Work Performance of the Isolated Perfused Beating Heart in the Hereditary Myocardiopathy of the Syrian Hamster

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ABSTRACT

The work performance of the isolated beating heart of control Syrian hamsters and hamsters suffering from an inbred myocardiopathy was studied in a system using a myographic differential force transducer. A stretch force of either 3.75 or 8.75 g was applied to the hearts. Myocardial metabolism of pyruvate-3-14C and palmitate-1-14C was studied with and without a stretch force. A definite reduction in work performance of the myopathic heart could be demonstrated. Peak height of contraction, tension-time index, tension time per minute and heart rate were significantly lower. The progressive myocardial fiber lengthening, caused by the stretch force, was less in the myopathic hearts.

No difference was observed between the uptake and oxidation of pyruvate-3-14C and palmitate-1-14C by control and myopathic hearts. The presence of a stretch force affected metabolism of both hearts in a similar manner.

Two mechanisms for explaining the reduction in work performance by the myopathic heart were observed, namely, a reduction in heart rate and a relative inability of the myopathic muscle fibers to lengthen. The depressed mechanical performance could not be related directly with altered substrate metabolism or with reduction in total muscle mass.

ADDITIONAL KEY WORDS myographic differential force transducer stretch force myocardial metabolism heart rate muscle fiber lengthening tension time per minute total muscle mass

We have attempted to determine the mechanisms involved in the congestive cardiac failure which occurs in the Syrian hamster (Mesocricetus auratus), suffering from an inbred muscular dystrophy and myocardiopathy (1).

The condition is characterized by a necrosis and degeneration of cardiac muscle with replacement by fibro-fatty tissue (2, 3). The hamsters develop congestive cardiac failure at the age of 60 to 100 days, and usually die in about 220 days. Cardiac failure in these animals shows up with all the known features of congestion, i.e. pulmonary edema, liver congestion, ascites and generalized edema. The animals respond to therapy with digitalis, diuretics, and salt loading and restriction in the same way as humans with congestive cardiac failure (4). It is therefore possible that investigations on these animals may shed some light on the mechanism of heart failure in human conditions with similar, if not identical, pathology.

Biochemical studies showed that sarcosomal oxidative phosphorylation was significantly reduced in all the hamsters of the myopathic strain, suggesting an inherited inborn error of metabolism.1 Uncoupling of oxidative phosphorylation in these hearts was accompanied

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by a reduction in adenosine triphosphate (ATP) and creatine phosphate contents.

In this study we attempted a quantitative assessment of the myocardial work performance of the isolated perfused beating heart of the myopathic animals. Furthermore, an evaluation was made of the influence on the myocardial work performance of a total reduction in muscle mass, and changes in heart rate and the nature of the work response to preloading the heart with a stretch force. The myocardial usage of palmitate and pyruvate was also studied.

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vate was also observed to determine whether the impaired work performance may be related to a disturbance in the energy supply mechanisms.

Since no technique was available for functional studies on the isolated perfused beating heart of such small animals, we devised a system in which a myographic differential force transducer was employed and adapted to the modified Langendorff (5) assembly for rat heart perfusions.

**Methods**

Myopathic hamsters (*Mesocricetus auratus*) and controls of the London School of Hygiene strain were used for both mechanical and metabolic studies. Animals were fed ad lib until decapitation.

**WORK PERFORMANCE STUDIES**

The isolated hamster heart was kept beating by retrograde perfusion through the aorta at a constant pressure of 60 mm Hg. The hearts were perfused for 30 min with 40 ml of a modified Krebs-Henseleit buffer (6) containing glucose (10 mM) as substrate by means of a modified Langendorff system (5) using a closed recirculatory system. The system was continuously gassed with 95% O₂ and 5% CO₂ through an inlet at the lower end of the perfusion chamber (Fig. 1, 15). Coronary flow was measured as the runoff of perfusion fluid from the right auricle and ventricle (7).

**Modification of Perfusion System**

The perfusion system is shown in Figure 1. The component parts are numbered 1-18 and this description refers to the parts by numbers. Gassing, was done through an inlet (15) at the lower end of the perfusion chamber, while a clamp (9) was firmly fixed at the upper end of the chamber to prevent any movement of the cannula assembly.

