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ANAEROBIC ENERGY PRODUCTION AND O_2 DEFICIT–DEBT RELATIONSHIP DURING EXHAUSTIVE EXERCISE IN HUMANS

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SUMMARY

1. Eight subjects performed one-legged, dynamic, knee-extensor exercise, first at 10 W followed by 10 min rest, then at an intense, exhaustive exercise load (65 W) lasting 3·2 min. After 60 min recovery, exercise was performed for 8–10 min each at 20, 30, 40 and 50 W. Measurements of pulmonary oxygen uptake, heart rate, blood pressure, leg blood flow, and femoral arterial–venous differences of oxygen content and lactate were performed as well as determination of ATP, creatine phosphate (CP) inosine monophosphate (IMP) and lactate concentrations on biopsy material from the quadriceps muscle before and immediately after the intense exercise, and at 3, 10 and 60 min into recovery.

2. Individual linear relations ($r = 0{\cdot}95$–$1{\cdot}00$) between the power outputs for submaximal exercise and oxygen uptakes (leg and pulmonary) were used to estimate the energy demand during intense exercise. Pulmonary and leg oxygen deficits determined as the difference between energy demand and oxygen uptake were 0·46 and 0·48 l (kg active muscle)$^{-1}$, respectively. Limb and pulmonary oxygen debts (oxygen uptake during 60 min of recovery − pre-exercise oxygen uptake) were 0·55 and 1·65 l (kg active muscle)$^{-1}$, respectively.

3. During the intense exercise, muscle [ATP] decreased by 30% and [CP] by 60% from resting concentrations of 6·2 and 22·4 mmol (kg wet wt)$^{-1}$, respectively, and [IMP] increased to 1·1 mmol (kg wet wt)$^{-1}$. Muscle [lactate] increased from 2 to 28·1 mmol (kg wet wt)$^{-1}$, and the concomitant net lactate release was 14·8 mmol (kg wet wt)$^{-1}$ or about 1/3 of the total net lactate production. During recovery 70% of the accumulated lactate was released to the blood, and the nucleotides and CP returned to about 40 and 85% of pre-exercise values at 3 and 10 min of recovery, respectively.

4. Total reduction in ATP and CP (and elevation of IMP) during the intense exercise amounted to 16·4 mmol ATP (kg wet wt)$^{-1}$, which together with the lactate production accounted for 83·1 mmol ATP (kg wet wt)$^{-1}$. In addition 6–8 mmol ATP (kg wet wt)$^{-1}$ are made available related to accumulation of glycolytic intermediates including pyruvate (and alanine). Estimated leg oxygen deficit corresponded to an ATP production of 94·7 mmol ATP kg^{-1}; this value included 3·1 mmol kg^{-1} related to unloading of HbO_2 and MbO_2. Resynthesis of nucleotides and CP could account

for less than 10% of the leg oxygen debt, and lactate elimination including resynthesis of glycogen for another 25%.

5. The anaerobic energy contribution during the first half-minute of intense exercise accounted for 80% of the total energy turnover and this decreased to 30% during the last phase of the exercise. The mean anaerobic energy contribution was 45% for the 3·2 min of exhaustive exercise.

6. The maximal anaerobic capacity of human muscle amounted to the equivalent of close to 0·5 l O_2 kg^{-1}. An extrapolation to whole-body anaerobic capacity cannot be made, as the magnitude of neither [ATP] and [CP] reduction nor lactate release from the muscle is likely to be comparable in all muscles when the human performs whole-body exercise.

7. When exercising with a small muscle group the measurements of (i) oxygen deficit and (ii) energy yield, based on metabolic alterations of the active muscle, give similar values for the anaerobic energy release. The dominant fraction of the elevation in recovery oxygen uptake (i.e. oxygen debt) is not accounted for, as normalization of nucleotides, CP, muscle and blood lactate only amounted to about $\frac{1}{3}$ of the debt measurement. Elevation in hormones such as adrenaline and noradrenaline as well as temperature do not appear to play a role in the high recovery oxygen uptake in the present study.

INTRODUCTION

The aerobic contribution to the energy turnover in dynamic exercise as well as a person's maximal aerobic power can be readily quantified. In contrast the magnitude of the anaerobic energy metabolism is much more difficult to determine and therefore its significance is less well understood. This is not due to a lack of effort, but rather to the fact that the techniques available have limitations. The three routes used to assess anaerobic energy production are to measure (i) oxygen deficit, (ii) debt, or (iii) the lactate produced combined with the depletion of ATP and creatine phosphate (CP) concentrations of muscle (for references see Karlsson, 1971).

In the initial phase of submaximal exercise the oxygen deficit, as defined by Krogh & Lindhard (1920), probably provides an accurate assessment of anaerobic energy release when the unloading of oxygen from haemoglobin (Hb) and myoblobin (Mb) is considered. However, the use of oxygen deficit measurements in intense, exhaustive exercise are questionable as it is uncertain whether mechanical efficiency remains at values observed during submaximal exercise (Saltin, Gagge, Bergh & Stolwijk, 1972; Saltin, 1989).

Through the years measurements of lactate concentrations, made predominantly in the blood, have been used both as indicators of anaerobic energy release and for the quantitative evaluation of the lactate in the anaerobic energy release (Margaria, Edwards & Dill, 1933; for further references see di Prampero, 1981). However, the dilution space for lactate is undefined and the turnover of lactate is high (Brooks, 1985). Improvements in these estimations may be achieved if measurements of lactate are restricted to the muscles that are active in the exercise. Further, if the size of the active muscle's mass is known and the amount of lactate which has escaped the muscles during the exercise can be determined, total net lactate produced and its energy equivalents in ATP equivalents can be estimated.

The present study is an attempt to use this latter approach in the assessment of an anaerobic energy production. The accumulation of lactate as well as changes in ATP and CP concentrations were determined in the active muscle, whose mass could be determined. Further, lactate released from the muscle during and after the exercise was estimated from measurements of limb blood flow and arteriovenous difference for lactate. The oxygen uptake of the active leg and the whole body were also determined to compare the obtained values for the anaerobic energy contribution with the more traditional measurements of oxygen deficit and debt.

METHODS

Subjects

Eight, healthy, male subjects aged 23–29 years, with an average height of 182 cm and an average weight of 73 kg participated in the experiment. Five of the subjects had participated in previous experiments of similar design and measurements. All were habitually physical active, but none trained for competition. The subjects were fully informed of any risks and discomfort associated with these experiments before they gave their informed consent to volunteer, and the study was approved by the local ethical committee.

Measurement

Blood flow. Femoral venous blood flow was measured by the thermodilution technique (Andersen & Saltin, 1985). Briefly, ice-cold saline at 0 °C was infused at a constant rate into the femoral vein to achieve a drop in femoral venous blood temperature of approximately 0·8–1·0 °C. During times of high blood flow (exercise and early recovery) an infusion rate of 115 ml min^{-1} for 10–15 s achieved this change in venous blood temperature and allowed rapid blood flow determinations. At rest and in late recovery, when blood flows are low and more constant, an infusion rate of 45 ml min^{-1} for 30–45 s was used (Richter, Mikines, Galbo & Kiens, 1989). Because of the small magnitude of these data bolus injections (3 ml) of ice-cold saline were also commonly used to confirm the values obtained from constant infusions (Gaffney, Sjøgaard & Saltin, 1989).

Blood pressure was followed with a Statham transducer connected to the femoral artery catheter with the reference point at the heart level. Heart rate was obtained from the pressure curves.

Blood analysis. Oxygen saturation of blood was determined spectrophotometrically (Radiometer OSM-2 Haemoximeter). Haemoglobin concentration was also determined with the Haemoximeter which was calibrated spectrophotometrically by the cyanomethaemoglobin method (Drabkin & Austin, 1935). The P_{O_2} was measured with the Astrup technique (ABL Radiometer). Haemoglobin concentrations at low oxygen saturation were adjusted with a correction factor obtained from multiple measurements of oxygen content of fully oxygenated blood samples by Van Slyke analysis (Holmgren & Pernow, 1959). Blood lactate was determined by a fluorometric assay (Lowry & Passonneau, 1972). Noradrenaline and adrenaline concentrations in arterial blood were determined with an immunoassay technique (Christensen, Vestergaard, Sørensen & Rafaelsen, 1980).

