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PULMONARY FUNCTION AND ACID-BASE BALANCE DURING HIGH INTENSITY CONSTANT-LOAD EXERCISE

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DEDICATED TO MY PARENTS

DIRK and ENA

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DECLARATION

I, Elsabe Odendal, hereby declare that the work on which this thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part thereof has been, is being, or is to be submitted for another degree in this or any other university.

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ABSTRACT

The possibility that an inadequate response of the pulmonary system might limit high intensity exercise in man has received increasing attention over the past few years. However, very few scientific investigations have focused systematically on pulmonary function during high intensity constant-load exercise. Furthermore, many studies have examined only one part of the pulmonary system during exercise and some have not included blood gas measurements as a measure of the adequacy of pulmonary function.

The studies reported in this thesis were designed to investigate the possible failure of the gas exchanging and pump functions of the pulmonary system during high intensity constant-load exercise. In particular, the aim was to determine the extent to which the pulmonary system might be a factor causing fatigue during this form of exercise.

Pulmonary function was investigated in 10 well-trained endurance athletes [age, 27 $\pm$ 6 yrs; maximal oxygen consumption [VO_2 max], 60 $\pm$ 5 ml/kg/min; maximum work rate capacity [WR max], 335 $\pm$ 30 W/min during high intensity constant-load

cycling exercise at 70% [234 ± 18 W/min; n = 5] and 80% [268 ± 33 W/min; n = 8] of WR max, as determined during an incremental test to exhaustion for the measurement of maximal oxygen consumption.

Ventilation [Vi], oxygen consumption [VO_2], carbon dioxide expiration [VCO_2] and arterialized venous pH [pHa], arterialized venous carbon dioxide tension [$PaCO_2$], arterialized venous bicarbonate ion [HCO_3^-] and venous blood lactate concentrations were measured during both work rates to investigate the adequacy of the gas-exchanging function of the pulmonary system. The data were analyzed with the aim of answering the following:

a] to evaluate whether ventilation increased sufficiently during exercise to ensure an adequate oxygen supply to the working tissues;

b] to assess whether the increased ventilation maintained acid-base homeostasis by lowering arterialized venous carbon dioxide tension [$PaCO_2$], and thereby preventing a continuous fall in arterialized venous pH [pHa].

Maximal voluntary ventilation tests lasting 20 seconds [MVV_{20}] were also measured before and after exercise at both constant work rates to evaluate the possibility of respiratory muscle fatigue prior to, or coincidental with exhaustion.

The increase in ventilation recorded at the end of exhaustive exercise at 70% WR max [94.6 $\pm$ 8.8 l/min] and 80% WR max [109.5 $\pm$ 8.6 l/min] was associated with a constant VO_2 of 3.1 $\pm$ 0.3 l/min and 3.4 $\pm$ 0.1 l/min respectively vs 3.4 $\pm$ 0.4 l/min and 3.5 $\pm$ 0.4 l/min from the 5th minute until the end of exercise (N.S.) at both 70% and 80% WR max respectively. As the VO_2 values were less than the VO_2 max values of 3.9 $\pm$ 0.5 l/min and 4.0 $\pm$ 0.4 l/min, there was probably an adequate oxygen supply to the working muscles at both 70% and 80% WR max.

The decrease in $PaCO_2$ from a normal resting value of 46.0 $\pm$ 3.2 mmHg to 34.2 $\pm$ 3.3 mmHg at the end of exhaustive exercise at 70% WR max and from 42.5 $\pm$ 3.3 mmHg to 36.2 $\pm$ 3.7 mmHg at 80% WR max prevented a continuous fall in arterialized venous pH. At 70% WR max, pHa remained constant from the 5th minute at 7.32 $\pm$ 0.02 and, at 80% WR max, pHa decreased over the first 6 minutes to 7.27 $\pm$ 0.04 ($P < 0.05$) and thereafter remained constant (N.S.).

A marked metabolic acidosis during exercise at 80% WR max was demonstrated by significant ($P < 0.05$) decreases in buffer base, base excess and arterialized venous HCO_3^- concentrations. All concentrations were decreased more at 80% WR max exercise than at 70% WR max, but none of the between work rate differences reached statistical significance. Compared to exercise at 70% WR max, at the end of exercise at 80% WR max the base excess [BE] was -10.1 $\pm$ 2.9 mEq/l vs -7.7 $\pm$ 1.9 mEq/l (N.S.); the buffer base [BB] was 37.9 $\pm$ 2.9 mEq/l vs 40.3 $\pm$ 1.9 mEq/l (N.S); the bicarbonate ion concentration [HCO_3^-] was 15.3 $\pm$ 2.6 mmol/l vs 17.2 $\pm$ 1.2 mmol/l; (N.S.). The only statistically significant differences to indicate a more marked metabolic acidosis during the 80% WR max were the lower pHa of 7.23 $\pm$ 0.03 vs 7.31 $\pm$ 0.03; ($P < 0.05$) and the higher venous blood lactate concentration [LACTATE] of 10.0 $\pm$ 2.4 mmol/l vs 7.6 $\pm$ 0.9 mmol/l ($P < 0.05$).

Furthermore, there was no significant difference (N.S.) between pre-exercise maximal voluntary ventilation [MVVREST] values and post-exercise maximal voluntary ventilation [MVVPOST-EX] values recorded in the minute immediately following exercise at 70% WR

max [MVVREST, 176 ± 5.0 l/min; MVVPOST-EX, 177 ± 6.0 l/min]. In contrast at 80% WR max, the MVVREST values [174 ± 7.0 l/min] differed significantly from the MVVPOST-EX values [186 ± 6.0 l/min]. There was also a small ($P < 0.05$) decrease in MVV values recorded after a 10 [158 ± 10 l/min; n = 4], a 15 [157 ± 6 l/min; n = 4] and a 20 minute period of recovery [159 ± 10 l/min; n = 4] following 80% WR max exercise compared to the resting values [174 ± 7.0 l/min].

