

MALLEABILITY OF THE SYSTEM IN OVERCOMING LIMITATIONS: FUNCTIONAL ELEMENTS

By B. SALTIN

August Krogh Institute, Copenhagen University, Copenhagen

SUMMARY

Three different views can be found in the literature concerning the classical question in exercise physiology: what limits maximal oxygen uptake in man? Some authors believe that the limitation is the maximal rate of oxygen delivery by the cardiovascular system. Others argue that oxygen uptake is limited by the capillary bed or metabolic capacity of skeletal muscle, and the third line of thought is that no single factor can be found to be directly limiting as all links in the oxygen transport are so closely matched. The stand taken in this paper is that the skeletal muscle of man can be excluded as a limiting factor for maximal oxygen uptake in whole body exercise. It can be shown, by direct measurements, that in sedentary and in trained man maximal perfusion and oxygen utilization of skeletal muscle is so high that if all muscles in the body were engaged in intense exercise, the cardiac pump function would have to be 2–3 fold larger than it is. What happens in whole body exercise is that each muscle group receives only a fraction of the blood it can accommodate. The primary role for a larger capillary network observed in trained muscles is to keep or extend mean transit time. Elevated mitochondrial enzyme activities affect the metabolic response (i.e. lipid oxidation is elevated in trained muscles). However, these adaptations are not necessary for increasing the maximal oxygen uptake of man, as the capacity of the heart is limiting. Improved training techniques (which induce even larger improvements in cardiac pump function) may reveal that pulmonary diffusion capacity is the limiting factor.

INTRODUCTION

Adaptations to physical activity or inactivity can be described in terms of performance criteria or functional criteria. Performance criteria include the ability to perform work at specified rates and durations. Physical training increases the ability to perform work; a period of inactivity decreases it.

Functional criteria of adaptation include the magnitudes of alterations in various systems (e.g. in respiration, circulation and metabolism). A good way to quantify the adaptation to physical activity or inactivity in functional terms has been to determine maximal oxygen uptake ($\dot{V}_{O_2 \max}$). The test provides an objective measurement of the functional capacity of whichever system or systems may limit oxygen uptake (i.e. respiratory, cardiovascular and/or metabolic systems). The respiratory system is

Key words: Work capacity, circulation, muscle blood flow.

thought to impose no limitation in normal man (Holmgren & Åstrand, 1966). Some see $\dot{V}_{O_2\max}$ as a limit set on the body's maximal rate of oxygen delivery by the cardiovascular system (Ekblom, 1969; Rowell, 1974), a view favoured in this presentation. Others argue that oxygen uptake is limited by the capillary bed or the metabolic capacity of skeletal muscle (Kaijser, 1970; Holloszy & Booth, 1976; Ingjer, 1978, 1979). The view is also advanced that all links of the oxygen transporting system of man are so closely related that no single factor can be found to limit maximal oxygen uptake (Di Prampero, 1985). It is questionable whether the observed close statistical relationship between respiratory, cardiovascular and skeletal muscle variables observed by many (Åstrand, 1952; Holmgren & Åstrand, 1966; Ingjer, 1978; Mathieu *et al.* 1981) really can be used as an argument for one link not being limiting.

The functional capacity of human skeletal muscle for an increase in blood flow and oxygen consumption is unknown. To approach this problem investigations have been made in which a small fraction of the muscle mass is engaged in the exercise. By studying the circulatory response at various levels of work, including exhaustive exercise, the maximal capacity of the muscle to accommodate a flow and consume oxygen per unit of muscle mass can be measured.

EXERCISE MODEL AND MUSCLE MASS ENGAGED IN THE EXERCISE

The knee-extensors of one limb were chosen to perform the exercise. The contractions could readily be limited to this muscle as verified by EMG recordings (Andersen *et al.* 1985). Further, the exercise caused a marked haemodynamic response not only in the exercising limb, but also in the whole body. The dynamic work with the knee-extensors was performed at a rate of 60 contractions per minute, using the experimental set-up shown in Fig. 1. The contraction of the quadriceps femoris muscle caused the lower part of the leg to extend from about 90° to 160° flexion. The angle of the hip was fixed at 90°. Fly-wheel momentum helps to return the leg to its relaxed position. In order to familiarize the subjects with the exercise and establish their performance capacity, they had to practise several times before the actual experiments. In this way it was possible for the subjects to exercise exclusively with the knee-extensors at all work loads.

