Pulmonary Gas Exchange Dynamics and the Tolerance to Muscular Exercise: Effects of Fitness and Training

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Oxygen uptake (\(\dot{V}O_2\)) kinetics are generally agreed to be first-order for moderate work rates with a time constant (\(\tau\dot{V}O_2\)) that is thought to reflect the kinetics of intramuscular creatine phosphate depletion. However, when there is a concomitant lactic acidosis, \(\tau\dot{V}O_2\) is appreciably longer, reflecting an additional, delayed and slowed component that leads to \(\dot{V}O_2s\) greater than the aerobic equivalent of that work rate and which therefore invalidates current techniques for \(O_2\) deficit estimation. This "excess" \(\dot{V}O_2\) is no more than \(~250-300\) ml/min at work rates for which (lactate) and (H\(^+\))a can be stabilized. At higher work rates which demand sustained and progressive increases in (lactate) and (H\(^+\))a, however, \(\dot{V}O_2\) also continues to increase progressively, yielding excess \(\dot{V}O_2s > 11\) /min at exhaustion. The trajectory of excess \(\dot{V}O_2\) therefore is to the maximum \(\dot{V}O_2\): the resulting exercise limitation becomes progressively more pronounced the higher the work rate, which accounts for the hyperbolic character of the power-duration curve. Factors which speed \(\dot{V}O_2\) kinetics in this domain reduce the excess \(\dot{V}O_2\) mechanism and lead to improved exercise performance. We have demonstrated that, in addition to appropriately-designed training regimens, induction of a metabolic acidosis prior to exercise speeds \(\dot{V}O_2\) kinetics at high work rates, reducing the increase in both (lactate) and (H\(^+\))a and reducing the \(CO_2\) load to ventilation during the transient phase of the work. The optimum procedure for inducing these improved pulmonary gas-exchange kinetics, however, remains to be determined.


Key words: Oxygen uptake kinetics, "Excess" oxygen uptake, Power-duration curve, Lactic acidosis, Exercise performance

The ability to sustain high-intensity exercise is dependent, in large part, upon the body's ability to transport and utilize oxygen at rates commensurate with imposed energy demands. However, while indices such as maximum \(O_2\) uptake (\(\mu\dot{V}O_2\)) and the lactate threshold (\(\theta L\)) have proven useful in predicting the ability to sustain exercise, it should be remembered that it is not the \(O_2\) which is utilized but rather the difference between the energy demands of the task and that provided by the oxidative processes which results in the mediators of muscular fatigue.

For moderate-intensity exercise (i.e., with no sustained metabolic acidosis, \(<\theta L\)), pulmonary \(O_2\) uptake (\(\dot{V}O_2\)) increases towards its steady state with first-order kinetics (following a short "cardio-dynamic" phase of response) (Linnarsson, 1974, Whipp et al., 1982, Miyamoto et al., 1982, Yoshida, 1990):

\[
\Delta \dot{V}O_2 (t) = \Delta G \cdot (1 - e^{-t/\tau})
\]

where \(\Delta G\) is the steady-state gain, i.e., \(\Delta \dot{V}O_2\) (ss), and \(\tau\) is the \(\dot{V}O_2\) time constant. In this intensity domain, neither \(\Delta G\) nor \(\tau\) are appreciably affected.
Fig. 1 Time course of the $O_2$ uptake ($\dot{V}O_2$) response to a moderate-intensity, constant-load cycling test in a normal subject. The pre-exercise control was unloaded cycling ('0' Watts). Reproduced with permission from Whipp et al. (1986).

by work rate. The $O_2$ deficit ($O_2$ Def) (Fig. 1), therefore, will be:

$$O_2 \text{ Def} = \Delta G \cdot t - \Delta G \left(1 - e^{-t/\tau}\right) \cdot dt$$  \(\text{(ii)}\)

which, as $t$ becomes long with respect to $\tau$, yields:

$$O_2 \text{ Def} = \Delta G \cdot \tau$$  \(\text{(iii)}\)

However, as $\Delta G$ has been widely demonstrated to be effectively unchanged by either fitness or training (Astrand and Rodahl, 1970, Casaburi et al., 1987), $O_2$ Def is therefore largely determined by the current level of $\tau$. Consequently, subjects capable of sustaining high work rates tend to have short $\tau$s; physical training has also been shown to reduce $\tau$ (Hickson et al., 1978, Hagberg et al., 1980, Cerretelli et al., 1979).

