Liver Function Tests in Chronic Congestive Heart Failure

By Leonard Felder, M.D., Alvin Mund, M.D. and Julius G. Parker, M.D.

It has been difficult for the clinician to evaluate quantitatively and qualitatively the degree of damage to the liver in the presence of congestive heart failure. This paper gives a statistical analysis of the results of various liver function tests on a group of patients with congestive heart failure. The analysis includes comparisons based on etiology, type of rhythm, duration of heart failure, and nutrition.

INTRODUCTION

ONE OF THE most common manifestations of congestive heart failure is enlargement of the liver. This fact has led several investigators to study liver function tests in an attempt to evaluate hepatic dysfunction in congestive heart failure. Historically, the first association of liver pathology and congestive heart failure was noted by Kiernan who described the “nutmeg liver.” Seventy-eight years later Mallory described the typical microscopic appearance of central congestion with focal necrosis. Other authors pointed out the fatty changes and the compression of capillaries by edema fluid accumulated between the liver cell cords and capillaries.

The three main theories of the pathogenesis of the altered liver anatomy are: infection, mechanical compression and hypoxia with secondary nutritional deficiency. The deficiency in oxygen supply to liver cells in heart failure seems to be due not only to the slowing of blood flow through the liver but even more so to arterial unsaturation resulting from pulmonary lesions. This was stressed by Rich and others who pointed out that jaundice of heart failure is especially apt to develop following pulmonary infarction. Ingelfinger's studies of bromsulfalein removal rates by means of hepatic vein catheterization, and the studies of blood flow to other organs in congestive heart failure make it reasonable to assume that there is a decrease in blood flow to the liver in the presence of cardiac decompensation.

There is other evidence for impaired liver function in congestive heart failure. Hepatic fibrosis has been found three times as great in patients with heart failure as in patients without heart failure. More significantly, central fibrosis, so common in decompensated cardiac patients, did not occur at all in patients who were not in heart failure. Hyperbilirubinemia has been found in patients who were in severe chronic heart failure. Jolliffe and Cantarow noted that bromsulfalein was not cleared from the blood at a normal rate in the presence of heart failure. Blood cholesterol levels do not seem to be altered by circulatory embarrassment. In a detailed study of patients, Jolliffe found some alteration in liver function in 15. Most reports in the literature have utilized from one to five specific liver function tests. Studies have been correlated on the basis of etiology of heart disease, on the type of rhythm present or on the presence or absence of heart failure. The consensus is that there is a severe aberration in liver function in association with a failing heart.

It is the purpose of this paper to show the qualitative and quantitative alteration in liver function tests produced by congestive heart failure; to consider briefly the correlation between pathologic changes and functional alterations revealed by the liver tests used; and to discuss the effects of nutrition, per se, on the metabolic functions of the liver.

Clinical Materials and Methods

The material for this study was obtained from the case records and pathologic reports of patients attended at the Montefiore Hospital during the five-year period, 1944–48, inclusive. All hospital records of patients on the medical service during

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this period were reviewed and only those cases pertinent to the present study were selected. This series consists of 135 cases of which 54 came to autopsy. To be included in the data of this report, a case must have satisfied the criteria for congestive heart failure as set forth by the American Heart Association. The patient must have had congestive heart failure uncomplicated by other disease so far as could be ascertained by examination of clinical and pathologic data.

Under the term “other disease” are included diabetes mellitus, hyperthyroidism, rheumatic fever, subacute bacterial endocarditis, any infectious process, liver cirrhosis, or a cirrhotic process of other than cardiac origin. In patients who did not come to autopsy all the clinical and laboratory criteria at our command were utilized in ruling out complicating disease. For the purposes of this report, cardiac cirrhosis was not considered a complication of congestive heart failure.

Although there were no clear-cut criteria employed for evaluating the nutritional status of our patients from the records, an estimate was made on the basis of the subjective impressions of the examiners.

