The Relationship of Sodium Retention and Venous Pressures to Edema Formation

By RALPH GOLDMAN, M.D. AND SAMUEL H. BASSETT, M.D.

Two patients with congestive cardiac failure were placed on a metabolic balance regimen and supplemental sodium chloride was administered. Weight changes in these patients could be closely correlated with the amount of sodium retention and appeared to be initially independent of brachial venous pressure thus supporting the concept that edema in congestive failure results from primary sodium retention rather than primary elevation in venous pressure.

The demonstration by Warren and Stead\(^*\) that administration of sodium to patients with compensated heart failure resulted in gain in weight, followed by a rise in venous pressure, was a departure from the concept of edema formation current at the time. It is now generally assumed that factors, other than increased venous pressure may initiate the retention of salt and water. However, it may still be of interest to note that an increase of several kilograms in the amount of extracellular fluid can occur prior to any demonstrable change in the measurement of pressure in the median cubital vein at the elbow. Electrolyte and nitrogen balances, observations of venous pressures, and body weights acquired in the course of a metabolic balance study lent themselves to a quantitative examination of these relationships.

METHODS

The actual variations in weight of two patients with congestive cardiac failure (patients EHP and EVJ) were related to weight changes arrived at theoretically and calculated from balance data, using the constants proposed by Reifenstein, Albright and Wells.\(^2\) The derived values for the retention of water were then compared with carefully obtained venous pressures.

The metabolic data and the methods employed were obtained by conventional balance techniques. Analytic methods were as follows: nitrogen by the Hiller, Plazin and Van Slyke modification of the Kjeldahl procedure directly on the urine and emulsified samples of diet, stool, etc.;\(^3\) chloride by modification of the Volhard silver nitrate–ammonium thiocyanate titration directly on specimens of diluted urine and on solutions of aliquots of diet, feces, emesis and sputum;\(^4\) sodium and potassium by the Beckman flame photometer directly on specimens of diluted urine and on solutions of the ash of aliquots of diet, feces, emesis and sputum. Ashing was performed in a muffle furnace at temperatures not exceeding 450°C. Each patient was maintained on two levels of sodium intake, and the effect of adrenocorticotropicin was observed at each level. Actual changes in weight were measured on a scale accurate to 10 Gm. Gain or loss in tissue weight was computed as nitrogen balance in grams times 32.\(^2\) This value represents not only the cell increase, but the normally associated extracellular water as well. Total weight change (cell weight plus all fluid change, including both normal and edema fluid) was calculated on the basis of nitrogen balance in grams times 27 (cell weight alone) plus a value for grams of extracellular fluid obtained by dividing the sodium balance by the sodium concentration per milliliter of serum.\(^*\) The difference between the two calculated values was assumed to constitute edema.

Venous pressures were obtained under basal conditions. The patients were placed supine on a firm bed. At the initiation of the study a horizontal line was painted on the chest wall parallel to, and 10 cm. above, the level of the bed. The patient was rotated until the line was exactly 10 cm. above the bed at each test, and the same arm was always used. This line was the zero level of reference. The skin of the forearm was infiltrated with procaine and a no. 16 needle inserted into the vein. Sodium citrate was used as the anticoagulant. Five minutes were allowed for relaxation of venous spasm, and the fluid column was permitted to rise and to fall to the point of equilibrium as a check of free flow in the system.

* Correction for the Donnan effect was not applied.

From the Research Service, Veterans Administration Center, Los Angeles, and the University of California Medical Center, Los Angeles, Calif.

This work was supported in part by a grant-in-aid from the U. S. Public Health Service, Heart Institute, Grant No. H-1004(e)(e2).
Fig. 1. The relationship of the observed weight changes to weight changes calculated from metabolic balance data. Dotted lines (graph of calculated weight) indicate gains in tissue associated with positive nitrogen balance; solid lines depict the variations in extracellular fluid.

A small carpenter's level was used to relate the zero line on the chest to the column of sodium citrate solution in the manometer.

Results

Figure 1 shows the result of the calculations based on the metabolic balance data. The upper diagram in each pair indicates the actual changes in weight; the solid line in the lower diagram, the total calculated change, tissue plus edema. The dashed line reveals the portion of the weight curve attributable to tissue gain only. The area between the solid and the dashed lines represents edema (when the solid line is above) or dehydration (when the solid line is below). In both patients the diet was apparently sufficiently high in calories and protein to permit a significant gain of tissue.