To obtain values for the thigh volume, surface measurements of the subjects' thigh lengths and circumferences were taken together with skinfold measurements of the thigh. Thigh volume could then be calculated (Jones & Pearson, 1969; Andersen & Saltin, 1985). The anthropometric method to determine the mass of the thigh was verified using computerized assisted tomography. A close correlation was found between the two methods using six subjects ($r = 0.96$; $P < 0.001$).

WHOLE BODY RESPONSE TO KNEE-EXTENSOR EXERCISE

Most subjects could perform at a work load of 40–45 W with the knee-extensors of one limb for at least 10 min. Some exceptional subjects could handle both 70 and 80 W without fatiguing. The pulmonary oxygen uptake increased linearly with the work

intensity from no-load exercise to the work levels just mentioned, with only a small inter-individual variation (Fig. 2). Based on the increase in oxygen uptake from a

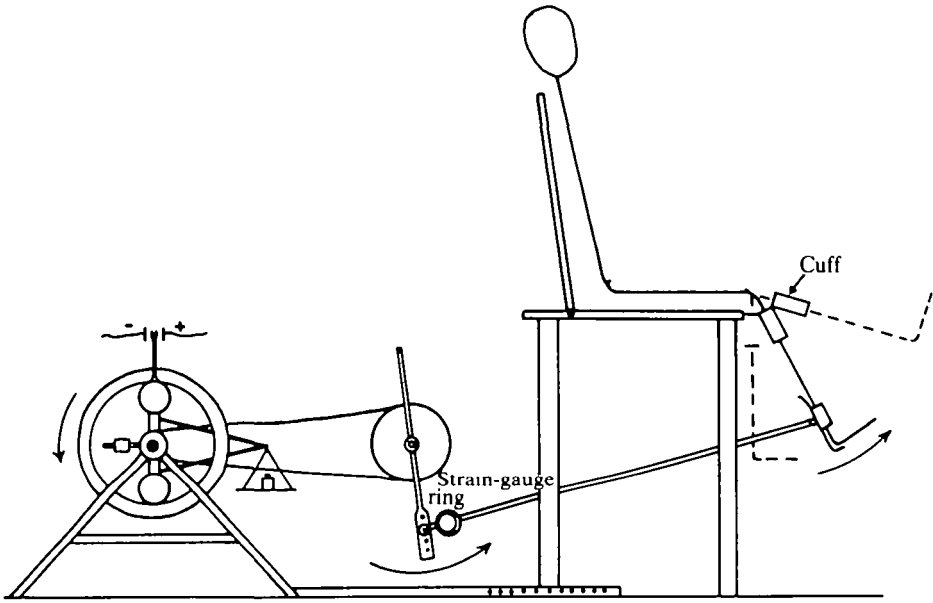


Fig. 1. A schematic drawing of the exercise-machine used (the modified Krogh bicycle ergometer for knee-extensor). (For details, see text.)

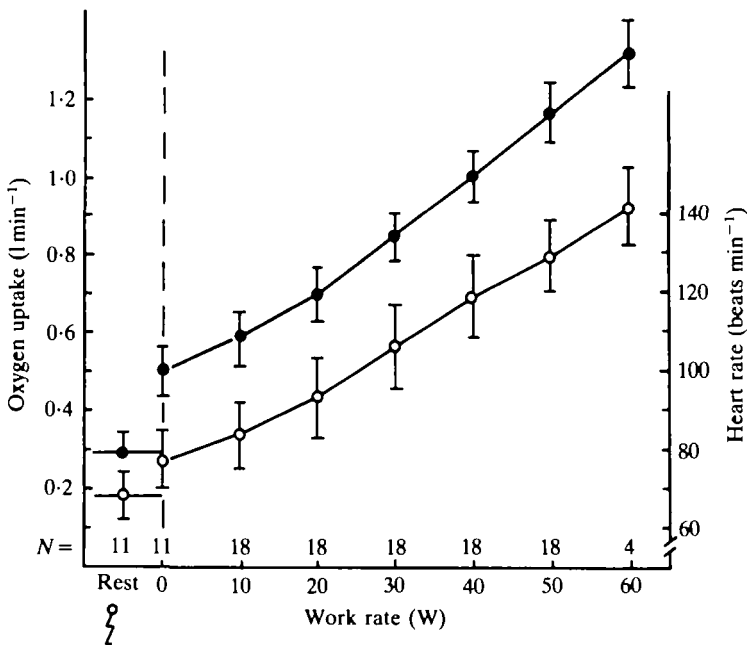


Fig. 2. Mean values (± 1 S.D.) for pulmonary oxygen uptake (●) and heart rate (○) at rest and when exercising with various work loads with the knee-extensors. (Adapted from Andersen *et al.* 1985.)

