Fluid and Electrolyte Balance during Recovery from High-Output Heart Failure Due to Beri-beri

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The pathogenesis of congestive heart failure is still obscure. Previous studies showed a decrease in cellular osmolarity during recovery from low output failure. A similar trend was found during recovery from high output failure due to beriberi, suggesting an analogous cellular disturbance. It is postulated that increased cellular osmolarity is an important factor in the retention of water and sodium associated with the development of congestive failure.

Studies of water and electrolyte balance during recovery from the usual type of low cardiac output congestive failure have shown cellular uptake of potassium and sodium and loss of water. By inference, the development of congestive failure is characterized by changes in the opposite direction, namely, cellular loss of potassium and sodium and gain of water. Such movements of water and electrolytes were explained by the hypothesis that cellular osmolarity increased during circulatory insufficiency. Partial support of this hypothesis was derived from the demonstration of concomitant increase in extracellular osmolarity, as reflected by elevation of plasma sodium concentration in decompensated cardiac patients. The following studies were conducted to investigate the movements of electrolytes and water during recovery from high-output type of congestive heart failure.

Method

Three patients admitted with severe congestive heart failure due to beriberi were studied on the metabolic ward. Cardiac catheterization was performed soon after admission and before institution of any specific therapy. The cardiac output and the customary intravascular and intracardiac pressures were obtained in each of the three patients. These studies were repeated after recovery from the congestive failure. Specific renal function tests were performed before and after recovery from congestive failure in two of the patients. The renal vein was catheterized and the true renal plasma flow was calculated from para-aminohippurate extraction and clearance. Glomerular filtration rate was obtained by mannitol clearance.

Total balance studies for water, sodium, potassium and chloride were carried out for 8 to 12 days during recovery in each of the three cases. In addition, nitrogen balance was determined in two of the three cases. Metabolic studies were divided into periods of three to five days each and the stools were pooled and analyzed for each period. Urine was collected and analyzed daily. Blood samples were obtained at the beginning of each period and at the conclusion of the metabolic studies. The exact weight of food ingested was determined by weighing all food served and rejected. Foods were prepared by high pressure steam. The electrolyte and nitrogen content of each food was obtained from appropriate tables. The patients were weighed on the Troemmer beam balance.

Intracellular and extracellular partition of water and electrolytes was calculated according to the method of Darrow and Elkinton, Winkler and Danowski. Reference point for the total extracellular volume was selected at the end of the study after edema had been eliminated, 16 per cent of the body weight being taken as equivalent to the extracellular water at that moment. Calculations of the extracellular water were then carried back to the initial period, utilizing the total chloride balance and the plasma chloride concentrations. Primary interest was not in the absolute volume of extracellular water, but, rather, in the changes occurring in this volume during recovery. Changes in extra-
cellular electrolyte content were then computed from the extracellular volumes and the plasma electrolyte concentrations at the beginning and end of each period. Total body water balance was calculated from changes in weight corrected for true internal nitrogen balance, 1 Gm. of metabolized protein nitrogen being considered equivalent to 33.3 Gm. of tissue weight. Since nitrogen balance was not determined in case 3, no such correction was made. The difference between total and extracellular balance represented intracellular balances. The insensible loss of weight was determined according to the method of Newburg. This was assumed to be essentially equal to insensible loss of water. The total intracellular osmolar change was calculated by Elkington’s method.

Sodium and potassium were analyzed by flame-photometry, according to methods described previously. Chloride was determined manometrically and polarographically, and nitrogen was determined by micro-Kjeldahl method.

Case Reports

Case 1 (D. R. H. no. 50-15822)

L. P., a 53 year old male bartender, was admitted on Nov. 1, 1950 because of severe dyspnea and edema. There was a weight gain of 35 pounds over the preceding two months, and for 10 days prior to admission there was progressive swelling of ankles, legs and abdomen, followed by dyspnea and orthopnea. There was a slight nonproductive cough. Review of the past history revealed no evidence suggestive of cardiovascular, pulmonary, or renal diseases. There was, however, a long history of chronic alcoholism and poor dietary intake.

