Muscle metabolism in patients with chronic obstructive lung disease and acute respiratory failure

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Summary

1. The concentration of metabolites in intercostal and quadriceps muscle, and pulmonary function, were studied in twelve patients with chronic obstructive lung disease and acute respiratory failure before, during and after standardized treatment at an intensive care unit. The findings were compared with those obtained in hospitalized patients of comparable age with non-pulmonary diseases.

2. On admission, when the patients had marked hypoxaemia, hypercapnia and acidosis, the concentrations of ATP and creatine phosphate were low in both intercostal and quadriceps muscle, particularly the latter. The lactate concentration was increased in relation to control values but glycogen did not differ significantly.

3. In response to therapy, the Pa,co2 and the patient's acidosis decreased, the vital capacity increased and lung mechanics improved along with the clinical condition. At the same time there were significant increases in the concentrations of ATP, creatine phosphate and glycogen in intercostal and quadriceps muscles, to values similar to, and for glycogen in excess of, those found in control subjects. Lactate concentration fell significantly during treatment.

4. In view of the low initial muscle concentrations of ATP and creatine phosphate in the patients, it is suggested that dysfunction of the respiratory muscles may be an important component of respiratory failure. Moreover, the concentration of energy-rich compounds in muscle rose significantly as the patients responded to treatment, which emphasizes the importance of adequate nutritional therapy in this disorder.

Key words: adenosine triphosphate, creatine phosphate, muscle, lung disease, respiratory failure.

Abbreviations: Pa,o2, Pa,co2, partial pressure in arterial blood of oxygen and carbon dioxide; FEV1.o, forced expiratory volume in 1 s; FVC, forced vital capacity.

Introduction

Acute deterioration of respiratory function in patients with chronic obstructive lung disease is usually caused by a bronchial or pulmonary infection. When the infection is adequately treated, most patients gradually recover the respiratory function they had before the infection. However, it is not uncommon for the recovery to be very slow, with persistent dyspnoea and hypoxaemia in the resting state, even though signs of acute infection are no longer present. In such patients there is frequently a nutritional deficiency, in both calories and protein, particularly during acute exacerbations of their disease. This nutritional deficiency might limit the response of the respiratory muscles to the extra demands of acute respiratory failure and slow recovery.

The present study was undertaken to examine...
<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Chronic bronchitis (years)</th>
<th>Acute exacerbation</th>
<th>Arterial blood (on admission)</th>
<th>Duration of treatment (days)</th>
</tr>
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<tr>
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</tr>
<tr>
<td>O.R.</td>
<td>M</td>
<td>46</td>
<td>169</td>
<td>51</td>
<td>18</td>
<td>2-3 weeks</td>
<td>$P_{aO_2}$ 5.2, $P_{aCO_2}$ 8.0, pH 7.30</td>
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<tr>
<td>G.O.</td>
<td>M</td>
<td>65</td>
<td>178</td>
<td>79</td>
<td>10</td>
<td>2-3 weeks</td>
<td>$P_{aO_2}$ 5.5, $P_{aCO_2}$ 7.9, pH 7.30</td>
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<tr>
<td>S.Z.</td>
<td>M</td>
<td>65</td>
<td>174</td>
<td>80</td>
<td>35</td>
<td>2-3 weeks</td>
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<td>G.L.</td>
<td>M</td>
<td>67</td>
<td>168</td>
<td>66</td>
<td>10</td>
<td>2 days</td>
<td>$P_{aO_2}$ 5.7, $P_{aCO_2}$ 8.1, pH 7.30</td>
<td>10</td>
</tr>
<tr>
<td>A.S.</td>
<td>M</td>
<td>67</td>
<td>171</td>
<td>45</td>
<td>10</td>
<td>8 days</td>
<td>$P_{aO_2}$ 4.5, $P_{aCO_2}$ 7.7, pH 7.32</td>
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<tr>
<td>O.S.</td>
<td>M</td>
<td>67</td>
<td>171</td>
<td>50</td>
<td>10</td>
<td>3-4 weeks</td>
<td>$P_{aO_2}$ 4.5, $P_{aCO_2}$ 7.3, pH 7.29</td>
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<td>G.C.</td>
<td>M</td>
<td>68</td>
<td>184</td>
<td>75</td>
<td>20</td>
<td>2 days</td>
<td>$P_{aO_2}$ 5.6, $P_{aCO_2}$ 11.8, pH 7.15</td>
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<tr>
<td>B.H.</td>
<td>M</td>
<td>69</td>
<td>178</td>
<td>49</td>
<td>20</td>
<td>2 days</td>
<td>$P_{aO_2}$ 7.1, $P_{aCO_2}$ 6.5, pH 7.34</td>
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<td>A.N.</td>
<td>M</td>
<td>72</td>
<td>167</td>
<td>70</td>
<td>30</td>
<td>3 weeks</td>
<td>$P_{aO_2}$ 5.9, $P_{aCO_2}$ 9.6, pH 7.24</td>
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<td>E.E.</td>
<td>M</td>
<td>75</td>
<td>170</td>
<td>52</td>
<td>4</td>
<td>3 weeks</td>
<td>$P_{aO_2}$ 5.5, $P_{aCO_2}$ 10.2, pH 7.35</td>
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<td>R.K.</td>
<td>F</td>
<td>65</td>
<td>161</td>
<td>68</td>
<td>15</td>
<td>2 days</td>
<td>$P_{aO_2}$ 3.7, $P_{aCO_2}$ 9.0, pH —</td>
<td>17</td>
</tr>
<tr>
<td>N.K.</td>
<td>F</td>
<td>66</td>
<td>154</td>
<td>47</td>
<td>1</td>
<td>4 weeks</td>
<td>$P_{aO_2}$ 5.2, $P_{aCO_2}$ 8.9, pH 7.33</td>
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the concentrations of energy-rich compounds and carbohydrate metabolites in muscle tissue from patients with chronic obstructive lung disease and acute respiratory failure. Intercostal and quadriceps muscle was studied before, during and after therapy at an intensive care unit.

