Patterns of Electrolyte Excretion in Edema Loss without the Use of Diuretics

By D. ROBERT AXELROD, M.D.

During the loss or gain of edema the composition of the extracellular fluid remains remarkably constant despite the large changes in volume. A number of studies have indicated that the renal excretion of body water and electrolytes does not completely account for this constancy. In studies of edema loss, electrolytes and water were not lost in the same proportions that exist in extracellular fluid or in a combination of extracellular and intracellular fluids. Sodium depletion and subsequent sodium replacement, in both edematous and nonedematous patients, produced changes in body sodium without proportional changes in the extracellular water. Sodium was retained by pre-edematous patients before edema appeared, and by post-edematous patients after the edema was lost. These studies do not necessarily contradict the idea that edema is excess extracellular fluid but indicate that, during the loss or gain of edema, sodium and water are not excreted or retained in the same proportion as they exist in extracellular fluid.

Few balance studies were found in which all the edema of congestive heart failure was lost without the use of diuretics. The present report is of 15 edematous male patients studied on a metabolic ward who lost all of their edema on a regimen of bed rest and a fixed, low-sodium diet. The net urinary balance of sodium, potassium, and chloride has been related to weight change, which was used as the measure of change of body water. In all of the studies presented here, the loss of sodium per kilogram of weight loss was less than the concentration of sodium in extracellular fluid. There were two patterns of edema loss; in one the sodium loss was approximately 100 mEq/Kg. of weight lost, and in the other sodium loss was less than 50 mEq/Kg. There is an indication that the difference in pattern was related to the underlying disease. These studies indicate that edema loss is not solely the result of renal excretion of the excess sodium, but that there is also an internal redistribution of sodium. In some instances this redistribution appeared to be the major mechanism accompanying edema loss.

Materials and Methods

Patients with edema were admitted directly to the metabolic ward where they were weighed and the urinary collection was started. At 8:00 a.m. of each day during the study, the patient emptied his bladder, completing the day's urinary collection; and was then weighed on a kilogram scale sensitive to changes of 10 Gm. Urinary volume, sodium, potassium, and chloride were measured daily. Analyses of serum sodium, potassium, chloride, and carbon dioxide-combining power were done approximately three times a week. Stool analyses were not done, but the stools were inspected. None of these patients had diarrhea or bulky stools during the study.

The diet consisted of approximately 2 liters of a prepared liquid formula containing 1,950 calories; 329 Gm. of carbohydrate, 63 Gm. of protein, and 42 Gm. of fat (calculated from tables of composition). A kilogram of formula was made up of 240 Gm. of low-sodium milk, 25 Gm. of "Casee," 150 Gm. of dextrose, 60 Gm. of 11.5 per cent cream, and 525 Gm. of water. Thirty quarts, enough for about 15 days of study, were prepared at one time and put into 1-quart waxed cardboard containers and frozen. Each thirty-quart batch was analyzed for sodium, potassium, and chloride, and since there was little variation from batch to batch, the average values of 8 mEq. of sodium, 12 mEq. of potassium, and 12 mEq. of chloride per liter, were used. Distilled water for drinking was allowed as desired.

Patients were kept at bed rest or restricted activity during the study, and each patient was studied until it appeared that the weight was stable and there was no evidence of edema. Therapy consisted of bed rest and low-sodium diet for three patients; in addition the patient

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with beriberi heart disease was given thiamine after the fifth day; one patient with cor pulmonale had two phlebotomies; and the patient with Hodgkin's disease received nitrogen mustard, which eliminated the inguinal lymphadenopathy that had produced unilateral leg edema. The other nine patients received digitalis and one of these (De) also received apresoline, hydralazine, and hexamethonium without any decrease in his hypertension. Balance of electrolytes was taken as the difference between the urinary excretion and the amount taken in the diet. Insensible water loss was calculated as the fluid intake minus the urinary volume, minus the weight change.

Sodium and potassium were analyzed with an internally compensated flame spectrophotometer; the food aliquot was treated in the method described by Wallace et al. Serum and urine chlorides were measured by the method of Schales and Schales, food chloride by the second open Carius method described by Cheek and West. Serum carbon dioxide-combining power was done by the Van Slyke and Cullen method. Serum osmolality was determined by freezing-point depression, with use of a thermistor for temperature measurements. The carbon dioxide-combining power was done by the routine clinical laboratory. All other analyses were done in duplicate in the research laboratory.

