Mercurial Diuresis in Edematous Individuals

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The electrolyte and water losses in 75 instances of diuresis following Mercuhydrin were studied in 17 edematous patients. The loss of potassium was appreciable following exhibition of the drug to patients who retained their dietary sodium almost completely. Occurrence of such clinical symptoms as weakness, nausea, and ventricular premature contractions might be attributed to this loss of potassium. The fluid lost by mercurial diuresis was isotonic with body fluids. The chloride concentration was fairly constant at 151 mEq per liter. The concentrations of sodium and potassium were more variable, the average concentrations being 97 and 35 mEq per liter, respectively. Loss of water and electrolyte in these concentrations leaves the patient in relative alkalosis, with a loss of intracellular potassium and a gain in intracellular sodium.

The effect of mercurial diuretics on the renal excretion of electrolytes has been thoroughly investigated in the dog and in the normal man.1-4 The electrolyte losses in the edematous patient, however, have been studied less extensively.4-7 There is general agreement that in both the normal individual and in the edematous patient the diuresis is predominantly one of sodium and chloride. There is also agreement that potassium excretion is not increased in normal individuals while in the edematous patient an examination of the reported data reveals potassium loss of varying magnitude.4-8 The present study was designed to extend the information concerning the relative losses of sodium, potassium and chloride following administration of a mercurial diuretic in edematous patients and to assess the changes in body fluid compartments resulting from these losses.

**METHODS**

Twenty-four hour losses of water and electrolyte were measured following the administration of Mercuhydrin to 13 patients with congestive heart failure and to 4 with ascites due to cirrhosis of the liver. In all, 75 diureses were studied in these 17 patients. Although the daily intake of sodium was approximately 70 mEq., 24 hour specimens prior to the administration of Mercuhydrin all contained less than 10 mEq and 55 of the 75 contained less than 2 mEq of sodium. A period of at least four days was allowed between injections of the mercurial diuretic in the same patient. The patients with congestive heart failure were all receiving maintenance doses of digitalis.

The effect of adjuvants to the mercurial salts was also observed. Ammonium chloride, when used, was administered continuously as nonenteric coated tablets in daily doses of 100 mEq. Ammonium carboxylic resin, when used, was given in dosage of 45 Gm. per day.* The exchange capacity of this resin in terms of removal of sodium and potassium from the body was estimated as 2 mEq per Gm.

Ammonium chloride induces acidosis by the addition of excess anion to the body pool; ammonium cation exchange resin, by depletion of body base, particularly potassium.9 Whether or not acidosis per se potentiates the diuresis is unknown,10 but in either instance the adjunct therapy potentiates the mercurial diuresis.

Urine was collected during two consecutive 24 hour periods. At the beginning of the second period 2 or 3 ml. of Mercuhydrin was administered intravenously. In order to express the electrolyte and water losses due to the Mercuhydrin the electrolyte and water excretion during the 24 hours prior to the injection was subtracted from the excretion during the 24 hours following mercurial administration. It was assumed that extrarenal water losses were the same on both days. The electrolyte and water loss due to the mercurial injection is regarded as a bloc of fluid which is called, for want of a better term, the “diuretic urine,” and its components, “diuretic

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* The resin used (Amberlite IRC-50 of Rohm and Haas Co., Philadelphia, Pa.) was kindly packaged and supplied in the ammonium form by Smith, Kline and French Laboratories, Philadelphia, Pa.
water, sodium, potassium and chloride.” Because of
the inherent variability in daily water and electro-
yte excretion, the control urine does not precisely
represent the electrolyte excretion on the day of
the mercurial if a diuretic had not been admin-
istered. This error may be appreciable in small diu-
reses but is minimized in larger ones. In this report,
therefore, only those diureses have been included in
which there was an increase of at least 1000 cc. of
urine over the previous day’s output.