Material and methods

Patients

Ten male and two female patients with chronic obstructive lung disease (Table 1) were studied at the time of admission to the hospital, after 1 week of treatment and at discharge from hospital 6–8 weeks later. The diagnosis was based on a history of a chronic productive cough either in the morning or persisting throughout the day, rhonchi, prolonged expiration and pulmonary function tests demonstrating airway obstruction and arterial hypoxaemia. All had smoked more than 10 cigarettes a day for more than 10 years, and all had a history of chronic bronchitis ranging from 1 to 35 years. All patients but two (A.N. and E.E.) had experienced increasing effort dyspnoea over the past 6 months to 20 years. Three patients (G.O., O.R. and N.K.) had had pulmonary tuberculosis. One patient (B.H.) had had a myocardial infarction 16 years previously and another (G.C.) had had congestive heart failure for 2 years. One patient (N.K.) was on anticoagulants because of a suspected pulmonary embolus shortly before her admission to the intensive care unit.

All patients had an acute exacerbation of the disease over a period of 2–30 days before admission; in four the acute even lasted no more than 2 days but in the others its duration varied from a week to 30 days. The exacerbation was usually due to a bronchial or pulmonary infection. Respiratory distress and loss of appetite had prevented the patients from either eating or sleeping adequately. On admission all were in respiratory failure according to the criteria of Campbell (1965) (\(P_{a,o_2}\) 8 kPa or less and/or \(P_{a,co_2}\) 6.5 kPa or more; see Table 1). Three patients (G.O., O.S. and N.K.) had polycythaemia and an increased packed cell volume. Seven (G.O., R.K., A.S., G.C., O.R., O.S. and N.K.) had right-heart failure, as evidenced by distended jugular veins, palpable liver and leg oedema.

Control subjects

Twelve patients (four male and eight female) served as control subjects. Their mean age was 62 (range 48–78) years. None of them had a history of lung disease and they smoked less than five cigarettes a day or not at all. All were in hospital at the time of the study, with disorders which included inguinal hernia, gall-bladder disease, varicose veins, rupture of the Achilles tendon and, in four of the patients in whom intercostal muscle biopsy was performed, cancer of the breast. A biopsy specimen was obtained in six patients from the quadriceps muscle and in the other six from the intercostal muscles. Arterial blood gases were measured in the latter group and were normal.

The nature, purpose and possible risks involved in the study were carefully explained to all patients and control subjects before obtaining their consent to participate. The protocol was approved by the Ethical Committee of the Serafimer Hospital. There were no complications.

Procedure

In the patients with lung disease, biopsy specimens were obtained from the intercostal and quadriceps femoris muscles within the first day after admission to intensive care and before the institution of full therapy, though oxygen administration and intermittent assisted ventilation had usually been started and in two patients artificial ventilation had commenced. Arterial blood samples, spirometric recordings and measurements of breathing mechanics were obtained. After 1 week of intensive care the quadriceps muscle biopsy and the lung-function tests were repeated. Finally, after 6–8 weeks of treatment, both an intercostal and a quadriceps femoris muscle biopsy was taken and the lung-function tests were repeated.