Each of the ten liver function studies was treated statistically in order to permit the recognition of significant differences between specific paired groups; for example, between patients with rheumatic heart disease and those who did not have rheumatic heart disease; between patients with chronic congestive failure of less than three years' duration and those with failure of more than three years' duration; between patients who had auricular fibrillation and those with regular sinus rhythm. The method of statistical analysis used was the standard error of the difference of two proportions.

The total serum protein was determined by the Kjeldahl method; the normal range being 6–8 Gm. per 100 cc. The serum albumin and serum globulin determinations were based on salting-out procedures; the normal ranges being 3.5–5 Gm. per 100 cc. for the former and 1.5–3 Gm. per 100 cc. for the latter. The intravenous 5 mg. per Kg. bromsulfalein test was used; 0–10 per cent retention of dye in the blood after thirty minutes was considered normal. For the cephalin-cholesterol flocculation, the Hanger procedure was employed considering 0–2+ as the normal range. A modified Maclagan's thymol turbidity test was used, considering a normal range to be 0–5 units. For bilirubin, the VandenBergh reaction was performed, a range of 0–1 mg. per 100 cc. being considered normal. The Bodansky's method for alkaline phosphatase was used; 0–4 Bodansky units was accepted as the normal range. For the cholesterol and cholesterol ester determinations, a modified Bloor method was used and the normal ranges applied were 150–270 mg. per 100 cc. for the former and 60 per cent or more of the total for the latter.

**Control Studies.** The ten liver function tests used in this study were performed on a control group of 20 presumably normal adults consisting of 10 male and 10 female subjects. The mean values and ranges for each test are given in Table 1. The control figures are generally in agreement with those in the literature. However, certain tests show a variable percentage of abnormal values.

**RESULTS AND DISCUSSION**

**Thymol Turbidity**

We have tested a total of 84 patients on whom 162 determinations were run. In 31 per cent the findings were abnormal (Table 2). This

**Table 1.—Results of Liver Function Tests in 20 Normal Hospital Employees**

<table>
<thead>
<tr>
<th>Tests</th>
<th>No. determinations</th>
<th>% Abnormal</th>
<th>Average</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein, Gm. Cc</td>
<td>20</td>
<td>0</td>
<td>6.8</td>
<td>6.5-7.3</td>
</tr>
<tr>
<td>Albumin, Gm. Cc</td>
<td>20</td>
<td>0</td>
<td>5</td>
<td>4.4-5.3</td>
</tr>
<tr>
<td>Globulin, Gm. Cc</td>
<td>20</td>
<td>0</td>
<td>1.9</td>
<td>1.6-2.4</td>
</tr>
<tr>
<td>Cholesterol, mg. Cc</td>
<td>20</td>
<td>15</td>
<td>183</td>
<td>124-243</td>
</tr>
<tr>
<td>Cholesterol esters, Cc</td>
<td>20</td>
<td>5</td>
<td>72</td>
<td>59-80</td>
</tr>
<tr>
<td>Cephalin flocculation, 0-4+</td>
<td>20</td>
<td>10</td>
<td>1</td>
<td>0-3+</td>
</tr>
<tr>
<td>Thymol turbidity, units</td>
<td>20</td>
<td>0</td>
<td>2</td>
<td>1-3</td>
</tr>
<tr>
<td>Alkaline phosphatase, B.U.</td>
<td>20</td>
<td>0</td>
<td>1.9</td>
<td>1.2-3.3</td>
</tr>
<tr>
<td>Bilirubin, mg. Cc</td>
<td>20</td>
<td>15</td>
<td>0.56</td>
<td>0.13-1.2</td>
</tr>
<tr>
<td>Bromsulfalein, Cc</td>
<td>20</td>
<td>45</td>
<td>11.5</td>
<td>3-26</td>
</tr>
</tbody>
</table>

is a significant figure and is similar to the ones described in the literature. The average value was 4.8 units with a range of 1–15 units. We could find no significant differences in any of the subgroups.

Carter and Maclagan observed that 10 of 28 patients with heart disease had positive thymol turbidity tests. Stollerman noted that 50 per cent of 56 patients with heart disease of all types, with or without failure, gave positive tests. There was only a 36 per cent incidence in those with congestive heart failure, and 6 of 11 patients with acute rheumatic fever showed positive tests. In Stollerman's series most of
those giving positive tests were very weak. The average was 6.7 units.

