DETERMINANTS OF VENTILATION DURING EXERCISE

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ABSTRACT

The anaerobic threshold hypothesis suggests a causal link between the ventilatory and lactate responses to exercise. If such a causal link exists, it should be evident in all subjects, regardless of fitness levels. There is also evidence to support a role of potassium in the regulation of ventilation. Further, numerous authors have suggested that submaximal threshold indices can accurately predict performance.

Sixteen male subjects participated in two studies involving incremental work tests and prolonged exercise on a bicycle ergometer. Measurements of respiratory gases and ventilation ($\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$) were made continuously during exercise, while metabolite and electrolyte concentrations (La^-, K^+, pH) were measured on arterialised blood samples taken via an indwelling catheter, both before and during exercise.

Eight endurance trained (ET) and eight untrained (UT) subjects completed a fast incremental work test, during which there was significant correlation between both V_E and $[La^-]$ (UT $r = 0.877$, ET $r = 0.848$, $p < 0.05$) and $\dot{V}_E$ and $[K^+]$ (UT $r = 0.869$, ET $r = 0.774$, $p < 0.05$). $\dot{V}_E$ was significantly lower in ET relative to UT at 330W ($p < 0.05$), the highest workload the two groups had in common. Similarly, $[K^+]$ was significantly lower at 300W and 330W and $[La^-]$ was significantly lower at all work loads in excess of 90W. From graphs of respiratory and lactate responses, the first and second ventilatory thresholds and the first lactate threshold (VT_1, VT_2 and LT_1) were determined. Maximum oxygen consumption ($\dot{V}O_2max$) and all thresholds were significantly higher ($p < 0.05$) for ET than for UT, both in terms of absolute $\dot{V}O_2$ and $\%\dot{V}O_2max$. VT_1 was coincident with LT_1 for both groups.

The eight ET subjects also completed the second study involving a slow incremental work test for assessment of the individual anaerobic threshold (IAT), and a one hour

self-paced trial, both on the bicycle ergometer. During the self-paced trial, there was again significant correlation between $\dot{V}_E$ and $[La^-]$ ($r = 0.738$ to 0.756, $p < 0.05$). Although statistically significant, correlations between $\dot{V}_E$ and $[K^+]$ were low ($r = 0.371$ to 0.373, $p < 0.05$). All subjects reached steady state $[K^+]$ between the 20th and 50th minutes of the trial ($p < 0.05$). Similarly, four subjects reached steady state $[La^-]$ in the same time period, three of whom also attained steady state $\dot{V}O_2$. Only one subject reached a steady state $\dot{V}_E$. No IAT was calculable in two of the eight subjects and the mean IAT was significantly different from the mean VT_2. Neither these, nor the VT_1 or LT_1 could accurately predict performance.

The following conclusions were drawn from the results of this thesis:

(1) changes in ventilation during exercise are regulated by a number of inputs including La^- and K^+, both of which are important,

(2) the LT_1 and the VT_1 may have a causal relationship even considering the role of K^+ in the regulation of ventilation, and

(3) threshold indices measured during incremental work tests do not accurately predict endurance performance, represented by a one hour self-paced trial.

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LIST OF ABBREVIATIONS

AnT	Anaerobic threshold
CLW	Constant load work
IAT	Individual anaerobic threshold
IW	Incremental work
LT_1	First lactate threshold
LT_2	Second lactate threshold
MSS	Maximum steady state
OBLA	Onset of blood lactate accumulation
OPLA	Onset of plasma lactate accumulation
RCT	Respiratory compensation threshold
TDMA	Threshold of decompansation for metabolic acidosis
$\dot{V}_E/\dot{V}CO_2$	Ventilatory equivalent for carbon dioxide
$\dot{V}_E/\dot{V}O_2$	Ventilatory equivalent for oxygen
VT_1	First ventilatory threshold
VT_2	Second ventilatory threshold
VT_{long}	Ventilatory threshold for long term exercise

CHAPTER 1.

REVIEW OF LITERATURE

1. Introduction

Both aerobic and anaerobic metabolism play a role, at any exercise intensity, in the resynthesis of adenosine triphosphate (ATP) for continued muscular contraction. The relative importance of one metabolic pathway over the other varies with exercise intensity. At low exercise intensity, ATP resynthesis occurs primarily via aerobic metabolism. As exercise intensity increases, so does the proportion of anaerobic metabolism involved. This results in a progressive increase in the production of lactate and hydrogen ions by the active muscles, which in turn leads to an increase in their concentrations in the blood. Accompanying this there is an elevation in 'non-metabolic' carbon dioxide production as a result of the buffering of hydrogen ions, which in turn leads to an increase in ventilation.

The concept of the 'Anaerobic Threshold' (AnT) was proposed to explain the relationship between metabolic events at the site of muscular contraction and the respiratory response to exercise of increasing intensity. Far from consensus being reached however, there has developed much conflict and controversy over the AnT.

More recently, there has been increased interest in the role of potassium in the regulation of ventilation. Potassium efflux occurs with every muscular contraction, an event which is at least partially countered by the activity of the Na-K pumps. The resultant increase in plasma potassium concentration may regulate an elevation in ventilation via both neural and humoral input mechanisms.

This review of literature will consider the mechanisms advanced in interpretation of the AnT concept, as well as the influence of potassium on ventilation. The validity and reliability of AnT measurement, and its usefulness as a guide to endurance performance will also be discussed.

2. Development of the concept and the controversy.

Building on the work of Naimark, Wasserman and McIlroy (1964) which showed that the increase in respiratory exchange ratio reflects a developing metabolic acidosis during incremental exercise, the concept of the AnT was developed by Wasserman and McIlroy (1964). They suggested that the increase in anaerobic metabolism occurring at the AnT was due to hypoxia in the actively contracting muscle fibres. The threshold of anaerobic metabolism could, they suggested, be measured in three ways: "(1) as an increase in lactate concentration in the blood, (2) as a decrease in arterial blood bicarbonate and pH and, (3) as an increase in the respiratory exchange ratio".

Research in this area had begun at least half a century earlier. Christiansen, Douglas and Haldane (1914), discussed what they termed the absorption and dissociation of carbon dioxide in the blood during exercise. Hill, Long and Lupton (1924) noted an increase in lactic acid formation when muscles lack oxygen. Douglas (1927) wrote of the association he observed between 'physicochemical' changes in arterial blood, brought about by variation in the metabolic rate of the tissues, and the equivalent respiratory response. Owles (1930) observed that blood lactate concentrations began to increase from resting concentrations once a critical metabolic rate was breached.

The publication of the articles by Wasserman and his colleagues along with a later article (Wasserman, Whipp, Koyal and Beaver, 1973) heralded the present interest, as well as the controversy, in the AnT. Wasserman et al. (1973) defined the AnT as

"the level of work or O_2 consumption just below that at which metabolic acidosis and the associated changes in gas exchange occur". Again the inadequate supply of O_2 to the working muscles was suggested as the stimulus for the threshold phenomenon.

With continued research a number of areas of conflict have arisen, many of which are yet to be resolved. The most contentious issues surrounding the AnT are:
(1) is muscle tissue hypoxic at the work intensity corresponding to the AnT?
(2a) is there a cause and effect relationship between the ventilatory and local metabolic responses to exercise, or are they merely coincident and reliant upon circumstance?
(2b) are there physiologic changes other than that associated with the increase in anaerobic metabolism, which could also significantly effect ventilation?
(3) does blood lactate concentration accurately reflect intramuscular lactate concentration?
(4a) is there a threshold phenomenon in the response to incremental work tests, or do lactate and ventilation rise exponentially from rest?
(4b) is there a second discernable threshold in both/either of the lactate and ventilatory responses to incremental work tests and if so, at what intensity does it occur?
(5) are the subjective methods of threshold detection reliable given inter- and intra-investigator variability?
(6) does the AnT or any of the other threshold variable, accurately predict endurance performance?

3. Definition of the anaerobic threshold

According to Wasserman, the AnT consists of a lactate threshold with an associated ventilatory threshold. Other investigators have proposed alternative threshold reponses with alternative definitions, which vary in degree of similarity to that

proposed by Wasserman. As a result, there exists in the literature a broad array of terminology, all purporting to describe specific changes in the ventilatory and lactate responses to exercise of progressively increasing intensity. Table 1 lists a selection of the differing thresholds under four broad headings as employed by McLellan (1987). The entries in this table are by no means exhaustive, but instead represent alternative definitions and methods of detection from those of the other entries within each group. The concepts accompanying each different term listed under a particular heading are not necessarily equivalent. For example, both the individual anaerobic threshold (IAT) of Stegmann, Kindermann and Schnabel (1981) and the AnT of Kindermann, Simon and Kuel (1979) are listed under 'Rapid increase' in lactate response, since both occur during the latter stages of a progressive incremental work test, even though they describe two quite different events. Appendix 1 gives a more complete list with accompanying definitions for each term.

For the remainder of this review, the following terms will be used to denote the ventilatory and metabolic responses to incremental exercise:
First ventilatory threshold (VT_1) - initial increase in ventilation relative to oxygen consumption with no change relative to carbon dioxide production.
Second ventilatory threshold (VT_2) - increase in ventilation relative to carbon dioxide production with a further increase with respect to oxygen consumption.
First lactate threshold (LT_1) - initial continuous increase in blood lactate concentration, above that existing at rest.
Second lactate threshold (LT_2) - subsequent rapid increase in blood lactate concentration.

These terms will be used where a general descriptor is appropriate. Where a specific definition is being considered, the terminology proposed by the original investigators will be preferred.

VENTILATORY RESPONSE	
Increase in $\dot{V}E$ compared with $\dot{V}O_2$	**Increase in $\dot{V}_E$ compared with both $\dot{V}CO_2$ and $\dot{V}O_2$**
Anaerobic threshold (Wasserman et al., 1973)	Threshold of decompensated metabolic acidosis (Reinhard et al.,1979)
Aerobic threshold (Skinner and McLellan, 1980)	Anaerobic threshold (Skinner and McLellan, 1980)
Ventilation threshold (Jones and Ersham, 1982)	Ventilation threshold for long-term exercise (Reybrouk et al., 1983)
First ventilatory threshold (McLellan, 1985)	Second ventilatory threshold (McLellan, 1985)
LACTATE RESPONSE	
Initial continuous increase	**Rapid increase**
Anaerobic threshold (Wasserman et al., 1973)	Anaerobic threshold (Kindermann et al., 1979)
Maximum steady state (Londeree and Ames, 1975)	Individual anaerobic threshold (Stegmann et al., 1981)
Aerobic thresold (Kindermann et al., 1979)	Lactate turnpoint (Davis et al., 1983)
Lactate threshold (Ivy et al., 1980)	

Table 1.1: A classification of the different terminologies that exist in the literature to define specific changes in the ventilatory and lactate responses to incremental exercise (Adapted from McLellan, 1987).

4. Current Concepts

The interpretation of the mechanisms underlying the response to continuous incremental work (IW) offered here, is based on that developed by Wasserman et al. (1973) and later summarised by Davis (1985) and McLellan (1987). It serves as a beginning against which the various aspects of the concept which are subject to disagreement can be compared.

At rest or during low exercise intensities (ie. those below 40% $\dot{V}O_2max$), aerobic metabolism provides the primary mechanism for ATP repletion. This excludes the possibility of a temporary utilization of anaerobic metabolism associated with an abrupt onset of exercise. Oxidation of carbohydrates and free fatty acids predominates and the subsequent production of carbon dioxide (CO_2) is accompanied by an increase in CO_2 flux to the lungs.

Receptors sensitive to variations in the partial pressure of CO_2 (PCO_2) and/or hydrogen ion (H^+) in the blood are activated causing an increase in ventilation ($\dot{V}_E$) which, at low intensity exercise, occurs in direct proportion to changes in both $\dot{V}O_2$ and $\dot{V}CO_2$. Ventilatory control will be discussed in greater depth later in this review.

Anaerobic metabolism is active at low intensity exercise, but the increase in the rate of accumulation of lactate (La^-) in the blood is minimal over that at rest, since mechanisms of its removal are able to match those of its production. As exercise intensity is progressively increased a work load is reached, which varies from one person to the next, where a rise in blood La^- concentration occurs corresponding to an increase in anaerobic metabolism. The anaerobic metabolism becomes more active since the O_2 demands of the exercising muscles have exceeded the O_2 supply to the mitochondria. The rise in La^- concentration above those existing at rest, marks the LT_1 and occurs at between 40-60 % of $\dot{V}O_2$ max.

Lactic acid is almost completely dissociated at physiological pH into lactate and H^+. The majority of H^+ produced in the cytoplasm is buffered primarily by bicarbonate ion (HCO_3^-) and the non-metabolic CO_2 generated by this is released into the blood. This causes a further increase in the CO_2 flux to the lung, above that generated from aerobic metabolism, and consequently there is an elevation in $\dot{V}_E$ at a rate greater than that in $\dot{V}O_2$ and metabolic rate. These ventilatory changes begin at the VT_1, which coincides with the same work intensity and $\dot{V}O_2$ as the LT_1.

The drop in pH that occurs at the LT_1 as a result of the generation of H^+ is only evident during fast IW tests (ie. increases of greater than 30W/minute). The metabolic acidosis accompanying exercise in slower IW tests (ie. increases of 30W/ 4 minutes) is delayed until a higher work load. The difference is a result of the delay time needed for the attainment of new 'steady state' metabolic and ventilatory responses at each succesive work load, steady state being achieved in a slow IW test but not in a fast IW test. This will be discussed in more detail later in this review. Figure 1.1 summarises these changes (McLellan, 1987).

After the first threshold, the ventilatory response to IW tests of different protocols also varies according to the rate of work load increment. During fast incremental tests, a period of 'isocapnic buffering' occurs at work loads in excess of VT_1. In this period $\dot{V}_E$ remains closely linked to $\dot{V}CO_2$, but while end-tidal CO_2 remains constant HCO_3^- and pH fall progressively, causing a metabolic acidosis to develop with only partial respiratory compensation at most.

The metabolic acidosis continues until the VT_2, which marks the beginning of the more complete respiratory compensation for the developing metabolic acidosis at work loads between 65 and 85 % $\dot{V}O_2max$. As work loads are increased beyond VT_2, this respiratory compensation is manifested as a further increase in the rate of the ventilatory response, in excess of that in $\dot{V}CO_2$ as well as $\dot{V}O_2$.

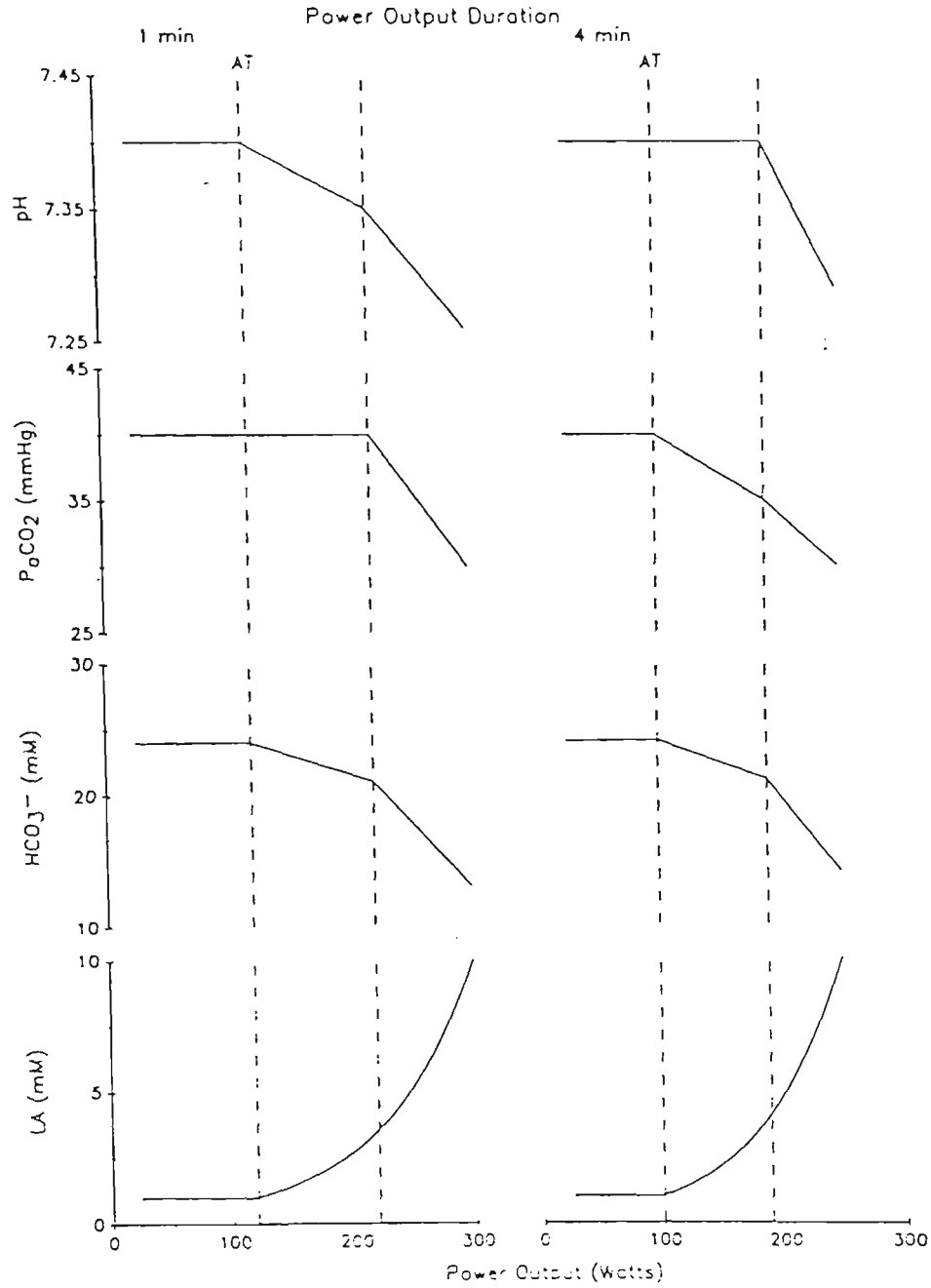

Figure 1.1: A schematic representation of the changes in blood pH, carbon dioxide (PCO_2), bicarbonate (HCO_3^-) and lactate (LA) concentrations throughout exercise tests employing either fast (one minute) or slow (four minute) power output increments (McLellan, 1987).

There is no direct correlate of VT_2 in the pattern of La^- accumulation in the blood, although many investigators have identified a critical point of La^- concentration, in excess of LT_1, occuring just prior to the phase of rapid increase in La^- accumulation in the blood (LT_2). In spite of there being quite considerable variation in the work rate and/or the $\dot{V}O_2$ required to produce these different LT_2 values, some researchers accredit their LT_2 'equivalent' as representing the point where the rate of lactate removal is maximal (Davis, Bassett, Hughes and Gass, 1983; Stegmann et al., 1981). At exercise intensities above LT_2, the rate of La^- production occurs in excess of its maximal removal rate, resulting in the rapid rise in blood La^- concentration.

In slow incremental tests there is no period of isocapnic buffering, since pH does not begin to drop until VT_2. As a result, $\dot{V}_E$ and $\dot{V}CO_2$ continue to remain closely linked at all exercise intensities above VT_1, so that no second threshold is observed. Because of this, most investigators orignally ascribed little importance to the VT_2 (Wasserman and Whipp, 1975), although it has more recently been the subject of more attention as regards its significance (McLellan and Gass, 1989; Reybrouk, Ghesquiere, Cattaert et al., 1983).

Whipp, Davis and Wasserman (1989) have suggested that 'isocapnic buffering' is the result of a ventilatory response, short of that producing complete compensation for the metabolic acidosis, which causes the levelling out of arterial PCO_2. During the early phases of a rapid incremental test, arterial PCO_2 increases up to VT_1, the levelling off above VT_1 being caused by an increased breathing frequency. However, the response is not yet strong enough to result in respiratory compensation, as reflected by a declining arterial PCO_2. In tests employing a slower increment, there is time at these lower supra-VT_1 workloads for the ventilatory response to provide more complete compensation for the metabolic acidosis.

The ventilatory equivalents for oxygen ($\dot{V}_E/\dot{V}O_2$) and carbon dioxide ($\dot{V}_E/\dot{V}CO_2$) are often used as markers for the ventilatory thresholds. Prior to VT_1, both ventilatory equivalents decrease as work loads increase from rest, due to a decrease in the ratio of the physiological dead space to tidal volume (Jones and Ersham, 1982).

At VT_1, $\dot{V}CO_2$ and $\dot{V}_E$ begin to increase more rapidly than $\dot{V}O_2$, so $\dot{V}_E/\dot{V}O_2$ reaches a minimum value and progressively rises thereafter. During fast incremental tests, $\dot{V}_E/\dot{V}CO_2$ continues to drop during the period of isocapnic buffering. These two criteria, introduced by Davis, Frank, Whipp and Wasserman (1979), constitute the most accepted method of VT_1 assessment. $\dot{V}_E/\dot{V}CO_2$ reaches its minimum at VT_2 during fast IW tests, before progressively rising at higher exercise intensities.

During slow IW tests, both ventilatory equivalents reach a minimum at VT_1 and rise progressively at higher work loads because of the absence of isocapnic buffering. These relationships are summarised in Figure 1.2 (Wasserman and Whipp, 1975).

Later, McLellan (1985) assessed the relationship of $\ln\dot{V}_E/\dot{V}CO_2$ to $\dot{V}O_2$ and found an inflection point corresponding to VT_2 at identical $\dot{V}O_2$ values during IW tests employing both fast and slow work load increments. On this basis, he suggested that VT_2 may have greater physiological significance than had been previously suggested.

A number of authors have rejected the threshold phenomenon in favour of exponential models of ventilatory and lactate response (Campbell, Hughson and Green, 1989; Hughson, 1984; Hughson, Weisiger and Swanson, 1987, Yeh, Gardner, Adams et al., 1983). The IAT of Stegmann, Kindermann and Schnabel (1981) is also based on an exponential rise in blood lactate after an initial linear segment. Mathematical models of response patterns will be discussed in detail later in this review.

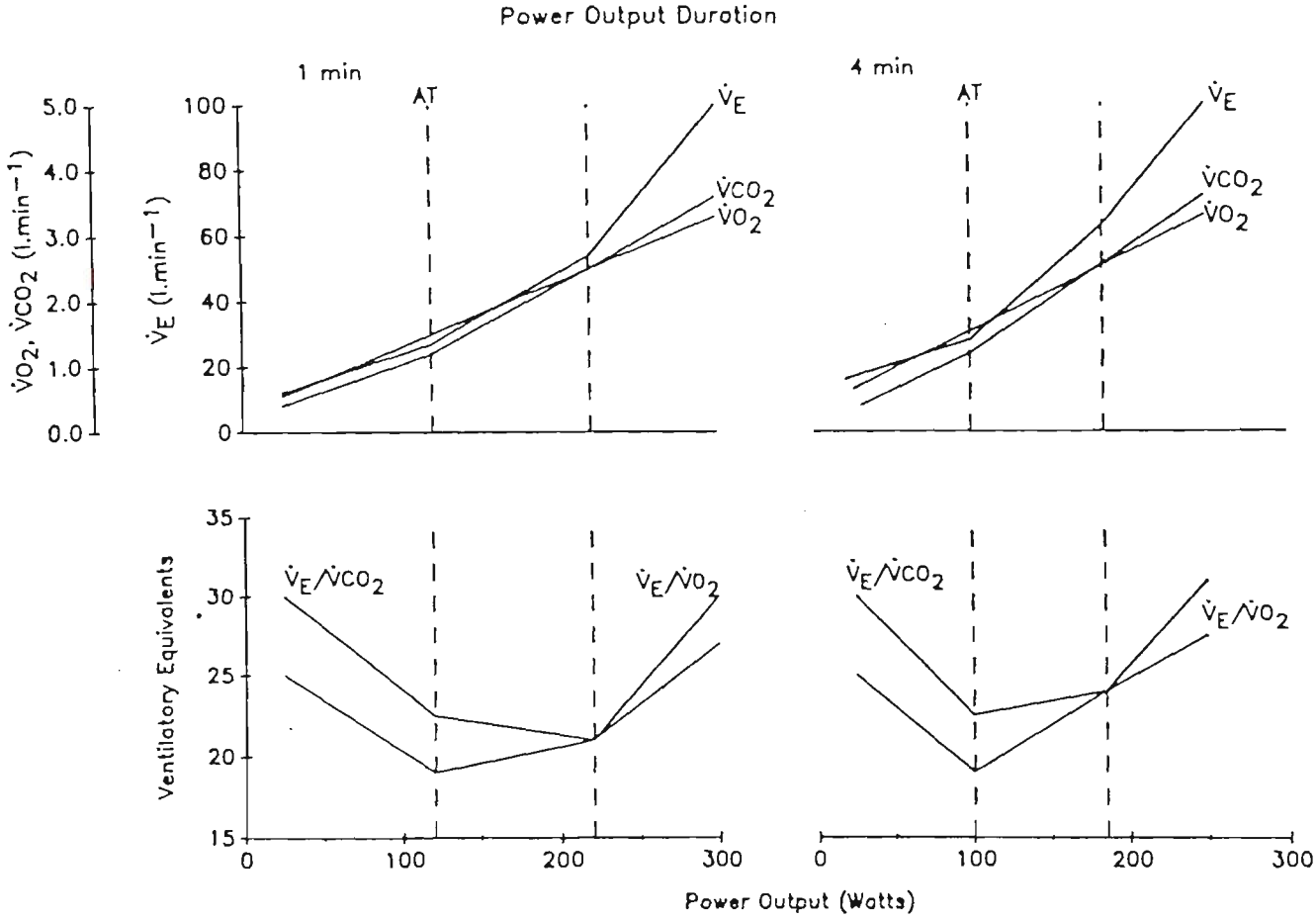

Figure 1.2: A schematic representation of the changes in ventilation, oxygen uptake, carbon dioxide output and the ventilatory equivalents for oxygen and carbon dioxide throughout an exercise test involving either fast (one minute) or slow (four minute) power output increments (modified from Wasserman and Whipp, 1975, in McLellan, 1987).

5. Allied Concepts

A number of other physiological variables have also been used to denote changes in the response to incremental exercise.

Heart rate breakpoint.

Conconi, Ferrari, Ziglio et al. (1982) studied the relationship between running speed and heart rate response. They concluded that the relationship could be described as having an initial linear segment separated from a curvilinear segment, corresponding to higher running speeds, by a point of deflection which correlated well ($r = 0.93$) with LT_1. They were unable to reproduce the same high correlation in other sports. Ribeiro, Fielding, Hughes et al. (1985) found that the heart rate 'break point' correlated better with LT_2 ($r = 0.97$) than with LT_1 ($r = 0.89$).

Critical power.

The critical power concept was initially proposed for single muscle groups by Monod and Scherrer (1965). It was later reported by Moritani, Nagata, De Vries and Muro (1981), that the concept was equally valid for whole body exercise. Through a series of constant load work (CLW) tests, a critical power was established which was equal to "the rate of energy supply at which work can be sustained without fatigue". A high correlation has been found between critical power and the VT_1 (De Vries and Moritani, 1980, $r = 0.93$, Moritani et al., 1981, $r = 0.91$, De Vries et al., 1982, $r = 0.88$). An earlier study by Gleser and Vogel (1973) had also derived a relationship between endurance time and work load during a series of CLW tests but did not correlate their findings with either VT_1 or LT_1.

Fatigue threshold.

Whipp, Huntsman, Storer et al. (1982), also followed a similar path with their 'fatigue threshold' concept. Again, in a series of CLW tests, subjects exercised to exhaustion at a number of different work loads. From a relationship between power output and time to fatigue, the fatigue threshold, being the power output that can be maintained for an infinite time, was calculated. These authors suggest that the fatigue threshold occurs at a higher power output than the VT_1/LT_1.

Further work has been conducted on this concept by Hughson, Orok and Staudt (1984), who suggest that it may provide a more accurate estimate of endurance performance than VT_1 or LT_1. Poole, Ward and Whipp (1986) suggest that it represents the CLW at which a maximum steady state of $\dot{V}O_2$, blood La^- and pH is attained. Exercise at higher intensity will result in a steadily increasing $\dot{V}O_2$ and blood La^- and a steadily decreasing pH.

EMG studies.

De Vries et al. (1982) also developed a fatigue threshold which they defined as the highest constant power output requiring no increase in electromyographic (EMG) activity for its maintenance. They reported a correlation of $r = 0.90$ between their fatigue threshold and VT_1. Moritani and De Vries (1980) had previously correlated integrated EMG (IEMG) with VT_1 ($r = 0.973$). Nagata, Moritani and Muro (1983) again found a significant correlation ($r = 0.927$) between critical power and VT_1 and also suggested a link between neuromuscular fatigability (determined from IEMG measurements during a series of CLW tests) and critical power. Indirectly then, this supports the work of De Vries et al. (1982). Viitasalo, Luhtanen, Rahkila and Rusko (1985) compared IEMG activity with both first and second thresholds (determined

by both gas exchange and blood La^- criteria). They concluded that the IEMG could be used to indicate the first but not second threshold.

Potassium threshold.

Gleim, Zabetakis, Coplan et al. (1988) have demonstrated a relationship between the changes in potassium and lactate concentrations during IW. They reported that serum potassium levels rose minimally at power outputs below that corresponding to the LT_1, but at power outputs in excess of the LT_1 there was a consistent and significant increase in serum potassium concentration. Although they do not directly correlate the 'potassium threshold' with the LT_1, they inferred coincidence between the two. No comparisons with ventilatory response were reported.

6. Proposed mechanisms producing the lactate threshold (LT_1)

Although a great deal of research supports the direct association of the ventilatory and lactate responses to IW tests, there is perhaps an equal volume which rejects the association. Because of this, discussion of the proposed mechanisms for the ventilatory and lactate thresholds will be considered separately. A number of propositions have been raised to explain the threshold phenomena and the main ones will be considered in turn.

6.1 Tissue Hypoxia

In developing their original anaerobic threshold concept, Wasserman and McIlroy (1964) and Wasserman et al. (1973) suggeted that tissue hypoxia was the major cause of the rise in blood [La^-]. As the supply of O_2 to exercising muscles falls behind demand, the rate of anaerobic glycolysis is increased to meet this added demand and

the elevated blood lactate concentration reflects similarly elevated production of lactate in the muscle.

In the presence of hypoxia, pyruvate is produced during glycolysis at a rate above that at which it can be oxidised in the Kreb's cycle. As a result, it is reduced to lactate with the accompanying regeneration of nicotinamide adenine dinucleotide (NAD), which is necessary for the maintenance of glycolysis. (Stainsby, 1986). Mader and Heck (1986) claim that the limiting factor in the oxidation of pyruvate is 'saturation' of pyruvate dehydrogenase (PDH) activity, the enzyme necessary for the conversion of pyruvate to acetyl CoA.

To support his hypothesis, Wasserman (1984) cites a number of studies in which an alteration to oxygen supply produces a relative alteration in blood lactate concentration. Among them are experiments in which induced hyperoxia caused a decrease in blood lactate concentration and muscle lactate release (Banister, Taunton, Patrick et al., 1970; Hughes, Clode, Edwards et al., 1968; Linnarsson, Karlsson, Fagraeus et al., 1974). Walsh and Banister (1988) point out that although this may be explained by a decrease in the number of hypoxic loci within muscle tissue, it could also be explained by the inhibitory effect of hyperoxia on glycolysis.