The biopsy specimens were taken from control subjects in the morning after an over-night fast, usually immediately before surgery. The procedures for obtaining the specimens were the same as in the patients with lung disease.

Treatment

Treatment consisted of oxygen administration, ventilatory support, physiotherapy and
early mobilization, spasmolytic, mucolytic and diuretic drugs, antibiotics and parenteral nutrition.

Oxygen was administered by means of a nasal catheter delivering 0.25-2 l/min. Steps were taken to maintain $P_aO_2$ at 6.5-9.5 kPa without simultaneous carbon dioxide retention. Assisted ventilation was performed, with a mask and bag, for a few minutes every 15-60 min. Four patients were ventilated mechanically for 10-16 days, the indications being increasing hypoxaemia or hypercapnia, or increasing mental or physical exhaustion despite all other therapeutic measures. Artificial ventilation was undertaken with an Engström ventilator and was adjusted to give a $P_aO_2$ of 10-13 kPa and a $P_aCO_2$ of 4.5-5.5 kPa. The patients were tracheostomized during the first day of respirator treatment, which was continuous for about a week, and the patients were then gradually weaned from the ventilator over a period of 3-8 days. Breathing exercises were given under the guidance of a physiotherapist. In addition to mucolytic agents and antibiotics, aminophyllin (1-1.6 g/day) was given by continuous intravenous administration. Diuretic therapy (frusemide) was given when the patients showed clinical signs of fluid retention.

Parenteral nutrition included the daily administration of 100-200 g of carbohydrate, amino acids corresponding to 50-70 g of protein, 100 g of fat and vitamins, and was continued until the patients could eat normally. In two patients (G.O. and S.Z.) the parenteral nutrition was confined to 200 g of carbohydrate daily.

All patients survived during hospitalization and all were discharged improved, except one (S.Z.) who left the hospital at his own request. Three patients (G.O., S.Z. and A.S.) died 2-10 months later in respiratory failure.

Muscle biopsy

The intercostal muscle biopsy was obtained under local anaesthesia through a 2-3 cm oblique incision in the seventh or eighth intercostal space in the anterior axillary line. The external intercostal membrane was divided and two specimens of the external intercostal muscle were obtained. One was immersed in liquid nitrogen within 2-3 s and kept frozen until analysed. The other was used for histological examination based on Haematoxylin/Eosin and van Gieson stains.

A biopsy specimen from the lateral portion of the quadriceps muscle was obtained with the percutaneous needle biopsy technique described by Bergström (1962). The specimen was immersed in liquid nitrogen within 2-3 s and kept frozen until analysed. Enzymatic analyses of ATP, creatine phosphate, lactate, glucose, glucose 6-phosphate and glycogen in both intercostal and quadriceps muscle tissue were carried out as described by Karlsson (1971).

Lung function

Dynamic spirometry was undertaken with a bellows spirometer (Vitalograph, Moreton House Ltd) during the acute phase, and with a water-sealed Bernstein spirometer (KIFA) during the rehabilitation period. With the subjects seated, a forced vital capacity (FVC) was recorded and the volume expired during the first second (FEV$_{1.0}$) was measured.

The mechanics of breathing were measured with an oesophageal balloon, 10 cm long and 2.5 cm in diameter, fastened to a polyethylene catheter (PE 200). The balloon was introduced into the oesophagus through the nose so that its tip was 40 cm from the nostril. The patient was asked to strain so as to empty the balloon, which was then filled with 0.2 ml of air (Milic-Emili, Mead, Turner & Glauser, 1964). Changes in pressure were measured by means of an inductive pressure transducer (EMT 490 with amplifier EMT 460, Siemens–Elema) feeding a storage oscilloscope (564 B with amplifier 2 a 63, Tektronix).

Ventilation was measured with a dry spirometer (Wedge 570, Med Science) coupled to the oscilloscope, which registered pressure–volume curves, and gas flow was recorded by an ink-jet writer (Mingograph 42, Siemens–Elema). Dynamic lung compliance was determined from the ratio between the volume and pressure recorded by the oscilloscope. However, lung compliance could not be determined during the acute stage because of the patient's breathlessness. The maximum resistance (mean of inspiratory and expiratory resistance) was calculated from the recordings of pressure, volume and gas flow.

