J. exp. Biol. **115**, 319–331 (1985)
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METABOLIC AND CIRCULATORY LIMITATIONS TO $\dot{V}_{O_2}max$ AT THE WHOLE ANIMAL LEVEL

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SUMMARY

The O_2 path from environment to mitochondria can be viewed as a cascade of resistances in series, each being overcome by a specific pressure gradient (O_2 conductance equation). To assess the relative importance of the different factors that can set a limit to $\dot{V}_{O_2}max$, three sets of resistances will be identified, RQ, Rc and Rm, inversely proportional to: O_2 transport ($\dot{Q}max \times [Hb]$), RQ; capillary cross section, Rc; and succinic dehydrogenase (SDH) activity, Rm. Published data show that changes of $\dot{V}_{O_2}max$ can be induced by altering the blood O_2 capacity, or by training, and that these changes are accompanied by measured changes of the above identified resistances. From these data, the ratio of each resistance to the overall resistance can be calculated by algebraic manipulation of the O_2 conductance equation, expressed in relative form. It can thus be shown that: (1) in two-legged exercise, about 75 % of $\dot{V}_{O_2}max$ is set by O_2 transport, the remaining fraction being about equally partitioned between the two peripheral factors indicated above, and that (2) in one-legged exercise, the limits to $\dot{V}_{O_2}max$ are about equally set by central and peripheral factors.

Maximal O_2 consumption ($\dot{V}_{O_2}max$) increases with increasing O_2 partial pressure in inspired air (Bannister & Cunningham, 1954; Fagraeus, Karlsson, Linnarsson & Saltin, 1973; Kaijser, 1970; Margaria, Camporesi, Aghemo & Sassi, 1972; Margaria, Cerretelli, Marchi & Rossi, 1961; Nielsen & Hansen, 1937; Welch & Pedersen, 1981) and following the transfusion of red blood cells (Buick *et al.* 1980; Ekblom, Goldbarg & Gullbring, 1972; Ekblom, Wilson & Åstrand, 1976); it decreases in hypoxia (both acute and chronic) (see Cerretelli, 1981 for review), following CO inhalation (Ekblom & Huot, 1972; Ekblom, Huot, Stein & Sthorstenson, 1975; Pirnay, Dujardin, Deroanne & Petit, 1971; Raven *et al.* 1974; Vogel & Gleser, 1972) and after acute anaemia (Woodson, Wills & Lenfant, 1978).

It is generally inferred from these data that, at sea level, $\dot{V}_{O_2}max$ is limited essentially by the O_2 transport system (cardiac output times blood O_2-carrying capacity). However, several other factors, such as peripheral circulation, O_2 diffusion at the muscle level and mitochondrial capacity, have also been considered among the

Key words: $\dot{V}_{O_2}max$ limitations, blood infusion, two-legged *vs* one-legged training.

possible factors that set a limit to $\dot{V}_{O_2}max$, particularly during exercise with small muscle groups (see for instance, Kaijser, 1970; Saltin, 1977).

The following article is devoted to a discussion of the factors limiting $\dot{V}_{O_2}max$.

The O_2 path from the environment to the mitochondria can be viewed as a cascade of resistances in series, each individual resistance (Ri) being overcome by a specific O_2 pressure gradient (ΔPi). In this model, the O_2 flow through each section is equal to the overall flow through the system, and the overall resistance, R_T is given by the sum of the n resistances in series:

$$\dot{V}_{O_2} = \frac{\Sigma_{i=1}^{n} \Delta Pi}{\Sigma_{i=1}^{n} Ri} = \frac{\Delta P_T}{R_T} \quad , \tag{1}$$

where ΔP_T is the overall O_2 pressure gradient from the environment to the mitochondria.

Equation 1 can be utilized to calculate each individual Ri, provided that the corresponding pressure gradient can be measured, or estimated. However, the procedure requires several assumptions and complex calculations (Shephard, 1976).

A somewhat different approach is developed here. Published values of the change in $\dot{V}_{O_2}max$, induced by altering acutely the blood O_2 capacity or by training, and resulting from (or accompanied by) measured changes of other physiological parameters that can be likened to individual resistances, are entered into equation 1 expressed in relative form. It is then possible to calculate the ratio of each individual Ri to the overall resistance R_T.