The figure illustrates the close parallel between the actual changes in weight of patient EHP (table 1) and the theoretical weights as computed. The cause of the asymmetry of the figure is apparent when it is seen that at the end of 60 days the patient had gained 2.5 kg. in tissue as based on calculations made from retention of nitrogen. In patient EVJ (table 2) as in patient EHP, the actual and theoretic weights were closely comparable. An estimate of the amount of edema is plotted in figure 2 and compared with the measurements of the venous pressures. It is evident that both patients could increase fluid retention by 3 kg., present clinical evidence of edema, and yet have no significant change in the brachial venous pressure.

Discussion

The present study confirms the report of Warren and Stead who demonstrated that edema formation in congestive heart failure precedes the increase in venous pressure and depends upon retention of sodium and water. In our study, the close agreement between the theoretical and the actual fluctuations in weight supports the assumptions made in the calculations. Values based upon nitrogen and sodium balances (as well as nitrogen and chloride) resulted in estimations of weight change which were substantially the same as those observed. It is also apparent from the data that the frequent practice of discounting nitrogen retention in short balance studies is not justified. It can be seen that in 60 days of observation both patients disclosed a tissue gain of over 2 kg. Each had been debilitated by his disease, and it is probable that the weight gain was due to the enforced intake of the test diet which was undoubtedly hypercaloric for the individual.

Earlier studies of the edema in congestive failure, such as those by Schroeder, suggested that, as sodium excretion decreased, water was retained to restore isotonicity. More recent studies have implied that water may be retained primarily, as well as in response to sodium retention. Thus, Schroeder has subsequently found that in one-third of his patients, the chloride loss was less than the proportionate amount of water during recompensation, although chloride and water loss were comparable in the remaining two-
thirds. Lombardo noted that on injecting hypotonic sodium chloride there was a relatively greater retention of water than of sodium, and a subsequent fall in the serum sodium. Miller also suggested that water retention preceded sodium retention, since in eight subjects sodium loss during recovery from congestive heart failure was much less than the amount anticipated from fluid and weight loss.

Recently, Squires and his associates found that during recovery from cardiac edema there was a positive potassium balance as well as a loss of water in excess of sodium chloride. This would imply that during the development of cardiac edema there is a dilution of intracellular electrolyte and a loss of cellular potassium. The work of Iseri and associates also revealed a positive potassium balance during loss of cardiac edema. Laragh has observed that the hypernatremia which occurs in certain cardiac patients can be relieved by the ingestion of potassium chloride. It is presumed in this instance that potassium enters the cells and releases sodium to the extracellular fluid. On the other hand, Schwartz and Wallace and Lesser and co-workers noted that, during mercurial diuresis, chloride is the ion that is preferentially excreted (although not in excess of the amount anticipated from the loss of water), while sodium and potassium are both lost in large quantities as the major accompanying cations. Undoubtedly, further work is required to clarify the relationship of potassium exchange to congestive failure, for in our subjects the balances of this element were not significantly affected by mercurial diuretics. The actual decreases in weight compared

