Substrate depletion in different types of muscle and in liver during prolonged running

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Baldwin, K. M., J. S. Reitman, R. L. Terjung, W. W. Winder, and J. O. Holloszy. Substrate depletion in different types of muscle and in liver during prolonged running. Am. J. Physiol. 225(5):1045-1050. 1973.—Depletion of glycogen and triglyceride stores in red, white, and intermediate types of skeletal muscle and of glycogen in liver was studied in rats subjected to prolonged exercise. Groups of rats were killed after 15, 60, and 120 min of running up an 8° incline at a) 1 mph, b) 1 mph with 1 min at 1.5 mph every 9 min, and c) alternate 30-sec intervals at 0.5 and 1.5 mph. White muscle underwent little or no change in glycogen and triglyceride concentrations in response to the three exercise tests. In red muscle and intermediate muscle, the decrease in glycogen concentration ranged from 42 to 72% after 2 hr; glycogen decreased most sharply during the first 15 min of all three exercise tests and then stabilized or decreased more slowly. Triglyceride concentration in red muscle decreased approximately 40% after 2 hr of all three exercise tests. Little or no change in triglyceride concentration occurred in white and intermediate muscle. Liver glycogen decreased progressively during all three exercise tests and was depleted approximately 85% after 2 hr. These results suggest that in the rat performing prolonged moderate exercise, a) white muscle contracts infrequently and b) liver glycogen can be a more important source of energy than muscle glycogen.

Three types of muscle fibers have been identified in skeletal muscles of rodents. These are the white fibers which have a low respiratory capacity, a high glycolytic capacity, high myosin ATPase activity, and are fast twitch; the red fibers which have a high respiratory capacity, a high glycolytic capacity, high myosin ATPase activity, and are fast twitch; and the intermediate fibers which have a moderately high respiratory capacity, a low glycolytic capacity, low myosin ATPase activity, and are slow twitch (3, 5, 7, 18, 35, 40).

Skeletal muscle adapts to regularly performed endurance exercise, such as prolonged running, with an increase in the levels of activity of hexokinase (5, 27, 32, 36) and of the mitochondrial enzymes involved in the oxidation of carbo hydrate and fat (3, 23, 26, 31). In our studies of this phenomenon we have routinely trained rats by means of a program of treadmill running which results in enzymatic adaptations in all three types of muscle fibers (3, 5). However, the magnitude of the adaptive response varies considerably among the fiber types. For example, the increase in respiratory capacity of red muscle was found to be roughly twice as great as in intermediate and 5 times as great as in white muscle (3); hexokinase activity in red muscle was found to increase approximately 3 times as much as in intermediate and 15 times as much as in white muscle (5).

Since the extent of an adaptive response is usually related to the magnitude of the inducing stimulus, it may be that the smaller increase in enzyme levels in white muscle, relative to red, might reflect a lesser participation in the work performed during the training sessions. Previous studies have shown that glycogen and triglyceride stores in skeletal muscle are depleted during muscular work (1, 4, 6, 10, 11, 17, 21, 37, 41). It seemed possible, therefore, that measurements of the concentrations of these substrates, as indicators of prior contractile activity, might provide some information regarding the degree of involvement, relative to each other, of the three types of muscle fibers in exercise of various intensities.

This approach was used in the present study in which the time course of depletion of substrate stores in the three types of skeletal muscle was determined during an exercise session of the type we routinely employ in our training studies. In addition, responses to two other exercise tests were examined to obtain information regarding the degree of involvement of each of the three types of muscle fibers in exercise of various intensities.

Methods

Animal care and training program. Male rats of a Wistar strain (specific pathogen-free CFN rats) weighing approximately 150 g were obtained from Carworth Farms and were provided with food and water ad libitum. The animals were trained to run on a Quinton 42-15 animal treadmill for 4 weeks. They were exercised 5 days/week with the treadmill set at an 8° incline. The duration and speed of the run were progressively increased until the animals were running for 1 hr/day at 1 mph. After the 4 weeks, the rats were tested, and it was determined that they could all complete the 2-hr-lug exercise tests to which they were subjected. They were then maintained on the training program, with 1 hr/day of running at 1 mph, for another 5–10 days.

Acute exercise tests. The animals were randomly assigned to four groups and killed approximately 24 hr after their last
training session. The six animals in group A, which were used as rested controls, were not exercised for the 24 hr preceding sacrifice.