The physiological basis of the $O_2$ deficit at this work intensity is (a) the reduction in muscle (creatinine phosphate) (CP) and (b) the utilization of $O_2$ stores. As the amount of $O_2$ dissolved in muscle tissue water is trivially small and there is little or no reduction in oxymyoglobin levels ($P_{50} \sim 5$ mmHg) at these work rates, then the volume of stored $O_2$ utilized in the transient phase of the exercise will be: $V_v \cdot \Delta \dot{V}O_2$, where $V_v$ is the venous blood volume and $\Delta \dot{V}O_2$ is the change in the mixed venous $O_2$ content. $V_v$ is effectively unchanged (in short-term exercise). However, $\Delta \dot{V}O_2$ decreases hyperbolically with increasing work rate; i.e.,

$$\Delta \dot{V}O_2 = CaO_2 - \left(\dot{V}O_2/\dot{Q}\right)$$  \(\text{(iv)}\)

This relationship forms the basis of the useful rule-of-thumb that the arterio-venous $O_2$ difference, $C(a-v)O_2$, for various work rates may be closely estimated as:

$$C(a-v)O_2 = \left(20 \cdot \dot{V}O_2\right)/\left(1 + \dot{V}O_2\right)$$  \(\text{(v)}\)

The linear increase in the $O_2$ deficit as work rate increases (eq. (iii)), coupled with the proportionally reduced contribution from the $O_2$ stores, puts progressively greater demands on the local CP stores. When these become inadequate to maintain ATP
concentrations, then there is an obligatory demand for supplemental energy transfer from anaerobiosis.

When blood and muscle lactate levels begin to increase systematically (i.e., above \( \theta L \)), \( \dot{V}O_2 \) kinetics become appreciably more complex (Fig. 2), requiring at least two terms to characterize the behavior (Linnarsson, 1974, Paterson and Whipp). There are two most compelling features of the supra-threshold \( \dot{V}O_2 \) kinetics. The first is that the early phase of the response is slower than characteristic of sub-threshold exercise (i.e., \( \tau \) is increased). Although steady states are commonly not attainable at these work rates, it appears that this early component of \( \dot{V}O_2 \) projects to the same \( \Delta G \) as that for sub-threshold exercise (Paterson and Whipp). However, a second component for \( \dot{V}O_2 \) is subsequently superimposed on this initial response component, which leads to \( \dot{V}O_2 \) increasing to values appreciably greater (\( \Delta G' \)) than those projected from sub-threshold exercise (Paterson and Whipp, Whipp and Mahler, 1980, Roston et al., 1987); i.e., there is "excess" \( \dot{V}O_2 \), which equals \( \Delta G' - \Delta G \). The demonstration that this component is of delayed onset (Paterson and Whipp) obviates the traditional procedure for computing the \( O_2 \) deficit at these work rates.

There is a range of supra-threshold work rates for which the excess \( \dot{V}O_2 \) eventually becomes constant (Roston et al., 1987, Poole et al., 1988); that is, for a given work rate in this range, \( \dot{V}O_2 \) can attain a steady state, with the excess \( \dot{V}O_2 \) typically not exceeding \( \sim 500 \text{ ml/min} \) (Whipp, 1987). In this work-rate range (i.e., the heavy-intensity domain), both the elevated blood (lactate) and \( (H^+)^* \) can also be stabilized (Roston et al., 1987, Poole et al., 1988). A work rate (or \( \dot{V}O_2 \)) is reached, however, for which \( \dot{V}O_2 \), (lactate) and \( (H^+)^* \) all increase progressively throughout the work bout, eventually reaching values that limit tolerance (i.e., the severe-intensity domain).