Results

Weight change and net urinary electrolyte balances for each patient are tabulated in table 1, which also includes the diagnosis, calculated losses of electrolytes per kilogram of weight loss, and the ratio of sodium to chloride losses. The patients lost from 4 to 18 Kg. of weight in periods of 5 to 20 days. On the basis of the loss of sodium per kilogram of weight loss, they were divided into two groups. The first group lost 81 to 132 mEq. Na/Kg. In the second group there was a range of values from a gain of 11 mEq. Na/Kg. to a loss of 48 mEq./Kg. Losses of chloride per kilogram of weight loss were more variable than sodium, which is reflected by the wide range in the ratio of sodium to chloride losses. In general, the loss of Cl/Kg. was greater in group I than in group II. There was a total loss of body potassium in all but four of the studies. These losses were small, 37 to 169 mEq., except for the patient with Cushing's syndrome who lost 444 mEq. in 11 days. The gain of potassium in four studies was also small, ranging from 20 to 164 mEq.

The loss or gain of K/Kg. varied a great deal. Average extrarenal water loss ranged from 1,090 to 1,870 ml./day, with one value of 2,430 ml./day in a patient with advanced pulmonary disease. There were occasional fluctuations in the extrarenal water loss per day by some individuals, and in some instances this could be related to a change in acid-base balance, as reflected by changes in serum carbon dioxide-combining power.

Table 2 contains the average serum electrolyte concentrations, and the first and final concentrations for sodium and osmolality. The average values fall within the normal ranges except for the expected changes associated with the underlying disease. For example, the patient with Cushing's syndrome (Mn) had a hypokalemic alkalosis; the patients with cor pulmonale in group II had elevated concentrations of carbon dioxide-combining power. There do not appear to be any other differences of average serum electrolyte or osmolar concentrations between the groups. There was no consistent change in serum sodium or osmolar concentration between the first value and the value obtained after all the edema was lost; the changes that occurred were small.

The daily losses of weight and electrolytes are depicted in figures 1 to 5. The scale has been arranged so that 100 mEq. of electrolyte is equivalent to 1 Kg. of weight, and the net loss of each day is added to the cumulative balance of the preceding days. The parallel course of the sodium and weight curves in these figures indicates a consistent relationship of these losses at a rate of 100 mEq./Kg. The chloride curves maintained a consistent relationship to the weight curves, except in one case, and to the sodium curves except in the instances discussed later. In figure 1 the sodium and weight curves are parallel from the third day to the end of the study. In figure 2 they are almost identical, whereas the chloride loss was very small and not related to the other losses. In the study shown in figure 3, all three of the curves are essentially the same for the first 9 days, then the rate of sodium loss exceeded the rates of weight and
**Table 1**

**Edema Loss Without Diuretics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Diagnosis*</th>
<th>No. of days</th>
<th>Initial weight</th>
<th>Total net loss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weight Kg.</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
<td>------------</td>
<td>-------------</td>
<td>----------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Eg.</td>
<td>68</td>
<td>Varicose veins</td>
<td>11</td>
<td>78.14</td>
<td>8.39</td>
</tr>
<tr>
<td>Qn.</td>
<td>69</td>
<td>Varicose veins</td>
<td>11</td>
<td>79.02</td>
<td>4.80</td>
</tr>
<tr>
<td>So.</td>
<td>38</td>
<td>Hodgkin's disease</td>
<td>9</td>
<td>107.21</td>
<td>6.92</td>
</tr>
<tr>
<td>Ao.</td>
<td>62</td>
<td>ASHD</td>
<td>11</td>
<td>67.29</td>
<td>10.34</td>
</tr>
<tr>
<td>Lt.</td>
<td>63</td>
<td>HHD</td>
<td>11</td>
<td>91.69</td>
<td>4.81</td>
</tr>
<tr>
<td>Ch.</td>
<td>65</td>
<td>ASHD</td>
<td>17</td>
<td>64.07</td>
<td>15.56</td>
</tr>
<tr>
<td>Sf.</td>
<td>60</td>
<td>ASHD, diabetes</td>
<td>5</td>
<td>63.12</td>
<td>4.40</td>
</tr>
<tr>
<td>Mn.</td>
<td>48</td>
<td>Cushing's syndrome</td>
<td>11</td>
<td>112.03</td>
<td>12.60</td>
</tr>
<tr>
<td>Sn.</td>
<td>64</td>
<td>Total</td>
<td>13</td>
<td>75.36</td>
<td>8.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before KCl</td>
<td>5</td>
<td>6.44</td>
<td>605</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After KCl</td>
<td>8</td>
<td>1.78</td>
<td>377</td>
</tr>
<tr>
<td>Ec.</td>
<td>37</td>
<td>Beriberi</td>
<td>15</td>
<td>82.70</td>
<td>18.56</td>
</tr>
</tbody>
</table>

*ASHD, arteriosclerotic heart disease; HHD, hypertensive heart disease.