Arterial blood samples were taken from the femoral or brachial artery, into 10 ml heparinized syringes. The oxygen tension ($P_aO_2$) was
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Table 2. Measurements of lung function in the patient group

Data from four patients on artificial ventilation are not included in the results 'After 1 week'. \( \Delta P_{es} \) = oesophageal pressure variation during tidal ventilation. Significance of differences from corresponding value recorded before therapy: \*\( P<0.01 \); \**\( P<0.05 \); \***\( P<0.001 \).

<table>
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<th></th>
<th>Before therapy</th>
<th>After 1 week</th>
<th>At discharge</th>
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<tbody>
<tr>
<td><strong>Blood gases</strong></td>
<td></td>
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<tr>
<td>( Pa_o_2 ) (kPa)</td>
<td>5.6±0.3</td>
<td>7.7±0.5*</td>
<td>7.7±0.4***</td>
</tr>
<tr>
<td>( Pa_co_2 ) (kPa)</td>
<td>8.4±0.5</td>
<td>6.7±0.4**</td>
<td>5.9±0.4***</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>7.31±0.02</td>
<td>7.39±0.02**</td>
<td>7.39±0.02**</td>
</tr>
<tr>
<td>Base excess (mmol/l)</td>
<td>1.6±1.0</td>
<td>4.5±2.1</td>
<td>0.6±1.2</td>
</tr>
<tr>
<td><strong>Spirometry</strong></td>
<td></td>
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</tr>
<tr>
<td>VC (l)</td>
<td>1.3±0.2</td>
<td>2.2±0.3**</td>
<td>2.2±0.2*</td>
</tr>
<tr>
<td>FEV(_1.0) (l)</td>
<td>0.5±0.1</td>
<td>0.9±0.1</td>
<td>1.0±0.1</td>
</tr>
<tr>
<td><strong>Lung mechanics</strong></td>
<td></td>
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<tr>
<td>( \Delta P_{es} ) (cm water)</td>
<td>21±1.6</td>
<td>18.3±2.0</td>
<td>13.4±0.7***</td>
</tr>
<tr>
<td>Compliance (ml/cm water)</td>
<td></td>
<td>112±23</td>
<td>147±35**</td>
</tr>
<tr>
<td>Resistance (cm water 1(^{-1}) s(^{-1}))</td>
<td>11.8±0.8</td>
<td>10.4±0.5</td>
<td>7.6±1.0*</td>
</tr>
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</table>

Determined by a Clark electrode and the carbon dioxide tension (\( Pa_co_2 \)) by a Severinghaus electrode (E 5046 and E 5036, Radiometer). Both electrodes were calibrated at a standard temperature with gases saturated with water. A correction was made for body temperature, with a slide rule (Severinghaus, 1966). pH was measured with a glass electrode with a calomel cell as reference (Radiometer), and the base excess was calculated with the same slide rule.

**Statistics**

Standard statistical methods were employed (Snedecor & Cochran, 1967), the paired \( t \)-test being used when applicable. Data in the text, Tables and Figures are presented as mean values ± SEM.

**Results**

**Pulmonary function**

On admission all patients showed signs and symptoms of respiratory distress. They had moderate to marked degrees of hypoxaemia and hypercapnia (Table 1). Most patients also displayed uncompensated respiratory acidosis, with a mean pH of 7.31±0.02. Their vital capacity was severely reduced, as was their FEV\(_1.0\). Lung resistance was considerably increased compared with data for healthy subjects (Frank, Mead & Ferris, 1957) and the oesophageal pressure variations during tidal ventilation were severely augmented (Nisell, 1960).

After 1 week of treatment at the intensive care unit, all patients noted a considerable improvement in subjective symptoms. The hypoxaemia, hypercapnia and the respiratory acidosis were less marked (\( P<0.05 − 0.01 \)) and the vital capacity had increased by 70% (\( P<0.05 \), Table 2).

At 6–8 weeks after admission, when the patients had recovered from the acute exacerbation, \( Pa_co_2 \) was further decreased, to an average of 5.9±0.4 kPa, but the average \( Pa_o_2 \) (7.7±0.4 kPa) did not differ significantly from that measured earlier during therapy. Measurements of lung mechanics showed that lung resistance had fallen 35% (\( P<0.01 \)) compared with the initial values and dynamic compliance was 30% higher than it had been after 1 week of intensive care (\( P<0.05 \)) (Table 2). The oesophageal pressure variations during tidal ventilation had likewise diminished 35% since admission.