The cannula assembly (18) consisted of a round Teflon body through which passed the aortic cannula (11) and an adjustable stainless steel wire (12), the lower tip of which was used to fix the apex of the mounted heart. A slot in the cannula assembly allowed passage of a traction cord (Fig. 1, 7) from the heart base to the lower driving rod of a differential myographic force transducer (Fig. 1, 4 (Sanborn Model FTA 1.1)). Axial traction was transferred to the force transducer by the traction cords and the amount of tension transmitted to the cord could be regulated by moving the force transducer in a vertical direction. A desired load could be applied to the upper driving rod of the force transducer by a cord and weighing pan (Fig. 1, 5). The system was suitably calibrated and recordings made with a Sanborn carrier preamplifier (model no. 150-1100 AS) and a Sanborn single-channel recorder. It was also observed that stress relaxation or creep (8) occurred progressively during the course of the experiment. Measurement of the degree of creep was used as an index of fiber lengthening.

**Perfusion Technique**

The heart was removed from the animal and mounted on the aortic cannula (7) and perfused at a constant aortic pressure of 60 mm Hg. The transfer procedure and adjustment took 2 to 3 min and the hearts were allowed to beat 5 min before recording started. With weights of 10 g and 5 g in the weighing pan, this system allowed satisfactory recordings with a stretch force of 8.75 g and 3.75 g on the heart.

Since the traction cords were fixed to the heart by tiny steel hooks, it was ascertained at the end of each experiment if any displacement of the hooks might have occurred through tearing of the myocardium. No instance of tearing was experienced.

**Measurement of Myocardial Mechanical Performance and Coronary Flow Rate.** A recording was made of the heart's contractions every 5 min and peak height in millimeters of developed tension, developed tension-time index in milligram seconds (the area under the systolic curve of developed tension) and developed tension-time per minute (the product of tension-time index and heart rate) measured. The mean of seven such measurements was used to represent the work performance of the heart over a 30-min perfusion period. Each recording included a short segment of the electrical average position, indicating the average tension of the heart muscle. Although developed tension was either maintained or tended to increase for both normal and myopathic animals after the first 5 min of perfusion, a gradual stress relaxation of the recorded average tension running parallel to a similar change in the initial tension (resting length) was observed. This displacement indicated muscle fiber lengthening and its measurement in millimeters was used as an index of muscle fiber lengthening (FL). We preferred measurement of displacement of the electrical average tension because it could be more accurately defined at all stages of the experiment. Recordings at a paper speed of 25 mm/sec from a normal and a myopathic hamster heart subjected to a stretch force of 8.75 g are illustrated in Figure 2. The electrical average tension, developed systolic tension, and degree of fiber lengthening as indicated by displacement of the electrical average tension and the initial tension are demonstrated. Coronary flow rate was estimated by the rate at which the effluent dropped.
Recordings from a control and myopathic hamster heart subjected to a stretch force of 8.75 g.

from the heart and this was converted to milliliters per minute by a curve in which drops per minute were correlated with milliliters per minute (7).

**METABOLIC STUDIES**

After decapitation, the hearts were rapidly removed and arrested in ice-cold saline, mounted onto a cannula and perfused with 15 ml Krebs-Henseleit bicarbonate buffer (pH 7.4) for 30 min in a closed recirculating system. Chromatographically pure pyruvate-3-¹⁴C (6 mm) and palmitate-1-¹⁴C (0.7 mm) were used as substrates obtained from Radiochemical Centre. Albumin-bound palmitate was prepared, using a particular batch of albumin (Fraction V, Pentex Inc.) that was made available to us through the courtesy of Dr. D. Challoner, Seattle, Washington. A nondialyzed solution, freshly prepared on the day of perfusion, gave consistently good results.

Pyruvate uptake, lactate production, titratable fatty acid uptake, and incorporation of palmitate-¹⁴C into tissue lipids were calculated (9, 10). ¹⁴CO₂ production was measured in both the liquid and gas phases. All radioactivity was assayed in an alcohol-toluene based gel scintillator by a Packard Tri-Carb scintillation spectrometer with appropriate corrections for quenching (11).

To determine the effect of a stretch force on myocardial metabolism, a weight of 8.75 g was attached to the apex of the heart and the metabolism compared with and without this load. For accurate assessment of metabolic change, values were related to the myocardial noncollagen protein nitrogen (NCPN) concentration. The methods for determination of myocardial nitrogen fractions are described elsewhere (12).