THEORY

As a first approximation, when exercising at $\dot{V}_{O_2}max$, equation 1 becomes:

$$\dot{V}_{O_2}max = \frac{\Delta P_T}{R_T} = \frac{\Delta P_T}{RQ + Rc + Rm} \quad , \tag{2}$$

where the following three individual resistances have been identified.

(1) RQ, inversely proportional to maximal cardiac output and to the average slope of the blood O_2 dissociation curve.

(2) Rc, inversely proportional to peripheral diffusion and perfusion, which in turn depend on the O_2 diffusion coefficient from the capillary to the cells, on the surface and volume of the capillary bed, and on the average distance between capillary and cell.

(3) Rm, inversely proportional to mitochondrial O_2 utilization capacity. The latter depends on the molecular conductance for O_2, the surface of the inner mitochondrial membrane, and on the total volume of mitochondria.

The reader is referred to Taylor & Weibel (1981), for a detailed discussion of the physiological and morphological parameters on which RQ, Rc and Rm depend, and to

Table 1. *Average effects on the indicated number of subjects* (N) *of withdrawal or infusion of red blood cells (or blood) on* $\dot{V}_{O_2}max$ *(1 min^{-1}),* $\dot{Q}max$ *(1 min^{-1}) and [Hb] (g dl^{-1}), taken from the quoted references*

Reference	$\dot{V}_{O_2}max$	$\Delta\dot{V}_{O_2}max$	$\dot{Q}max$	$\Delta\dot{Q}max$	[Hb]	Δ [Hb]	Δ RQ/RQ	*N*	Notes
Buick *et al.* (1980)	5·33	+ 0·25	–	–	15·1	+ 1·2	− 0·080	6	
	4·85	+ 0·26	–	–	15·8	+ 0·9	− 0·057	5	
Ekblom, Goldbarg & Gullbring (1972)	4·57	− 0·48	–	–	14·6	− 1·9	0·130	3	
	4·40	+ 0·39	–	–	13·2	+ 1·7	− 0·129		
	4·49	− 0·28	–	–	14·9	− 1·6	0·107		Subsequent withdrawals (at
	4·49	− 0·46	–	–	14·9	− 2·3	0·154	4	2-day intervals) of 400,
	4·49	− 0·71	–	–	14·9	− 2·7	0·221		800 and 1200 ml blood
Ekblom, Wilson & Åstrand (1976)	4·27	− 0·24	28·7	+ 0·8	15·4	− 1·6	0·079	5	
	4·27	+ 0·34	28·7	− 0·4	14·7	+ 1·4	− 0·080		
Woodson, Wills & Lenfant (1978)	43·1	− 12·4	284	− 21	15·3	− 5·3	+ 0·395	4	Established anaemia. Not included in Fig. 1

In the experiments of Woodson, Wills & Lenfant (1978) $\dot{V}_{O_2}max$ and $\dot{Q}max$ are given in ml kg^{-1} min^{-1} and refer to conditions of established anaemia. Other reported data were measures immediately before, and within 2 days after, the experimental manipulation.

Δ RQ/RQ is the relative change of the resistance to O_2 transport calculated from the product $\dot{Q}max \cdot$ [Hb], when available, or from [Hb] alone, an increase of O_2 transport capacity leading to a negative value of Δ RQ/RQ.

The data obtained by Woodson *et al.* (1978) were not included in Fig. 1 since in conditions of established anaemia, the two peripheral resistances Rc and Rm may also have changed (see text for details).

Shephard (1969, 1976) for an analytical formulation of the corresponding pressure gradients.

Endurance training, or acute alterations of blood O_2 capacity, lead, as is well known, to changes of $\dot{V}_{O_2}max$. Under these conditions, *ceteris paribus*, the overall pressure gradient cannot be expected to change (ΔP_T = constant). Hence, assuming that the system behaves linearly, the changes of $\dot{V}_{O_2}max$ must be due to an equal (and opposite) change of the total resistance to flow:

$$\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max = \frac{\Delta P_T}{R_T + \Delta R_T} \quad . \tag{3}$$

Dividing equation 3 by equation 2 and rearranging:

$$\frac{\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max}{\dot{V}_{O_2}max} = \frac{1}{1+\Delta R_T/R_T} \quad . \tag{4}$$

