EFFECTS OF EXOGENOUS AND ENDOGENOUS POSTERIOR PITUITARY ANTIDIURETIC HORMONE ON WATER AND ELECTROLYTE EXCRETION

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EFFECTS OF EXOGENOUS AND ENDOGENOUS POSTERIOR PITUITARY ANTI DiURETIC HORMONE ON WATER AND ELECTROLYTE EXCRETION

BY RICHARD J. F. MURPHY AND EUGENE A. STEAD, JR.

(From the Department of Medicine, Duke University School of Medicine, Durham, N. C.)

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The urine output of normal subjects varies greatly from hour to hour. Two of the important factors affecting the urine volume are the degree of activity of the posterior pituitary gland and the amount of solids to be excreted in the urine. In general, whenever the normal kidney is excreting a concentrated urine of low volume, secretion of the antidiuretic hormone (ADH) of the posterior pituitary gland is occurring. This secretion may be due to emotional, drug, or other nervous stimulation, or to an increased osmotic pressure in the extracellular fluid. The excretion of a large amount of very dilute urine by the normal kidney occurs when ADH production is inhibited either by nervous or osmotic stimuli. When concentrated electrolyte solutions are administered intravenously, a large quantity of concentrated urine is produced. This large urine volume appears to be the result of the osmotic effects of the solids in the urine, and the volume is not decreased by secretion of ADH.

While there is general agreement as to the effects of ADH on water excretion, there has been little information on its effects on sodium, chloride and potassium excretion in man. The purposes of this study were (1) to determine the effect of endogenously produced ADH on the excretion of water, sodium and chloride, (2) to determine whether minute doses of commercial Pitressin given intravenously had the same effects on water and electrolyte excretion as endogenously produced ADH, (3) to determine whether the rate of excretion of sodium modified the antidiuretic effectiveness of Pitressin, and (4) to determine whether Pitressin given intravenously in minute doses altered glomerular filtration rate or renal plasma flow.

MATeRIALS AND METHODS

All of the following studies have been carried out on human subjects without endocrine, renal, cardiac, or other disease which has a known effect on water and electrolyte metabolism. All had been on normal salt and water intakes in the past. All subjects were studied in the post-absorptive state as regards food. The differing water and electrolyte conditions which were introduced as a part of the study will be mentioned specifically in the results.

In all studies the same lot of Pitressin (commercial ADH prepared by Parke, Davis and Company) has been used. Fresh solutions of Pitressin in 9% NaCl were prepared for each experiment. The doses varied somewhat as specifically mentioned but where it is not mentioned, the dose was arbitrarily fixed at 1.0 milliunit per kilo of body weight.

Urine collections were made from an indwelling urethral catheter which was placed at the bladder neck with considerable care. Throughout the full period of each study, which was carried out in a quiet, isolated environment, the patient was recumbent but not sleeping. As much assurance as possible was given to avoid any emotional upset during the simple procedures that were carried out.

In all cases except the clearance studies, urine was collected at arbitrary time intervals of 10 minutes. Individual samples were measured for chloride by the Van Slyke and Hiller modification of the method of Sendroy (1). Sodium and potassium were measured with the Perkin-Elmer flame photometer.

In measuring the renal hemodynamic effect of Pitressin, the clearance techniques of Smith, Goldring, and Chasis have been followed using inulin and sodium paraminohippurate (PAH) as the test substances (2).

RESULTS

Endogenous secretion of pituitary ADH. After collecting urine for 20–30 minutes, sodium chloride solution in doses of 20–30 cc. per kilo of body weight was given intravenously over a period of 30–60 minutes to 21 normal subjects. These individuals may be divided into two groups, depending on the concentration of the salt used. Group I consisted of 15 subjects who received a solution with a concentration of 125–146 millimols of sodium chloride; Group II of six subjects who re-

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1 This work was supported by a grant from the Life Insurance Medical Research Fund and the Anna H. Hanes Memorial Fund.

2 Present Address: Department of Medicine, Royal Victoria Hospital, Montreal, Canada.
Fig. 1. Effect of NaCl infusions on urine volume in three normal subjects and one patient with diabetes insipidus

The findings in normal subjects are shown in the three lower curves. The subjects receiving NaCl solution of 155 millimols are represented by the continuous line; that of 142 millimols by short dashes; and that of 125 millimols by long dashes. The concentration of the NaCl solution in the patient with diabetes insipidus was 139 millimols (dotted line).

received a solution with a concentration of 149–155 millimols. It is generally stated that .9% sodium chloride solution (155 millimols) is isotonic with plasma.