Physical Examination. The patient was a well-developed, plethoric white male with anasarca and orthopnea. The blood pressure was 130/60. No evidence of hypertension was seen in the ocular fundi. A conspicuous rhinophyma and dilated telangiectasies of the cheeks were present. The skin was flushed and warm. The tongue was smooth, red and atrophic. Vein necks were distended. There was a pleural effusion on the right and moist rales were heard above this and in the left base. The heart was enlarged to both right and left. A diffuse apical impulse with a rate of 140 per minute was felt. There was a mesodiastolic gallop and a soft systolic murmur at the apex. The abdomen was protuberant with ascites and edema of the wall. A tender liver extended 6 cm. below the right costal margin. The genitalia and extremities showed massive edema and the skin over the legs was indurated and brawny. Neurologic examination revealed no abnormalities.

Laboratory Studies. The complete blood count was normal except for hemoglobin of 10 Gm. per 100 cc. The hematocrit was 40 per cent. Urinalysis was negative except for 1 plus albuminuria. Fasting blood sugar was 92 mg. per 100 cc.; nonprotein nitrogen, 70 mg. per 100 cc.; serum albumin, 4.99 Gm.; serum globulin, 2.06 Gm.; and serum bilirubin, 2.4 mg. per 100 cc. The Kline test was negative. Plasma sodium concentration was 129 mEq.; potassium, 5.3 mEq.; chloride, 101.1 mEq. per liter; and carbon dioxide combining power, 32 volumes per cent. Chest x-ray films and fluoroscopy showed congestion of the lungs, right pleural effusion, and a poorly contracting, hyperactive heart, which was enlarged to 60.5 per cent of the diameter of the chest. The electrocardiogram showed sinus tachycardia and low voltage complexes in all leads. The basal metabolic rate was plus 35 per cent. The arm-to-tongue circulation time, using Decholin, was 17 seconds, and the venous pressure was 340 mm. of water. Total plasma volume, using T-1824 dye, was 6,804 ml. and the total blood volume, 11,423 ml. Soon after admission 1500 ml. of straw-colored pleural effusion were removed.

Hospital Course. Cardiac catheterization studies, performed on the third day, demonstrated an increase in right ventricular diastolic and pulmonary “capillary” pressures. The cardiac output was 14.4 liters per minute and the cardiac index, based on “dry weight,” was 7.75 liters. The arteriovenous oxygen difference and the peripheral vascular resistance were well below normal. These findings were consistent with high-output failure due to beriberi.

The first two hospital days constituted a brief control period on bed rest and a 200 mg. sodium diet without supplementary vitamins. Dyspnea was partially relieved initially by thoracentesis. There was an additional weight loss of 2.5 Kg. over the 48-hour period. No change in physical findings with respect to heart and peripheral vessels was observed.

Following cardiac catheterization on the third day of metabolic study, the patient was started on 200 mg. of crystalline thiamine hydrochloride, intramuscularly, three times a day, and, in addition, was given supplementary oral “B” complex vitamins. He was also kept on a weighed 200 mg. sodium diet. On this regimen, the patient improved rapidly and steadily with disappearance of peripheral and pulmonary congestion and with a decrease in cardiotoracic ratio to 48.5 per cent. The venous pressure fell to 90 mm. of water and the circulation time fell to 12 seconds. The plasma volume on the ninth day was 6,250 ml. The metabolic studies were continued from the first through the twelfth day, by which time the edema had all disappeared and the weight had stabilized at approximately 34 Kg. below the initial weight.

Cardiac catheterization, performed again after full compensation of cardiovascular function, showed a decrease in cardiac index to 5.8 liters per minute, a decrease in end-diastolic right ventricular and pulmonary “capillary” pressures to normal,
and an increase in arteriovenous oxygen difference and peripheral vascular resistance.

