Body Composition in Experimental Congestive Heart Failure

By Robert J. Adolph, M.D., and Harry A. Bliss, M.D.

Body fluid and electrolyte composition in congestive heart failure has been studied by the metabolic balance technique,1-4 by analysis of skeletal muscle and other tissues5-9 and by the administration of tracer substances10-11 but not by whole body analysis. As part of another study evaluating the effects of digitalis-like compounds on myocardial composition, we thought it appropriate to analyze carcass homogenates of dogs with experimental heart failure for water, fat, nitrogen, and electrolytes.

The physiological aspects of the syndrome produced in this study, and of a similar syndrome produced by progressive pulmonary artery constriction, have been extensively studied by Barger12 and Davis,13, 14 and their associates. The low cardiac output which responds inadequately to exercise, high venous pressure, tachycardia, reduced renal blood flow and glomerular filtration rate, increased aldosterone excretion, salt and water retention, hepatomegaly, ventricular hypertrophy, and evidence of malnutrition seen in these syndromes all resemble the abnormalities of human congestive failure. The technique of Barger and co-workers, used in this study, produces heart failure often lasting many months, whereas the method originated by Davis and associates yields a more rapidly progressive disability, usually terminating in death within a few weeks. Unlike the situation in human congestive failure, subcutaneous edema is rarely seen in these animals.

Rather, fluid retention manifests itself as ascites often of large volume.

Ascitic fluid was discarded before preparing the carcass homogenates in the belief that elimination of this large pool of interstitial fluid would permit a more fruitful comparison of tissue composition in the two groups of animals. Since ascitic fluid resembles a transudate,15 its contribution to total body composition may be approximated, if desired, from a knowledge of its volume and of serum electrolyte concentrations.

Methods

Tricuspid insufficiency and pulmonary artery stenosis were created at separate operations 10 to 14 days apart in four well-nourished female mongrel dogs by the technique of Barger and associates. Animals were fed ad libitum a diet consisting of one part ground horse meat, one part Miller's Puppy Meal, and two parts Purina Kibble Meal, offered once daily six days a week. During the first month of confinement, animals consumed about three-quarters of a pound of this mixture daily, but subsequently appetite diminished somewhat and they ate only about one-half pound a day. As ascites accumulated, appetite was further dulled and less food was eaten. Table 1 details the weights and chronological course of the heart failure syndrome in these animals. Volume of ascitic fluid and ascites-free weight were measured at autopsy. No animal demonstrated subcutaneous edema.

During the 24 hours before death, only water was offered to the animals. Pentobarbital, 25 mg./Kg. estimated ascites-free weight, was injected intravenously. Just before death, blood was taken for serum sodium, potassium, and chloride analyses. Nine minutes before sacrificing the animal by removing the heart, each animal was given acetyl strophanthidin, 0.015 mg./Kg. estimated ascites-free weight, to determine the effect of the drug on myocardial electrolytes. Since nothing was excreted between the time of strophanthidin administration and death, the drug did not alter total body composition.

At autopsy, ascitic fluid was removed and dis...
TABLE 1

Clinical Data for Animals with Congestive Heart Failure

<table>
<thead>
<tr>
<th>Dog</th>
<th>Weight at first operation (Kg.)</th>
<th>Ascites-free weight (Kg.)</th>
<th>Weight of ascites (Kg.)</th>
<th>Time 1* (days)</th>
<th>Time 2† (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.8</td>
<td>18.7</td>
<td>5.2</td>
<td>42</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>15.0</td>
<td>15.7</td>
<td>2.7</td>
<td>88</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>17.0</td>
<td>16.3</td>
<td>7.6</td>
<td>59</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>20.2</td>
<td>16.4</td>
<td>11.6</td>
<td>114</td>
<td>286</td>
</tr>
</tbody>
</table>

*Time 1 represents the time between the second operation and the appearance of ascites.
†Time 2 indicates the duration of life after the onset of ascites.