In Group I the initial effect was the production of a water diuresis (i.e., the urine minute volumes increased markedly to levels of 6–12 cc./min. and sodium and chloride concentrations decreased) beginning about 30 minutes after the infusion was started. After a variable but short period of time there was an abrupt antidiuresis. As shown in Figure 1, the more concentrated solutions in Group I produced an earlier antidiuresis. In Group II, who received saline in slightly greater concentration, no water diuresis was produced. The urine volume increased slowly over the period of observation but did not rise above 3 cc./min., and there was no abrupt antidiuresis. As the urine volume increased in this group the sodium concentration in the urine rose and did not decrease as it did in Group I. In Figure 1 the effect of giving 1,400 cc. of sodium chloride solution with a concentration of 139 millimols to a patient with diabetes insipidus is shown. There was an immediate large increase in urine volume with a slow fall over the next two hours. There was no abrupt antidiuresis as there was in Group I.

The following interpretation of these data is offered: Solutions containing a concentration of between 125 and 146 millimols of sodium chloride do not stimulate the production of ADH. Their initial effect is to cause a water diuresis either by dilution of existing ADH or by inhibition of its secretion. During water diuresis the loss of water greatly exceeds the loss of salt and the electrolytes in the body are concentrated. In due time this causes an osmotic stimulus for ADH secretion and antidiuresis occurs. The absence of a water diuresis when the concentration of sodium chloride is slightly increased in the fluid administered suggests that the osmotic mechanism is a sensitive one and that the amount of water lost does not have to be large to cause the production of endogenous ADH. As the concentration of the NaCl solution approaches 150 millimols, the duration of the water diuresis is progressively reduced (Figure 1). The fact that the patient with diabetes insipidus

<table>
<thead>
<tr>
<th>Subj.</th>
<th>Water excretion (cc./min.)</th>
<th>Chloride excretion (meq./10 min.)</th>
<th>Sodium excretion (meq./10 min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. A.</td>
<td>10.8 9.0 8.1 7.2 3.8 2.8 3.5</td>
<td>7.0 7.0 6.6 6.5 5.1 4.3 5.3</td>
<td>7.8 6.9 5.8 6.4 5.3 4.4 5.4</td>
</tr>
<tr>
<td>W. M.</td>
<td>7.5 12.6 12.8 8.5 4.3 3.5 2.9</td>
<td>4.5 7.1 6.3 5.4 6.2 5.9 5.4</td>
<td>3.4 6.1 5.5 4.4 5.6 5.4 4.7</td>
</tr>
<tr>
<td>H. C.</td>
<td>4.0 5.6 4.7 4.5 2.9 2.4 2.4</td>
<td>1.6 1.8 1.7 2.1 2.7 4.6 3.0</td>
<td>2.2 2.2 2.0 2.4 3.2 3.1 3.1</td>
</tr>
<tr>
<td>E. T.</td>
<td>15.7 13.5 9.4 8.0 8.0 5.5 5.8</td>
<td>4.4 4.4 4.2 4.5 4.6 4.2 4.8</td>
<td>2.4 5.5 4.8 5.4 5.7 4.3 5.9</td>
</tr>
<tr>
<td>G. H.</td>
<td>12.5 15.4 8.2 4.5 4.6 5.2 5.4</td>
<td>6.8 7.1 6.9 6.6 7.6 7.8 7.9</td>
<td>2.4 6.9 7.3 7.4 8.4 9.7 8.3</td>
</tr>
<tr>
<td>E. A.</td>
<td>14.0 13.4 11.8 9.5 6.2 5.1 3.9</td>
<td>4.5 4.6 4.6 4.5 4.2 4.3 4.3</td>
<td>3.2 3.0 3.1 3.0 2.9 2.6 2.9</td>
</tr>
<tr>
<td>A. M.</td>
<td>13.2 13.3 14.1 10.7 4.2 3.2 3.5</td>
<td>5.3 4.5 4.9 5.0 4.2 4.8 5.1</td>
<td>5.7 4.9 5.2 6.0 4.6 5.9 6.3</td>
</tr>
<tr>
<td>E. T.</td>
<td>9.8 8.5 6.3 3.7 2.6 2.7 2.6</td>
<td>2.3 2.0 1.9 1.7 1.7 1.8 1.9</td>
<td>2.0 1.6 1.8 1.8 1.9 1.9 2.0</td>
</tr>
</tbody>
</table>
TABLE II