Sodium and potassium were determined in an
internal standard flame photometer,11 chloride by
the method of Wilson and Ball,12 ammonium accord-
ing to Summerson's modification of the Van Slyke
and Cullen procedure.13

The mean increase in urinary chloride (di-
uretic chloride) was 425 mEq. Chloride did not
appear in the urine exclusively as the sodium salt.
The average diuretic sodium was 281 mEq., the average diuretic potassium 92 mEq. Diuretic potassium ranged from 7 to 200 mEq. The largest potassium losses occurred in those diureses where the patient received ammonium chloride. The patients receiving resin did not lose as much potassium in the urine as those receiving ammonium chloride, but they were,
at the time of mercurial administration, losing
potassium in the stool.9

<table>
<thead>
<tr>
<th>Adjunct therapy</th>
<th>No. of observations</th>
<th>Mean 24 hour losses</th>
<th>Mean concentration in diuretic urine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diuretic water</td>
<td>Diuretic chloride</td>
<td>Diuretic sodium</td>
</tr>
<tr>
<td>None</td>
<td>mL</td>
<td>mEq.</td>
<td>mEq.</td>
</tr>
<tr>
<td>Ammon. chloride</td>
<td>2396</td>
<td>359</td>
<td>245</td>
</tr>
<tr>
<td>Resin</td>
<td>2858</td>
<td>440</td>
<td>266</td>
</tr>
<tr>
<td>Mean</td>
<td>3215</td>
<td>471</td>
<td>314</td>
</tr>
<tr>
<td>100 σ/m</td>
<td>40</td>
<td>36</td>
<td>48</td>
</tr>
</tbody>
</table>

\[ \sigma^2 = \sqrt{\frac{\sum x^2}{N} - \overline{x}^2} \]

Observations

Seventy-five diureses following the admin-
istration of Mercuhydrin were studied in pa-
ients who were accumulating fluid. The mean
increase in urinary volume over the previous
day’s excretion (diuretic water) for the entire
group was 2855 ml. (table 1). There is no sig-
nificant statistical difference between the mean
diuretic water in the groups with and without
adjunct therapy (ammonium chloride or resin).
Since diuretic volumes under 1000 cc. have
been excluded from this series, a comparison of
these mean volumes should not be interpreted
as meaning that the adjunct therapeutic agent
was ineffective. Ammonium chloride or resin
usually potentiated the response to Mercuhy-
drin in a given patient in whom diuretic water
would have been less than 1000 cc. without ad-
junction therapy. Moreover, cation exchange resin
often potentiated the diuresis when ammonium
chloride failed to do so.

The relationship of sodium and potassium
losses to chloride loss is illustrated by 20 diu-
reses which were selected from the group to
cover the range of chloride losses (fig. 1). Al-
though most of the chloride may be accounted
for as the sodium and potassium salt, the
equivalents of chloride are usually in excess of
the equivalents of sodium and potassium. There
is probably a small increase in the excretion of
other cations to balance the diuretic chloride
excretion. An attempt was made to account for
this relative cation deficit. The pH of the urine
varied less than ±0.5 pH units between the
control and diuretic day in 37 of 62 observa-
tions. In the other 25 observations the pH
shifted 1 to 2 units to the acid side. A shift of
1 to 2 pH units at pH values of 5.0 or 6.0, how-
ever, contributes only negligibly to free hydro-
gen ions in the urine. In 27 of 62 observations
the ammonia excretion was the same (+30
mEq.) on the control day as on the day of the
mercurial, but increased more than 30 mEq. in 33 diureses. It may be that calcium and magnesium appear in increased amounts as well.4, 6

When the chloride loss is plotted against water loss for the 75 mercurial injections, it becomes clear that the chloride concentration is quite constant for all diureses and independent of the extent of the diuresis and of the adjunct therapy (fig. 2). The mean concentration of chloride in diuretic urine was 151 mEq. per liter ±14 per cent* (table 1). When sodium and potassium losses are compared with water loss it was found that the mean sodium concentration was 97 mEq. per liter and the mean potassium concentration 35 mEq. per liter, but the individual values varied considerably (±26 and ±43 per cent respectively). The sum of the sodium and potassium concentrations, however, had about the same variability (±17 per cent) as the chloride.

When chloride is removed from the body in concentration of 151 mEq. per liter, sodium in concentration of 97 mEq. per liter and potassium in concentration of 35 mEq. per liter, changes in the plasma concentration of the electrolytes may be anticipated. Plasma sodium, potassium and chloride were therefore determined at the time of mercurial administration and again 24 hours later in 13 diureses in 6 patients (table 2). Plasma chloride fell in every instance14-18; the average fall was 5.1 mEq. per liter. Plasma potassium remained unchanged or fell slightly. Sodium values did not change significantly.

*100 s/mean.