Other interventions cited by Wasserman (1984) involved those where the delivery of oxygen to the exercising muscles was decreased by various methods, resulting in an increase in blood [La^-] and a shift in the threshold to lower $\dot{V}O_2$ (Hughes et al., 1968; Linnarsson et al., 1974). Numerous studies offer evidence which weakens the validity of this observation. Jobsis and Stainsby (1968) observed that with isolated muscle preparations, NAD levels were never low enough to reflect a limitation of oxidative metabolism, suggesting instead that a mass action effect due to the increased availability of pyruvate and extramitochondrial NADH caused the increased lactate production. But in studies involving exercising humans Graham,

Sjogaard, Lollgen and Saltin (1978) observed changes in mitochondrial redox state reflecting a lower NAD concentration and/or higher NADH concentration. This contradiction was addressed by Graham and Saltin (1989) who found in favour with the original results of Jobsis and Stainsby (1968) that NAD/NADH did not decrease but actually rose during exercise.

Katz and Sahlin (1988) argue however that neither the surface fluorometry technique used by Jobsis and Stainsby (1968), nor the glutamate dehydrogenase technique of Graham and Saltin (1989) give accurate estimation of mitochondrial redox state. Instead they use a method involving chemical determination of total tissue NADH, finding that muscle NADH is increased above resting values during high intensity exercise (Sahlin and Katz, 1987). The technique they used for NADH determination also suffers from criticisms regarding its validity, based on its inability to differentiate NADH concentrations between cytoplasmic and mitochondrial compartments.

In defence of his anaerobic threshold hypothesis, Wasserman (1984) refers to the fact that the lactate/pyruvate ratio rises coincidently with the increase in blood [La^-], rather than before it, as suggested by the mass action hypothesis.

Kaijser (1970) has shown that altering partial pressure of arterial oxygen from 5% below to 30 % above normal values produces little variation in (a-$\bar{v}$) O_2 difference. This is supported by Connett, Gayeski and Honig (1984) who showed that the lowest mitochondrial PO_2 required for uninhibited production of ATP is not reached in electrically stimulated isolated dog gracilis muscle, even though increases in lactate production occur. In a later paper, the same authors (Connett, Gayeski and Honig, 1986) reject the concept of Wasserman's anaerobic threshold and state that neither tissue nor blood [La^-] reflect muscle O_2 availability or glycolytic rate.

Pirnay, Marechal, Radermecker and Petit (1972) demonstrated that the O_2 tension in venous blood was significantly greater than the critical mitochondrial O_2 tension. Using radioactively labelled lactate 'tracers', Mazzeo, Brooks, Schoeller and Budinger (1983), Donovan and Brooks (1983) and Brooks (1986b), have all shown that lactate is produced under fully aerobic conditions. However, tracer methodology has been criticised for its inability to distinguish between lactate and pyruvate, with the result that instead of measuring lactate production, it may detect the rate of total pyruvate production (Wolfe, Jahoor and Miyoshi, 1988) which is far in excess of that of lactate.

Wasserman addresses the question of adequacy of O_2 supply in recent reviews (Wasserman, 1986a; Wasserman, Beaver and Whipp, 1990). He suggests that hypoxic loci, resulting from perfusion non-uniformity within an exercising muscle, cannot be detected by methods that measure mean or predominant O_2 pressures across a number of cells. Also, Bylund-Fellenius, Walker, Elander et al., (1981) suggest that in intact tissue, end capillary PO_2 must be maintained above 8 mm Hg to avoid anaerobiosis, not the minimum 1 mm Hg required by an individual mitochondrion. So, while some or even the majority of mitochondria within a muscle may have an adequate supply of O_2 at LT_1, others may be functioning anaerobically. Katz and Sahlin (1988) agree with Wasserman adding that O_2 in isolated mitochondria cannot be taken as being representative of intact tissues or cells.

Holloszy (1973) interprets the muscle hypoxia theory to infer that the lower lactate levels seen in endurance trained individuals are explained by improved oxygen delivery. However, since it is well documented that oxygen consumption does not vary at any given absolute work intensity as a result of training, the concept, in his words 'needs revision'. Davis (1985) defends the original concept pointing out that after training, the drift in $\dot{V}O_2$ at exercise intensities above the threshold is

diminished and that 'steady state' $\dot{V}O_2$ is lower. He agrees with Holloszy regarding work intensities below the LT_1, but not for intensities exceeding it.

Eldridge (1975) states that blood lactate concentrations are the sum of the rate of appearance (turnover) of lactate in the blood and the rate of its clearance. The presence of a sudden and continuous rise in blood La^- concentration in IW tests would appear to be explained, not as the point of sudden onset of anaerobic metabolism as originally proposed by Wasserman, but as the point where turnover of lactate in the blood exceedes clearance rate. Wasserman (1986b) accepts that La^- concentration relies on a balance between production and clearance, but that this does not conflict with his theory of a sudden rise in glycolytic rate at the LT_1. In support of the threshold representing an increased glycolytic rate, he notes that the time to exhaustion during CLW above the LT_1 is less than that during CLW below the LT_1 and suggests that this is due to depletion of intramuscular glycogen used in anaerobic metabolism. In contrast, Wasserman suggests that work below the LT_1 may involve lactate production under predominantly aerobic conditions. Katz and Sahlin (1988) reject criticisms against Wasserman's O_2 dependent lactate production hypothesis since data are either questionable as a result of inappropriate experimental methods, or can be interpreted in a way which supports the hypothesis. A conclusion to this disagreement awaits more sensitive analytical methods.

6.2 Muscle fibre recruitment pattern

At exercise intensities below the first threshold, slow twitch muscle fibres, with high oxidative metabolic capacity, provide most of the contractile activity. During exercise above LT_1 fast twitch fibres, with higher concentrations of glycolytic enzymes, are recruited (Moritani and De Vries, 1980). Clausen (1976) linked the progressive recruitment of the fast twitch fibres to lactate production.

Moritani and de Vries (1980), Nagata et al. (1981; 1983), De Vries et al. (1982) and Viitasalo et al. (1985) all reported strong correlation between the increase in IEMG activity and Wasserman's AnT during bicycle ergometry, as previously discussed. Nagata et al. (1981) suggest that at the LT_1, slow twitch fibres are contracting at maximal frequency. The recruitment of fast twitch fibres and the resultant decrease in pH has an inhibitory effect on the contractile capacity of individual fibres.As further fast twitch fibres are recruited there is an increase in blood La^- concentration because of their greater glycolytic capacity.

In support of these investigations, Farrell, Wilmore, Coyle et al. (1979) found that treadmill velocity at the onset of plasma lactate accumulation (OPLA), $\dot{V}O_2max$ and % slow twitch fibres correlated best with 15 km running performance. Ivy, Withers, Van Handel et al. (1980) found correlations between % slow twitch fibres and absolute ($r = 0.70$) and relative ($r = 0.74$) LT_1. Coyle, Coggan, Hopper and Walters (1988) were less successful in correlating LT_1 and % slow twicth fibres ($r = 0.55$). Tesch, Sharp and Daniels (1981) observed significant correlation ($r = 0.75$) between the relative muscle mass occupied by slow twitch fibres and the $\dot{V}O_2$ at OBLA; however Aunola and Rusko (1986) suggest that muscle fibre type alone has little effect on the $\dot{V}O_2$ at either the first or second threshold. Jacobs and Kaiser (1982) observed no significant difference in lactate concentrations at OBLA in fast or slow twitch fibre populations after incremental cycle exercise. Finally, Saltin, Nazar, Costill et al., (1976) found only a minor change in the distribution of fibre types after training, despite a reduction in lactate production from the trained muscles.

6.3 Aerobic metabolism and substrate utilisation

Closely associated with fibre type is the metabolic profile of the muscle. The greater the aerobic capacity of a muscle, the less lactate it will produce at a given work output. Holloszy and coworkers (Holloszy, 1973; Holloszy and Booth, 1976; Holloszy and Coyle, 1984; Holloszy, Rennie, Hickson et al., 1977) suggest that it is the muscle's enhanced capacity to oxidise fats, due to an increase in mitochondrial density, concentration of oxidative enzymes and electron transport systems, that causes the delay in the LT_1 after exercise training.

Gollnick, Bayly and Hodgson (1986) and Jobsis and Stainsby (1986) suggest that lactate is formed via a mass action effect of lactate dehydrogenase converting pyruvate to lactate. After training, the increased mitochondrial density results in a higher ATP/ADP ratio because the entry of ADP into the mitochondria is enhanced. Glycolysis and glycogenolysis will then remain supressed. Wasserman (1986a) argues against this by citing data which suggests that the increase in pyruvate concentration occurs after the increase in lactate concentration during incremental exercise.

Ivy, Costill, Van Handel et al. (1981) altered substrate availability with dietary manipulations. They tested the hypotheses that elevating blood free fatty acid (FFA) levels prior to exercise would slow carbohydrate metabolism and thus lower La^- production, and conversely that prior ingestion of glucose would stimulate glycolysis and prematurely raise blood [La^-]. During the trials where blood FFA were elevated, blood [La^-] was lowered and LT_1 delayed relative to control trials. No effect was observed however in the trials where glucose was ingested. Hickson, Rennie, Conlee et al. (1977) had found delayed exhaustion in rats following trials in which plasma FFA were raised, suggesting that FFA have a carbohydrate sparing effect via the inhibition of phosphofructokinase by citrate.

In a review of the effect of dietary modification on LT_1, Yoshida (1986) concludes that both of the above hypotheses put forward by Ivy et al. (1981) were valid. Also glycogen depletion via prior exercise led to a delay in LT_1. However, Quiron et al. (1988) observed that while a fat rich diet increased mobilisation of FFA and a carbohydrate rich diet increased the respiratory exchange ratio, neither diet altered LT_1, VT_1 or OBLA.

6.4 Lactate kinetics

As previously mentioned, Eldridge (1975) stated that blood La^- concentration was dependent on its production rate and the clearance rate. Brooks (1985a) has suggested that the LT_1 occurs as a result of the drop in the clearance rate relative to the production rate. As production rate increases with increasing work load, an exercise intensity is reached beyond which the ability to clear lactate becomes progressively inadequate.

The fate of lactate has been subject to considerable scrutiny. Karlsson and Jacobs (1982) point out that lactate produced in one part of a muscle can be partially or completely oxidised in another part of the same muscle, or in a less active neighbouring muscle. Donovan and Brooks (1983) reason that the relative decrease in the clearance rate at the LT_1 is due to a reduction in blood flow to the tissues which oxidise the lactate. The blood flow reduction occurs as a result of vasoconstriction to non-active muscle tissue and other tissues capable of oxidising lactate during exercise. They propose cardiac muscle as another possible site of lactate oxidation.

In a series of papers Brooks (1985c; 1986a; b; c) develops the concept of the 'lactate shuttle' whereby lactate is shuttled from areas of high glycogenolytic rate to areas of high oxidative rate for re-use as a substrate for ATP repletion. He suggests that

although the predominant fate of lactate produced during exercise is oxidation in skeletal and cardiac muscle (up to 75%), a significant proportion (up to 20%) is 'shuttled', firstly from the site of its production to the liver for conversion into glucose via gluconeogenesis, and then back to areas of high metabolic rate. The kidney is also mentioned by Brooks as another potential site of lactate metabolism.

Brooks (1985c; 1986a; b; c) states that the shift in the LT_1 to higher work loads and oxygen consumptions after training is well explained by this theory. An increase in the oxidative profile of muscle, in capillary density of muscle, and in hepatic flow during exercise would all favour improved removal of lactate from the blood and thus delay the LT_1. Sjodin (1976) suggests that slow twitch fibres possess relatively more heart type LDH (H-LDH) than skeletal muscle type LDH (M-LDH) and also that training increases the proportion of H-LDH, another adaptation that would favour the capacity of trained muscle to oxidise lactate.

Davis (1985) raises doubts about the validity of isotopic tracer studies, the method favoured by Brooks and co-workers, while Katz and Sahlin (1988) and Wolfe, Jahoor and Miyoshi (1988) suggest that the isotopic carbon is in equilibrium with pyruvate. Thus, tracer techniques may overestimate the importance of the lactate shuttle since they cannot distinguish between pyruvate and lactate metabolism.

6.5 Catecholamines

Davies, Few, Foster and Sargeant (1974) noted that changes in plasma catecholamines and blood lactate shared a close association during a series of CLW tests of increasing intensity. The changes in the two variables from resting values were both curvilinear and correlated well with each other ($r = 0.88$-0.94) varying slightly depending on the type of exercise. Van Harn and Brooks (1985) observed thresholds during IW tests in both adrenaline and noradrenaline which correlated

($r = 0.96$ and $r = 0.92$ respectively) with LT_1. Similarly Lehmann, Berg, Kapp et al. (1983) found good correlation between the product of lactate and noradrenaline response during IW and running performance ($r = 0.79$).

In a series of experiments, Stainsby and co-workers (1984; 1985; 1987) studied the link between catecholamines and lactate production. They found that adrenaline infusion was more effective in elevating blood La^- and that this metabolic action of adrenaline was due to stimulation of beta receptors in skeletal muscle resulting in increased glycogenolysis via a cyclic-AMP mediated mechanism. Hespel, Lijnon, Vanhees, et al.(1986) showed that beta blockade during exercise reduced glycolysis by inhibiting the effect of catecholamines.

Mazzeo and Marshall (1989) detected a high correlation between catecholamine inflection points and LT_1 ($r = 0.97$) in both trained cyclists and runners performing on bicycle ergometers and treadmills. The inflection point shifted with LT_1 to different % $\dot{V}O_2max$ regardless of ergometer type or specificity of the subjects training background. They proposed that a cause and effect relationship may exist between adrenaline and lactate via the regulation of glycogenolysis by adrenaline.

6.6 Potassium

With every muscular contraction, there is an efflux of intracellular potassium which is countered by the activity of the sodium-potassium pump (Na-K pump). Catecholamines, as well as exercise, stimulate the Na-K pump (Clausen, 1989). Adrenaline infusion has been shown to result in a decrease in arterial plasma potassium (Everts, Retterstol and Clausen, 1988; Lim, Linton and Band, 1982; Sahlin, Henriksson and Juhlin-Dannfelt, 1984) and beta blockade produces an exaggerated rise in plasma potassium during exercise (Linton, Lim, Wolff et al., 1984), providing evidence for the link between catecholamines and potassium.

The association between plasma potassium and lactate during exercise was investigated by Gleim et al. (1989). As mentioned earlier, they found significance between the patterns of plasma potassium and blood lactate increase during incremental work and suggested the presence of a potassium threshold. Also, Band et al. (1982), Conway et al. (1988), Newstead (1988) and Paterson et al. (1989) have all found strong correlations between plasma potassium and ventilation during CLW. The proposed mechanisms of action of potassium and its links to ventilatory and lactate responses during exercise will be discussed in detail later.

6.7 Summary of mechanisms producing the lactate threshold

The original hypothesis put forward by Wasserman et al. (1973) that the AnT represented the onset of anaerobic metabolism due to tissue hypoxia has come under considerable criticism. A great deal of data has been reported to show that lactate is produced under fully aerobic conditions and that O_2 supply to the exercising muscle tissue at LT_1 does not reach the critically low levels required for anaerobic metabolism. That lactate is produced at low work loads seems to be well accepted, so the initial and continuous rise in blood lactate at the LT_1 during IW is more likely a result of lactate production rate exceeding that of removal, rather than the onset of lactate production. But the presence of hypoxic loci in otherwise adequately perfused tissue cannot be discounted. Methods of determining redox state and lactate turnover which would refute the hypoxia hypothesis have been questioned and data showing decreased O_2 availability during submaximal exercise via alternative methods of redox state estimation have been reported.

Patterns of motor unit recruitment and the associated change in the profile of active fibre types may also have bearing in the lactate response. Substrate utilisation, and the enzymatic capacities of different fibre types could also be of importance. Finally, adrenergic stimulation and changes in plasma $[K^+]$ may also be significant, also

providing additional potential mechanisms for the coupling of the ventilatory and lactate responses.

7. Proposed mechanisms producing the ventilatory thresholds.

7.1 Respiratory mechanics

During an IW test both tidal volume (V_T) and breathing frequency (f_B) increase with work load. At work loads up to VT_1, the increase in $\dot{V}_E$ is largely due to increases in the V_T. At workloads above the VT_1, f_B is of more importance in producing the elevation in $\dot{V}_E$, a plateau occurring in V_T at higher intensities. These changes occur at around the VT_1 but may not be associated with it, in spite of the coincidence.

As power output is increased towards that producing VT_1, the ratio of dead space to tidal volume (V_D/V_T) decreases due to a relatively greater progressive increase in V_T than in V_D (Jones and Ersham, 1982). While this ratio decreases, both $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ also decrease as a result of the relative increase in alveolar ventilation ($\dot{V}_A$).

It seems likely that beyond a certain point, further increases in V_T come at the cost of a progressively greater increase in respiratory work, so it becomes more efficient to increase $\dot{V}_E$ via f_B. This maintains the matching between $\dot{V}CO_2$ and $\dot{V}_A$ but also leads to the disproportionate increase in $\dot{V}_E$ relative to $\dot{V}O_2$ (and $\dot{V}CO_2$ in all but fast IW tests) occuring at VT_1. As stated earlier, Whipp, Davis and Wasserman (1989) have suggested that the increased f_B is responsible for the isocapnic buffering short of respiratory compensation for the developing metabolic acidosis.

7.2 Ventilatory Control

The concept of ventilatory control during exercise achieving most consensus accepts that various neural and humoral stimuli are involved in an integrated regulation of breathing. Information regarding the types of stimuli, the location of the receptors and the precise mechanisms which mediate the response are equivocal.

When beginning exercise, or changing from a low constant intensity to a higher constant intensity, the ventilatory response is divided temporally into three phases. The first phase begins within the first breath and involves an initial rapid increase in $\dot{V}_E$. Because of the speed of the response, this phase is thought to be governed by neurological control (Dejours, 1963). The second phase begins after about 15 seconds, with $\dot{V}_E$ rising exponentially before reaching a plateau after approximately four minutes (Whipp, Wasserman, Davis et al., 1980). The third phase involves either constant $\dot{V}_E$ for exercise below VT_1, or a slowly increasing $\dot{V}_E$ at supra-VT_1 intensities, the drift being the result of a gradual increase in f_B (Whipp et al., 1980).

The overall mechanism most commonly accepted to describe this response pattern is the neurohumoral theory. Although many have contributed to its development, Dejours has written about it most extensively. The theory holds that a combination of a rapid neurogenic component (phase I) and a slower humoral component (phases II and III) adequately describes the ventilatory response to exercise. It makes the assumption that the initial rapid ventilatory response must be neurogenically mediated, due to the time delay in transmission of humoral information from muscle to a site of known chemoreception being too long to allow its involvement. It also assumes that a slow response must be humoral since neurogenic responses are more quickly mediated. The neurogenic and humoral

EXERCISE HYPERPNEA HYPOTHESIS

REFLEX:	CENTRAL NEUROGENIC	PERIPHERAL NEUROGENIC	NEUROHUMORAL		HUMORAL	CARDIODYNAMIC
			NEUROGENIC	HUMORAL		
STIMULUS:	AROUSAL, CONDITIONING	MOTION, TENSION	pHa, PCO2, PO2 CATECHOLAMINES			DOWNSTREAM CHEMICAL ERROR (FEED-BACK) / HAEMODYNAMIC EFFECTS (FEED-FORWARD)
				pHa, PCO2, PO2	CO2 FLUX	
MECHANISM:	CORTICAL OR HYPOTHALAMIC IRRADIATION TO RESPIRATORY CENTRES		PERIPHERAL (CAROTID) OR CENTRAL CHEMORECEPTORS		MIXED VENOUS CHEMORECEPTORS	DECREASED VA/Q / BLOOD FLOW
		PROPRIOCEPTORS, MUSCLE SPINDLES, METABOLORECEPTORS		PERIPHERAL (CAROTID BODIES) AND/OR CENTRAL CHEMORECEPTORS		

Figure 1.3: A summary of proposed mechanisms of ventilatory control based on Wasserman, Whipp and Casaburi (1986).

components are added in the overall response seen in phases II and III. These assumptions have not been universally accepted (Whipp, 1981).

A number of contributing mechanisms have been suggested and these are summarised in Fig. 1.3 (Wasserman, Whipp and Casaburi, 1986). Apart from being either neurogenic or humoral, some are feedforward, providing the stimulus for ventilation based on a projection of metabolic need, while others are feedback, modifying the projected estimates with information regarding actual metabolic rate.

It is most likely that at any given time there are a number of mechanisms active and that the mechanism(s) primarily responsible for the ventilatory response vary with both time and exercise intensity. Cunningham (1987) suggested that the number of stimuli contributing to respiratory drive is likely to provide more information than is necessary, resulting in a redundancy of some of the stimuli. This is in line with other control systems in the body.

7.2.1 Neurogenic control

There appear to be two basic classifications of neurogenic ventilatory control. The first involves a central descending drive and the second a peripheral ascending drive.

Central drive

The descending neural stimulus to hyperpnoea is based on the observation that $\dot{V}_E$ increases immediately with the initiation of exercise, a response far too quick to be humorally mediated (Dejours, 1963). The corticohypothalamic activity responsible for the initiation of muscular contraction with exercise also triggers hyperpnoea by irradiation of neural activity to the respiratory centres in the brain stem. The greater the muscular force generated, the greater the irradiation, and thus the greater the ventilatory response. This is not a recent theory, being first proposed by Geppert and

Zuntz (1888) then later refined by Krogh and Lindhard (1913), and in spite of conflicting data (reviewed by Dempsey, Vidruk and Mitchell, 1985) is well accepted.

Eldridge (1976) has suggested a 'slow' central neurogenic input which he terms 'reverberation', whereby the respiratory centres are capable of sustaining an increased $\dot{V}_E$, albeit exponentially decaying, after the removal of the causal stimulus.

Peripheral drive

The ascending stimulus is thought to be transmitted from contracting skeletal muscles by group III and IV afferents (Kao, 1963; McCloskey and Mitchell, 1972) to respiratory centre neurons. Dejours, Mithoeffer and Labrousse (1957b) had earlier thought that muscle spindles were involved, transmitting their information via group I and II afferents, but the subsequent work of Hornbein, Sorensen and Parks (1969) and McCloskey and Mitchell (1972) has shown involvement of this pathway to be unlikely.

The identity of stimulus to group III and IV afferents is unclear. Local release of K^+ (Tibes, 1977; Tibes, Hemmer and Boning, 1977), increases in La^- and H^+, and/or decreases in PO_2 (Cunningham, Lloyd and Spurr, 1966a; 1966b) are all possible stimuli. However, since spinal cord transection does not abolish the ventilatory response to exercise (Dempsey, Vidruk and Mastenbrook, 1980), this mechanism could only be, at best, one of a number acting to regulate exercise hyperpnoea.

7.2.2 Cardiodynamic control

This theory states that as pulmonary blood flow increases, if not matched by $\dot{V}_A$, the change in blood gases and pH will be measured downstream and serve as a possible stimulus for hyperpnoea (Wasserman, Whipp and Castagna, 1974). Increased CO_2

flow may be able to act as a stimulus for ventilation by the fact that the more quickly elevated cardiac output could increase the flow of blood containing only resting levels of CO_2. Such a feedback mechanism has proved unlikely (reviewed in Wasserman, Whipp and Casaburi, 1986) but instead a feedforward mechanism originating in receptors in the right ventricular wall and transmitted by the vagus and sympathetic nerves has been suggested (Jones, Huszczuk and Wasserman, 1981).

7.2.3 CO2 flow

Yamamato and Edwards (1960) proposed that CO_2 flow to the lung served as a stimulus for a mechanism mediated by the vagus nerve, linking $\dot{V}CO_2$ to $\dot{V}_A$ via the brainstem respiratory centre. Receptors for the mechanism have proved difficult to find (Coleridge, Coleridge and Howe, 1967; Dawes and Comroe, 1954; Gonzalez, Fordyce and Grodins, 1977) strengthening the belief that changes in PCO_2 accompanying the change in CO_2 flow, are measured by arterial chemoreceptors which can independently provide the link between $\dot{V}_E$ and $\dot{V}CO_2$ (Gonzalez et al. 1977; Sylvester, Whipp and Wasserman, 1973). More recently, evidence in favour of lung receptors has been provided by Sheldon and Green (1982), although it is still unclear whether the stimulus is CO_2 flow or pulmonary arterial CO_2 content.

7.2.4 Peripheral chemoreceptors

The carotid bodies are the main arterial chemoreceptors in man (Mitchell, 1966). These receptors respond to hypoxia, but also to hypercapnia and decreased pH (Cunningham, 1963). Their responsiveness to hypoxia is reduced in the presence of eucapnia and heightened by hypercapnia. Similarly responsiveness to hypercapnia is greater with simultaneous hypoxia and less with hyperoxia (Cunningham 1974). Cunningham (1987) refers to them as 'asphyxia receptors' in reference to the fact that in natural conditions (eg. exercise), PCO_2 goes up and PO_2 down.

During exercise, they are crucial in the ventilatory response to metabolic acidosis, although they appear to have little effect on the initial rapid increase in ventilation at the onset of exercise (Wasserman, Whipp, Koyal and Cleary, 1975). Also, during CLW below the VT_1, subjects who had previously undergone resection of the carotid bodies showed a normal ventilatory response once steady state had been reached. During CLW above the VT_1 however, the developing metabolic acidosis was not matched by increased ventilation (Wasserman et al., 1975). It appears from these results that there has to be a change in PCO_2 and/or H^+ for the carotid bodies to be active.

Yamamoto and Edwards (1960) suggested that it is the oscillatory nature of PCO_2 and H^+ within each respiratory cycle, rather than the mean value, which provides the stimulus for ventilatory control. This concept allows for the carotid bodies to be active in ventilatory regulation even in isocapnic conditions. It has been variously suggested that the maximal rate of change in the oscillation, the peak value and amplitude and/or the number of oscillations per second (Whipp, 1981), may all provide stimuli for ventilatory control in the absence of variation in the mean PCO_2 or pH. Possibly supporting this, it has been observed that afferent discharge from the carotid bodies is phasic (Biscoe and Purves, 1967).

The sensitivity of the carotid bodies appears to be modified under particular situations. Whether the reduced ventilatory response to exercise observed in athletes (Casaburi, Storer and Wasserman, 1987b; Yerg, Seals, Hagberg and Holloszy, 1985), thought by many to be due to reduced sensitivity of the peripheral chemoreceptors to PCO_2 (Byrne-Quinn, Weil, Sodal et al. 1971, Miyamura, Yamashina and Honda, 1976) is a result of training (Blum, Kanarek, Callahan et al., 1979; Yerg et al., 1985) or is genetically inherited (Kelley, Laufe, Millin et al., 1984; Saunders, Leeder and Rebuck, 1976) is unclear. Increases in catecholamines and plasma potassium appear

to stimulate ventilation, via direct or indirect activity on carotid bodies. Catecholamine infusion (Joels and White, 1968) and increases in plasma potassium (Band and Linton, 1989) in cats have caused increased carotid body discharge. In both experiments, there was a concurrent increase in $\dot{V}_E$. Further, Band, Linton, Kent and Kurer (1985) found the effect of K^+ was negated after sectioning of the carotid sinu and aortic nerves.

Wasserman et al. (1975) found that subjects whose carotid bodies had been surgically resected, did not exhibit a VT_1 due to their failure to develop the respiratory compensation for the metabolic acidosis associated with moderate to high intensity exercise. However, subjects with McArdle's disease, do show a VT_1 in the absence of an increased blood lactate or the accompanying H^+ (Hagberg, Coyle, Carol et al. 1982). McArdle's disease involves a genetic abnormality of carbohydrate metabolism involving absence of the enzyme myophosphorylase B and thus an inability to produce lactate in the muscle (McArdle, 1951). This would suggest that either the carotid bodies are not involved or that the stimulus is other than H^+. McLellan (1985) has suggested, given the high (75%$\dot{V}O_2max$) threshold values obtained by Hagberg et al., that they actually measured VT_2 and that at these intensities, as the authors stated, neurogenic control is more active. More recently, (Hagberg, King, Rogers et al., 1990) re-examined the response to incremental work in McArdle's patients, finding in favour of their original data and conclusions. Again in this paper, they report an uncharacteristically high VT_1 (71% $\dot{V}O_2max$), which would appear to be the result of a misinterpretation of the definition of the VT_1. They suggest that "McArdle's patients .... were already hyperventilating somewhat during low levels of exercise (30-60% $\dot{V}O_2max$)", contradicting their own assessment of the VT_1.

Alternatively, Paterson, Friedland, Bascom, et al., 1990) showed that there is a close temporal relationship between arterial $[K^+]$ and $\dot{V}_E$ during exercise in McArdle's disease subjects, suggesting that potassium may excite arterial chemoreceptors to increase $\dot{V}_E$, as proposed by Band and Linton (1989) and Band et al. (1985). K^+ may also exert this control via group III and IV afferents as previously discussed.

7.2.5 Central Chemoreceptors

In contrast to resting conditions, it would appear unlikely that central chemoreceptors, located in the medulla oblongata, play a significant role in the regulation of exercise hyperpnoea since cerebrospinal fluid does not become acidic during exercise in animal experiments (Bisgard, Forster, Byrnes et al., 1978; Kao, Wang, Mei and Michel, 1965) and no other stimulus for ventilatory regulation is apparent.

7.3 Summary of the mechanisms producing the ventilatory threshold

Ventilatory control of arterial PO_2, PCO_2 and pH during exercise is governed by a number of different mechanisms, the relative importance of each varying with exercise intensity.

A number of these stimuli can account for the presence of the VT_1, either independently of, or in association with LT_1. The possible role of potassium in producing the VT_1 as well as providing a link with LT_1 will be discussed in depth later in this review. Catecholamines would also appear to be important in the production of both thresholds and thus in their association.

Of the control mechanisms proposed, the carotid bodies and the skeletal muscle metaboloreceptors provide the strongest possible links between VT_1 and LT_1 with

descending neural control also providing a potential link. Aspects of respiratory mechanics may also contribute to the VT_1.

8. Experimental comparisons of the lactate and ventilatory thresholds

There have been numerous studies which either support or reject the original hypothesis of Wasserman et al. (1973) on the basis of coincidence of the breakpoints in the lactate and ventilatory responses to incremental work. A number of investigators have provided data compatible with the concept of association between VT_1 and LT_1. However, whether the coincidence of VT_1 and LT_1 signifies a direct causal relationship is still doubtful and an equal volume of data have been reported in which the VT_1 and LT_1 has been experimentally dissociated. Once dissociation is proven, any causal relationship can be rejected.

8.1 Coincidence

Coincidence between VT_1 and LT_1 has been observed during experiments employing both slow and fast incremental tests on both the treadmill and the bicycle ergometer (Aunola, Marniemi, Alanen et al., 1988; Caiozzo, Davis, Ellis et al., 1982; Davis, Basset, Hughes and Gass, 1983; Davis, Vodak, Wilmore et al., 1976; Haverty, Kenney and Hodgson 1988; Ivy, Withers, Van Handel et al., 1980; McLellan, 1985; Reinhard, Muller and Schmulling 1979; Wasserman et al. 1973, Yoshida, Suda and Takeuchi et al., 1982).

Less work has been done involving coincidence between the second thresholds, although Aunola et al. (1988), Davis et al. (1983) and McLellan (1985) report such evidence.