Oxygen uptake. Pulmonary oxygen uptake was determined by collection of expired air in Douglas bags. The volume of air was measured in a Tissot spirometer and the concentrations of O_2 and CO_2 were determined with Servomex and Beckman LB-2 analysers, respectively. The instruments were regularly calibrated with known gas mixtures.

Muscle mass. Surface measurements of the subject's thigh length (L) and circumferences (O_1, O_2 and O_3) were performed together with skinfold (S) measurements of the thigh. Thigh volume (V) was then calculated from the formula:

$$V = L \times (12\pi)^{-1} \times (O_1^2 + O_2^2 + O_3^2) - (S - 0{\cdot}4) \times 2^{-1} \times L \times (O_1 + O_2 + O_3) \times 3^{-1}$$

(cf. Jones & Pearson, 1969). The quadriceps femoris muscle mass (M) was then calculated as:

$$M = 0{\cdot}307 \times V + 0{\cdot}353 \; (n = 12, r = 0{\cdot}93, P < 0{\cdot}001)$$

(autopsy study, O. Halskov, personal communication).

This anthropometric approach gave values similar to those from estimations based on multiple

CAT-Scans (Saltin, 1985). The present subjects had a mean knee-extensor mass of 2·8 kg with a range of 2·5–3·5 kg.

Muscle biopsies

Muscle samples were analysed for total water by weighing the samples before and after freeze-drying and for lactate and CP by fluorometric assays (Lowry & Passonneau, 1972). The ATP and inosine monophosphate (IMP) concentrations were determined with a high-performance liquid chromatography technique (Magnson & Perryman, 1980).

Procedures

Subjects performed one-legged exercise in the supine position on a specially designed ergometer that permitted graded intensities of exercise to be confined only to the quadriceps muscles (Andersen, Adams, Sjøgaard, Thorboe & Saltin, 1985). All subjects practised the exercise several times before the final experiment was performed.

At the time of the actual experiment a catheter was placed in the femoral artery with the Seldinger technique with the tip placed 1–2 cm proximal to the inguinal ligament. The tip of one of the two femoral vein catheters was placed approximately 8 cm in the retrograde direction, i.e. 12–14 cm distal to the inguinal ligament. This catheter was used for collecting blood samples and for infusing the ice-cold saline. Another venous catheter was placed in the inguinal region with the tip 1–2 cm distal to the ligament. The thermistor for measurement of leg blood flow was inserted through this catheter and was advanced just proximal to the tip.

Protocol

On the morning of the final experiment, subjects arrived after a light breakfast. Placement of catheters was followed by 30 min of rest in the supine position. The first exercise was performed for 10 min with the experimental leg at a work load corresponding to about 25% of its peak aerobic work capacity (10 W). After at least 10 min rest a muscle biopsy was taken from m. vastus lateralis and blood was drawn from the femoral artery and vein simultaneously. Then an intense work load (mean 65; range 52–79 W) was performed to exhaustion (mean 3·2; range 2·2–4·9 min) followed by a recovery period of 1 h. The force of each kick and its rate were monitored continuously. Either a change in the force tracing (see Andersen *et al.* 1985) or a drop in rate were the objective determinants for terminating the exercise.

After 10 s of the intense exercise, and during early recovery (0–5 min), blood flows were determined as frequently as possible, followed by blood sampling from the femoral artery and vein. At least two complete measurements per 90 s and a minimum of four determinations were accomplished during the exercise. Beyond the 5 min of recovery, blood flows were measured and blood samples were collected at about 7, 10, 13, 16, 20, 30, 45 and 60 min (Fig. 1). An occlusion cuff placed just below the knee was inflated (220 mmHg) during the entire period of the intense exercise and during recovery, except for three to four 'breaks' (about 30 s) during recovery at approximately 8, 25, 40 and 50 min. The expired air was collected continuously in Douglas bags during the intense exercise and in the recovery period. Additional muscle biopsies were taken immediately at exhaustion and 3, 10 and 60 min of recovery.

Finally a progressive, continuous exercise protocol was performed at power outputs of 10–50 W, each lasting for 7–8 min. Blood flow determinations and blood sample collections were performed during the last 2–3 min of the exercise when expired air was also collected for oxygen uptake determination. In some subjects a blood sample was also taken after 3 min of each exercise. The cuff was inflated during the measurements. Figure 1 summarizes the protocol, including sampling times.

Calculations

Leg oxygen uptake and lactate efflux

Oxygen uptake of and lactate efflux from the knee extensors were calculated by multiplying the blood flow with femoral arterial–venous difference for oxygen and lactate. A continuous blood flow

curve was constructed for each subject by linear connection of the consecutive data points to obtain time-matched values for the blood flow measurements with the latter two variables. No difference between 'time-matched' and measured blood flow was larger than 0·3 l min^{-1} in the last part of recovery.

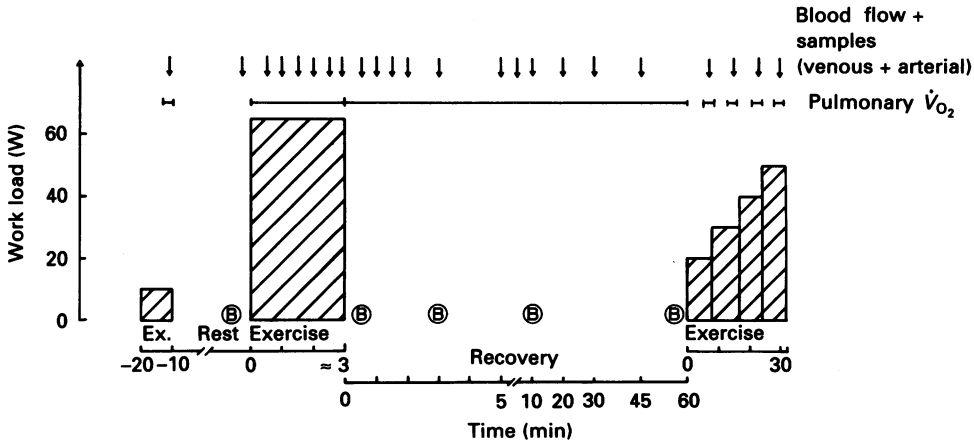

Fig. 1. Schematic representation of the experimental design. Ⓑ, muscle biopsy.

Total oxygen uptake and total lactate efflux

The total oxygen uptake (except the oxygen unloaded from haemoglobin (Hb) and myoglobin (Mb)) and total lactate efflux during the very intense exercise as well as during the recovery period are given by the time integral

$$\int_0^x f(t)\,dt,$$

where 0 is the start of intense exercise or recovery, x is either the time for exhaustion or the end of recovery, and $f(t)$ is oxygen uptake or lactate efflux at a given time during exercise or recovery. In practice, the total oxygen uptake and lactate efflux were determined as the areas under the oxygen uptake and lactate efflux curves, respectively, with time on the x-axis. The curves were produced on the assumption that there was a linear relationship between two measured values. When the above approach for calculations was compared with the method of matching blood flow with blood concentration measurements nearest in time, the largest difference in total oxygen uptake or total lactate efflux was 3%. In most instances deviations were less than 1%.

Oxygen deficit and debt

The oxygen uptake (leg and pulmonary) during the submaximal exercise bouts was used to estimate the energy demand of the very intense exercise by linear extrapolation (Broun & Hollander, 1977). Then the leg and pulmonary oxygen deficit for the very intense exercise was calculated as the difference between this estimated energy demand and the actual (measured) oxygen uptake (see Fig. 2).

Oxygen debt (leg and pulmonary) was determined as the difference between total oxygen uptake during recovery and calculated total resting oxygen uptake (i.e. 60 min times measured oxygen uptake per minute at rest before exercise).