Ernst and Dotti\textsuperscript{24} tested 44 cardiac patients in failure. In 12 patients or 27 per cent the results were abnormal. Of these 44 patients, only 14 had rheumatic heart disease and the incidence of elevated thymol tests in these was three. They also tested 25 patients who were
duration or rhythm was considered. Using 2+ as the upper limit of normal, we found no difference between malnourished and well-nourished patients (table 3).

Kissane, Fidler and Clark\textsuperscript{31} reported that 84 per cent of patients with rheumatic fever and congestive heart failure had abnormal cephalin-cholesterol flocculation tests. They used 1+ as

<table>
<thead>
<tr>
<th>Test</th>
<th>Rheumatic</th>
<th>Non-rheumatic</th>
<th>Under 3 years failure</th>
<th>Over 3 years failure</th>
<th>Regular sinus rhythm</th>
<th>Auricular fibrillation</th>
<th>Totals</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>D.*</td>
<td>A.†</td>
<td>D. A.</td>
<td>D. A.</td>
<td>D. A.</td>
<td>D. A.</td>
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<tr>
<td>Thymol turbidity</td>
<td>99</td>
<td>28</td>
<td>63 35 67 23</td>
<td>95 29 57 31</td>
<td>105 31</td>
<td>162 31</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Cephalin flocculation</td>
<td>134</td>
<td>26</td>
<td>94 16 90 23</td>
<td>138 21 87 18</td>
<td>141 24</td>
<td>228 22</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>50</td>
<td>52</td>
<td>28 34 28 32</td>
<td>50 54 33 33</td>
<td>45 56</td>
<td>78 46</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Serum bilirubin</td>
<td>85</td>
<td>53</td>
<td>41 50 48 48</td>
<td>78 54 50 50</td>
<td>76 54</td>
<td>126 52</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Bromsulfalein</td>
<td>19</td>
<td>84</td>
<td>14 86 12 75</td>
<td>21 90 10 80</td>
<td>23 87</td>
<td>33 85</td>
<td>20</td>
<td>45</td>
</tr>
<tr>
<td>Plasma cholesterol</td>
<td>73</td>
<td>55</td>
<td>58 28 48 35</td>
<td>83 47 52 35</td>
<td>79 48</td>
<td>131 43</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Plasma cholesterol esters</td>
<td>39</td>
<td>26</td>
<td>22 27 18 33</td>
<td>43 32 22 27</td>
<td>39 36</td>
<td>61 33</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Total plasma protein</td>
<td>83</td>
<td>36</td>
<td>66 20 59 23</td>
<td>90 33 61 21</td>
<td>88 34</td>
<td>149 29</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Plasma albumin</td>
<td>83</td>
<td>28</td>
<td>66 23 59 32</td>
<td>90 21 61 16</td>
<td>88 32</td>
<td>149 26</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Plasma globulina</td>
<td>83</td>
<td>16</td>
<td>66 21 59 20</td>
<td>90 17 61 15</td>
<td>88 20</td>
<td>149 18</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

* No. of determinations.
† Per cent abnormal.

<table>
<thead>
<tr>
<th>Test</th>
<th>Control</th>
<th>Cardiac Failure Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well Nourished</td>
<td>Mal- nourished</td>
</tr>
<tr>
<td>Total protein, Gm.%</td>
<td>6.8</td>
<td>6.6</td>
</tr>
<tr>
<td>Albumin, Gm.%</td>
<td>5</td>
<td>4.08</td>
</tr>
<tr>
<td>Globulin, Gm.%</td>
<td>1.9</td>
<td>2.52</td>
</tr>
<tr>
<td>Cholesterol, mg.%</td>
<td>183</td>
<td>190</td>
</tr>
<tr>
<td>Cholesterol esters, % esterification</td>
<td>72</td>
<td>66</td>
</tr>
<tr>
<td>Cephalin flocculation, 0-+</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Thymol turbidity, units</td>
<td>2</td>
<td>4.6</td>
</tr>
<tr>
<td>Alkaline phosphatase, B. U.</td>
<td>1.9</td>
<td>5</td>
</tr>
<tr>
<td>Bilirubin, mg.%</td>
<td>0.56</td>
<td>1.6</td>
</tr>
<tr>
<td>Bromsulfalein, % retention</td>
<td>11.5</td>
<td>45</td>
</tr>
</tbody>
</table>

not in failure and found 36 per cent of their tests abnormal.