The 12 animals in group B were exercised at a treadmill speed of 1 mph up an 8° incline; four animals from group B were sacrificed after 15 min of running (23 hr and 15 min after their last training session); four more animals were sacrificed after 60 min of running (24 hr after their last training session); the last four animals were sacrificed after 2 hr of running (25 hr after their last training session).

The 12 rats in group C were exercised at 1 mph up an 8° incline with intervals of running at 1.5 mph, each lasting 1 min, spaced 9 min apart through the exercise session. As in groups B and C, groups of four animals were sacrificed after 15, 60, and 120 min of running.

The animals were not fasted prior to the exercise tests. There were no differences in mean body weight among the four groups. The final average body weight for all the animals was 270 ± 4 g.

Tissue preparation. The animals were anesthetized with 94 mg Na pentobarbital given intraperitoneally immediately after the exercise. Approximately 5 min later the muscles of the right lower extremity were rapidly exposed. The soleus muscle, which is made up of intermediate fibers, was excised and frozen with Wollenberger tongs (43) cooled in liquid nitrogen. Next, the quadriceps muscle group was excised and frozen. The skeletal muscles removed prior to exsanguination were used for measurement of glycogen content, and those removed after exsanguination were used for determination of triglyceride content. The tissues were stored at -70 °C until they were analyzed.

**Assay methods.** Tissue glycogen concentrations were determined with an anthrone reagent as described by Hassid and Abraham (20).

Intramuscular triglycerides were extracted from muscles that had been carefully cleaned free of any adherent adipose tissue and connective tissue with alcohol ether (3:1) according to the method of Entenman (15). Triglycerides were measured by the method of Kaplan and Lee (29).

Blood glucose levels were determined on Nelson-Somogyi filtrates of whole blood by the enzymatic method of Stein (39).

Serum free fatty acids were measured as described by Novak (33).

**RESULTS**

**Red muscle.** As shown in Tables 1–3, the sharpest reduction in muscle glycogen concentration occurred during the first 15 min of running. The greatest loss of glycogen occurred in the red vastus muscle, which consists predominantly of red fibers (3), and of the deepest portion of the vastus lateralis, which consists predominantly of red fibers (3), were excised and frozen with Wollenberger tongs. One lobe of the liver was then frozen. Next, the rats were exsanguinated via the abdominal aorta. Following exsanguination, the heart, the left soleus muscle, and samples of the superficial, white and deep, red regions of the left vastus lateralis muscle were excised and frozen. The skeletal muscles removed prior to exsanguination were used for measurement of glycogen content, and those removed after exsanguination were used for determination of triglyceride content. The tissues were stored at -70 °C until they were analyzed.

TABLE 1. Endogenous substrate depletion in red, white, and intermediate skeletal muscle, heart, and liver in group B after 15, 60, and 120 min of running

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Substrate</th>
<th>Rest (6)</th>
<th>15 min (4)</th>
<th>60 min (4)</th>
<th>120 min (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red vastus</td>
<td>Glycogen*</td>
<td>9.51 ± 0.90</td>
<td>5.61 ± 0.25</td>
<td>5.79 ± 0.18</td>
<td>5.14 ± 0.40</td>
</tr>
<tr>
<td></td>
<td>Triglyceride†</td>
<td>2.43 ± 0.19</td>
<td>1.87 ± 0.25</td>
<td>1.47 ± 0.24</td>
<td>1.38 ± 0.16</td>
</tr>
<tr>
<td>White vastus</td>
<td>Glycogen</td>
<td>8.07 ± 0.26</td>
<td>7.49 ± 0.17</td>
<td>7.08 ± 0.26</td>
<td>7.57 ± 0.42</td>
</tr>
<tr>
<td></td>
<td>Triglyceride</td>
<td>1.37 ± 0.22</td>
<td>1.65 ± 0.20</td>
<td>1.79 ± 0.55</td>
<td>1.69 ± 0.23</td>
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<tr>
<td>Soleus</td>
<td>Glycogen</td>
<td>6.36 ± 0.67</td>
<td>2.80 ± 0.16</td>
<td>3.07 ± 0.13</td>
<td>3.17 ± 0.39</td>
</tr>
<tr>
<td></td>
<td>Triglyceride</td>
<td>1.35 ± 0.11</td>
<td>1.89 ± 0.19</td>
<td>1.33 ± 0.05</td>
<td>1.29 ± 0.12</td>
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<tr>
<td>Heart</td>
<td>Glycogen</td>
<td>4.80 ± 0.39</td>
<td>4.05 ± 0.32</td>
<td>4.46 ± 0.37</td>
<td>4.51 ± 0.27</td>
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<td>Triglyceride</td>
<td>1.72 ± 0.18</td>
<td>1.65 ± 0.14</td>
<td>1.89 ± 0.09</td>
<td>1.95 ± 0.05</td>
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<tr>
<td>Liver</td>
<td>Glycogen</td>
<td>54.37 ± 5.46</td>
<td>37.55 ± 9.46</td>
<td>21.20 ± 4.10</td>
<td>7.13 ± 2.43</td>
</tr>
</tbody>
</table>