Comments on methods and procedure

In the original use of the one-legged knee-extensor exercise model (Andersen *et al.* 1985) the subjects were sitting whereas a supine position was used in the present study. The main reason for this change in position was to facilitate easy access to the catheters in the groin and thereby allow

for frequent multiple blood sampling and blood flow measurements during the exercise and during early recovery.

Another difference compared to earlier studies was that the venous catheters and thus both sampling of the blood and the site for the blood flow measurements in the vein were more distal (≈ 10 cm). This was done to avoid or minimize contamination of the blood from the skin. Thus, the

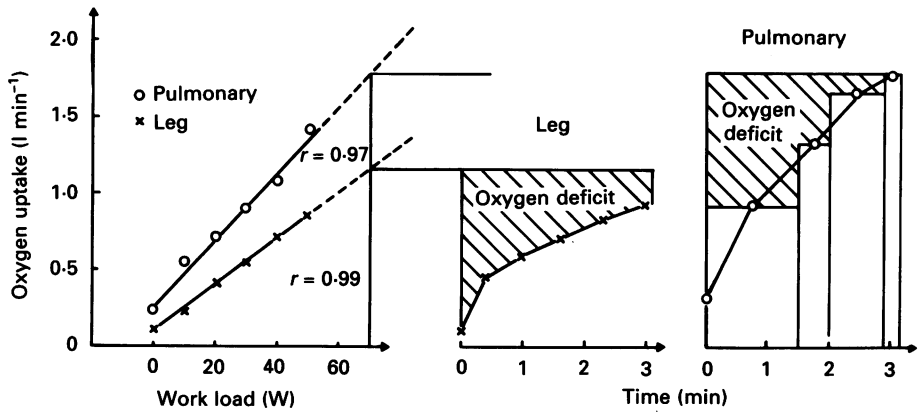

Fig. 2. Determination of oxygen deficit. From the relationship between work intensity and leg or pulmonary oxygen uptake (left) the leg and whole-body energy demand during intense exercise was estimated. The leg (middle) and whole-body (right) oxygen deficit were determined as the difference between this energy demand and total oxygen uptake measured during the exercise. Data from one representative subject is illustrated. Individual r values for the remaining subjects were all above 0·95 (pulmonary) and 0·98 (leg).

blood samples were all taken distal to the entrance of the saphenous vein and the flows represent femoral vein blood flows. This flow originates from the quadriceps femoris (knee extensor) muscle with a contribution from the hamstrings and from the overlying skin vasculature. When the measurements are performed ≈ 10 cm more proximal in the femoral vein than in the present study, it has been shown that during exercise thigh skin blood flow contributes about 2% and non-active tissues contribute another 0·4–0·5 l min^{-1} to the measured blood flow (Savard, Nielsen, Laszczynska, Larsen & Saltin, 1988). When comparing the present results with earlier results for leg blood flow, leg oxygen uptake and pulmonary oxygen uptake there were some systematic differences (Fig. 3). In the present study leg blood flow was lower (0·5–1·0 l min^{-1}) and the femoral arterial–venous O_2 difference was wider (20–40 ml l^{-1}); the latter was not enough to give the same leg oxygen uptake. Thus leg oxygen uptake was up to 0·1 l min^{-1} lower during the present exercises. Nevertheless the present data yielded a similar slope for the work intensity – submaximal leg oxygen uptake or blood flow relationships for the leg (Fig. 3). Pulmonary oxygen uptake was the same in the supine as in the sitting position during the submaximal work. The slightly steeper elevation in pulmonary oxygen uptake than in leg oxygen uptake at increasing exercise intensities relates to the fact that the heavier the work load the more muscles of the torso are active to keep the pelvis stable (Fig. 3). It could have been anticipated that this effect would be less in the supine position, but this was obviously not the case.

RESULTS

Systemic response (Fig. 3)

Pulmonary oxygen uptake at rest was 0·31 ± 0·01 l min^{-1} (mean ± S.E.M.) and it increased linearly with the work intensity during the submaximal exercises from 0·50 l min^{-1} at 10 W to 1·45 l min^{-1} at 50 W. During the exhaustive exercise (65 W) the oxygen uptake increased gradually and reached 1·85 l min^{-1} before exhaustion.

A sharp, initial drop occurred in pulmonary oxygen uptake in the recovery period, followed by a gradual decline from $0{\cdot}34 \pm 0{\cdot}02$ l min^{-1} at 15 min to $0{\cdot}30 \pm 0{\cdot}02$ l min^{-1} at 35 and 60 min.

Heart rate was 60 ± 2 beats min^{-1} at rest, increased with the submaximal exercises to 130 ± 13 beats min^{-1} at 50 W, and reached 145 ± 6 beats min^{-1} during the exhaustive exercise. In recovery the heart rate changed in concert with oxygen uptake.

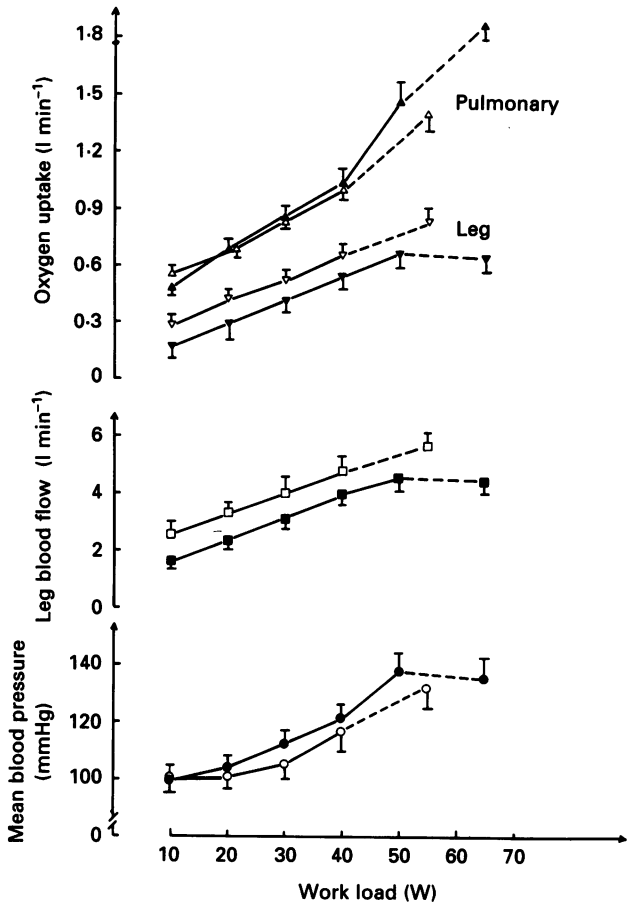

Fig. 3. Comparison of some variables obtained during one-legged knee-extensor exercise performed in the upright (Andersen & Saltin, 1985, open symbols) and the supine position (present study, filled symbols). The measurements of leg blood flow and arterial–venous O_2 difference were performed 10 cm more distal in the femoral vein in the present as compared to our previous study.

Mean arterial blood pressure was 98 ± 4 mmHg at rest and remained unaltered at the low exercise intensities. It became elevated to 138 mmHg at 50 W and to 135 mmHg during the very intense exercise. In recovery the pressure decreased promptly to 105 ± 7 mmHg after 1 min and to 100 ± 5 mmHg after 2 min.