Case 2 (D. R. H. no. 51-4151)

L. B., a 40 year old white male, brewery employee, was admitted on March 20, 1951 because of severe swelling of the lower extremities, genitalia and abdomen. The patient was a chronic alcoholic and had been drinking excessively for five months, averaging 40 to 50 bottles of beer per day. His intake of food became progressively more restricted and, with the development of anorexia in the few weeks preceding his admission, was virtually nil. For one week before admission, he noted increasing dyspnea and progressive edema, but denied orthopnea, palpitation and cough. For two days he suffered from pain in his calves, but gave no other symptoms of peripheral neuritis. A careful interrogation of his past medical history revealed no evidence of any previous cardiovascular, pulmonary or renal disease.

Physical Examination. The patient was a well-developed white male with warm flushed skin and anasarca. The temperature, pulse, and respirations were normal and the blood pressure was 115/65. The sclerae were slightly icteric. The fundi showed no evidence of hypertension. The tongue was smooth and red, and perleche was present. There was no thyroid enlargement or evidence of hyperthyroidism. Occasional rales were heard in both lower lobes and signs of pleural effusion were present in the left. The heart was enlarged and a protodiastolic gallop and a soft systolic murmur were heard at the apex. The abdomen was protuberant and signs of ascites were present. A tender liver was palpable 10 cm. below the right costal margin. The spleen and kidneys could not be felt. The external genitalia and the lower extremities revealed marked pitting edema. Neurologic examination revealed bilateral calf tenderness, plantar hyperalgesia, and decreased knee and ankle jerks.

Laboratory Studies. The hemoglobin was 12.0 Gm. per 100 cc. and the hematocrit, 42 per cent. Urinalysis was negative. Serologic tests for syphilis were negative. Blood urea nitrogen was 9 mg. per 100 cc.; total serum protein, 5.97 Gm. per 100 cc. with 3.65 Gm. albumin and 2.32 Gm. globulin per 100 cc. Total serum bilirubin was 1.2 mg. per 100 cc., and inorganic phosphorus 6.5 mg. per 100 cc. Plasma carbon dioxide combining power was 35 volumes per cent; sodium, 130, and potassium 3.6 mEq. per liter. The cephalin flocculation test was 1 plus in 24 hours. Total plasma volume was 4,310 ml., and the total blood volume was 7,431 ml. The electrocardiogram was suggestive of right ventricular dilatation. Arm-to-tongue circulation time was 11 seconds, and the venous pressure 168 mm. of water. Chest x-ray films showed a cardiothoracic ratio of 51.2 per cent, pulmonary congestion, and mild emphysema.

Hospital Course. Cardiac and renal vein catheterization was performed on the second and twenty-first days of hospitalization. The initial studies, which required 450 ml. of saline during the procedure, showed a cardiac output of 8.33 liters per minute and a "dry weight" cardiac index of 4.73 liters per minute. End-diastolic right ventricular and pulmonary "capillary" pressures were elevated, whereas the arteriovenous oxygen difference and the peripheral vascular resistance were decreased. In spite of the high cardiac output, the true renal blood flow was decreased, so that the fraction of cardiac output going to the kidneys was only 5.8 per cent. There was proportionately less reduction in glomerular filtration rate than in renal plasma flow, with consequent elevation in filtration fraction to 35.0 per cent. Following the initial studies and during the 10-day metabolic period, the patient was maintained on a weighed 200 mg. sodium diet rich in vitamins. No cardiac glycosides, diuretics or supplementary vitamins were given. The plasma volume and blood volume fell to 2,873 and 5,861 ml., respectively. The patient lost over 16 Kg. of fluid and showed improvement in both cardiac and renal functions. Pulmonary rales and signs of pleural fluid and peripheral edema disappeared. The cardiothoracic ratio decreased from 51.2 to 43.6 per cent. Venous pressure fell to 85 mm. of water, but the circulation time lengthened slightly to 14 seconds. The end-diastolic right ventricular and pulmonary "capillary" pressures fell to normal levels. There was, however, a paradoxic increase in cardiac output to 11.15 liters per minute, directly referable to considerable amount of apprehension, obvious during the second cardiac catheterization procedure. Both renal plasma flow and glomerular filtration rate became normal, as did the filtration fraction and the renal blood flow–cardiac output ratio.