Values are means ± se. Number of animals per group is given in parentheses. Animals in group B ran up an 8° incline at 1 mph. *Glycogen concentrations are expressed as mg/g wet wt. †Triglyceride concentrations are expressed as μmoles/g wet wt.

TABLE 2. Endogenous substrate depletion in red, white, and intermediate skeletal muscle, heart, and liver in group C after 15, 60, and 120 min of running

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Substrate</th>
<th>Rest (6)</th>
<th>15 min (4)</th>
<th>60 min (4)</th>
<th>120 min (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red vastus</td>
<td>Glycogen*</td>
<td>9.51 ± 0.90</td>
<td>5.84 ± 0.25</td>
<td>3.17 ± 0.03</td>
<td>3.90 ± 0.44</td>
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<tr>
<td></td>
<td>Triglyceride†</td>
<td>2.43 ± 0.19</td>
<td>1.44 ± 0.18</td>
<td>1.17 ± 0.10</td>
<td>1.38 ± 0.11</td>
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<tr>
<td>White vastus</td>
<td>Glycogen</td>
<td>8.07 ± 0.26</td>
<td>7.47 ± 0.46</td>
<td>7.10 ± 0.39</td>
<td>7.82 ± 0.52</td>
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<td>Triglyceride</td>
<td>1.57 ± 0.22</td>
<td>1.59 ± 0.22</td>
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<td>1.64 ± 0.25</td>
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<tr>
<td>Soleus</td>
<td>Glycogen</td>
<td>6.36 ± 0.67</td>
<td>3.55 ± 0.31</td>
<td>3.17 ± 0.13</td>
<td>3.67 ± 0.28</td>
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<tr>
<td></td>
<td>Triglyceride</td>
<td>1.35 ± 0.11</td>
<td>1.02 ± 0.10</td>
<td>1.23 ± 0.14</td>
<td>1.16 ± 0.06</td>
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<tr>
<td>Heart</td>
<td>Glycogen</td>
<td>4.80 ± 0.39</td>
<td>4.61 ± 0.45</td>
<td>3.90 ± 0.35</td>
<td>5.45 ± 0.37</td>
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<tr>
<td></td>
<td>Triglyceride</td>
<td>1.72 ± 0.18</td>
<td>1.12 ± 0.09</td>
<td>1.09 ± 0.04</td>
<td>1.16 ± 0.09</td>
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<td>Liver</td>
<td>Glycogen</td>
<td>54.75 ± 5.46</td>
<td>35.12 ± 4.68</td>
<td>22.57 ± 12.9</td>
<td>7.60 ± 2.80</td>
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</tbody>
</table>

Values are means ± se. Number of animals per group is given in parentheses. Animals in group C ran up an 8° incline at 1 mph with intervals of running at 1.5 mph, each lasting 1 min, spaced 9 min apart through the exercise session. *Glycogen concentrations are expressed as mg/g wet wt. †Triglyceride concentrations are expressed as μmoles/g wet wt.
TABLE 3. Endogenous substrate depletion in red, white, and intermediate skeletal muscle, heart, and liver in group D after 15, 60, and 120 min of running