Noradrenaline concentration averaged $0{\cdot}30 \pm 0{\cdot}07$ ng ml^{-1} at rest and increased during the exhaustive exercise to $0{\cdot}35 \pm 0{\cdot}08$ ng ml^{-1} and remained at that level early

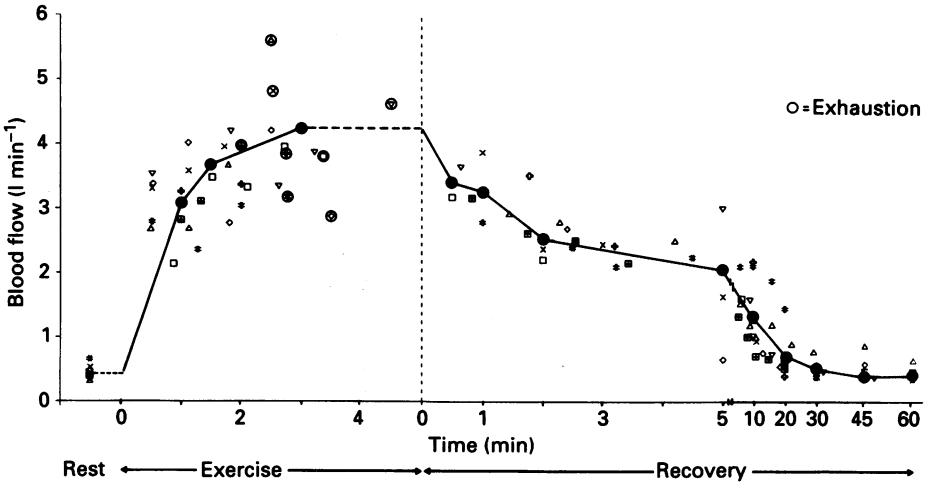

Fig. 4. Individual and mean values for femoral vein blood flow during and after intense exercise. The various symbols represent one individual, except the filled circles which give the mean values. Note that a circle around an individual value marks the measurement performed just before exhaustion. The vertical dashed line denotes start of recovery.

TABLE 1. Leg blood flow, oxygen uptake and lactate efflux at rest, at different submaximal work loads, and during exhaustive exercise

Work load (W)	Leg blood flow (l min^{-1})	Leg oxygen uptake (l min^{-1})	Lactate efflux (mmol min^{-1})
0 (n = 8)	0·39±0·01	0·023±0·004	0·05±0·01
10 (n = 8)	1·55±0·10	0·176±0·017	0·0±0·1
20 (n = 8)	2·29±0·21	0·279±0·028	0·0±0·1
30 (n = 7)	3·04±0·19	0·415±0·029	1·6±0·7
40 (n = 7)	3·93±0·31	0·551±0·034	5·6±1·0
50 (n = 7)	4·42±0·38	0·651±0·035	8·4±1·7
65 (n = 8) (peak exercise)	4·26±0·26	0·616±0·038	16·2±2·7

Means±S.E.M. are given.

in recovery. At 10 min the noradrenaline concentration was again at resting level (0·29±0·06 ng ml^{-1}).

Adrenaline concentration was 0·17±0·04 ng ml^{-1} pre-exercise and it increased to 0·24±0·06 ng ml^{-1} at exhaustion, but was already close to pre-exercise level (0·18±0·05 ng ml^{-1}) at 3 min post-exercise.

Local response

Leg blood flow (Fig. 4; Table 1)

Leg blood flow was less than 0·4 l min^{-1} before the exercise. It increased with increasing submaximal exercise intensities reaching 4·42 l min^{-1} at 50 W. Leg blood flow increased rapidly during exhaustive exercise reaching 3·16 and 3·69 l min^{-1} after

1 and 1·5 min, respectively, and a final rate of 4·26 l min^{-1}. The return of the blood flow to pre-exercise level was quite slow. It was still 3·28, 2·06 and 1·32 l min^{-1} at 1, 5 and 10 min of recovery, respectively. At 30 and 60 min leg blood flow had reached 0·52 and 0·43 l min^{-1}, respectively, compared to 0·39 l min^{-1} at rest.

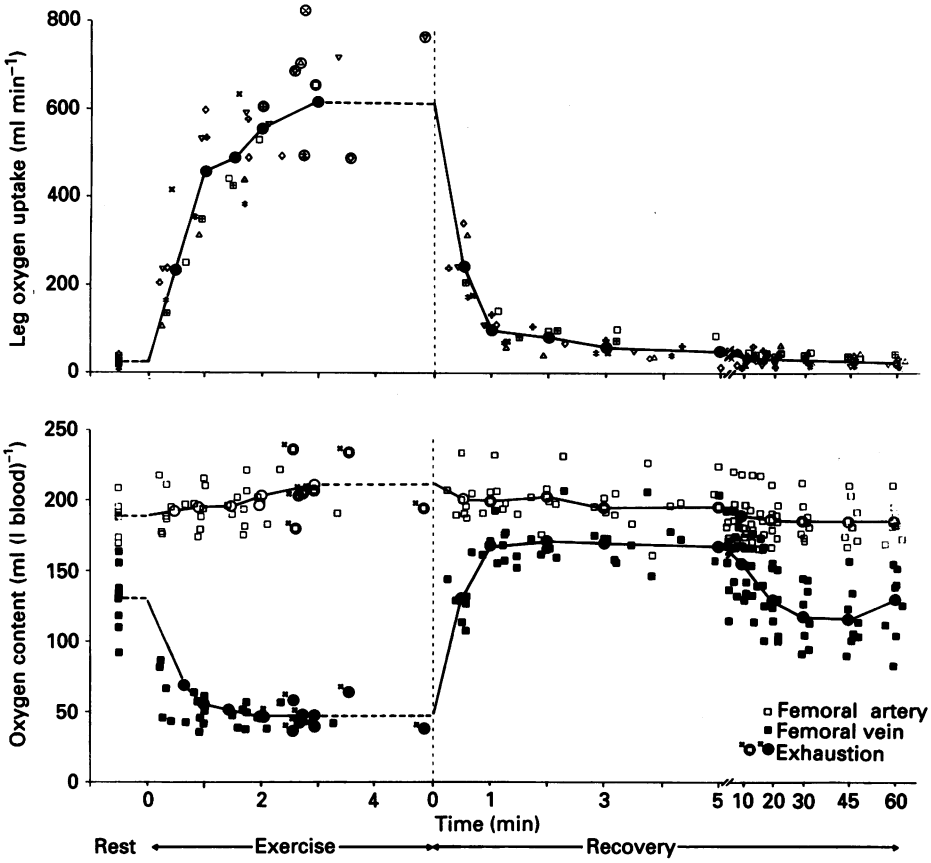

Fig. 5. Individual and mean values for oxygen content in femoral vein and artery (lower panel), and leg oxygen uptake (upper panel), during and after intense exercise. The organization and symbols are the same as in Fig. 4, with the addition of open circles denoting mean values for the femoral artery measurements.

Leg oxygen uptake (Fig. 5; Table 1)

Arterial oxygen saturation (S_{a,O_2}) was 97·8±0·3% at rest and was essentially unaltered during the exercises whereas oxygen content (C_{a,O_2}) increased from 183·3±7·6 to 194·1±4·4 ml l^{-1} during the submaximal exercise, and to 211±5·8 ml l^{-1} in the exhaustive exercise. Early in recovery S_{a,O_2} and C_{a,O_2} were above pre-exercise values, but by 10 min the C_{a,O_2} was 189±4·7 ml l^{-1} compared to 188±4·1 ml l^{-1} at rest.

Femoral venous oxygen saturation (S_{fv,O_2}) was 71·8±3·2% at rest, which with a haemoglobin concentration of 144±4 g l^{-1} gave a C_{fv,O_2} of 138·5±7·8 ml l^{-1}. Increasingly submaximal exercise intensities resulted in a lowering of O_2 saturation

to $26 \pm 1{\cdot}4\%$ and C_{fv,O_2} was $53{\cdot}2 \pm 3{\cdot}5$ ml l^{-1} at 10 W with small further reductions at the higher exercise intensities. During the exhaustive exercise the S_{fv,O_2} became reduced to $33 \pm 4\%$ within 30 s of exercise and it was $22 \pm 2\%$ at exhaustion. At these corresponding times C_{fv,O_2} was $68 \pm 8{\cdot}2$ and $48 \pm 4{\cdot}3$ ml l^{-1}, respectively.

At the termination of the exhaustive exercise, S_{fv,O_2} and C_{fv,O_2} increased sharply to a level much above the resting value, and remained so for some 20 min of the recovery period.