Effect of small, intravenous doses of Pitressin on urine volume and sodium and chloride excretion in the absence of endogenous secretion of ADH

Observations were made during infusion of PAH and insulin

<table>
<thead>
<tr>
<th>Subj.</th>
<th>Urine volume (cc./min.)</th>
<th>Urine chloride (meq./min.)</th>
<th>Urine sodium (meq./min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Pitressin</td>
<td>After Pitressin</td>
<td>Before Pitressin</td>
</tr>
<tr>
<td>D. W.</td>
<td>9.6</td>
<td>12.0</td>
<td>1.9</td>
</tr>
<tr>
<td>M. B.</td>
<td>9.6</td>
<td>10.1</td>
<td>2.0</td>
</tr>
<tr>
<td>L. C.</td>
<td>6.8</td>
<td>8.3</td>
<td>0.2</td>
</tr>
<tr>
<td>E. M.</td>
<td>10.2</td>
<td>12.2</td>
<td>0.3</td>
</tr>
<tr>
<td>L. H.</td>
<td>14.6</td>
<td>14.9</td>
<td>0.8</td>
</tr>
<tr>
<td>R. T.</td>
<td>12.3</td>
<td>13.8</td>
<td>1.1</td>
</tr>
<tr>
<td>M. C.</td>
<td>17.1</td>
<td>17.7</td>
<td>0.3</td>
</tr>
<tr>
<td>H. R.</td>
<td>8.2</td>
<td>6.2</td>
<td>2.3</td>
</tr>
<tr>
<td>R. T.</td>
<td>10.9</td>
<td>11.5</td>
<td>1.0</td>
</tr>
</tbody>
</table>

did not have the abrupt anti-diuresis which the normal subjects had supports the above interpretation. O'Connor (3) has shown that in the dog changes between a fall of 2.5% and an increase of 5% from the resting level of blood chloride were sufficient to cause the tubules to respond over the full range of their functional capacity from maximal selective reabsorption of water when salt was given to minimal reabsorption in water diuresis.

Granting that the anti-diuresis produced when NaCl solutions between 125 and 146 millimols are given intravenously results from the secretion of endogenous ADH, we are in a position to determine the effect of this material on electrolyte excretion. Table I shows these results in eight normal subjects in whom complete data on sodium and chloride excretion are available. Despite a change in urine volume from a mean of 11 cc./min. to 3.8 cc./min. the excretion of sodium and chloride remained constant. Under the conditions of these observations endogenous ADH neither increases nor decreases sodium and chloride excretion.

EFFECT OF MINUTE DOSES OF PITRESSIN ON THE EXCRETION OF WATER AND ELECTROLYTES

Shannon has shown that the full range of antidiuretic effects can be produced in the intact dogs by the intravenous administration of 1–5 milliunits of Pitressin per hour (4). Lauson and his colleagues reported identical findings in man with allowance for weight differences (5). In the dog (6) and presumably in man, much greater quantities of ADH are produced in response to certain physiologic stimuli than are needed for maximal antidiuretic activity. In five normal subjects the endogenous secretion of ADH was reduced to a minimum by oral administration of 1,000–2,000 cc. of water and the antidiuretic effects of giving a single intravenous injection of 5 to 70 milliunits of Pitressin were observed (Figure 2). If one allows five minutes as an average figure for the passage of urine from the renal tubules to the bladder, it appears that the antidiuretic effect is produced immediately. It is also apparent that over a fairly wide range of this drug, the duration of maximal anti-diuresis is relatively fixed. In

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**Fig. 2. Effect of Small Varying Doses of Pitressin on the Course of Water Diuresis in Normal Subjects**

Each point represents the average minute volume of a 10 minute collection period and is placed at the five minute point in the period.
four of these five subjects receiving doses varying from 10–70 milliunits, maximal antidiuresis lasted about 40 minutes and an additional 30–40 minutes were required for the tubules to "escape" from the antidiuretic effect. In the one subject receiving only 5 milliunits, onset of maximal antidiuresis was similar to the other individuals but the duration of maximal antidiuresis was shorter and the "escape" from its effect more immediate.

Doses of 0.5 to 2 milliunits of Pitressin per kilo of body weight given intravenously over a two minute period of time produced no detectable effect on pulse rate, blood pressure, skin color, or gastrointestinal activity.