Table 1.—Comparison of Theoretic with Observed Weight Changes

<table>
<thead>
<tr>
<th>Period</th>
<th>No. of Days</th>
<th>1 N-Bal. Gm.</th>
<th>2* Cal. Tissue Wt. Change Gm.</th>
<th>3* Cal. Tissue + ECW Change Gm.</th>
<th>4 Sodium Balance Gm.</th>
<th>5 Cal. ECW Change Gm.</th>
<th>6 Cal. Tot. Wt. Change Gm.</th>
<th>7 Cal. Edema Gm.</th>
<th>8 Observed Total Wt. Change Gm.</th>
<th>9 Observed Total Wt. Kg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5</td>
<td>7.80</td>
<td>213</td>
<td>252</td>
<td>0.483</td>
<td>154</td>
<td>360</td>
<td>117</td>
<td>490</td>
<td>56.33††</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>8.78</td>
<td>237</td>
<td>281</td>
<td>0.944</td>
<td>300</td>
<td>537</td>
<td>256</td>
<td>490</td>
<td>56.82</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>8.89</td>
<td>240</td>
<td>284</td>
<td>6.399</td>
<td>2030</td>
<td>2270</td>
<td>1986</td>
<td>1080</td>
<td>59.20</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>8.50</td>
<td>232</td>
<td>275</td>
<td>3.207</td>
<td>1020</td>
<td>1252</td>
<td>977</td>
<td>1200</td>
<td>60.49</td>
</tr>
<tr>
<td>V</td>
<td>5</td>
<td>1.06</td>
<td>29</td>
<td>34</td>
<td>-3.478</td>
<td>-1110</td>
<td>-1081</td>
<td>-1115</td>
<td>-1260</td>
<td>59.23</td>
</tr>
<tr>
<td>VI</td>
<td>5</td>
<td>9.50</td>
<td>259</td>
<td>306</td>
<td>-7.619</td>
<td>-2420</td>
<td>-2161</td>
<td>-2467</td>
<td>-1830</td>
<td>57.40</td>
</tr>
<tr>
<td>VII †</td>
<td>5</td>
<td>4.40</td>
<td>121</td>
<td>144</td>
<td>0.884</td>
<td>281</td>
<td>402</td>
<td>258</td>
<td>380</td>
<td>57.78</td>
</tr>
<tr>
<td>VIII ‡</td>
<td>5</td>
<td>5.01</td>
<td>135</td>
<td>160</td>
<td>7.105</td>
<td>2260</td>
<td>2395</td>
<td>2235</td>
<td>1940</td>
<td>59.72</td>
</tr>
<tr>
<td>IX**</td>
<td>6</td>
<td>9.81</td>
<td>265</td>
<td>314</td>
<td>3.357</td>
<td>1070</td>
<td>1335</td>
<td>1021</td>
<td>1460</td>
<td>61.18</td>
</tr>
<tr>
<td>X</td>
<td>5</td>
<td>5.61</td>
<td>151</td>
<td>179</td>
<td>-2.796</td>
<td>-890</td>
<td>-739</td>
<td>-918</td>
<td>-660</td>
<td>60.52</td>
</tr>
<tr>
<td>XI</td>
<td>8</td>
<td>11.43</td>
<td>309</td>
<td>366</td>
<td>-5.316</td>
<td>-1690</td>
<td>-1381</td>
<td>-1747</td>
<td>-1400</td>
<td>59.12</td>
</tr>
</tbody>
</table>

* Tissue weight change in grams calculated from the constants of Albright, Reifenstein and Wells, i.e., nitrogen balance (Gm.) times 27.
† Tissue plus ECW (extracellular water) weight change in grams calculated from constants, i.e., nitrogen balance times 32.
‡ Sodium balance in grams divided by sodium per gram of ECW equals total ECW change in grams (no correction was made for the Donnan effect). Serum sodium concentration averaged 3.18 Gm. per L. with only minor fluctuations.
§ Calculated by adding tissue weight change (column 2) and total ECW change (column 5).
|| Calculated by subtracting tissue weight change with accompanying ECW (column 3) from total weight change (column 6).
# ACTH, 200 mg., 10 mg. every 6 hours.
** ACTH, 480 mg., 20 mg. every 6 hours.
†† This value represents weight for the beginning of the period, all the others are for the end of the period designated.
closely with those calculated from the negative sodium balances. This observation is considered important since technical errors in collecting specimens ordinarily result in unexplained deficits in recovery of sodium. However, in view of the variable findings of other authors, it would be fallacious to generalize on the basis of these two patients. No inference can be drawn other than that, in these individuals under the conditions specified, the changes in sodium and extracellular water appeared to be closely and directly related.

**SUMMARY**

In carefully-controlled electrolyte balance studies on two patients with congestive heart failure, retention of water induced by sodium supplementation amounted to over 3 kg. and presented as clinical edema.

In neither instance was the edema preceded by an increase in the brachial venous pressure.

The data thus support the concept that retention of fluid in heart failure does not depend upon an initial elevation in venous pressure.

**SUMMARIO IN INTERLINGUA**

In cautemente controlate studios del balans electrolytico in duo patientes con congestive dysfunctionamento cardiaque, la retention de aqua inducita per un supplementazione de natrium amontava a plus que 3 kg. Illo se presentava sub le forma de edema clinic.

Le edema non esseva precedite per un augmento del pression venose brachial in o le un o le altere del casos.
SODIUM RETENTION AND VENOUS PRESSURES

Le constatationes del studio assi supporta le conception que le retention de fluido in dysfunctionamento cardiac non depende de un elevation initial del pression venose.

REFERENCES


The Relationship of Sodium Retention and Venous Pressures to Edema Formation

RALPH GOLDMAN and SAMUEL H. BASSETT

Circulation. 1955;12:630-634
doi: 10.1161/01.CIR.12.4.630

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1955 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/12/4/630

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/