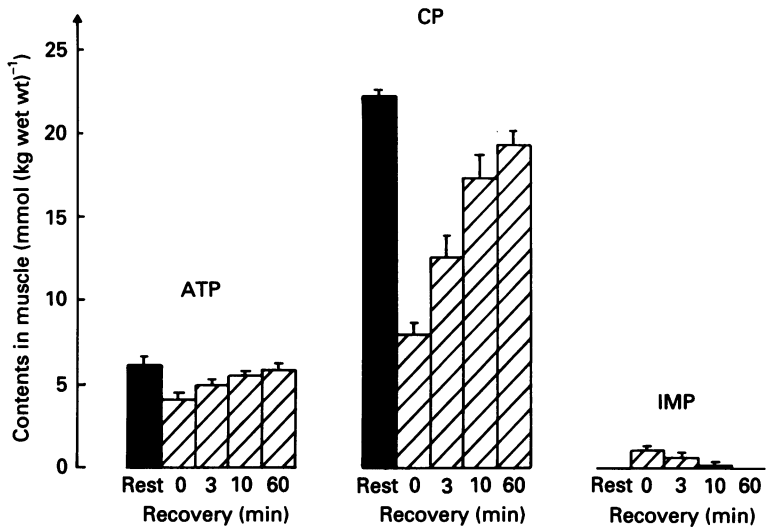

Fig. 6. ATP, CP and IMP contents in muscle at rest (■) and at various points after intense exercise (▨). Means ± S.E.M. are given.

Oxygen tension of arterial (P_{a,O_2}) and femoral vein (P_{fv,O_2}) blood followed the same pattern as S_{O_2} and C_{O_2} during the exhaustive exercise and in recovery. It may be noteworthy that P_{fv,O_2} was lowered to 18 ± 1 mmHg within 30 s of intense exercise and was unchanged thereafter to exhaustion.

Leg oxygen uptake was 0·023 l min^{-1} at rest and increased during the submaximal exercises to 0·176 l min^{-1} at 10 W and to 0·651 l min^{-1} at 50 W. During the exhaustive exercise the oxygen uptake by the exercising limb increased within 1 min to 0·459 l min^{-1} and to 0·616 l min^{-1} at exhaustion. In the post-exercise recovery period the oxygen uptake fell quite markedly; although leg blood flow stayed high, the femoral arterial–venous O_2 difference narrowed. By 45 and 60 min of recovery leg oxygen uptake had decreased to 0·032 and 0·026 l min^{-1}, respectively.

Muscle water, ATP, creatine phosphate, inosine monophosphate and lactate (Fig. 6)

The water content of the knee-extensor muscle was $76{\cdot}0 \pm 0{\cdot}3\%$ at rest and it increased to $78{\cdot}0 \pm 0{\cdot}3\%$ during the intense exercise. It was still at $77{\cdot}6 \pm 0{\cdot}3\%$ after 60 min of recovery.

The ATP concentration of the muscle at rest was 6·2 mmol (kg wet wt)$^{-1}$ and declined to 4·1 mmol (kg wet wt)$^{-1}$ at exhaustion; a reduction of about 30%. After 10 and 60 min of recovery the [ATP] was 5·6 and 5·9 mmol (kg wet wt)$^{-1}$,

respectively. *The IMP concentration*, which was below 0·2 mmol (kg wet wt)$^{-1}$ at rest, increased to 1·1 mmol (kg wet wt)$^{-1}$ at exhaustion. After 10 min of recovery [IMP] was 0·18 mmol kg^{-1} and it was undetectable after 60 min.

The CP concentration which averaged 22·4 mmol (kg wet wt)$^{-1}$ at rest, was reduced at exhaustion to 8·0 mmol (kg wet wt)$^{-1}$ (a decrease of 60%). The return of [CP] to control level during recovery was slow; and at 10 and 60 min the concentrations were 17·4 and 19·5 mmol (kg wet wt)$^{-1}$, respectively. The total reduction in [ATP] and [CP] (and elevation in [IMP]) amounted to 17·4 mmol (kg wet wt)$^{-1}$, which after adjustments for water content of the muscle tissue was equivalent to 16·4 mmol ATP (kg wet wt)$^{-1}$

The muscle lactate concentration was $2{\cdot}0 \pm 0{\cdot}4$ mmol (kg wet wt)$^{-1}$ at rest and during the intense exercise it accumulated in the knee-extensor to $28{\cdot}1 \pm 1{\cdot}5$ mmol (kg wet wt)$^{-1}$. This lactate accumulation corresponded to an ATP production of 44·9 mmol ATP (kg wet wt)$^{-1}$ during the exhaustive exercise. In the recovery period muscle lactate was $17{\cdot}0 \pm 1{\cdot}5$, $8{\cdot}1 \pm 1{\cdot}3$, and $3{\cdot}4 \pm 0{\cdot}7$ mmol (kg wet wt)$^{-1}$ at 3, 10 and 60 min, respectively.

Lactate efflux from muscle (Table 1, Fig. 7)

At rest and at the two lowest submaximal exercise intensities no net exchange of lactate was observed for the limb, and both femoral arterial and venous lactate concentrations were below 1 mmol l^{-1}. At 30 W femoral venous lactate concentration increased to $2{\cdot}1 \pm 0{\cdot}6$ mmol l^{-1} which represented a net release of 1·6 mmol min^{-1}. At the two highest submaximal exercise intensities (40 and 50 W) a further elevation in femoral venous lactate concentration was seen and a net release of lactate occurred (5·6 and 8·4 mmol min^{-1}, respectively).

During the exhaustive exercise both femoral arterial and venous lactate rose continuously and the latter more than the former, reaching 4·5 mmol l^{-1} and 8·5 mmol l^{-1}, respectively, at exhaustion. Thus, a net release of lactate occurred amounting to 12·4, 14·8 and 16·2 mmol min^{-1} at 1 and 2 min of exercise, and at exhaustion, respectively. This resulted in a total net lactate efflux during the exhaustive exercise of $41{\cdot}8 \pm 8{\cdot}8$ mmol or $14{\cdot}8 \pm 3{\cdot}0$ mmol (kg wet wt)$^{-1}$. This was approximately 50% of the lactate that accumulated in the muscle over the same period of time. The net lactate release during the exercise represents an ATP production of 22·2 mmol (kg wet wt)$^{-1}$. A dominant fraction or about 70% of the lactate that accumulated in the muscle at exhaustion left the muscle for the blood stream in the recovery period. At the end of recovery a very small net release was still present.

Oxygen deficit–oxygen debt (Fig. 2)

The linear regression analysis between work intensities (submaximal) and the individual oxygen uptakes gave r values above 0·95 (leg: 0·984–0·999; pulmonary: 0·952–1·000). The energy demand of the work intensity used for the exhaustive exercise was estimated by extrapolation of these relationships. For the duration of the whole exhaustive exercise period it amounted to $1{\cdot}00 \pm 0{\cdot}10$ l O_2 (kg active muscle)$^{-1}$ and $1{\cdot}86 \pm 0{\cdot}19$ l O_2 (kg active muscle)$^{-1}$ for the leg and whole body, respectively. Subtracting the actual total oxygen uptake which occurred during the exhaustive exercise, the estimated oxygen deficit was $0{\cdot}46 \pm 0{\cdot}04$ l O_2 (kg active

muscle)$^{-1}$ for the leg and $0{\cdot}48 \pm 0{\cdot}05$ l O_2 (kg active muscle)$^{-1}$ for the whole body (i.e. pulmonary oxygen data). The corresponding oxygen debts (recovery–pre-exercise oxygen uptake) were $0{\cdot}55 \pm 0{\cdot}05$ and $1{\cdot}47 \pm 0{\cdot}26$ l (kg active muscle)$^{-1}$ for the leg and for whole body, respectively.