The reversal of exercise-induced bronchodilation and or a decreased contractility of the respiratory muscles are possible reasons for the lower recorded maximal voluntary ventilation after a recovery period of 10, 15 and 20 minutes.

Peak ventilation at 70% WR max and at 80% WR max did not even approach values close to MVVREST. At both work rates the "dyspnoea index" [Vi/MVVREST x 100] was less than 65%. Thus, these data suggest that pulmonary fatigue is probably not a factor limiting high intensity constant-load exercise at 70% WR max [80 - 85% VO_2 max] and at 80% WR max [85 - 90% VO_2 max].

Reasons for excluding pulmonary fatigue as a factor limiting high intensity exercise are as follows:

a] There was an adequate hyperventilatory response for the developing metabolic acidosis. The added increment in ventilation caused a progressive fall in arterialized venous carbon dioxide tension which was sufficient to prevent arterialized venous pH falling continuously during the exercise period.

b] Oxygen uptake [VO_2] remained constant throughout the exercise period and was less than the VO_2 maximum values, indicating that the oxygen supply to the working muscles was adequate.

c] There was no evidence of ventilatory muscle fatigue at 70% WR max as maximal voluntary ventilation recorded before exercise [MVVREST] and maximal voluntary ventilation recorded after the cessation of exercise [MVVPOST-EX] were not different. MVVPOST-EX values at 80% WR max were increased if compared to corresponding 70% WR max MVVPOST-EX values.

d] Final ventilation recorded at the end of the 70% and 80% WR max work rates did not reach values close to the maximal voluntary ventilation values.

e] The "dyspnoea index" was much less than the maximum value of 100% at exhaustion. Hence, breathlessness was not a factor limiting exercise at these work rates.

Metabolic changes in the working skeletal muscles causing muscular fatigue are the more likely factors limiting performance at these work rates. The more marked metabolic acidosis may explain why subjects exercised for only 12 minutes at 80% WR max, whereas subjects were able to continue exercise for 22 minutes at 70% WR max.

CHAPTER 1

INTRODUCTION TO, AND SCOPE OF, THE THESIS

The question addressed in this thesis is whether pulmonary fatigue limits continued high intensity exercise.

The pulmonary system is responsible for ensuring adequate gas exchange by maintaining iso-capnic and iso-oxic conditions in arterial blood as well as regulating acid-base balance [McArdle WD et al, 1981]. During high intensity exercise, the increased oxygen consumption and carbon dioxide production by the working skeletal muscles causes an increasing oxygen desaturation and acidity in the venous blood presented to the lung for gas exchange. Hence, the requirement of the pulmonary system for maintaining arterial oxygen content and lowering carbon dioxide tension in order to maintain acid-base balance, is increased several fold during exercise [Dempsey JA et al, 1980].

Some researchers contend that the pulmonary system has a surplus capacity to meet the homeostatic demands of short-term exercise,

even of high intensity in normal adults [Shephard RJ, 1966; Hughes RL et al, 1968; Åstrand P-O et al, 1977; Brooks GA et al, 1984; Bender PR et al, 1985; Anholm JD et al, 1989].

Arguments against any failure of pulmonary function during exercise have centered around the following observations:

1. The ability of subjects to increase minute ventilation even during maximal exercise [Shephard RJ et al, 1966; Åstrand P-O et al, 1977].

2. The fact that ventilation during maximal exercise does not usually approach the maximal voluntary ventilation [MVV] recorded in those subjects at rest [Freedman S, 1970; Brooks GA et al, 1984].

3. The normal arterial oxygen tension is maintained during maximal exercise [Hughes RL et al, 1968].

4. The absence of respiratory muscle fatigue following short duration exercise of high intensity [Bender PL et al, 1985; Anholm JD et al, 1989].

However, others argue that no organ system has limitless functional capacity and that the capacity of even the healthy pulmonary system may be exceeded in some individuals during exercise that is either intense or prolonged [Campbell EJM et al, 1970; Freedman S, 1970; Roussos CM et al, 1979; Dempsey JA et al, 1985, 1986; Inbar O et al, 1987; Hopkins SR et al, 1989]. These authors have provided the following evidence to support their argument that the response of the pulmonary system during exercise is inadequate and that its functional and regulatory capacities may be limited during exercise of high intensity. Their arguments are as follows:

1. The respiratory compensation for the progressively developing metabolic acidosis of high intensity exercise is incomplete as arterial carbon dioxide tension usually falls only to the range of 25 - 32 mmHg. Thereafter the arterial blood pH falls during high intensity exercise. Hence, the pulmonary system does not increase alveolar ventilation sufficiently to maintain acid-base regulation [Inbar O et al, 1987; Hopkins SR et al, 1989; Dempsey JA et al, 1990].

2. Dempsey JA, [1986] has suggested that the healthy pulmonary system may also limit oxygen transport and carbon dioxide elimination due to an inadequate compensatory hyperventilation during very intense exercise. He showed an inappropriately low hyperventilatory response during intense exercise in some highly trained athletes despite a marked metabolic acidosis and arterial hypoxaemia [Dempsey JA et al, 1984].

