Journal of Physiology (1991), **443**, *pp.* 575–586
With 5 figures
Printed in Great Britain

ASYMMETRIES OF OXYGEN UPTAKE TRANSIENTS AT THE ON- AND OFFSET OF HEAVY EXERCISE IN HUMANS

BY DONALD H. PATERSON AND BRIAN J. WHIPP*

From the Division of Respiratory Physiology and Medicine, Harbor–UCLA Medical Center, Torrance, CA 90509, and Faculty of Physical Education, University of Western Ontario, London, Ontario, Canada N6A 3K7

(*Received 27 February 1991*)

SUMMARY

1. At work rates which do not result in a sustained increase in blood lactate ($[L^-]$), oxygen uptake ($\dot{V}_{O_2}$) approaches the steady state with first-order kinetics. However, when $[L^-]$ is increased, at least two kinetic components are required to characterize the $\dot{V}_{O_2}$ response dynamics. The purpose of the present investigation was to determine whether these more-complex kinetics are best represented as: (a) two components which operate throughout the exercise or (b) a delayed slow component which is consequent to the lactic acidaemia and which does not influence the early development of the O_2 deficit.

2. Six healthy subjects underwent an incremental ramp test on a cycle ergometer, to the limit of tolerance, for determination of the maximum $\dot{V}_{O_2}$ ($\mu\dot{V}_{O_2}$) and estimation ($\hat{}$) of the threshold for lactic acidaemia ($\hat{\theta}_L$) non-invasively. Subjects then performed, on different days, two to four repetitions of square-wave exercise from a baseline of unloaded pedalling ('O' Watts (W)) to work rates (WR) $< \theta_L$ (90% $\hat{\theta}_L$) and $> \theta_L$ (half-way between $\hat{\theta}_L$ and $\mu\dot{V}_{O_2}$). Ventilatory and pulmonary gas exchange variables were determined breath-by-breath. For each subject, the $\dot{V}_{O_2}$ transitions were averaged prior to fitting a least-squares algorithm to the on- and off-transient responses.

3. The $< \theta_L$ test resulted in a mono-exponential $\dot{V}_{O_2}$ response, with a time constant of 31·3 and 31·5 s for the on- and off-transients, respectively.

4. The $\dot{V}_{O_2}$ responses to the $> \theta_L$ test were fitted to three competing models: (a) a single exponential for the entire period; (b) a double exponential for the entire period; and (c) an initial single exponential with a subsequent phase of delayed onset. Model (c) yielded a significantly lower residual mean-squares error than methods (a) and (b), with a time constant for the initial component of 40·2 s for the on-transient and 32·9 s for the off-transient and a subsequent phase of $\dot{V}_{O_2}$ increase for the on-transient which averaged 230 ml min^{-1}. The $\Delta\dot{V}_{O_2}/\Delta$WR for the early kinetics of the $> \theta_L$ test were not different from the $< \theta_L$ test (9·6 and 9·5 ml min^{-1} W^{-1}, respectively).

* Present address: Department of Physiology, Center for the Health Sciences, UCLA, Los Angeles, CA 90024, USA.

MS 9185

5. These data suggest that the slow phase of the $> \theta_L$ $\dot{V}_{O_2}$ kinetics is a delayed-onset process. This being the case, the O_2 deficit during heavy exercise, as conventionally estimated, would be overestimated.

INTRODUCTION

Following the onset of constant-load muscular exercise, the exponential increase in pulmonary oxygen uptake ($\dot{V}_{O_2}$) may be characterized with a single time constant (τ) and a delay (d) which reflects the tissue-to-lung vascular transit delay (Linnarsson, 1974; Whipp, Ward, Lamarra, Davis & Wasserman, 1982), if the work rate is of moderate intensity (i.e. below the subject's lactate threshold, θ_L). For heavy exercise (i.e. $> \theta_L$), the $\dot{V}_{O_2}$ kinetics become more complex, with a slow component being evident (Linnarsson, 1974; Whipp, 1987) which leads to the steady-state or asymptotic $\dot{V}_{O_2}$ being greater than that predicted from the sub-θ_L relationship between $\dot{V}_{O_2}$ and work rate (Whipp, 1987). As very little is known about these supra-θ_L kinetic characteristics, we attempted to determine: (a) whether the more complex $\dot{V}_{O_2}$ dynamics reflect two (or more) components induced from time zero or whether the slow component is an additional one of delayed onset, i.e. which may not influence the early response; and (b) whether the on- and off-transient kinetics are symmetrical.

An abstract of this work has been published previously (Paterson & Whipp, 1987).

METHODS

Six healthy subjects who were physically active but not in competitive training, with maximum $\dot{V}_{O_2}$ s which ranged from 36 to 54 ml kg^{-1} min^{-1} (Table 1), gave informed consent for the study, which was approved by the Institutional Human Subjects Protection Committee. They performed ramp and square-wave exercise tests on a computer-controlled, electromagnetically braked cycle (Lanooy) at a pedalling frequency of 60–70 rev min^{-1}. Throughout the tests, inspired and expired volumes were measured by a turbine volume sensor (Alpha Technologies), calibrated by using known volumes of room air at mean flows and flow profiles spanning the exercise range. Respired air was sampled continuously at the mouthpiece (1 ml s^{-1}) for continuous measurement of P_{O_2}, P_{CO_2} and P_{N_2} by mass spectrometry (Perkin–Elmer, MGA 1100); the mass spectrometer was calibrated using precision-analysed mixtures. The time delay between the volume and gas concentration signals was measured by passing a bolus of gas through the system, as previously described (Beaver, Wasserman & Whipp, 1973). Electrical signals from these devices underwent analog-to-digital conversion and were processed for breath-to-breath determination of ventilatory and pulmonary gas exchange variables (Beaver, Lamarra & Wasserman, 1981): O_2 uptake ($\dot{V}_{O_2}$, STPD (standard temperature and pressure dry)), CO_2 output ($\dot{V}_{CO_2}$, STPD), ventilation ($\dot{V}_E$, BTPS (body temperature and pressure when saturated with water vapour)), respiratory exchange ratio (R), ventilatory equivalents for CO_2 and O_2 ($\dot{V}_E/\dot{V}_{CO_2}$, $\dot{V}_E/\dot{V}_{O_2}$), and end-tidal P_{CO_2} and P_{O_2} (P_{ET,CO_2}, P_{ET,O_2}). The breath-to-breath data were displayed on-line (Beckman, R711 Dynograph) and stored on digital tape for subsequent analysis.