### Table 2.—The Effect of the Electrolyte Losses following Mercuhydrin on Plasma Electrolyte Concentrations

<table>
<thead>
<tr>
<th>Diuresis</th>
<th>Adjunct therapy</th>
<th>Change in plasma sodium concentration mEq./L.</th>
<th>Change in plasma potassium concentration mEq./L.</th>
<th>Plasma chloride mEq./L. before Mercuhydrin</th>
<th>Plasma chloride mEq./L. 24 hrs. after Mercuhydrin</th>
<th>Change in plasma chloride concentration mEq./L.</th>
<th>Diuretic water ml./24 hrs.</th>
<th>Diuretic chloride mEq./24 hrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ammon. chloride</td>
<td>-1.8</td>
<td>-0.7</td>
<td>110.5</td>
<td>109.2</td>
<td>-1.3</td>
<td>2120</td>
<td>312</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>-1.2</td>
<td>0.0</td>
<td>115.0</td>
<td>112.8</td>
<td>-2.2</td>
<td>1490</td>
<td>222</td>
</tr>
<tr>
<td>3</td>
<td>Ammon. chloride</td>
<td>-3.8</td>
<td>-0.7</td>
<td>114.8</td>
<td>112.0</td>
<td>-2.8</td>
<td>1840</td>
<td>290</td>
</tr>
<tr>
<td>4</td>
<td>None</td>
<td>0.0</td>
<td>-0.3</td>
<td>112.0</td>
<td>109.2</td>
<td>-2.8</td>
<td>2360</td>
<td>344</td>
</tr>
<tr>
<td>5</td>
<td>None</td>
<td>0.0</td>
<td>0.0</td>
<td>114.8</td>
<td>111.3</td>
<td>-3.5</td>
<td>1690</td>
<td>222</td>
</tr>
<tr>
<td>6</td>
<td>None</td>
<td>-2.6</td>
<td>+0.1</td>
<td>110.8</td>
<td>106.8</td>
<td>-4.0</td>
<td>1340</td>
<td>181</td>
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<tr>
<td>7</td>
<td>None</td>
<td>+1.6</td>
<td>-0.4</td>
<td>104.5</td>
<td>100.2</td>
<td>-4.3</td>
<td>2360</td>
<td>356</td>
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<tr>
<td>8</td>
<td>None</td>
<td>0.0</td>
<td>-0.1</td>
<td>113.5</td>
<td>109.0</td>
<td>-4.5</td>
<td>2040</td>
<td>331</td>
</tr>
<tr>
<td>9</td>
<td>Ammon. chloride</td>
<td>0.0</td>
<td>-1.2</td>
<td>111.0</td>
<td>105.5</td>
<td>-5.5</td>
<td>1340</td>
<td>231</td>
</tr>
<tr>
<td>10</td>
<td>Ammon. chloride</td>
<td>-4.6</td>
<td>-0.6</td>
<td>116.0</td>
<td>108.0</td>
<td>-8.0</td>
<td>1560</td>
<td>236</td>
</tr>
<tr>
<td>11</td>
<td>Ammon. chloride</td>
<td>-1.6</td>
<td>-1.4</td>
<td>103.8</td>
<td>95.5</td>
<td>-8.3</td>
<td>3020</td>
<td>432</td>
</tr>
<tr>
<td>12</td>
<td>Ammon. chloride</td>
<td>+3.4</td>
<td>-1.5</td>
<td>104.0</td>
<td>94.5</td>
<td>-9.5</td>
<td>3190</td>
<td>438</td>
</tr>
<tr>
<td>13</td>
<td>Ammon. chloride</td>
<td>-1.8</td>
<td>—</td>
<td>108.1</td>
<td>98.3</td>
<td>-9.8</td>
<td>2320</td>
<td>364</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>-1.0</td>
<td>-0.5</td>
<td>110.7</td>
<td>105.6</td>
<td>-5.1</td>
<td>2054</td>
<td>304</td>
</tr>
</tbody>
</table>
DISCUSSION

Appreciable potassium losses following mercurial administration have not ordinarily been observed in normal individuals.\(^1\)\(^-\)\(^4\) Edematous patients studied in this laboratory who still have the capacity for excreting a fair proportion of dietary sodium in the urine also do not lose significant amounts of potassium. The present group of patients, who were, however, excreting negligible amounts of dietary sodium in the urine, invariably lost potassium following the use of a mercurial diuretic. The distinction between these two types of reaction to Mercuhydrin was also observed in a single individual who was not included in the series because she did not consistently excrete less than 10 mEq. of sodium per day. During the course of congestive heart failure in this patient there were periods when more sodium was excreted in the urine than at others. When, on a diet containing 70 mEq. of sodium, daily urinary sodium excretion was 40 to 60 mEq., there was little change in potassium excretion (−17 to +23 mEq.) following Mercuhydrin. On other occasions on the same diet, when the daily urinary sodium was less than 10 mEq., the diuretic potassium ranged from 60 to 150 mEq.