work load of 10 W to one of 40 W, apparent mechanical efficiency was in the range of 22–25 %, just as is observed during ordinary bicycle exercise (Åstrand, 1960). In contrast to treadmill and two-legged bicycle exercise, no levelling off could be established for whole body oxygen uptake when exercising with the knee-extensors of one limb. Instead an upward deflection in pulmonary oxygen uptake was observed when the exercise intensity was such that exhaustion in the knee-extensor occurred within 3–5 min. This point of deflection was closely related to the work capacity of the subject (Fig. 3). The explanation for this finding is that at these intense work rates additional muscle groups are engaged to stabilize the hip.

Heart rate increased linearly with the work load up to a peak value of 141 beats min^{-1} (Fig. 2). The individual variation both at submaximal and at maximal work rates was noticeable. Blood pressure during knee-extensor exercise did not vary much between subjects. No elevation in mean blood pressure was recorded at low work loads. Beyond a work load of 30 W (over 50–60 % of knee-extensor oxygen uptake)

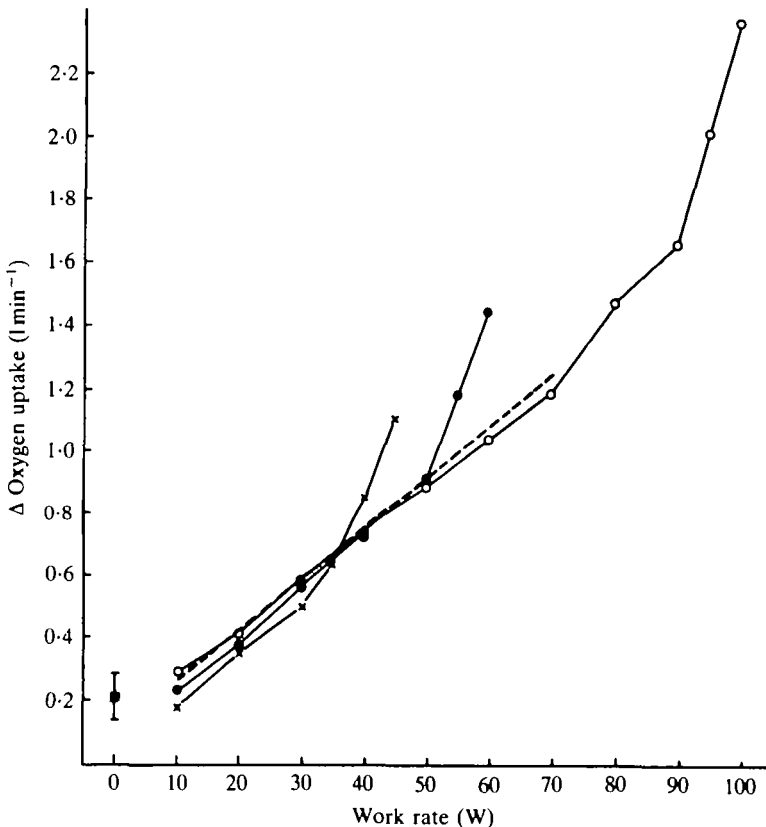


Fig. 3. Individual values for three subjects (●, ○ and ×) with marked variation in work performance. Pulmonary oxygen uptake (observed \dot{V}_{O_2}) during exercise—resting \dot{V}_{O_2} at no-load exercise and various work intensities are given. Note the upward deflection in pulmonary oxygen uptake occurring at quite different levels of exercise related to the work capacity of the subject. (---), mean $\Delta\dot{V}_{O_2}$, $N = 18$. (From Andersen *et al.* 1985.)

mean blood pressure became elevated and reached 133 mmHg at 60 W. The increase in mean blood pressure was due to an elevation in both systolic and diastolic pressures.