In the severe-intensity domain, excess \( \dot{V}O_2 \) can exceed a liter per minute for work rates that can be tolerated for 10-15 minutes (Roston et al.,1987, Whipp,1987). And, therefore, it is the trajectory of excess \( \dot{V}O_2 \), (lactate) and \( (H^+)^* \) towards their respective maxima - at a rate, of course, that dependent on work rate increment in this domain - that determines exercise tolerance.

Although the mechanisms of the excess \( \dot{V}O_2 \) remain to be elucidated, circulating levels of catecolamines, body temperature and respiratory work are unlikely to be major determinants (Casaburi et al., 1987, Poole et al., 1988). Routes of lactate metabolism or proportionally greater utilization of the alpha-glycero-phosphate shuttle, however, appear likely candidates (Whipp and Ward, 1990).

Physical training has been shown to speed the supra-threshold \( \dot{V}O_2 \) kinetics and reduce the magnitude of both excess \( \dot{V}O_2 \) and blood (lactate) (Casaburi et al., 1987). Consequently, this allows higher work rates to be sustained.

In summary, therefore, it appears that the initial slowing of the \( \dot{V}O_2 \) kinetics at these work rates results in a metabolic acidosis, a sequella of which is excess \( \dot{V}O_2 \).

It has recently been demonstrated (Gausche et al., 1989, Gerbino et al., 1990) that an appropriate

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**Fig. 2** Breath-by-breath responses of \( O_2 \) uptake (\( \dot{V}O_2 \)) and the respiratory exchange ratio (R) to a single 6-min bout of constant-load cycling in a normal subject above the lactate threshold (\( \theta L \)) (190 Watts) with on- and off-transients to "0" Watts. Vertical lines indicate onset and cessation of work. Reproduced with permission from Paterson and Whipp (in press).
with a reduced lactic acidosis. This prediction was confirmed by Gerbino et al. (1990), who demonstrated that the increase of blood (lactate) and (H⁺) were markedly attenuated following a high-intensity warm-up. These findings are compatible with the slow supra-threshold \( \dot{V}O_2 \) kinetics being a consequence of circulatory (and hence \( O_2 \) flow) limitation. The optimum warm-up protocol, however, remains to be characterized.

The domain transitions, therefore, are crucial parameters for both determining the relative stress of a particular task and also for determining optimum training strategies to improve exercise tolerance. As the dynamics of the nonsteady state \( \dot{V}O_2 \) are characteristic of the intensity domain, one could perform a range of constant-load work bouts and determine when the first-order \( \dot{V}O_2 \) kinetics change to second-order with a delayed steady state (this transition is the lactate threshold), and the highest attainable steady-state \( \dot{V}O_2 \) changes to an obligatory progressive increase to the maximum (this transition may be termed the "fatigue threshold", \( \theta F \), or "critical power"). Such a procedure would be greatly time- and laboratory-intensive, however. Consequently, non-invasive, incremental tests employing standardized gas-exchange criteria (Beaver et al., 1986, Whipp et al., 1986) are utilized to determine \( \theta L \) and the \( \mu \dot{V}O_2 \); the difference between these parameters being termed "Delta".

Delta is a useful construct, as it is representative of the mean rate of (lactate) increase between \( \theta L \) and \( \mu \dot{V}O_2 \). Although the physiological mechanisms which determine Delta have not been resolved, it is likely to reflect in large part the characteristics of lactate clearance mechanisms in addition to its production rate (Brooks, 1985, Jorfeldts et al., 1978). Endurance training which increases both \( \mu \dot{V}O_2 \) and \( \theta L \) has been shown not to affect Delta significantly (Davis et al., 1979). This accounts for the threshold fraction of the \( \mu \dot{V}O_2 \) increasing with physical training. In general, however, subjects with large \( \mu \dot{V}O_2 \)s tend to have larger Deltas, although the great varia-