The breath-to-breath gas exchange measurements were calibrated by means of a respiratory gas exchange simulator (Huszczuk, Whipp & Wasserman, 1990). This device utilizes a pump which takes in a mixture of atmospheric air and a flow of a precision-analysed calibration gas. The resulting mixture is then expelled with a profile of flow and respiratory gas concentrations which closely resembles that of normal expiration. The known flow of calibration gas allows the 'O_2 uptake' and 'CO_2 output' of the system to be pre-set independent of the minute ventilation of the simulator. Changes in the calibration mixture inflow therefore allow a range of 'metabolic rates' to be established between 0·2 and 5·0 l min^{-1}, with a resulting accuracy of $\pm 2\%$ (Huszczuk *et al.*

1990); i.e. beyond, but incorporating, the metabolic rates encountered in this study. Further details of this procedure may be found in the article by Huszczuk *et al.* (1990).

Each subject performed a ramp exercise test (15 W min^{-1}) to the limit of tolerance to determine the maximal $\dot{V}_{O_2}$ ($\mu\dot{V}_{O_2}$) and to estimate ($\hat{}$) the lactate threshold (θ_L) using gas-exchange criteria (Whipp, Ward & Wasserman, 1986).

TABLE 1. Subject characteristics

Subject no.	Sex	Age (years)	Weight (kg)	$\hat{\theta}_L$ (l min^{-1})	$\mu\dot{V}_{O_2}$ (ml kg^{-1} min^{-1})
1	M	37	70·5	2·00	44
2	M	48	81·7	2·05	37
3	M	36	78·0	2·65	54
4	F	22	50·0	1·20	43
5	F	26	65·5	1·34	36
6	F	38	62·3	1·44	39

$\hat{\theta}_L$ is the lactate threshold, in units of $\dot{V}_{O_2}$; $\mu\dot{V}_{O_2}$ is the maximum $\dot{V}_{O_2}$.

Over a 2 week period, subjects completed a series of square-wave exercise tests at work rates chosen to elicit: (a) a $\dot{V}_{O_2}$ of 90% of $\hat{\theta}_L$ and (b) a $\dot{V}_{O_2}$ midway between $\hat{\theta}_L$ and $\mu\dot{V}_{O_2}$ (i.e. 0·5 Δ). For each test, following a control phase of 4 min of unloaded pedalling ('O' W), the work rate was abruptly increased to the appropriate value for a period of 6 min, and then abruptly decreased back to 'O' W for 15 min recovery. Two to four repetitions of the $< \theta_L$ and $> \theta_L$ protocols were completed by each subject. The order of the tests was randomly assigned among subjects, with subjects completing no more than one test on a particular day.

The breath-by-breath data of each test were interpolated (1 s) and temporally aligned to a signal marking the points at which the work rate was increased and then subsequently decreased. The responses to each particular work rate were then averaged prior to the parameter estimation.

To characterize the kinetic behaviour of $\dot{V}_{O_2}$, the averaged response data of each subject were fitted by using various models. The first model was a monoexponential (including a delay term) throughout a fitting window extending from 20 to 360 s after the transition, for both the on- and off-transients, using a non-linear least-squares algorithm (Lamarra, Whipp, Ward & Wasserman, 1987); i.e. the exponential of the kinetic phase is not distorted by any early 'cardiodynamic' influences (Whipp *et al.* 1982). The second model considered the response to be comprised of two exponential components over the entire fitting window; i.e. two parallel compartments. The third model considered there to be a monoexponential component over the entire fitting window, but upon which an additional, delayed component was subsequently superimposed. In this model, the monoexponential phase of the fitting (typically 3 min or less) – i.e. '3 min fit' – was extrapolated to 6 min to establish the steady-state equivalent of this exponential component. This allowed us to determine the magnitude of the additional, delayed component at the end of the transition by taking the actual 6 min value and subtracting from it the steady-state equivalent of the monoexponential response.

Comparison between models was based on the residual mean square of the $\tau\dot{V}_{O_2}$ estimate, for both the onset and recovery, using paired t tests with significance levels set at $P < 0·05$.