LIMB RESPONSE

Blood flow measured in the femoral vein was between 0.15 and 0.40 l min⁻¹ at rest in the sitting position. During no-load exercise the mean blood flow rose to 1.45 l min⁻¹. From this level, flow increased linearly with increasing work rate, with no tendency to decline at the very intense work rates. Mean maximal blood flow reached 6.2 l min⁻¹ (Fig. 4).

Some variations in blood flow were observed between the various subjects at a given work rate. In general, this variation was a function of a haemoglobin content (i.e. a low haemoglobin concentration and a low arterial oxygen content were compensated for by a large flow). Arterial oxygen saturation averaged 98% at rest and remained at this level at all work rates. A small haemoconcentration from rest to maximal work was noticed, which caused arterial oxygen content to increase from 19.6, at rest, to 20.6 vol% at 60 W.

Mean femoral vein O₂ saturation was 74% at rest and dropped to 40% at no-load exercise. A further gradual reduction occurred reaching 26% (range 24–29%) at the heaviest work rate. This resulted in a femoral vein oxygen content of 6 vol% at peak exercise and an a-v_{O₂} difference over the exercising limb of 'only' 14.6 vol% during exhaustive exercise (Fig. 4).

A further indication of a rather incomplete extraction of oxygen by the exercising muscles comes from the P_{O₂} values in the femoral vein blood. At rest (sitting) a mean P_{O₂} of 48 mmHg was measured and at no-load exercise, 32 mmHg was found. Maximal exercise caused P_{O₂} only to drop to a mean of 24 mmHg (Fig. 5).

At rest, knee-extensor oxygen uptake (blood flow × a-v_{fem} oxygen difference) was between 6 and 12 ml min⁻¹. At no-load exercise it increased to 0.19 l min⁻¹. Similarly to pulmonary oxygen uptake, leg oxygen uptake increased linearly up to the maximal level of work reaching an average of 0.72 l min⁻¹ (Fig. 4). At 60 W, the upper values for limb oxygen uptake varied closely with the work performed just as did the maximal blood flow. The oxygen uptake of the sedentary subjects ranged from 0.52 to 0.76 l min⁻¹, whereas it reached values of up to 1.0 l min⁻¹ in the very fit subjects.

Arterial and femoral vein lactate concentrations were low at rest and with work loads of up to 30 W (50–60% of knee-extension oxygen uptake). At 40 W a significant increase in femoral vein lactate above arterial blood lactate occurred. At exhaustive exercise the a-v difference for lactate (2–2.5 vs 4–6.5 mmol l⁻¹ lactate in arterial and femoral vein blood, respectively) was in the range of 1.5–3.0 mmol l⁻¹. With blood flows of around 6 l min⁻¹ the lactate release was 9 mmol min⁻¹ or more. The pH averaged around 7.4 in arterial and venous blood at light work loads. At peak exercise the pH in femoral vein blood was reduced to 7.18, whereas arterial blood was still only reduced to 7.34.

THIGH VOLUME AND ITS CONTENT OF CAPILLARIES

The mass of the thigh, measured using anthropometric methods, gave a mean value of 2.6 kg, which corresponded with the 2.5 kg value obtained using the CAT-