8.2 Dissociation

8.2.1 Via protocol.

A number of different interventions have been used to dissociate VT_1 from LT_1. Some investigations have even revealed differences in the thresholds for some if not all subjects during IW tests without any intervention (Green, Hughson, Orr and Ranney, 1983; Simon, Young, Gutin, et al., 1983; Powers, Dodd and Garner, 1984).

In a review supporting the anaerobic threshold hypothesis, Davis (1985) points out that in the experiments by Powers et al. (1984), only one of the 13 subjects tested showed a significant difference between LT_1 and VT_1. Although this is true, there were also five occasions on which the two methods of VT_1 detection did not give the same result. Davis (1985) also rejects the data of Green et al. (1983) because the algorithms used for detection overestimate the points where systematic increases in $\dot{V}_E/\dot{V}O_2$ and blood La^- begin. Using the original data of Green et al. (1983), Davis (1985) shows that by employing the definition for the thresholds proposed by Wasserman, VT_1 and LT_1 differ by only 50 ml/min.

Hughes, Turner and Brooks (1982) used changes in test protocol to dissociate the thresholds by altering pedalling rate, while Hughson and Green (1982) changed work rate increment with a similar effect. Wasserman (1983) argues that Hughes et al. (1982) failed to find coincidence because of insensitive methodology - not using ventilatory equivalents to determine VT_1 and graphing lactate and ventilation not against $\dot{V}O_2$, but against a work load which employed too large an increment. The work of Hughson and Green (1982) must stand against that of Wasserman et al. (1973) and Yoshida (1985) who found no variation in the association between VT_1 and LT_1 with varying rates of work load increment.

8.2.2 Via prior exercise.

The use of prior exercise has provided another means of dissociation via its ability to elevate blood La^- before an IW test (Davis and Gass, 1979; Farrell and Ivy, 1987). In these studies the VT_1 did not change subsequent to the prior exercise, whereas the lactate response was significantly different. Although this intervention provides evidence of dissociation between VT_1 and LT_1 in the circumstances under which the tests were conducted, it does nothing to discredit the association under normal conditions. The results of Farrell and Ivy (1987) show that both $\dot{V}_E/\dot{V}O_2$ and blood La^- concentration are elevated in the IW test which followed prior exercise, even if the breakpoints are no longer coincident. This does not preclude association between the two factors. That the influence of lactate is one of numerous inputs to ventilatory control is not questioned (Wasserman, Whipp and Casaburi 1986). The question that is raised by the data of Farrell and Ivy (1987) is whether blood La^- concentration represents the primary stimulus to ventilation during a continuous IW test. By their intervention they have shown that other factors may also be involved in the response, but not that lactate is not of major importance.

8.2.3 Via glycogen depletion.

The work of Heigenhauser, Sutton and Jones (1983), Hughes, Turner and Brooks (1982), and Neary, MacDougall, Bachus and Wenger (1985) examined the effect of glycogen depletion by diet and/or prior exercise on the lactate and ventilatory response to exercise. Taken together these papers point to a delay in lactate response but an enhanced ventilatory response after glycogen depletion, resulting in a relative delay in the LT_1. McLellan and Gass (1989) refer to methodological inadequacies in two of these papers, (Hughes et al., 1982; Neary et al., 1985) and that an alternative interpretation could equally well explain the results observed by Heigenhauser et al. (1983). They conducted an experiment using a similar

intervention to deplete glycogen and found that, although blood lactate was reduced and $\dot{V}_E/\dot{V}CO_2$ was increased, the coincidence between VT_1 and LT_1 was not affected. Thus, the cause and effect relationship could not be rejected. They suggest that lower PCO_2 values are the cause of the differences following glycogen depletion and that a reduced $\dot{V}CO_2$, rather than an elevated $\dot{V}_E$, causes the increase in $\dot{V}_E/\dot{V}CO_2$. They also suggest that neurological mechanisms may exert greater ventilatory control in the absence of the usual increases in $\dot{V}CO_2$. The results of Yoshida (1986) and Quirion, Brisson, Laurencelle et al. (1988) support these findings.

8.2.4 Via endurance training.

Dissociation has been reported after exercise training. Poole and Gaesser (1985) found that the thresholds occurred at different percentages of $\dot{V}O_2max$ before training and that different training regimes caused differing degrees of improvement in the ventilatory and lactate responses. Later, Gaesser and Poole (1986) observed that the LT_1 was quicker to respond to a retraining stimulus than the VT_1. The results of Simon et al. (1986) indicate that VT_1 and LT_1 were coincident for trained but not untrained subjects. Similarly, Aunola and Rusko (1986) found greater coincidence between VT_1 and LT_1 in subjects with a greater proportion of slow twitch muscle fibres than in a group with more fast twitch fibres. The use of venous rather than arterial blood samples (all four studies) and graphical analysis of variables against work load rather than $\dot{V}O_2$ (Simon et al., 1986) weaken the accuracy of conclusions drawn, but do not necessarily negate them.

8.2.5 Via McArdle's disease.

As has been previously mentioned, Hagberg et al. (1982; 1990) detected a VT_1 in the absence of an LT_1 in subjects with McArdle's disease. Pain (Whipp, 1983), elevated

plasma potassium (Paterson et al., 1990) and methodological problems or neurological control of ventilation (McLellan, 1987) have all been put forward as reasons to explain this phenomenon.

8.3 Summary.

Better understanding of the control of the lactate and ventilatory responses to exercise must be established before the validity of the proposed cause and effect relationship between VT_1 and LT_1 can be verified.

9 . The relationship between exercise protocol and threshold detection

9.1 Incremental work tests

The importance of protocol in the determination of the ventilatory and lactate thresholds is evident not only from the definition of anaerobic threshold proposed by Wasserman et al. (1973) - where different responses to fast and slow incremental protocols were delineated - but also in that variation in protocol has been used as a tool to display dissociation between the thresholds, as previously discussed. Whipp, Davis, Torres and Wasserman (1981) concluded that the optimal test for determination of VT_1 was one of four to eight minutes duration which employed a ramped (ie. increasing progressively rather than in discrete steps) work rate of 50 Watts/minute. This allowed $\dot{V}O_2$ kinetics to accurately track the progressively increasing work load after a initial brief period where they lagged behind. If the ramp slope is too steep, $\dot{V}O_2$ will continue to lag behind work load and the method will be invalid. On the other hand, longer tests with slower ramps were thought to 'waste' time. Whipp et al. (1981) also observed that the VT_1 measured during their ramp test occurred at the same $\dot{V}O_2$ as that measured during IW tests with

increment rates of from 15W/min to 25W/5min. Davis, Whipp, Lamarra et al. (1982) added that ramp slopes between 20 and 50 W/min were optimal. In agreement with this, Buchfuhrer, Hansen, Robinson et al. (1983) suggested that although VT_1 was independent of test duration, $\dot{V}O_2max$ was highest when tests ranged from 8 to 17 minutes, with the optimal test duration being 10 minutes. McLellan (1985) reported similar findings.

The most important question surrounding the validity of the incremental tests centres on the kinetics of the ventilatory and lactate responses. Those who favour longer work durations (3 to 5 minutes) at each increment do so since this allows a steady state to be reached at each work load, below the first threshold at least. The results of the incremental tests can then be used to infer responses to prolonged steady state exercise with greater validity.

Davis, Whipp and Wasserman (1984) point out that the cause of the progressive respiratory acidosis in rapid IW tests is the difference in the time delay to steady state for $\dot{V}CO_2$ and $\dot{V}_E$, that of the former being 10-15 seconds less. Heck, Mader, Hess et al. (1985) and Oxenreider and Sharp (1987) found that blood lactate increased more slowly relative to $\dot{V}O_2$ with faster incremental tests, resulting in an overestimation of the lactate response. However, McLellan (1985) found no significant differences in VT_1, VT_2, LT_1 or OBLA with increment durations ranging from 1 to 5 minutes per 30W increase.

It would seem apparent that too fast an increment rate will result in overestimation of both ventilatory and lactate responses due to time delays in reaching steady state values. For similar reasons it would seem appropriate to increment work loads by a small amount as often as possible (ie. 20W/min would be better than 40W/2min), thus more closely approximating a ramp protocol. What constitutes 'too fast' in IW

tests if not ramp tests seems less clear, although an increase of 20 to 30W/min is commonly used.

9.2 Mode of exercise

In subjects not specifically trained for any single mode of exercise, the thresholds vary when expressed both in absolute terms and as a percentage of $\dot{V}O_2max$, depending on what type of ergometer is used. The smaller the active muscle mass, the smaller the absolute $\dot{V}O_2$ at both VT_1 and LT_1 (Davis, Vodak, Wilmore et al. 1976; Kreider, 1988). Davis et al. (1976) reported that VT_1 and LT_1 occurred at a higher % VO_2max, albeit insignificant, for treadmill exercise than for bicycle ergometer exercise and that this in turn produced significantly higher relative thresholds than did arm cranking. Jacobs and Sjodin (1985) found that OBLA for running occurred at a significantly higher % $\dot{V}O_2max$ than for cycling. These relative differences could be due to a number of factors related to oxidative capacity of the muscle and/or variations in efficiency causing differences in muscle fibre recruitment patterns.

The question of varying efficiency is important when conducting tests on the bicycle ergometer. Efficiency varies with seat height measured as a percentage of leg length, but perhaps more importantly as a function of pedal frequency. The most economical pedalling frequency, measured by way of $\dot{V}O_2$ at various frequencies for the same work output, would seem to vary with the degree of prior training and experience. Trained cyclists are most efficient at higher pedal frequencies ie. 60-80 rpm (Coast, Cox and Welch, 1986) and 91 rpm (Hagberg, Mullin, Giesse and Spitznagel, 1981), whereas non-cyclists reach optimum efficiency between 30 and 60 rpm (Dickinson 1929, Garry and Wishart 1931). Coast and Welch (1985) have reported that the optimum pedal rate also increases with power output.

The other important consideration regarding pedal frequency is that the higher the pedal frequency, the lower the proportion of maximal force required per pedal stroke to maintain power output at any given submaximal level of $\dot{V}O_2$ (Greig, Rutherford and Sargeant, 1986). The force required per pedal stroke could have significant effects on the LT_1, due to higher intramuscular pressures altering the adequacy of O_2 supply, or by changing the pattern of muscle fibre recruitment.

When using the same mode of ergometer and the same protocol, Heck, Mader, Hess et al. (1985) found variation in the OBLA as measured on two different treadmills. Whether the differences could be due to other sources of variation like calibration differences, different ambient temperatures or time of day, or different dietary or activity patterns prior to assessment was not discussed.

10. Lactate sampling

10.1 Muscle lactate versus blood lactate concentration

The theory of the anaerobic threshold as proposed by Wasserman et al. (1973) suggests that changes in blood lactate concentration accurately mirror the changing metabolic status of the muscle cell. Bylund-Fellenius, Walker, Elander, et al. (1981); Jorfeldt, Juhlin-Dannfelt and Karlsson (1978); Karlsson (1971) and Knuttgen and Saltin (1972) all support the coincidence of changes in muscle and blood lactate at a given $\dot{V}O_2$.

The data of Knuttgen and Saltin (1972) and Jorfeldt et al. (1978) are similar in that they both show only non-significant rises in both muscle and blood lactate before a threshold (corresponding to 60% $\dot{V}O_2max$ in the former and 70% $\dot{V}O_2max$ in the latter) beyond which appreciable increases occurred. At exercise intensities beyond that eliciting the threshold response, muscle lactate increased at a rate greater than that of blood lactate. The results of Karlsson (1971) show less coincidence between

muscle and blood lactate, with the concentration of muscle lactate always higher than that of blood lactate, the difference increasing with exercise intensity. Bylund-Fellenius et al. (1981) found that lactate/pyruvate ratios in the muscles correlated with those in the blood.

Jacobs and Kaiser (1982) observed a direct relationship between muscle and blood lactate levels only at the work intensity corresponding to OBLA. At other intensities of exercise, both above and below OBLA, the relationship was variable. Tesch, Daniels and Sharp (1982) have reported results similar to these. Furthermore, Green et al. (1983) showed that muscle lactate increased before the VT1 and LT1 (which were not coincident) while Rusko, Luhtanen, Rahkila et al. (1986) observed similar results with respect to LT_1.

More recently, data reported by Chwalbinska-Moneta, Robergs, Costill and Fink (1989) support that of Knuttgen and Saltin (1972) and Jorfeldt et al. (1978). They found a close relationship between blood and muscle lactate thresholds, a threshold in muscle La^- occurring just before the blood LT_1 (51% compared with 54% $\dot{V}O_2max$). They questioned the validity of the findings of Green et al. (1983) on a number of points. First, the use of a one minute IW test would have favoured the early rise in muscle lactate observed, as well as preventing stability between muscle and blood lactate levels, due to the time required to establish steady state associated with normal lactate kinetics. Second, Green et al. (1983) chose their work loads for biopsy relative to the VT_1, which they found at a significantly higher work load and $\dot{V}O_2$ than LT_1. This dissociation, having been previously discussed, raised the possibility that the VT_1 was overestimated. As a result, their sub-VT_1 work load may well have been supra-LT_1, so an elevation in muscle lactate would be expected.

Whether transport of lactate from muscle to blood is active or passive is also open to question. Opinion seems divided between a passive or 'facilitated diffusion'

mechanism, which could be governed by concentration gradients (Karlsson, 1971; Mader and Heck, 1986), versus an active one (Jorfeldt et al., 1978).

10.2 Arterial versus venous blood lactate concentration

Yeh et al. (1983) and Yoshida et al. (1982) have both reported that increases in lactate concentration in arterial blood precede those in venous blood, so that LT_1 determined from venous samples will be over-estimated. Davis (1985) suggests that this discrepancy can be overcome by minimising forearm movements. Given that oxidation in non-active muscle and gluconeogenesis in the liver are both possible fates of lactate, it would seem that sampling site is important and that venous sampling should be avoided.

Ideally, the sampling site should be just downstream from the principally active muscles to reduce the degree of potential metabolism of lactate. Arterial sampling involves a number of potential complications and sampling from the femoral vein is even more obtrusive. Arterialised sampling, from a hyperaemic ear lobe (McEvoy and Jones, 1975) or from a heated dorsal hand vein (Forster, Dempsey, Thomson et al,. 1972) have been shown to provide accurate representations of arterial blood pH, PCO_2, PO_2 and also arterial lactate in the latter study.

11 . Data analysis

11.1 Parameters chosen to detect thresholds

11.1.1 Lactate response

The primary difference between the various thresholds defined for the blood lactate response to exercise is in whether or not they represent a fixed absolute lactate value or a variable inflection point. Of the definitions listed in Appendix 1 as representing

the initial increase in lactate, those offered by Hurley, Hagberg, Allen et al. (1984); Kindermann, Simon and Keul (1979); LaFontaine, Londeree and Spath (1981) and Londeree and Ames (1975), all use fixed lactate concentrations of 2.0 to 2.5 mM. Those of Farrell, Wilmore, Coyle et al. (1979); Ivy et al. (1980) and Wasserman et al. (1973) use the inflection point.

The rapid increase in lactate is determined at 4.0 mM blood La^- by Kindermann, Simon and Keul (1979) and Sjodin and Jacobs (1981), whereas Davis et al. (1983) and Stegmann, Kindermann and Schnabel (1981) opt for the use of a change in the rate of lactate accumulation. There are other differences in the definitions, for example, whether IW or CLW tests are used, but the difference in fixed versus variable values indicates an important theoretical departure.

The main problem with the use of a fixed value of blood lactate is that it cannot accommodate for variability in the lactate concentration corresponding to the initial or rapid increases between individuals, or within the same individual before and after training. With training, the blood lactate corresponding to any submaximal exercise intensity, measured either in terms of absolute or relative $\dot{V}O_2$, is reduced (Hurley et al., 1984). This means that after training, the OBLA for example, represents a greater metabolic stress than it did before training. Since it is the inflection point rather than any fixed value which represents a change in metabolism, if fixed values are not coincident with the inflection points, they are not representing that change in metabolic response to exercise. In light of their finding, it is surprising that Hurley et al., (1984) chose an absolute lactate value in their definition of LT_1.

Both 2 and 4 mM values have been arrived at as mean values for predicting performance, from groups of subjects with homogenous activity and training profiles. The homogeniety makes the selection of a fixed value more likely. Stegmann and Kindermann (1982) compared the IAT and OBLA and found that for subjects of

higher aerobic capacity, OBLA occurred at a significantly higher work load and % $\dot{V}O_2$max than IAT, with the result that OBLA overestimated maximal steady state lactate. For subjects of lesser aerobic capacity, OBLA occurred before IAT. Given that 4.0 mM La was chosen as representing the optimal training intensity corresponding to maximal steady state lactate, the findings of Stegmann and Kindermann (1982) reduce the validity of using fixed lactate values for such purposes.

11.1.2 Respiratory response

The respiratory markers used to detect the anaerobic threshold during IW tests have changed from those used in the original definition of Wasserman and McIlroy (1964). They defined the respiratory equivalent of their anaerobic threshold as an increase in the respiratory gas exchange ratio (R). Wasserman et al. (1973) used the work rate at which $\dot{V}CO_2$ and $\dot{V}_E$ deviated from linearity as the VT_1 markers, after concluding that the increase in R was a transitory phenomenon caused by the buffering of lactate by bicarbonate.

Davis, Frank, Whipp and Wasserman (1979) modified the criteria for detection, preferring a systematic increase in $\dot{V}_E/\dot{V}O_2$ without any increase in $\dot{V}_E/\dot{V}CO_2$, and a coincident systematic increase in the end-tidal PO_2 without a decrease in end-tidal PCO_2. Caiozzo, Davis, Ellis et al. (1982) reported that the use of $\dot{V}_E/\dot{V}O_2$ for VT_1 detection has the best test-retest reliability and correlates most highly with LT_1 when compared with the other respiratory markers ($\dot{V}_E$, $\dot{V}CO_2$ and R). Wasserman, Whipp and Davis (1981) also favour this method since it delineates VT_1 from other causes of nonlinear increase in ventilation such as hypoxia and/or neurogenic factors.

More recently, Beaver, Wasserman and Whipp (1986) have preferred the use of the "V-slope" method, which defines the first threshold as the inflection point in the

relationship between $\dot{V}O_2$ and $\dot{V}CO_2$. In the same article they assessed the second threshold at the inflection point in the relationship between $\dot{V}_E$ and $\dot{V}CO_2$. They suggest that this method is preferable since it is independent of sources of potential variability in the ventilatory response, such as those caused by obesity, obstructed airflow or chemoreceptor insensitivity.

Volkov, Shirkovets and Borilkevich (1975) used excess CO_2 generated from the buffering of hydrogen ions to detect the VT_1, but McLellan (1985) found that it did not correlate well with other measures of the VT_1 and noted that its validity was questionable since it relies on R in its calculation.

11.2 Mathematical Models

Another objection that critics of the threshold theory put forward is the lack of objectivity in selecting the breakpoint. To counter the problem of assessor subjectivity, a number of computer detection methods have been produced. Orr et al. (1982) fit both two and three line linear regression equations in series to the ventilatory data (against $\dot{V}O_2$) during IW tests, depending on whether one or two thresholds were to be determined. They found a correlation of $r = 0.94$ between their two line regression analysis and the visually determined VT_1 assessed from ventilatory equivalents. The "V-slope" analysis of Beaver et al. (1986) also makes use of a computerised two-line regression analysis. Wasserman, Beaver and Whipp (1990) suggest that this latest method is more reliable than using the ventilatory equivalents due to subjectivity associated with high inter-assessor variability in the latter method. However, in the original paper, Beaver et al. (1986) say that "in some cases the curve (of $\dot{V}CO_2$ vs. $\dot{V}O_2$) has a bend above the respiratory compensation point, showing the importance of excluding this region from the calculation", suggesting that subjective analysis also affects this latest method.

Hughson (1984) suggested that breath-by-breath analysis of ventilatory response shows a curvilinear pattern, adding that although fitting two linear segments to the ventilatory response above VT_1 more closely fit the data than if only one breakpoint is considered, an exponential response fits the data better again.

Mathematical methods used to detect the LT_1 include the plotting of lactate regression residuals (Davis et al., 1983) and the log-log transformation of Beaver, Wasserman and Whipp (1985). The log-log model of Beaver et al. (1985) allows greater ease of detection since the data are presented with a more abrupt breakpoint.

Campbell, Hughson and Green (1989), Hughson, Weiseger and Swanson (1987) and Yeh et al. (1983) have all proposed exponential models of lactate increase during incremental work tests. Hughson et al. (1987) and Campbell et al. (1989) both fit exponential models to the relationship between lactate and $\dot{V}O_2$, since they believe that there is no breakpoint in the relationship and concluded that a slope index is a more valid measure of changing metabolism than any particular 'threshold'.

When comparing their model with that of Beaver et al. (1985), Hughson et al. (1987) found that the exponential model more closely fit the data. Both Beaver, Wasserman and Whipp (1988) and McLellan and Gass (1989) reject the exponential model for numerous reasons, including the dependence of the accuracy of the model on a very high rate of work load increase, the inability of the model to fit sets of data which show a decrease in lactate from resting levels at work loads below LT_1, and the almost identical ability of the two models to explain variance in test data. Hughson and Swanson (1988) responded that the log-log model is based on the prior assumption that a threshold exists and so will always find one, while Campbell et al. (1989) reported lower mean square error for their exponential model than for the log-log model over a range of work rate increases from 8W/min to 50W/min.

Yeh et al. (1983) also concluded that there was no discernible lactate threshold, the rise in blood lactate during IW being more accurately described by an exponential relationship, and further that there was so much variability in detection of VT_1 amongst different assessors (16%) that it was unreliable. They suggested that computer algorithms could be used to avoid assessor bias. Gladden, Yates, Stremmel and Stamford (1985) found not only that VT_1 and LT_1 were poorly correlated ($r = 0.53$), but also agreed with Yeh et al. (1983) that the correlation between thresholds picked by different assessors was not high ($r = 0.70$ for VT_1 and $r = 0.81$ for LT_1).

The failure of Yeh et al. (1983) to find a LT_1 could be explained by the high exercise intensity at which they began collecting blood samples. The first samples were taken two minutes before $R = 1.0$ which may have given only a few points below the breakpoint in lactate response and could thus have made the LT_1 more difficult to detect.

McLellan (1987) has suggested that as long as the assessors have a clear understanding of the changes in gas exchange there should be no reason for variation in VT_1 detection. The assessors used in the study of Gladden et al. (1985) ranged from those with "little experience" (defined by the authors as those having no papers published on VT/LT) to "experienced" (6 papers published). Also, the assessors independently chose which method of threshold detection they would use, rather than uniform definitions being supplied by the principal researchers. Given these circumstances, the inter-assessor variability they found is less surprising.

11.3 Mean versus individual data

McLellan (1985b) points out that although VT_1 and VT_2 occur at approximately 50% and 75% of $\dot{V}O_2max$ respectively, individual values can vary significantly. If

mean data are graphed, there is a smoothing effect of any changes in response patterns. For example, a break in the linearity of the $\dot{V}_E$ vs. $\dot{V}O_2$ may be not detected and the accuracy of the methods used to detect breakpoints cannot be assessed.

12 . Physiological adaptations following endurance training

12.1 Effect on thresholds

The observation that endurance athletes can continue to improve their performances without improving their $\dot{V}O_2max$, and that athletes with similar VO_2max values can perform at different levels, has prompted investigation into the effect of endurance training on the VT_1 and LT_1. After nine weeks of endurance training, Davis, Frank, Whipp and Wasserman (1979) found that previously sedentary men improved their VT_1 by 44% in terms of absolute $\dot{V}O_2$ and by 15% relative to $\dot{V}O_2max$. That VT_1 improved relative to $\dot{V}O_2max$ indicates that the two measures may be dependent on different physiological mechanisms.

This dissociation between $\dot{V}O_2max$ and VT_1 has since been observed by Gaesser, Poole and Gardner (1984) and Poole, Ward and Whipp (1986). Gaesser et al. (1984) also noted that the alterations in VT_1 initially lagged behind those in $\dot{V}O_2max$. Casaburi, Storer and Wasserman (1987b) and Casaburi, Storer, Sullivan and Wasserman (1989) found that the reduced ventilatory response to exercise after training was well correlated with reductions in blood lactate.

LT_1 has also been found to respond to training in a similar way. Coyle, Martin, Ehsani, et al. (1983) detected LT_1 at 100% of $\dot{V}O_2max$ in a group of well-trained ischaemic heart disease patients. Hurley et al. (1984) and Henritze, Weltman, Schurrer and Barlow (1985) both showed lower blood lactate levels at all submaximal exercise intensities relative to $\dot{V}O_2max$ after training while Denis,

Foquet, Poty et al. (1982) observed relative improvements in both VT_1 and LT_1. In agreement with their earlier findings concerning ventilatory adaptation, Gaesser and Poole (1988) again found that the adaptations causing the decreased lactate response initially lagged behind the increases in $\dot{V}O_2max$.

The adaptations gained as a result of the training would appear to be specific to the mode of exercise in which the training was completed. Withers, Sherman, Miller and Costill (1981) found that cyclists had a significantly higher VT_1 than runners when tested on the bicycle ergometer but that the results were reversed on the treadmill. Verstappen, Huppertz and Snoeckx (1982) found a direct relationship between work efficiency and training mode in cyclists and runners.

Training intensity also affects the relative improvements in thresholds. Henritze et al. (1985) found that after 12 weeks, a group of subjects who trained at an intensity greater than LT_1 showed significant improvements in their LT_1 whereas training at LT_1 caused only minor changes in another group. Supporting these results, studies on rats by Harms and Hickson (1983) revealed that training at 50% $\dot{V}O_2max$ was enough to produce adaptation in the mitochondria of slow twitch fibres but that higher intensity exercise was needed to produce similar adaptations in fast twitch fibres.

Katsuta, Kanao and Aoyagi (1988) found that beyond a certain duration of exercise, no further increases in capillary density or succinate dehydrogenase (SDH) activity were found.

Information regarding the relative merits of continuous versus interval training in producing adaptation are less consistent. Henriksson and Reitman (1976) observed that continuous training produced increases in SDH activity of slow twitch muscles only, while interval training isolated increases in SDH activity to fast twitch fibres.

McLellan and Skinner (1983) found that continuous training at an intensity between VT_1 and VT_2 improved VT_1 only, but that an interval training program, equal in overall work load, improved neither threshold. Poole and Gaesser (1985), in showing a dissociation of VT_1 and LT_1 after training, observed no difference in the increase in LT_1 after continuous and interval training, but a greater increase in VT_1 after interval training. Finally, critical power (which correlates well with the first threshold as has been discussed earlier) did not differ after continuous or interval training programs (Gaesser and Wilson, 1988).

12.2 Oxidative metabolism

There are a number of adaptations to both the structure and function of skeletal muscle resulting from endurance training, which explain the observed dissociation between the $\dot{V}O_2max$ and thresholds (Holloszy, 1973; Holloszy, Rennie, Hickson et al., 1977). When comparing the trained with the untrained individual, these include slower heart rate, greater stroke volume, lower blood flow to working muscles (which is compensated for by a greater arterio-venous O_2 ($a\text{-}\bar{v}O_2$) difference across the muscle), slower depletion of muscle and liver glycogen stores, a lower R (respiratory quotient) and a smaller rise in muscle and blood lactate concentration at any absolute work load or $\dot{V}O_2$. When considered relative to the athlete's higher $\dot{V}O_2max$, the $a\text{-}\bar{v}O_2$ difference is still greater, muscle and blood lactate concentrations are still less and R is still lower. These measurements all point to the likelihood that it is an improved ability to oxidise fats which primarily accounts for the enhanced performance of trained athletes.

Holloszy (1967) concluded from training studies on rats that it was the enhanced capacity of mitochondria for the oxidation of fatty acids that was the source of the improvement. Increases were noted in respiratory chain enzymes as well as enzymes

involved in the Kreb's cycle. Hoppeler, Luthi, Claasen et al. (1973) reported that there was an increase in both the size and the number of mitochondria after training.

Baldwin, Klinkerfuss, Terjung et al. (1972); Dudley, Abraham and Terjung (1982); Harms and Hickson (1983) and Soussi, Idstrom, Schersten and Bylund-Fellenius (1989) are just a few of the authors who have reported increases in oxidative enzyme activity after training in rats. Henriksson and Reitman (1976), Sjodin (1976) and Rusko and Rahkila (1980) have presented data showing similar changes in human skeletal muscle. By comparison, only relatively small changes in glycolytic enzyme activity after training have been reported, but these enzymes would appear to be present in sufficient concentration to preclude them as rate limiting at any exercise intensity (Gollnick, 1982).

The capacity to oxidise both fats and carbohydrates is enhanced by endurance training (Holloszy, 1973; Holloszy and Booth, 1976) but it is fatty acids which represent the preferential source of oxidisable substrate. The reason for this appears to be that the accumulation of citrate associated with the oxidation of fatty acids inhibits phosphofructokinase activity and thus glycolysis (Rennie, Winder and Holloszy, 1976). This is thought to be responsible, in part for the glycogen sparing effect observed after endurance training (Hickson, Rennie, Conlee et al., 1977).

This enhanced respiratory capacity and its link to elevating LT_1 has been studied by Ivy et al. (1980) who found significant correlations between pyruvate oxidation and absolute ($r = 0.94$) and relative ($r = 0.83$) LT_1. Aunola et al. (1988) correlated a number of markers of oxidative capacity with VT_1, VT_2, LT_1, LT_2 and OBLA. Cumulatively they explained between 58% and 74.5% of the variation in the thresholds of different subjects, citrate synthase having the strongest correlations of 0.72 to 0.85.

The number of active contractions seems to be important to the degree of mitochondrial change. Dudley, Abraham and Terjung (1982) and Harms and Hickson (1983) concluded that increasing contractile activity by either increased frequency (analagous to increased intensity) or by prolonging duration resulted in an increase in mitochondrial density.

12.3 Contractile properties of muscle fibres

Associated with this adaptive increase in oxidative capacity of muscle, which Baldwin, Reitman, Terjung et al. (1973) suggests affects all fibre types equally, is the possibility of transition of fast twitch muscle to slow twitch. Pette (1984) suggests that beyond a biochemical "white to red" transition, there is also a contractile "fast to slow" transition involving a change in myosin composition. A number of fibres in transition from fast to slow are also thought to be present at any time. Green, Klug, Reichmann et al. (1984) showed that endurance training in rats was a sufficient stimulus to produce the fast to slow transitions. Baumann, Jaggi, Soland et al. (1987) and Kovanen (1989) both found transition of fast to slow fibres as a response to endurance training and also transition of type IIb to IIa fibres through an intermediate transitional IIc fibre, in humans and rats respectively.

Ivy et al. (1980) observed a correlation between % slow twitch fibres and absolute ($r = 0.74$) and relative ($r = 0.70$) LT_1. Aunola et al. (1988); Coyle, Coggan, Hopper and Walters (1988) and Sjodin and Jacobs (1981), also found significant correlations between % slow twitch fibres and threshold values.

12.4 Adaptation in peripheral vasculature

A further adaptation noted after endurance training is an increase in the capillary density of trained muscle (Andersen and Henriksson, 1977; Katsuta, Kanao and Aoyagi, 1988), resulting in greater exposure of the blood to the muscle fibres. This

would mean that although the blood flow to the working muscles may be lower, and the $\dot{V}O_2$ of the muscles is not enhanced in the trained state, there may be improved delivery and transport of fatty acids to the muscle (Matoba and Gollnick, 1984). This may have a bearing on the increased metabolism of fatty acids since availability of fuels to working muscle has been shown to modify which fuels are metabolised (Hickson et al., 1977). Sjodin and Jacobs (1981) have found correlations between capillary density and OBLA ($r = 0.52$-0.63).