In view of these considerable losses of potassium, in one instance 200 mEq. (7 per cent of the total potassium content of the body\(^1\)\(^9\), the reasons for some of the untoward signs and symptoms which may follow the injection of mercurial diuretics should be reconsidered. The weakness and nausea which sometimes follow a large diuresis have usually been attributed to sodium depletion\(^2\)\(^0\), \(^2\)\(^1\) but may be related to the loss of potassium. The occurrence of arrhythmias after mercurial diuresis in digitalized patients, usually attributed to mobilization of digitalis from edema fluid\(^2\)\(^2\)\(-\)\(^2\)\(^4\) may also be due to potassium depletion. A relationship between digitalis toxicity and available potassium has been reported.\(^2\)\(^5\), \(^2\)\(^6\) Additional evidence for a relationship between the occurrence of arrhythmias and potassium depletion has been observed in this laboratory. Patients in congestive heart failure receiving ammonium or hydrogen cation exchange resin lose large amounts of potassium in the stool. When these patients are on maintenance doses of digitalis, it is not uncommon for them to develop premature contractions. The abnormal rhythm may be terminated by administering potassium or by withdrawing the resin or digitalis.\(^2\)\(^7\)

It has been observed (fig. 2) that the mean concentration of chloride in the diuretic urine was 151 mEq. per liter. This concentration of chloride is essentially isotonic with body fluids.\(^2\)\(^8\), \(^2\)\(^9\) Thus a bloc of fluid has been lost during the diuresis which leaves the tonicity of body fluid unchanged but alters the concentrations of individual ions.

The concentrations of sodium, potassium and chloride in the diuretic urine yield certain information concerning their origin. The concentrations of potassium and of chloride are greater and that of sodium is less in diuretic urine than in extracellular fluid. If all the electrolytes and water came from extracellular fluid alone, it would be expected that plasma chloride and potassium would fall following Mercuhydrin while plasma sodium would rise. The mean fall in plasma chloride was of the magnitude one would expect if water with chloride in a concentration of 151 mEq. per liter is re-
moved from extracellular fluid with a concentration of chloride of 110 mEq per liter.* Thus the chloride and water loss following Mercuhydrin can be accounted for as originating entirely from extracellular sources. In fact, if significant amounts of water had come from intracellular sources of low chloride concentration, the high concentration of chloride in the urine would be difficult to explain. (The possibility remains that some portion of the water loss may come from intracellular sources of high chloride concentration. Skin has been observed to have an unusually high concentration of chloride.39)

The fall in plasma potassium, however, is by no means great enough to account for the potassium loss as coming from the extracellular fluid alone. Indeed, the potassium loss in certain diureses was larger than the total calculated amount of extracellular potassium, so that intracellular loss of potassium seems unquestionable. The concentration of sodium in the diuretic urine is less than that in the extracellular fluid and a rise in serum sodium might be expected. Since this was not observed, sodium presumably entered the intracellular fluid in exchange for intracellular potassium, the loss of which has already been indicated. Thus, the mercurial diuresis in a patient who is actively accumulating edema fluid leaves the patient relatively alkalotic, with a loss of intracellular potassium and a gain in intracellular sodium.*

**Summary**

The electrolyte and water losses in 75 instances of diureses following Mercuhydrin were studied in 17 edematous patients.

The loss of potassium was appreciable following the injection of Mercuhydrin to patients who almost completely retained their dietary sodium. Occurrence of such clinical symptoms as weakness, nausea, and ventricular premature contractions might be attributed to this loss of potassium.

The fluid lost by mercurial diuresis was isotonic with body fluids. The chloride concentration was fairly constant at 151 mEq per liter. The concentrations of sodium and potassium were more variable, the average concentrations being 97 and 35 mEq per liter, respectively. Loss of water and electrolyte in these concentrations leaves the patient in relative alkalosis, with a loss of intracellular potassium and a gain in intracellular sodium.

**Acknowledgment**

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**References**


* On the basis of balance studies in six patients with congestive heart failure, similar conclusions have been recently reported in abstract form by Schwartz and Wallace.24
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