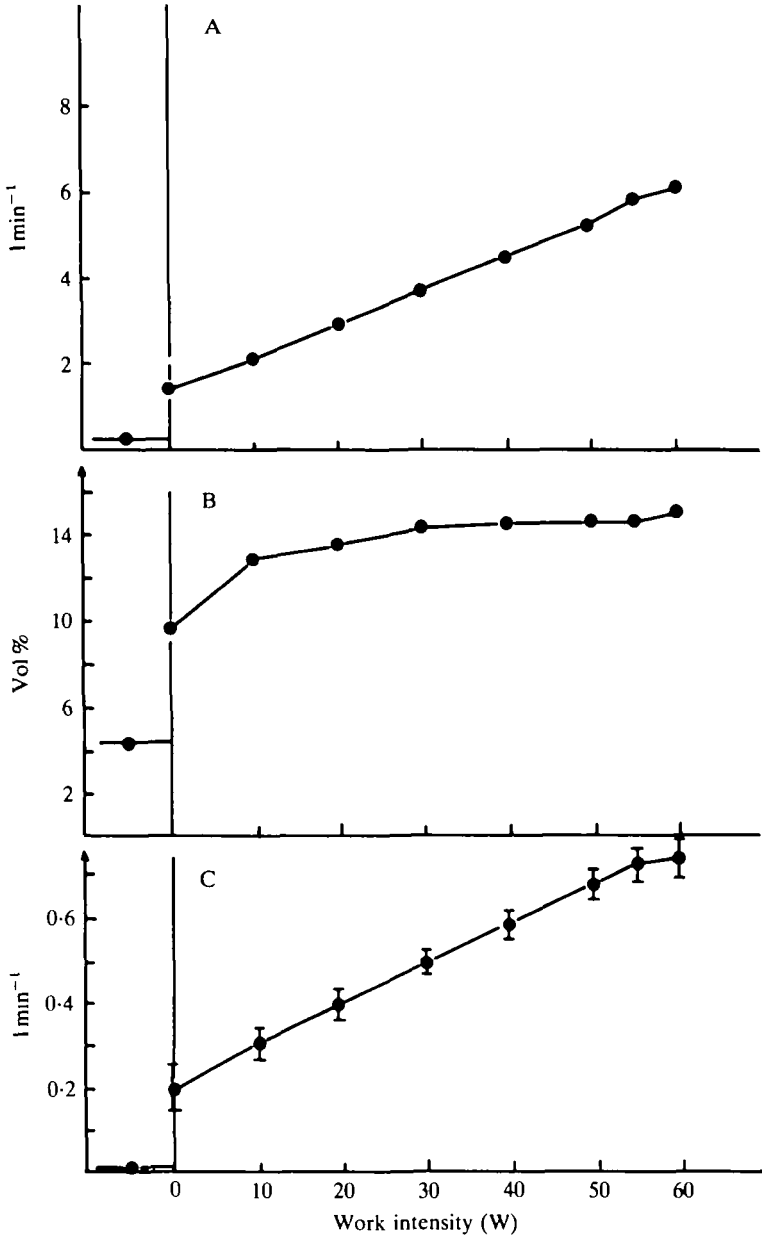


Fig. 4. Mean values for (A) blood flow, measured with a thermodilution technique in the femoral vein (Andersen & Saltin, 1985), (B) $a-v_{\text{fem}}$ oxygen difference and (C) muscle oxygen uptake at rest and various work intensities performed with the knee-extensors of one limb. $N = 12$ at work loads up to 50 W, 8 at 55 W and 4 at 60 W.

technique. For the whole group of subjects, the mean was 2.7 kg with a range of 2.15–3.05 kg. Capillaries in the thigh muscles averaged 376 mm⁻² with a marked variation between the subjects, related mainly to the training status; the range was from 270 to 520 mm⁻² (Table 1).

DISCUSSION

A calculation of maximal perfusion of skeletal muscle based on the present results gives values of 2.35 l min⁻¹ kg⁻¹ or 235 ml 100 g⁻¹ min⁻¹ with a range among the

Table 1. Mean values for certain variables for subjects grouped as low performers (low; N = 5) or high performers (high; N = 3) and in four subjects who have trained one leg (non-trained leg = NT-leg and trained leg = T-leg)

	Flow (ml kg ⁻¹ min ⁻¹)	a-v _{fem} O ₂ (ml l ⁻¹)	Capillary density (mm ⁻²)	Capillary blood volume (vol %)	Mean transit time (ms)
'Low'	2100	123	280	0.8	380
NT-leg	2350	131	320	0.9	395
'High'	2750	149	440	1.4	425
T-leg	2600	138	380	1.1	510

The mean transit time is estimated based on a capillary diameter of 6 μm and on the assumption that 90–100 % of all capillaries have a flow.