TABLE 2

Carcass Data

<table>
<thead>
<tr>
<th>Dog sample</th>
<th>Fat</th>
<th>H2O</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>N</th>
<th>K/N</th>
</tr>
</thead>
</table>
| Congestive heart failure
| 1 A       | 381 | 2,970 | 254 | 208 | 145 | 116 | 1.80 |
|           | 304 | 2,590 | 246 | 200 | 146 | 110 | 1.82 |
| 2 A       | 271 | 2,710 | 238 | 184 | 198 | 121 | 1.53 |
|           | 249 | 2,750 | 253 | 222 | 152 | 111 | 1.90 |
| 3 A       | 1,010 | 3,310 | 278 | 211 | 151 | 112 | 1.75 |
|           | 885  | 3,170 | 291 | 214 | 171 | 114 | 1.88 |
| 4 A       | 307  | 2,820 | 300 | 178 | 147 | 113 | 1.57 |
|           | 110  | 2,960 | 316 | 195 | 173 | 116 | 1.68 |
| Mean      | 414  | 2,910 | 272 | 202 | 192 | 115 | 1.74 |
| Control
| 5 A       | 315  | 2,630 | 222 | 189 | 123 | 114 | 1.65 |
|           | 310  | 2,500 | 225 | 208 | 139 | 117 | 1.73 |
| 6 A       | 1,680 | 3,040 | 225 | 237 | 124 | 120 | 1.97 |
|           | 1,930 | 2,610 | 212 | 199 | 134 | 119 | 1.67 |
| 7 A       | 2,480 | 2,580 | 214 | 181 | 107 | 114 | 1.33 |
|           | 2,440 | 2,800 | 210 | 186 | 130 | 122 | 1.52 |
| 8 A       | 244  | 2,770 | 221 | 187 | 117 | 117 | 1.56 |
|           | 344  | 2,640 | 253 | 198 | 132 | 115 | 1.73 |
| Mean      | 1,150 | 2,740 | 216 | 193 | 126 | 117 | 1.65 |

*Values for all constituents are given as Gm. or mEq. per Kg. dry fat-free carcass.
\( K/N \) is given as mEq. per Gm.
†Values are falsely low (see text).

Carded. After weighing, the carcass was placed in a plastic bag which was tightly sealed and frozen at -7 °C.

Four healthy female dogs, full grown but of unknown age, served as controls. None was given acetyl strophanthidin. These animals, noted in table 2 as numbers 5, 6, 7, and 8, weighed 15.0, 20.9, 16.4, and 17.5 Kg., respectively.

Although all carcasses from both groups were homogenized on the same day, those from animals with heart failure had remained frozen in individual plastic bags for 17 months before homogenization. Normal carcasses, on the other hand, were in bags for only 5 days. It was later found that ice placed in similar bags loses weight at a very slow but definite rate (about 0.02 per cent per day), so that the water content of animals with congestive heart failure noted in table 2 is falsely low by an unknown amount.

At the time of homogenization, the carcasses were clipped as free of hair as possible and sawed into small pieces. While still frozen, they were passed through grinders with increasingly fine outlet holes so that finally a thick paste was produced containing all parts of the body except teeth. This paste was vigorously homogenized by manual kneading. Two aliquots, each weighing 4 to 8 Gm., were taken for analysis from widely separated areas in the large container of homogenate from each carcass. The first samples from all dogs

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were analyzed concomitantly. The second samples were also analyzed, together, but at a different time.

Water content was found by heating the samples to constant weight in a 105 to 110°C oven. After repeated extractions with dry ethyl ether, weight, free of neutral fat, was determined. The dry, fat-free tissue was then ground into a powder in a pepper mill, mixed, and stored in glass vials in a desiccator. A 5-ml 0.75 N HNO₃ extract of 300 mg of the powder was made for electrolyte determinations. Sodium and potassium were analyzed with a lithium internal-standard flame photometer. Chloride values were determined by the Van Slyke and Hiller modification of the Sendroy iodometric method. Duplicate 10-mg portions of powder were treated by the micro-Kjeldahl digestion technique, with distillation and titrimetric estimation of nitrogen.

Serum sodium and potassium were analyzed in duplicate with a flame photometer. Chloride was determined in duplicate on Folin-Wu filtrates of serum by the method of Schales and Schales.

Results

Table 2 summarizes the carcass analytical data, which were subjected to an analysis of variance. Because the two samples from each dog were analyzed in separate groups, the experimental design was that of a split-plot. Main plots were represented by treatments, i.e., normal or congestive failure, while the two samples from each individual animal represented subplots. Accordingly, the differences between animals within each treatment constituted the appropriate error term for testing the significance of differences between treatments in the case of each carcass constituent. Table 3 presents a summary of this analysis and of the significance of differences observed.