Since $\Delta RT = \Delta RQ + \Delta Rc + \Delta Rm$, equation 4 becomes:

$$\frac{\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max}{\dot{V}_{O_2}max} = \frac{1}{1 + \frac{\Delta RQ}{R_T} + \frac{\Delta Rc}{R_T} + \frac{\Delta Rm}{R_T}} \quad , \tag{5}$$

which can be written in the equivalent form:

$$\frac{\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max}{\dot{V}_{O_2}max} = \frac{1}{1 + \frac{RQ}{R_T}\cdot\frac{\Delta RQ}{RQ} + \frac{Rc}{R_T}\cdot\frac{\Delta Rc}{Rc} + \frac{Rm}{R_T}\cdot\frac{\Delta Rm}{Rm}} \quad . \tag{5'}$$

By setting $\frac{RQ}{R_T} = FQ$, $\frac{Rc}{R_T} = Fc$, and $\frac{Rm}{R_T} = Fm$, equation 5′ becomes:

$$\frac{\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max}{\dot{V}_{O_2}max} = \frac{1}{1 + FQ\cdot\frac{\Delta RQ}{RQ} + Fc\cdot\frac{\Delta Rc}{Rc} + Fm\cdot\frac{\Delta Rm}{Rm}} \quad . \tag{6}$$

Thus, in equation 6, the three terms FQ, Fc and Fm indicate the fractional limitations of $\dot{V}_{O_2}max$ due to O_2 transport, peripheral perfusion and diffusion and mitochondrial capacity, respectively; while $\Delta RQ/RQ$, $\Delta Rc/Rc$ and $\Delta Rm/Rm$ are the relative

changes of the appropriate resistances. The resistances will be assumed to be inversely proportional:

(i) RQ, to maximal cardiac output ($\dot{Q}$max) times blood Hb concentration:

$$RQ = \frac{kQ}{\dot{Q}max \times [Hb]} ; \tag{7}$$

(ii) Rc, to capillary cross sectional area:

$$Rc = \frac{kc}{\text{capillary cross section}} ; \tag{8}$$

(iii) Rm, to mitochondrial SDH activity:

$$Rm = \frac{km}{SDH} . \tag{9}$$

When considering only the relative changes of resistance, as is the case in equation 6, the three constants kQ, kc and km cancel out. However, they have to be introduced for dimensional uniformity and they can be assigned, conventionally, the value of 1·0.

The changes of $\dot{Q}$max, [Hb], capillary cross section and SDH activity, elicited by appropriate experimental manipulations or by training, will be entered into equation 6 together with the corresponding changes of $\dot{V}_{O_2}$max. As detailed in the next section it will then become possible to estimate FQ, Fc and Fm from published data.

In this approach, it is assumed that pulmonary ventilation and lung diffusion are not among the major limiting factors, which seems justified for healthy subjects at sea level (Shephard, 1971).

It is interesting to note that the control of metabolic pathways has been analysed in a similar way by Kacser & Burns (1973, 1979). These authors define as 'sensitivity coefficient', Z, the very analogue of the quantity which is here defined as 'fractional limitation' of $\dot{V}_{O_2}$max, and given the symbol F.

CALCULATIONS

This section is devoted to an attempt to calculate the fractional limitations of $\dot{V}_{O_2}$max due to O_2 transport (FQ), peripheral perfusion and diffusion (Fc) and mitochondrial capacity (Fm) as from published data. Firstly, FQ will be estimated from the results of experiments in which the blood O_2-carrying capacity was acutely altered by withdrawal, or infusion, of red blood cells (or blood) and the resulting changes of $\dot{V}_{O_2}$max measured. Secondly, the three fractional limitations, FQ, Fc and Fm, will be estimated from the changes of $\dot{V}_{O_2}$max elicited by training and from the accompanying measured changes of maximal cardiac output, capillary cross sectional area and mitochondrial capacity.

The changes in $\dot{V}_{O_2}max$ resulting from manipulation of the blood are indicated in Table 1, together with the corresponding changes of Hb concentrations and, when available, of $\dot{Q}max$, as from the data of Buick *et al.* (1980); Ekblom *et al.* (1972, 1976) and Woodson *et al.* (1978). The corresponding changes of the resistance to O_2 transport, $\Delta RQ/RQ$ are also given. Since the experiments were done acutely, the other two sets of resistances (Rc and Rm) can reasonably be assumed not to change significantly. Hence $\Delta Rc = \Delta Rm = 0$, so that equation 6, once rearranged reduces to:

$$\frac{\dot{V}_{O_2}max}{\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max} = 1 + FQ\frac{\Delta RQ}{RQ} \cdot \qquad (10)$$