Cephalin-Cholesterol Flocculation

Our series of 228 determinations performed on 132 patients showed 22 per cent abnormal tests, using 2+ as the upper limit of normal. There was no significant difference in the percentage of abnormal readings when etiology, abnormal. Most observers, however, prefer to disregard any flocculation under 3+.\textsuperscript{11, 74} Were we to consider 1+ as abnormal, we would have 40 per cent positive tests instead of 22 per cent. There was a significant difference in all classifications on this basis. The rheumatic patients in failure for over three years, with auricular fibrillation, were much more prone to have positive tests. Using 1+ as the upper limit of normal,
the poorly nourished were also much more likely to have abnormal flocculation.

**Alkaline Phosphatase**

Sixty-three patients had 78 alkaline phosphatase determinations. Forty-six per cent of these tests showed elevated values. The mean value was 5.8 Bodansky units and the range was between 1.8 and 14.4 Bodansky units. Only 7 determinations were above 10 Bodansky units. According to our material the alkaline phosphatase is one of the more sensitive mechanisms to be impaired by congestive heart failure although the degree of elevation is not remarkably great. There is a significant difference when the groups are broken down into those with auricular fibrillation and those with regular sinus rhythm, although duration of heart failure or etiology does not seem to play any significant role (table 2).

Every attempt was made to rule out bone diseases and extrahepatic biliary tract obstruction. Renal insufficiency with secondary parathyroid hyperfunction, however, may contribute to some of the elevations noted.

Only a few reports dealing with the serum phosphatase values in cardiac failure have appeared in the literature. Gutman, and co-workers reported that in 10 patients with chronic passive congestion of the liver, proved at autopsy, 7 had values between 6.7 and 8.6 Bodansky units. None had values over 10 Bodansky units. The alkaline phosphatase values in 3 patients with cardiac cirrhosis varied between 4.4 and 10.9 Bodansky units. In portal cirrhosis the alkaline phosphatase values vary over a much wider range. Gutman and Hanger found phosphatase values below 10 Bodansky units in all of 9 patients with chronic passive congestion of the liver.

**Bilirubin**

In our series, 52 per cent of 126 determinations on 76 patients showed abnormally elevated serum bilirubin values (table 2). Etiology, duration of failure and type of cardiac rhythm bore no relation to the incidence of jaundice. Next to the bromsulfalein test, the bilirubin determination was the most sensitive of the liver function tests performed. The range was 0.1–13 mg. per 100 cc. with an average of 1.9 mg. per 100 cc. A point of importance is the fact that in 54 autopsied cases, 18 had hyperbilirubinemia. Of these 18, 12 showed pulmonary infarction while 6 were jaundiced in the absence of pulmonary infarction.

The occurrence of jaundice in chronic congestive heart failure is not rare. Both the lungs and the liver are implicated in this complication. In 1910 Oertel named this condition "multiple non-inflammatory necrosis of the liver with jaundice in chronic cyanosis" and ascribed to the liver the chief role in the production of the jaundice. Fishberg emphasized the serious prognostic import of jaundice in heart failure and attributed it to increased red cell destruction. Jolliffe reported a 5 per cent incidence of visible jaundice in 231 cases, there being no apparent relation to the severity of heart failure. Keeler and Resnik found jaundice most commonly in rheumatic patients with auricular fibrillation and long-standing failure. Nine out of their 10 jaundiced patients had pulmonary infarcts. Robertson, Swahm and Konzelmann and White considered serum bilirubin of little importance in the study of cardiac patients.