RESULTS

The mean $\mu\dot{V}_{O_2}$ of the subjects was 2·9 l min^{-1} or 43 ml kg^{-1} min^{-1} with $\hat{\theta}_L$ averaging 60% of $\mu\dot{V}_{O_2}$ (Table 1). Figure 1 shows breath-by-breath responses of pulmonary gas exchange from 'O' W (unloaded) cycling to constant-load exercise at a sub-threshold and a supra-threshold work rate, and recovery to unloaded cycling. For sub-threshold exercise, a steady-state $\dot{V}_{O_2}$ was attained within 3 min (i.e. the $\dot{V}_{O_2}$

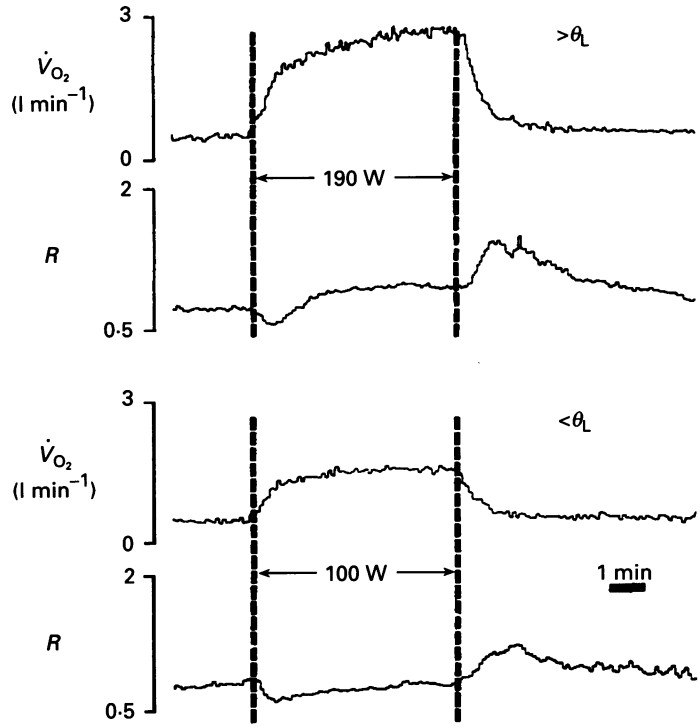

Fig. 1. Breath-by-breath responses of O_2 uptake ($\dot{V}_{O_2}$) and respiratory exchange ratio (R) to a single 6 min bout of constant-load work below θ_L (100 W; lower panel) and above θ_L (190 W; upper panel) with on- and off-transients to 'O' W; subject 2. Vertical dashed lines indicate onset and cessation of work.

TABLE 2. $\dot{V}_{O_2}$ time constant ($\tau\dot{V}_{O_2}$), O_2 deficit and O_2 debt for 3 min and 6 min model fits in response to square-wave exercise below and above θ_L

	3 min fit				6 min fit			
	On-transient		Off-transient		On-transient		Off-transient	
	τ (s)	O_2 deficit (ml)	τ (s)	O_2 debt (ml)	τ (s)	O_2 deficit (ml)	τ (s)	O_2 debt (ml)
$< \theta_L$	31·3	540·9	31·5	531·1	41·3	670·8	36·8	616·3
±S.E.M.	3·3	112·7	3·4	86·2	5·0	136·6	1·9	113·2
$> \theta_L$	40·2	1085·1	32·9	1124·5	68·8	1836·5	39·2	1262·2
±S.E.M.	2·7	205·9	2·0	148·3	4·8	310·2	2·0	189·5

time constant, $\tau = 31{\cdot}3 \pm 3{\cdot}3$ s: Table 2). For the supra-threshold work, $\dot{V}_{O_2}$ time constant, $\tau = 31{\cdot}3 \pm 3{\cdot}3$ s: Table 2). For the supra-threshold work, $\dot{V}_{O_2}$ kinetics appear more complex with a steady state not attained within 6 min of exercise. Below θ_L, the symmetry of the on/off $\dot{V}_{O_2}$ kinetics is characterized in Table 2, which shows that both τ and the O_2 deficit are not significantly different from the on- and off-transient, with τ being 31·3 and 31·5 s and the O_2 deficit 671 and 616 ml min^{-1}, respectively.

This is characteristic of a linear system. For the supra-threshold work, the on-transient response is discernibly slower than that in recovery (e.g. Figs 2 and 3). The on-transient best-fit τ (i.e. the early kinetic component) is some 8 s longer than that of the off-transient (40·2 *vs.* 32·9 s).

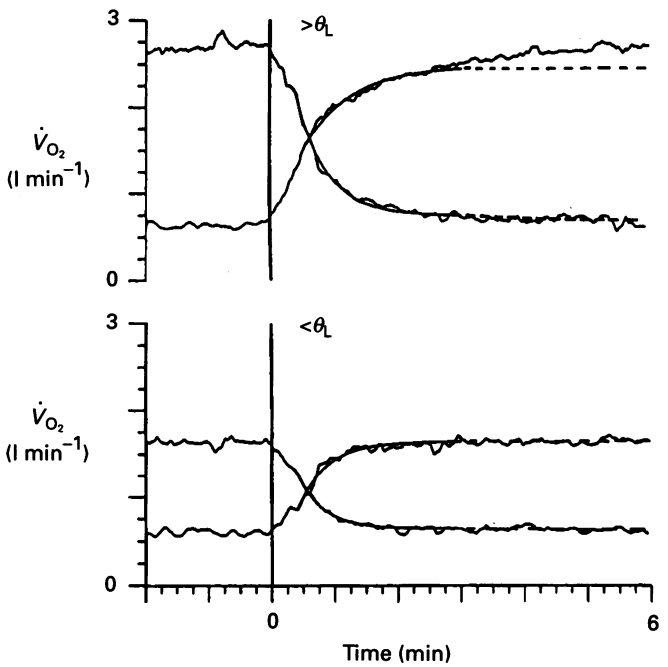

Fig. 2. On- and off-transient responses of $\dot{V}_{O_2}$ to 6 min bouts of constant-load work below θ_L (110 W; lower panel) and above θ_L (210 W; upper panel); subject 1. The responses are the averaged responses of four tests. Superimposed on the $\dot{V}_{O_2}$ responses are the monoexponential fits to 3 min (continuous lines, with the dashed lines indicating the extension of the monoexponential to 6 min). See text for further detail.