13. Prediction of endurance performance

VO_2max has traditionally been used to predict performance in endurance events (Costill, 1967; Saltin and Astrand, 1967). However, $\dot{V}O_2$max changes little in response to modifications in the training programs of well conditioned athletes (Pollock, 1977) and gives no insight into the reasons behind the differences in performance between athletes with similar maximal aerobic capacities (Costill, Thomason and Roberts, 1973).

A large volume of data is available which relates the various threshold measures with running events of distances ranging from two miles to the marathon. Table 1.2 summarises some of this work. Similar tests have been performed on the bicycle ergometer (Coyle et al., 1988, McLellan and Skinner, 1985; Vago, Mercier, Ramonatxo and Prefaut, 1987; Whipp, Huntsman, Storer et al. 1982). Theoretically, submaximal intensities should show closer correlation to endurance performance than $\dot{V}O_2$max and this is born out in practice with correlations of up to $r = 0.997$ having been reported. Regression equations have been developed, based on a particular threshold measurement, to predict running pace for different race distances (Farrell et al., 1979; LaFontaine et al., 1981; Sjodin and Jacobs, 1981; Tanaka and Matsuura, 1984; Tanaka et al., 1984).

EVENT	THRESHOLD	r	AUTHORS
Marathon	$OPLA_{VEL}$	.98	Farrell et al., 1972
"	$OPLA_{\dot{V}O2}$	.89	" "
"	$LA4_{VEL}$	.88 to .98	Fohrenbach et al., 1987
"	$LA3_{VEL}$	.88 to .99	" "
"	$LA2.5_{VEL}$	.88 to .99	" "
"	$OBLA_{VEL}$	.96	Sjodin and Jacobs, 1981
"	$LA4_{VEL}$	.682	Tanaka and Matsuura, 1984
"	$LT1_{VEL}$	.781	" "
20 km	MSS_{VEL}	.917	La Fontaine et al., 1981
19.3 km	$OPLA_{VEL}$	.97	Farrell et al., 1972
"	$OPLA_{\dot{V}O2}$	.91	" "
9.7 km	$OPLA_{VEL}$	.96	" "
"	$OPLA_{\dot{V}O2}$	.89	" "
10 km	$LT1_{VEL}$	.709	Iwaoka et al., 1988
"	RCT_{VEL}	.899	" "
8.05 km	MSS_{VEL}	.995	La Fontaine et al., 1981
10 km	$VT1_{\dot{V}O2}$	.94	Powers et al., 1982
"	$LT1_{\dot{V}O2}$	.70 to .88	Tanaka et al., 1984
"	$LT1_{VEL}$	.81 to .84	" "
"	$LT1_{\dot{V}O2}$	-.69 to -.92	Tanaka et al., 1986
3.2 km	$OPLA_{VEL}$	.91	Farrell et al., 1972
"	$OPLA_{\dot{V}O2}$	.85	" "
5 km	$LT1_{VEL}$	.597	Iwaoka et al., 1988
"	RCT_{VEL}	.786	" "
3.22 km	MSS_{VEL}	.993	La Fontaine et al., 1981
12 min run	$VT1_{\dot{V}O2}$	.73	Reybrouk et al., 1983
"	$VTlong_{\dot{V}O2}$	.82	" "
5 km	$LT1_{\dot{V}O2}$	.72 to .86	Tanaka et al., 1984
"	$LT1_{VEL}$	.79 to .83	" "
1500 m	$LT1_{VEL}$	.246	Iwaoka et al., 1988
"	RCT_{VEL}	.776	" "
800 m	$LT1_{VEL}$	.036	" "
"	RCT_{VEL}	.760	" "
402.3 m	MSS_{VEL}	.834	La Fontaine et al., 1981

Table 1.2: Summary of correlations between threshold measurements and running performance (VEL = velocity).

To say that one threshold more accurately predicts performance than another is not possible given the many sources of individual variation. However, those that occur at greater metabolic rates, ie. VT_2, IAT and OBLA, would seem to be closer to the intensities maintained by athletes during endurance events of up to marathon duration. This is in agreement with the observations of Costill and Fox (1969) that marathon runners could maintain a running pace requiring 75% of $\dot{V}O_2max$, but conflicts with Yoshida et al. (1987) who found that LT_1 was a better predictor of endurance performance than LT_2 or OBLA. That the subjects in the latter study were sedentary could explain this contradiction by way of differences in motivation and experience during performance.

14. Maximal steady state metabolism

Closely associated with the predictive capacity of the thresholds is their role in determining the maximal steady state (MSS) of blood lactate, ventilation and oxygen consumption during constant load exercise.

Whipp and Wasserman (1972) found that $\dot{V}O_2$ reached steady state after three minutes during CLW of low intensity exercise but that it was delayed for a further three minutes in work of moderate intensity. At high intensities, no steady state was achieved. The difference between $\dot{V}O_2$ at 3 and 6 minutes was increasingly greater the higher the work load and was thought to provide an index of the amount of anaerobic metabolism. Casaburi et al. (1987a) suggest four possible sources for this drift in $\dot{V}O_2$ during moderate intensity exercise; 1) the calorigenic effect of an elevated body temperature, 2) increased blood catecholamine concentration resulting in increased lipolysis and glycogenolysis, 3) ventilation increases resulting in an increased work of breathing, and 4) blood lactate elevations reflecting anaerobic metabolism.

Hagberg, Mullin and Nagle (1978) concluded that body temperature was the primary mediator of the $\dot{V}O_2$ drift but Casaburi et al. (1987a) reject this possibility due to a dissociation in the relationship between body temperature and $\dot{V}O_2$ after training. They concluded that blood lactate concentrations and thus anaerobic metabolism showed the closest affinity to $\dot{V}O_2$ drift, with the work of breathing associated with the increased $\dot{V}_E$ as another important factor. The exercise intensity above which a delay in steady state $\dot{V}O_2$ is observed is the VT_1 and/or LT_1 (Casaburi et al., 1987a, Ribiero, Hughes, Fielding et al., 1986, Whipp 1987).

Ribiero et al. (1986) suggested that VT_2 and/or LT_2 was coincident not only with the maximal steady state $\dot{V}O_2$ but also with MSS$\dot{V}_E$ and MSSLa. Casaburi et al. (1987b) linked the mediation of ventilatory response during CLW to reduced blood lactate. Haverty, Kenney and Hodgson (1988) found a correlation of $r = 0.90$ between MSS$\dot{V}O_2$ and MSSLa. All these findings suggest that the steady state responses of $\dot{V}O_2$, $\dot{V}_E$ and blood La^- are intimately associated.

Further evidence for the MSS being at the second threshold is presented by McLellan and Gass (1989). They found that when the response to CLW (at 2/3 of the difference between $\dot{V}O_2$max and VT_1/LT_1) of subjects with a high VT1 was compared with that of subjects with a low VT_1, only the high VT_1 group maintained a steady state response. They suggested that this may be because the fit group, whose MSS would be at a higher relative $\dot{V}O_2$, were exercising at an intensity below MSS but the unfit group were above it. They refer to the VT_{long} (Reybrouk, Ghesquiere, Cattaert et al., 1983) and the IAT of Stegmann, Kindermann and Schnabel (1981) as possible indicators of the MSS. Jacobs and McLellan (1988) validated the use of the IAT in identifying the MSSLa, while McLellan (1985a) had previously found that IAT occurred at a lower intensity than VT_2.

In contrast, Coyle et al. (1988) found that the highest steady state $\dot{V}O_2$ that can be maintained during endurance performance is correlated well with $\dot{V}O_2$ at LT_1 ($r = 0.90$). They defined their LT_1 as a 1mM increase in blood [La^-] above baseline which, in the highly trained subjects they used in their study, would represent a higher metabolic rate than that at an LT_1 defined by the inflection point. That the LT_1 in their study occurred at up to 86% of $\dot{V}O_2max$ would seem to verify this and bring the finding more into line with the results of previous work.

15. Determining endurance training intensities using threshold values.

The OBLA as defined by Kindermann, Simon and Keul (1979) was thought to represent the optimum blood lactate at which to train, because they found it to be coincident with the MSSLa. Later, Heck et al. (1985) produced data which they claimed justified this choice, but their results showed that the chosen blood lactate concentration of 4.0 mM was actually the average for their subjects, the range being 3 to 5 mM. It was this variability which prompted the development of the IAT by Stegmann, Kindermann and Schnabel (1981). Stegmann and Kindermann (1982) compared CLW at OBLA and IAT and found that in more highly trained subjects OBLA represented an intensity above the MSSLa, the converse being true for untrained subjects. IAT on the other hand defined MSSLa for individuals of varying fitness levels.

In a review of the use of thresholds for determining training intensities, MacDougall (1977) suggested that VT_1 be used. However, his finding that VT_1 occurred at 85% of $\dot{V}O_2max$, together with analysis of his graphical presentation of results would suggest that he has in fact detected VT_2 instead of VT_1. Olbrecht, Madsen, Mader et al. (1985) observed that elite swimmers maintained a velocity during training below that corresponding to 4.0 mM blood [La^-], while Fohrenbach, Mader and Hollman

(1987) found that a blood [La^-] of 2.5 to 3.0 mM correlated best with marathon running velocity in trained athletes.

These findings suggest that MSS may represent the optimal intensity at which to train. Whether MSS is coincident with IAT, VT_2/LT_2 or another measure such as VT_{long} is less certain.

16. Plasma potassium during exercise

16.1 Regulation of potassium by skeletal muscle during exercise

The acute regulation of plasma K^+ is primarily a function of the skeletal muscles (Bia and De Fronzo, 1981). K^+ efflux from the muscle cell occurs with each depolarisation preceding muscular contraction (Hodgkin and Horowicz, 1959), a positive linear relationship existing between efflux and the frequency of contractions (Clausen and Everts, 1989). The Na-K pumps attempt to maintain the gradients of Na^+ and K^+ across the sarcolemma by pumping K^+ back into the cell (and Na^+ back out) so that the propagation of action potentials may continue. Incomplete re-uptake of K^+ by Na-K ATPase appears to be the cause of the rise in extracellular K^+ after each repolarisation (Clausen, Everts and Kjeldsen, 1987). There exists a maximum level of Na-K pump activity and if K^+ efflux exceeds this, rapid accumulation of plasma K^+ occurs with the resulting impairment to muscular contraction (Clausen, Everts and Kjeldsen, 1987).

Major stimuli for the Na-K pump include: muscular excitation, catecholamines and insulin (Clausen and Everts, 1989). The mechanism of action of insulin is additive to that of catecholamines (Clausen and Everts, 1989) so is different, but also probably of less importance in the regulation of plasma K^+ during exercise (Jarhult and Holst, 1979). However, the effect of local release of adrenaline is not additive to muscular excitation suggesting they may act by the same mechanism (Everts,

Retterstol and Clausen, 1988). Catecholamines may either induce pump activity or alter its sensitivity to intracellular Na^+.The pump is sensitive to both intracellular Na^+ and extracellular K^+, the former being of greater significance (Sejersted, Wasserstrom and Fozzard, 1988). This would provide a direct link between muscular activity and excitation of the pump.

16.2 Links between muscle metabolism and plasma potassium

A rise in plasma [K^+] with exercise was reported by Fenn in 1936. Since then, numerous attempts have been made to link K^+ changes in the muscle with other metabolic events during exercise. Kilburn (1966) suggested that K^+ was exchanged for H^+ during exercise-induced acidosis and that both were released from skeletal muscle. Tibes et al. (1974) studied the relationship between plasma [K^+], [H^+] and [La^-] and concluded that K^+ efflux from the muscle cell was dependent on ionic transport through the muscle cell membrane, which was modified by [H^+].

Laurell and Pernow (1966) found that the rise in serum [K^+] at the onset of exercise and the fall after exercise, was more rapid than the changes in [La^-], pH and heart rate, although well correlated with them. Medbo and Sejersted (1988) showed that the $t_{1/2}$ for the rise in plasma [K^+] during exercise was around 25 seconds, far quicker than for the rise in blood [La^-]. If it is accepted that changes in blood [La^-] accurately reflect those in muscle [La^-], these results would suggest that K^+ efflux is not primarily dependent on H^+.

Heigenhauser et al. (1990) suggest that the link may be a result of mechanisms involved in ionic homeostasis, large increases in intracellular [H^+] being accounted for by decreases in [K^+] and increases in [La^-] and PCO_2. In venous plasma, increases in PCO_2, and [La^-] are balanced by increases in [H^+], [K^+] and [Na^+].

16.3 Coincidence between changes in blood lactate and plasma potassium

Gleim et al. (1988) have reported a threshold response in serum [K^+] during progressive IW that corresponded to the LT_1. As has been discussed previously, catecholamines may stimulate lactate production (Stainsby et al., 1984; 1985; 1987) and a threshold response in plasma catecholamine concentration has been observed which is coincident with the LT_1 (Van Harn and Brooks, 1985). Mazzeo and Marshall (1989) conclude that a cause and effect relationship exists between the breakpoint in the plasma adrenaline response and the LT_1 during IW.

Walsh and Bannister (1988) have suggested that local nervous reflex activity may increase sympathetic activity, with K^+ having a major role as a modulator of such control. However, catecholamines also increase the activity of the Na-K pumps during exercise (Everts, Reterstol and Clausen, 1988), which has the effect of preventing plasma K^+ from rising further. So, although at high exercise intensities there is an increase in both plasma catecholamines and plasma K^+, whether or not they are causally linked is yet to be verified.

16.4 Links between ventilation and plasma potassium

Band, Lim, Linton and Wolff (1982) continuously monitored arterial plasma potassium during CLW and found a marked temporal similarity between the changes in $\dot{V}_E$ and [K^+]. Later, Conway, Paterson, Petersen and Robbins (1988) and Paterson, Robbins and Conway (1989), conducted experiments where their subjects performed separate bouts of moderate and high intensity exercise, their findings agreeing that both during exercise and at its termination, there was a close temporal relationship between $\dot{V}_E$ and [K^+]. Conway et al. (1988) reported a correlation of $r = 0.97$ between $\dot{V}_E$, measured breath by breath, and [K^+]. Paterson et al. (1990) showed however, that there was no very fast (phase 1) component in the time course

of K^+ response during the recovery from exercise, suggesting that K^+ mediates $\dot{V}_E$ solely via arterial chemoreceptors.

Newstead (1988) also found correlations between $\dot{V}_E$ and $[K^+]$ of 0.932 to 0.987 at different work loads and observed a similar relationship between $[K^+]$ and $\dot{V}CO_2$. Donaldson, Newstead and Sneyd (1989) quantified this relationship between $\dot{V}CO_2$ and $[K^+]$, finding correlation coefficients of 0.792 to 0.929. Given the disparity in rate of increase between $\dot{V}_E$ and $\dot{V}CO_2$ at exercise intensities above VT_2, it is possible that the less significant correlations may have been for exercise intensities in excess of VT_2, although this was not reported.

In the discussion of ventilatory control earlier in this review, potassium was mentioned as a possible mediator of ventilation via two distinct mechanisms. First, it may act via a peripheral neurogenic effect, with local release of K^+ stimulating receptors of group III and IV afferents, the signal being transmitted to respiratory centre neurons (Kao, 1963). Second, elevated arterial plasma $[K^+]$ is thought to have a stimulatory effect on the carotid bodies (Band et al., 1985; Paterson and Nye, 1988). The results of Paterson et al. (1990) do not discount the possibility of mediation of $\dot{V}_E$ by the metaboloreceptor mechanism, but suggest that it may be of lesser importance than the humorally mediated mechanism, at least during the transitional phases of exercise.

16.5 Coincidence between changes in ventilation and plasma potassium

The rapid increase in both plasma $[K^+]$ and $\dot{V}_E$ at the onset of exercise would appear to be due to the delay between the increase in muscular contraction rate and the development of adequate stimulation to produce Na-K pump activity strong enough to counter the K^+ efflux (Vollestad and Sejersted, 1989). Once the efflux of K^+ can be balanced by the influx, $[K^+]$ remains stable, coincident with the

attainment of steady state $\dot{V}_E$. If the rate of efflux of K^+ exceeds the capacity of the pump, plasma [K^+] will continue to rise (Clausen, Everts and Kjeldsen, 1987) again coincident with the drift in $\dot{V}_E$ (Paterson et al., 1990).

How K^+ and H^+ co-exist in their effect on ventilation is not certain. Tibes et al. (1976) found similar levels of coincidence between [H^+], [K^+] and $\dot{V}_E$ during various intensities of exercise and concluded that both metabolites exerted a regulatory effect on ventilation. Tibes, Hemmer and Boning (1977) then studied the transition from rest to exercise and concluded that the rapid adjustments to $\dot{V}_E$ at the onset of exercise were related to K^+ release rather than H^+ production. The more rapid response of K^+ at the onset of exercise supports the relative importance of K^+ as a ventilatory regulator, at least in the rest to exercise transition.

Busse et al. (1989a) found no correlation between [K^+] and [H^+] during CLW tests in conditions of either metabolic acidosis or alkalosis. Good correlation was found between [K^+] and $\dot{V}_E$ during acidosis ($r = 0.90$), but the correlation was not reported for the alkalotic test. The same group (Busse et al., 1989b) also attempted to dissociate the effects of H^+ and K^+ on $\dot{V}_E$ during IW through a combination of dietary and exercise manipulation. They observed that although glycogen depletion caused relative alkalinity during the IW tests as compared with normal or high glycogen stores, the K^+ response to exercise was not altered and its relationship to $\dot{V}_E$ remained unaffected.

As discussed earlier, ventilatory control is no doubt dependent on a number of inputs and there is likely to be a surplus of stimuli at any instance. Although these arguments do not dismiss the effect of H^+ and therefore, by association, La^- on the ventilatory response to exercise, they suggest that other stimuli may be of equal or greater importance, at least during non-steady state exercise.

16.6 The effect of endurance training on acute potassium regulation

The concentration of Na-K pumps in the skeletal muscle of dogs is increased by endurance training (Knochel, Blachley, Johnson and Carter, 1985). Klitgaard and Clausen (1989) found a 30-40% greater concentration of Na-K pumps in biopsies of the vastus lateralis of endurance trained men compared with age-matched untrained subjects. Kjeldsen, Richter, Galbo et al. (1986) reported similar findings after endurance training in rats, observing that the change was restricted to the exercising muscles and that pump concentration was decreased by detraining.

Everts et al. (1988) found that stimulation of active Na^+-K^+ transport by adrenaline infusion is more pronounced in slow than fast twitch muscle. Everts, Lomo and Clausen (1989) added that in vitro activation of pumps in slow twitch muscles of rats was three times greater than that in fast twitch muscles at the same electrical stimulation frequency. Coupled with this is the observation that hyperkalemia is reduced after endurance training in man (Tibes, Hemmer, Schweigart et al. 1974), dogs (Knochel et al., 1985) and calves (Fosha-Dolzeal and Fedde, 1988). Increases in % slow twitch fibres in terms of oxidative capacity (Holloszy, 1983) and contractile properties (Pette, 1984), have both been previously discussed. Everts et al., (1988) reported equal pump concentration in muscle fibres of different types in young untrained rats, but no published data suggesting that there is a greater pump concentration in slow twitch muscle, or that endurance training causes such an adaptation could be found. However, such a possibility cannot be dismissed.

17 . Aims and objectives

The present series of experiments was undertaken to further investigate selected contributing factors to the metabolic and respiratory response to endurance exercise. The study was divided into two sections, the first of which involved trained and untrained subjects, each of whom performed a fast IW test. The purpose of this first study was to:

(1a) analyse and correlate the changes in ventilation, gas exchange, blood lactate and pH, and plasma potassium,

(1b) compare ventilatory thresholds with those in blood lactate and, if evident, in plasma potassium,

(1c) determine whether prior training affects the response of individual variables or the relationship between the variables.

The second section involved trained subjects who performed a further slow IW test and a one hour self-paced trial, the purpose being to:

(2a) analyse and correlate the changes in ventilation, gas exchange, blood lactate and pH, and plasma potassium during prolonged self-paced exercise,

(2b) analyse the accuracy of the various threshold indicies (LT_1, IAT, VT_1, VT_2) in predicting endurance performance.

CHAPTER 2

METHODOLOGY

This chapter outlines experimental techniques common to the two studies undertaken. More detailed descriptions of the experimental protocols, outlining additional information relevant to each study individually, can be found in the subsequent chapters.

Subjects.

The subjects were male volunteers, allotted to one of two groups on the basis of activity level. One group consisted of active but untrained men, recruited from the Footscray campus of Victoria University of Technology. The other group were elite triathletes with a minimum of two years continuous endurance training. Subject characteristics are given in Table 2.1. Prior to participation, written informed consent was given by all subjects in accordance with the guidelines for human experimentation provided by the National Health and Medical Research Council of Australia. Studies had the approval of the Institute's Human Experimentation Ethics Committee.

Subjects reported to the Human Performance Laboratory in the Department of Physical Education and Recreation after a fast of at least six hours and having abstained from exercise, alcohol, tobacco and caffeine for 24 hours.

Exercise Apparatus

All exercise bouts were performed on a modified, mechanically braked cycle ergometer (Monark). The frame geometry was changed to provide a position equivalent to typical racing bicycles, and adjustable for different body dimensions. The ergometer was also equipped with toe-clips and dropped racing handlebars.

In order to obtain accurate instantaneous power output values, the bicycle ergometer was fitted with an electronic tachometer, which measured crank R.P.M., and a strain gauge (X-TRAN S1W load cell), which measured the friction belt tension. The output of both devices was fed to an IBM XT personal computer. Data acquisition and analysis software were written using DAOS, and a sample rate of 10 samples/second was used to collect data. The strain gauge was calibrated against known weights prior to all exercise bouts.

Analysis of Expired Gas

During all tests subjects breathed through a low-resistance valve (Hans-Rudolph 2700 series 2-way valve), the expiratory side of which was connected to a four litre mixing chamber. Gas was continuously sampled from the mixing chamber for analysis of oxygen and carbon dioxide contents by Applied Electrochemistry S-3A and CD-3A gas analysers respectively. The analysers were calibrated using standard gases of known concentration prior to each test. Expired volume was measured by a turbine ventilometer.

Oxygen uptake, carbon dioxide production, respiratory exchange ratio and the ventilatory equivalents for both oxygen and carbon dioxide were calculated using standard equations. Together with ventilation, these measures were averaged every 30 seconds and recorded by computer (IBM XT PC), with software written using

DAOS. All data are reported under STPD conditions throughout this thesis, with the exception of V_E which is reported under BTPS conditions.

Blood sampling and analysis.

All blood samples were obtained from indwelling 20 or 22 gauge teflon catheters (Jelco). Catheters were introduced percutaneously into a left dorsal forearm vein, lying up to a maximum of four centimeters proximal to the wrist, and kept patent by frequent flushings with heparinised saline (10 IU/ml). Venous blood was arterialised by warming the subject's left hand in a hot water bath, thermostatically maintained at 45 degrees celsius. This method has been shown to produce values of PO_2 and PCO_2 to within less than 1 mm Hg, pH to within .001 units and blood lactate to within .21 mg/100ml of values obtained from arterial samples (Forster et al., 1972).

Samples were drawn through a three way stop cock and collected in a heparinised 5ml syringe. The sample was then divided, with 25 microlitres being allotted to a capillary tube containing anticoagulant, and a further 1ml to a 1.5 ml Eppendorf tube, the remainder being retained in the sampling syringe from which all air was expelled prior to being capped. The Eppendorf tubes and the syringes were placed on ice until analyses could be performed.

The samples in the Eppendorf tubes were spun at 2,000 R.P.M. for 10 minutes and the plasma then analysed for potassium concentration (Radiometer KNA2 Na^+/K^+ analyser). The samples in the capillary tubes were analysed for blood lactate concentration (Analox micro-stat P-LM4 lactate analyser). The samples in the capped syringes were analysed for blood PO_2, PCO_2 and pH (Radiometer ABL30 acid-base analyser) and for haemoglobin concentration and O_2 saturation (Radiometer OSM2 Hemoximeter). All analyses were conducted immediately after the termination of each test and were completed within 90 minutes.

GROUP	n	AGE (years)	WEIGHT (kg)	HEIGHT (cm)	$\dot{V}O_2max$ (ml/kg.min)
ET	8	25.6 ± 1.7	71.5 ± 5.1	179.5 ± 6.1	64.29 ± 4.01*
UT	8	29.4 ± 2.3	71.5 ± 5.2	174.4 ± 2.8	53.36 ± 5.88

Table 2.1: Physiological characteristics of subjects. Endurance trained (ET) subjects participated in both studies. Untrained subjects (UT) participated in the incremental exercise study only. Values are means ± 1 SD, * denotes different from UT.

CHAPTER 3

PHYSIOLOGICAL RESPONSES TO INCREMENTAL EXERCISE IN TRAINED AND UNTRAINED MEN

Introduction

Based on the long established observations of Hill, Long and Lupton (1924), that lactate formation increases when muscles lack oxygen, the concept of the anaerobic threshold was developed by Wasserman, Whipp, Koyal and Beaver (1973). They suggested that the ventilatory response to exercise accurately reflects changes in blood lactate concentration, and proposed that buffering of lactate by bicarbonate causes an increase in non-metabolic CO_2 production which, when sensed by the respiratory control mechanisms, results in an increase in $\dot{V}_E$.

Whether the relationship between the lactate and ventilatory responses is cause and effect, or merely coincidental, continues to be an area of controversy. Many authors have found reason to suggest a causal relationship (Aunola, Marniemi, Alanen et al., 1988; Caiozzo, Davis, Ellis et al., 1982; Davis, Basset, Hughes and Gass, 1983; Davis, Vodak, Wilmore et al., 1976; Haverty, Kenney and Hodgson, 1988; Ivy, Withers, Van Handel et al., 1980; McLellan, 1985; Reinhard, Muller and Schmulling, 1979; Wasserman et al., 1973; Yoshida, Suda and Takeuchi, 1982). However, the responses have been dissociated via manipulation of exercise protocol (Hughes, Turner and Brooks, 1982; Powers, Dodd and Garner, 1984; Simon, Young, Gutin et al.,1983), after prior exercise (Davis and Gass, 1979; Farrell and Ivy, 1987), via glycogen depletion (Fric et al., 1988; Heigenhauser et al., 1983; Hughes et al., 1982; Neary et al., 1985), as a result of endurance training (Poole and Gaesser, 1985; Simon, Young, Blood et al., 1986) and in subjects with McArdle's disease (Hagberg et al., 1982; 1990). Proponents of the cause and effect relationship between the lactate and

ventilatory thresholds have offered alternative interpretations and explanations of these results (Davis, 1985; McLellan, 1985; McLellan and Gass, 1989; Wasserman, 1983; Yoshida, 1986). Dissociation precludes a direct cause and effect relationship, but does not preclude lactate being of significance in regulating ventilatory response. Coincidence, on the other hand, does not guarantee a causal relationship, even though such an association may appear a strong possibility.

Tibes et al. (1977) have suggested that during the transition from rest to exercise, the increase in plasma [K^+] exerts a greater influence on ventilatory control than do increases in blood [La^-] or [H^+]. Also, Band et al. (1982), Conway et al. (1988), Newstead (1988), and Paterson et al. (1989) have reported high correlations between changes in plasma potassium concentrations and the ventilatory response to constant load exercise. Gleim et al. (1989) suggest that there is a breakpoint in the relationship between plasma potassium concentration and workload during IW, which is coincident with the lactate threshold, although no comparison with ventilatory response was reported.

Ventilatory control during exercise is subject to numerous stimuli. It seems likely that some stimuli assume greater or lesser importance depending on the intensity and the nature of the exercise being performed. To what extent changes in ventilation are affected by changes in lactate and/or potassium is the source of conjecture. The purpose of this experiment was to:

(1) analyse and correlate the changes in ventilation, gas exchange, blood lactate and pH, and plasma potassium,

(2) compare ventilatory thresholds with that in blood lactate and, if evident, in plasma potassium, and

(3) determine whether prior training affects individual responses during exercise or the relationship between responses during exercise.

Methods

Two groups of eight male subjects whose physical characteristics have previously been described (Table 2.1) participated in this study, which involved a single test on the bicycle ergometer. After an initial four minute warm-up period at 30W, work load was increased by 30W/min until volitional fatigue. All subjects pedalled at a constant rate of 90 rpm. Blood samples were taken at rest and then during the last fifteen seconds of each work load. Expiratory gases were collected continuously throughout each test.

The first and second ventilatory thresholds were determined by visual inspection of the graphs of $\dot{V}_E/\dot{V}O_2$ vs. $\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ vs. $\dot{V}O_2$. The criterion for VT_1 was the initial continuous increase in $\dot{V}_E/\dot{V}O_2$ without such an increase in $\dot{V}_E/\dot{V}CO_2$, as outlined by Caiozzo et al. (1982). VT_2 was determined as the initial continuous increase in $\dot{V}_E/\dot{V}CO_2$ (Reinhard et al., 1979).

The first lactate threshold was determined from a plot of lactate versus work load. LT_1 was defined as occurring at the work load that immediately preceded a continuous rise in lactate values above those at low work loads. The $\dot{V}O_2$ at the LT_1 was then assessed from a linear regression between $\dot{V}O_2$ and work load. The $\dot{V}O_2$ co-ordinate on the regression line corresponding to the work load at the inflection point in the work-lactate relationship was taken to represent the $\dot{V}O_2$ at LT_1. This method was used to reduce the likelihood of error caused by deviations in the $\dot{V}O_2$ response from its linear relationship with work load.

The existence of a possible inflection point in the plasma potassium concentration was also assessed using this method. All graphs were coded and randomised prior to threshold determination to ensure objectivity of analysis. The author was the sole assessor.

Statistics

The correlation between the mean response of $\dot{V}_E$, $\dot{V}O_2$, $[La^-]$, $[K^+]$ and pH was calculated for each group. Mean relationships were determined from analyses of individual responses, and linear regression equations were generated for each group for the following relationships: $\dot{V}_E$ vs. $[K^+]$, $\dot{V}_E$ vs. $[La^-]$, $\dot{V}_E$ vs. pH and $[K^+]$ vs $[La^-]$. A t-test was conducted on the slopes of the regression equations to determine whether one group's response was different from the other. An analysis of variance assessed differences between groups for $[K^+]$, $[La^-]$, pH and $\dot{V}_E$ at each individual work load. Student's t-test was used to compare the $\dot{V}O_2max$ and threshold values between groups, while analyses of variance were used to compare the methods of threshold estimation. All results are expressed as mean $\pm$ one standard deviation (SD).

Results

The average PO_2 for all samples taken during incremental work tests was 72.6 $\pm$ 13.0 mmHg, while the mean oxygen saturation was 95.0 $\pm$ 4.6 %. There was close correlation between the individual responses of the subjects of each group for $[K^+]$, $[La^-]$, $\dot{V}_E$ and pH (Table 3.1). For both the untrained and trained groups, all correlations were significant ($p < 0.05$). In both groups, $[La^-]$ was most closely related to $\dot{V}_E$ (UT $r = 0.877$, ET $r = 0.848$), while $[K^+]$ was also strongly related to $\dot{V}_E$ (UT $r = 0.869$, ET $r = 0.774$). The relationship between $[La^-]$ and $[K^+]$ for each group was also strong (UT $r = 0.815$, ET $r = 0.867$).