Kugel and Lichtman carefully studied 424 autopsied cases of primary heart disease. One hundred fifty-one showed pulmonary infarcts. Frank jaundice was present in only 4 per cent of the entire series and 10.5 per cent of those with pulmonary infarction. Only one of the 273 cases without pulmonary infarct had jaundice, but serum bilirubin values were not determined. They stressed the rarity of jaundice in the absence of pulmonary infarction and the importance of the duration of failure and the degree of pulmonary congestion in the development of frank jaundice.

Boland and Willius noted icterus in 14.6 per cent of 75 patients and emphasized the fact that repeated bouts of cardiac failure contributed to the incidence of jaundice. Halsted and Bauer, Meakins, Chavez, Sepulveda and Ortega all report elevated bilirubin values in from 37 to 84 per cent of their patients and again correlate degree and duration of failure with the incidence of jaundice.

Ottenberg summarized what we believe to
be the most rational sequence of events: (1) hypoxic depression of excretory function of the liver; (2) increased production of bilirubin in all infarcted areas; (3) actual central atrophy or necrosis of liver cells; and (4) slowing of the circulation with decreased clearance of blood bilirubin.

**Bromsulfalein**

This test was performed on the smallest number of patients but gave the highest percentage of abnormal determinations. Thirty patients were tested 33 times and in 85 per cent the findings were abnormal. Using 5 mg. per Kg. of body weight, injected intravenously, we considered a retention of over 10 per cent of dye in the blood after one-half hour as abnormal. Since all of our patients had severe heart failure, no conclusions could be drawn as to a parallelism between bromsulfalein retention and severity of heart failure; nor were any significant relationships noted between retention and the duration of failure or the cardiac rhythm (table 2). The range was 5 per cent to 100 per cent retention.

Our results are in general agreement with previous investigations of the bromsulfalein test in congestive failure. Thus, Jolliffe, using a 2 mg. per Kg. test, found that 75 per cent of his experimental group of patients with heart failure had bromsulfalein retention of 5–20 per cent. With compensation, 66 per cent of them showed normal bromsulfalein removal. He assumed a relationship between changes in liver function, degree of edema, and liver size in congestive failure. Similarly, Bernstein, LeWinn and Simkins, using the 5 mg. per Kg. test in a group of 59 cardiac patients with varying grades of failure, found normal bromsulfalein removal in the absence of failure, and increasing bromsulfalein retention with increasing impairment of the circulation. Chavez, Sepulveda and Ortega similarly analyzed 35 cases of congestive failure and arrived at the same conclusions, although the significance of the differences between their four grades of decompensation is questionable, especially since 50 per cent of the control patients showed abnormal bromsulfalein retention. Blumberg and Schloss studied the bromsulfalein retention (5 mg. per Kg.) in 6 patients who had intrinsic liver disease and cardiac decompensation. They found a rise in bromsulfalein retention as the circulation was impaired, while return of compensation restored bromsulfalein values to pre-decompensation or normal levels. Ingelfinger catheterized the hepatic vein in human subjects and studied the bromsulfalein "removal rate." He found it to be 10–15 per cent per minute in normal subjects and 6–7 per cent per minute in decompensated patients. Additional data regarding bromsulfalein retention or removal in congestive failure were provided by Cantarow, Meakins, and Robertson. Swahn and Konzelmann.

**Cholesterol and Cholesterol Esters**

The results of this study (table 2) are based on a total of 131 serum cholesterol determinations of which 56 were normal. Of the latter, 52 were below 150 mg. per 100 cc. and only 4 were above 270 mg. per 100 cc. There is a significant difference only between the rheumatic and nonrheumatic groups, the former having 55 per cent abnormal values and the latter 28 per cent. Each classification or group shows an appreciable percentage of abnormal values.

The cholesterol ester determination was performed 61 times. There was a 33 per cent incidence of low values. This is fairly constant for each of the groups tested. Eighty per cent of the abnormally low esters were associated with low total cholesterol.

Plasma cholesterol has been thoroughly studied, as indicated by the extensive review of Weinhouse in 1943. In spite of a tremendous volume of work, there is practically no direct reference to changes in blood cholesterol and its ester fraction in congestive heart failure. However, Weinhouse, quoting Bodansky and Bodansky and Port, states that in cardiac patients with edema there is no increase in blood cholesterol.