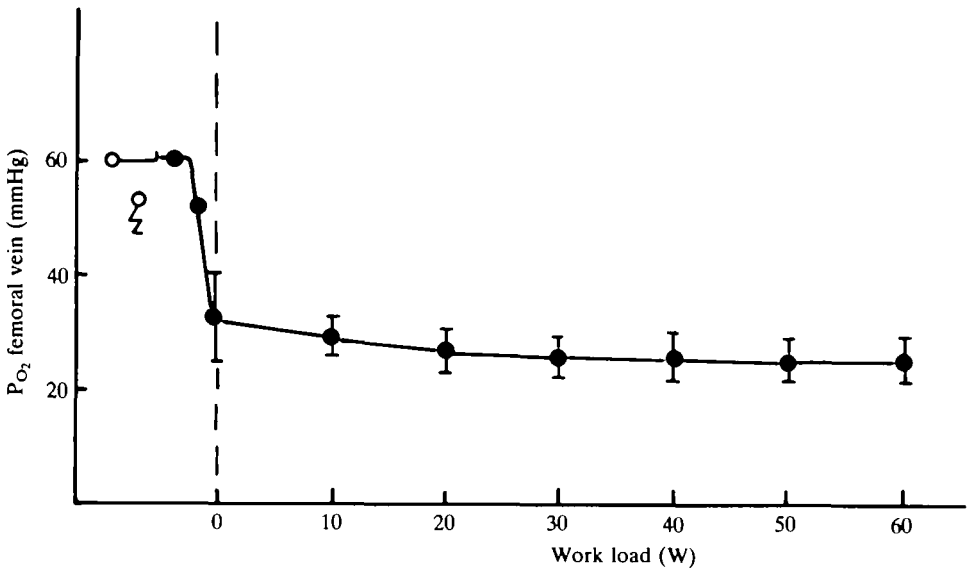


Fig. 5. Oxygen tension in the femoral vein blood draining the contracting knee-extensor muscles (N, see Fig. 4).

present subjects of $185\text{--}280\text{ ml } 100\text{ g}^{-1}\text{ min}^{-1}$ (Fig. 6). These values are very probably overestimated as the measured flow in the femoral vein not only includes a drainage from the knee-extensors, but also from the inactive hamstrings and other tissues of the thigh. There are good reasons to assume that this 'extra' flow at the most amounts to 10% of the observed values as discussed by Andersen & Saltin (1985). However, even after correcting the observed perfusion values by a 10% reduction, it is apparent that skeletal muscle of man can accommodate quite a high flow. In fact, the present findings for muscle blood flow are larger than those earlier reported by a factor of two (Grimby, Häggendal & Saltin, 1967; Clausen, 1976; Mellander, 1981). It is of note that, in recent studies of skeletal muscle blood flow in species other than man, a perfusion of $200\text{ ml } 100\text{ g}^{-1}\text{ min}^{-1}$ or more is frequently observed (Laughlin & Armstrong, 1982; Mackie & Terjung, 1983). The degree of capillarization in the muscles of these animals is in the same range as found in man (see also Mellander, 1981). As skeletal muscle is able to accommodate a flow of $200\text{ ml } 100\text{ g}^{-1}\text{ min}^{-1}$ or more, it is easy to see that if all muscles of man were intensely engaged in the exercise, a cardiac output of $50\text{--}60\text{ l min}^{-1}$ or more would be required. Such high values have never been reported; this is true even for the very best trained endurance athletes (Ekblom & Hermansen, 1968). Normal values of cardiac output in sedentary and trained subjects are $20\text{--}30\text{ l min}^{-1}$ (Blomqvist & Saltin, 1983).

Support for the view that the flow is 'excessive' in knee-extensor exercise is the finding of a rather low extraction of oxygen by the exercising muscles. In intense two-

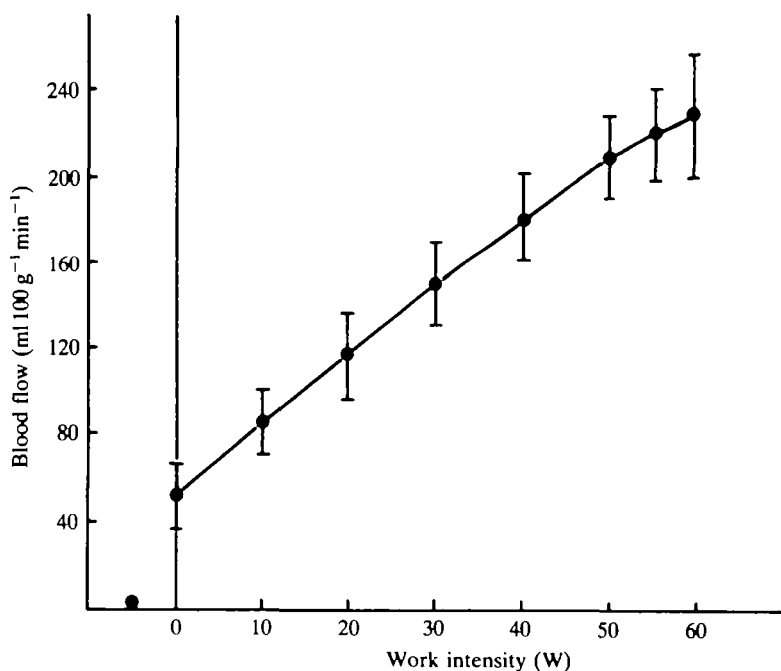


Fig. 6. Mean (\pm S.D.) knee-extensor blood flow expressed in $\text{ml } 100\text{ g}^{-1}\text{ min}^{-1}$ at rest and at various work loads. The small decline at the most intense exercise rate is not significant, but due to varying N , which is the same as in Fig. 4.