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Substrate</th>
<th>Rest (μ)</th>
<th>15 min (μ)</th>
<th>60 min (μ)</th>
<th>120 min (μ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red vastus</td>
<td>Glycogen*</td>
<td>9.51 ± 0.90</td>
<td>6.68 ± 0.28</td>
<td>5.89 ± 0.64</td>
<td>4.12 ± 0.52</td>
</tr>
<tr>
<td></td>
<td>Triglyceride†</td>
<td>2.43 ± 0.19</td>
<td>2.36 ± 0.13</td>
<td>2.10 ± 0.13</td>
<td>1.50 ± 0.25</td>
</tr>
<tr>
<td>White vastus</td>
<td>Glycogen</td>
<td>8.07 ± 0.26</td>
<td>7.88 ± 0.33</td>
<td>7.47 ± 0.30</td>
<td>6.80 ± 0.63</td>
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<td></td>
<td>Triglyceride</td>
<td>1.57 ± 0.22</td>
<td>1.55 ± 0.12</td>
<td>1.76 ± 0.18</td>
<td>1.21 ± 0.02</td>
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<tr>
<td>Soleus</td>
<td>Glycogen</td>
<td>6.36 ± 0.67</td>
<td>3.29 ± 0.20</td>
<td>2.90 ± 0.23</td>
<td>1.76 ± 0.18</td>
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<tr>
<td></td>
<td>Triglyceride</td>
<td>1.35 ± 0.11</td>
<td>1.17 ± 0.09</td>
<td>1.19 ± 0.12</td>
<td>1.21 ± 0.02</td>
</tr>
<tr>
<td>Heart</td>
<td>Glycogen</td>
<td>4.80 ± 0.39</td>
<td>4.24 ± 0.45</td>
<td>4.44 ± 0.35</td>
<td>4.14 ± 0.37</td>
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<tr>
<td></td>
<td>Triglyceride</td>
<td>1.72 ± 0.18</td>
<td>1.60 ± 0.14</td>
<td>1.45 ± 0.04</td>
<td>1.27 ± 0.10</td>
</tr>
<tr>
<td>Liver</td>
<td>Glycogen</td>
<td>54.75 ± 5.46</td>
<td>50.00 ± 4.62</td>
<td>19.85 ± 1.92</td>
<td>5.21 ± 1.65</td>
</tr>
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</table>

Values are means ± se. Number of animals per group is given in parentheses. Animals in group D ran up an 8° incline for alternate 30-sec periods at 0.5 and 1.5 mph. * Glycogen concentrations are expressed as mg/g wet wt. † Triglyceride concentrations are expressed as pmoles/g wet wt.

15 min of all three exercise tests. Thereafter, glycogen levels stabilized or decreased more slowly. The total reduction of glycogen concentration in red muscle after 2 hr was similar for the three exercise tests, ranging from 4.37 mg/g muscle in group B (Table 1) to 5.55 mg/g muscle in group C (Table 2).

The concentration of triglycerides in red muscle after 15 and 60 min of running varied considerably among the three groups; however, after 120 min, the concentration of triglycerides had decreased approximately 40% in response to all three exercise tests (Tables 1–3).

White muscle. In contrast to red muscle, white muscle underwent minimal changes in glycogen concentration in response to the three exercise tests (Tables 1–3). The greatest reduction in glycogen concentration in white muscle occurred in group D (Table 3) and amounted to only 1.27 mg/g or 16%. No decrease in triglyceride concentration occurred in white muscle in response to exercise in any of the three groups.

Soleus (intermediate) muscle. As in red muscle, the sharpest decrease in glycogen concentration in intermediate muscle occurred during the first 15 min of exercise (Tables 1–3). Thereafter, glycogen concentration remained stable (groups B and C) or decreased more slowly (group D). The decrease in glycogen concentration in soleus muscle after 2 hr of running ranged from 2.69 mg/g in group C to 4.60 mg/g in group D. The exercise appeared to have little or no effect on the concentration of the triglycerides in soleus muscle.

Comparison of three types of skeletal muscle. There are considerable differences between the normal, resting levels of glycogen in the three types of skeletal muscle. Therefore, a somewhat different perspective is obtained when the muscle glycogen concentrations after exercise are expressed in relative terms, as a percentage of the resting values (Fig. 1), instead of in absolute terms (Tables 1–3). As shown in Fig. 1, the percentage reductions of glycogen stores in soleus muscle in response to the three exercise tests were similar to or greater than those in red muscle, even though the absolute changes (mg/g) were smaller.