The effect of Pitressin on electrolyte excretion was measured under three differing circumstances. The first was in conjunction with the study of renal blood flow and glomerular filtration rate. These subjects were previously water-loaded to suppress endogenous secretion of ADH. It has been stated that in dogs, this is the only way to demonstrate the "chloruretic" properties of this preparation (7). All these subjects were given a standard volume of water to drink (20 cc. per kilo of body weight) 30–50 minutes before the onset of the studies so that they had a good water diuresis by the time the pre-Pitressin collections were made. These measurements were made during the infusion of inulin and PAH. Hippurate, being an acid salt which is rapidly cleared by the tubules, has an effect on the excretion of sodium. This effect was present in the study periods before and after the injection of Pitressin. The data are recorded in Table II and the values are expressed in terms of excretion per minute because the time of the individual periods ranged from 13–18 minutes. Despite the striking change in urine volume from 11.0 ± 1.1 cc. and 11.9 ± 1.1 cc. in the two periods before Pitressin to 1.1 ± 0.3 cc. and 1.4 ± 0.2 cc. in the two periods after Pitressin the excretion of sodium and chloride was not significantly changed. Potassium excretion was not measured in this group.

The second group of seven subjects received a water load of 20 cc. per kilo of body weight. They differed from the first group in that they had had no injections of inulin or hippurate. A 30 minute collection of urine was made before and after the injection of Pitressin. The urine was not collected during the first 10 minutes after the injection of Pitressin. In this group there was a slight but constant decrease in the excretion of sodium. The excretion of chloride in those cases where it was measured followed sodium. Potassium excretion was not measured. The data are recorded in Table III.

The third group of eight subjects received 1,000–1,500 cc. of 0.8–0.9% NaCl solution intravenously before urine collections were started. The infusion was finished one to two hours before Pitressin was given. This insured a relatively high concentration of sodium and chloride in the urine. These patients undoubtedly had some endogenous ADH effect because the urine volume was considerably smaller than in the previous study. They received no inulin or hippurate. In this group, urine collections were made at 10 minute intervals to note any pattern responses. Figure 3 shows the effect

<table>
<thead>
<tr>
<th>Subj.</th>
<th>Before Pitressin</th>
<th>After Pitressin</th>
<th>Before Pitressin</th>
<th>After Pitressin</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. C.</td>
<td>10.5</td>
<td>1.2</td>
<td>.084</td>
<td>.078</td>
</tr>
<tr>
<td>C. I.</td>
<td>18.2</td>
<td>1.0</td>
<td>.109</td>
<td>.069</td>
</tr>
<tr>
<td>M. J.</td>
<td>5.7</td>
<td>0.3</td>
<td>.040</td>
<td>.029</td>
</tr>
<tr>
<td>D. B.</td>
<td>6.6</td>
<td>0.3</td>
<td>.007</td>
<td>.003</td>
</tr>
<tr>
<td>A. W.</td>
<td>11.0</td>
<td>1.3</td>
<td>.132</td>
<td>.127</td>
</tr>
<tr>
<td>A. D.</td>
<td>9.5</td>
<td>2.4</td>
<td>.143</td>
<td>.134</td>
</tr>
<tr>
<td>A. M.</td>
<td>9.6</td>
<td>0.9</td>
<td>.211</td>
<td>.157</td>
</tr>
</tbody>
</table>

TABLE III

Differing effects on sodium excretion of small doses of intravenous Pitressin in two groups, one excreting small amount of salt in large volume of urine and the other excreting larger amount of salt in a smaller volume of urine.

Each figure represents the average of a 30 minute collection period.

<table>
<thead>
<tr>
<th>Subj.</th>
<th>Before Pitressin</th>
<th>After Pitressin</th>
<th>Before Pitressin</th>
<th>After Pitressin</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. M.</td>
<td>2.9</td>
<td>1.7</td>
<td>.67</td>
<td>44</td>
</tr>
<tr>
<td>H. C.</td>
<td>2.4</td>
<td>2.2</td>
<td>.35</td>
<td>39</td>
</tr>
<tr>
<td>E. T.</td>
<td>4.7</td>
<td>2.6</td>
<td>.57</td>
<td>47</td>
</tr>
<tr>
<td>M. M.</td>
<td>5.5</td>
<td>2.8</td>
<td>.51</td>
<td>52</td>
</tr>
<tr>
<td>H. L.</td>
<td>6.9</td>
<td>4.1</td>
<td>.55</td>
<td>52</td>
</tr>
<tr>
<td>E. A.</td>
<td>3.1</td>
<td>2.0</td>
<td>.27</td>
<td></td>
</tr>
<tr>
<td>G. H.</td>
<td>5.1</td>
<td>2.3</td>
<td>.85</td>
<td>51</td>
</tr>
</tbody>
</table>
of intravenous Pitressin on the excretion of sodium, chloride, and potassium. The sodium and chloride excretion in this group previous to Pitressin was approximately three times as large as in the water diuresis group. The excretion of sodium and chloride was not significantly changed by Pitressin. Potassium excretion showed a highly significant increase in the group from a mean of 70 ± 10 microequivalents per minute to 120 ± 14 in the first 10–20 minutes following Pitressin administration. In the two following 10 minute periods, potassium excretion began to return toward the control values. Observations on the effect of Pitressin on potassium excretion after water loading were not made.