The metabolic studies in this patient were carried out for 10 days from the second to eleventh day, inclusively, in two five-day periods.

Case 3 (D. R. II. no. 51-15894)

J. K., a 34 year old white male laborer, was admitted on Nov. 19, 1951 because of severe progressive dyspnea. There was a long history of chronic alcoholism, poor diet, and neglected personal hygiene. Exertional dyspnea had been noted intermittently for five years. This had become increasingly severe during the last year and was complicated by dependent edema over the last five months and swelling of the abdomen for one month. A chronic cough had been productive of a white frothy spumut, but hemoptysis had never occurred. On the day of admission, there was an exacerbation of cough and dyspnea, accompanied by fever, but not by chills or pleural pain. Past history was otherwise negative.

Physical Examination. The patient was an obese, orthopneic white male. The temperature was 101 F., pulse 100 per minute, and respirations 24 per minute. The blood pressure was 140/75. The skin was warm and flushed. The fundi showed no evidence of ante-
cedent hypertension. Signs of avitaminosis were evident in the tongue. The neck veins were distended. The trachea was in the midline and the thyroid was not palpable. A slight enlargement of the heart was present, with the apical impulse beyond the midclavicular line. The heart was hyperactive, with a regular rhythm and a rate of 104 per minute. The heart sounds were of poor quality and a soft systolic murmur was heard at the apex. The lungs revealed scattered rhonchi, fine rales at the bases, and definite signs of early pulmonary consolidation of the right upper lobe. The abdomen was distended with ascites. The liver was enlarged 5 fingerbreadths below the right costal margin and was firm, but nontender and nonpulsatile. The spleen could not be felt. There was marked tenderness of the calves, but there were no associated signs of peripheral neuritis. There was moderate soft pitting edema of the lower extremities and the trunk.

**Laboratory Studies.** A complete blood count showed a hemoglobin of 13.0 Gm. per 100 cc., hematocrit of 50.2 per cent, white blood cells 13,600 per cu. mm., with 84 per cent polymorphonuclears, 6 per cent lymphocytes, and 8 per cent monocytes. The Westergren sedimentation rate was 18 mm. in one hour. Urinalysis was negative. The sputum contained type III pneumococci. On admission, the blood urea nitrogen was 12 mg. per cent, plasma carbon dioxide combining power 50 volumes per cent, plasma chloride 96 mEq. per liter, plasma sodium 140 mEq. per liter, and plasma potassium 5.9 mEq. per liter. The total serum bilirubin on the seventh day was 1.2 mg. per 100 cc. Total serum protein was 7.6 Gm. per 100 cc., with 3.9 Gm. of albumin and 3.7 Gm. of globulin. Liver function studies showed a prothrombin time 85 per cent of normal, cephalin flocculation 3 plus in 24 hours, and bromsulphalein retention of 26 per cent in 45 minutes. Roentgenogram of the chest on admission showed a slightly enlarged heart, 49.5 per cent of intrathoracic diameter, and a pneumonitis of the right upper lung field. There was no pleural effusion. The arm-to-tongue circulation time, using Decholin, was 9 seconds, and the venous pressure was 150 mm. of water.

**Hospital Course.** Intensive antibiotic therapy was instituted and effected considerable improvement in the pneumonia, reducing the temperature to 99 F. on the second hospital day, when cardiac catheterization and renal function studies were performed. The cardiovascular-pulmonary hemodynamic measurements confirmed the clinical impression of high-output heart disease with left and right ventricular failure. The cardiac output was 11.4 liters per minute and the cardiac index 5.8 liters per minute. The peripheral vascular resistance was markedly decreased, but the arteriovenous oxygen difference was within normal limits. It is noteworthy that the renal plasma flow and the renal blood flow were normal. The glomerular filtration rate was supernormal.

Following this initial evaluation of cardiac and renal function, the patient received thiamine, 100 mg. three times a day, with other vitamins of the "B" complex group.