3. It has also been argued by Campbell EJM et al, [1970] that the extra energy cost of hyperventilation during maximal exercise may become a factor limiting exercise. They felt that eventually a point might be reached at which the oxygen cost of any further increases in ventilation might compromise the oxygen supply to the working muscles.

4. Finally, it has also been proposed that fatigue of the respiratory muscles may occur prior to, or coincidental with the termination of prolonged high intensity exercise [Freedman S, 1970; Roussos CM et al, 1979]. Such fatigue might explain inadequate alveolar ventilation and hypercapnia at high work rates [Roussos C et al, 1982].

Accordingly, the aim of this study was to eliminate or implicate the pulmonary system as a possible cause of fatigue during continued high intensity constant-load exercise at more than 80% of maximum oxygen consumption [VO_2max]. To accomplish this aim subjects first performed a preliminary test for measurements of their maximum oxygen consumption [VO_2 max], peak minute ventilation [Vi max] and maximum work rate capacity [WR max] on an electronically braked cycle ergometer. The results of these tests were used to calculate work rates which represented 70% and 80% WR max for more prolonged exercise.

During more prolonged exercise mean minute ventilation [Vi], oxygen consumption [VO_2], carbon dioxide expiration [VCO_2] and respiratory exchange ratio [RER] were measured. At the same time, arterialized venous blood samples were taken for determination of pH [pHa], buffer base [BB], base excess [BE], bicarbonate ion concentrations [HCO_3^-], carbon dioxide tension [$PaCO_2$] and venous blood was taken for measurements of lactate concentrations [LACTATE]. Together with respiratory muscle endurance values (resting maximal voluntary ventilation [MVVREST]) and ratings of perceived exertion for effort [RPE]

and ventilation [RVE] during the two work rates, such measurements were used to assess whether or not:

1. the increased ventilation achieved during high intensity exercise was sufficient to maintain an adequate oxygen supply to the working skeletal muscles;

2. respiratory compensation for the developing metabolic acidosis was sufficient to ensure acid-base homeostasis;

3. the high rates of ventilation achieved during high intensity exercise caused significant respiratory muscle fatigue that could lead to the termination of exercise;

4. progressive dyspnoea developed which ultimately limited exercise performance.

In addition, maximum voluntary ventilation over 20 s was recorded at the end [MVVPOST-EX] of constant-load exhaustive exercise at 70% and 80% WR max to determine whether there was respiratory muscle fatigue.

CHAPTER 2

REVIEW OF LITERATURE

As explained in Chapter One, this study examined a number of aspects of pulmonary function during continued constant-load exercise at intensities greater than 80% of maximum oxygen consumption [VO_2max] to determine whether or not the pulmonary system may become a limiting factor in such exercise. In this review, the background to that question is described. Specific attention is focused on the different ventilatory thresholds as described by various investigators and on the VO_2, blood lactate concentration, the respiratory compensation for the developing metabolic acidosis and dyspnoea during exercise at work rates above the "second ventilatory threshold", described in section 2.3.

2.1 Ventilatory threshold for short-term exercise:

It is traditionally taught that during a progressive exercise test to exhaustion, ventilation rises as a linear function of oxygen uptake [VO_2] to 50 - 70% of VO_2 max after which ventilation begins to rise exponentially whereas VO_2 continues to rise linearly [Wasserman K et al, 1973; Davis JA et al, 1976; Davis JA et al, 1979; Reinhard U et al, 1979; Reybrouck T et al, 1983; Powers SK et al, 1984].

This ventilatory [V_T] [Hagberg JM et al, 1982; Powers SK et al, 1985] or "anaerobic" threshold [A_T] [Wasserman K et al, 1973; Davis JA et al, 1976; Stamford BA et al, 1978; Mickelson TC et al, 1982] has been used to define the work rate during progressive exercise above which ventilation and plasma lactate concentration increase continuously [Davis JA et al, 1976; Reybrouck T et al, 1983]. This has been interpreted to indicate that the lactate and ventilation thresholds are coincidental and causally related [Wasserman K et al, 1983; 1984a, b; 1990; Caiozzo V et al, 1982; Hughes EF et al, 1982; Whipp BJ et al, 1984], but this has been questioned [Brooks GA, 1985; Walsh ML et al, 1988] as lactate and ventilation thresholds can be dissociated [Hagberg JM et al, 1982; Hughes EF et al, 1982; Heigenhauser GJF et al, 1983; Gaesser GA et al, 1986;

Yamamoto Y et al, 1989]. Furthermore, several investigators have shown that both muscle [Green HJ et al, 1983; Connett RJ et al, 1986] and "arterialized" venous blood [Hughson RL et al, 1982; Campbell ME et al, 1989; Dennis SC et al, 1992] lactate concentrations increase as a continuous rather than as a threshold function of VO_2.

However, irrespective of this controversy, work rates at or above the V_T or A_T can be sustained for only relatively short periods of time and interest in identifying those work rates persists [Wasserman K et al, 1977; Wasserman K, 1981].

2.2 Ventilatory threshold for long-term exercise:

For sustained exercise, Reybrouck T et al, [1983] have identified a work rate [20 W above the V_T for short-term exercise corresponding to about 73% VO_2max] which they define as a "second ventilatory threshold" for long-term exercise. When

prolonged exercise is undertaken at that work rate, lactate concentration, VO_2 [Moritani T et al, 1981; Hughes RL et al, 1984; Roston WL et al, 1987; Poole DC et al, 1988] and ventilation are maintained at steady state levels and subjects can continue to exercise for at least 20 - 40 minutes.