Effect of sodium chloride excretion on water excretion after Pitressin. Table III compares the urine volume after Pitressin in two groups of individuals. Group A had received a water load of 20 cc. per kilo of body weight, and Group B had been given 0.8–0.9% NaCl solution as described above. The chief distinguishing features between the two groups so far as this point is concerned is that the water-loaded individuals were excreting relatively small amounts of salt in a large volume of water and the group who had received intravenous saline were excreting considerably larger quantities of salt in smaller amounts of water. Observation periods were 30 minutes before Pitressin and 30 minutes after Pitressin. From the previous studies, this was felt to be within the limits of the period of maximal antidiuresis. In all cases, a 10 minute period was allowed to elapse after the administration of Pitressin to correct for renal tubule to bladder delay. The dose of Pitressin in the saline group was constant, 1.0 milliunits per kilo. In the water group in some cases, it was less, but never more. The mean urine minute volume expressed in cc./min. for the 30 minute period in the saline group following Pitressin was 2.5 ± 0.29, and for the water group, 1.06 ± 0.27. Comparing these two groups statistically, the difference is of significance with a p value equal to 0.01. In terms of Pitressin effect, the experiment was weighted against the results because in some of the water experiments, Pitressin dosage was less than 1.0 milliunit per kilo. We take these results to indicate that changes in sodium excretion of a degree that is well within the average physiological range, has a modifying influence on the antidiuretic effectiveness of Pitressin.

Effect of Pitressin on renal hemodynamics. In dogs and rats no consistent effect has been found on renal blood flow and glomerular filtration rate (8, 9). Table IV shows the effect of intravenous Pitressin on these same functions in normal subjects. All studies were prepared and carried through under identical conditions. All subjects were given a similar amount of water to drink previous to starting the clearances (20 cc. per kilo of body weight) to suppress endogenous ADH. Following the initial control period (two clearances), all received intravenous Pitressin in the dose of 1 milliunit per kilo of body weight. A pe-

### Table IV

The effect of intravenous Pitressin on renal plasma flow and glomerular filtration rate in normal subjects

<table>
<thead>
<tr>
<th>Subj.</th>
<th>CIN (cc./min.)</th>
<th>CPAH (cc./min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>R. T.</td>
<td>131</td>
<td>116</td>
</tr>
<tr>
<td>M. C.</td>
<td>141</td>
<td>132</td>
</tr>
<tr>
<td>A. C.</td>
<td>113</td>
<td>117</td>
</tr>
<tr>
<td>L. C.</td>
<td>102</td>
<td>106</td>
</tr>
<tr>
<td>H. R.</td>
<td>111</td>
<td>109</td>
</tr>
<tr>
<td>R. T.</td>
<td>115</td>
<td>118</td>
</tr>
<tr>
<td>L. H.</td>
<td>115</td>
<td>101</td>
</tr>
<tr>
<td>E. M.</td>
<td>111</td>
<td>110</td>
</tr>
<tr>
<td>M. B.</td>
<td>106</td>
<td>112</td>
</tr>
<tr>
<td>D. W.</td>
<td>85</td>
<td>98</td>
</tr>
<tr>
<td>Mean</td>
<td>113</td>
<td>112</td>
</tr>
<tr>
<td>S. D.</td>
<td>15.2</td>
<td>9.5</td>
</tr>
<tr>
<td>S. E.</td>
<td>4.8</td>
<td>3.0</td>
</tr>
</tbody>
</table>
period of 10–15 minutes was allowed before starting
the first post-Pitressin period to allow for the
mechanical effects of an abrupt change in urine
volume to wear off. Then two or more additional
clearance periods were carried out, each preceded
by a similar dose of intravenous Pitressin to in-
sure continuity of Pitressin effect. There was no
demonstrable change in renal plasma flow and
glomerular filtration rate.