All metabolic data were expressed in terms of the noncollagen protein nitrogen content of the heart. Work parameters were expressed in terms of fresh wet weight. Tension-time index was calculated in terms of both wet weight and noncollagen protein nitrogen content. All results are expressed as means ±SEM (number of observations). P values are derived from Student's t-test (Snedecor) (13).

**Results**

**Noncollagen Nitrogen, Nonprotein Nitrogen and Noncollagen Protein Nitrogen Contents of the Hearts**

The noncollagen nitrogen, nonprotein nitrogen, and noncollagen protein nitrogen contents of control and myopathic hearts are summarized in Table 1. In animals aged 90 days the noncollagen protein nitrogen content
TABLE 1

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Type of hamster</th>
<th>No. of animals</th>
<th>Noncollagen nitrogen (mg/g wet wt.)</th>
<th>Nonprotein nitrogen (mg/g wet wt.)</th>
<th>Noncollagen protein nitrogen (mg/g wet wt.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>Control</td>
<td>11</td>
<td>31.26 ± 0.92</td>
<td>2.70 ± 0.08</td>
<td>28.56 ± 0.90</td>
</tr>
<tr>
<td>90</td>
<td>Myopathic</td>
<td>8</td>
<td>24.89 ± 0.20</td>
<td>2.39 ± 0.14</td>
<td>22.50 ± 0.17</td>
</tr>
<tr>
<td>270</td>
<td>Control</td>
<td>6</td>
<td>26.98 ± 1.89</td>
<td>2.94 ± 0.23</td>
<td>24.04 ± 1.71</td>
</tr>
<tr>
<td>270</td>
<td>Myopathic</td>
<td>7</td>
<td>21.13 ± 1.08</td>
<td>2.43 ± 0.16</td>
<td>18.70 ± 1.13</td>
</tr>
</tbody>
</table>

**Coronary flow (ml/min)**

- Control: 115000 ± 3000
- Myopathic: 110000 ± 2000

**Heart rate (beats/min)**

- Control: 250 ± 5
- Myopathic: 250 ± 5

**TTM (tension-time per minute)**

- Control: 31.26 ± 0.92
- Myopathic: 24.89 ± 0.20

**Noncollagen protein nitrogen (mg/sec/min/100mg NCPN)**

- Control: 2.70 ± 0.06
- Myopathic: 2.39 ± 0.14

**Fiber lengthening (mm)**

- Control: 20 ± 1.0
- Myopathic: 18 ± 1.0

**TIME (minutes)**

- Control: 20 ± 1.0
- Myopathic: 18 ± 1.0

**FIGURE 3**

Work performance of control and myopathic hamster hearts loaded with 8.75 g. Abbreviations:

- TTM = tension-time per minute; NCPN = noncollagen protein nitrogen.

of the myopathic hearts averaged 22.50 ± 0.17 mg/g heart tissue, compared to 28.56 ± 0.90 mg/g in the control hearts, a reduction of 21.2% (P < 0.001). A similar reduction in noncollagen protein nitrogen content (22.2%) was obtained in the hearts of the animals aged 270 days, the myopathic myocardial noncollagen protein nitrogen content being 18.70 ± 1.13 mg/g, compared to 24.04 ± 1.71 mg/g in the control hearts (P < 0.025).

**Work Performance of the Hearts**

The mechanical performance was determined in 5 control and 6 myopathic hearts preloaded with a stretch force of 8.75 g, while a second series consisting of 3 control and 3 myopathic hearts was studied with a stretch force of 3.75 g. Animals aged 114 to 149 days were used in this study.

In comparison with the control hearts, the work performance of the myopathic hearts was significantly reduced with both stretch forces. All parameters measured, i.e. peak tension developed, tension-time index, and tension-time per minute, remained depressed in the myopathic hearts throughout the observation period, resulting in a significant re-
duction in mean work performance over the 30-min perfusion period (Figures 3 and 4, Table 2).

A comparison of the work performance of the normal hamster heart loaded with 8.75 and 3.75 g showed no significant difference. The myopathic hamster heart, however, showed a lower level of work performance when subjected to the 3.75 g load.

The reduction in work performance per heart beat as measured by tension-time index was significant when expressed both in terms of wet weight and noncollagen protein nitrogen.