legged exercise, femoral vein oxygen saturation is usually 2–4% and P_{O_2} may be as low as 8–12 mmHg (Doll & Keul, 1968; Saltin *et al.* 1968). This poor oxygen extraction may be explained by extremely short mean transit times (MTT). From the capillary counts, the volume of the capillary bed can be estimated fairly well, as the mean diameter of capillaries in skeletal muscles of man is approximately 6 μm . Whether all capillaries are open during maximal exercise is not known, but it is likely, as Gray, McDonagh & Gore (1983) have shown that 80% or more of the capillaries are open when the muscle is in use. The estimated MTT in the present subjects at peak exercise amounts to only 400–500 ms (Table 1). It is interesting that a relationship appears to exist between capillary density and MTT: the subjects having the largest MTT also had the largest extraction (i.e. the highest $a-v_{\text{fem}}$ difference). The primary reason for the observed alteration in capillary density of the skeletal muscle in relation to its usage is thus not the ability to accommodate a large flow but to enable an adequate MTT, thereby making it possible for an optimal exchange of gases, substrates and metabolites as the blood passes through the capillary. If the data in Table 1 are extrapolated to a value of MTT which would allow for an $a-v_{\text{fem}}$ oxygen difference of 170–180 ml l^{-1} (as measured in whole body exercise), the value obtained would be in the range of 800–900 ms. With a capillary density of 350 mm^{-2} (capillary blood volume, 1.0 vol%) and flow in all capillaries, muscle blood flow could, at the most, be in the range of 1.2–1.3 $\text{l kg}^{-1} \text{min}^{-1}$ (i.e. 50–60% of the values observed in the present study). Thus, it would seem that during exercise, each muscle group does indeed only receive a fraction of the blood flow, which it would otherwise get if it was the only group exercising in the body.

The question then arises whether an elevation in mitochondrial enzyme activity is a prerequisite for an elevation in maximal oxygen uptake. The answer appears to be no. In sedentary as well as in trained man the high oxygen delivery to the knee-extensor muscle results in peak oxygen uptake of the muscle which is of the order of 0.25 $\text{l kg}^{-1} \text{min}^{-1}$ up to close to 0.45 $\text{l kg}^{-1} \text{min}^{-1}$ in the fittest subjects. Thus, when more oxygen is offered to the muscles than they usually are supplied with, the muscle has the capacity to utilize it. This is in line with the fact that the aerobic metabolic potential of skeletal muscle of man exceeds the amount of oxygen made available for it during exercise (cf. Gollnick, Riedy, Quintinskie & Bertocci, 1985).

In summary, it can be said that it is possible to identify one link which limits oxygen transport and utilization in man during intense exercise. The skeletal muscles do not limit maximal oxygen if more than one-third or more of the muscle mass is intensely involved in the exercise. Instead it is the heart and its capacity to supply the contracting muscles with a blood flow which is limiting. However, as concluded elsewhere (Blomqvist & Saltin, 1983), training techniques that induce even larger improvements in cardiac pump performance than observed today may reveal that pulmonary diffusing capacity is the ultimate limiting factor.

REFERENCES

- ANDERSEN, P., ADAMS, R. P., SJØGAARD, G., THORBOE, A. & SALTIN, B. (1985). Dynamic knee-extension as a model for the study of an isolated exercising muscle in man. *J. appl. Physiol.* (in press).