†These values are for total, rather than net losses, with the patient on a diet not exceeding 10 mEq. of sodium and 25 mEq. of chloride per day.
chloride losses. The relationship of losses in figure 4 were consistent for the first 5 days, and sodium diverged from the weight and chloride curves when supplemental potassium chloride was given. All of the patients in group I lost approximately 100 mEq Na/Kg. for most of their weight loss. A study of a patient in group II is presented in figure 5. The over-all ratio of losses was 47 mEq Na/Kg. and the curves show that this ratio was consistent after the first 3 days. Despite the variations in the ratio of sodium to weight losses among the studies in group II, there was little variation within an individual study in either group.

In an attempt to determine whether the balances during accumulation of edema were the same as during loss of edema, sodium solutions were given intravenously to three patients who had lost all or most of their edema. One patient with a history of repeated episodes of congestive failure secondary to arteriosclerotic heart disease, received 298 mEq. of sodium chloride as isotonic saline in a 2-hour period. He retained all of it, gained 2.11 Kg. of weight, and after 5 days there was no change in sodium balance or weight. A patient in group II (Hn) received 425 mEq. of sodium chloride as 5 per cent saline in a 1-hour period. One day later he had retained 342 mEq. of sodium with a weight gain of .35 Kg.; 5 days later he had still retained 295 mEq. of sodium, and his weight was .21 Kg. less than before the saline administration. Another patient with nutritional heart disease, who had lost 95 mEq. Na/Kg. and 7 Kg. of weight, received 298 mEq. of sodium chloride as isotonic saline within 2 hours. He retained 171 mEq. of sodium 1 day later, with a weight gain of .68 Kg. Five days later he still retained 135 mEq. of sodium and his weight was .20 Kg. less than before the saline had been given.

**Discussion**

The composition of the fluid lost during the disappearance of edema was studied in a series of patients who lost all of their edema on a regimen of rest, low-sodium diet, and, in some instances, digitalis. The fluid lost was hypotonic to body fluids in respect to the fixed cations, i.e., sodium and potassium. This is similar to the findings in previous studies of

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**Table 2**

*Serum Values during Edema Loss without Diuretics*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sodium mEq./L.</th>
<th>Potassium mEq./L.</th>
<th>Chloride mEq./L.</th>
<th>CO₂ Combining power—mM./L.</th>
<th>Osmolarity mOsM./L.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Initial Final</td>
<td>Mean Initial Final</td>
<td>Mean Initial Final</td>
<td>Mean Initial Final</td>
<td>Mean Initial Final</td>
</tr>
<tr>
<td>Eg.</td>
<td>140 138 141</td>
<td>4.7 107 25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qn.</td>
<td>141 139 143</td>
<td>4.6 107 26</td>
<td>277 281 276</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ao.</td>
<td>140 140 140</td>
<td>5.3 98 26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lt.</td>
<td>138 134 139</td>
<td>5.1 106 22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ch.</td>
<td>137 137 141</td>
<td>5.0 100 21</td>
<td>292 291 298</td>
<td></td>
<td></td>
</tr>
<tr>
<td>St.</td>
<td>145 146 145</td>
<td>5.0 106 28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mn.</td>
<td>143 146 147</td>
<td>3.0 96 35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sn.</td>
<td>142 139 137</td>
<td>5.3 111 24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ee.</td>
<td>138 134 131</td>
<td>4.8 102 23</td>
<td>280 271 281</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rs. (a)</td>
<td>147 140 147</td>
<td>4.9 104 32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rs. (b)</td>
<td>144 141 147</td>
<td>5.5 96 30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men.</td>
<td>138 135 137</td>
<td>5.1 103 25</td>
<td>282 302 286</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lo.</td>
<td>145 147 143</td>
<td>5.6 100 34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De.</td>
<td>142 141 143</td>
<td>4.1 103 26</td>
<td>283 280 285</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hn.</td>
<td>137 142 140</td>
<td>4.5 99 28</td>
<td>282 281 289</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There were 4 to 10 determinations for each mean, except for Sf. and the CO₂ value for Rs (a).
Electrolyte and weight losses during edema loss. Patient Ch with arteriosclerotic heart disease. After the third day the sodium and weight curves were essentially parallel; the ratio of losses was 100 mEq. of sodium per kilogram. The sodium and chloride losses maintained a consistent relationship throughout the study.