Muscle Fiber Lengthening

With a load of 8.75 g, there was a gradual lengthening of both control and myopathic hearts. Both groups showed a similar degree of lengthening for the first 15 min of perfusion. In the second 15-min period, the amount of lengthening was significantly less in the myopathic heart (Fig. 3). Using a 3.75 g weight to produce stretch, the myopathic hearts showed less lengthening at each period of observation (except at 20 min), and the total cumulative lengthening was significantly less over the 30-min period of perfusion ($P < 0.05$) (Figure 4, Table 2).

Heart Rate and Work Performance

The mean heart rate of all the myopathic animals studied was significantly lower than that of control animals (Table 2). The lowest heart rate observed in the control animals was 120/min, the majority being over 160/min. On the other hand, the heart rate of the majority of myopathic animals did not rise above 120/min (Table 3).

With both loads studied the developed tension as measured by tension-time index was significantly less for the myopathic animals at any particular heart rate chosen for comparison.

Results of the Metabolic Studies

Metabolism of pyruvate-$3^{14}$C was studied in 8 control and 8 myopathic animals (age = 90 days) without a stretch force, and in 7 control and 6 myopathic animals (age = 270 days) with 8.75 g attached to the apex. The results are summarized in Table 4.
Without a stretch force, the uptake of pyruvate was significantly higher in myopathic animals ($P < 0.01$). However, the increase in pyruvate uptake was not significant when these two groups were subjected to a load of 8.75 g. Lactate production was similar in control and myopathic hearts both with and without a stretch force. Similarly, $^{14}$CO$_2$ production was identical in both types of hearts with and without a stretch force. The percentage of pyruvate-3-$^{14}$C oxidized to $^{14}$C O$_2$, as well as the total pyruvate recovery, was lower in control and myopathic hearts when subjected to a stretch load.

Since stretch force studies had been performed on hamsters 270 days of age and compared to the mean age of 90 days in experiments without a stretch force, an attempt was made to determine whether the altered metabolic pattern was due to the difference in age or the presence of a stretch force. Hence, the effect of a 8.75 g stretch force on the myocardial metabolism of pyruvate-3-$^{14}$C was studied in a series of control hamsters aged 90 days. This effect on the metabolic pattern of pyruvate-3-$^{14}$C in these hearts was similar to that obtained previously in different age groups, indicating that it was indeed a result of the stretch force (unpublished observations).

Metabolism of Palmitate-1-$^{14}$C

Palmitate-1-$^{14}$C metabolism was observed in 8 control and 8 myopathic hearts in animals aged 90 days without a stretch force and in 6 control and 6 myopathic hearts in animals aged 270 days with a weight of 8.75 g attached to the apex (Table 5).

Palmitate-1-$^{14}$C uptake, $^{14}$CO$_2$ production, and palmitate-$^{14}$C recovery as tissue lipid tended to be higher in myopathic hearts both with or without a stretch force, but the change was not significant. The presence of a stretch force in control and myopathic hearts had no significant effect on the metabolic pattern of palmitate-1-$^{14}$C, as indicated by the percentage of palmitate oxidized and palmitate recovery.

Since there was a marked age difference...
### TABLE 3

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Stretch force = 8.75 g</th>
<th>Stretch force = 3.75 g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of observations</td>
<td>TTI</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Myopathic</td>
</tr>
<tr>
<td>80</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>110</td>
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<td>1</td>
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<td>120</td>
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<td>10</td>
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<td>140</td>
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<td>1</td>
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<td>160</td>
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<td>6</td>
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<tr>
<td>180</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>2</td>
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<tr>
<td>200</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>220</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>230</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Mean age = 114 to 149 days.