2.3 Exercise at work rates above the "second ventilatory threshold":

Exercise at intensities above the "second ventilatory threshold" [20 W above the V_T for long-term exercise; > 73% and 80% VO_2 max] causes continuous rises in ventilation ["VE drift"], heart rate, VO_2 and blood lactate concentration, to the point of exhaustion. [Linnarsson D, 1974; Hagberg JM et al, 1978; Wasserman K, 1984; Mole PA et al, 1985; Whipp BJ, 1987; Poole DC et al, 1988]. Reasons for the slow rise in VO_2 [VO_2 drift] from the 5th minute until the end of high intensity exercise have not been established.

a] Mediators of the slow rise in VO_2 during high intensity exercise:

Several factors have been suggested to contribute to the VO_2 drift during high intensity exercise at work rates above the "second ventilatory threshold". These include an increase in core temperature [Hagberg JM et al, 1978], an increased metabolic acidosis [Whipp BJ, 1987] and a progressive rise in circulating catecholamine concentrations [Galbo H, 1983 and Fellows IW et al, 1985].

In addition, the additional energy costs of the upward drift in ventilation during high intensity exercise have also been identified as a possible cause of the curvilinear rise in VO_2 [Bradley ME et al, 1978; Hagberg JM et al, 1978; Roussos C et al, 1982]. As argued in Chapter One, the metabolic and circulatory costs of additional ventilation may limit blood flow to the active muscles [Campbell EJM et al, 1970; Anholm J et al, 1987; Jones NL et al, 1990].

In the past, some investigators have suggested that rises in blood lactate concentration may cause the slow increase in VO_2

during high intensity exercise [Whipp BJ et al, 1972; Casaburi R et al, 1987; Roston WL et al, 1987; Poole DC et al, 1988]. These suggestions were based on the belief that the rises in VO_2 after the initial 3 minutes of exercise at work rates requiring more than 60% VO_2 max were due to blood lactate oxidation [Henry FM et al, 1951; Volkov NI et al, 1969; Poole DC et al, 1988]. Results of Hagberg JM et al, [1978], however, repudiate this explanation for the slow rise in VO_2 during constant-load exercise. They showed a slow rise in VO_2 at work rates where blood lactate concentrations did not change appreciably during exercise.

b] <u>Blood lactate turnover during high intensity exercise:</u>

Based on recent evidence, it appears that rises in circulating lactate concentrations are not a product of muscle hypoxia, as has been proposed [Wasserman K et al, 1964; 1967; 1973;

Karlsson J, 1971; Gautier H et al, 1978]. A number of investigators have argued that there is always an adequate oxygen supply to the muscle mitochondria during exercise [Jobsis FF et al, 1968; Holloszy JO, 1973; 1976; Chance B et al, 1978; Connett RJ et al, 1984; Stainsby WN et al, 1990]. Furthermore, a large part of the lactate formed by some muscle fibers is oxidized by other, more oxidative muscle fibers [Brooks GA, 1985].

Hence, the rises in blood lactate concentrations at work rates above the "second ventilatory threshold" may not necessarily indicate muscle hypoxia in non-steady state conditions [Jobsis FF et al, 1968; Brooks GA et al, 1984; Connett RJ et al, 1984; Gaesser GA et al, 1984; Mazzeo RS et al, 1986]. Instead, rises in blood lactate concentration may be due to a stimulation of glycogenolysis by rising plasma catecholamine concentrations [Issekutz B, 1984; Stainsby WN et al, 1987; Gregg SG et al, 1989; Brooks GA et al, 1991] or as a consequence of metabolic acidosis or both [Dennis SC et al, 1991].

c] Metabolic acidosis of high intensity exercise:

Metabolic acidosis at high work rates results from the acceleration of carbohydrate oxidation and the resultant increase in glycolytic ATP turnover. When ATP is resynthesized by glycolysis, rather than by creatine phosphate hydrolysis or oxidative phosphorylation, the hydrogen ions arising from its hydrolysis are not re-consumed in its resynthesis [Gevers W, 1977; Alberti KGMM et al, 1982; Hochachka PW et al, 1983; Dennis SC et al, 1991]. Since any acceleration of carbohydrate metabolism increases hydrogen ion production, rises in blood lactate concentration are more a consequence of, than a cause of, metabolic acidosis [Dennis SC et al, 1992]. When the capacity of the muscle to exchange intracellular hydrogen ions for extracellular sodium ions [Na^+] is exceeded, increases in cytosolic hydrogen ion concentration shift the lactate dehydrogenase and lactate permease equilibria towards lactate formation and hydrogen ion [H^+] + lactate co-efflux [Dennis SC et al, 1985; Walsh ML et al, 1988].

With the development of a progressive acidosis during exercise at work rates above the "second ventilatory threshold" , the pH of

skeletal muscle falls from about 7.0 to between 6.4 and 6.5 and arterial pH declines from 7.4 to about 7.2 [Hermansen L et al, 1972; Sahlin K, 1978] and this acidosis causes fatigue by combining with $H.PO_4^{2-}$ ions from net creatine phosphate breakdown to form $H_2PO_4^-$ ions. An increased $H_2PO_4^-$ ion concentration slows cross-bridge cycling [Jones NL, 1980; Mainwood GW et al, 1985], decreases tension-developing capacity [Fitts RH et al, 1976; Donaldson SKB et al, 1978; Fabiato A et al, 1978] and may also adversely affect sarcoplasmic reticulum function [Nakamaru Y et al, 1972; Fabiato A et al, 1978; Mandel F et al, 1982; Byrd SK et al, 1989].