Digitalis and mercurial diuretics were withheld. Sodium intake was limited to 200 mg. daily.

On this regimen the heart became compensated. There was a weight loss of 4.8 Kg. during the first two days before metabolic studies were instituted and a total loss of 10.4 Kg. over the first 10 days with complete disappearance of the peripheral edema. A decrease of cardiothoracic ratio to 42.2 per cent was evident on the x-ray films. The venous pressure and circulation time showed only minimal changes. Cardiac and renal vein catheterizations were repeated four weeks after admission. The cardiac output, pulmonary capillary pressure and right ventricular pressure decreased to normal, and the peripheral vascular resistance increased to a nearly normal value. There was no change in the true renal plasma flow, but the glomerular filtration rate fell from supernormal to normal values.

The metabolic studies were carried out for eight days, from the third to the tenth day, inclusive. The study was divided into two four-day periods.

**Results of the Metabolic Studies.**

The results of the metabolic studies carried out during recovery in each of the three patients proven to have a high-output type of congestive heart failure are presented in tables 1 and 2.

**Changes in Water Metabolism.** As expected, all three patients lost weight during the 8- to 12-day period of study. The total water balance, estimated from weight changes and corrected for true nitrogen balance in cases 1 and 2, but not corrected in case 3, indicated a total loss of 22.02, 17.71 and 5.50 Kg. of water, respectively.

Calculation of extracellular water balance demonstrated total losses of 20.70, 19.52, and 2.25 Kg. in each of the three cases, respectively. Loss of extracellular water was maximal during the first period in cases 2 and 3 and appeared to represent a prompt response to either dietary or supplementary thiamine. In case 1, the greater loss of extracellular water occurred during period II, presumably due to delay in specific therapy. The total extracellular water at the onset of study was calculated to be 34, 41, and 17.6 per cent of the edematous body weight, respectively, in the three cases.
### Table 1.—Intake and Output Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Period Days</th>
<th>Weight $K_L$</th>
<th>Intake</th>
<th>Output</th>
<th>Stool</th>
<th>Plasma</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>$H_2O$ mEq.</td>
<td>$Na$ mEq.</td>
<td>$K$ mEq.</td>
<td>$Cl$ mEq.</td>
<td>$N$ Gm.</td>
</tr>
<tr>
<td>Case 1</td>
<td>I</td>
<td>94.27</td>
<td>9,207</td>
<td>351</td>
<td>135</td>
<td>53.0</td>
<td>11,050</td>
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<tr>
<td></td>
<td>1-4</td>
<td>97.03</td>
<td>10,575</td>
<td>26</td>
<td>356</td>
<td>113</td>
<td>51.1</td>
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<tr>
<td></td>
<td>5-8</td>
<td>77.70</td>
<td>8,903</td>
<td>36</td>
<td>599</td>
<td>335</td>
<td>44.8</td>
</tr>
<tr>
<td></td>
<td>9-12</td>
<td>56.90*</td>
<td>7,994</td>
<td>54</td>
<td>540</td>
<td>155</td>
<td>70.6</td>
</tr>
<tr>
<td>Case 2</td>
<td>I</td>
<td>80.53</td>
<td>20,910</td>
<td>110</td>
<td>463</td>
<td>199</td>
<td>56.8</td>
</tr>
<tr>
<td></td>
<td>2-6</td>
<td>67.80</td>
<td>57,954</td>
<td>51</td>
<td>540</td>
<td>155</td>
<td>70.6</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>54.40*</td>
<td>57,954</td>
<td>51</td>
<td>540</td>
<td>155</td>
<td>70.6</td>
</tr>
<tr>
<td>Case 3</td>
<td>I</td>
<td>92.7</td>
<td>18,555</td>
<td>41</td>
<td>401</td>
<td>116</td>
<td>13,400</td>
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<tr>
<td></td>
<td>3-6</td>
<td>90.9</td>
<td>18,238</td>
<td>42</td>
<td>515</td>
<td>137</td>
<td>13,100</td>
</tr>
<tr>
<td></td>
<td>7-10</td>
<td>87.2*</td>
<td>18,238</td>
<td>42</td>
<td>515</td>
<td>137</td>
<td>13,100</td>
</tr>
</tbody>
</table>

* Values obtained at end of study. Other values obtained at beginning of each period.  † Interpolated between preceding values and values obtained four days later.  ‡ Blood urea nitrogen.  § One-half of eight-day pooled sample.