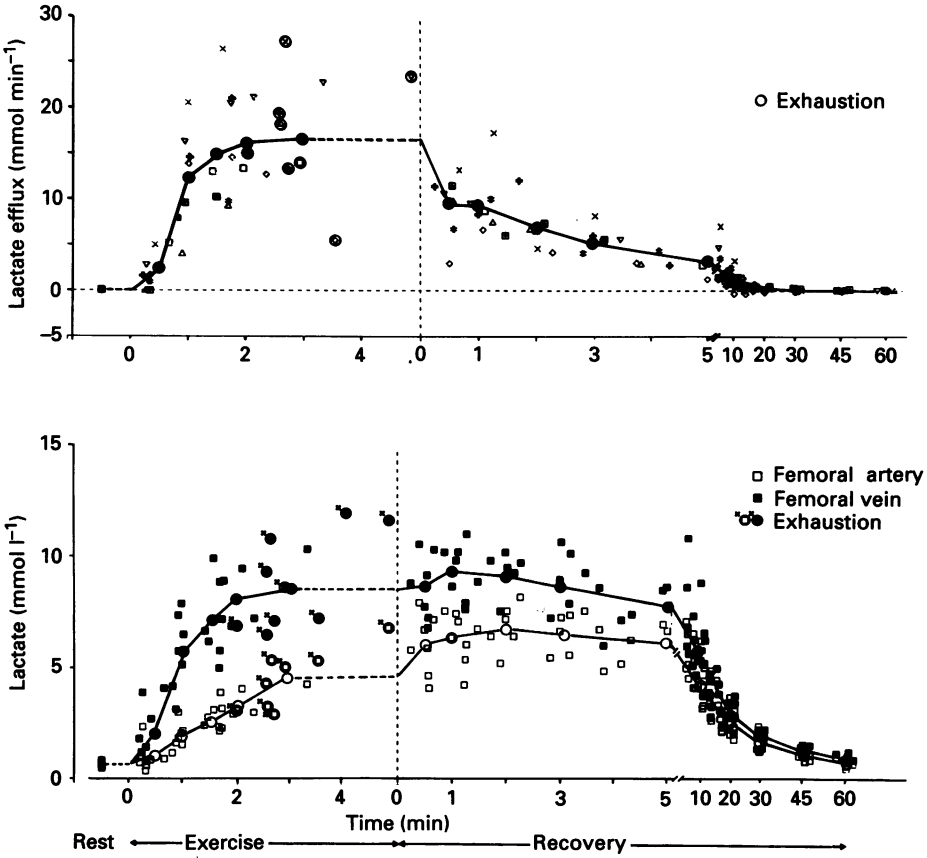

Fig. 7. Individual and mean values for lactate concentrations in femoral vein and artery (lower panel), and leg lactate efflux (upper panel), during and after intense exercise. The organization and symbols are the same as in Fig. 4, with the addition of open circles denoting mean values for the femoral artery measurements.

Alactacid and lactacid energy yield and oxygen deficit (Table 2A)

The measurements of changes in the concentrations of ATP, CP and IMP coupled with the lactate production of the active knee-extensor muscles were equivalent to an ATP production of 83·1 mmol (kg wet wt)$^{-1}$ (Table 2A). The estimated oxygen deficit expressed in the same units was 94·7 mmol (kg wet wt)$^{-1}$ which includes desaturation of HbO_2 (equivalent to 1·9 mmol ATP (kg wet wt)$^{-1}$ and MbO_2.

Recovery in ATP, creatine phosphate, lactate and O_2 debt (Table 3)

In sharp contrast to the close match that existed between the two methods to determine the anaerobic energy yield during the intense exercise, is the lack of

congruity between these estimations and the oxygen debt measurements. This relates both to its value for the leg as well as for the whole body. The temporal pattern for change in the leg oxygen debt per kilogram active muscle was a quick drop from $54{\cdot}8 \pm 3{\cdot}7$ ml min^{-1} during the first 3 min of recovery of $11{\cdot}4 \pm 2{\cdot}1$ ml min^{-1}

TABLE 2. Factors contributing to oxygen deficit

A. Measurements (means ± S.E.M., $n = 7$)

	Exercise (mmol ATP (kg wet wt)$^{-1}$)
Changes in ATP, CP, IMP	$16{\cdot}4 \pm 0{\cdot}8$
Lactate production*	$66{\cdot}7 \pm 6{\cdot}6$
Total	$83{\cdot}1 \pm 7{\cdot}0$
Oxygen deficit*	$94{\cdot}7 \pm 6{\cdot}5$
Changes in HbO_2*	$1{\cdot}9 \pm 0{\cdot}2$
Total	$92{\cdot}8 \pm 6{\cdot}4$

B. Measurements and estimations (means)

	Exercise (mmol ATP (kg wet wt)$^{-1}$)
Determined ATP production*	83·1
Alanine + pyruvate release† (maximum)	≈ 0·8
Accumulated glycolytic intermediates and alanine‡	≈ 5·3
Lactate taken up by flexors (maximum)	≈ 2·0
Total	91·2
Oxygen deficit	94·7
Changes in HbO_2, MbO_2§	3·1
Total	91·6

* 1 mmol lactate = 1·5 mmol ATP ≈ 6·70 ml equiv O_2. † Katz *et al.* (1986). ‡ Spriet, Söderlund, Bergström & Hultman (1987*b*); Katz *et al.* (1986). § Svedenhag, Henriksson & Sylvén (1983).

from 3 to 10 min and $6{\cdot}1 \pm 1{\cdot}0$ ml min^{-1} for the remaining time. This relates to the fact that the resynthesis of the ATP, CP and reloading of Hb and Mb with O_2 occurs early in recovery. However, the magnitude of these processes only accounts for some 10% of the observed oxygen debt. Another minor fraction (less than 10%) can probably be explained by the energy needed for lactate conversion to glycogen in the muscle, but the remaining large fraction of the O_2 debt does not appear to be directly related to the metabolites of the compounds which create the alactacid and lactacid energy yield. This discrepancy becomes markedly enlarged when comparison is made with the whole-body O_2 debt, which was almost threefold larger than the leg O_2 debt.

DISCUSSION

The principal findings of the present study are that the anaerobic energy release during the intense exercise estimated from metabolic measurements relates extremely well in quantity to the estimated O_2 deficit, and that the O_2 debt measurements, determined for the leg or for the whole body, were much higher than

TABLE 3. Factors contributing to oxygen debt (for a discussion of energy needed for lactate elimination and resynthesis of glycogen, see text)

	Recovery (mmol ATP (kg wet wt)$^{-1}$)			
	0–3 min	3–10 min	10–60 min	Total
Changes in ATP	0·9±0·3	0·4±0·3	0·5±0·2	1·8±0·4
Changes in CP	5·0±1·4	4·4±0·9	2·7±1·2	12·1±1·2
Changes in IMP	0·4±0·2	0·6±0·1	—	1·0±0·2
Total	6·3±1·4	5·4±1·0	3·2±1·5	14·9±0·8
Oxygen debt	36·8±2·5	17·9±3·3	68·4±11·0	123·1±11·2
Changes in MbO_2, HbO_2	3·9	−0·3	−0·6	3·0
Total	32·9	18·2	69·0	120·1

Means±S.E.M.; values for S.E.M. for changes in MbO_2 and HbO_2 are not included because MbO_2 was not measured, but taken from Svedenhag *et al.* (1983).

could be accounted for by the reloading of haemoglobin and myoglobin, resynthesis of ATP and CP stores, and glycogen resynthesis from lactate.