A decreased pH may also decrease the activities of key glycolytic and oxidative enzymes [Newsholme EA et al, 1973; Jones NL, 1980; Sutton JR et al, 1981; Hochachka PW, 1983; Graham TE et al, 1986] but that probably follows the reduced demand for ATP arising from less cross-bridge cycling. Thus, the capacity for high intensity exercise probably depends as much on the removal of hydrogen ions from the muscles as on the delivery of oxygen [Jones NL, 1980].

Several studies have shown that metabolic acidosis reduces endurance time during high intensity exercise [Dennig H et al,

1931; Wenger HA et al, 1976; Jones NL et al, 1977; Jacobs I, 1986]. Significant relationships between time to fatigue and muscle pH have also been demonstrated during maximal exercise bouts [Fitts RH et al, 1976; Stevens ED, 1980].

In response to the metabolic acidosis of high intensity exercise, most healthy subjects hyperventilate to maintain acid-base balance [Davis JA et al, 1976; Reinhard U et al, 1979; Belman MJ et al, 1980; Caiozzo VJ et al, 1982]. H^+ ions in the blood combine with bicarbonate ions [HCO_3^-] to form carbon dioxide [CO_2] and water [H_2O] according to the following equation.

$$H^+ + HCO_3^- \longleftrightarrow H_2CO_3 \longleftrightarrow H_2O + CO_2$$

Higher arterial carbon dioxide tensions [$PaCO_2$] increase ventilation. The greater ventilation then "drives" off the excess carbon dioxide formed by the dissociation of H_2CO_3 and the pulmonary control mechanisms return the arterial carbon dioxide tension [$PaCO_2$] to its set-point of 40 mmHg or less [Wasserman K, 1984].

i] Accepted indicators of an adequate response by the pulmonary system for maintaining acid-base homeostasis during high intensity exercise:

The ventilatory equivalent for arterial carbon dioxide tension [$VE/PaCO_2$] is an accepted indicator of the adequacy of alveolar ventilation in meeting the body's metabolic needs [Severinghaus JW, 1965]. Values above 2 l/min/mmHg are considered to indicate adequate respiratory compensation.

The ventilatory equivalent for carbon dioxide expiration [VE/VCO_2] and oxygen consumption [VE/VO_2] are also used to define appropriate levels of ventilation. Values above 26 for the VE/VCO_2 ratio are considered to indicate hyperventilation [Flenley DC et al, 1983; Whipp BJ et al, 1984].

The VE/VO_2 ratio averages about 25 at work rates not associated with metabolic acidosis [Asmussen E, 1965; Wasserman K et al, 1967]. An increase in the VE/VCO_2 and VE/VO_2 ratios to values greater than 26 and 25 respectively are therefore believed to reflect an adequate respiratory compensation for metabolic acidosis [Wasserman K, 1984].

One theory therefore suggests that the healthy pulmonary control system shows a remarkably precise and efficient response to even severe exercise. Respiratory compensation for the developing metabolic acidosis of high intensity exercise seems to be complete. The added increment in ventilation exceeds that necessary to accommodate the increased rate of carbon dioxide production with a resultant decrease in $PaCO_2$. The result is that a continuous fall in arterial pH is constrained.

ii] <u>Inadequate compensatory hyperventilation as a possible cause of fatigue during high intensity exercise:</u>

In contrast, others have found that even the healthy pulmonary system may fail to maintain acid-base balance during intense exercise [Dempsey JA, 1986]. A failure of hydrogen ion homeostasis by the pulmonary system is shown by an increase in chemical stimuli without an adequate increase in ventilation resulting in arterial hypoxaemia with either normo- or

hypercapnia [Roussos C et al, 1982]. Dempsey JA et al, [1981], [1984] and Hopkins SR et al, [1989] have also reported an inappropriately low hyperventilatory response during exercise in some trained athletes despite severe metabolic acidosis and arterial hypoxaemia.

These researchers believe that there might be limits to the pulmonary system's homeostatic capabilities during high intensity exercise. They provide examples in which the compensatory hyperventilation for the developing metabolic acidosis associated with severe exercise was incomplete [Dempsey JA et al, 1981, 1984 and Hopkins SR et al, 1989]. The decrease in arterial carbon dioxide tension did not compensate for the developing metabolic acidosis. As a result pHa fell progressively during exercise until exhaustion. The result was that the pulmonary system allowed some error in its acid-base regulation in lieu of increasing the overall oxygen cost of exercise by increasing alveolar ventilation to achieve complete respiratory compensation for the metabolic acidosis.

Given these two opposing schools of thought, the purpose of this study was to examine the respiratory compensation for metabolic

acidosis during high intensity constant-load exercise at work rates above the "second ventilatory threshold" in an attempt to contribute towards resolving this controversy.

The study calculated the ventilatory equivalent for $PaCO_2$, VO_2 and VCO_2 as these ratios are accepted indicators of the adequacy of the respiratory compensation for the metabolic acidosis of exercise. Furthermore, measurements of arterialized venous carbon dioxide tension, pH and HCO_3^- concentrations were included to determine whether or not the respiratory compensation for the developing metabolic acidosis was sufficient to ensure acid-base homeostasis.

d] <u>The development and measurement of progressive dyspnoea during high intensity exercise at work rates above the "second ventilatory threshold":</u>

i] <u>The development of progressive dyspnoea:</u>

Dyspnoea is the sensation of increased respiratory effort, and is usually thought to be due to a combination of increased metabolic demand in the working muscles, increased ventilatory demand, increased rates of ventilation, increased impedance to breathing and reduced respiratory muscle power [Jones NL, 1984]. However, the precise mechanism by which respiratory effort is sensed remains poorly understood and direct experimental data are presently unavailable [Poon C, 1987]. It appears that sensory pathways relaying signals of respiratory effort are present as shown by the ability of human subjects to appreciate impediments to ventilation [Killian KJ et al, 1982] as well as their ability to accurately detect changes in lung volume, respiratory muscle force, and respiratory mechanical load [Zechman FW et al, 1986].