### Table 2.—Derived Values of Total, Extracellular, and Intracellular Balances

<table>
<thead>
<tr>
<th>Patient</th>
<th>Period Days</th>
<th>Total Balance</th>
<th>Extracellular Balance</th>
<th>Intracellular Balance</th>
<th>Extracellular Volume L.</th>
<th>Insens Loss of Weight m/d.</th>
<th>Total Intracellular Osmolar Change mEq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>I</td>
<td>—6.95 -190 -87</td>
<td>-268 -8.7 -3.15 +72 -60</td>
<td>-3.80 -262 -6</td>
<td>31.90</td>
<td>2,045</td>
<td>+283.8</td>
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<tr>
<td></td>
<td>1-4</td>
<td>—8.33 -1240 +101</td>
<td>-894 -29.9 -10.19 -1532 -26</td>
<td>+1.86 +292 +199</td>
<td>28.75</td>
<td>1,968</td>
<td>-332.8</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>—6.74 -1186 +37</td>
<td>-716 -29.1 -7.36 -981 -30</td>
<td>+0.62 +205 +136</td>
<td>11.20</td>
<td>1,240</td>
<td>+301.3</td>
</tr>
<tr>
<td></td>
<td>5-8</td>
<td>—13.52 -1273 +106</td>
<td>-1416 +23.6 -13.07 -1778 -27</td>
<td>-0.45 +505</td>
<td>76</td>
<td>29.82</td>
<td>-750.7</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>—4.19 -467 +120</td>
<td>-515 +21.8 -6.45 -746 +32</td>
<td>+2.26 +279</td>
<td>106</td>
<td>17.75</td>
<td>+306.2</td>
</tr>
<tr>
<td>Case 2</td>
<td>I</td>
<td>—13.52 -1273 +106</td>
<td>-1416 +23.6 -13.07 -1778 -27</td>
<td>-0.45 +505</td>
<td>76</td>
<td>29.82</td>
<td>-750.7</td>
</tr>
<tr>
<td></td>
<td>2-6</td>
<td>II</td>
<td>—4.19 -467 +120</td>
<td>-515 +21.8 -6.45 -746 +32</td>
<td>+2.26 +279</td>
<td>106</td>
<td>17.75</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>—2.40 -391 +3</td>
<td>-0.30 -130</td>
<td>90</td>
<td>16.20</td>
<td>13.80</td>
<td>2,540</td>
</tr>
<tr>
<td>Case 3</td>
<td>I</td>
<td>—13.52 -1273 +106</td>
<td>-1416 +23.6 -13.07 -1778 -27</td>
<td>-0.45 +505</td>
<td>76</td>
<td>29.82</td>
<td>-750.7</td>
</tr>
<tr>
<td></td>
<td>3-6</td>
<td>II</td>
<td>—4.19 -467 +120</td>
<td>-515 +21.8 -6.45 -746 +32</td>
<td>+2.26 +279</td>
<td>106</td>
<td>17.75</td>
</tr>
<tr>
<td></td>
<td>7-10</td>
<td>—2.40 -391 +3</td>
<td>-0.30 -130</td>
<td>90</td>
<td>16.20</td>
<td>13.80</td>
<td>2,540</td>
</tr>
</tbody>
</table>

* Change in weight corrected for true nitrogen balance (1 Gm. $N = 3.33$ Gm. $H_2O$).
† True internal nitrogen balance (corrected for total nonprotein nitrogen balance calculated on assumption of equal distribution of nonprotein nitrogen throughout entire body fluids).
‡ Corrected for true nitrogen balance (1 Gm. $N = 2.4$ mEq. $K$) in cases 1 and 2.
§ Final extracellular volume (16% of compensated weight).
¶ Corrected for true nitrogen balance in cases 1 and 2.