The question that arises is: how reasonable are our metabolic measurements during the exercise? We observed reductions in ATP and CP of 30 and 60% as well as an elevation of IMP to 1 mmol (kg wet wt)$^{-1}$ during the intense exercise, which correspond well with previous results (Karlsson, 1971; Jones, McCartney, Graham, Spriet, Kowalchuk, Heigenhauser & Sutton, 1985; Cheetham, Boobis, Brooks & Williams, 1986; Katz, Broberg, Sahlin & Wahren, 1986). The same is true for the lactate accumulation in the muscle of close to 30 mmol (kg wet wt)$^{-1}$ at exhaustion (Jones *et al.* 1985; Cheetham *et al.* 1986; Katz *et al.* 1986; Spriet, Söderlund, Bergström & Hultman, 1987*a*). The actual mean rate of a total net lactate production of 0·24 (0·19–0·30) mmol (kg wet wt)$^{-1}$ s^{-1} also appears quite likely. Values ranging from 0·5 to 1·7 mmol (kg wet wt)$^{-1}$ s^{-1} have been reported in exercises lasting 10–30 s (Jacobs, Tesch, Bar-Or, Karlsson & Dotan, 1983; Jones *et al.* 1985; Cheetham *et al.* 1986). In longer exercises, i.e. lasting some minutes as was the case for our subjects, rates of lactate production similar to those reported here have been observed (Karlsson, 1971; Katz *et al.* 1986; Spriet *et al.* 1987*a*). Additional components of the lactacid anaerobic energy release are the small amounts related to the accumulation of alanine and glycolytic intermediates in the muscle, loss of pyruvate (alanine) from the muscle as well as possibly a very small underestimation of lactate production (Table 2B). The latter is due to a minor uptake of lactate from the blood in the 'resting' hamstring muscles of the active limb (< 1·0 mmol (kg wet

wt)$^{-1}$). Based on our own measurements, and data published by others, this additional glycolytic energy contribution may amount to 5–9 mmol ATP (kg wet wt)$^{-1}$ which suggests a total anaerobic energy yield of some 90 mmol ATP (kg wet wt)$^{-1}$ (Table 2B). Of this the alactacid compounds contributed about 15–20% with the remainder being supplied by glycolytic processes.

What is striking is how closely this estimate of anaerobic energy production during the intense exercise relates to the observed O_2 deficit (note: some 3 mmol ATP (kg wet wt)$^{-1}$ of the deficit measurements relate to unloading of haemoglobin and myoglobin; see Table 2A and B). This fact gives support to the use of O_2 deficit measurements as a quantitative measure of anaerobic energy metabolism during very intense exercise. Our estimation of oxygen deficit was based on the determination of the energy demand of the peak exercise intensity from a linear extrapolation of the submaximal aerobic energy cost ($\dot{V}_{O_2}$)–work relationship. Thus, such an extrapolation appears to be a satisfactory procedure at least when exercising with a small muscle group. The importance of the lactate production during the demanding submaximal exercise must be considered. It is quite substantial and represents at 50 W an estimated energy contribution of about 10% above that produced by aerobic metabolism (Fig. 8). It is of note that the lactate release is of equal magnitude at 3–4 and 7–8 min at 50 W. The magnitude of the anaerobic contribution is a minimum value as some accumulation of lactate may also occur at the 'steady-state' phase at this exercise intensity. The possibility exists that this anaerobic energy yield from glycolysis compensates for a reduction in free energy (ΔG) from ATP hydrolysis when increases take place in factors such as temperature and P_i and reduction in pH (Kawai, Guth, Winnikes, Haist & Ruegg, 1987; Cooke, Franks, Luciani & Pate, 1988). If this assumption is correct, one would have anticipated that the same would occur during the intense exercise, i.e. anaerobic energy production ought to have given a larger ATP yield than the estimate from the oxygen deficit measurement and this was not observed.

However, there is an alternative possibility. The force production per unit at ATP utilized is highly dependent upon speed of contraction and fibre recruitment pattern (Kushmerick, 1985; di Prampero, Boutellier & Marguerat, 1988). In the submaximal exercises the contractions were fast, only occupying 0·35–0·45 s of the 1 s duty cycle. In the intense exercise leading to exhaustion the contraction gradually became elongated to 0·6 s. Thus, the energy demand per contraction may have been reduced as a function of the slower contraction, although work output was unaltered. This could compensate for a possible reduction of free energy from ATP hydrolysis during the exhaustive exercise; at least in its later phase. From the above discussion it is clear that some very basic questions remain to be answered in relation to why lactate is formed during exercise and the mechanical efficiency of muscle contraction, including possible variation in ΔG for the ATP hydrolysis.

It has been known for a long time that O_2 debt measurements produce erroneously high estimates of anaerobic energy liberation (Margaria *et al.* 1933; Knuttgen, 1962; Margaria, Cerretelli, di Prampero, Massari & Torelli, 1963). However, the reason for this is unclear. Exercise, particularly when it is very intense leading to exhaustion, causes the oxygen uptake during recovery to return to pre-exercise or basal levels very slowly. As pointed out early in this century, it may not return to pre-exercise

level on the same day (Krogh & Lindhard, 1919; see also: Bahr, Ingnes, Vaage, Sejersted & Newsholme, 1987). This was not the case in the present subjects as the oxygen uptake measured at either the leg or the lungs was at the pre-exercise level by 60 min of recovery. In spite of this the O_2 debt measurement for the whole body was three times larger than the O_2 deficit value.

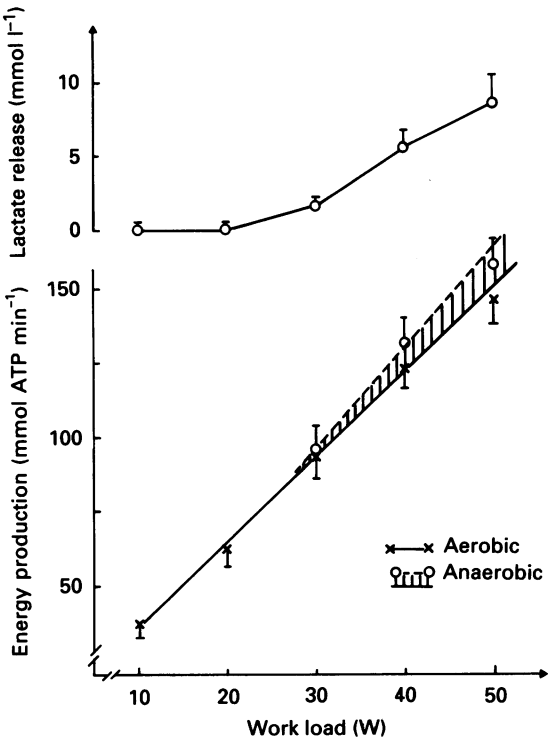

Fig. 8. Lactate release (upper panel) and energy production expressed as mmol ATP min^{-1} (○) at the end of various work rates sustained for 7 min (lower panel). The aerobic part (×) of total energy production is determined from leg oxygen uptake and the anaerobic part from lactate efflux. The shaded area represents the anaerobic addition to the aerobic energy yield. Means ± S.E.M. are given.

The O_2 debt measurement for the leg was also much too high. Initially this may appear to be a surprising statement at the O_2 deficit and debt values are of similar magnitude. However, the extra energy demand for resynthesis of the ATP and CP could only account for 6–7 mmol ATP (kg wet wt)$^{-1}$ during the first 3 min of recovery ('fast component'). This alactacid component can contribute no more than 20% to the 'fast component' of the O_2 debt. The re-loading of Hb and Mb may account for another 2–4 mmol ATP (Table 3). The fate of lactate is more difficult to account for on a precise time base. There is good reason to believe that the lactate metabolism did take place throughout recovery. A utilization of lactate, glycolytic intermediates and glucose uptake by the muscle from the blood for glycogen resynthesis within the knee-extensors during the entire 60 min of recovery can be

estimated to demand some 25 mmol ATP kg^{-1} or $\approx$ 0·4–0·5 mmol kg^{-1} min^{-1}, based on the increase in glycogen (Bangsbo, Juel & Kiens, 1989). However, after adding this amount to the ATP demands documented above for the 'fast component', we can only account for 10–12 mmol ATP kg^{-1} or less than $\frac{1}{3}$ of the leg oxygen debt (36·8 mmol ATP (kg wet wt)$^{-1}$ for the first 3 min. The discrepancy was not reduced in the remaining 57 min of the recovery (Table 3). During the last 50 min of recovery the repayment of the lactacid energy yield including possible resynthesis of glycogen from glycolytic intermediates and glucose can maximally amount to 20 mmol ATP kg^{-1}. This together with about 3 mmol ATP kg^{-1} for ATP and CP resynthesis is far from the measured leg oxygen debt of 66·0 mmol ATP kg^{-1}. Of note is how little lactate elimination contributes to the slow component of the oxygen debt, a point also recently made by Roth, Stanley & Brooks (1988).