Although there is very little information at present regarding the importance of dyspnoea limiting constant-load exercise at high intensities, the consciousness of increased respiratory effort [Dockter R et al, 1971] may indicate the limit of one's endurance [Scharf S et al, 1984]. Furthermore, the development of dyspnoea during exercise might be the way in which ventilation acts as a sensory cue for the perception of effort [Mihevic P, 1981].

The "VE drift" during high intensity exercise might be a source of considerable discomfort in many subjects and may even cause a reduction in exercise tolerance [Hanson P et al, 1982; Whipp BJ, 1990]. It has been proposed that as ventilation increases, the only possible way to reduce breathlessness is to stop exercising. The level of ventilation is therefore optimized to minimize discomfort. The sensation of breathlessness may also be the stimulus that protects the respiratory muscles from fatigue [Killian KJ et al, 1982; El-Manshawi A et al, 1986; Scharf S et al, 1984].

Hyperventilation at exercise intensities above the "second ventilatory threshold" has been shown to be one contributor to the sensation of dyspnoea. Thus, exercise at work rates above the "second ventilatory threshold" in which high rates of ventilation are maintained and in which there is a continuous increase in sensations of respiratory effort may ultimately be limited by the development of progressive dyspnoea.

ii] <u>The measurement of dyspnoea:</u>

Breathlessness is difficult to quantify and its perception and description will differ from person to person. Many of the measurements of dyspnoea have been validated by psychophysical methods [Borg G et al, 1982]. The Borg scale was designed to describe the sensations of perceived exertion of physical effort and respiratory effort. The sensations of respiratory effort increase very little at low and moderate work rates but accelerate more rapidly at higher work rates.

Measurements during exercise allow quantification of the symptom of dyspnoea in terms of the balance between ventilatory demand and the ability to meet that demand with the maximum ventilatory volume [MVV]. This concept is expressed as the "dyspnoea index" viz:

$$\text{"DYSPNOEA INDEX"} = \frac{\text{VE in exercise}}{\text{MVV}} \times 100$$

The "dyspnoea index" often approximates 100% in patients with chronic obstructive pulmonary disease [Gandevia B, 1963; Cotes JE, 1979; Roussos C, 1982; Jones NL et al, 1990; Whipp BJ, 1990]. Values for the "dyspnoea index" recorded in the subjects during high intensity exercise at work rates above the "second ventilatory threshold" were compared with values reported in studies of patients with chronic obstructive pulmonary disease [COPD], whose exercise intolerance is thought to be exclusively due to shortness of breath [Roussos C, 1982].

The extent to which dyspnoea represents a true limitation to high intensity exercise at work rates above the "second ventilatory threshold", however, remains uncertain and awaits further investigation. Accordingly this study examined the ratings of perceived exertion for ventilation during constant-load high intensity exercise in an attempt to establish whether the intensity of dyspnoea limited further exercise.

2.4 Respiratory muscle fatigue:

Another possible mechanism by which the pulmonary system might

limit exercise of very high intensity could be through the development of respiratory muscle fatigue.

a] Physiological and biochemical characteristics of the respiratory muscles:

The work of the respiratory muscles consists primarily of overcoming elastic resistance and the flow-resistive forces. A number of factors determine the energy expenditure of the respiratory muscles; these include the frequency of contraction, the magnitude of pressure development and the velocity of shortening [Åstrand P-O, 1977].

Respiratory muscles, especially the diaphragm, differ from locomotor muscles in that their biochemical and electromechanical characteristics are much closer to those of cardiac muscle [Derenne P et al, 1978; Aubier M et al, 1985, 1986; Dempsey JA et al 1986; Gosselin LE et al, 1988; Viires N et al, 1988]. The diaphragm has an oxidative capacity and capillary density which is 2 - 3 times that of slow-twitch locomotor muscle. It also has a high capacity for lactate oxidation during high intensity exercise [Rochester DF et al, 1979; Saltin B et al, 1983 and Fregosi RF et al, 1984].

b] Respiratory muscle fatigue during exercise:

The literature on respiratory muscle fatigue during exercise is abundant, but inconclusive. Questions still exist as to (i) whether respiratory muscle fatigue occurs during intense exercise in healthy subjects, and if so, (ii) whether it actually limits exercise capacity and (iii) whether exercise performance could be improved if the endurance of the respiratory muscles was improved with training.

In addition, studies have used a wide variety of methods to assess respiratory muscle fatigue which makes it difficult to compare results.

The identification of respiratory muscle fatigue ultimately depends on the demonstration of a decrease in force development by the respiratory muscles which could lead to a decreased capacity to maintain or increase alveolar ventilation appropriately [Roussos C et al, 1982].

The different measurements used include electromyograms recorded from oesophageal or chest electrodes, recording the intensity of

dyspnoea, measurements of maximal inspiratory and expiratory pressure developed by the respiratory muscles against an occluded airway and the maximal voluntary ventilation test [MVV].

Some authors failed to show respiratory muscle fatigue after short-term exercise of high intensity [Bender PL et al, 1985; Anholm JD et al, 1989]. Bender PL et al, [1985] found that a 3 - 10 minute run to exhaustion did not change the ability to ventilate maximally but that this capacity declined only in long-term exhaustive exercise lasting 60 minutes. Similarly Anholm JD et al, [1989] also showed that there was no decrement in the MVV of highly trained elite athletes after short-term exhaustive exercise.