In contrast to the paucity of data in congestive failure, there is abundant material dealing with blood cholesterol changes in various types of heart disease. Poindexter and Bruger observed that cholesterol values were low in patients with rheumatic heart disease...
and elevated in patients with hypertensive and arteriosclerotic disease. They found no difference in the ratio of ester-free cholesterol in the three types of heart disease. On the other hand, Elliot and Nuzum found no hypercholesteremia in uncomplicated arterial hypertension, vascular degeneration or renal impairment complicating hypertension. This latter point of view was substantiated and extended to include all the lipid fractions by the work of Page, Kirk and Van Slyke who studied a group of 16 patients with uncomplicated essential hypertension. By contrast, the reports of Gorham and Myers and Davis, Stern and Lesnick support the findings of Poindexter and Bruger showing a hypercholesteremia in arteriosclerotic cardiac patients. There is considerable overlap between the figures for arteriosclerotic patients and normal subjects. If cholesterol metabolism is disturbed in congestive failure, the etiology of the heart disease must be considered in some relation to this disturbance, as emphasized in two recent reviews.

Our own results substantiate the reports by Poindexter and Bruger of significant differences of the blood cholesterol level in patients with rheumatic heart disease and those with nonrheumatic heart disease. Since rheumatic heart disease is acquired earlier and cardiac decompensation usually occurs at a much younger age than hypertensive or arteriosclerotic heart disease, the question arises as to whether age is a factor in changing the blood cholesterol. However, Page and his associates in a very careful statistical analysis showed that variations of age, from 20–90 years, were not found to have a determinable influence on either the amount or the composition of plasma lipids.

It must also be emphasized that patients with rheumatic heart disease are in congestive failure for longer periods and suffer greater degrees of malnutrition than patients with hypertensive or arteriosclerotic heart disease. Man and Gildea in a study of the serum lipids in malnutrition found that the cholesterol varied with the state of nutrition, increasing with improvement in nutrition.

Finally, the factor of active infection must be considered in patients with rheumatic fever. Thus, King and Bruger report subnormal serum cholesterol values in tuberculosis. Stoesser observed a low ester fraction in children suffering from pneumonia and acute upper respiratory infections. Kipp reported the same for pneumonia in the adult. Knudson, Ordway and Ferguson found marked depression of the cholesterol ester fraction in patients with a positive Wassermann, despite no change in the total cholesterol level.

**Total Plasma Proteins, Albumin and Globulin**

We had 149 total protein determinations performed on 104 patients. Of these tests, 29 per cent were abnormal, i.e., below 6.0 Gm. per 100 cc., but excluding values above 8.0 Gm. per 100 cc., in which the elevation was due solely to hyperglobulinemia and of which 6 are included in the abnormal globulin series.

As indicated (table 2), 36 per cent of the tests in the rheumatic group and 20 per cent in the nonrheumatic group were abnormal. This difference is statistically significant. On the other hand, there is no significant difference between groups analyzed with respect to duration of failure and the type of cardiac rhythm.

As for albumin determinations (table 2), 26 per cent of the determinations were abnormal, i.e., below 3.5 Gm. per 100 cc. Patients with auricular fibrillation showed 32 per cent abnormal determinations, while those with regular sinus rhythm were significantly different, having only 16 per cent abnormal determinations. There was no significant difference when etiology or duration of failure was considered.

Of 149 globulin determinations (table 2), 18 per cent were abnormal, i.e., above 3.1 Gm. per 100 cc. However, four values of 0.8, 0.7, 1.2 and 1.3 Gm. per 100 cc. were not included among the abnormal values. No significant differences were noted when groups were compared on the basis of etiology of heart disease, duration of failure, or type of cardiac rhythm.

The average plasma protein values were as follows: total proteins 6.50 Gm. per 100 cc., with a range of 4.0–8.9 Gm.; albumin 3.93 Gm. per 100 cc., with a range of 2.4–5.5 Gm.; and globulin 2.65 Gm. per 100 cc., with a range of 0.7–4.6 Gm.