**Intramuscular metabolites**

Table 3 shows the concentrations of metabolites in the samples of intercostal and quadriceps muscle in the patients and in the control subjects. The concentration of ATP in intercostal muscle was lower in the patients at the
TABLE 3. Concentrations of metabolites in muscle biopsy samples from the intercostal and quadriceps muscles in the patient group and in healthy control subjects

Results are presented as mean values ± SEM. Significance of difference from corresponding value recorded in patients before therapy: *P<0.05; **P<0.01.

<table>
<thead>
<tr>
<th></th>
<th>Concentration (μmol/g wet wt. of muscle)</th>
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<tr>
<td></td>
<td>ATP</td>
<td>Creatine phosphate</td>
</tr>
<tr>
<td>Intercostal muscle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, before therapy</td>
<td>2.4±0.4</td>
<td>10.6±1.8</td>
</tr>
<tr>
<td>Patients, at discharge</td>
<td>3.4±0.2*</td>
<td>16.2±1.9**</td>
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<tr>
<td>Healthy control subjects</td>
<td>2.9±0.1</td>
<td>11.0±0.5</td>
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<tr>
<td>Quadriceps muscle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, before therapy</td>
<td>3.2±0.3</td>
<td>12.5±0.7</td>
</tr>
<tr>
<td>Patients, after 1 week</td>
<td>3.1±0.2</td>
<td>15.9±1.2*</td>
</tr>
<tr>
<td>Patients, at discharge</td>
<td>4.1±0.3**</td>
<td>17.0±2.0**</td>
</tr>
<tr>
<td>Healthy control subjects</td>
<td>4.0±0.1*</td>
<td>16.7±1.2*</td>
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than the control values (P < 0.05), although the contents of creatine phosphate and glycogen did not differ significantly. The intercostal muscle samples obtained after 6-8 weeks of therapy contained, compared with the pre-treatment values, more ATP (+40%, P < 0.05), creatine phosphate (+50%, P < 0.01) and glycogen (+70%, P < 0.01) but less lactate (-60%, P < 0.05) and glucose (-45%, P < 0.05).

The concentrations of metabolites in quadriceps muscle changed in parallel with those in intercostal muscle (Table 3). On admission the patients had, when compared with control subjects, a reduced quadriceps muscle content of both ATP (-20%, P < 0.05) and creatine phosphate (-25%, P < 0.01) and a two- to three-fold increase in lactate and glucose concentrations (P < 0.05-0.01), although the glyco-
gen concentration was similar in patients and control subjects. As with intercostal muscle, the metabolite concentrations in quadriceps muscle changed with treatment. After 1 week of treat-
ment the only change was in creatine phosphate, which had increased by 25% (P < 0.05). After treatment for 6-8 weeks there was an increase in ATP concentration (+30%, P < 0.01) to a value similar to that in the control subjects, and in glycogen concentration (50%, P < 0.05) to a concentration greater than that in the control subjects (P < 0.05). Lactate and glucose con-
tentions were lower after treatment than at the time of admission (P < 0.05).

Discussion

The present group of patients with chronic obstructive lung disease and acute respiratory failure showed a marked decrease in the muscle concentrations of ATP and creatine phosphate compared with control subjects. The decrease in the content of energy-rich compounds was less for intercostal than for quadriceps muscle (Table 3), but there was a substantial increase of ATP and creatine phosphate in both types of muscle after treatment, which suggests that both muscles were depleted at the time of the initial measurements. The control subjects used in this study were patients of comparable age who had been hospitalized for non-pulmonary disorders. There are no other reference data for intercostal muscle but a comparison of the quadriceps muscle metabolite concentrations in the present patients with lung disease and healthy young subjects (Karlsson, Diamant & Saltin, 1970) or well-trained middle-aged men (Saltin, Wahren & Pernow, 1974) gives differences which are still more marked.

The magnitude of the reduction of the ATP concentration in these patients is illustrated by the fact that the patients' values on admission are lower than those found for quadriceps muscle during maximal physical exertion both in healthy subjects (Saltin et al., 1974) and in patients with occlusive arterial disease of the leg (Pernow, Saltin, Wahren, Cronestrand & Ekeström, 1975). Moreover, the present values are comparable with the ATP concentration in quadriceps muscle in patients in cardiogenic shock or severe congestive heart failure (Karlsson, Willerson, Lestin, Mullins & Mitchell, 1975).

The concentration of ATP in muscle is normally maintained relatively stable even in situations involving a sharply increased intracellular ATP turnover, as for example during physical exercise (Hultman, Bergström & Andersson, 1967). Similarly, the ATP is largely unchanged even during acute tissue hypoxia, induced by arterial occlusion (Harris, Hultman, Kaijser & Nordesjö, 1975).