Regression lines drawn for the relationship between $\dot{V}_E$ and $[K^+]$ for each group show the slope of the relationship to be significantly greater ($p < 0.05$) for the endurance trained group. The same analyses were conducted for the relationships between $\dot{V}_E$ and $[La^-]$, $\dot{V}_E$ and pH and between $[K^+]$ and $[La^-]$, with significantly greater slopes (Table 3.2) being observed for the endurance trained group ($p < 0.05$) in all cases.

Mean response patterns of $\dot{V}_E$, $[K^+]$, $[La^-]$ and pH for the two groups are shown in Figure 3.1. There was a general shift to the right in all parameters for subjects in the endurance trained group. Analysis of variance revealed that $\dot{V}_E$ was significantly higher in the untrained group at 330W ($p < 0.05$), the highest work load the two groups had in common. $[K^+]$ values were significantly higher ($p < 0.05$) in the trained group at rest and in the untrained group at 300W and 330W. In the untrained group, $[La^-]$ was significantly higher at 90W and above, while pH was significantly lower at 210W and above ($p < 0.05$).

The $\dot{V}O_2max$ scores (UT = 53.4 $\pm$ 5.9 ml/kg.min, ET = 64.3 $\pm$ 4.0 ml/kg.min) for the endurance trained group were significantly higher ($p < 0.05$). As inferred by the rightward shift of the response patterns of the subjects of the endurance trained group, they also had significantly higher threshold values ($p < 0.05$), both when compared in terms of absolute $\dot{V}O_2$ and as a percentage of $\dot{V}O_2max$ (Table 3.3). LT_1 did not vary significantly from the VT_1 in both groups, expressed in either absolute or relative terms.

Typical examples of individual responses from both groups are shown in Figures 3.2 and 3.3. The pattern of increase in plasma potassium concentration, although being well correlated with those of ventilation and blood lactate, did not, in the majority of cases, show a clear breakpoint similar to those associated with VT_1 and LT_1.

	UT				ET		
	$[La^-]$	**pH**	**$\dot{V}_E$**		**$[La^-]$**	**pH**	**$\dot{V}_E$**
$[K^+]$	.815	-.785	.869	**$[K^+]$**	.867	-.784	.774
$[La^-]$		-.920	.877	**$[La^-]$**		-.864	.848
pH			-.797	**pH**			-.675

Table 3.1: Correlation coefficients for individual responses to the fast IW test, averaged by group. All correlations significant ($p < 0.05$).

COMPARISON	GROUP	SLOPE
$\dot{V}_E$ vs $[K^+]$	ET	84.849
	UT	67.549
$\dot{V}_E$ vs $[La^-]$	ET	18.134
	UT	4.755
$\dot{V}_E$ vs pH	ET	-1355.698
	UT	-968.468
$[K^+]$ vs $[La^-]$	ET	0.256
	UT	0.233

Table 3.2: Linear regression analysis data. All slope coefficients significantly greater for ET group ($p < 0.05$).

	UNTRAINED		ENDURANCE TRAINED	
	ml/kg.min	**% $\dot{V}O_2$max**	**ml/kg.min**	**% $\dot{V}O_2$max**
$\dot{V}O_2$max	53.36 ± 5.88		64.29 ± 4.01	
LT_1	27.23 ± 3.45	51.34 ± 6.75	38.99 ± 3.59	60.25 ± 5.28
VT_1	27.39 ± 3.53	51.76 ± 7.68	38.26 ± 3.40	59.62 ± 5.01
VT_2	37.53 ± 5.20	70.62 ± 8.70	51.43 ± 3.42	79.26 ± 4.74

Table 3.3: $\dot{V}O_2$max and threshold data expressed in absolute (ml/kg.min) and relative (%$\dot{V}O_2$max) terms. $\dot{V}O_2$max and all threshold values significantly higher in ET group ($p < 0.05$). LT_1 not significantly different from VT_1 in either group.

.

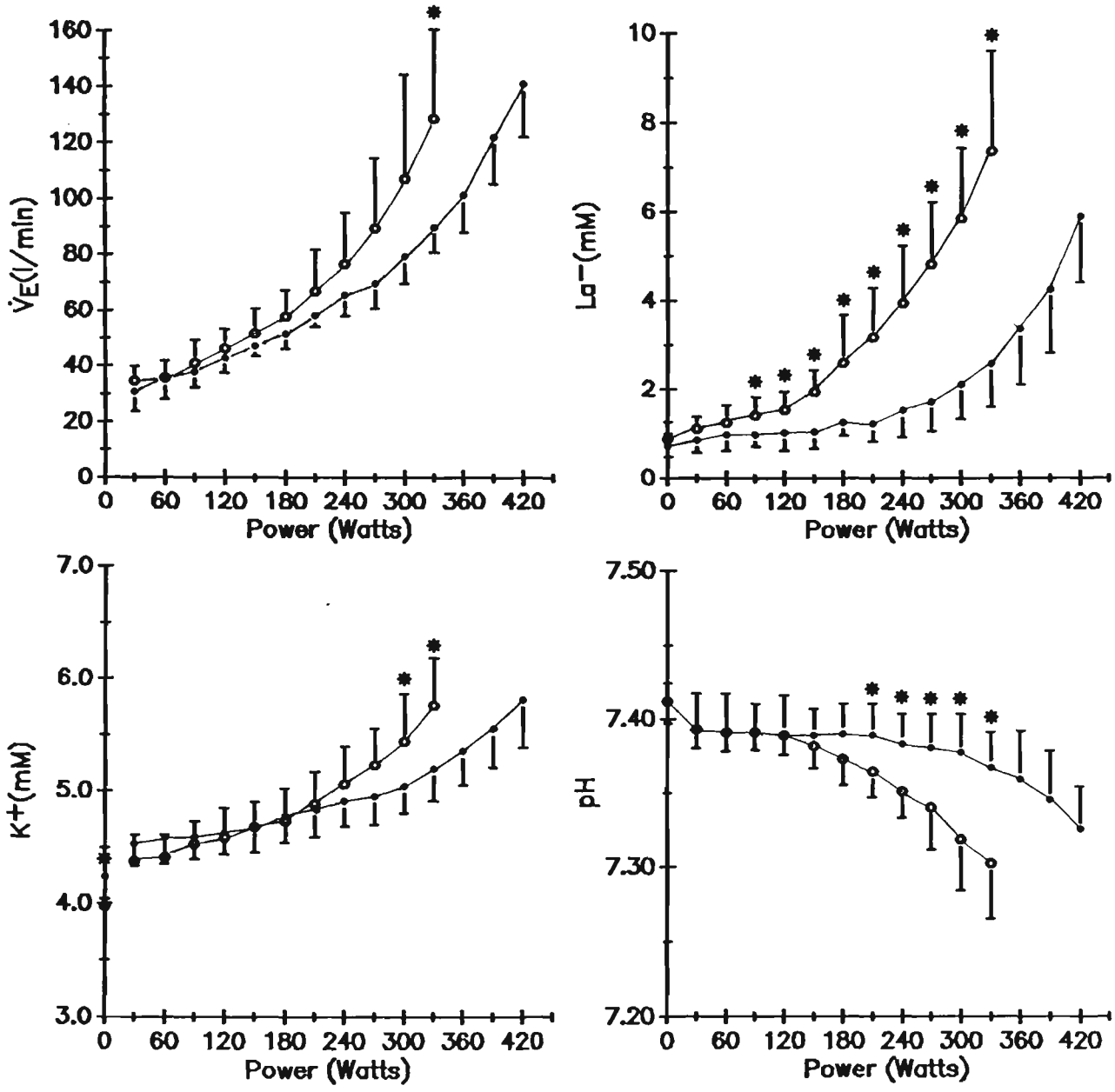

Figure 3.1: Group responses for $\dot{V}_E$, $[K^+]$, $[La^-]$ and pH against power output.

o untrained subjects, • endurance trained subjects. Values are mean ± 1 SD.

* significantly different ($p < 0.05$).

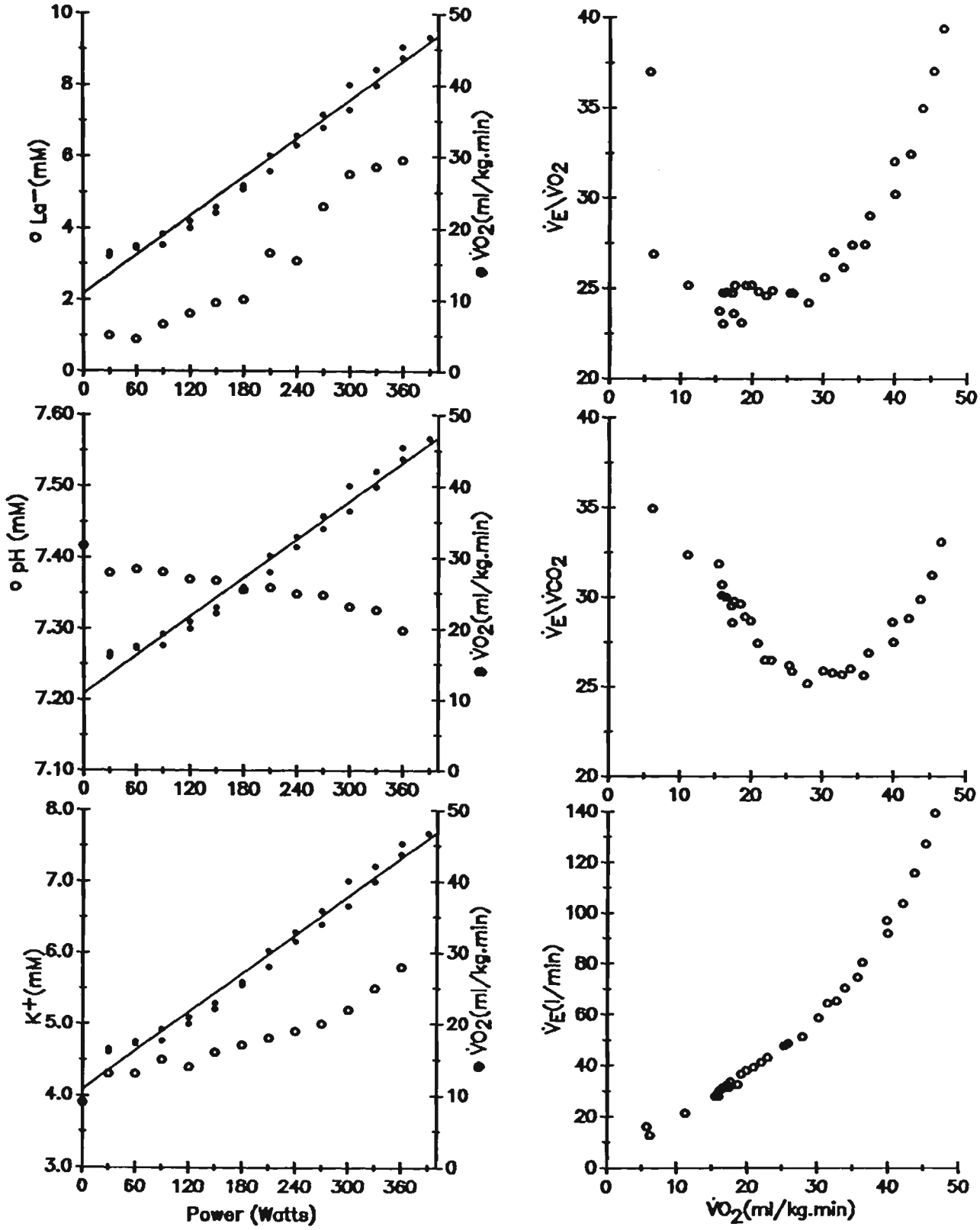

Figure 3.2: Typical individual response of an untrained subject to the fast IW test, for $[La^-]$, pH and $[K^+]$ vs. power output, and $\dot{V}E/\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$ and $\dot{V}E$ vs. $\dot{V}O_2$.

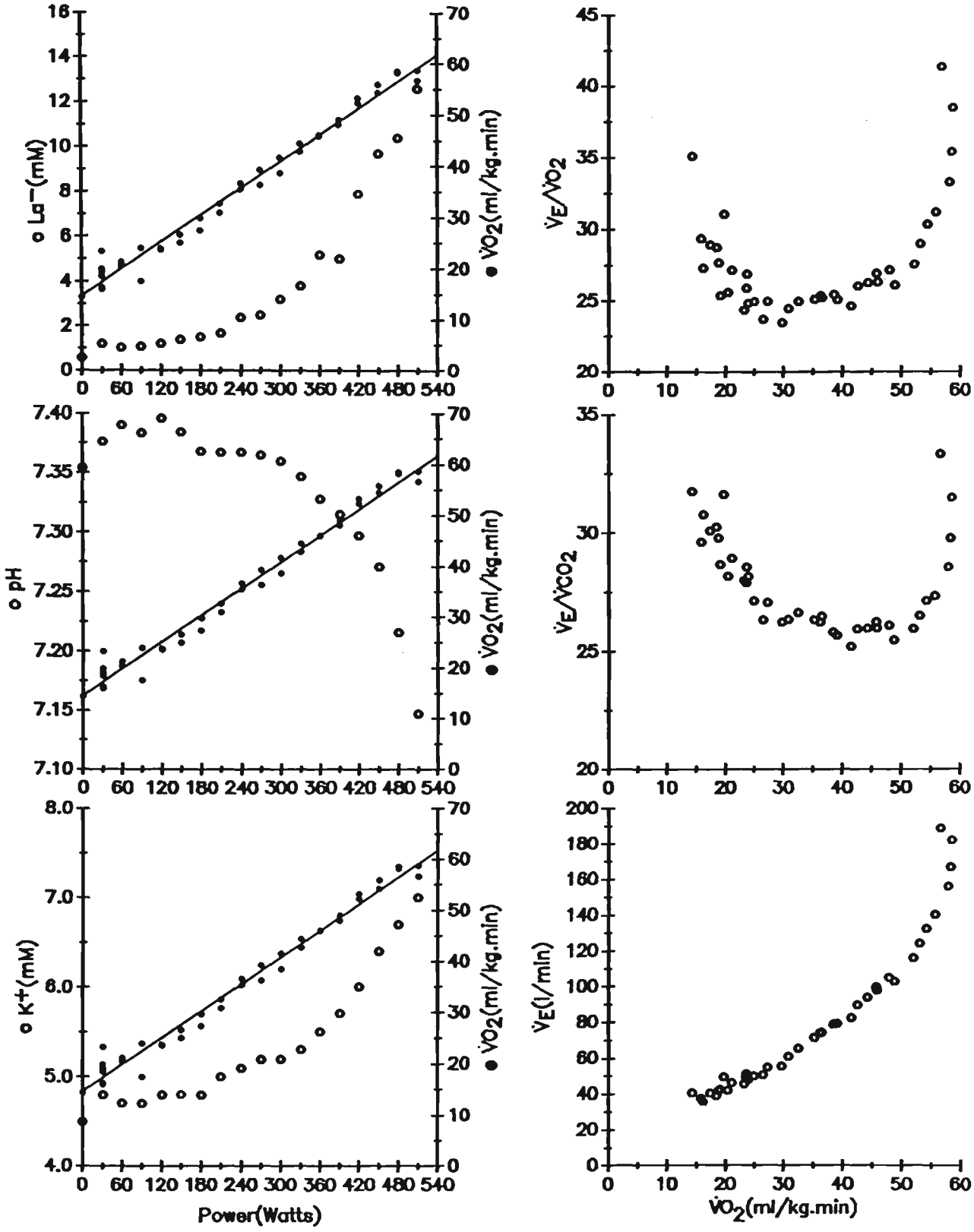

Figure 3.3: Typical individual response of an endurance trained subject to the fast IW test, for $[La^-]$, pH and $[K^+]$ vs. power output, and $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$ and $\dot{V}_E$ vs. $\dot{V}O_2$.

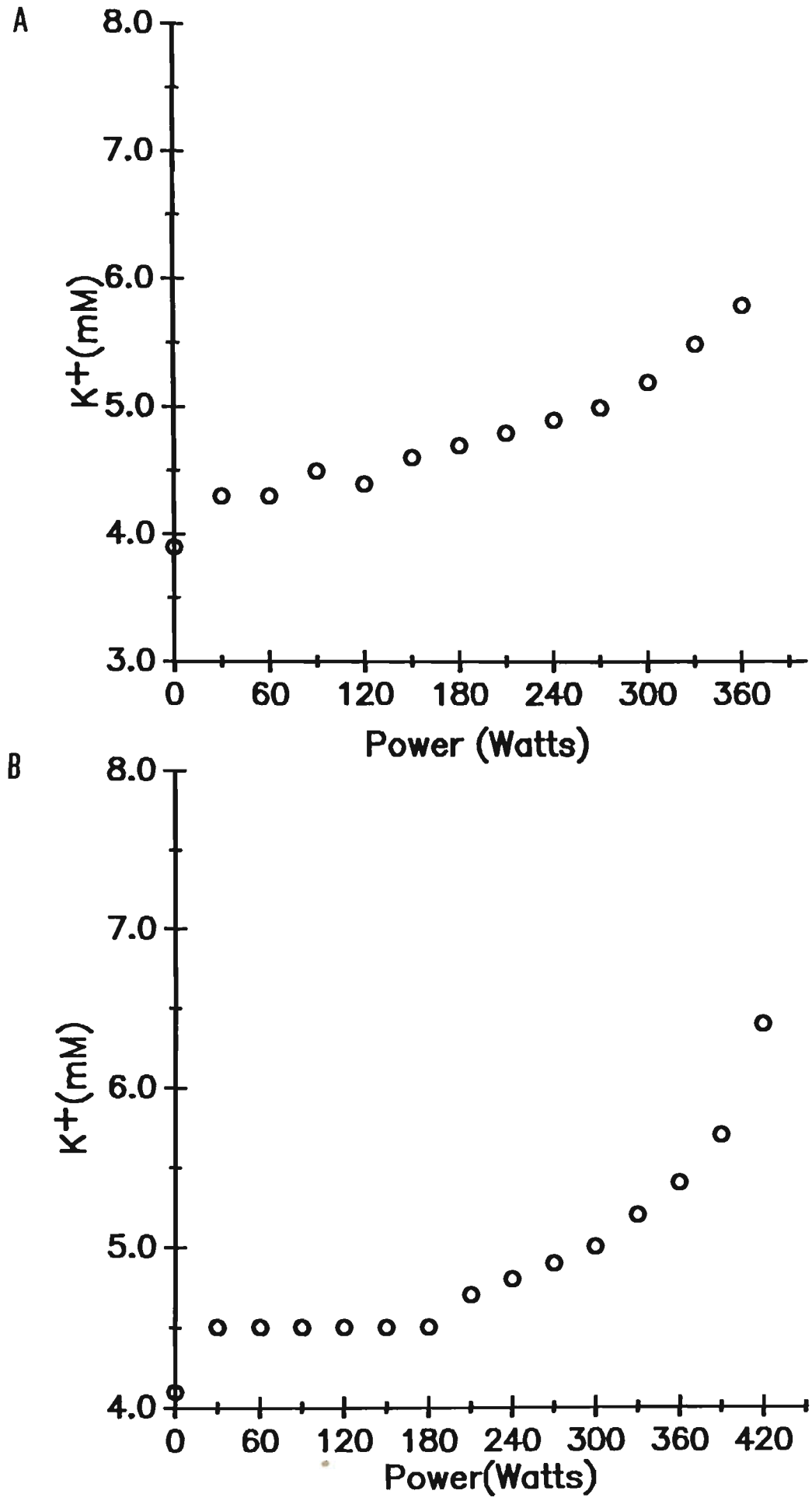

Figure 3.4: Increase in plasma [K^+] during the fast incremental work test.

A) Typical response without inflection point, B) Typical response with inflection point

Typically there was an initial rise from resting values at the onset of exercise, followed by a gradual progressive increase in concentration. Some subjects (2 UT, 4 ET) in each group showed a threshold phenomenon (Figure 3.4). After the initial increase in $[K^+]$ a temporary plateau occurred, followed by a gradual, progressive increase. These inflection points did not correlate well with either VT_1 or LT_1.

Discussion

The close correlation between blood $[La^-]$ and the ventilatory response to incremental exercise observed during this study has often been noted and provided the basis for the development of the anaerobic threshold hypothesis (Wasserman et al., 1973). Changes in both $[La^-]$ and pH were well correlated with $\dot{V}_E$, as were increases in plasma $[K^+]$ (Table 3.1). Tibes et al. (1977) have reported that during the transition from rest to exercise, ventilatory adjustments were more closely related to K^+ release than to H^+ production, while Laurell and Pernow (1966) found that the rise in serum $[K^+]$ at the onset of exercise was more rapid than for either of $[La^-]$ or pH. Medbo and Sejersted (1988) calculated the $t_{1/2}$ (half time) for the rise in $[K^+]$ at the onset of exercise to be around 25 seconds, far quicker than for the rise in blood $[La^-]$. This would suggest that during an IW test, K^+ may more closely affect $\dot{V}_E$ than would La^- or pH. In the present study however, although both La^- and K^+ were significantly correlated with $\dot{V}_E$, the association between La^- and $\dot{V}_E$ was greater. Thimm and Gerber (1988) found strong correlation for both La^- and K^+ with respiratory rate in endurance trained and untrained rats. They also found that the correlation with La^- was stronger. That both La^- and K^+ were strongly correlated with $\dot{V}_E$ lends support to the contention that ventilatory control is mediated via a number of inputs (Cunningham, 1987).

Gleim et al. (1989) reported similarities between the response patterns of K^+ and La^- during IW. These two metabolites were also strongly correlated with each other, as well as individually with $\dot{V}_E$ (Table 3.1), in this study. Whether this relationship is based upon coincidence or causality is unclear. Walsh and Bannister (1988) have suggested that local nervous reflex activity may induce sympathetic activity and that K^+ may be a major modulator of such control. Since catecholamines are thought to stimulate La^- production (Stainsby et al., 1984; 1985; 1987), this would provide a causal link between $[K^+]$ and $[La^-]$. However, catecholamines also increase the activity of the Na-K pump during exercise (Everts et al., 1988), which would then lower plasma $[K^+]$ and negate the possibility of causality. Alternatively, if both La^- and K^+ are considered simply as modulators of $\dot{V}_E$, coincidence between their response patterns is possible.

The finding that $\dot{V}_E$, pH and La^- responses to IW displayed a rightward shift in the endurance trained relative to the untrained subjects is in agreement with previously published results (Casaburi et al., 1987b; Coyle et al., 1983; Davis et al., 1979; Holloszy and Coyle, 1984; Hurley et al., 1984; Yerg et al., 1985). $\dot{V}_E$ in endurance trained subjects is significantly reduced at work loads in excess of VT_1 (Casaburi et al., 1987b). The attenuation in $\dot{V}_E$ sensitivity during exercise is thought to be due to a reduction in CO_2 sensitivity by the arterial chemoreceptors, although whether this is a genetically inherited trait (Kelley, et al., 1984; Saunders, et al., 1976) or a response to endurance training (Blum, et al., 1979; Yerg et al., 1985) is unclear. In fact, while some studies have shown reduced CO_2 sensitivity in athletes (Byrne-Quinn et al., 1971; Miyamura et al., 1976), others have found no such change (Mahler et al., 1982; Saunders et al., 1976).

The lower blood $[La^-]$ seen in endurance trained subjects would suggest that CO_2 flux to the lung is also reduced. The buffering of La^-, however, occurs primarily in

the cytoplasm of the active cell, before the fate of the La^- is decided. The lactate shuttle, proposed by Brooks (1986a, b, c) suggests that La^- is shuttled from areas of high glycolytic rate to areas of high oxidative rate for re-use as a substrate for ATP resynthesis. He suggests that this ability is greatly enhanced in endurance trained subjects and is at least partly responsible for the delay in the LT_1 observed in these subjects. Given that lactate production in endurance trained subjects is greatly reduced at the same absolute work loads relative to untrained subjects since they have higher oxidative capacity in active muscles (Holloszy and Coyle, 1984), that vasoconstriction to non-active muscle beds may be less at the same absolute work load in endurance trained subjects (Katz, Sharp, Armstrong and King, 1984) and that endurance trained subjects will have a higher capillary density (Andersen and Henriksson, 1977; Katsuta et al., 1988), not only will less lactate be produced by the endurance trained subjects, but it will also be more efficiently cleared and re-metabolised. This greater ability to clear and re-use La^- could help to explain why $\dot{V}_E$ did not vary as much as $[La^-]$ between trained and untrained subjects, in spite of any possible reduction in the CO_2 sensitivity of the chemoreceptors.

Increases in plasma $[K^+]$ have been shown to increase carotid body discharge in cats (Linton and Band, 1985; Band and Linton, 1989), with consequent increases in $\dot{V}_E$. The type III and IV nerve fibres are also thought to have a major role in contraction induced changes in $\dot{V}_E$ (McCloskey and Mitchell, 1972; Tibes, 1977) and La^-, pH and K^+ are all potential stimuli to the associated metabolic receptors (Tibes et al., 1977). However, during the recovery from exercise, the time course of $[K^+]$ change lacked a very fast (phase 1) component (Paterson et al., 1989), suggesting that K^+ does not mediate $\dot{V}_E$ via neural pathways but via direct stimulate the carotid chemoreceptors. When integrated with the effect of La^- on $\dot{V}_E$, this would also help to explain these experimental observations.

Along with Tibes et al. (1977), other investigators including Band et al. (1982), Conway et al. (1988), Newstead, (1988) and Paterson et al. (1989) have also reported a close correlation between changes in plasma [K^+] and $\dot{V}_E$ during exercise. Furthermore, Tibes et al. (1974) observed a reduction in hyperkalemia following constant load exercise in endurance trained men. On this basis, the observation that the K^+ response to IW also showed a shift to the right in the endurance trained subjects is not surprising. Kjeldsen et al. (1986) found that endurance training in rats resulted in an increase in the concentration of Na-K pumps, while Everts et al. (1988) noted a more pronounced activation of Na-K pumps in type I compared with type II fibres of rats. Similarly, Klitgaard and Clausen (1989) found a greater concentration of Na-K pumps in biopsies of vastus lateralis muscle of trained men compared with untrained men. When considered along with the observed increase in numbers of type I fibres following endurance training in rats (Green et al., 1984) and humans (Baumann et al., 1987), the possibility that pump concentration in type I fibres is higher than in type II fibres offers an attractive explanation for the observed responses in this experiment.

The slopes of the regression equations for the endurance trained group all show that a greater change in $\dot{V}_E$ is elicited for any given change in [K^+], [La^-] or pH, when compared with the untrained group (Table 3.2). Although responses for $\dot{V}_E$, plasma [K^+], and blood pH and [La^-] were all reduced relative to absolute work load in the endurance trained subjects, the $\dot{V}_E$ response underwent the least change. So in spite of the attenuation in the ventilatory response, the results would also seem to suggest a greater sensitivity of the ventilatory control mechanisms to K^+, La^- and pH changes in the endurance trained subjects.

In terms of the relationship between $\dot{V}_E$ and [K^+], these results are also supported by the observations of Newstead (1988). In 6 renal transplant recipients, the mean

slope coefficient for the relationship between $\dot{V}_E$ and $[K^+]$ was 34.7. When considered with the slope coefficient for healthy untrained subjects (67.55) and endurance trained subjects (84.85), a trend of increasing slope coefficient with increasing fitness is evident.

The $\dot{V}O_2max$ and threshold scores (both absolute and relative) of the endurance trained subjects were significantly greater than those of the untrained subjects (Table 3.3). It is well accepted that the delay in the thresholds relative to $\dot{V}O_2max$, observed in endurance trained subjects, indicates that the metabolic response to submaximal exercise and exercise at $\dot{V}O_2max$ are at least partially dependent on different physiological processes (Coyle et al., 1983; Gaesser et al., 1984; Gaesser and Poole, 1988; Hurley et al., 1984; Mahon and Vaccaro, 1989; Poole et al., 1986). Adaptations within the muscles of endurance trained subjects which could lead to such a result include increased concentration of mitochondrial enzymes (Holloszy and Coyle, 1984), increased size and number of mitochondria (Hoppeler et al., 1973), enhanced oxidation of fats (Holloszy, 1973) and the associated inhibition of glycolysis (Rennie et al., 1976), transition of type IIb to IIa as well as II to I fibres (Baumann et al., 1987) and increases in capillary density (Andersen and Henriksson, 1977).

One of the major misgivings with the anaerobic threshold hypothesis is the reported ability to dissociate the VT_1 from the LT_1. Simon et al. (1986) found that VT_1 and LT_1 were coincident only in trained subjects, the LT_1 being significantly higher than VT_1 in untrained subjects. In the present study, the thresholds were coincident in both groups. A possible explanation for the lack of coincidence found by Simon et al. (1983) lies in the relative rate of ventilatory and lactate kinetics and the site of blood sampling. Whipp and Wasserman (1972) found that steady state in $\dot{V}O_2$ is achieved only after up to three minutes of exercise at work loads below that corresponding to

VT_1, and is delayed beyond three minutes at work above the threshold. Casaburi et al. (1987a) observed that blood La^- and $\dot{V}_E$ showed the closest affinity to $\dot{V}O_2$ drift and that the time taken to attain steady state ventilation is longer in untrained subjects, the pattern of its increase being most closely linked to increases in arterial blood [La^-]. Added to this, when venous blood samples are taken, the sampled blood [La^-] is modified by the effect of lactate metabolism in resting muscle (Poortmans, Bossche and Le Clercq, 1979; Yeh et al., 1983). Once steady state has been reached, the difference between arterial and venous [La^-] is small, but during IW, increases in venous blood [La^-] lag behind those in arterial blood [La^-]. So during a fast IW test (Simon et al. used an increment of 30W every 2 minutes), the slower kinetics of untrained subjects increases the likelihood that venous sampling will cause dissociation between the VT_1 and the LT_1, the LT_1 being overestimated relative to VT_1.

The possibility of a 'potassium threshold' has been raised by Gleim et al. (1989), who found similarity between the point of inflection of lactate and potassium responses during IW tests. In the present study, most commonly there was an initial rise in the plasma [K^+] at the onset of exercise, which was then followed by a further more gradual increase. However, the response pattern in two of the untrained and four of the endurance trained subjects exhibited a temporary plateau in plasma [K^+] after the initial increase, which preceded the eventual progressive rise. In these cases, there was a clear inflection point between the plateau phase and the beginning of the progressive rise (Figure 3.4), but there was no correlation between the inflection point for potassium response and those in lactate or ventilatory responses.

The delay in the activation of the Na-K pump at the onset of exercise (Vollestad and Clausen, 1989) might explain the initial increase in plasma [K^+]. Once the pump has been activated by the increase in extracellular [K^+] (and intracellular [Na^+]), it can

balance the rate of efflux of K^+ from the exercising muscles associated with low intensity work loads (Clausen et al., 1987), so plasma [K^+] would plateau. Beyond a certain intensity, further increases in K^+ efflux associated with increases in exercise intensity, are not matched by increases in Na-K pump activity, presumably because the intracellular [Na^+] does not reach the level required for complete activation of all the available Na^+-K^+ ATPase (Clausen et al., 1987). This results in a progressive accumulation of K^+ in the plasma above a threshold work load.