GENERAL DISCUSSION

The data recorded here are consistent with the
view that the physiologic effects of small doses of
Pitressin on the excretion of water, sodium and
chloride are quantitatively and qualitatively simi-
lar to those caused by endogenously produced
ADH. Observations of others comparing the antidi-
uresis caused by Pitressin with that produced by
smoking support this thesis (10).

The effect of Pitressin on electrolyte excretion
in the dog has not been consistent. O’Connor (3)
found no effect on chloride excretion. Anslow and
his colleagues (7) and Sartorius and Roberts (11)
have shown that under certain conditions Pitres-
sin causes a definite increase in sodium and chlo-
ride excretion in the dog. However, since in the
latter studies Pitressin apparently increased glo-
merular filtration rate, these experiments probably
cannot be directly applied to man.

In the experiments reported here there was no
effect on the excretion of sodium and chloride in
the water-loaded subjects receiving inulin and
PAH, and in the salt- and water-loaded subjects
who did not receive inulin and PAH. In the wa-
ter-loaded group who received no inulin or PAH,
there was a slight, but consistent, decrease in so-
dium excretion. The salt- and water-loaded sub-
jects had a lower urine flow before Pitressin and
a higher urine flow after Pitressin than the water-
loaded group. It has been reported that Pitressin
in man produces no change in the excretion of so-
dium chloride (10) and that it decreases the ex-
cretion of sodium slightly in the water-loaded sub-
ject (12). The latter authors believe that the re-
duction in the excretion of sodium is due to the
low rate of urine flow which causes sodium to be
more completely reabsorbed. Our data fit nicely
into this hypothesis as the retention of sodium
occurred only when the average excretion of water
was reduced to 1 cc./min.

The data in Table III show that a moderate in-
crease in the rate of excretion of sodium chloride
influences the volume of urine formed after Pitres-
sin. The factors determining the rate of sodium
chloride excretion seem to be little changed by
ADH, but under maximal ADH effect the amount
of urine formed is greatly influenced by the amount
of sodium chloride excreted. The mechanism by
which increased sodium chloride excretion limits
the antidiuretic effect of ADH remains to be de-
termined. A simple osmotic effect of the salt re-
jected by the tubules seems the most likely ex-
planation.

This dependence of water excretion on salt ex-
cretion has been studied in a different manner by
Rosenbaum, Nelson and Strauss (13). They
found a decreasing water excretion in the pres-
ence of a constant water load despite a constant fil-
tration rate with the only variable being a dimin-
ishing sodium chloride excretion. Their results
show that a maximum urine flow cannot be main-
tained without a considerable excretion of salt.

The increase in potassium excretion following
Pitressin in the salt-loaded subjects was striking
and immediate and suggests that it is caused by a
change in renal tubular function. Assuming that
Pitressin does affect the tubular mechanism re-
ponsible for potassium excretion, two possibili-
ties exist since as Berliner, Kennedy and Hilton
have shown potassium is both reabsorbed and excreted
by the tubules (14). The tubular transport mecha-
nism for reabsorption may be inhibited or the ex-
cretory mechanism intensified.

CONCLUSIONS

1. In normal subjects rapid intravenous infu-
sion of saline with a concentration of 125–146
millimols NaCl produced a diuresis within 30
minutes which in terms of urine volume and sodium
and chloride concentration is indistinguishable
from a water diuresis.

2. After a short period of time this is succeeded
by an abrupt antidiuresis due to posterior pituitary
activity. Sodium and chloride excretion during
this period is unchanged.

3. A comparison of the effects of Pitressin given
intravenously and endogenously produced ADH
was made in subjects receiving 0.8 to 0.9% saline
solution. The effects on the excretion of water,
sodium and chloride are similar.
4. Commercial ADH (Pitressin) given intravenously in small doses causes a slight decrease in the excretion of sodium in water-loaded subjects in whom urine flow is reduced to around 1 cc./min. No effect was demonstrable in water-loaded subjects receiving inulin and PAH for clearance studies or in salt-loaded subjects. After salt loading Pitressin caused a transient increase in the excretion of potassium.

5. The urine volume after intravenous Pitressin is influenced by the excretion of amounts of sodium and chloride in the urine which are within the physiological range.

6. Small doses of Pitressin given intravenously have no effect on glomerular filtration rate and renal plasma flow.

REFERENCES