As shown in Fig. 2, the interpolated (1 s) and time-aligned averaged responses of the $\dot{V}_{O_2}$ on- and off-transients, for one subject, during the sub-threshold exercise are characterized by a monoexponential fit, with delay. The goodness of fit is not different for the first 3 min or the full 6 min; the resultant τ was $\sim$ 30 s and the steady-state $\Delta\dot{V}_{O_2}/\Delta$WR was 9·9 ml min^{-1} W^{-1}. Above θ_L, using a two-compartment model, the early component (i.e. 3 min fit) clearly yields the better representation of the early kinetic phase of the response (i.e. Fig. 2); in no case did the 6 min, one-compartment fit adequately describe the kinetics (Fig. 3). The early monoexponential response evinced a best-fit time constant of 44 s and a steady-state gain (i.e. $\Delta\dot{V}_{O_2}/\Delta$WR) of 9·1 ml min^{-1} W^{-1} (i.e. the dashed line in Fig. 2). The time constant was appreciably slower than for the sub-θ_L work rate but the asymptote was not different for the two work intensities. We could not discriminate between an exponential or linear fit to the slow phase of the $\dot{V}_{O_2}$ response. This was also true for the group as a whole and hence we can only state, from these data, that the time course of this later component of increase is slow and, at 6 min, leads to an 'excess'

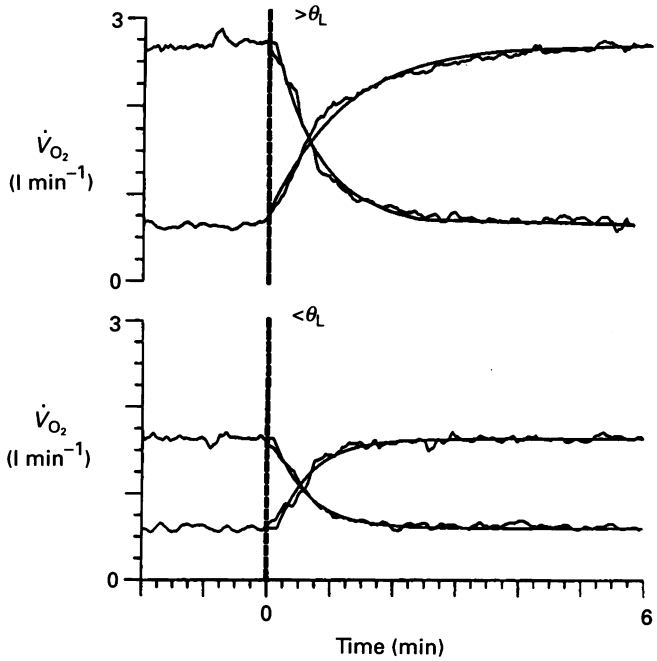

Fig. 3. On- and off-transient responses of $\dot{V}_{O_2}$ to 6 min bouts of constant-load work below θ_L (110 W; lower panel) and above θ_L (210 W; upper panel); subject 1. The responses are the averaged responses of four tests. Superimposed on the $\dot{V}_{O_2}$ responses are the monoexponential fits (with delay) to the entire 6 min of the response.

TABLE 3. Change in $\dot{V}_{O_2}$ between 3 min and 6 min in response to square-wave exercise below and above θ_L

Subject no.	$\Delta\dot{V}_{O_2}$ (6−3 min) (ml min^{-1})	
	$< \theta_L$	$> \theta_L$
1	−8	+230
2	+30	+320
3	+32	+250
4	+47	+105
5	+74	+174
6	−4	+137
Mean	+29	+230*
±S.E.M.	31	32

* $\Delta\dot{V}_{O_2}$ (6−3 min) significantly > 0.

$\dot{V}_{O_2}$ of 230 ml min^{-1} (e.g. Fig. 2 and Table 3). A continuous double-exponential fit (i.e. compartments in parallel) for exercise above θ_L yielded a poor fit to the data with a rapid-component time constant of 17 s in this subject. Four of the six subjects showed a similarly rapid time constant using this model, and the time constant was highly variable among subjects. If we compute the O_2 deficit in the traditional manner as recently characterized by Casaburi, Storer, Ben Dov & Wasserman (1987) – i.e. to establish the effective gain and single time constant to the entire data set (as shown in Fig. 3) – then the O_2 deficit per Watt for supra-θ_L exercise was 11·0 ± 0·69 ml

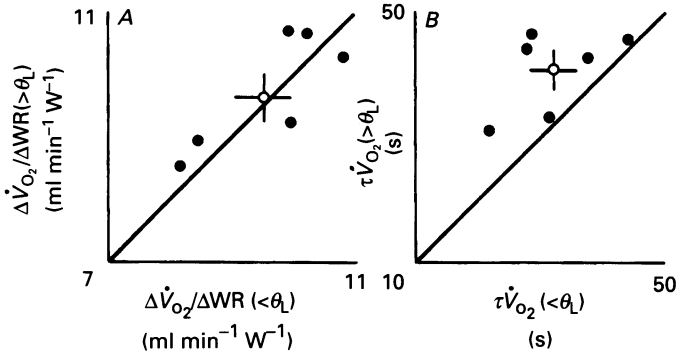

Fig. 4. *A*, the $\dot{V}_{O_2}$ amplitude ($\Delta\dot{V}_{O_2}$) at 3 min (mean: 160–180 s) expressed per Watt of work rate increment for the mean response of four tests in each of the six subjects $< \theta_L$ and $> \theta_L$. Note the asymptotic $\dot{V}_{O_2}$ of the 3 min fit was the same for work rates $< \theta_L$ and $> \theta_L$. *B*, the time constant ($\tau\dot{V}_{O_2}$) of the on-transient responses for the 3 min fit $< \theta_L$ and $> \theta_L$. Note that $\tau\dot{V}_{O_2} > \theta_L$ was significantly greater than $\tau\dot{V}_{O_2} < \theta_L$.