The view of Cunningham (1987) that ventilation is mediated by a number of inputs, is supported here. The significance of K^+ in ventilatory control is suggested in its close association with $\dot{V}_E$. However, the stronger association between $\dot{V}_E$ and La^-, also reflected in the coincidence of VT_1 and LT_1, suggests that changes in La^- may be of primary importance in regulating ventilatory change during exercise.

CHAPTER 4

PHYSIOLOGICAL RESPONSES TO PROLONGED EXERCISE IN TRAINED MEN

Introduction

Both lactate and ventilatory threshold indices have been shown to correlate well with endurance performance. This has been most commonly observed in running events, ranging from two miles to marathon distance (Table 1.2).

Trained marathon runners can maintain a pace requiring 75% of $\dot{V}O_2max$ for the duration of the event (Costill and Fox, 1969). The threshold measures which represent the rapid increase in blood lactate accumulation and the onset of hyperventilation with respect to $\dot{V}CO_2$ (IAT, OBLA and VT_2), occur at approximately this relative intensity of exercise and so should most accurately predict performance.

Closely associated with the ability of the thresholds to predict endurance performance is the assertion by some investigators that the thresholds occur at maximum steady state blood lactate concentration and/or ventilation. Fohrenbach, Mader and Hollman, (1987) found that lactate reached steady state at around 3mM during a marathon, which compares favourably with the results of Stegmann and Kindermann (1982) who claimed that IAT defined the work load for maximum lactate steady state. Ribeiro et al., (1986) and Rusko et al., (1986) found similar relationships for their definitions of AnT (both being the point of rapid rise in blood lactate during an IW test), while Reybrouk et al., (1986) reported that VTlong was the most accurate ventilatory measure of maximum steady state. Earlier, Kindermann et al., (1979) had suggested the higher value of 4mM to define

maximum steady state lactate concentration while LaFontaine et al., (1981) defined their maximum steady state lactate concentration at 2.2mM.

Casaburi et al., (1987b) suggest that lactate is the primary factor influencing steady state ventilation. A close relationship between changes in plasma potassium concentration and ventilation during CLW has also been reported (Band et al., 1982; Linton et al., 1984; Conway et al., 1988; Paterson et al., 1989). Vollestad and Sejersted (1989) noted a steady state in arterial plasma potassium during CLW requiring up to 85% $\dot{V}O_2max$, with the steady state being progressively delayed at higher work loads. Ventilation was not reported for these experiments.

During the IW study reported in this thesis, the changes in $\dot{V}_E$ were strongly associated to changes in $[K^+]$, $[La^-]$ and pH. Whether these associations are maintained during maximal self-paced exercise bouts is unknown. Furthermore, there is a lack of consistency in the reported abilities of the various thresholds to predict endurance performance. The purpose of this study therefore was to examine:

(1) the ventilatory response during prolonged, self-paced exercise, and compare it with those of blood lactate, blood pH and plasma potassium concentration,

(2) the accuracy of the various threshold indices (LT_1, IAT, VT_1, VT_2) in predicting endurance performance as measured by work output and average $\dot{V}O_2$ during one hour of continuous self-paced exercise.

Methods

The group of eight endurance trained males (Table 2.1) each performed three separate bouts of exercise on the bicycle ergometer, with at least four days between each test. The first was a fast incremental exercise test as described in the previous chapter. The second was also an incremental test but on this occasion, after the

initial warm up period at 30W, work load was increased firstly to 120W and then by 30W every third minute until volitional fatigue. Blood samples and expired gases were collected during exercise as in the first incremental test. At the conclusion of exercise, subjects remained seated while further blood samples were taken at 1, 2, 3, 5, 7 and 10 minutes post-exercise.

The individual anaerobic threshold (IAT) was established from the blood lactate data, according to the method of Stegmann et al. (1981). Individual data points for exercise and recovery were plotted as a continuous function against time. The exercise portion of the curve was fitted to a single exponential equation for all points beyond the LT_1, while the recovery curve was fitted to a single third order polynomial. These equations have been found to accurately describe lactate kinetics during the two phases of the test (McLellan and Jacobs, 1989). The time during recovery when blood lactate concentration equalled the value at the end of exercise was determined via interpolation of the recovery regression equation. From this point a straight line was drawn to form a tangent to the exercise lactate curve. The point of intersection of the tangent line with the exercise curve is defined as the IAT (Stegmann et al., 1981).

In the third exercise bout, subjects were required to perform as much work as they could in a self-paced, one hour trial. To ensure that exercise intensity remained 'steady' and to avoid a sprint towards the end of the bout, subjects were told that the test was a simulated 40km. time trial. From prior experience, subjects knew that such a trial would take approximately one hour to complete but no feedback was given during the test as to what 'distance' had been covered. Blood samples were collected at the following times: rest, 2.5, 5, 7.5, 10, 15, 20, 30, 40, 50 and 60 minutes, and later analysed using the methods previously outlined. Expired gases were collected continuously and analysed as previously described. Haemoglobin concentration was

determined to indicate whether haemoconcentration had significantly affected results.

Statistics

An analysis of variance was performed on group results to assess first whether the concentrations of K^+, La^- or pH were different from those at rest, and secondly whether any of the six variables (power, $\dot{V}_E$, $\dot{V}O_2$, K^+, La^- and pH) changed with respect to time throughout the 60 minute self-paced trial. Fisher's procedure was then used to locate specific differences.

For further statistical analyses, data collected during this trial were separated into two phases. The first 20 minutes formed the early phase, where the response to exercise was progressively changing, while the late phase included the data collected from the 20th minute to the 50th, where responses were more steady. Data at 60 minutes were not used in these subsequent analyses due to increased work rates in the last few minutes of exercise.

The correlation between the changes in power, $\dot{V}_E$, $\dot{V}O_2$, $[La^-]$, $[K^+]$, and pH during both the early and late phases were assessed. As well as the analysis of variance mentioned previously, where any change in variables for the entire trial duration was assessed, linear regression equations were generated to test for steady state in individual responses between minutes 20 and 50. In this case, steady state was accepted only if the slope of the linear regression equation did not vary significantly from zero. A t-test was used to assess this.

A comparison of the LT_1 with the VT_1 has been conducted for this group in the previous section. Student's t-test was used to compare the IAT assessed from the slow IW test, with the VT_2 assessed from the fast IW test. Correlative methods were

used to assess whether the threshold variables accurately predicted performance, as indicated by total work done. All results are expressed as mean ± 1 SD.

Results

The mean PO_2 and oxygen saturation values for the fast IW tests were reported in the previous section. The mean PO_2 values for the slow IW tests and the one hour self-paced trial were 68.7 ± 9.6 mmHg and 67.0 ± 8.9 mmHg respectively. Corresponding oxygen saturation values were 94.8 ± 3.1% and 93.9 ± 2.9% respectively. Although these results suggest incomplete arterialisation, the longer duration of each work load in the slow incremental test, and the continuous nature of the self-paced trial, allow for better equilibration of ion concentrations between arterial and venous blood since both production and metabolism of lactate is relatively stable (Ahlborg et al., 1975). Under these conditions, venous samples provide a good representation of arterial blood.

Mean increases in haemoglobin concentration over the duration of the one hour self-paced trial amounted to 9.9 ± 3.1% of the resting values, not large enough to alter the significance of other findings.

Figure 4.1 shows the individual response patterns of a typical subject for each variable measured during the self-paced trial. The mean group responses are shown in Figure 4.2. During the self-paced trial, there was a trend towards progressive increases in $\dot{V}O_2$ and plasma $[K^+]$, which continued for the first 5 minutes of exercise. Similarly, there were trends of increasing power output for the first 7.5 minutes and in $\dot{V}_E$ and blood $[La^-]$ for the first 10 minutes. Blood pH decreased for the first 10 minutes, in line with the increases in blood $[La^-]$. All results then tended towards resting values for the duration of the test, excluding the final sample where

subjects sensed they were nearing the end of the trial and subsequently increased their work rate.

The initial values included in the analyses for power, $\dot{V}_E$ and $\dot{V}O_2$ were those taken after 2.5 minutes of exercise, not those taken at rest, as was the case for $[K^+]$, $[La^-]$ and pH. Analysis of variance revealed significant increases in $[K^+]$, $[La^-]$ and pH during exercise relative to those at rest. For $[K^+]$ and $[La^-]$, all exercise samples were higher ($p < 0.05$) than those at rest. A similar pattern was evident for pH, all samples excluding the final two values, being significantly lower ($p < 0.05$) than those at rest.

There was variation in the power output within the 60 minute trial, that recorded at 30, 40 and 50 minutes being significantly lower than other values. The $\dot{V}O_2$ values at 5, 7.5, 10, 15 and 60 minutes were all significantly higher than those at 2.5 minutes, while $\dot{V}O_2$ at 60 minutes was significantly higher than that at 50 minutes, reflecting the increase in metabolic rate towards the end of the trial. $\dot{V}_E$ showed no significant variation during exercise and none of the parameters showed any variation during the steady phase of the test, between 20 and 50 minutes.

There were a number of significant correlations in the response patterns during both phases of the self-paced trial (Tables 4.1 and 4.2). The strongest correlations were between $\dot{V}_E$ and $[La^-]$ ($r = 0.738$ in phase 1 and $r = 0.756$ in phase 2). However, many correlations attained statistical significance in spite of accounting for only a relatively small degree of the variance in $\dot{V}_E$. For example, the correlation between $\dot{V}_E$ and $[K^+]$ reached statistical significance ($p < 0.05$) for both phases of the trial with r values of 0.371 and 0.373. This means that plasma $[K^+]$ could account for only 14% of the variance in $\dot{V}_E$.

When linear regression equations were generated for individual responses between

20 and 50 minutes, the only parameter whose equation had a slope which did not vary significantly from zero (ie. achieved steady state) in all eight subjects was $[K^+]$. Four of the eight subjects reached a steady state $[La^-]$, three of whom also reached a steady state $\dot{V}O_2$. One other subject also reached a steady state $\dot{V}_E$. No individual subjects reached a steady state in power output or pH.

The mean values of the correlation coefficients associated with the regression equations used to approximate lactate kinetics during exercise and recovery in the three minute exercise test were 0.98 ± 0.01 and 0.97 ± 0.01 respectively.

No IAT was calculable in two of the eight subjects. In these instances, lactate concentration decreased immediately after the cessation of exercise, thus not allowing for completion of the detection method. Figure 4.3A shows an example of a typical lactate response against time, in an instance where the IAT was calculable. Figure 4.3B shows one of the two cases where it was not calculable.

The mean absolute values for IAT and VT_2 were 51.91 ± 4.58 ml/kg.min and 51.43 ± 3.42 ml/kg.min respectively while the values expressed relative to $\dot{V}O_2max$ were 82.31 ± 8.44% and 79.26 ± 4.74% (Table 4.3). Although the mean values of IAT and VT_2 appear to be closely associated, there was in fact no significance in this relationship. This is due to differences in the rank order of the values obtained by the subjects for the two thresholds.

None of the threshold variables could accurately predict total work done, in either absolute terms or relative to body weight. Nor could they predict mean $\dot{V}O_2$ during the trial (Table 4.4). The mean $\dot{V}O_2$ at IAT and VT_2 was similar to the mean $\dot{V}O_2$ for the trial (54.01 ± 3.28), but the lack of correlation again appears to be due to differences in the rank order of the different parameters. Greater subject numbers may have provided significant correlations for some of these comparisons.

	$[La^-]$	$[K^+]$	pH	$\dot{V}_E$	$\dot{V}O_2$
POWER	.223	.307*	-.075	.244	.322*
$[La^-]$		.539*	-.659*	.738*	.276
$[K^+]$			-.564*	.371*	.521*
pH				-.480*	-.481*
$\dot{V}_E$					.165

Table 4.1: Correlation coefficients for individual response patterns for the first twenty minutes of the self paced exercise test. * significant ($p < 0.05$).

	$[La^-]$	$[K^+]$	pH	$\dot{V}_E$	$\dot{V}O_2$
POWER	.008	-.449*	-.081	-.159	.507*
$[La^-]$		.463*	-.703*	.756*	.210
$[K^+]$			-.506*	.373*	-.125
pH				-.628*	-.318
$\dot{V}_E$					.041

Table 4.2: Correlation coefficients for individual response patterns for the 20th to 50th minutes of the self paced exercise bout. * significant ($p < 0.05$).

	ml/kg.min	% $\dot{V}O_2$max
$\dot{V}O_2$max	64.29 ± 4.01	
LT_1	38.99 ± 3.59	60.25 ± 5.28
VT_1	38.26 ± 3.40	59.62 ± 5.01
IAT	51.91 ± 4.58	82.31 ± 8.44
VT_2	51.43 ± 3.42	79.26 ± 4.74

Table 4.3: $\dot{V}O_2$max and threshold values expressed in absolute (ml/kg.min) and relative (% $\dot{V}O_2$max) terms. LT_1 coincident with VT_1 ($p < 0.05$), IAT not coincident with VT_2.

		WORK	WORK/kg	$\bar{x}\dot{V}O_2$
LT_1	(ml/kg.min)	.24	.507	.144
	(% $\dot{V}O_2$max)	.012	.191	-.024
VT_1	(ml/kg.min)	-.432	-.114	-.005
	(% $\dot{V}O_2$max)	-.614	-.499	-.403
IAT	(ml/kg.min)	.22	.181	.003
	(% $\dot{V}O_2$max)	.098	-.199	-.326
VT_2	(ml/kg.min)	.037	-.028	.096
	(% $\dot{V}O_2$max)	-.345	.396	-.299

Table 4.4: Correlation coefficients for the relationship between threshold values and work parameters from the 60 minute self paced exercise bout. No significant correlations.

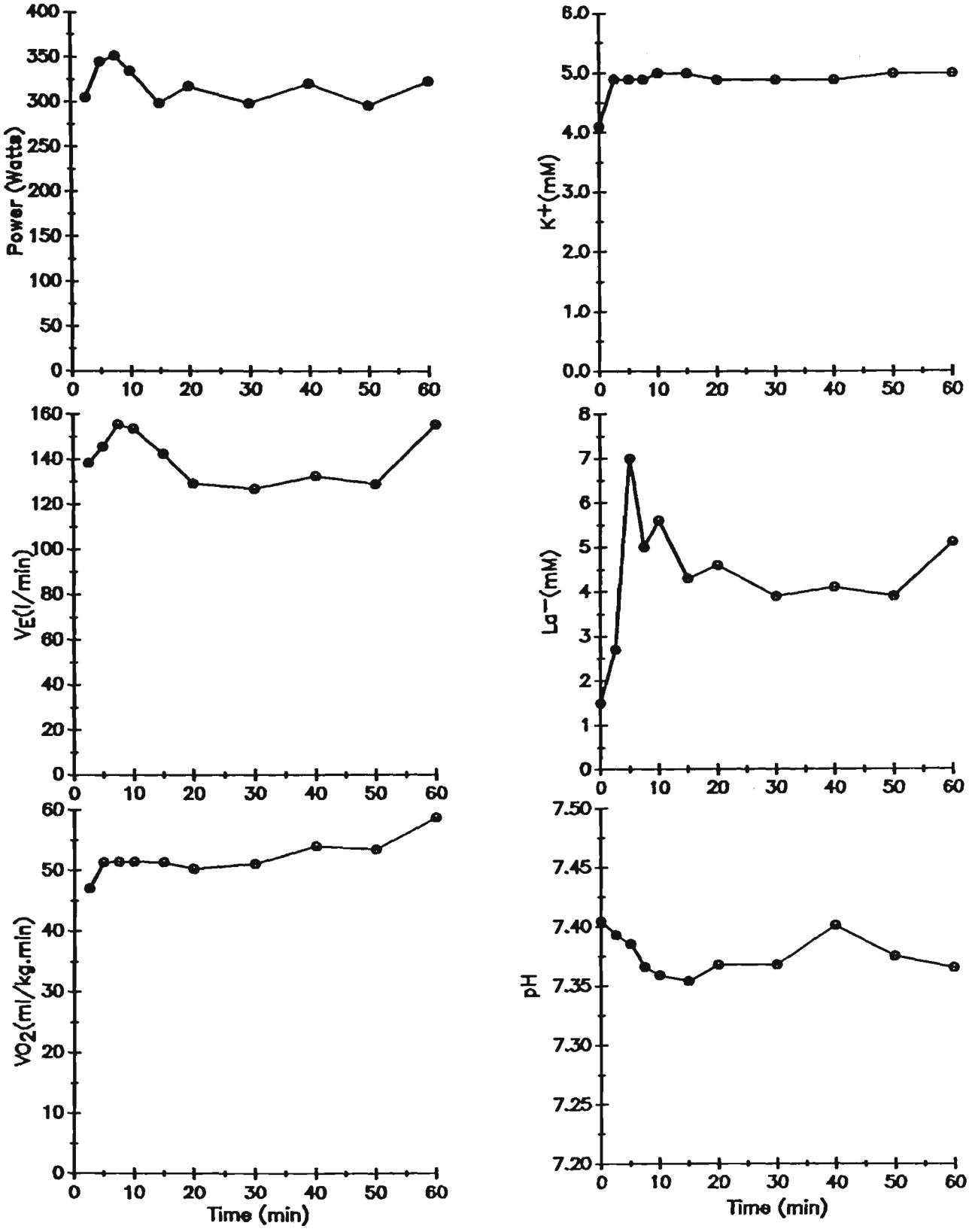

Figure 4.1: Typical individual response to self-paced one hour trial. Power output, $\dot{V}_E$, $\dot{V}O_2$, $[K^+]$, $[La^-]$ and pH vs. time.

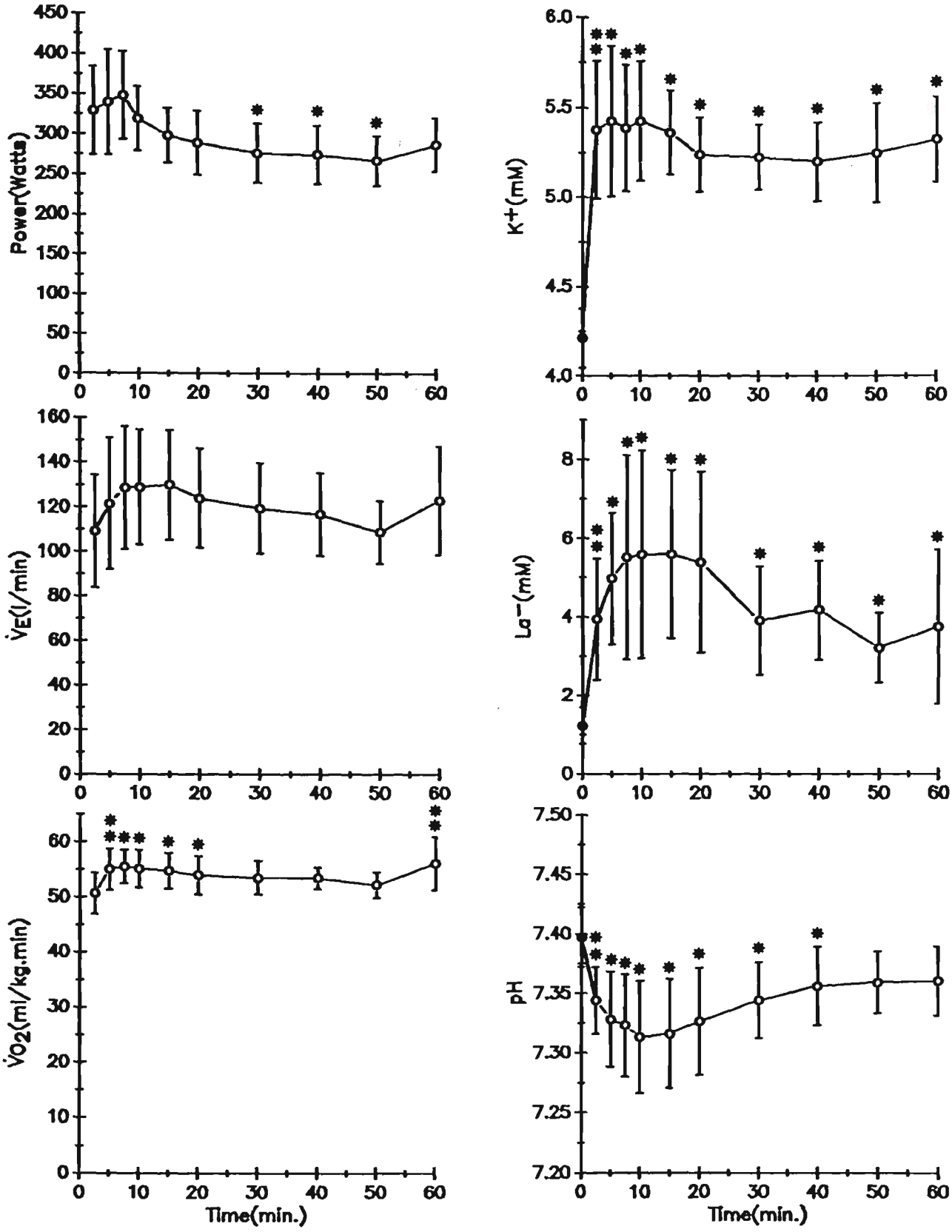

Figure 4.2: Group response to self-paced one hour trial. Power output, $\dot{V}_E$, $\dot{V}O_2$, $[K^+]$, $[La^-]$ and pH vs. time. Values are mean ± 1 SD. * significantly different from initial measurement, ** significantly different from previous measurement ($p < 0.05$).

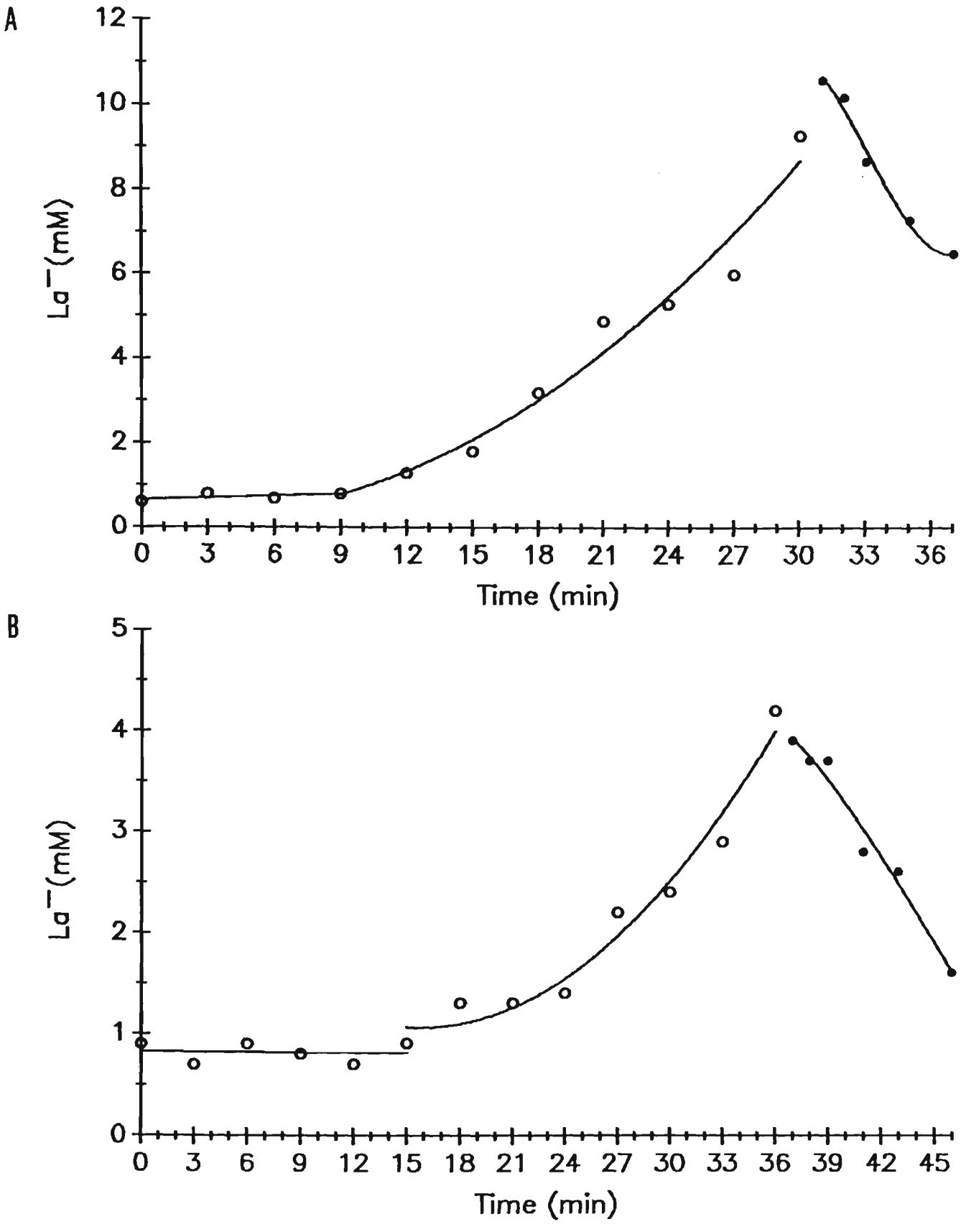

Figure 4.3: Typical response to slow incremental work test for IAT determination. Blood lactate concentration vs. time. A) IAT calculable, B) IAT not calculable. o exercise, ● recovery

Discussion

Most prolonged exercise trials conducted in laboratories to assess metabolic and respiratory responses employ protocols using pre-selected work loads. While the use of this type of exercise protocol provides important information, it is not valid to generalise results gained from such a test to actual performance, where work rate and thus physiological response, is not so stringently regulated. For this reason, a self-paced trial was preferred in this study. That none of the subjects maintained a steady power output over the duration of the trial vindicates the choice of protocol on these grounds.

Only one subject reached a steady state $\dot{V}_E$ between the 20th and 50th minute of exercise. Generally $\dot{V}_E$ showed a progressive increase for up to 15 minutes before undergoing a steady decline, which continued up to the 50th minute of exercise. That mean values were not different between the 20th and 50th minute, even though seven individuals showed significant decline, is a result of the variability of the responses (Figure 4.2). However, power output was showing a decline after only 7.5 minutes of exercise, indicating that subjects may have begun exercise at an intensity above their maximal steady state $\dot{V}_E$ (Whipp and Wasserman, 1972).

Four mM has been suggested as defining the maximal steady state [La^-] (Kindermann et al., 1979). Stegmann et al. (1982) compared prolonged exercise at the IAT with exercise at 4mM and found that maximum steady state [La^-] corresponded better with IAT. They suggested that the higher the aerobic power of an athlete, the more the maximum steady state [La^-] would be overestimated if determined at 4mM. From the 20th to the 50th minute of the self-paced trial, four of the subjects reached a statistical steady state blood [La^-]. Those four subjects had mean blood [La^-] of between 1.8 and 4.1 mM, the corresponding mean $\dot{V}O_2$ values

during this period being higher for the subjects who's lactate values were lowest. This supports the findings of Stegmann et al. (1982).

The mean $\dot{V}O_2$ maintained by all subjects throughout the trial was 54.01 $\pm$ 3.54 ml/kg.min or 84% of $\dot{V}O_2$max. Hamilton, Beltz, Montain and Coyle (1989) performed a study with elite cyclists involving a one hour trial and the mean $\dot{V}O_2$ their subjects maintained was in the range of 85-95% $\dot{V}O_2$max. Of the four subjects previously mentioned who attained a statistical steady state [La^-], three also achieved a steady state $\dot{V}O_2$ between the 20th and 50th minute. Lactate may be the primary regulator of $\dot{V}O_2$ drift during heavy exercise (Casaburi et al., 1987a). The observation that those subjects whose [La^-] showed a slow negative drift during the 20th and 50th minutes also showed a slow negative drift in $\dot{V}O_2$, and that those whose [La^-] was steady also tended to have steady $\dot{V}O_2$ values, concurs with the results of Casaburi et al. (1987a).

All subjects attained a steady state in plasma [K^+] during the 20th to 50th minute of exercise. Steady state plasma [K^+] has previously been reported at 85% $\dot{V}O_2$max (Vollestad and Sejersted, 1989). The fact that this occurred in the present study in spite of a relative lack of steady state response in the other variables, suggests that plasma [K^+] may not exert as much influence over $\dot{V}_E$ as it appeared to do in the fast IW test.

The low correlation values between plasma [K^+] and $\dot{V}_E$ for both phases of the self-paced trial would also suggest this (Tables 4.1 and 4.2). These results were surprising given the previous findings of Band et al. (1982), Conway et al. (1988), Newstead (1988) and Paterson et al. (1990), who all observed close temporal relationships between [K^+] and $\dot{V}_E$ during exercise and recovery. Newstead (1988) reported correlation coefficients within the range of 0.932-0.987. There are however, differences between those studies and the present one which may lead to this

discrepancy. First, the present study employed endurance trained athletes, whose potassium flux and ventilatory response vary significantly from one another. Secondly, although the changes in plasma [K^+] during exercise observed during this study were often comparable to those reported in previous studies, the work loads and durations involved in the present trial were both considerably greater, as were the mean $\dot{V}_E$ values.

The best of the correlations was between La^- and $\dot{V}_E$. Koyal et al. (1976) suggested that changes in blood [La^-] were responsible for the increased ventilation associated with high intensity exercise. Other researchers have found relationships between body temperature (Hagberg, Mullin and Nagle, 1978), catecholamines (Butland, Pang and Geddes, 1983) and ventilatory response. Casaburi et al. (1987b) concluded that the mediation of the reduced ventilatory response to exercise above the VT_1 after endurance training was primarily due to the lower blood [La^-].

Individually, the plasma [K^+] and blood [La^-] can account for only 14% and 55-57% of the variance in $\dot{V}_E$ during the self-paced trial respectively. If and how they interact is not certain, but since K^+, La^- and pH (Tibes et al., 1977) can all mediate change in ventilation via group III and IV afferents (McCloskey and Mitchell, 1972; Tibes, 1977), and since both H^+ (Yamamoto and Edwards, 1960; Wasserman et al., 1975) and K^+ (Linton and Band, 1985; Band and Linton, 1989) stimulate the carotid chemoreceptors, interaction is at least possible.

Further, Kilburn (1966) suggested that K^+ was exchanged for H^+ during exercise-induced acidosis. Tibes et al. (1974) studied the relationship between plasma [K^+], [H^+] and [La^-] and concluded that K^+ efflux from the muscle cell, dependent on ionic transport through the cell membrane, was modified by [H^+].

However, Laurell and Pernow (1966) found that the rise in serum [K^+] at the onset of exercise and the fall after exercise, was more rapid than the changes in [La^-], pH and heart rate, although well correlated with them. Medbo and Sejersted (1988) showed that the $t_{1/2}$ for the rise in plasma [K^+] during exercise was around 25 seconds, far quicker than for the rise in blood [La^-]. If it is accepted that changes in blood [La^-] accurately reflect those in muscle [La^-] (Chwalbinska-Moneta et al., 1989), these results would suggest that K^+ efflux is not primarily dependent on H^+.

Heigenhauser et al. (1990) suggest that the link may be a result of mechanisms involved in ionic homeostasis, large increases in intracellular [H^+] being accounted for by decreases in [K^+] and increases in [La^-] and PCO_2. In venous plasma, Heigenhauser et al. (1990) suggest that increases in PCO_2, and [La^-] are balanced by increases in [H^+], [K^+] and [Na^+]. Hence, even though the metabolic changes which produce the K^+ and La^- may be independent, the appearance of the two ions in the blood and their effects on ventilation would appear to be inter-related. Whether these effects are additive, or whether they augment or interfere with one another is uncertain. Paterson et al. (1990) suggested that stimulation of $\dot{V}_E$ by K^+ appears to be mediated via its effect on the peripheral chemoreceptors, since no very fast (phase 1) component of the time course in plasma [K^+] change is evident at the cessation of exercise. This would seen to be supported by the $t_{1/2}$ for K^+ accumulation in the blood, previously mentioned (Medbo and Sejersted, 1988). Although this may be the case, it does not preclude the possibility of this mechanism being active during prolonged steady state exercise.