Edema loss;¹⁻⁶ only one study showed that the fluid lost had the composition of extracellular fluid.¹⁸ In these reports, the fluid lost was described in terms of extracellular and intracellular fluid losses, and shifts of ions from one compartment to the other. By this interpretation, the proportion lost from each compartment varied from patient to patient, and there was water loss that could not be ascribed to either compartment. In the present study, by using the loss of sodium per kilogram of weight loss, two patterns occurred and within each pattern the findings were quite consistent.

Table 1 shows the two groups of patients, separated on the basis of sodium loss per kilogram of weight lost. The 10 patients in the first group lost approximately 100 mEq Na/Kg, and the five patients in the second group lost less than 50 mEq Na/Kg. In group I the edema was secondary to venous stasis or hypertensive arteriosclerotic, or beriberi heart disease. The results of the three patients in this group whose edema was due to venous stasis were essentially the same as the results from the patients whose edema was due to cardiac disease. The interpretations, based on the findings in this group, would be the same, whether or not these three patients are included in the group. In group II, the edema was secondary to cor pulmonale, or a combination of liver cirrhosis and heart disease in four of the five cases. The difference in the ratio of sodium to water losses in the two groups may be due to liver damage, which is more likely to occur with cor pulmonale, and is similar to the report of Farber and Soberman¹² that patients with edema of liver cirrhosis had a lower sodium to water ratio than patients with edema of heart failure. Only four studies of edema loss were found in which no diuretics other than digitalis were used. The data of these 11 patients have been recalculated on the basis of sodium and chloride losses per kilogram of weight lost and are presented in table 3. The results are quite similar to those in group I.

In this study the weight loss was relatively large over a short period of time, and the diet was adequate to maintain caloric and protein

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balances. Under these conditions weight change can be used as a measure of water balance. Skin and fecal losses of electrolytes are small when there is no sweating or diarrhea. In studies of edema loss, fecal excretion of sodium was almost always less than 2 mEq./day, chloride excretion was even smaller, and potassium excretion was more variable, but usually less than 10 mEq./day.7,9,19 Skin losses of sodium, potassium, and chloride ranged from 3 to 6 mEq./day in a study done under controlled conditions.20 In this study the stools were inspected and there were no instances of diarrhea or bulky stools. At times patients were noted to have visible sweating, but this was infrequent and sporadic. The sodium or chloride loss per kilogram of weight loss would not change much if calculations for fecal and skin losses were included. Since the ratios of sodium to weight and of sodium to chloride losses remained essentially constant during the course of an individual study, it appears that variations in fecal and skin losses were small and did not affect the over-all results. The consistency of the relationships of sodium, chloride, and weight losses in the individual studies is emphasized because this supports the over-all results of each study.

Average daily values for extrarenal water loss are given in table 1. This includes respiratory, skin, and fecal water, but does not include metabolic water of oxidation. The values are a little larger than reported by Jaenike and Waterhouse,18 but are within the range of values reported by Iseri et al.,19 and Squires, Crosley, and Elkinton,21 who also noted deviations from average values within an individual study. D’Alton et al.22 found a change of insensible water loss after edema cleared, in only one of three patients, and Jaenike et al.18 found no difference in average insensible water loss on days of mercurial diuresis from days of no mercurial administration. Since a large portion of insensible water loss is via the lungs, and in some instances the fluctuations in this study could be related to changes in serum carbon dioxide-combining power, the variations of insensible or extrarenal water loss may well be due to changes in acid-base balance.