TABLE 4. Residual mean square of best-fit $\tau\dot{V}_{O_2}$ for 3 min and 6 min model fits in response to square-wave exercise below and above θ_L

Subject no.	3 min fit		6 min fit	
	$< \theta_L$	$> \theta_L$	$< \theta_L$	$> \theta_L$
1	0·095	0·078	0·088	0·091
2	0·043	0·076	0·064	0·090
3	0·059	0·074	0·092	0·130
4	0·058	0·068	0·062	0·078
5	0·047	0·052	0·046	0·056
6	0·046	0·045	0·043	0·055
Mean	0·058	0·066	0·066	0·083*†
±S.E.M.	0·008	0·006	0·008	0·011

* Significant difference within models for $< \theta_L$ *vs.* $> \theta_L$.
† Significant difference between models for 3 min *vs.* 6 min fit.

compared with 7·22±0·57 ml for the sub-θ_L test ($P < 0·05$) and was appreciably greater than the calculated recovery V_{O_2} (Table 2).

Statistical analyses of the 3 min and 6 min fits to the data are given in Table 4. Comparing models, the 6 min fit for the supra-θ_L exercise showed a significantly poorer fit, as evidenced by the greater residual mean square error for both the on- and off-transients. Considering the early kinetic component (i.e. 3 min) of the two-compartment fits, a monoexponential fit was equally good (with the same magnitude of error) above and below θ_L. The $\Delta\dot{V}_{O_2}/\Delta WR$ for the six subjects below θ_L and to the end of the first-component (3 min) fit above θ_L were not significantly different at $\simeq$ 9·5 ml min^{-1} W^{-1} (Fig. 4*A*). The second component of the two-compartment fit, from 3 to 6 min, showed a significant slow phase of increase in $\dot{V}_{O_2}$ during the supra-threshold exercise of 230 ml min^{-1}. There was no 'slow component' increase of $\dot{V}_{O_2}$ in the sub-threshold exercise (e.g. Figs 2 and 3). Even using the '3 min fit' for the supra-θ_L exercise, the on-transient time constant was significantly longer (40 s) than for the sub-θ_L exercise (31 s) (Fig. 4*B*). The off-transient time constant was similar for the supra- and sub-θ_L exercise (31·5±3·4 and 32·9±2·0 s, respectively; Table 2).

Figure 5 shows the averaged responses and the early component monoexponential '3 min fits' for two subjects performing the same work rates (to within 5 W); the work rate, however, was above θ_L in one subject and below it in the other. Note, that although a similar $\dot{V}_{O_2}$ is achieved by the subjects within 3 min, the early kinetic

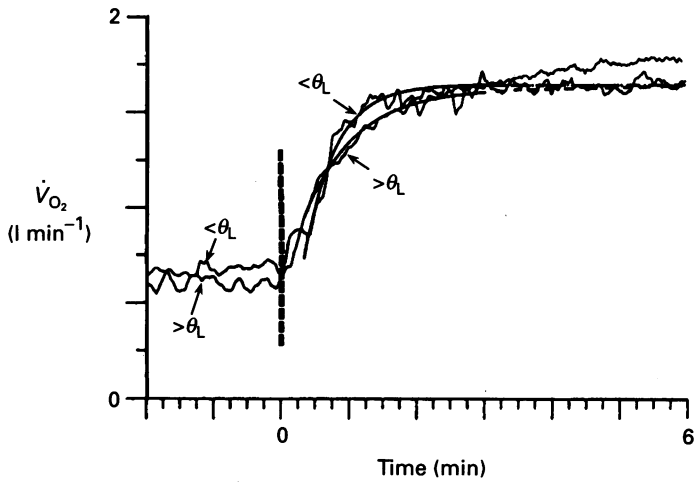

Fig. 5. The averaged $\dot{V}_{O_2}$ response (subject 4) for $> \theta_L$ exercise (115 W) compared with those (subject 1) for $< \theta_L$ exercise (110 W). Monoexponential fits to 3 min (with extrapolation to 6 min, and shown by dashed lines) are superimposed. Note that a similar $\dot{V}_{O_2}$ is achieved for the two subjects by 3 min. Subject 4, however, showed a slow component of increasing $\dot{V}_{O_2}$ between 3 and 6 min.

behaviour is slowed in the subject working above θ_L. The slowed on-transient time course in the subject exercising above θ_L yields an O_2 deficit approximately 0·5 l larger than that of the subject working below the threshold. The subsequent slow component is only apparent for the subject performing the supra-θ_L exercise.