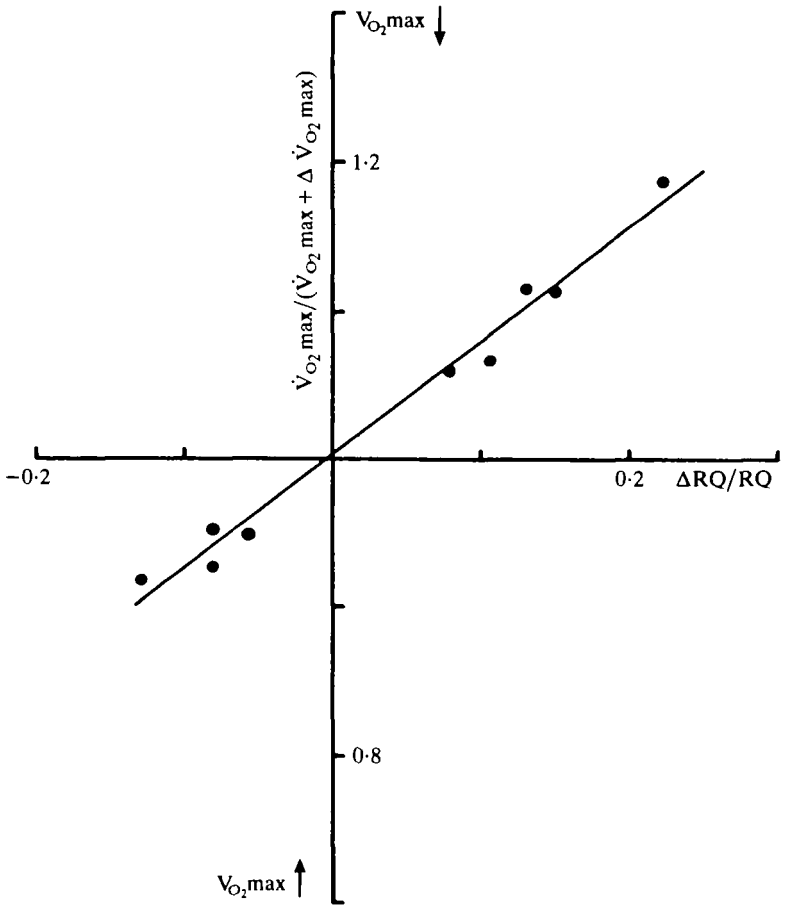

Fig. 1. Average changes of $\dot{V}_{O_2}max$ are plotted as a function of the changes of the resistance to O_2 transport, from the data of Table 1. The slope of the regression is the fractional limitation of $\dot{V}_{O_2}max$ due to O_2 transport, FQ = 0·775 (see text, equations 10 and 11). For references, see Table 1. $y = 1{\cdot}003 + 0{\cdot}775x$ ($r^2 = 0{\cdot}98$).

Least squares linear regression of the data of Table 1 yields (see Fig. 1):

$$y = 1{\cdot}003 + 0{\cdot}775x, \tag{11}$$

($r = 0{\cdot}99$; $N = 9$; $P < 0{\cdot}001$) where $y = \dot{V}_{O_2}max/(\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max)$ and $x = \Delta RQ/RQ$. Thus $FQ = 0{\cdot}78$.

From this first series of calculations it can then be concluded that the limitation of $\dot{V}_{O_2}max$ due to O_2 transport ($\dot{Q}max$ times blood O_2 capacity) amounts to about 80 % under these experimental conditions.

The percentage increase with training of: (1) $\dot{V}_{O_2}max$, (2) mitochondrial SDH activity, (3) capillary cross section per unit muscle surface and (4) maximal cardiac output are presented in Fig. 2, for two-legged (cycling) endurance training in man as from several sources (Andersen & Henriksson, 1977; Henriksson & Reitman, 1976, 1977; Ekblom *et al.* 1968; Saltin *et al.* 1968). (For a comprehensive review of skeletal muscle adaptations to training, see Saltin & Gollnick, 1983.) The subjects' mean increase in $\dot{V}_{O_2}max$ amounts to 18 %, while the corresponding increase in enzymatic activity amounts to 31·2 %, of capillary cross sectional area to 20 % and of maximal cardiac output to 11·3 %. Thus: $(\dot{V}_{O_2}max + \Delta\dot{V}_{O_2}max)/\dot{V}_{O_2}max = 1{\cdot}180$, $\Delta Rm/Rm = -0{\cdot}312$; $\Delta Rc/Rc = -0{\cdot}200$ and $\Delta RQ/RQ = -0{\cdot}113$. Inserting these values into equation 9, and rearranging, one obtains:

$$0{\cdot}132Fm + 0{\cdot}200Fc + 0{\cdot}113FQ = 0{\cdot}1525. \tag{12}$$

If it assumed that no other limiting factors exist besides the three considered,

$$Fm + Fc + FQ = 1{\cdot}0, \tag{13}$$

Table 2. *Fractional limitations of $\dot{V}_{O_2}max$, during one- and two-legged maximal exercise, due to: (1) O_2 transport ($\dot{Q}max$ times blood O_2 capacity), FQ, (2) capillary perfusion and diffusion, Fc, and (3) mitochondrial capacity, Fm*

	Two legs			One leg		
α	FQ	Fc	Fm	FQ	Fc	Fm
0·02	0·80	0·005	0·195	0·61	0·01	0·38
0·10	0·79	0·02	0·19	0·60	0·03	0·37
0·5	0·77	0·05	0·18	0·55	0·15	0·30
1·0	0·72	0·14	0·14	0·52	0·26	0·26
2·0	0·68	0·21	0·11	0·47	0·35	0·18
10	0·59	0·37	0·04	0·38	0·56	0·06
100	0·55	0·44	0·01	0·35	0·64	0·01

The three factors, FQ, Fc and Fm, are expressed in relative units ($FQ + Fc + Fm = 1{\cdot}0$), and the two peripheral ones are assumed to be interdependent, being related by the coefficient α: $Fc = \alpha Fm$. See text for details.

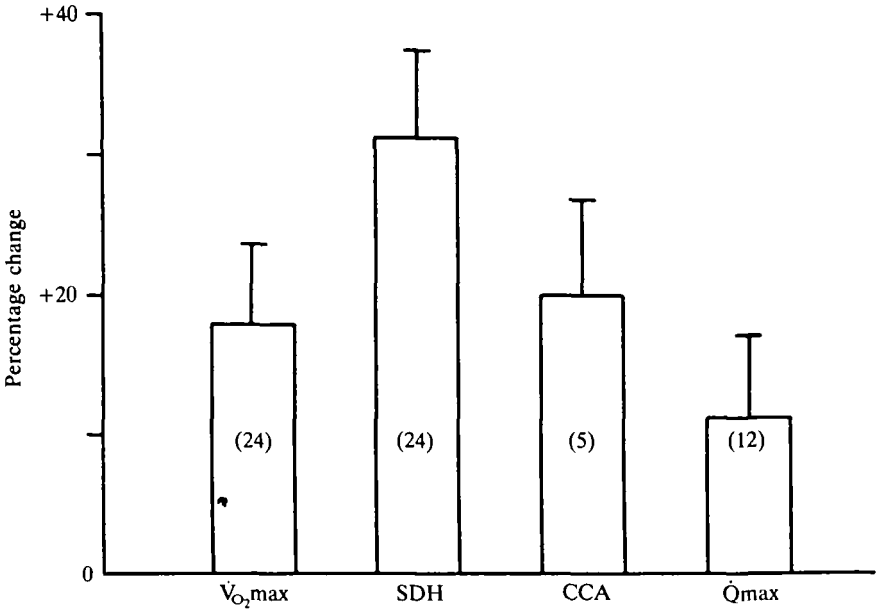

Fig. 2. Average changes (±S.D.) of $\dot{V}_{O_2}$max, SDH activity, capillary cross sectional area (CCA) and maximal cardiac output ($\dot{Q}$max) following two-legged endurance training. Number of observations in brackets. Data from Andersen & Henriksson (1977); Henriksson & Reitman (1976, 1977); Ekblom *et al.* (1968) and Saltin *et al.* (1968).