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**Fig. 3** Time course of pulmonary gas exchange (\( \dot{V}O_2 \), \( \dot{V}CO_2 \), R) to two consecutive square-wave bouts of exercise performed from a background of unloaded cycling to 250 Watts, (i.e., \( > \theta L \)). Note that the \( \dot{V}O_2 \) time course during the on-transient is faster for the second exercise bout, while the corresponding \( \dot{V}CO_2 \) time course is slower. As a result, the transient undershoot in R is more striking for the second work bout. Reproduced with permission from Whipp and Ward (1990).
Fig. 4 Relationship between Delta (the difference between the maximum $\dot{V}O_2$ ($\mu \dot{V}O_2$) and $\theta L$) and $\mu \dot{V}O_2$ in a large sample of normal subjects. Note the wide variability of Delta at any given value of $\mu \dot{V}O_2$. Furthermore, the bounds on Delta, as represented by the dashed lines, appear to extrapolate to a $\dot{V}O_2$ consistent with the resting metabolic rate, rather than zero. We thank Drs. R. Casaburi, J. A. Davis and D. Y. Sue for allowing us to use some of their unpublished data in the compilation of this figure.

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Fig. 5 Upper panel: The power-duration (\(W\cdot t\)) relationship for high-intensity cycling exercise in a single subject. Lower panel: Determination of parameters \(W'\) and \(\theta_F\) from the linear \(\dot{W} \cdot 1/t\) formulation; see text for further details. \(\theta_L\) is the estimated lactate threshold.

Reproduced with permission from Poole et al. (1988).

Fig. 6 The "fatigue threshold" (\(\theta_F\)) represents the transition between heavy- and severe-intensity exercise. Work rates that exceed \(\theta_F\) elicit an obligatory increase in \(\dot{V}O_2\) which attains the maximum \(\dot{V}O_2\) (\(\mu\dot{V}O_2\)), in progressively shorter intervals the higher the work rate (\(\# 3 \rightarrow \# 2 \rightarrow \# 1\)) (upper panel), as dictated by the power-duration (\(W\cdot t\)) relationship (lower panel). In contrast, work rates which approach \(\theta_F\) (\# 4) result in a \(\dot{V}O_2\) steady state being attained, such that the work may be continued for a prolonged duration. See text for further details.

range of lactate levels among individual subjects (up to 8 mM or more, for example), \(\theta_F\) may prove to be the better index of the transition between heavy and severe exercise in individual subjects (Fig. 6).

\(\theta_F\) has been shown to be highly correlated with physical fitness; \(W'\), however, seems to be relatively independent of fitness (Poole et al., 1988, Moritani et al., 1981), although much more investigation is needed before the latter point can be made with assurance. By the same token, \(W'\) was not increased by endurance training, whereas \(\theta_F\) increased systematically (Poole et al., 1990). In both conditions, the \(\dot{W} \cdot t\) relationships were well-fit by a hyperbola (Poole et al., 1990).

Attempts to model the physiological basis of the hyperbolic \(\dot{W} \cdot t\) relationship would seem, we firmly believe, to require parameters of the model formula-
tion which include multi-compartment \( \dot{V}_O_2 \) kinetics with parameter values that cohere with those experimentally determined. That is, unless the model actually characterizes the temporal behavior of \( \dot{V}_O_2 \), the parameters of the model are unlikely to have plausible physiological correlates.

In conclusion, therefore, pulmonary \( \dot{V}_O_2 \) kinetics during muscular exercise, which are so crucial for exercise tolerance, are both a determinant and a consequence of the magnitude and time course of the metabolic (chiefly lactic) acidosis. The kinetics of the \( \dot{V}_O_2 \) response to high-intensity exercise may therefore be considered to be a "proxy" variable (Yamamoto, 1978) for the fatigue processes which constrain the tolerable duration of a particular work task. They also, therefore, provide a non-invasive basis for work-rate optimization strategies in physical training and rehabilitation.

REFERENCES


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