There are several possible explanations for the reduced concentrations of ATP and creatine in this patient group. Arterial hypoxaemia, which in some patients was as low as 4-5 kPa, in conjunction with a markedly increased work of breathing, may have contributed to low concentrations of ATP. One would also expect both of these factors to accelerate muscle glyco-
genolysis and lactate formation, yet the lactate concentrations were only moderately increased and considerable amounts of glycogen were still available in the muscle tissue. It is not clear why the low ATP did not stimulate anaerobic glycolysis to a greater extent, but the findings suggest that additional factors may contribute to the disturbed regeneration of muscle-cell adenine nucleotides.

The reduced concentrations of ATP and creatine phosphate could be due to a lack of their precursors. Purine and creatine synthesis occurs mainly in the liver and requires energy (Walker & Walker, 1959). In the present hypoxaemic and nutritionally depleted patients,
any disturbance of the purine or creatine metabolism would probably be reflected in a reduced content of total adenine nucleotides or total creatine in muscle. These variables were not measured in the present study, but observations in severely ill patients with primarily circulatory and intestinal disorders have, in fact, shown a decreased content of both total adenine nucleotides and creatine in quadriceps muscle (Bergström, Fürst, Hultman & Vinnars, 1976).

In this context it is noteworthy that the duration of the acute exacerbation before admission appeared to influence the degree of alteration in intramuscular metabolites. Fig. 1 and Fig. 2 present the results for the eight patients with a 1–4 weeks history and the four with less than 3 days duration of the acute phase respectively. It will be seen that the former group, which probably had the most marked nutritional depletion, displayed the lowest ATP values and a marked improvement in response to therapy, whereas the latter, with a short period of acute exacerbation, exhibited only minimal changes in ATP concentrations. Instead, in the patients with less than 3 days history higher initial lactate concentrations were seen, which fell significantly in response to therapy. The findings for this patient group thus resemble the responses of healthy subjects to physical exercise or acute hypoxia (Harris et al., 1975; Saltin et al., 1974).

An alternative possibility is that the low ATP and creatine phosphate concentrations in the patients' muscle were a consequence of structural alterations, for example increased fibrosis of the muscle tissue. However, histological examination of the intercostal biopsy samples revealed consistently normal muscle tissue without an increased incidence of connective tissue components. Moreover, after treatment the ATP and creatine phosphate concentrations were comparable with those found in healthy subjects. The third possibility is that variations in water content of the muscle tissue contributed to the observed changes in concentration of energy-rich compounds. However, the water content in five patients was 74.0–75.5%, which is within the normal range (Karlsson, 1971). It seems unlikely that abnormal composition of the muscle tissue contributed to the altered concentrations of intramuscular metabolites.

The low concentrations of ATP and creatine phosphate, particularly in intercostal muscle, make it unlikely that the patients' respiratory muscles were able to perform adequately, especially in view of the augmented work of breathing. This assessment is supported indirectly by electromyographic findings from

**FIG. 1.** Concentrations of metabolites in quadriceps muscle in eight patients who had had an acute exacerbation lasting 1–4 weeks before their admission to hospital. Pa, Results obtained in patients at the time of admission; Pt, values measured after 6–8 weeks of treatment. C, Control values.

**FIG. 2.** Concentrations of metabolites in quadriceps muscle in four patients who had had acute exacerbation lasting less than 3 days before admission to hospital. Pa, Results obtained in patients at the time of admission; Pt, values measured after 6–8 weeks of treatment. C, Control values.
intercostal muscles in patients of this type (Campbell, 1954). It would thus appear that
dysfunction of the respiratory muscles may be an
important component of acute respiratory failure in these patients.

Treatment caused an improvement in the patients' lung function (Table 2), which was
accompanied by marked changes in the concentra-
tions of intramuscular metabolites. As
discussed above, the ATP and creatine phospho-
cracteristics were comparable with those for the control
subjects, whereas the glycogen content increased to
levels greater than in the control group. A
similar overshoot in muscle glycogen con-
centration is seen when healthy subjects ingest a carbohydrate-rich diet after heavy exercise
(Hultman & Bergström, 1967).

The present findings thus emphasize the
importance of adequate nutritional therapy in
these patients and suggest that the restoration of
energy and substrate stores in muscle is an
important aspect of the treatment of patients with chronic obstructive lung disease and acute respiratory failure.

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