Coyle et al. (1983; 1988) report that endurance performance is determined by maximal steady state $\dot{V}O_2$ and that the $\dot{V}O_2$ maintained during competition is related to that at which La^- begins to accumulate in the blood. Cycling performance varied considerably in two groups of subjects, both of whom had similar high

$\dot{V}O_2max$ scores, depending largely on a positive relationship ($r = 0.90$) with % $\dot{V}O_2max$ at LT_1 (Coyle et al., 1988).

Other researchers have also found good correlation between the LT_1/VT_1 and performance (Farrell et al.,1979; Londeree and Ames, 1975; Tanaka and Matsuura, 1984; Tanaka et al., 194; 1986). Different threshold indicies have also been suggested to accurately predict performance, including the IAT (Stegmann et al., 1982), the VT_{long} (Reybrouk et al., 1983), and the OBLA or work load/$\dot{V}O_2$ representing 4mM [La^-] (Heck et al., 1985; Kindermann et al., 1979; Sjodin and Jacobs, 1981). The finding in the present study (Table 4.4) that none of the threshold indicies measured could accurately predict performance, is in conflict with previous results.

Protocol is of vital importance to the ability of threshold parameters measured during an IW test to predict performance (Heck et al., 1985). Although the above list of threshold parameters also represents a considerable number of different protocols, they all had successful prediction outcomes. The self-paced trial protocol chosen in the current experiment to assess the predictive capacities of the threshold indicies, represents a departure from previous bicycle ergometer protocols, which commonly measured endurance time at a set work load. Nevertheless, strong correlations between threshold indicies and running performance have been reported (Farrell et al., 1979; LaFontaine et al,. 1981; Tanaka and Matsuura, 1984; Tanaka et al., 1984; 1986), in events which were also self-paced.

Mognoni, Sirtori, Lorenzelli and Ceretelli (1990) found that performance could not be predicted from OBLA measured via the results of an incremental work test, while Denis, Dormois, Castells et al. (1988) concluded that IW tests could not evaluate endurance training effects. In the present study, it is possible that small subject numbers may have reduced the likelihood of statistically significant correlations.

However, a number of trends from the above studies are apparent and are verified by the results of the present study. First, there exists a work load in excess of the LT_1/VT_1 which defines an individual's maximal cardiorespiratory and metabolic steady state of exercise (McLellan and Gass, 1989). Secondly, this maximal steady state level is enhanced by endurance training, relative to both absolute $\dot{V}O_2$ and % VO_2max (Hurley et al., 1984) and thirdly, those subjects with the highest $\dot{V}O_2/La^-$ ratio are able to maintain a higher level of work output for a longer period of time.

The physiological adaptations to exercise that explain these observations include an increase in the concentration of mitochondrial and respiratory chain enzymes (Holloszy and Coyle, 1984), an increase in the size and number of mitochondria (Hoppeler et al., 1973), an increased capacity to oxidise fats (Holloszy, 1973) with a resultant inhibition of glycolysis (Rennie et al., 1976), an increased oxidative capacity of all muscle fibre types (Baldwin et al., 1983), a possible structural change of fibre type from I to II, as well as from IIb to IIa (Baumann et al., 1987), an increase in capillary density (Andersen and Henriksson, 1977) and an enhanced ability to oxidise lactate (Donovan and Brooks, 1983; Brooks, 1986a; b; c). The combined effect of these adaptations is that, relative to $\%\dot{V}O_2max$, oxygen extraction and utilisation by active skeletal muscle is enhanced and blood $[La^-]$ is lower.

It would appear that the choice of the threshold index, the threshold definition used, the protocol during both the IW test and the performance trial and the fitness and motivation of the subjects, can all affect the accuracy of the ability of the threshold indices to predict performance, thus clouding the existence or otherwise of any direct physiological relationship. However, where strong correlation is reported between threshold indices measured during IW tests and endurance performance, causality cannot necessarily be assumed from coincidence.

CHAPTER 5

OVERVIEW AND CONCLUSIONS

The anaerobic threshold hypothesis (Wasserman et al., 1973) suggests a causal link between specific metabolic changes in active skeletal muscle and changes in gas exchange and ventilation. By buffering the H^+ associated with the La^- produced during anaerobic metabolism, there is an increase in CO_2 production which can be measured non-invasively as an accurate reflection of muscle metabolism. Potassium efflux from contracting skeletal muscle cells is only partly balanced by Na-K pump activity, so increases with exercise intensity. Plasma [K+] has also been suggetsed as a mediator of ventilation (Paterson et al., 1990). It was the aim of this research project to examine the influence La^- and K^+ on the ventilatory response to both incremental and prolonged exercise in trained and untrained men, and to assess whether or not the response to incremental exercise can predict performance in prolonged exercise.

Physiological response to incremental exercise in trained and untrained men.

Ventilatory control is governed by both neural and humoral mechanisms (Dejours, 1963). Among the numerous inputs, the control of exercise hyperpnoea is partially dependent on the stimulation of the carotid chemoreceptors by blood-borne stimuli and on peripheral neurogenic drive from the exercising muscles transmitted via group III and IV afferents. Increases in blood PCO_2 and [H^+] (Yamamoto and Edwards, 1960) and in plasma [K^+] (Linton and Band, 1985) can all increase the firing frequency of the chemoreceptors, while La^-, H^+ and K^+ efflux from active skeletal muscle is sensed by metaboloreceptors associated with the group III and IV afferents. However, whether the metaboloreceptors are active in mediating the very

fast (phase 1) component of ventilatory response during the start of and the recovery from exercise is uncertain (Paterson et al., 1990).

The coincidence between ventilatory and lactate responses during incremental work has been questioned by many researchers and has been dissociated in a number of studies. Dissociation excludes the possibility of a direct causal relationship between V_E and La^-, whereas coincidence does not necessarily prove it.

This first study reported the relationships between K^+, La^-, pH and $\dot{V}_E$ during an incremental work test in both endurance trained and untrained subjects. The degree of coincidence between the VT_1 and the LT_1 was assessed in both groups. Good correlations were observed between $\dot{V}_E$ and both $[K^+]$ and $[La^-]$ (Table 3.1) in both groups of subjects, the stronger association being between $[La^-]$ and $\dot{V}_E$. There was also strong correlation between $[K^+]$ and $[La^-]$, although this would appear to be an indirect relationship via their mutual regulation of $\dot{V}_E$, rather than a direct one. There was a rightward shift in $\dot{V}_E$, $[K^+]$, $[La^-]$ and pH relative to work load in the trained compared with the untrained subjects (Figure 3.1). Attenuation in $\dot{V}_E$ was significant only at higher work loads, as has been previously noted (Koyal et al., 1967), while significantly higher $[La^-]$ and lower pH values were observed for untrained subjects at much lower work loads. The attenuation in plasma $[K^+]$ in the trained group followed a similar pattern to that of $\dot{V}_E$.

The endurance trained subjects registered significantly higher scores for $\dot{V}O_2max$ and for all threshold indices, relative to both absolute $\dot{V}O_2$ and $\%\dot{V}O_2max$. VT_1 was coincident with LT_1 in both groups (Table 3.3).

The results concurred with the anaerobic threshold theory in as much as it proposes a strong link between changes in blood $[La^-]$ and ventilation. The results also highlight the likelihood that there are numerous stimuli having input into regulation

of ventilation (Cunningham, 1987), of which K^+ and La^- seem to be of considerable importance. That both K^+ and La^- seem to have important roles need not negate a causal link between [La^-] and $\dot{V}_E$.

Physiological responses to prolonged exercise in trained men.

Blood [La^-] is an important regulator of $\dot{V}_E$ during prolonged exercise (Casaburi et al., 1987b). Strong correlations have also been noted between increases in plasma [K^+] and $\dot{V}_E$ during constant load work (Paterson et al., 1990). It was one aim of this second study to examine whether the mechanisms of ventilatory control and their interactions noted during IW are also apparent during exercise of prolonged duration and relatively steady intensity.

Endurance performance is thought to be associated with a maximal steady state $\dot{V}O_2$ and metabolism (Coyle et al., 1988). That $\dot{V}O_2max$ lacks power in predicting endurance performance is well accepted (Farrell et al., 1979). That some submaximal work intensity should more accurately predict performance is also well accepted (McLellan and Gass, 1989). Most of the defined thresholds, in both lactate and ventilatory responses, have been shown to correlate well with some measure of performance. However, given the disparity of the threshold definitions, as well as the diversity of events for which they are said to be able to predict performance, no unequivocal evidence is available to suggest which, if any, of the threshold indices offers the best prediction outcome. A second aim of this study was to determine whether performance in a one hour self-paced trial could be accurately predicted by threshold indices (VT_1, VT_2, LT_1, IAT) measured in incremental work tests.

Correlations between $\dot{V}_E$ and [K^+], [La^-] and pH were not as strong during the self-paced trial as they were during incremental work, even though all were

statistically significant (Tables 4.1 and 4.2). Again, [La^-] correlated most strongly with $\dot{V}_E$, although the most interesting finding was the weakness of the correlation between [K^+] and $\dot{V}_E$, which was in contrast to previous findings (Newstead, 1988). This was highlighted by the fact that all eight subjects reached a statistical steady state plasma [K^+] during the second phase of the trial, while only one of the eight subjects attained a steady state $\dot{V}_E$ (Figure 4.2).

The performance of the endurance trained subjects in the one hour trial was similar to that of the elite cyclists reported by Hamilton et al. (1989); however, whereas the same group had recently found strong correlation between performance and LT_1 (Coyle et al., 1988) in well trained cyclists, no such correlation was observed in this study (Table 4.4). A similar finding was recently reported by Mognoni et al. (1990). The only conclusion that could be drawn from the performance study was that there exists an exercise intensity above VT_1/LT_1 which is enhanced by training and which represents the maximal steady state.

Conclusions

Based on the results of the studies comprising this thesis, the following conclusions can be drawn:

1) changes in ventilation during exercise are regulated by a number of inputs, La^- and K^+ both being important,

2) the LT_1 and the VT_1 may have a causal relationship even considering the role of K^+ in the regulation of ventilation,

3) threshold indices measured during incremental work tests did not have the ability to accurately predict endurance performance, represented by a one hour self-paced trial, in the subjects studied in the present investigation.

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APPENDIX 1.

A summary of the different terms used to denote changes in the ventilatory and lactate responses to incremental exercise, with their accompanying definitions and methods of assessment.

VENTILATORY RESPONSE

First Ventilatory Threshold

Anaerobic threshold

(Wasserman, Whipp, Koyal and Beaver, 1973)

-"the level of work or oxygen consumption just below that at which metabolic acidosis and the associated changes in gas exchange occur".

N = 85, 17-91 years of age, predominantly sedentary,
n = 61, bicycle ergometer (BE), power incremented by 15 watts each minute (15W/min) n = 24, BE, 25W/min.

Detected by "the work rate at which CO_2 production and minute ventilation deviate from linearity as compared with the rate of rise in oxygen consumption as work rate is incremented". Also used "the associated increase in R, and the decrease in the difference in O_2 tension between inspired and end-tidal values without a comparable change in end-tidal CO_2 (hyperventilation with respect to O_2)."

Aerobic threshold

(Skinner and McLellan, 1980)

-"initial rise in lactate and non-linear increases in $\dot{V}_E$ and $\dot{V}CO_2$" during progressive exercise from rest to $\dot{V}O_2$max. Review paper.

Ventilation threshold

(Jones and Ersham, 1982)

-"during exercise of increasing power, $\dot{V}_E$ increases linearly with $\dot{V}O_2$, but in most healthy subjects this straight line gives way to a curve of increasing $\dot{V}_E$ to $\dot{V}O_2$ at high levels of exercise. A line drawn through the initial points of this relationship permits the identification of a VO_2 at which V_E 'breaks away'". Review paper.

Ventilation threshold 1

(McLellan, 1985)

-"the first 'break' in the plot of $\dot{V}_E$ versus $\dot{V}O_2$" and "the first increase in $\dot{V}_E/\dot{V}O_2$ with no change in $\dot{V}_E/\dot{V}CO_2$".

N = 10 males, 20.5 $\pm$ 0.3 yr, BE, 30W/min, /3min, /5min to fatigue.

V-Slope

(Beaver, Wasserman and Whipp, 1986)

-"a transition in the relationship between the $\dot{V}CO_2$ and $\dot{V}O_2$, which is the underlying element in all methods of anaerobic threshold detection by gas exchange".

N = 10 males, 19-39 yr., BE, 15W/min to fatigue.

Second Ventilatory Threshold

Threshold of decompensated metabolic acidosis

(Reinhard, Muller and Schmulling, 1979)

-a "definite increase in $\dot{V}_E/\dot{V}CO_2$ after its minimum (during incremental exercise) determines approximately the work load level where a marked fall of capillary pH occurs".

N = 116, M + F, 20-65, BE, 100kpm/min (16 1/3 W/min).

Anaerobic threshold

(Skinner and McLellan, 1980)

-"the sharp rise in lactate and the 'breakaway' in $\dot{V}_E$" during progressive exercise from rest to $\dot{V}O_2$max. Review paper.

Respiratory compensation for metabolic acidosis

(Wasserman, Whipp and Davis, 1981)

After the period of isocapnic buffering, end-tidal CO_2 tension decreases, reflecting respiratory compensation for the metabolic acidosis of exercise. This respiratory compensation for the non-respiratory lactic acidosis is reflected by an increase in $\dot{V}_E/\dot{V}CO_2$ as well as by a further increase in $\dot{V}_E/\dot{V}O_2$. Review paper.

Respiratory compensation threshold

(Simon, Young, Gutin, Blood and Case, 1983)

-the "$\dot{V}O_2$ or work rate at which $\dot{V}_E$ increases disproportionately to $\dot{V}CO_2$ during IW". It "denotes the end of isocapnic buffering and the onset of hypocapnia".

N = 5, M, 30.2 ± 4.1, BE, 30W/2min at 60 rpm to exhaustion.

Ventilation threshold for long term exercise

(Reybrouck, Ghesquiere, Cattaert, Fagard and Amery, 1983)

-"the highest work rate at which V_E did not further increase after 20 minutes of exercise" during a 40 minute constant load exercise test.

N = 8, M ,20-53, inactive to well conditioned, BE.

Ventilation threshold 2

(McLellan, 1985)

-the second break in the plot of $\dot{V}_E$ versus $\dot{V}O_2$ "and an increase in the $\dot{V}_E/\dot{V}CO_2$". It is noted that "with longer power output durations, $\dot{V}_E$ increases out of proportion to $\dot{V}CO_2$ at VT_1 and a period of isocapnic buffering is not observed above V_{T1}". A "plot of $\ln\dot{V}_E/\dot{V}CO_2$ versus $\dot{V}O_2$ revealed, however, that an altered ventilatory response was observed at the same $\dot{V}O_2$ for all incremental test conditions".

N = 10, M, 20.5 ± 0.3 yr, BE, 30W/min, /3min, /5min to fatigue.

Respiratory compensation for metabolic acidosis

(Beaver, Wasserman and Whipp, 1986)

-A breakpoint in the relationship between $\dot{V}_E$ and $\dot{V}CO_2$. "This point of increased slope marks the start of respiratory compensation for metabolic acidosis, below which $\dot{V}_E$ is closely coupled to $\dot{V}CO_2$ but above which $\dot{V}E$ rises more rapidly in a phase of relative hyperventilation".

N = 10 males, 19-39 yr., BE, 15W/min to fatigue.

LACTATE RESPONSE

First lactate threshold

Anaerobic threshold

(Wasserman, Whipp, Koyal and Beaver, 1973)

-As above for same authors.

Maximum steady state

(Londeree and Ames, 1975)

-the O_2 uptake, heart rate and/or treadmill velocity at which plasma lactate concentration reaches 2.2 mmol/l after 10 minutes of constant load exercise.

N = 13, M, low (n = 4, 24.8 $\pm$ 3.3 yr), medium (n = 6, 23.7 $\pm$ 2.3 yr) and high (n = 3, 32.2 $\pm$ 8.0 yr) fitness groups, TM, 2-8 x 15 minute CLW tests.

Onset of plasma lactate accumulation

(Farrell, Wilmore, Coyle, Billing and Costill, 1979)

-the constant exercise intensity which elicits an increase in plasma lactate concentration over those observed at rest or low exercise intensity (40-60%$\dot{V}O_2$max).

N = 18, M, endurance trained, TM, 8X10 min CLW

Determined as the point where delta lactate (post- minus pre-test) values began to rise. This point was determined by both visual inspection and by the use of linear regression equations.

Aerobic threshold

(Kindermann, Simon and Keul, 1979)

-"approximately 2 mmol/l lactate - first significant elevation of lactate, nonlinear increase in $\dot{V}_E$, RQ" during a continuous IW test.

N = 7, M, trained, TM, starting 5% gradient, 8kph then increased by 2kph/3min.

Lactate threshold

(Ivy, Withers, Van Handel, Elger, and Costill, 1980)

-the work load "just before the onset of blood lactate accumulation" (here taken to mean the work load just below that which produces a continuous and significant rise in blood lactate concentration from that observed at rest) during a continuous IW test.

N = 13, M, 23.8 $\pm$ 5.0 yr, BE, 60rpm, 25W/min to fatigue.

Lactate threshold

(Hurley, Hagberg, Allen, Seals, Young, Cuddihee and Holloszy, 1984)

-the work load resulting in a blood lactate concentration of 2.5mM, which correlates well with maximal steady state and endurance performance.

N = 8 untrained M, 29 ± 1 yr, TM, 6 x 10 min CLW, pre and post training.

Second lactate threshold

Anaerobic threshold

(Kindermann, Simon and Keul, 1979)

-"approximately 4 mmol/l lactate - steep part of exponential increase in lactate concentration" during a continuous IW test.

Protocol as above for same authors.

Onset of Blood Lactate Accumulation

(Sjodin and Jacobs, 1981)

-"A blood lactate concentration of 4 mmol/l has been widely accepted as representing the limit between exercise intensities, which are predominantly aerobic or anaerobic in nature with regard to energy supply.".

N = 18, M, marathon runners, 32 ± 7 yr, TM, 4X4min work loads during continuous IW with increments of 0.5 to 2.0 kph.

Individual Anaerobic Threshold

(Stegmann, Kindemann and Schnabel, 1981)

-the exercise intensity during a continuous IW test just before that where the rate of lactate elimination falls below the rate of lactate production, resulting in a rapid accumulation of blood lactate at higher exercise intensities.

N = 62, M and F, various fitness levels.

n = 38, M, TM, started at 6 or 8kph and 5% gradient and increased by 2kph/3min.

n = 16M + 8F, BE, started at 50 or 100W and increased by 50W/3min.

Lactate turnpoint

(Davis, Bassett, Hughes, Gass, 1983)

-"a second, sharp elevation in the rate of increase of venous lactate concentrations (breakpoint)" during continuous IW tests.

N = 16, M, 27 ± 7.5 yr, BE, 10W/20 sec to fatigue.

APPENDIX 2.

Experimental data and statistical analyses.

UTW	UTxK	UTsdK	UTxLa	UTsdLa	UTxpH	UTsdpH	UTxDE	UTsdDE
0	3.98	.07	.89	.37	7.412	.015	•	•
30	4.38	.23	1.11	.29	7.393	.013	34.70	5.25
60	4.41	.20	1.25	.39	7.391	.013	35.63	6.12
90	4.53	.20	1.41	.41	7.391	.012	41.15	8.23
120	4.58	.27	1.53	.40	7.389	.013	46.42	6.72
150	4.68	.22	1.94	.50	7.382	.015	51.90	8.88
180	4.73	.29	2.61	1.08	7.373	.018	57.76	9.57
210	4.88	.29	3.19	1.11	7.364	.017	66.83	15.07
240	5.06	.33	3.94	1.30	7.351	.019	76.70	18.41
270	5.23	.33	4.83	1.39	7.340	.028	89.57	25.18
300	5.44	.42	5.85	1.58	7.318	.034	107.26	37.42
330	5.76	.42	7.36	2.25	7.302	.037	128.90	33.42

ETW	ETxK	ETsdK	ETxLa	ETsdLa	ETxpH	ETsdpH	ETxDE	ETsdDE
0	4.24	.20	.73	.24	7.399	.025	•	•
30	4.53	.20	.86	.29	7.393	.024	30.75	7.18
60	4.58	.23	.98	.35	7.390	.027	34.87	6.82
90	4.59	.20	.98	.26	7.390	.020	37.90	5.47
120	4.63	.19	1.03	.41	7.390	.026	42.91	5.38
150	4.68	.23	1.04	.36	7.389	.018	47.14	3.34
180	4.78	.24	1.25	.29	7.390	.020	51.52	5.12
210	4.84	.25	1.23	.40	7.389	.021	57.98	3.83
240	4.91	.22	1.51	.59	7.383	.020	65.57	7.49
270	4.95	.25	1.73	.67	7.380	.023	69.55	8.80
300	5.04	.24	2.10	.77	7.377	.026	79.24	9.41
330	5.19	.28	2.58	.97	7.367	.024	89.80	9.04
360	5.35	.30	3.36	1.25	7.359	.033	101.32	13.26
390	5.55	.34	4.25	1.43	7.345	.033	122.18	16.51
420	5.81	.43	5.90	1.49	7.325	.029	141.21	18.70
450	6.00	.38	6.68	1.89	7.296	.031	159.67	18.75

Table A.1: Mean results for fast incremental work test.

	TRAINING	V̇O2MAX	LT1	LT1%	IAT	IAT%	VT1	VT1%	VT2	VT2%
1	UT	46.60	27.27	58.52	•	•	27.92	59.91	35.83	76.89
2	UT	64.29	31.80	49.46	•	•	32.07	49.88	38.43	59.78
3	UT	52.09	31.62	60.69	•	•	28.81	55.31	37.31	71.63
4	UT	53.11	24.73	46.57	•	•	31.33	58.99	36.95	69.57
5	UT	53.09	30.04	56.59	•	•	27.18	51.20	37.76	71.12
6	UT	52.16	24.37	46.72	•	•	22.31	42.77	29.58	56.71
7	UT	46.73	23.86	51.07	•	•	26.72	57.18	35.89	76.80
8	UT	58.78	24.18	41.13	•	•	22.81	38.81	48.45	82.43
9	ET	65.82	44.19	67.14	•	•	32.53	49.42	44.37	67.41
10	ET	68.20	40.40	59.25	46.73	68.52	36.54	53.86	51.82	75.98
11	ET	58.66	32.95	52.78	54.99	93.74	30.85	52.59	48.92	83.40
12	ET	69.04	36.78	53.27	•	•	40.35	58.44	57.53	83.33
13	ET	63.68	41.25	64.78	54.06	84.89	38.39	60.29	48.25	75.77
14	ET	63.75	41.16	64.56	53.72	84.27	39.19	61.47	49.21	77.19
15	ET	58.47	35.88	61.37	45.54	77.89	39.64	67.79	50.94	87.12
16	ET	66.71	39.27	58.87	56.41	84.56	38.97	58.42	49.11	73.62

Table A.2: $\dot{V}O_2max$ and threshold values from both fast and slow incremental work tests. All absolute results expressed in ml/kg.min.

Unpaired t-Test X_1 : TRAINING Y_1 : $\dot{V}O_2MAX$

DF	Unpaired t Value	Prob. (1-tail)
14	-4.349	.0003

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	53.356	5.876	2.077
ET	8	64.291	4.005	1.416

Unpaired t-Test X_1 : TRAINING Y_2 : LT1

DF	Unpaired t Value	Prob. (1-tail)
14	-6.684	.0001

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	27.234	3.446	1.218
ET	8	38.985	3.585	1.267

Unpaired t-Test X_1 : TRAINING Y_3 : LT1%

DF	Unpaired t Value	Prob. (1-tail)
14	-2.941	.0054

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	51.344	6.745	2.385
ET	8	60.253	5.281	1.867

Unpaired t-Test X_1 : TRAINING Y_4 : VT1

DF	Unpaired t Value	Prob. (1-tail)
14	-5.486	.0001

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	27.394	3.525	1.246
ET	8	37.058	3.521	1.245

Unpaired t-Test X_1 : TRAINING Y_5 : VT1%

DF	Unpaired t Value	Prob. (1-tail)
14	-1.775	.0488

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	51.756	7.682	2.716
ET	8	57.785	5.771	2.04

Unpaired t-Test X_1 : TRAINING Y_6 : VT2

DF	Unpaired t Value	Prob. (1-tail)
14	-5.514	.0001

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	37.525	5.2	1.838
ET	8	50.019	3.746	1.324

Unpaired t-Test X_1 : TRAINING Y_7 : VT2%

DF	Unpaired t Value	Prob. (1-tail)
14	-1.933	.0369

Group	Count	Mean	Std. Dev.	Std. Error
UT	8	70.616	8.704	3.077
ET	8	77.978	6.345	2.243

Table A.3: t-test results for $\dot{V}O_2max$ and threshold comparisons between UT and ET.

Anova table for a 2-factor repeated measures Anova.

Source:	df:	Sum of Squares:	Mean Square:	F-test:	P value:
TRAINING (A)	1	917.204	917.204	56.445	.0001
subjects w. groups	14	227.492	16.249		
Repeated Measure (B)	1	6.248	6.248	.733	.4065
AB	1	8.715	8.715	1.022	.3292
B x subjects w. groups	14	119.401	8.529		

Anova table for a 2-factor repeated measures Anova.

Source:	df:	Sum of Squares:	Mean Square:	F-test:	P value:
TRAINING (A)	1	446.258	446.258	7.544	.0157
subjects w. groups	14	828.158	59.154		
Repeated Measure (B)	1	8.446	8.446	.356	.56
AB	1	16.589	16.589	.7	.4168
B x subjects w. groups	14	331.776	23.698		

Table A.4: Analysis of variance results for comparison between VT_1 vs. LT_1. A) Absolute values, B) relative values.

TIME	POWER	LA-	K+	pH	VE	VO2	TIME	POWER	LA-	K+	pH	VE	VO2
0	0	1.5	4.1	7.405	•	•	0	•	.5	4.2	7.445	•	•
2.5	305	2.7	4.9	7.393	138.35	47.07	2.5	403	4.5	6.0	7.322	127.16	58.08
5.0	345	7.0	4.9	7.385	145.59	51.32	5.0	407	5.5	6.0	7.299	141.26	63.11
7.5	351	5.0	4.9	7.366	155.64	51.47	7.5	381	10.9	5.8	7.274	141.30	60.48
10.0	334	5.6	5.0	7.359	153.64	51.39	10.0	307	5.9	5.8	7.267	146.40	61.54
15.0	298	4.3	5.0	7.354	142.39	51.30	15.0	271	7.0	5.5	7.274	147.69	58.76
20.0	317	4.6	4.9	7.368	129.21	50.24	20.0	277	6.8	5.4	7.307	152.76	59.41
30.0	297	3.9	4.9	7.368	126.89	51.06	30.0	279	5.2	5.4	7.329	135.06	57.22
40.0	320	4.1	4.9	7.401	132.54	54.00	40.0	276	6.1	5.3	7.349	119.01	53.38
50.0	296	3.9	5.0	7.375	114.28	53.47	50.0	274	3.6	5.3	7.375	111.73	52.62
60.0	323	5.1	5.0	7.365	165.37	65.50	60.0	258	2.5	5.3	7.398	108.28	51.80
0	0	.8	3.9	7.387	•	•	0	•	4.2	1.0	7.386	•	•
2.5	282	1.9	5.1	7.343	72.03	49.56	2.5	304	5.1	3.7	7.355	76.02	48.94
5.0	290	2.1	4.9	7.352	72.68	51.02	5.0	313	5.2	3.6	7.374	87.86	55.11
7.5	354	1.9	5.0	7.354	89.00	56.16	7.5	348	5.2	3.8	7.386	92.80	56.78
10.0	329	1.8	5.1	7.343	92.42	57.01	10.0	310	5.2	3.3	7.385	91.85	54.15
15.0	335	3.9	5.2	7.327	92.62	57.82	15.0	321	5.4	2.6	7.395	93.71	56.50
20.0	335	3.1	5.0	7.322	95.77	58.05	20.0	293	5.2	2.3	7.396	87.98	50.66
30.0	326	2.3	5.2	7.329	95.69	57.14	30.0	297	5.1	1.5	7.395	87.20	53.46
40.0	319	3.7	5.1	7.344	94.73	56.39	40.0	291	5.0	1.7	7.399	86.66	53.20
50.0	320	3.0	5.1	7.348	94.82	56.38	50.0	278	5.0	1.5	7.390	84.80	53.08
60.0	323	1.9	5.2	7.341	101.97	60.49	60.0	300	5.1	2.0	•	89.05	52.68
0	•	1.8	4.2	7.404	•	•	0	•	1.8	4.3	7.409	•	•
2.5	424	4.3	5.5	7.361	129.75	49.72	2.5	335	6.3	5.6	7.342	116.97	52.16
5.0	455	6.2	5.8	7.321	159.18	55.40	5.0	249	4.7	5.8	7.317	126.89	54.18
7.5	449	6.7	5.7	7.309	162.89	55.89	7.5	263	5.4	5.7	7.329	130.46	52.19
10.0	397	10.8	5.8	7.261	157.69	53.62	10.0	260	6.3	5.7	7.328	136.26	52.59
15.0	352	9.4	5.7	7.249	160.28	55.12	15.0	255	6.8	5.6	7.349	127.16	49.66
20.0	330	9.3	5.5	7.247	140.68	53.97	20.0	221	4.8	5.4	7.349	117.54	50.67
30.0	291	4.5	5.4	7.301	142.68	50.99	30.0	204	3.8	5.4	7.376	106.04	48.96
40.0	274	4.8	5.5	7.310	134.65	52.11	40.0	213	3.9	5.5	7.379	107.30	49.88
50.0	249	3.3	5.5	7.323	127.76	49.32	50.0	223	3.9	5.8	•	106.43	49.32
60.0	317	3.3	5.7	7.337	132.63	51.52	60.0	239	2.3	5.6	7.389	115.33	54.90
0	•	1.3	4.4	7.372	•	•	0	•	1.1	4.4	7.365	•	•
2.5	293	2.5	5.1	7.339	93.95	46.42	2.5	285	5.6	5.7	7.299	118.73	53.36
5.0	342	4.1	5.5	7.305	112.24	55.92	5.0	316	6.6	5.3	7.268	125.20	54.02
7.5	342	5.6	5.6	7.279	115.09	57.83	7.5	299	4.8	5.2	7.287	140.71	53.18
10.0	330	6.4	5.6	7.270	119.60	57.79	10.0	288	4.6	5.2	7.288	132.55	52.68
15.0	284	5.9	5.2	7.288	139.23	56.22	15.0	273	4.9	5.3	7.299	135.33	52.67
20.0	295	7.3	5.3	7.316	132.48	54.90	20.0	245	4.9	5.2	7.303	135.09	53.72
30.0	263	5.5	5.3	7.333	130.62	55.83	30.0	254	4.5	5.1	7.319	130.31	53.49
40.0	249	5.0	5.2	7.340	129.56	55.26	40.0	254	4.1	5.1	7.327	129.86	52.77
50.0	254	4.1	5.1	7.341	107.60	51.97	50.0	244	2.4	5.2	7.352	123.52	51.14
60.0	255	6.2	5.3	7.343	130.80	57.05	60.0	280	6.7	5.4	7.319	141.87	54.84

Table A.5: Individual results for the one hour self-paced trial.