The present study did not give any clues concerning why oxygen uptake remains elevated after intense exercise both in the exercising limb and the body. However, several factors can be ruled out. Catecholamines are suggested as a possible cause (Mæhlum, Grandmontagne, Newsholme & Sejersted, 1986). One of the features of exercising with a small muscle group such as the knee-extensors of one leg is that it causes negligible perturbations in the catecholamine levels of the blood. Noradrenaline and adrenaline are barely elevated during the exercise, and in recovery they rapidly return to resting level. Thus at least in the present study plasma catecholamines are unlikely explanations for the elevated recovery oxygen. Temperature is another factor thought to cause recovery oxygen uptake to remain elevated. However, it is also an unlikely factor in the present study as femoral vein blood temperature elevated very little during the intense exercise ($\approx$ 37 °C) and within 30 min in the recovery period it was at pre-exercise temperature. Before leaving the subject of oxygen debt it is worth emphasizing that the resynthesis of CP and ATP only accounts for about 20% of the oxygen debt during the first 10 min of recovery, and for the entire hour of recovery it accounts for less than 10%.

The absolute magnitude for the anaerobic energy production was 91·6 mmol ATP (kg wet wt)$^{-1}$ or the equivalent of 0·46 l O_2 (kg wet wt)$^{-1}$ of active muscle. The average human has 30–35 kg of muscle which theoretically should mean that the whole-body capacity for an anaerobic energy production approaches 15 l O_2 or 200 ml O_2 (kg body wt)$^{-1}$. Such high values have never been reported, and values of barely half this level are found in the literature (Åstrand & Saltin, 1961; Karlsson & Saltin, 1970; Linnarson, Karlsson, Fagraeus & Saltin, 1974; Hermansen & Medbø, 1984; Medbø, Mohn, Tabata, Bahr & Sejersted, 1988). There are several obvious explanations for this discrepancy. One is that probably the muscles of the body cannot all be active at the same time to the same extent as the knee-extensor group in the present study. Thus, neither the reduction in [CP] and [ATP] nor lactate production will be equally high in all muscles. Another factor is that if the systemic blood flow is to be distributed to a large fraction of the muscle mass, peak perfusion becomes reduced. This will affect the amount of lactate leaving the muscle during the exercise. In the present study $\frac{1}{3}$ of the lactate produced was released to the blood during the exercise and the rate of release was as high as 27 mmol min^{-1} for one subject. In ordinary two-legged exercise a rate of lactate entering the blood of 4–7 mmol min^{-1} has been found (Jorfelt, Juhlin-Dannfelt & Karlsson, 1978; Katz *et*

al. 1986). Thus, the present data for anaerobic energy yield obtained during exhaustive exercise with a small muscle group in man cannot be extrapolated to the whole body, and values of 100 ml O_2 (kg body wt)$^{-1}$ are likely peak values.

In this context recent data obtained on racehorses are of interest as they support this conclusion. A maximal oxygen deficit of up to 168 ml (kg body wt)$^{-1}$ has been

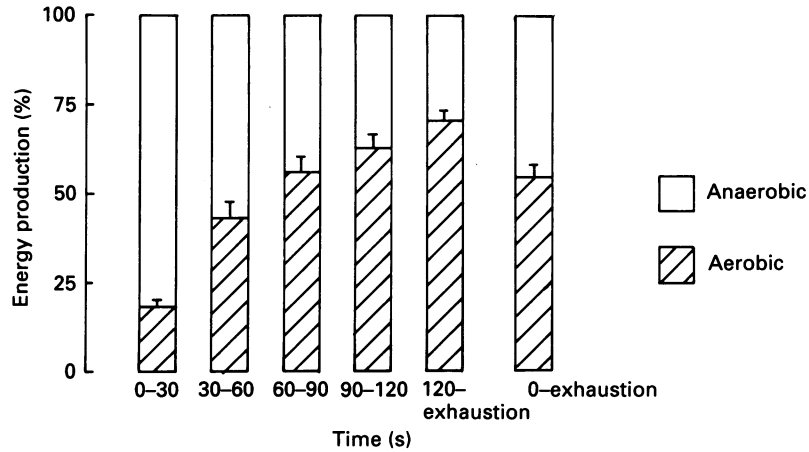

Fig. 9. The relative contribution of aerobic and anaerobic energy yield during different periods of intense exercise to exhaustion (left) and during the whole exercise period (0–exhaustion, right). Means ± S.E.M. are given.

reported (Rose, Hodgson, Kelso, McCutcheon, Reid, Bayly & Gollnick, 1988). A galloping horse can engage a very large fraction of its muscle maximally, and the elevation in muscle lactate as well as reductions in [ATP] and [CP] are slightly more pronounced than in the present study. Furthermore during exercise the horse can probably elevate the cardiac output to a value 2–3 times higher per kilogram body weight than man. Accordingly the horse is able to maintain a high perfusion of all muscles during the exercises, which optimizes the elimination of lactate from the muscles during the exhaustive exercise. Another example of the role of muscle perfusion and lactate elimination from the muscle during the exercise for the magnitude of the lactacid anaerobic energy release can be obtained by comparing our data on the total anaerobic yield which was 380 mmol ATP (kg dry wt)$^{-1}$ (= 92 mmol ATP (kg wet wt)$^{-1}$) with 295 mmol (kg dry wt)$^{-1}$ which is the value found for the same muscle group with arrested circulation (Spriet *et al.* 1987*a*).

The design of our study made it possible to evaluate the relative role of the anaerobic and aerobic energy yield at various phases of the exercise. In the first half-minute of exercise, oxygen uptake by the muscle accounted for 20% of the total energy turnover, in the second minute this increased to 50% and peaked at approximately 70% during the last phase of the exercise (Fig. 9). The measurements for the whole-body oxygen uptake have a similar time course for its contribution to the energy delivery, but they do not give a proper quantitative value for the oxygen utilization of the contracting muscles.

Both leg blood flow and leg oxygen uptake increased linearly with the submaximal exercise intensities. However, a further elevation did not occur in either variable at peak exercise, during which the values for leg blood flow and oxygen uptake barely reached those obtained at the highest submaximal work intensity (50 W; Table 1; Fig. 3). It could be argued that the work time was too short for these variables to accelerate to true peak values. However, 75% of the increase in flow occurred during the first minute of the intense exercise. Furthermore, systemic blood pressure was also elevated considerably. A more likely explanation for the levelling off is a mechanical hindrance to flow. In the supine position performing at the very high work intensity ($\approx$ 65 W) the contraction occupies a very substantial fraction of the 1 s duty cycle; indeed more than 50% or 0·6 s in comparison to 0·35–0·45 s during submaximal exercise. It is very unlikely that any perfusion occurs during the contraction (Walløe & Wesche, 1988). Moreover the duration of time between contractions becomes critical and the 0·4 s between contractions during the high work intensity may be too short for adequate perfusion. In the present study we are on the verge of demonstrating a functional significance both in regard to blood flow and oxygen extraction. The leg vascular resistance was slightly higher and the femoral arterial–venous O_2 difference narrower during the exhaustive exercise than that observed during the heaviest submaximal work intensity (50 W). Furthermore, blood flow and oxygen extraction could have been anticipated to be larger during the exhaustive exercise than at 50 W since pH and P_{CO_2}, factors related to vasodilatation and unloading of the oxygen from the Hb in the muscle capillary bed, were more extreme.

In conclusion, this study has proved that in small muscle group exhaustive exercise, oxygen deficit and estimations of the energy yield, based on ATP and CP reductions and lactate production of the active muscle, give similar values for the anaerobic energy release, where the nucleotides and CP, lactate accumulation and net release of lactate contributed with 20, 53 and 27%, respectively. The oxygen debt measurement, regardless of whether it was made over the active muscle or for the whole body, markedly overestimated the anaerobic energy release.

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