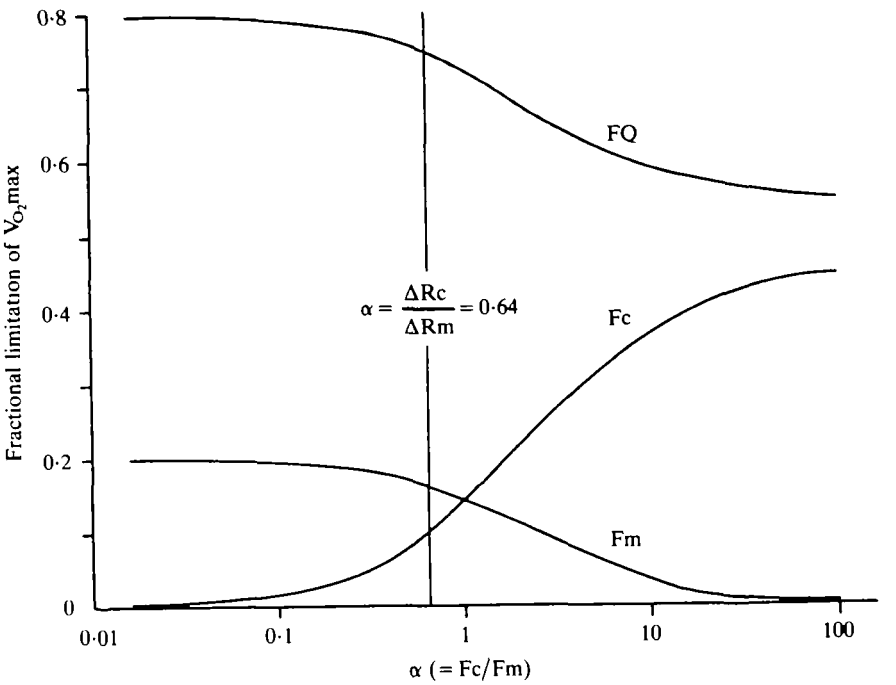

Fig. 3. Fractional limitations of $\dot{V}_{O_2}$max due to O_2 transport (FQ), capillary perfusion and diffusion (Fc) and mitochondrial capacity (Fm) during two-legged maximal exercise, as a function of the coefficient α (= Fc/Fm, equation 14). (See text for details.)

and that the two peripheral limiting factors are interdependent,

$$Fc = \alpha Fm, \tag{14}$$

then, Fm, Fc and FQ can be calculated with the aid of equation 12 for any predetermined value of α (Table 2, Fig. 3).

For low values of α, i.e. assuming that peripheral perfusion and diffusion do not limit $\dot{V}_{O_2}max$ to any significant extent, about 80 % of $\dot{V}_{O_2}max$ is set by O_2 transport, the remaining 20 % being due to mitochondrial capacity. On the contrary, if the assumption is made that the mitochondrial capacity does not set any limit to $\dot{V}_{O_2}max$ ($\alpha > 100$), about 55 % of $\dot{V}_{O_2}max$ depends on O_2 transport, the remaining 45 % being due to peripheral diffusion and perfusion (Table 2, Fig. 3).

A reasonable solution to this dilemma is to assume that the two peripheral factors in question are equally effective in limiting $\dot{V}_{O_2}max$. This amounts to saying that $\alpha = 1{\cdot}0$, a value close to that calculated from the ratio of $\Delta Rc/\Delta Rm = 0{\cdot}64$ (Fig. 2). If this is so, then $FQ = 0{\cdot}72$ and $Fc = Fm = 0{\cdot}14$ (Table 2). The obtained value of FQ is not far from that calculated from Fig. 1, thus supporting the hypothesis that $\dot{V}_{O_2}max$ is limited chiefly by the O_2 transport to tissues.

The percentage increases of $\dot{V}_{O_2}max$ and of mitochondrial enzyme activity during one-legged (cycling) exercise are indicated in Fig. 4, using the data of Henriksson