A direct correlation was generally noted be-
between downward aberrations of total protein and of albumin values. Conversely, a high total protein figure was invariably a reflection of hyperglobulinemia. There is rather universal agreement on these correlations among previous investigators. Ellis,24 Hand,38 Herrmann,41 Thomson,95 Moore and Van Slyke,79 Rowe,68 Payne and Peters,78 and Biorck and associates3 found low total plasma protein and plasma albumin values in patients with congestive heart failure. Stewart,82 however, found a normal specific gravity of the plasma in cardiac patients but made no chemical analyses. Thomson42 found in patients with cardiac decompensation an average total protein of 5.28 Gm. per 100 cc.; albumin, 2.69 Gm. per 100 cc.; and globulin, 2.59 Gm. per 100 cc. Similarly, Payne and Peters83 found that 13 of 24 patients in congestive heart failure had total protein values below 6.2 Gm. per 100 cc. Herrmann41 found that 100 patients in failure averaged 6.10 Gm. per 100 cc. for total protein with albumin of 3.54 Gm. per 100 cc. (subnormal by his standards) and globulin of 2.58 Gm. per 100 cc.

The factors playing a part in the development of abnormal protein values in chronic congestive heart failure are somewhat difficult to evaluate without adequate metabolic studies in view of the dynamic equilibrium of proteins in the body fluids.96 Herrmann41 noted the lowest plasma protein levels in patients who had had congestive failure for many months, especially in those with clinical evidence of cardiac cirrhosis. Thomson65 believed that the low protein and particularly the low albumin values were due to malnutrition. Only a broad general correlation can be drawn from our data between the duration of the congestive heart failure, the impaired state of nutrition, and the depression of total protein and albumin values. Since our patients are a selected socio-economic group with chronic congestive failure, rather than acute or recurrently acute failure with long periods of remission, it is virtually impossible to decide which of the following factors play the most important roles: (1) cardiac failure, per se; (2) inadequate protein and caloric intake; (3) interference with protein formation. The poor appetite of patients in chronic congestive failure is well known.44 There is little doubt that they suffer from insufficient protein intake. This is the only factor of which we can be certain.

Nutrition

The method employed in this survey was to record the observation of the admitting physician as to whether the patient was well nourished or poorly nourished. We were well aware of the fallacies in such measures but were not prepared to use more objective tests for nutrition. The results of various liver tests in different states of nutrition are shown in table 3.

It is significant that 54 per cent of our patients were considered to be poorly nourished. The longer the duration of heart failure, the greater the number of malnourished patients. Rheumatic patients and those with arrhythmias were more emaciated than those with other types of heart disease and those having normal sinus rhythm, perhaps because rheumatic heart disease patients live longer with cardiac symptoms.

Certain plasma constituents seem to be directly correlated with diet. Among these substances we have measured the cholesterol and protein fractions. Our findings are consistent with those of other studies.21, 41, 44 The average serum cholesterol was 175 mg. per 100 cc. in the entire cardiac group; in those patients who were malnourished, the average was 162 mg. per 100 cc. compared to a level of 190 mg. per 100 cc. for the well nourished.

The average value for total proteins in the entire series was 6.59 Gm. per 100 cc. This is considerably higher than those of other observers.41, 78, 95 The well nourished patients averaged 6.6 Gm. per 100 cc. as compared with a 6.5 Gm. per 100 cc. level for the poorly nourished. Serum albumin averaged 3.93 Gm. per 100 cc. In the well nourished it was slightly above at 4.08 Gm. per 100 cc. and in the malnourished 3.85 Gm. per 100 cc. Globulin levels averaged 2.65 Gm. per 100 cc., but were slightly higher in the malnourished than in the well nourished, 2.68 Gm. per 100 cc. and 2.52 Gm. per 100 cc., respectively.

There is marked individual variation in these tests and no definite conclusions can be drawn.
from the single case. Although there is an apparent correlation between the state of nutrition and the changes in the serum protein level, these changes are not statistically significant.