The extracellular volume shrank progressively throughout the first 10 days of study in cases 1 and 2 and reached a minimum by the end of five days in case 3. The intracellular water balance was negative in cases 1 and 3, but positive in case 2. There was considerable insensible loss of weight, exceeding 2.0 Kg. per day. during the
initial period of study in all three cases. With recovery, the insensible loss decreased progressively in the first two cases, but remained elevated in the last.

Changes in Sodium Metabolism. The sodium ion was eliminated from the body in large quantities, the total external balance being 

\[-2,616, -1,739, \text{and} -502 \text{ mEq.} \]

for the entire period of study, respectively, in the three cases. Natureasis occurred promptly in the first period in cases 2 and 3, but was delayed until the administration of thiamine in case 1, as shown in table 3. The urinary sodium concentration was very low during the two-day control period and rose abruptly and progressively after institution of thiamine to reach a maximum on the sixth day of treatment.

The total intracellular sodium balance over the entire period of study was quite variable, being negative in cases 1 and 3, but markedly positive in case 2. The variability was also apparent during the separate periods of observation in case 1. These variations may have been due, in part, to the possible inherent error in utilizing chloride balance as a criterion of extracellular balance.

Changes in Potassium Metabolism. All three patients had a positive total potassium balance,

\[
\begin{align*}
\text{Urine} & \quad \text{Na}^+ \quad \text{K}^+ \\
\text{Output mEq.} & \quad \text{Conc. mEq. L} & \quad \text{Conc. mEq. L} \\
1 & 1700 & 3.0 & 52.4 & 129.0 & 5.3 \\
2 & 1800 & 3.2 & 46.7 \\
3 & 3656 & 21.9 & 41.2 \\
4 & 3900 & 36.8 & 21.7 \\
5 & 2700 & 52.8 & 18.4 & 146.1 & 3.8 \\
6 & 4125 & 77.5 & 13.6 \\
7 & 4100 & 97.9 & 15.9 \\
8 & 4025 & 99.0 & 21.8 \\
9 & 4700 & 89.3 & 18.5 & 143.6 & 4.5 \\
10 & 4900 & 82.8 & 25.7 \\
11 & 3475 & 81.3 & 50.0 \\
12 & 2550 & 44.8 & 58.5 \\
13 & & & & 149.9 & 4.9
\end{align*}
\]

* Beginning of thiamine therapy.

resulting from cellular uptake. After correction of extracellular balance and the internal nitrogen balance, the intracellular potassium balance was +329 mEq. in case 1 and +182 mEq. in case 2. The intracellular balance, uncorrected for nitrogen, in case 3 was +256 mEq.

Cellular uptake of potassium in cases 2 and 3 was greater during the last half of the study than during the first half. In case 1 the balance was slightly negative during the initial period, but became strongly positive for the remainder of the study. The delay in uptake in case 1 was correlated with the poor renal conservation of potassium, which was present for two days before and on the day of institution of thiamine (table 3).

Total Change in Osmolar Activity of Intracellular Base. This was derived from the difference between the calculated total osmotically active base at the end and beginning of the period, corrected for the measured external balances of sodium and potassium. A negative value implies binding of osmotically active electrolyte in the body fluids into inactive complexes, and a positive value implies the reverse change. Since osmotically inactive base is negligible in the extracellular fluid, the data would represent intracellular changes. It must be admitted, however, that an indeterminate fraction of the changes in osmolar activity may occur in the bones. In cases 2 and 3 the total osmolar change over the entire period of observation was negative, signifying inactivation of cellular base. In case 1, the change during period I was positive, presumably from correction of the initial hyponatremia and delay in therapy. During period II the osmolar change was negative, although much of this was again reversed during period III.