*P < 0.025  
†P < 0.005

### TABLE 4

**Metabolism of Pyruvate-3-\(^1^C, 6 \text{ min}, \) by Control and Myopathic Hamster Hearts**

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Pyruvate uptake(\uparrow)</th>
<th>Lactate output</th>
<th>Pyruvate recovery as (^{14})CO(_2)</th>
<th>Pyruvate uptake oxidized ($)</th>
<th>Total pyruvate recovery ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>154.0 ± 12.7</td>
<td>70.66 ± 8.32</td>
<td>32.10 ± 18.61</td>
<td>2.94 ± 1.53</td>
<td>61.56 ± 12.7</td>
</tr>
<tr>
<td>90</td>
<td>204.78 ± 9.82</td>
<td>75.59 ± 9.52</td>
<td>39.39 ± 18.49</td>
<td>3.79 ± 0.81</td>
<td>57.70 ± 9.49</td>
</tr>
<tr>
<td>270</td>
<td>173.35 ± 11.38</td>
<td>54.91 ± 6.61</td>
<td>18.22 ± 3.79</td>
<td>10.03 ± 1.53</td>
<td>41.28 ± 6.75</td>
</tr>
<tr>
<td>270</td>
<td>197.11 ± 12.40</td>
<td>58.93 ± 8.13</td>
<td>14.33 ± 3.28</td>
<td>7.08 ± 1.28</td>
<td>36.66 ± 4.22</td>
</tr>
</tbody>
</table>

Number in parentheses indicates number of animals studied.

†Results expressed as \(\mu\)mole/100 mg of noncollagen protein nitrogen per 30 min.

### TABLE 5

**Metabolism of Palmitate-1-\(^1^C, 0.7 \text{ min,} \) by Control and Myopathic Hamster Hearts**

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Palmitate uptake(\uparrow)</th>
<th>Palmitate-(^1^C) recovery as tissue lipid</th>
<th>(^{14})CO(_2) production</th>
<th>Palmitate uptake oxidized ($)</th>
<th>Total palmitate recovery ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>13.44 ± 1.29</td>
<td>6.87 ± 0.51</td>
<td>1.71 ± 0.43</td>
<td>12.28 ± 2.35</td>
<td>65.61 ± 4.88</td>
</tr>
<tr>
<td>90</td>
<td>15.44 ± 1.64</td>
<td>8.52 ± 0.59</td>
<td>2.63 ± 0.92</td>
<td>16.15 ± 5.47</td>
<td>73.28 ± 4.11</td>
</tr>
<tr>
<td>270</td>
<td>11.50 ± 0.71</td>
<td>5.74 ± 0.21</td>
<td>1.29 ± 0.33</td>
<td>10.70 ± 2.53</td>
<td>59.8 ± 1.51</td>
</tr>
<tr>
<td>270</td>
<td>13.94 ± 2.06</td>
<td>7.35 ± 0.37</td>
<td>1.44 ± 0.27</td>
<td>10.24 ± 1.51</td>
<td>58.8 ± 5.8</td>
</tr>
</tbody>
</table>

*Number in parentheses indicates number of animals studied.
†Results expressed as \(\mu\)mole/100 mg of noncollagen protein nitrogen per 30 min.
between the two series of myopathic and control hamsters studied with and without a stretch force, the effect of a 8.75 g stretch force on the myocardial metabolism of palmitate-1-14C was subsequently studied in a series of control hamsters aged 90 days. The metabolic pattern was not significantly changed by the presence of a stretch force, establishing that the marked age difference between the two series of hamsters was not a factor in determining the metabolic patterns observed (unpublished observations).

**Discussion**

The results in this study clearly show a reduced work performance in the hearts of myopathic animals. This was evident from measurements of peak height of developed tension as well as the tension-time index and the tension-time per minute (Table 2). Cardiac rate was also significantly reduced in the myopathic hearts and accentuated the reduced work performance when calculated in terms of tension-time per minute. In an effort to explain this reduction in work performance of the myopathic hamster heart, several factors were considered.

1. **Heart Rate.** A definite relationship exists between chronotropism and inotropism (14-17). A variable relationship between developed tension and frequency may occur and an increase in heart rate has been shown either to increase developed tension (Barditch or staircase phenomenon) or decrease it (reversed staircase phenomenon).

Although little is known about the basis for the relationship between heart rate and contractile force, the present observations suggest that there is an association between the reduced work performance and the slower heart rate of the myopathic animals.

The difference in heart rates, however, cannot explain fully the difference in work performance of control and myopathic hearts. Comparison of tension-time index of control and myopathic hearts with similar heart rates, indicated that the difference in work performance was still evident and significant (Table 3). Sufficient observations were available to give a valid comparison at two rates, namely, 180/min and 180/min.

2. **Effective Myocardial Mass.** The reduced work capacity could not be ascribed purely to a disproportionate reduction in the total effective myocardial mass of the myopathic animal. Using the noncollagen protein nitrogen content of the heart as reference base, work performance per heat as measured by tension-time index could be related to the actual muscle mass. The reduction in work performance of the myopathic heart remained as significant as when the comparison was made on wet weight basis.