Animals with congestive heart failure showed significantly more sodium and chloride than controls. Mean values indicated somewhat less fat and slightly less nitrogen in animals with heart failure than in controls, but these differences were not statistically significant. Approximately the same amount of potassium was found in each group of dogs. In animals with heart failure, the increase in both sodium and chloride amounted to 20 to 25 per cent of the control concentration for each electrolyte. The number of milliequivalents accumulated in excess of control was about twice as great for sodium as for chloride.

Serum sodium ranged between 140 and 147 mEq per L in control animals and between 146 and 148 mEq per L in dogs with heart failure. Serum potassium varied from 3.45 to 4.11 mEq per L in controls and from 3.45 to 4.47 mEq per L in animals with heart failure. Serum chloride values were determined only for the group with heart failure where they varied between 112 and 124 mEq per L.

In table 4, data from our control dogs are compared with carcass analyses which have been reported in the literature. Variation among these results is large, and no major differences between our findings and those of other investigators can be distinguished.

Discussion

When ascitic fluid was discarded, it was seen that each of the animals had lost weight during the development of cardiac failure. Although the fat difference between groups was not statistically significant, probably because of the small number of animals and of
the scatter of the data, it seems likely that fat
loss was responsible for a considerable part of
the weight loss in animals with heart failure.
Although nitrogen concentrations were similar
in the two major groups of animals, our
data do not rule out the possibility that loss
of lean tissue may also have occurred.

Since appetite failure and loss of tissue
weight accompany both experimental and
clinical congestive heart failure, the effects
of undernutrition on the body constituents
measured in this study should be noted. Huth
and Elkin ton,28 in acutely fasted rats, found
that reduction of body fat was the major fac-
tor responsible for loss of weight, while pro-
tein loss contributed considerably less. Sodium
and chloride were increased, while both potas-
sium and potassium:nitrogen ratio were de-
creased. Widdowson and McCance,29 in
chronically undernourished rats, made rather
similar observations.

Sodium and chloride retention in the
amounts found in dogs with congestive heart
failure certainly comes as no surprise. Un-
questionably, its magnitude was greatly un-
derestimated since ascitic fluid was not in-
cluded in the analysis. Unreliability of the
water data in these animals precludes exami-
nation of the relationship of water to other
constituents.

These results fail to indicate any significant
differences between normal dogs and those
with heart failure with respect to carcass con-
centrations of potassium and nitrogen. In
this regard, they agree with some observations
in the literature and are at variance with others. Birkenfeld and collaborators9 found
exchangeable potassium in congestive heart
failure not significantly different from that
in a group of hospital "controls" of similar age. Aikawa and Fitz10 reported similar val-
ues for exchangeable potassium, which usu-
ally increased after restoration of cardiac
compensation. During recovery from cardiac
decompensation, some balance studies1,2 have
demonstrated considerable potassium reten-
tion with only slight nitrogen retention,
although two groups2,4 reported no significant
change in potassium.

Investigation of skeletal muscle in patients
with congestive heart failure2,5,6 and in ca-
nine experimental heart failure8 has shown
no significant change in potassium:nitrogen
ratio or in potassium per unit dry fat-free
muscle solids. Most of the available informa-
tion thus corroborates the data presented here
and indicates that although body weight may
decrease in this syndrome, the relationship of
potassium to nitrogen and to dry tissue solids
is not seriously disturbed.

Summary

The bodies of four dogs with experimental
congestive heart failure and of four normal

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*Gm. or mEq./100 Gm. wet fat-free carcass.
Data rearranged assuming 73.4 Gm. water/100 Gm. wet fat-free tissue. Original values
for water were 67.4 (1951 subject) and 70.4 (1953 subject) Gm./100 Gm. wet fat-free

tissue.
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dogs were homogenized. Analyses for water, fat, sodium, potassium, chloride, and nitrogen were carried out after discarding ascitic fluid in the animals with heart failure. Sodium and chloride concentrations were increased in dogs with heart failure. Otherwise the two groups did not differ significantly.

Acknowledgment

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