DISCUSSION

The O_2 deficit has proven to be a useful concept in exercise bioenergetics. It represents the O_2 equivalent of the energy that was utilized to fuel muscular contraction, but which was not derived from reactions involving atmospheric O_2, i.e. taken into the body after the start of the work. The quantification of the O_2 deficit, however, is based upon two assumptions. Firstly, it assumes that a steady-state or asymptotic $\dot{V}_{O_2}$ can be accurately determined or projected and, secondly, that this steady-state or asymptotic value is the appropriate one at all times during the test, i.e. throughout the *entire* non-steady-state phase. At work rates in which there is no sustained metabolic (lactic) acidosis, these criteria have been consistently shown to be met. After the muscle-to-lung transit delay, $\dot{V}_{O_2}$ approaches its steady-state level with first-order kinetics (Linnarsson, 1974; Whipp *et al.* 1982) and with a time constant which does not change appreciably with work rate. This allows the O_2 deficit to be computed and apportioned into its component parts. The O_2 stores component appears to become proportionally less important, the higher the work

rate; this is a consequence of the mixed venous O_2 content, which represents the dominant component of the utilized O_2 stores, decreasing hyperbolically rather than linearly with increasing work rate (Durand, 1980; Rowell, 1986). The remainder is provided by the reduction in the local creatine phosphate stores (Piiper, diPrampero & Cerretelli, 1968; Mahler, 1985) and possibly some transient lactate increase at the higher regions of this intensity range.

Our data are consistent with these concepts. Not only does $\dot{V}_{O_2}$ increase with first-order kinetics, but the on- and off-transient dynamics are symmetrical: neither the steady-state gains nor the time constants are significantly different. This is to be expected if in recovery the depleted O_2 and local creatine phosphate stores are replenished to the same pre-exercise levels.

At work rates above the lactate threshold, two features of our results bear upon the validity of the conventional means of O_2 deficit computation. Firstly, the best-fit time constant for the early dynamics is slow relative to the sub-threshold work and also projects to a 'steady-state' gain which is not appreciably different from that for sub-threshold exercise, i.e. $= 10$ ml min^{-1} W^{-1}. Consequently, the O_2 deficit for this early component becomes disproportionately large at these work rates, consistent with the increased blood and muscle lactate concentrations previously demonstrated at these work rates (Knuttgen & Saltin, 1972; Jorfeldt, Juhlin-Dannfelt & Karlsson, 1978; Bylund-Fillenius, Walker, Elander, Holm, Holm & Schersten, 1981; Roston, Whipp, Davis, Cunningham, Effros & Wasserman, 1987), being associated with – and likely to result from – relatively reduced O_2 utilization in the contracting muscles. This relative lack of O_2 utilization, which is a necessary requirement for the lactate threshold being attributable to anaerobiosis, has proved difficult to demonstrate during incremental exercise testing, where the $\dot{V}_{O_2}$–WR relationship commonly remains linear even above the lactate threshold (Whipp, Davis, Torres & Wasserman, 1981; Hughson & Inman, 1986). A likely reason for this is the influence of the second component of the kinetics. That is, an additional phase of O_2 uptake becomes discernible a few minutes into the test, which causes $\dot{V}_{O_2}$ to increase to a value at 6 min which is 230 ml min^{-1}, on average, *greater* than the steady-state requirement. In more prolonged tests and at even higher work intensities, this 'excess' $\dot{V}_{O_2}$ can exceed 1 l min^{-1} (Whipp, 1987).

To date, however, there is not a generally agreed-upon description of the slow phase of the pulmonary $\dot{V}_{O_2}$ kinetics for supra-threshold exercise. Certain features of the response profile do appear to be characteristic.

(a) The early component of the $\dot{V}_{O_2}$ kinetics is slowed compared with subthreshold exercise.

(b) The additional slow component is of delayed onset and results in an additional and progressive increase in $\dot{V}_{O_2}$; however, there is no convincing evidence that this process is exponential in form. In our study, the slow-phase data were not significantly better fitted by an exponential compared with a linear fit. Linnarsson (1974) noted the same uncertainty, as the best-fit group-mean exponential of this slow phase had a time constant of more than half an hour.

And (c) this slow component causes $\dot{V}_{O_2}$ to increase to values greater than those predicted from extrapolation of the subthreshold $\dot{V}_{O_2}$–WR relationship (Roston *et al.* 1987; Whipp, 1987). This is even apparent from measurements of the leg component

of total body $\dot{V}_{O_2}$ during leg-extension ergometry (Andersen & Saltin, 1985). The 'excess $\dot{V}_{O_2}$' at a particular work rate can be reduced or abolished by endurance training (Casaburi *et al.* 1987; Poole, Ward & Whipp, 1990). However, over a narrow range of supra-threshold work rates, a steady state may eventually be reached (Roston *et al.* 1987; Whipp, 1987; Poole, Ward, Gardner & Whipp, 1988). At even higher work rates, a steady state is unattainable; $\dot{V}_{O_2}$ continues to increase to the subject's maximum $\dot{V}_{O_2}$ (Roston *et al.* 1987; Whipp, 1987; Poole *et al.* 1988). The highest $\dot{V}_{O_2}$ at which a steady state can be attained appears to coincide with the highest work rate at which blood [lactate] does not continue to rise during the course of the work (Roston *et al.* 1987; Poole *et al.* 1988).