In contrast, others have provided experimental evidence to suggest that respiratory muscles may fatigue during severe exercise [Bye PTP et al, 1984; Martin BJ et al, 1984] as well as during a marathon [Loke J et al, 1982] and ultramarathon running race [Warren GL et al, 1989].

Bye PTP et al, [1984] noted a decreased maximal transdiaphragmatic pressure following high intensity short-term maximum exercise in highly trained athletes. They interpreted

this as an indication of a decreased capacity for force development by the respiratory muscles. Compensatory hyperventilation during maximum exercise was absent and respiratory muscle fatigue was considered to be the explanation for this phenomenon.

Martin BJ et al, [1982] provided indirect evidence that respiratory muscle fatigue could contribute to exercise limitations in normal humans. Short-term maximal running performance was reduced in subjects who had undergone a period of prior ventilatory work in the form of prolonged hyperpnea. This work consisted of 150 min of sustained ventilation performed isocapnically. Subjects maintained about 2/3 of their 12s MVV during the breathing test. Subjects also ceased exercise at significantly lower rates of ventilation [117 vs 124 l/min, BPTS; $P < 0.05$] during maximal running after ventilatory work. Martin BJ et al, [1982] concluded that reduced respiratory muscle endurance alone was sufficient to decrease short-term maximal running performance.

Loke J et al, [1982] found $\pm$ 10% decreases in the 15 s MVV and maximal inspiratory and expiratory pressures after marathon running, again suggesting respiratory muscle fatigue.

Warren GL et al, [1989] estimated that decrements in respiratory muscle endurance may have limited exercise performance in a 24-hour ultramarathon. They demonstrated a 17% decrease in MVV after 24 hours of running. They hypothesized that the decline in running speed during the ultramarathon may be explained, in part, by respiratory muscle fatigue as the variance in MVV accounted for about 39% ($P < 0.0001$) of the variance of running speed. They therefore concluded that the decrease in respiratory muscle endurance may constrain running speed in extremely prolonged running events.

In addition, several studies have shown that high levels of ventilation cannot be continued indefinitely and that attempts to maintain high levels of ventilation [55 - 80% of MVV] are associated with the development of respiratory muscle fatigue.

Bai TR et al, [1984] recorded a decrease in maximal inspiratory and transdiaphragmatic strength posthyperpnea at 76 and 79% MVV. Data from Zocche GP et al, [1960]; Tenney SM et al, [1968]; Freedman S, [1970] indicated that ventilation rates of 50 - 60% of MVV could be maintained for fifteen minutes, whereas Wilson SH et al, [1984] showed electromyographic evidence of ventilatory muscle fatigue

when ventilation was sustained at more than 65% of the maximal voluntary ventilation for 10 minutes or more.

c] Respiratory muscle training:

Furthermore, several studies have shown that respiratory muscle training increases exercise tolerance in subjects with normal lung function [Leith DE et al, 1976; Robinson EP et al, 1982; Coast JR et al, 1987] and in patients with lung disease [Pardy RL et al, 1981; Sonne LJ et al, 1982; Belman MJ et al, 1988]. Leith DE et al, [1976] were able to show increased strength and endurance of the respiratory muscles after a 5-wk programme designed specifically to train the respiratory muscles. They found an approximate 14% increase in the MVV after respiratory muscle endurance training in the form of voluntary normocapnic hyperpnea to exhaustion [30 - 45 min each day, 5 days a week].

Robinson EP et al, [1982], found significant improvements in respiratory muscle endurance after a 10- to 20-week physical

fitness program. Subjects showed a significant increase in both maximal sustainable ventilatory capacity lasting 15 minutes and MVV. There was no increase in the control group and they suggested that these data indicate that running training can improve respiratory muscle strength and endurance in healthy, previously sedentary individuals.

Coast JR et al, [1987], [1990] measured maximal inspiratory pressures in a group of sedentary students and a group of US national class cross-country skiers immediately after a maximal exercise test. In the sedentary students there was a significant drop in maximal inspiratory pressure compared to that measured before exercise, whereas the skiers did not show any reduction in this pressure.

These observations are consistent with the hypothesis that the untrained subjects developed inspiratory muscle fatigue following maximal exercise, whereas the trained subjects were able to maintain normal inspiratory muscle function due to a training effect on the respiratory muscles induced by chronic high intensity exercise training. Furthermore, these findings also suggest that differences in training status may influence the results of breathing tests performed in different subject groups.

Both strength and endurance of the respiratory muscles have been shown to be improved by breathing training against inspiratory resistance.

Belman MJ et al, [1988] and Sonne LJ et al, [1982] studied patients with COPD and found that resistive respiratory muscle training improved both respiratory muscle strength and endurance. Pardy RL et al, [1981] examined the exercise capacity of COPD patients after respiratory muscle training and also found an improvement in exercise capacity.

In summary, the possibility that exercise is terminated because the limits of ventilation are reached, has traditionally been dismissed as peak ventilation during maximal exercise never reaches or even approaches the maximal exercise ventilatory capacity measured by tests of maximal voluntary ventilation [Freedman S, 1970; Martin BJ et al, 1981; Brooks GA et al, 1984]. However, there is a body of evidence showing that respiratory muscle fatigue may develop during prolonged high intensity exercise when high levels of ventilation are maintained.

