td></td>
<td>(0.828)</td>
<td>(1.442)</td>
<td>(31.102)</td>
<td>(2.756)</td>
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</table>

F values computed using the within individuals mean square as the error mean square.

<table>
<thead>
<tr>
<th>Between groups</th>
<th>4</th>
<th>4.99*</th>
<th>4.42†</th>
<th>1.79</th>
<th>2.84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between individuals within groups</td>
<td>16</td>
<td>(21.321)</td>
<td>(18.239)</td>
<td>(817.426)</td>
<td>(45.101)</td>
</tr>
</tbody>
</table>

F values computed using the mean square between individuals within groups as the error mean square.

*Values significant at the 1 per cent level.
†Values significant at the 5 per cent level. F values are given except for numbers in parentheses which are mean squares.

tween the arterial blood pressure and the sodium clearances in the 12-hour period prior to testing, in the pre-load period, and in the load period, demonstrates that increments in sodium clearance under load increased with the blood pressure. The differences in sodium clearance were already present prior to testing and during the pre-load period. As shown in table 2, pre-load mean sodium clearance values in groups I, II, and III were 1.63, 2.60, and 4.67 ml. per minute, while the increments under load were 1.02, 1.20, and 2.06 ml. per minute, respectively.

The mean plasma sodium concentration during the pre-load period was in the same range for the normotensive, moderately severely, and severely hypertensive groups (143.6 mEq. per L.), whereas the mildly hypertensive group showed consistently a slightly higher sodium concentration (146.1 mEq. per L.). This difference was already present before the priming infusion (fig. 4). Under load, the group with mild hypertension reached a maximal plasma sodium concentration of 149.2 mEq. per L. (Δ = plus 2.1 per cent; the other groups 145.7 mEq. per L (Δ = plus 1.5 per cent); the differences in increments not appearing to be significant.

The filtered load of sodium (product of the plasma concentration of sodium and the inulin clearance rate) also showed no correlation with the arterial blood pressure. In the pre-load period, the mean filtered load of sodium was 13.6, 16.3, 15.4, and 10.0 mEq. per minute for the normotensive, mildly, moderately severely, and severely hypertensive patients while in the load period it was 14.8, 17.1, 14.8, and 10.2 mEq. per minute, respectively. In figure 5, it is demonstrated that the per cent of the filtered sodium which is excreted (sodium clearance divided by the inulin clearance) shows the same relationships as did the sodium clearance itself (fig. 2).

There was no correlation between sodium clearance and the clearance of inulin or para-aminohippurate. There was some correlation between sodium clearance and the calculated renal resistance and the filtration fraction. Figure 6 shows that the sodium clearance in hypertensive individuals parallels arterial blood pressure up to a critical renal resistance ranging from 12,000 to 16,000 dynes-sec.-cm.-5, beyond which it declines with increasing renal resistance. The chloride excretion followed the pattern of sodium; the potassium principally the one of water (table 2).

Because the number of individuals in each group was small, an analysis of variance is presented in table 3. This may be interpreted as follows: 1. Individuals (groups ignored) differ significantly in mean urine volume and sodium, potassium, and chloride clearances.

2. Group means differ significantly with respect to urine volume and sodium, potassium,
and chloride clearances. 3. Individuals within a group are not homogeneous. 4. The variation between groups is significantly greater than the variation within groups for the mean urine volume and sodium clearance (and for chloride clearance also if group IV is eliminated from the analysis). This must be viewed as an approximate test because of the known heterogeneity within groups.

**DISCUSSION**

These studies confirm the observations of others that most hypertensive individuals excrete more sodium, chloride, potassium, and water when loaded with sodium chloride than do normotensive individuals. There is a direct relationship between sodium clearance and mean arterial blood pressure as long as the renal plasma flow and glomerular filtration rate are normal. This correlation appeared to be present in the resting state, was clearly evident in the pre-load period and was improved by loading. The priming and sustaining infusions, both of which contained 0.9 per cent sodium chloride, might be considered in themselves to constitute a sodium chloride load. Under these load conditions, hypertensive individuals with normal renal function apparently excrete a higher percentage of filtered sodium than do normotensive subjects.

The overnight urine samples brought in by the patients are not as accurately collected as those during the renal excretory measurements and clearance values in the overnight "basal" state are obviously subject to considerable error. There was a slight elevation in the average basal excretion of sodium in the hypertensive patients. This tends to confirm the report of Green and Ellis\(^8\) that the basal excretion of sodium is elevated in hypertension. Not all investigators have found this to be true however. Since the correlation of blood pressure and sodium excretion improves with load, minor differences in sodium excretion in the basal state are made more evident by the pre-load infusion of isotonic sodium chloride and become more marked under loading with 2.5 per cent sodium chloride. It appears therefore that loading may bring out differences in sodium excretion which are not clearly apparent in the basal state.