We interpret the slowed early $\dot{V}_{O_2}$ kinetics as reflecting the inadequate O_2 utilization that results in the lactic acidosis. The physiological mechanisms of the delayed, slower phase remain to be resolved. As 'fast twitch' muscle fibres have been shown to be energetically inefficient compared to 'slow twitch' muscle fibres (Crow & Kushmerick, 1982) and tend to be recruited more at higher work rates (Henneman & Olsen, 1965; Saltin & Gollnick, 1983), they may play a role in this phenomenon. However, the dynamics of the 'excess' $\dot{V}_{O_2}$ appear to be related to the magnitude and the time course of the increase in blood [lactate] (Roston *et al.* 1987), both before and after endurance training (Casaburi *et al.* 1987; Poole *et al.* 1988, 1990). Other potential metabolic stimulators, such as catecholamine levels, body temperature and ventilation (Casaburi *et al.* 1987; Poole *et al.* 1988), correlate poorly with the time course of 'excess $\dot{V}_{O_2}$', although they each are likely to be involved to some extent. Furthermore, experimentally increased blood [lactate] in resting animals also stimulates $\dot{V}_{O_2}$ appreciably (Bertram, Wasserman & Van Kessel, 1967), whereas the increase resulting from elevating catecholamine levels is relatively small (Sjostrom, 1985; Staten, Matthews, Cryer & Bier, 1987). Roth, Stanley & Brooks (1988), however, were unable to discern any significant difference in the pattern of post-exercise $\dot{V}_{O_2}$ when blood [lactate] was elevated to a peak of approximately 5 mM l^{-1} by circulatory occlusion during the work. This would be consistent, however, with our results; the off-transient $\dot{V}_{O_2}$ kinetics following the supra-θ_L exercise were predominantly first-order and, as shown in Fig. 2 and Table 2, with a 'sub-threshold' time constant (discussed below).

A further feature of the dynamic non-linearity of the $\dot{V}_{O_2}$ responses to heavy exercise is that the off-transient kinetics are faster than those of the on-transient. At the off-transient, $\dot{V}_{O_2}$ was either monoexponential (e.g. Figs 2 and 3; Table 2) or had a slow component that was appreciably smaller ($\simeq 10\%$) than that of the on-transient. Linnarsson's (1974) data also show a markedly reduced slow phase of $\dot{V}_{O_2}$ at the off-transient, although his work rates were higher than those we utilized. Furthermore, Ren, Broberg & Sahlin (1989) recently demonstrated that, at 20, 40 and 60% of $\mu\dot{V}_{O_2}$, the O_2 debt and deficit were not significantly different in five healthy subjects; however, at 80% of $\mu\dot{V}_{O_2}$, the O_2 debt was less than the deficit. It is likely that this relative 'speeding' of the $\dot{V}_{O_2}$ kinetics at the off-transient operates only within a restricted range above the lactate threshold, as we and numerous other investigators have demonstrated a significant slow phase of the off-transient kinetics that becomes more prominent the higher the work rate (Margaria, Edwards & Dill, 1933; Knuttgen, 1962; Davies, DiPrampero & Cerretelli, 1972). Our present results

suggest, therefore, that the slow component becomes manifest at the off-transient at a higher work rate than for the on-transient. Consequently, the greater rate of change of the 'O_2 debt' which occurs over a small range of work rates above θ_L appears to be a result of – or is dominated by – the increased 'gain' factor consequent to the 'excess $\dot{V}_{O_2}$' with little or no slow dynamics, but that at higher work rates the slow phase of the recovery $\dot{V}_{O_2}$ compounds the effect, yielding even greater values of 'O_2 debt'. This asymmetry of $\dot{V}_{O_2}$ kinetics at these work rates suggests that the limitations to oxygen utilization during the exercise are alleviated, or less prominent, at the off-transient; i.e. that the lactate is cleared by predominantly aerobic mechanisms and that the other metabolic stimulants (e.g. catecholamines, Q_{10}, work of breathing) are either present at too low a value to educe discernible responses or that they induce an effect which operates with a time constant similar to that of the exercising muscle $\dot{V}_{O_2}$.

The consequence, however, is that dynamic system characterizations that yield lumped parameters for on- and off-transient behaviour are likely to suggest misleading physiological correlates in this intensity domain.

Supported by grants from NHLBI (No. 11907) and NSERC (No. A2787).

REFERENCES

ANDERSEN, P. & SALTIN, B. (1985). Maximal perfusion of skeletal muscle in man. *Journal of Physiology* **366**, 233–240.

BEAVER, W. L., LAMARRA, N. & WASSERMAN, K. (1981). Breath-by-breath measurement of true alveolar gas exchange. *Journal of Applied Physiology* **51**, 1662–1675.

BEAVER, W. L., WASSERMAN, K. & WHIPP, B. J. (1973). On-line computer analysis and breath-by-breath graphical display of exercise function tests. *Journal of Applied Physiology* **34**, 128–132.

BERTRAM, F. W., WASSERMAN, K. & VAN KESSEL, A. L. (1967). Gas exchange following lactate and pyruvate injections. *Journal of Applied Physiology* **23**, 190–194.

BYLUND-FILLENIUS, A. C., WALKER, P. M., ELANDER, A., HOLM, S., HOLM, J. & SCHERSTEN, T. (1981). Energy metabolism in relation to oxygen partial pressure in human skeletal muscle during exercise. *Biochemical Journal* **200**, 247–255.

CASABURI, R., STORER, T. W., BEN DOV, I. & WASSERMAN, K. (1987). Effect of endurance training on possible determinants of $\dot{V}_{O_2}$ during heavy exercise. *Journal of Applied Physiology* **62**, 199–207.

CROW, M. T. & KUSHMERICK, M. J. (1982). Chemical energetics of slow- and fast-twitch muscles of the mouse. *Journal of General Physiology* **79**, 147–166.

DAVIES, C. T. M., DIPRAMPERO, P. E. & CERRETELLI, P. (1972). Kinetics of cardiac output and respiratory gas exchange during exercise and recovery. *Journal of Applied Physiology* **32**, 618–625.