- ANDERSEN, P. & SALTIN, B. (1985). Maximal perfusion of skeletal muscle in man. *J. Physiol., Lond.* (in press).
- ÅSTRAND, I. (1960). Aerobic work capacity in men and women with special reference to age. *Acta physiol. scand. (Suppl.)* **49**, 169.
- ÅSTRAND, P.-O. (1952). *Experimental Studies of Physical Working Capacity in Relation to Sex and Age*. Copenhagen: Munksgaard.
- BLOMQUIST, C. G. & SALTIN, B. (1983). Cardiovascular adaptations to physical training. *A. Rev. Physiol.* **45**, 169–189.
- CLAUSEN, J. P. (1976). Circulatory adjustments to dynamic exercise and effect of physical training in normal subjects and in patients with coronary artery disease. *Prog. Cardiovasc. Dis.* **18**, 459–495.
- DI PRAMPERO, P. (1985). Metabolic and circulatory limitations to \dot{V}_{O_2} max at the whole animal level. *J. exp. Biol.* **115**, 319–331.
- DOLL, E. & KEUL, J. (1968). Zum Stoffwechsel des Skelettmuskels. II. Sauerstoffdruck, Kohlensäuredruck, pH, Standardbikarbonat und base excess im venösen Blut der arbeitenden Muskulatur. Untersuchungen an Hochleistungsportlern. *Pflügers Arch. ges. Physiol.* **301**, 214.
- EKBLOM, B. (1969). The effect of physical training on oxygen transport system in man. *Acta physiol. scand. (Suppl.)* **328**, 1–45.
- EKBLOM, B. & HERMANSEN, L. (1968). Cardiac output in athletes. *J. appl. Physiol.* **25**, 619–625.
- GOLLNICK, P. D., RIEDY, M., QUINTINSKIE, J. J. & BERTOCCI, L. A. (1985). Differences in metabolic potential of skeletal muscle fibres and their significance for metabolic control. *J. exp. Biol.* **115**, 191–199.
- GRAY, S. D., McDONAGH, P. F. & GORE, R. W. (1983). Comparison of functional and total capillarity densities in fast and slow muscles of the chicken. *Pflügers Arch. ges. Physiol.* **397**, 209–213.
- GRIMBY, G., HÄGGENDAL, E. & SALTIN, B. (1967). Local xenon 133 clearance from the quadriceps muscle during exercise in man. *J. appl. Physiol.* **22**, 305–310.
- HOLLOSZY, J. O. & BOOTH, F. W. (1976). Biochemical adaptations to endurance training in muscle. *A. Rev. Physiol.* **38**, 273–291.
- HOLMGREN, A. & ÅSTRAND, P.-O. (1966). DL and the dimensions and functional capacities of the O₂ transport system in humans. *J. appl. Physiol.* **21**, 1463–1470.
- INGJER, F. (1978). Maximal aerobic power related to the capillary supply of the quadriceps femoris muscle of man. *Acta physiol. scand.* **104**, 238–270.
- INGJER, F. (1979). Effects of endurance training on muscle fibre ATP-ase activity capillary supply, and mitochondrial content in man. *J. Physiol., Lond.* **294**, 419–422.
- JONES, P. R. M. & PEARSON, J. (1969). Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. *J. Physiol., Lond.* **219**, 63P.
- KAUSER, L. (1970). Limiting factors for aerobic muscle performance. *Acta physiol. scand. (Suppl.)* **346**, 1–96.
- LAUGHLIN, M. H. & ARMSTRONG, R. B. (1982). Muscular blood flow distribution patterns as a function of running speed in rats. *Am. J. Physiol.* **243**, H296–H306.
- MACKIE, B. G. & TERJUNG, R. L. (1983). Blood flow to different skeletal muscle fiber types during contraction. *Am. J. Physiol.* **245**, H264–H275.
- MATHIEU, O., KRAUER, R., HOPPELER, H., GEHR, P., LINDSTEDT, S. L., ALEXANDER, R. MCN., TAYLOR, C. R. & WEIBEL, E. R. (1981). Design of the mammalian respiratory system. VII. Scaling mitochondrial volume in skeletal muscle to body mass. *Respir. Physiol.* **44**, 113–128.
- MELLANDER, S. (1981). Differentiation of fiber composition, circulation, and metabolism in limb muscles of dog, cat and man. In *Mechanism of Vasodilation*, (eds P. M. Vanhoutte & J. Jensen), pp. 243–254. New York: Raven Press.
- ROWELL, L. B. (1974). Human cardiovascular adjustments to exercise and thermal stress. *Physiol. Rev.* **54**, 75–159.
- SALTIN, B., BLOMQUIST, G., MITCHELL, J. H., JOHNSON, R. L., JR., WILDENTHAL, K. & CHAPMAN, C. B. (1968). Response to exercise after bed rest and after training. *Circulation* **7**, 1–78.