Although these data suggest increased tubular rejection of sodium, chloride, and water as the primary mechanism for the augmented excretion, the possibility of minute, nondetectable increments of filtered load cannot be ruled out, as has been pointed out by many investigators.\(^{13-15}\) Experimental work on animals\(^{13, 16, 17}\) suggests that the increased excretion of water and electrolytes is due to a higher filtered load as a consequence of elevated filtration pressure. This is also reflected by an increased filtration fraction. The fact that the mean arterial blood pressure and filtration fraction parallel sodium and chloride clearance and urine flow in hypertensive subjects having no significant reduction of renal hemodynamics is the only evidence from our
EFFECT OF SODIUM CHLORIDE LOAD

FIG. 4. The mean plasma sodium concentrations of the normal (●), the mildly hypertensive (□), the moderately severely hypertensive (□□) and the severely hypertensive (■) groups are plotted before the start of the clearance determination (Plo), during the 3 pre-load (0.9 per cent sodium chloride), the 5 load (2.5 per cent sodium chloride), and the final recovery (0.9 per cent sodium chloride) periods. The vertical lines indicate the range of individual values.

data to support this view. Shipley and Study\textsuperscript{18} determined the effect of acute alterations in renal arterial blood pressure on renal blood flow, extraction of inulin, glomerular filtration rate, tissue pressure, and urine flow and thought that increased intravascular pressure caused increased tissue pressure which diminished the transfer of filtrate through the tubular wall with consequent increase in urine flow. This mechanism remains a possibility in essential hypertension.

No correlation between sodium clearance and para-aminohippurate or inulin clearance could be established. The filtration fraction paralleled sodium clearance in the groups with mild and moderately severe hypertension, but did not in the group with severe hypertension. The best correlation in the mild and moderately severe groups was between total renal resistance and sodium clearance (fig. 6). As the renal extraction of para-aminohippurate was not determined,

Fig. 5. Sodium clearance expressed as per cent of the filtered sodium excreted during the 3 pre-load, the 5 load, and the final recovery periods. Left, mean values for the normal (●), mildly hypertensive (□), and moderately severely hypertensive (□□) groups. Lined areas mark standard deviations of the means. Right, values given for individual severely hypertensive patients (■).

renal resistance values of the severely hypertensive patients must be judged with caution.
In spite of these limitations, one may speculate that renal resistance, reflecting arteriolar sclerosis as the basic pathologic process in the hypertensive kidney, may be related in a causative fashion to water and electrolyte excretion.

The plasma sodium concentration does not seem to regulate the response of sodium excretion under load since the normotensive, moderately severely, and severely hypertensive groups had the same concentrations. The results of Barger, Rudolph, Rokaw, and Yates, who found increased sodium excretion on the side where they injected hypertonic sodium chloride into the renal artery, suggests the possible importance of this factor. Taquini, Plesch, Carpis, and Badano found elevated serum sodium concentrations in 10 of 13 severely hypertensive patients. The finding in this study of a slightly elevated plasma sodium level only in mild cases of essential hypertension warrants further investigation.

When the patients studied here were examined according to the criteria of Green, Johnson, Bridges, and Lehmann, the "high salt-excretors" were found to belong to the groups with mild and moderately severe hypertension whereas the "normal salt-excretors" were in the group having severe hypertension. Such a simple classification therefore does not adequately describe these relationships in these patients since there was a progressively increasing salt excretion with increasing blood pressure until impairment of renal function became prominent.

The decreased sodium clearance of the severely hypertensive group is primarily due to reduction of filtered load. However, in the limited number of severely hypertensive cases studied, there did not appear to be a definite correlation between the filtration rate and the per cent of the filtered load of sodium and chloride excreted. Increased tubular reabsorption or decreased tubular rejection of sodium and chloride may have been an addi-

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**Fig. 6.** Sodium clearance expressed as milliliters per minute per 1.73 M.² body surface plotted against calculated renal resistance. Single values of the 3 pre-load periods are shown for the normal (●), the mildly hypertensive (□), and the moderately severely hypertensive (■) individuals with their calculated regression line on the left and for the severely hypertensive patients (■) on the right where the line has been drawn by inspection.
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759

tional factor in the 2 severely hypertensive pa-

tients who retained a greater proportion of

the administered load.

SUMMARY

The renal hemodynamic and excretory re-

sponses to an intravenous load of 2.5 per cent

sodium chloride were studied in 15 patients

with essential hypertension and in 5 normal

subjects, all on comparable salt intakes for

3 weeks prior to testing. Para-aminohippur-

rate and inulin clearances did not change

under load.

Sodium and chloride clearances and water

excretion following this load were proportion-

al to the degree of blood pressure elevation

and to the increase in renal resistance except

in 3 instances in which renal plasma flow and

glomerular filtration rate were greatly re-

duced.

No measurable increases in glomerular fil-

tration rate and only slight increases in plas-

ma sodium concentration, which were of sim-

ilar magnitude in all groups, were observed
during the sodium chloride loading. The

hypertensive patient appeared to reject a

greater portion of the filtered load of sodium

chloride and water.

This alteration in electrolyte excretion in

essential hypertension apparently is not re-

lated to renal plasma flow or glomerular fil-

tration rate, but parallels blood pressure and

renal resistance up to the point of a severe

reduction in renal hemodynamic function.

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Effect of an Intravenous Sodium Chloride Load on Renal Hemodynamics and Electrolyte Excretion in Essential Hypertension

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