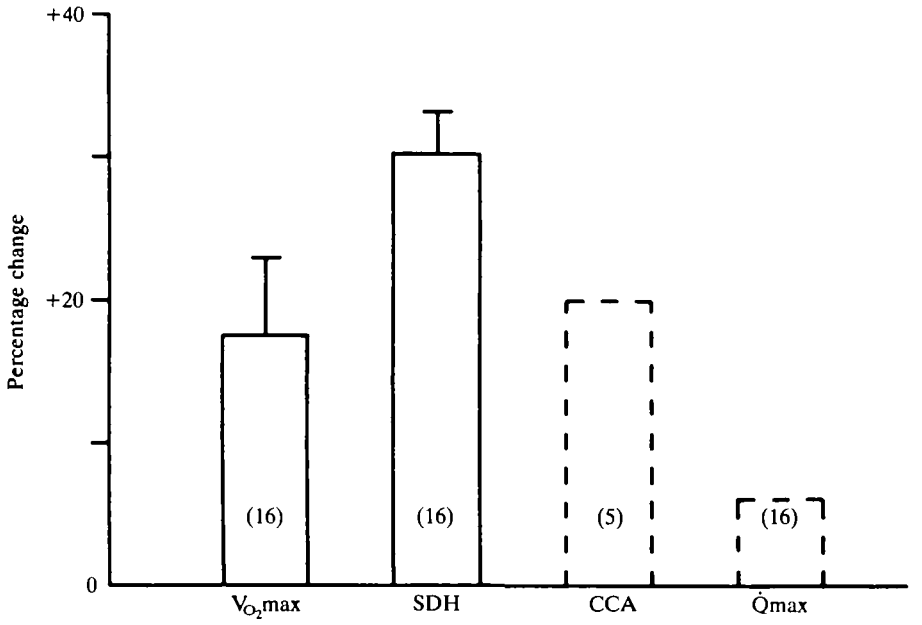

Fig. 4. Average changes (±S.D.) of $\dot{V}_{O_2}max$ and SDH activity following one-legged endurance training. Increases of capillary cross section (CCA) and of maximal cardiac output ($\dot{Q}max$) are assumed to be equal to that observed after two-legged training (Fig. 2) and to increase of $\dot{V}_{O_2}max$ of the untrained leg, respectively. Number of observations in brackets. Data from Henriksson (1977) and Saltin *et al.* (1976).

(1977) and Saltin *et al.* (1976). No measurements were made under these conditions of capillary cross section and cardiac output changes. It can be assumed however that: (a) the former is the same as in two-legged training, and (b) the latter is equal to the $\dot{V}_{O_2}max$ changes observed in the untrained leg in which no increase in enzymatic activity was observed (Henriksson, 1977; Saltin *et al.* 1976). If this is so (Fig. 4), and on the basis of the two assumptions outlined in equations 13 and 14, Fm, Fc and FQ can be calculated as a function of α (Table 2). The general trend that emerges is similar to that observed in two-legged exercise; for all values of α, however, FQ is smaller and Fc and Fm greater in one-legged (as compared to two-legged) exercise, thus indicating that O_2 transport is less crucial in setting $\dot{V}_{O_2}max$ during exercise with small muscle groups. If, once again, the assumption is made that the two peripheral factors have equal weight ($\alpha = 1{\cdot}0$), then FQ = 0·52 and Fc = Fm = 0·26 (Table 2).

DISCUSSION

The above analysis and calculations depend on a series of assumptions that need to be explicitly stated and discussed.

(1) Ventilation and pulmonary diffusing capacity for O_2 have not been considered among the possible factors limiting $\dot{V}_{O_2}max$. This view seems well supported, at least for healthy subjects in normoxia (Shephard, 1971) and will not be further discussed.

(2) The present approach can be meaningfully applied only if the overall pressure gradient from environment to mitochondria is not affected by the experimental manipulations affecting $\dot{V}_{O_2}max$. For all conditions here considered (blood loss or infusion and training) a different assumption would indeed seem rather awkward, even if small changes of O_2 partial pressure at the peripheral end may in fact occur.

(3) The three resistances RQ, Rc and Rm have been considered proportional to maximal O_2 transport capacity, capillary cross section and SDH activity (see equations 7–9). This simplification was introduced since the knowledge of the different morphological and physiological parameters that make up the various resistances (or conductances) is not detailed enough to warrant other approaches at present.

(4) In Table 1, the changes of the resistance to O_2 transport ($\Delta RQ/RQ$) have been calculated (in seven out of 10 cases) from the [Hb] changes, thus neglecting any eventual changes of $\dot{Q}max$. When measured, these were found to be rather small (Ekblom *et al.* 1972; Woodson *et al.* 1978) and, if taken into account, they tend to reduce the calculated value of $\Delta RQ/RQ$. This would therefore lead to an increase in the slope of the regression of Fig. 1, and hence to a greater value of FQ which, in this case, may approach 0·90.