Heart. The exercise tests had little or no effect on the glycogen content of the heart. However, all three groups had a reduction in the concentration of triglycerides in heart muscle, which ranged from 21% (group B) to 32% (group C) after 2 hr of running (Tables 1–3).

Liver. A progressive, marked decrease occurred in liver glycogen concentration. By the end of the 2 hr of running, approximately 85% of the livers' glycogen stores were depleted in all three groups (Tables 1–3).

Blood. Blood glucose levels averaged 125 ± 6 mg/100 ml in the rested, fed animals. After an initial moderate increase, the concentration of blood glucose fell slightly in all three groups, averaging 111 ± 7 mg/100 ml in group B, 106 ± 8 mg/100 ml in group C, and 98 ± 13 mg/100 ml in group D after 2 hr of running.

Plasma FFA levels increased from a resting level of 140 ± 20 μmoles/liter to 340 ± 50 μmoles/liter in group B, 360 ± 50 μmoles/liter in group C, and 380 ± 50 μmoles/liter in group D after 2 hr of running.
DISCUSSION

Studies employing either normal exercise (1, 10, 17, 21, 37, 41) or electrical stimulation of muscles in situ (4, 6, 11) have shown that endogenous muscle glycogen (1, 4, 11, 21, 37, 41) and triglyceride (6, 10, 17, 37) stores can be decreased by contractile activity. Studies comparing the responses of the three different muscle fiber types to repeated electrical stimulation through the nerve have shown that the white motor units lose their glycogen stores and fatigue very quickly compared to both the red and the intermediate fibers (9, 14). The results of these studies on muscle stimulated to contract in situ, which indicate that the same number of contractions produce a far greater depletion of glycogen in white than in red or intermediate fibers, are consistent with available biochemical and anatomical information. Compared to the red and the intermediate fibers, the white fibers have a poor blood supply (16, 30), a low respiratory capacity, and a high glycogenolytic capacity (3, 5, 7, 35, 40).

In the above context, the finding that the three exercise tests used in the present study resulted in minimal glycogen depletion in the white portion of the vastus lateralis over a 2-hr period provides strong evidence that these white fibers contracted infrequently during the exercise. The alternative possibility that the white fibers did contract frequently and obtained their energy from exogenous substrates (i.e., blood glucose and FFA) seems unlikely. In the first place, there is no reason to believe that the metabolic response of the muscle fibers to contractile activity induced by electrical stimulation of the nerve is grossly different from that seen when the stimulus to contract originates in the central nervous system. This is because the subsequent series of events, including membrane depolarization, release of calcium from the sarcotubular reticulum, splitting of ATP, etc., is presumably the same. In the second place, white muscle fibers have lower levels of hexokinase activity (5, 8, 35) and, as mentioned earlier, a poor blood supply and a low capacity to oxidize fat and carbohydrate.

We therefore interpret our results to indicate that when exercise is of an intensity that can be maintained for 2 hr or longer, the work is performed primarily by the red and intermediate fibers with little involvement of the white. On the other hand, if the work load exceeds the capacity of the red and intermediate fibers, the white motor units are also activated by the central nervous system, and if work is continued to the point of exhaustion, white muscle glycogen stores can be essentially completely depleted (41).

The exercise test to which the rats in group C in the present study were subjected was essentially the same as the maximum training stimulus in our studies of the adaptive response of muscle to exercise (23, 31). It seems reasonable to assume that a positive relationship exists between the magnitude of an inducing stimulus, in this case the customary level of physical activity, and the extent of the adaptive response. Thus, the finding that the white portion of the vastus lateralis is minimally involved in the exercise used to train the animals in our studies, as reflected in an essentially unchanged glycogen content after 2 hr of running, helps to explain why the absolute increases in respiratory capacity (3) and in hexokinase activity (5) with training are so much smaller in white than in red muscle.

Edgerton et al. (13) examined the effects of treadmill running on phosphorylase activity in red and white muscle fibers in guinea pigs and also came to the conclusion that the red fibers are activated more frequently than the white during prolonged, moderate intensity work. However, in their study, 21% of the white and only 10% of the red fibers were phosphorylase negative after 10 min of running, giving the impression that glycogen depletion was more rapid in white than in red fibers early during exercise. In contrast, in the present study the most rapid depletion of glycogen in red muscle occurred during the first 15 min of exercise, whereas white muscle glycogen stores were essentially unaffected. This difference could be due to differences in the species and the exercise tests in the two studies. However, another explanation for this apparent discrepancy could be that negative staining for phosphorylase, which is not a quantitative measure of glycogen, may, at best, be a crude indicator of glycogen depletion.