One Factor ANOVA X1 : T Y1 : POWER

Analysis of Variance Table

Source	DF	Sum Squares	Mean Square	F-test
Between groups	9	60967.7	6763.3	3.49
Within groups	70	135031.5	1643.307	0.0013
Total	79	195997.2		

Model II estimate of between component variance = 602.459

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T5 vs. T50	72.375	43.965*	1.198	3.384
T5 vs. T60	52.75	43.965*	.635	2.393
T8 vs. T10	29	43.965	.193	1.316
T8 vs. T15	49.75	43.965*	.566	2.257
T8 vs. T20	59.25	43.965*	.803	2.688

* Significant at 95%

One Factor ANOVA X1 : T Y1 : POWER

Group	Count	Mean	Std. Dev.	Std. Error
T3	8	328.875	55.605	19.447
T5	8	339.625	65.277	23.079
T8	8	348.375	54.767	19.363
T10	8	319.375	39.992	14.14
T15	8	299.625	34.247	12.109

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T8 vs. T20	72	43.965*	1.186	3.267
T8 vs. T40	73.875	43.965*	1.249	3.352
T8 vs. T50	81.125	43.965*	1.505	3.681
T8 vs. T60	61.5	43.965*	.865	2.79
T10 vs. T15	20.75	43.965	.356	.941

* Significant at 95%

One Factor ANOVA X1 : T Y1 : POWER

Group	Count	Mean	Std. Dev.	Std. Error
T20	8	289.125	40.244	14.229
T30	8	276.375	76.746	12.992
T40	8	274.5	36.21	12.802
T50	8	267.25	31.116	11.001
T60	8	286.875	33.549	11.861

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T10 vs. T20	30.25	43.965	.209	1.372
T10 vs. T30	43	43.965	.423	1.951
T10 vs. T40	44.875	43.965*	.461	2.036
T10 vs. T50	52.125	43.965*	.621	2.365
T10 vs. T60	32.5	43.965	.242	1.474

* Significant at 95%

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T3 vs. T5	-10.75	43.965	.026	-.488
T3 vs. T8	-19.5	43.965	.087	.885
T3 vs. T10	9.5	43.965	.021	.431
T3 vs. T15	30.25	43.965	.209	1.372
T3 vs. T20	39.75	43.965	.361	1.802

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T15 vs. T20	9.5	43.965	.021	.431
T15 vs. T30	22.25	43.965	.113	1.009
T15 vs. T40	24.125	43.965	.133	1.095
T15 vs. T50	31.375	43.965	.225	1.423
T15 vs. T60	11.75	43.965	.032	.533

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T3 vs. T30	52.5	43.965*	.62	2.382
T3 vs. T40	54.375	43.965*	.676	2.467
T3 vs. T50	61.625	43.965*	.869	2.796
T3 vs. T60	42	43.965	.403	1.905
T5 vs. T8	-8.75	43.965	.018	.397

* Significant at 95%

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T20 vs. T30	12.75	43.965	.037	.578
T20 vs. T40	14.625	43.965	.049	.664
T20 vs. T50	21.875	43.965	.103	.992
T20 vs. T60	2.25	43.965	.003	.102
T30 vs. T40	1.875	43.965	.006	.085

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T5 vs. T10	20.25	43.965	.209	.919
T5 vs. T15	40	43.965	.384	1.814
T5 vs. T20	50.5	43.965*	.583	2.291
T5 vs. T30	63.25	43.965*	.915	2.87
T5 vs. T40	65.125	43.965*	.97	2.955

* Significant at 95%

One Factor ANOVA X1 : T Y1 : POWER

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test	Dunnett t
T30 vs. T50	13.125	43.965	.079	.414
T30 vs. T60	-10.5	43.965	.051	-.474
T40 vs. T50	17.25	43.965	.142	.779
T40 vs. T60	-12.375	43.965	.085	-.561
T50 vs. T60	-29.625	43.965	.489	-.69

Table A.6: Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.

One Factor ANOVA X1 : T Y2 : ΔE

Analysis of Variance Table

Source	DF	Sum Squares	Mean Square	F-test
Between groups	9	4133.72	459.302	.827
Within groups	70	38856.605	555.094	Pr > .5931
Total	79	42990.325		

Model II estimate of between component variance = -11.974

One Factor ANOVA X1 : T Y2 : ΔE

Comparison:	Mean Diff.	Fisher PLSD	Scheffe F-test:	Dunnett t
T5 vs. T50	12.495	23.497	.125	1.061
T5 vs. T60	-1.8	23.497	.002	.153
T8 vs. T10	-.315	23.497	9.458E-5	.027
T8 vs. T15	-1.315	23.497	.001	.112
T8 vs. T20	4.568	23.497	.017	.366

One Factor ANOVA X1 : T Y2 : ΔE

Group:	Count	Mean	Std. Dev.	Std. Error
T3	8	109.12	25.244	8.926
T5	8	121.363	29.36	10.38
T8	8	128.486	27.389	9.683
T10	8	128.801	25.648	9.068
T15	8	129.801	24.55	8.68

One Factor ANOVA X1 : T Y2 : ΔE

Comparison:	Mean Diff.:	Fisher PLSD	Scheffe F-test:	Dunnett t
T8 vs. T20	9.175	23.497	.067	.779
T8 vs. T40	11.698	23.497	.11	.993
T8 vs. T50	19.619	23.497	.308	1.665
T8 vs. T60	5.324	23.497	.023	.452
T10 vs. T15	-1	23.497	.001	.085

One Factor ANOVA X1 : T Y2 : ΔE

Group:	Count	Mean	Std. Dev.	Std. Error
T20	8	123.939	22.244	7.864
T30	8	119.311	20.233	7.153
T40	8	116.789	18.479	6.533
T50	8	108.868	14.108	4.988
T60	8	123.162	24.422	8.634

One Factor ANOVA X1 : T Y2 : ΔE

Comparison:	Mean Diff.:	Fisher PLSD:	Scheffe F-test:	Dunnett t
T10 vs. T20	4.863	23.497	.019	.413
T10 vs. T30	9.49	23.497	.072	.806
T10 vs. T40	12.013	23.497	.116	1.02
T10 vs. T50	19.934	23.497	.318	1.692
T10 vs. T60	5.639	23.497	.025	.479

One Factor ANOVA X1 : T Y2 : ΔE

Comparison:	Mean Diff.:	Fisher PLSD:	Scheffe F-test:	Dunnett t
T3 vs. T5	-12.243	23.497	.12	1.039
T3 vs. T8	-19.366	23.497	.3	1.644
T3 vs. T10	-19.681	23.497	.31	1.671
T3 vs. T15	-20.681	23.497	.342	1.756
T3 vs. T20	-14.819	23.497	.176	1.258

One Factor ANOVA X1 : T Y2 : ΔE

Comparison:	Mean Diff.:	Fisher PLSD	Scheffe F-test:	Dunnett t
T15 vs. T20	5.863	23.497	.022	.498
T15 vs. T30	10.49	23.497	.088	.89
T15 vs. T40	13.013	23.497	.136	1.105
T15 vs. T50	20.934	23.497	.351	1.777
T15 vs. T60	6.639	23.497	.035	.564

One Factor ANOVA X1 : T Y2 : ΔE

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test:	Dunnett t
T3 vs. T30	-10.191	23.497	.233	.865
T3 vs. T40	-7.669	23.497	.047	.651
T3 vs. T50	252	23.497	5.105E-5	.021
T3 vs. T60	-14.043	23.497	.158	1.192
T5 vs. T8	-7.124	23.497	.041	.605

One Factor ANOVA X1 : T Y2 : ΔE

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test:	Dunnett t
T20 vs. T30	4.628	23.497	.017	.393
T20 vs. T40	7.15	23.497	.041	.607
T20 vs. T50	15.071	23.497	.192	1.279
T20 vs. T60	.776	23.497	4.625E-4	.066
T30 vs. T40	2.523	23.497	.005	.214

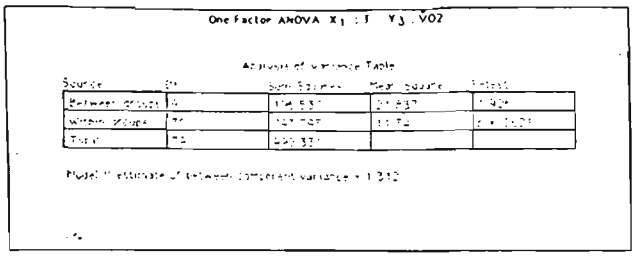
One Factor ANOVA X1 : T Y2 : ΔF

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test:	Dunnett t
T5 vs. T10	-7.439	23.497	.041	.631
T5 vs. T15	-8.439	23.497	.052	.716
T5 vs. T20	-2.576	23.497	.008	.219
T5 vs. T30	2.051	23.497	.003	.174
T5 vs. T40	4.574	23.497	.017	.388

One Factor ANOVA X1 : T Y2 : ΔF

Comparison	Mean Diff.	Fisher PLSD	Scheffe F-test:	Dunnett t
T20 vs. T50	10.444	23.497	.137	.887
T20 vs. T60	-3.351	23.497	.012	.284
T30 vs. T50	8.821	23.497	.08	.762
T40 vs. T50	5.874	23.497	.033	.541
T50 vs. T60	-14.295	23.497	.124	1.213

Table A.6: (cont.) Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.

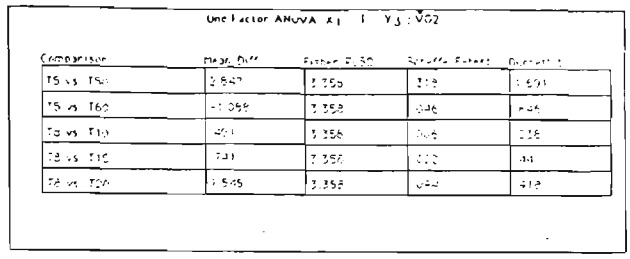


One Factor ANOVA X1 : T Y3 : V02

Analysis of Variance Table

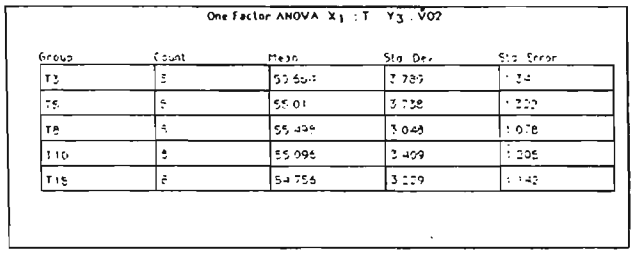
Source	DF	Sum Squares	Mean Square	F-test
Between Groups	5	124.637	24.927	7.904
Within Groups	72	227.027	3.153	
Total	77	350.331		

Model II estimate of between component variance = 1.312



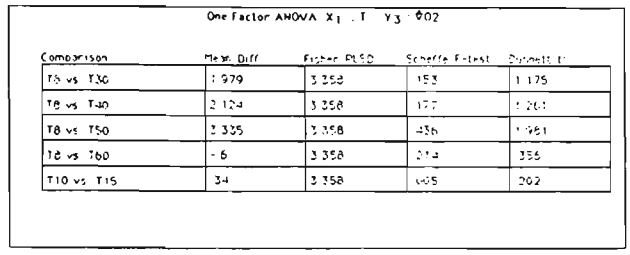
One Factor ANOVA X1 : T Y3 : V02

Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T5 vs T30	2.642	2.755	.318	1.691
T5 vs T60	-1.059	2.758	.046	.648
T8 vs T10	.451	2.756	.006	.228
T8 vs T30	.731	2.756	.012	.344
T8 vs T60	-1.649	2.756	.044	.619



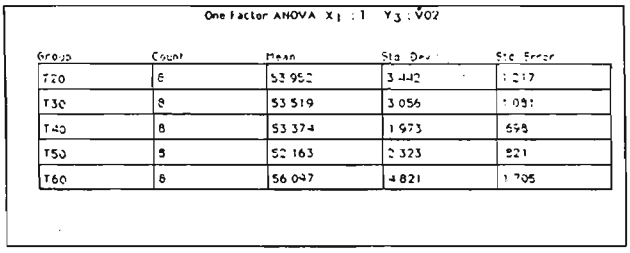
One Factor ANOVA X1 : T Y3 : V02

Group	Count	Mean	Std. Dev.	Std. Error
T3	8	59.604	2.789	1.34
T5	8	55.01	3.738	1.322
T8	8	55.494	3.048	1.078
T10	8	55.096	3.409	1.205
T15	8	54.756	3.229	1.142



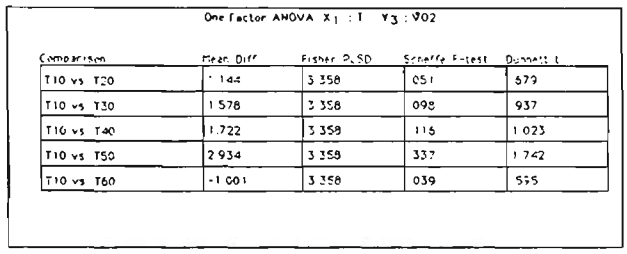
One Factor ANOVA X1 : T Y3 : V02

Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T5 vs T30	-1.979	3.358	.153	1.175
T8 vs T30	-2.124	3.358	.177	1.261
T8 vs T50	-2.335	3.358	.436	1.661
T8 vs T60	-.6	3.358	.014	.356
T10 vs T15	.34	3.358	.005	.202



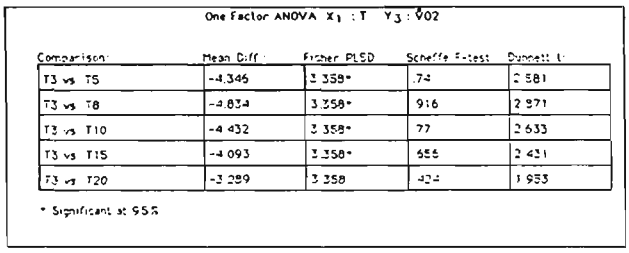
One Factor ANOVA X1 : T Y3 : V02

Group	Count	Mean	Std. Dev.	Std. Error
T20	8	53.952	3.442	1.217
T30	8	53.519	3.056	1.081
T40	8	53.374	1.973	.698
T50	8	52.163	2.323	.821
T60	8	56.047	4.821	1.705



One Factor ANOVA X1 : T Y3 : V02

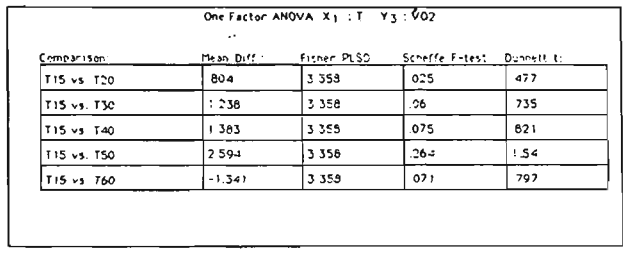
Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T10 vs T20	1.144	3.358	.051	.679
T10 vs T30	1.578	3.358	.098	.937
T10 vs T40	1.722	3.358	.116	1.023
T10 vs T50	2.934	3.358	.337	1.742
T10 vs T60	-1.001	3.358	.039	.595



One Factor ANOVA X1 : T Y3 : V02

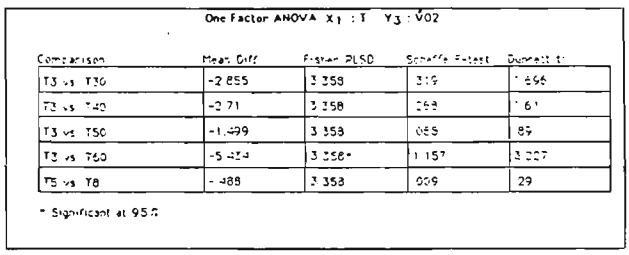
Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T3 vs T5	-4.346	3.358*	.74	2.581
T3 vs T8	-4.834	3.358*	.916	2.871
T3 vs T10	-4.432	3.358*	.77	2.633
T3 vs T15	-4.093	3.358*	.655	2.431
T3 vs T20	-3.289	3.358	.424	1.953

* Significant at 95%



One Factor ANOVA X1 : T Y3 : V02

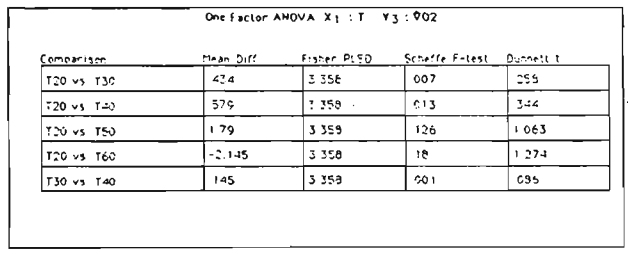
Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T15 vs T20	.804	3.358	.025	.477
T15 vs T30	1.238	3.358	.06	.735
T15 vs T40	1.383	3.358	.075	.821
T15 vs T50	2.594	3.358	.264	1.54
T15 vs T60	-1.341	3.358	.071	.797



One Factor ANOVA X1 : T Y3 : V02

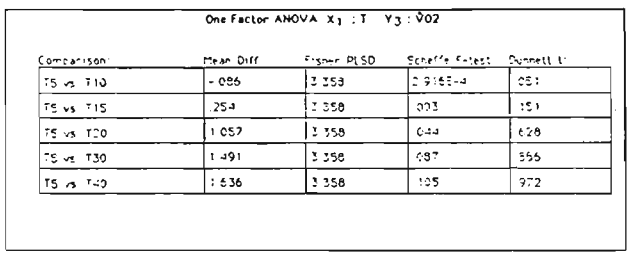
Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T3 vs T30	-2.855	3.358	.319	1.696
T3 vs T40	-2.71	3.358	.293	1.61
T3 vs T50	-1.499	3.358	.085	.89
T3 vs T60	-5.424	3.358*	1.157	3.227
T5 vs T8	-.488	3.358	.009	.29

* Significant at 95%



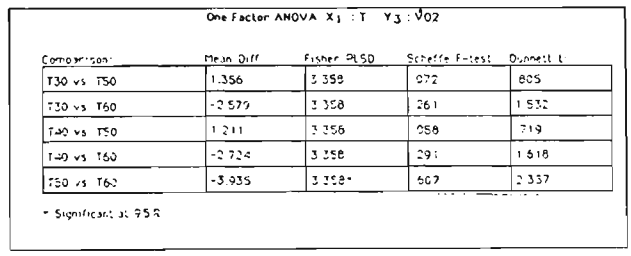
One Factor ANOVA X1 : T Y3 : V02

Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T20 vs T30	.424	3.358	.007	.255
T20 vs T40	.579	3.358	.013	.344
T20 vs T50	1.79	3.359	.126	1.063
T20 vs T60	-2.145	3.358	.18	1.274
T30 vs T40	.145	3.358	.001	.086



One Factor ANOVA X1 : T Y3 : V02

Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T5 vs T10	-.086	3.358	2.916E-4	.051
T5 vs T15	.254	3.358	.003	.151
T5 vs T20	1.057	3.358	.044	.628
T5 vs T30	1.491	3.358	.087	.886
T5 vs T40	1.636	3.358	.105	.972



One Factor ANOVA X1 : T Y3 : V02

Comparison	Mean Diff	Fisher PLSD	Scheffe F-test	Dunnett t
T30 vs T50	1.356	3.358	.072	.805
T30 vs T60	-2.579	3.358	.261	1.532
T40 vs T50	1.211	3.358	.058	.719
T40 vs T60	-2.724	3.358	.291	1.618
T50 vs T60	-3.935	3.358*	.607	2.337

* Significant at 95%

Table A.6: (cont.) Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.

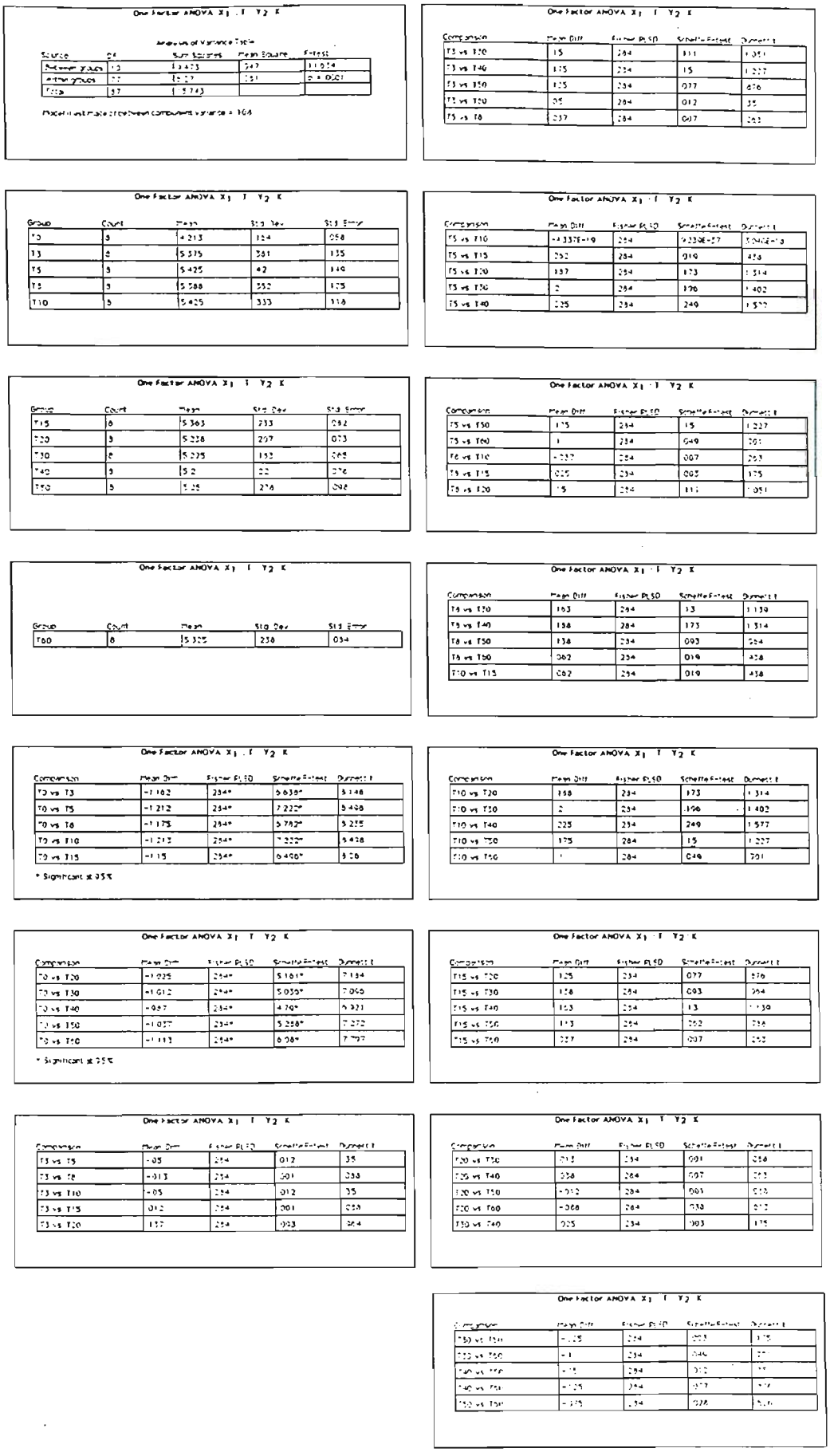


Table A.6: (cont.) Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.

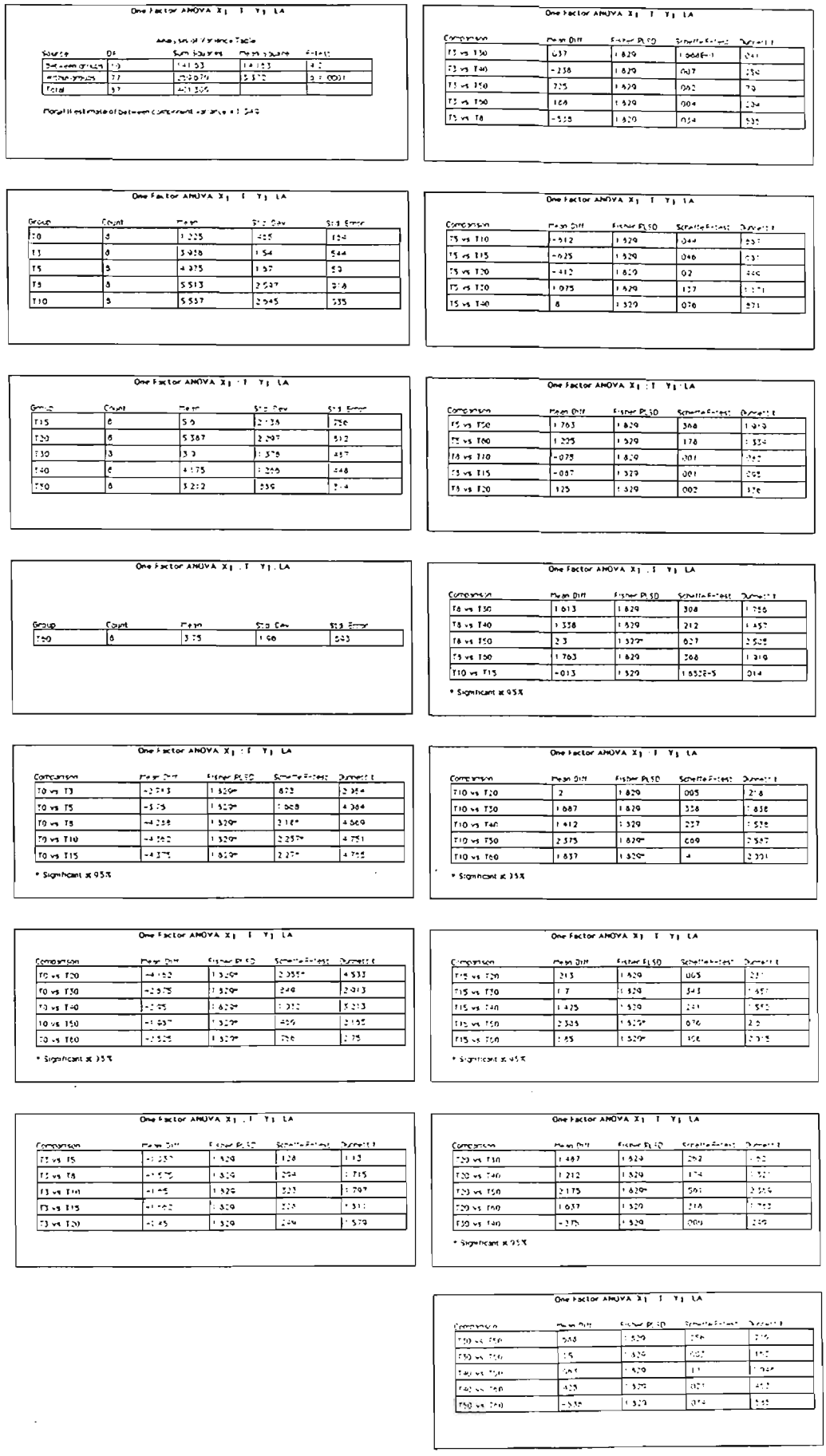


Table A.6: (cont.) Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.

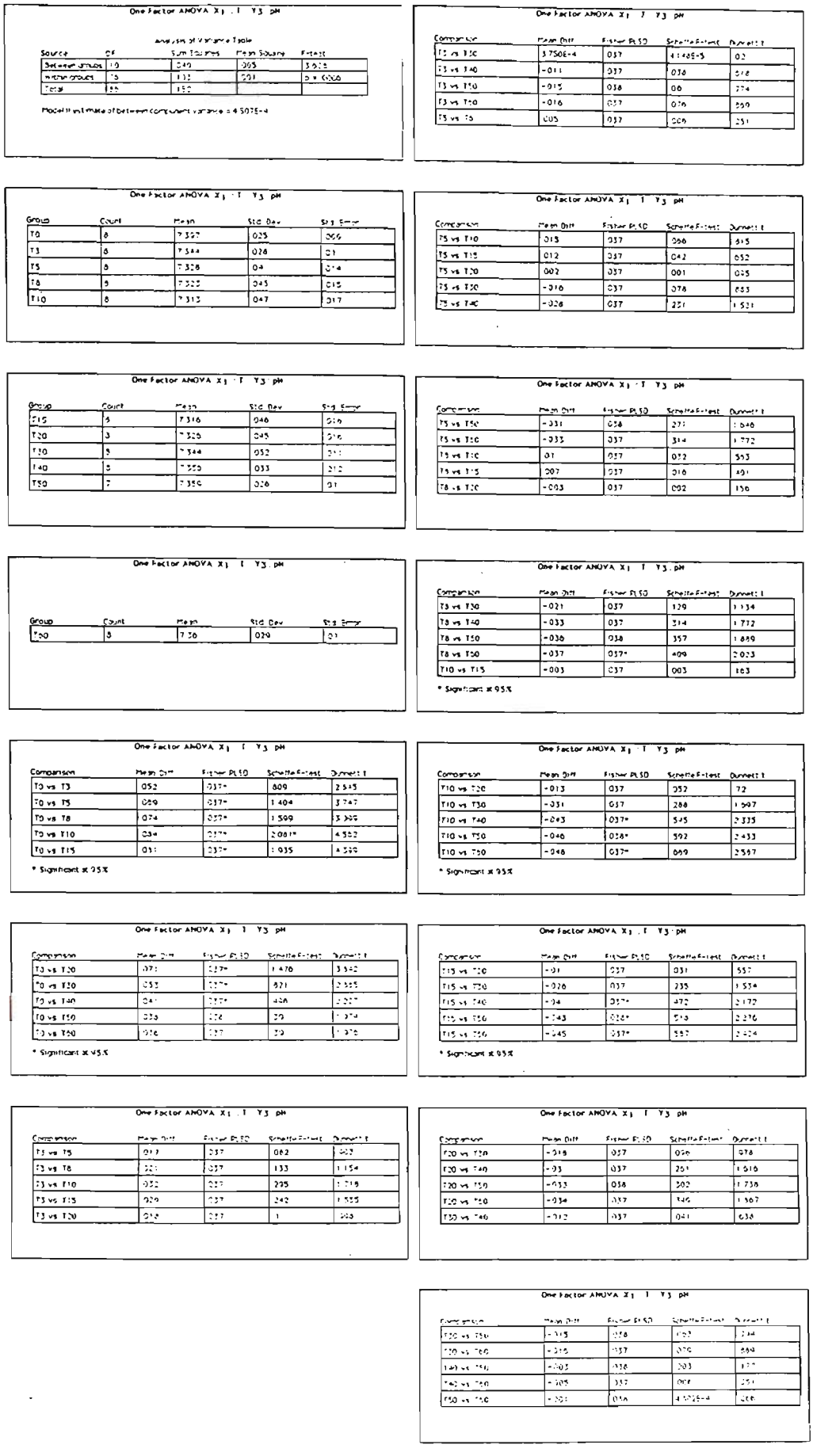


Table A.6: (cont.) Analysis of variance results for comparison of response to one hour self-paced trial. Time is the independant variable.