The ratios of chloride to water losses were also hypotonic to interstitial fluid and more variable than the sodium to water losses. The difference in the losses of sodium and chloride is also seen in the wide range in the ratios of sodium to chloride losses (table 1). These results indicate that some of the sodium and chloride are distributed and excreted independent of, and different from, each other, and suggests that the use of chloride excretions as a measure of extracellular fluid changes may be erroneous. Most of the patients had a small loss of potassium during the loss of edema. In two studies there was a gain of more than 100 mEq. of potassium, and the ratio of sodium to weight losses changed during the course of each of these

### Table 3

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of patients</th>
<th>Na loss mEq./Kg.</th>
<th>Cl loss mEq./Kg.</th>
<th>Na/Cl</th>
<th>Balance K mEq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iseri19</td>
<td>3</td>
<td>101, 108</td>
<td>120, 77</td>
<td>.90, 1.39</td>
<td>+182, +236</td>
</tr>
<tr>
<td>Iseri1</td>
<td>1</td>
<td>108</td>
<td>58</td>
<td>1.86</td>
<td>+329</td>
</tr>
<tr>
<td>Jaenike18</td>
<td>3</td>
<td>91, 119</td>
<td>79, 114</td>
<td>1.17, 1.64</td>
<td>-41, +69</td>
</tr>
<tr>
<td>Mader2</td>
<td>4</td>
<td>105, 114</td>
<td>164</td>
<td>.76</td>
<td>+ 42, + 75</td>
</tr>
<tr>
<td></td>
<td>184, 180+</td>
<td>178</td>
<td></td>
<td></td>
<td>+154, +123</td>
</tr>
</tbody>
</table>

*Total weight loss of 2 Kg.
+*Only a small proportion of the edema loss was studied in the patient who lost 184 mEq./Kg., and this is probably true of the one who lost 180 mEq./Kg.
Electrolyte and weight losses during edema loss. Patient Ee with beriberi heart disease. The slope of the sodium, chloride, and weight curves is steeper after thiamine was given. The sodium curve diverged from the weight and chloride curves on the ninth day. There was a steady gain in body potassium.

loss proceeded at a rate greater than 100 mEq. Na/Kg., and the curves diverged. As in the previous study there was no change in the relationship of the chloride and weight curves.

The results of this study indicate that in edema loss, without the use of specific diuretic drugs, the fluid that was lost from the body was hypotonic to body fluids. The serum sodium and osmolar concentrations did not increase after the edema loss, indicating that internal redistribution and osmotic inactivation of some of the ions had occurred. Others have also found no increase in serum sodium concentration after edema loss.1, 5, 18, 23 Bone solids, which can gain or lose large quantities of sodium, may be the site of osmotic inactivation of sodium.24-27 Recent studies, however, failed to show any changes of bone sodium in patients with cardiac disease.28, 29 Some of the chloride may have been exchanged for an intracellular anion that was excreted, or the chloride may have been held in an osmotically inactive form in connective tissue.
A sodium solution which was rapidly infused into patients who had lost all or most of their edema, contained more sodium than is present in 2 Kg. of extracellular fluid. Five days after the sodium administration there was a small decrease in body weight in two of the studies, but more sodium was retained than is present in a kilogram of extracellular fluid. In the other study, sodium retention and weight gain were in the proportions found in extracellular fluid. The retention and excretion of body sodium without proportional changes in body water have been reported by Lusk and Palmer,4 who found large retentions of sodium in patients before they reaccumulated edema; by McCance,10 who found a discrepancy between sodium and water during both depletion and repletion of sodium in normal subjects; by Aikawa,11 who found increased exchangeable body sodium in patients with rheumatic fever before they developed edema, and after they had lost their edema; by Farber and Soberman,12 and Birkenfeld et al.,13 who found increased exchangeable body sodium in patients after edema was lost. These observations indicate that the fluid lost during the disappearance of edema did not have the same composition as the edema fluid in the body, and that the accumulation or disappearance of edema is at least partially related to altered internal redistribution of sodium and is not solely due to inadequate renal excretion of sodium.

Summary

Sodium, potassium, chloride, and water losses were studied in patients while they lost all of their edema. The fluid which was excreted was hypotonic to body fluids, but did not change the osmotic concentration of the fluid that remained. Since the fluid excreted did not have the same composition as the edema fluid in the body, the interpretation of the results is that there is an internal redistribution and osmotic inactivation of a portion of the ions of the edema fluid of the body, and that the kidney is not the sole mechanism involved in the formation or loss of edema. Relating sodium loss to weight loss revealed two patterns; one group lost approximately 100 mEq. of sodium per kilogram of weight loss, and the other group lost less than 50 mEq. of sodium per kilogram. There is an indication that this difference is related to liver function.

Acknowledgment

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