(5) The peripheral limiting factors (diffusion and perfusion from capillary to cell, and O_2 utilization at the mitochondrial level) have been assumed to be interdependent (equation 14). The alternative assumption that the limitation due to peripheral perfusion and diffusion, Fc, is proportional to that due to O_2

transport, FQ ($Fc = \alpha FQ$), leads to quite different results from those in Table 2. On this basis, in fact, during two-legged exercise FQ is in the range 0·75–0·50 for small values of α ($\alpha < 1{\cdot}0$), but decreases dramatically for $\alpha > 1{\cdot}0$, to attain 0·12 for $\alpha = 10$. However, since the two sets of peripheral factors here considered are both affected by the same (presumably) local stimuli, it seems reasonable to assume that they are related to each other rather than to cardiac output. Hence the assumption that $Fc = \alpha Fm$ (equation 14).

(6) The fraction of $\dot{Q}max$ perfusing the working muscles has been implicitly assumed not to change with training. An eventual increase of this fraction with training would lead to values of FQ smaller, and of Fc and Fm greater, than those reported in Table 2.

The above analysis, assumptions and calculations suggest that, during maximal whole body exercise, $\dot{V}_{O_2}max$ is essentially limited by cardiac output, a conclusion that is shared by many authors although based on different grounds (e.g. Shephard, 1976; Saltin & Gollnick, 1983). Contrary to the above conclusions is the opinion of Ivy, Costill & Maxwell (1980) who assign a major role to muscle respiratory capacity in determining $\dot{V}_{O_2}max$. These authors base their conclusion on the results of a statistical analysis on 20 physically active subjects which showed that 72% of the variance in $\dot{V}_{O_2}max$ could be explained by the combined effects of muscle respiratory capacity and percentage of slow twitch (ST) fibres. However, since $\dot{Q}max$ was not measured, this type of analysis cannot show the fraction of the total $\dot{V}_{O_2}max$ variability that depends on $\dot{Q}max$. In addition, this type of statistical analysis cannot, in my opinion, be used to infer causal relationships between the investigated parameters. The relatively minor importance of the periphery as a limiting factor is also consistent with the data of Gollnick *et al.* (1973) who observed an average increase of $\dot{V}_{O_2}max$ by 13% after 5 months' endurance training in humans ($N = 6$) while mitochondrial SDH activity increased on average by 95%, i.e. to a much larger extent than reported in Fig. 2.

It must also be pointed out that the fractions of the $\dot{V}_{O_2}max$ limitation obtained from the training data were calculated assuming that ΔRm is proportional to the change of succinate dehydrogenase activity rather than from the increase of the overall mitochondrial capacity *in vitro*. The latter increases by 50–100% both in man (Holloszy *et al.* 1977) and in rats (Patch & Brooks, 1980), i.e. to a larger extent than the former (~30%) (Figs 2, 4). On the basis of these data, therefore, the importance of mitochondria as a limiting factor would become smaller, and that of O_2 transport larger, than reported in Table 2.

During one-legged exercise the fraction of $\dot{V}_{O_2}max$ limitation due to the periphery seems to become more important, although the general picture remains substantially unchanged (Table 2).

It becomes immediately apparent that the type of analysis presented above can, in principle, be extended to other situations of which the following seem to be of some interest. (1) Animals of different size, in which case the relative importance of the various limiting factors may be different from that in man and, eventually, size dependent. (2) Different types of training in man, in which case the adaptations of $\dot{Q}max$, capillary cross section and muscle enzymatic activity may change from one

type of training to another. This may allow the use of a system of three (or more) experimental equations with three unknowns (equation 6), thus eliminating the need for the coefficient α (equation 14). (3) High altitude acclimation in man, in which case $\dot{V}_{O_2}max$, $\dot{Q}max$, [Hb], capillary cross section and muscle enzymatic activity are known to change (Cerretelli, Marconi, Dériaz & Giezendanner, 1984; Boutellier *et al.* 1983). This may allow study of the behaviour of the various factors limiting $\dot{V}_{O_2}max$ in the course of the acclimation period. At present, there is insufficient data for a detailed analysis of these three situations.

In concluding, I would like to point out that the results of the above analysis should be viewed with care in the light of the many assumptions and approximations involved in the calculations. They do support the view, however, that whole body $\dot{V}_{O_2}max$ is mostly (~80%) limited by cardiac output, while for exercises with small muscle groups the role of the periphery becomes more important, attaining about 50% during one-legged maximal exercise.

This work was supported in part by the Fonds National Suisse de la Recherche Scientifique (Grant no. 3.364.082). The author wishes to thank all participants to the Meeting whose criticisms and comments have contributed to improving this paper.

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