The smaller adaptive increases in hexokinase activity (5) and respiratory capacity (3) in soleus than in red muscle in our studies on the effects of training had also led us to suspect that the intermediate fibers participate to a lesser extent in the work of running than do the red. Consistent with this view is the present finding that the combined decrease in glycogen and triglyceride stores in group C, after 2 hr of the exercise stress used in our training studies, was equivalent to approximately 30 cal/g red muscle, if completely oxidized, compared to 11 cal/g in soleus. However, the slow twitch fibers are thought to rely predominantly on aerobic metabolism and could, perhaps, obtain most of their energy from glucose and FFA extracted from the blood during exercise of moderate intensity. Furthermore, there is evidence that the slow twitch soleus muscle uses less ATP than fast twitch muscle in maintaining tension (19).

In view of these considerations and our lack of information regarding the total energy utilized by the muscle fibers, the interpretation that the red fibers do relatively more work than the intermediate during the exercise session is rather tenuous and must be viewed with caution.

In studies in which muscles were electrically stimulated through the nerve to contract repeatedly in situ, it was found that glycogen stores in intermediate fibers decreased minimally despite prolonged contractile activity (4, 14). This finding, together with the observation that soleus muscle has a low glycogenolytic and a relatively high respiratory capacity, makes it appear reasonable that intermediate fibers derive most of the energy utilized during prolonged work from oxidative metabolism. In this context, the responses of the soleus muscles in the present study are somewhat surprising in two respects. Despite the relatively low intensity of the work, as evidenced by the fact that it could be maintained for 2 hr without development of exhaustion, there was considerable glycogen depletion in soleus muscle in response to all three exercise tests. This ranged from 42% in group C to 72% in group D. Also puzzling is the finding that the exercise had little or no effect on the concentration of triglycerides in soleus muscle; in contrast,
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triglyceride stores decreased about 40% in red muscle after 2 hr in response to the three exercise tests. This finding is in keeping with the results of a previous study on the effects of exhausting exercise in which the decrease in endogenous triglycerides in soleus was small, amounting to only one-third that seen in red muscle (37). We have no explanation for these findings at present. However, the lack of response of muscle triglycerides does suggest that triglyceride lipase activity is perhaps lower in intermediate than in red fibers during exercise. The present results confirm our previous finding that, of the three types of skeletal muscle, only the red fibers appear to utilize a large portion of their intracellular triglyceride stores during exercise (37).

In both the red and the intermediate types of muscle, there was an initial rapid fall in glycogen concentration, followed by a leveling off or a more gradual decline in response to the exercise tests in the present study. This is very similar to the patterns of glycogen depletion found by Chapler and Stainsby (11) in dog gastrocnemius-plantaris muscles stimulated to contract in situ at frequencies between 2 and 10 twitches/min. In studies on humans, in which glycogen depletion in quadriceps muscle during exercise was examined by means of serial muscle biopsies, the concentration of muscle glycogen also dropped most sharply during the first few minutes (21). However, the subsequent decline in muscle glycogen concentration was almost linear, with no evidence of a tendency to level off until the glycogen concentration dropped to very low levels (21). This difference probably relates to the intensity of the work relative to the \( V_{\text{O}_{2\text{max}}} \) and the muscle mass involved in the exercise. For example, at a work rate requiring 80% of \( V_{\text{O}_{2\text{max}}} \) running, which involves a larger muscle mass, appears to result in slower depletion of muscle glycogen stores in men than does bicycling (12). This effect might be even more marked in animals as the work is performed by the musculature of all four extremities. It seems reasonable that some of the rapid early fall in glycogen concentration occurs during the development of the \( O_2 \) deficit, when ATP regeneration via mitochondrial oxidation of substrates is not activated sufficiently to balance ATP breakdown and inhibit glycolysis. It is well documented that during work of moderate intensity progressively less of the needed energy is derived from carbohydrate and more from fat (1, 12, 28, 34). In the present study blood FFA levels were very low at the start of exercise and increased only 2.5-fold; however, the increase in FFA turnover. Am. J. Physiol. 201: 9-15, 1961.


REFERENCES


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