DURAND, J. (1980). Circulatory responses to exercise. In *Lactate: Physiologic, Methodologic and Pathologic Approach*, ed. MORET, P. R., WEBER, J., HAISSLY, J. CL. & DENOLIN, H., pp. 25–34. Springer-Verlag, Berlin.

HENNEMAN, E. & OLSEN, C. B. (1965). Relations between structure and function in the design of skeletal muscle. *Journal of Neurophysiology* **28**, 581–598.

HUGHSON, R. L. & INMAN, M. D. (1986). Oxygen uptake kinetics from ramp work tests: variability of single test values. *Journal of Applied Physiology* **61**, 373–376.

HUSZCZUK, A., WHIPP, B. J. & WASSERMAN, K. (1990). A respiratory gas exchange simulator for routine calibration in metabolic studies. *European Respiratory Journal* **3**, 465–468.

JORFELDT, L., JUHLIN-DANNFELT, A. & KARLSSON, J. (1978). Lactate release in relation to tissue lactate and human skeletal muscle during exercise. *Journal of Applied Physiology* **44**, 350–352.

KNUTTGEN, H. G. (1962). Oxygen debt, lactate, pyruvate and excess lactate after muscular work. *Journal of Applied Physiology* **17**, 639–644.

KNUTTGEN, H. G. & SALTIN, B. (1972). Muscle metabolites and oxygen uptake in short-term submaximal exercise in man. *Journal of Applied Physiology* **32**, 690–694.

LAMARRA, N., WHIPP, B. J., WARD, S. A. & WASSERMAN, K. (1987). Breath-to-breath 'noise' and parameter estimation of exercise gas-exchange kinetics. *Journal of Applied Physiology* **62**, 2003–2012.

LINNARSSON, D. (1974). Dynamics of pulmonary gas exchange and heart rate changes at start and end of exercise. *Acta Physiologica Scandinavica* **415**, suppl., 1–68.

MAHLER, M. (1985). First order kinetics of muscle oxygen consumption and an equivalent proportionality between $\dot{Q}_{O_2}$ and phosphorylcreatine level. *Journal of General Physiology* **86**, 135–165.

MARGARIA, R., EDWARDS, H. T. & DILL, D. B. (1933). The possible mechanisms of contracting and paying the oxygen debt and the role of lactic acid in muscular contraction. *American Journal of Physiology* **106**, 689–715.

PATERSON, D. H. & WHIPP, B. J. (1987). The kinetics of oxygen uptake during heavy exercise in man. *Journal of Physiology* **394**, 56*P*.

PIIPER, J., DIPRAMPERO, P. E. & CERRETELLI, P. (1968). Oxygen debt and high-energy phosphates in gastrocnemius muscle of the dog. *American Journal of Physiology* **215**, 523–531.

POOLE, D. C., WARD, S. A., GARDNER, G. W. & WHIPP, B. J. (1988). Metabolic and respiratory profile of the upper limit for prolonged exercise in man. *Ergonomics* **31**, 1265–1279.

POOLE, D. P., WARD, S. A. & WHIPP, B. J. (1990). Effect of training on the metabolic and respiratory profile of heavy and severe exercise. *European Journal of Applied Physiology* **59**, 421–429.

REN, J. M., BROBERG, S. & SAHLIN, K. (1989). Oxygen deficit is not affected by the rate of transition from rest to submaximal exercise. *Journal of Physiology* **135**, 545–548.

ROSTON, W. L., WHIPP, B. J., DAVIS, J. A., CUNNINGHAM, D. A., EFFROS, R. M. & WASSERMAN, K. (1987). Oxygen uptake kinetics and lactate concentration during exercise in humans. *American Review of Respiratory Disease* **135**, 1080–1084.

ROTH, D. A., STANLEY, W. C. & BROOK, G. A. (1988). Induced lactacidemia does not affect post-exercise O_2 consumption. *Journal of Applied Physiology* **65**, 1045–1049.

ROWELL, L. B. (1986). *Human Circulation: Regulation during Physical Stress*. Oxford University Press, Oxford.

SALTIN, B. & GOLLNICK, P. D. (1983). Skeletal muscle adaptability: significance for metabolism and performance. In *Handbook of Physiology*, section 10, *Skeletal Muscle*, ed. PEACHEY, L. D, pp. 555–631. American Physiological Society, Washington, D.C.

SJOSTROM, L. (1985). Catecholamine sensitivity with respect to metabolic rate in man. *International Journal of Obesity* **9**, suppl. 2, 123–129.

STATEN, M. A., MATTHEWS, D. E., CRYER, P. E. & BIER, D. M. (1987). Physiologic increments in epinephrine stimulate metabolic rate in humans. *American Journal of Physiology* **253**, E322–330.

WHIPP, B. J. (1987). Dynamics of pulmonary gas exchange. *Circulation* **76**, suppl. VI, 18–28.

WHIPP, B. J., DAVIS, J. A., TORRES, F. & WASSERMAN, K. (1981). A test to determine the parameters of aerobic function during exercise. *Journal of Applied Physiology* **50**, 217–221.

WHIPP, B. J., WARD, S. A., LAMARRA, N., DAVIS, J. A. & WASSERMAN, K. (1982). Parameters of ventilatory and gas exchange dynamics during exercise. *Journal of Applied Physiology* **52**, 1506–1513.

WHIPP, B. J., WARD, S. A. & WASSERMAN, K. (1986). Respiratory markers of the anaerobic threshold. *Advances in Cardiology* **35**, 47–64.