Cardiac Cirrhosis

The type of liver function impairment noted in a group of patients with proven cardiac cirrhosis is shown in Table 3. It must be emphasized that the data recorded are based on a small series of 14 cases, having a maximum number of 47 determinations for the cephalin flocculation test and a minimum of 6 for the bromsulfalein determinations.

The results show, furthermore, that there are more abnormal determinations with each of the liver function tests in the cardiac cirrhotic patients as compared with the over-all group of cardiacs; the most significant changes occurring in the total proteins and albumin values of which the percentage of abnormal values is doubled in the cirrhotic group compared with the over-all cardiac group.

A comparison of the mean values and ranges in this cirrhotic group with those of the total observed group shows that the trends and actual values are almost the same. The only real differences to be noted are that the alkaline phosphatase reaches the relatively high value of 8 Bodansky units while the cholesterol and cholesterol esters are about 10 per cent lower in cirrhotic patients than in the total group of patients.

Conclusions and Summary

Ten liver function tests were evaluated in a study of 135 cases of chronic protracted congestive heart failure of which 54 came to autopsy. Two or more different tests were performed on each patient; 50 per cent of the patients had seven or more tests performed. Seventy-four per cent of the patients had at least one abnormal determination although only 30 per cent of the tests performed were out of the normal range. The greater the variety of tests made, the higher was the incidence of abnormality.

No significant differences were found when the etiology of the heart disease was considered, nor did the duration of heart failure or type of rhythm alter the liver function tests. The nutritional status of the patients was considered grossly, and, except for showing the expected shifts in average determinations, did not affect the results of the liver function tests significantly.

The thymol turbidity test was abnormal in 31 per cent of the tests. Cephalin flocculation was abnormal in 22 per cent of the determinations and showed a slight increment in the malnourished group of patients.

Alkaline phosphatase was elevated in 46 per cent of the determinations in the group as a whole and in 83 per cent in the cases of cardiac cirrhosis which were autopsied. There was no significant difference noted on the basis of nutrition.

Bilirubin was found to be elevated in 52 per cent of the tests performed. Sixty per cent of the cases with cardiac cirrhosis had abnormal values.

Bromsulfalein clearance was abnormal in 85 per cent of the determinations.

The serum cholesterol values were found abnormal in 43 per cent of all determinations and there was a significant difference between the rheumatic and nonrheumatic groups. The abnormal values were below 150 mg. per 100 cc., four determinations being abnormally high. The well nourished cardiac patients averaged 190 mg. per 100 cc. The poorly nourished patients averaged 162 mg. per cent, and the autopsied cases with cardiac cirrhosis averaged 154 mg. per 100 cc.

The cholesterol ester values were abnormal in 33 per cent of cases, but there were no significant differences between any of the cardiac groups. The values tend to parallel the cholesterol figures.

The total plasma proteins were found to be quantitatively abnormal in 29 per cent of the determinations. The average was 6.53 Gm. per 100 cc. The well nourished patients averaged 6.6 Gm. per 100 cc. as against 6.5 Gm. per 100 cc. for the malnourished and 6.14 Gm. per 100 cc. for those with proven cardiac cirrhosis.

The average albumin was 3.93 Gm. per 100 cc., and 26 per cent of the patients had less than 3 Gm. per 100 cc. The values for the well nourished patients averaged 4.08 Gm. per...
100 cc., for the malnourished 3.85 Gm. per 100 cc. and for the autopsied cirrhotic patients 3.63 Gm. per 100 cc.

Plasma globulin was elevated in 18 per cent of the patients. The average was 2.6 Gm. per 100 cc.

The possible mechanisms involved in the observed liver function abnormalities are discussed. The conclusion is drawn that since the liver is multifunctional a proper evaluation requires a multitude of tests. It is to be hoped that future studies utilizing the clearance technic and other specific methods will localize the exact site of anatomic damage.

On the basis of tests performed, there is apparently no pathognomonic pattern of impairment of liver function in congestive failure and cardiac cirrhosis. There is definite impairment of liver function in congestive heart failure. The exact basis for this change remains unknown.

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