**DISCUSSION**

In each of the three cases reported in this study, a diagnosis of congestive heart failure of the high-output type, due to beriberi, was made on the basis of the history of chronic alcoholism with poor dietary intake; avitaminosis; absence of pericardial, valvular or the usual myocardial diseases; congestive edema,
with elevated venous, right ventricular diastolic, and pulmonary "capillary" pressures; signs of hyperactive heart with increased pulse pressure and shortened circulation time; high cardiac output by direct measurements; and peripheral vasodilation with flushed warm skin, low arteriovenous oxygen difference, and low peripheral vascular resistances. Although blood lactate and pyruvate levels were not obtained, the improvement of all three patients on dietary and/or supplementary thiamin, without the use of digitalis or mercurial preparations, substantiated the diagnosis.

The metabolic studies during recovery in these three cases revealed a comparable trend to that observed during recovery from low-output failure. There was a pronounced cellular uptake of potassium in all three cases, and a significant negative intracellular water balance in two. The net result in all three cases indicated movements of sodium, potassium, and water in such a manner, which tended to increase the concentration of electrolytes in the cells. The capacity of the cells to take up additional electrolyte during recovery is presumably dependent upon osmotic inactivation of cellular base. This was demonstrable in cases 2 and 3.

Thus, the development of both low- and high-output congestive failure would, by inference, be accompanied by activation of cellular base. Squires, Crossley and Elkinston reached a similar conclusion, and the results obtained by Miller could be interpreted in the same manner. A primary increase in cellular osmolarity may lead to cellular extrusion of electrolytes and uptake of water, and may stimulate the kidneys (1) to retain water, through antidiuretic hormone, in order to lower the cellular osmolarity, and (2) to retain sodium, possibly through corticoid activity, in order to raise the extracellular osmolarity and maintain equilibrium. The characteristic interstitial edema would result when the excess water and sodium, retained during exercise, are incompletely eliminated during the succeeding rest.

In low-output failure, increased cellular osmolarity may be attributed to primary cardiac insufficiency with accumulation of metabolites in the tissues either from incomplete removal or from decreased oxygen transport and impaired oxidation. In beriberi, on the other hand, congestive failure may occur in the presence of high oxygen transport and may develop in the absence of myocardial failure. Moreover, in the present study, edema antedated dyspnea in one case, and occurred in the presence of normal renal blood flow in another. If myocardial failure, decreased renal blood flow and decreased oxygen transport are not obligatory for the development of edema in beriberi, the disturbance in the cells may be the primary factor provoking retention of sodium and water. Increased cellular osmolarity in beriberi may be the result of accumulation of pyruvate and lactate ions in the tissues and may be the initial step in the vicious cycle which eventuates in myocardial failure and reduced renal blood flow.

**Summary**

In three cases of beriberi with high-output congestive failure, established by clinical criteria together with cardiac catheterization, metabolic balances of sodium, potassium, chloride and water were determined during the period of recovery on a regimen consisting of bed rest, low sodium, and a vitamin-rich diet with or without thiamine supplements. Nitrogen balance was studied in two of the cases. Cellular uptake of potassium with or without sodium and cellular ejection of water was demonstrated in these patients. The consequent osmotic inactivation of cellular base was comparable with that associated with recovery from low-output congestive failure. The findings are discussed from the standpoint of pathogenesis of congestive heart failure.

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**Sumario Español**

En tres casos de beriberi en decompensación cardíaca de alta producción, establecida
mediante criterio clínico además de cateterismo cardíaco, estudios metabólicos del balance del sodio, potasio, cloruros y agua se determinaron durante el periodo de recuperación en un régimen que consistió en descanso en cama, bajo sodio y una dieta rica en vitaminas con y sin suplementos de tiamina. Estudios de balance de nitrógeno fueron hechos en dos casos. El “uptake” celular para el potasio con o sin el sodio y la expulsión de agua se demostró en estos pacientes. La consiguiente inactivación osmótica de base celular fué comparable con aquella asociada al recobro de la decompensación cardíaca de tipo de baja producción. Los hallazgos se discuten desde el punto de vista de la patogénesis de la decompensación cardíaca.

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Fluid and Electrolyte Balance during Recovery from High-Output Heart Failure Due to Beri-beri

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