3. **Muscle Fiber Lengthening.** In this preparation myocardial fiber lengthening occurs as a gradual progressive response with the same load. A slow adjustment in resting tension (stress relaxation) or length (creep) following an applied stretch or load has previously been described in the frog sartorius muscle (18). This change has been assigned to the viscoelastic elements within the muscle and these studies indicated that contraction acts to reset the resting length of the muscle system, as well as evokes the contractile response.

In contrast to the control hearts, work performance in the myopathic hearts was significantly lower with a stretch force of 3.75 g rather than with 8.75 g. In addition, it was observed that the smaller force produced less fiber lengthening in the myopathic hearts than in the control hearts throughout the period of observation (Fig. 4). The cumulative lengthening proved to be significantly less after 30 min (P < 0.05). When stretched with 8.75 g, it was also observed that fiber lengthening in the myopathic heart was of the same extent as in the control heart for a limited period of 15 min, but after this did not progress at the same rate as in the control hearts (Fig. 3).

The distensibility of the myopathic heart appears, therefore, to be less than in the control hearts. These findings suggest that some functional relationship might exist between the fiber lengthening produced by a constant preload and the work performance. It is
suggested that the lower work performance of the myopathic heart could be explained in part because it does not lengthen readily when subjected to a load.

Starling (19) stated that the energy of contraction (i.e., of the ventricular muscle) is a function of muscle fiber length. Although a Starling effect may be involved in this preparation, it is perhaps more likely that the extensive fibrosis of myopathic heart merely splints the myocardium, thus resisting stretch and permitting less work than in the normal animal. An altered physical state in the protein structure of the contractile mechanism may, however, make relaxation difficult, or on the other hand, allow near maximal stretch by the preload from the outset before recordings start. In the latter case little further stretch will be possible except by a heavier weight. It may be added that the myopathic hearts have the appearance of flabbiness rather than stiffness to ordinary observation. In normal frog sartorius muscle showing stress relaxation (creep), it has been suggested that contractions reset cross-linkages between myosin rods and actin filaments (18). This ability could be lacking in the myopathic hamster heart.

(4) Myocardial Metabolism. Comparison of the metabolic patterns of control and myopathic hearts showed that the metabolism of pyruvate-3-14C and palmitate-1-14C tended to be increased in the myopathic hearts with as well as without a load. However, only pyruvate uptake by the myopathic heart without a load and palmitate-1-14C incorporation into tissue lipids with a load were significantly higher (Tables 4 and 5). This observation suggests increased oxidative metabolism by the myopathic muscle. Further studies with regard to oxygen consumption by the myopathic hearts are in progress. Other studies indicated defective oxidative phosphorylation in myopathic sarcosomes and the possibility exists that oxidative metabolism in vivo is elevated to increase ATP production.

The metabolic pattern of pyruvate-3-14C, obtained when the heart was subjected to a stretch force, differed from those when no weight was attached to the hearts (Table 4). The percentage recovery of pyruvate-3-14C as lactate and 14CO2 was depressed in both control and myopathic hamsters, suggesting an altered pathway of pyruvate metabolism in the presence of a stretch force. It is possible that the physical changes occurring in the myocardium when subjected to a stretch force might affect the metabolism. Palmitate metabolism, on the other hand, was unaffected by the presence of a stretch load in both control and myopathic hearts (Table 5). Similar results were obtained when rat hearts were subjected to a stretch load (unpublished observations). Further studies, however, are needed to establish the exact mechanism by which a stretch force changes myocardial pyruvate metabolism.

The above results suggest that the depressed mechanical performance in the myopathic heart is probably not related to altered substrate metabolism. Unchanged substrate metabolism in the myopathic hearts, however, does not exclude the possibility that a biochemical lesion may influence the heart failure. It has been shown that defective oxidative phosphorylation is present in myopathic sarcosomes as well as a reduction in the myocardial high energy phosphate content. This biochemical defect, however, appears to occur at an early age in the myopathic hamsters, even before definite structural abnormalities can be demonstrated in the heart muscle. An impairment of myocardial energy production may in the course of time be responsible for defective protein synthesis, causing an altered physical state giving rise to congestive cardiac failure.

References


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