The following issues make it difficult to compare reported results: Firstly, a wide variety of experimental methods have

been used to assess respiratory muscle fatigue; secondly, different exercise modes were used. Whilst some studies have failed to show respiratory muscle fatigue after short-term exercise [Bender PL et al, 1985; Anholm JD et al, 1989], others have provided evidence which indicated the development of respiratory muscle fatigue during and after prolonged high intensity exercise [Bye PTP et al, 1984; Martin BJ et al, 1984; Loke J et al, 1982 and Warren GL et al, 1989] or after maximal exercise [Coast JR et al, 1987].

Further support for the possible development of respiratory muscle fatigue is supplied by studies showing that training improved both respiratory muscle strength and endurance [Belman MJ et al, 1988; Coast JR et al, 1990; Sonne LJ et al, 1982 and Pardy RL et al, 1981]. However, the effect of respiratory muscle training on exercise tolerance and its relative contribution to athletic [whole body] performance in the healthy remains unknown.

This study therefore investigated whether or not the high rates of ventilation achieved during high intensity constant-load exercise caused significant respiratory muscle fatigue that could lead to the termination of exercise. Specifically this was

achieved by comparing maximal voluntary ventilation over 20 seconds after exercise [MVVPOST-EX] to MVV before exercise [MVVREST] and to ventilation during exercise.

2.5 Conclusion:

Exercise capacity is not generally considered to be limited by the pulmonary system in healthy subjects. The response of the healthy pulmonary system to the substantial physiological requirements of exercise at or below the "second ventilatory threshold" usually maintains homeostasis. But, the functional capacity of the pulmonary system may be exceeded and or compromised during high intensity constant-load exercise at work rates above the "second ventilatory threshold". Under those conditions, the following limitations to exercise performance need to be considered:

1. One of the prime functions of the pulmonary system during exercise is to supply oxygen to the working muscles via the

circulatory system. The requirements for pulmonary gas exchange increase with severe sustained exercise and the pulmonary system may fail indirectly if the additional oxygen provided by an increased ventilation was used exclusively by the respiratory muscles, rather than the active skeletal muscles. The metabolic cost of ventilation may therefore limit oxygen transport to the locomotor muscle and thus play a role in restricting endurance during high intensity constant-load exercise.

2. The imprecise regulation of arterial carbon dioxide tension and pHa [acid-base homeostasis] appears to be another possible limitation to exercise performance. The pulmonary system may fail to increase alveolar ventilation sufficiently to achieve a complete respiratory compensation for the developing metabolic acidosis. It may rather accept some error in acid-base regulation possibly due to respiratory muscle fatigue instead of increasing the energy cost of ventilation. The more severe acidosis would be expected to impair exercise performance.

3. Furthermore, respiratory muscle fatigue may occur prior to, or coincide with the termination of exercise leading to an

absence of compensatory hyperventilation, resulting in hypercapnia and hypoxaemia. Consequently, respiratory muscle fatigue may be a factor limiting high intensity exercise.

4. A limiting factor to exercise capacity at exercise intensities above the "second ventilatory threshold" may be the discomfort associated with the act of breathing. There is a continuous increase in sensations of respiratory effort during prolonged high intensity exercise during which high levels of ventilation are maintained. The only possible option to reduce breathlessness, is to terminate the exercise.

So, in healthy subjects, there is a possibility that as high intensity exercise is prolonged and metabolic demands are rising (i) the oxygen supply to the working skeletal muscles becomes limiting; (ii) the pulmonary system becomes less capable of providing complete respiratory compensation for the developing metabolic acidosis; (iii) fatigue of the respiratory muscles results in an inadequate alveolar ventilation leading to hypercapnia and hypoxaemia; and (iv) progressive dyspnoea develops that may limit exercise tolerance.

Despite numerous studies, the question of whether or not high intensity constant-load exercise is limited by the pulmonary system is not resolved. The present study was therefore undertaken to reevaluate some aspects of pulmonary function, in particular, oxygen supply to the working skeletal muscles, respiratory compensation for the developing metabolic acidosis, respiratory muscle fatigue and dyspnoea during exercise at 70% WR max [80 - 85% VO_2 max] and 80% WR max [85 - 90% VO_2 max] to determine whether or not the pulmonary system may limit endurance in high intensity exercise.

CHAPTER 3

METHODS

Arterialized venous blood gas tensions, acid-base status, pulmonary gas exchange and respiratory muscle endurance during two cycle ergometer constant-load tests at 70% and 80% WR max were examined in 10 subjects [9 males; 1 female] who volunteered to participate in the study. All protocols were approved by the Ethics and Research Committee of the Faculty of Medicine of the University of Cape Town. All subjects were active in physically demanding sporting activities and were comfortable with the bicycle ergometer. None of the subjects smoked or had any history of exercise-induced asthma or other pulmonary diseases.

The individual physiological characteristics of the subjects are listed in Table 3.1. On arrival all subjects were weighed on an Avery scale [Birmingham, England] so that absolute VO_2 max values [described later] could be corrected for differences in body mass.

3.1 Lung function tests:

Table 3.1 Physiological characteristics of the subjects participating in either the 70% or 80% WR max constant-load cycle test or both.

Subject No	Gender M/F	Age [yrs]	Weight [Kg]	70% WR max [Watts]	80% WR max [Watts]	WR max [Watts]	VO_2max [ml/kg/min]
1	M	22	71		335	400	62
2	M	30	77		260	325	56
3	M	33	77	250	290	360	58
4	M	26	55		275	345	71
5	F	30	50	220	245	310	60
6	M	19	65		245	310	62
7	M	33	67	210	230	290	57
8	M	18	66		260	325	60
9	M	27	68	250		355	63
10	M	35	73	240		340	53
Mean		27	67	234	268	335	60
S.D.		±6	±8	±18	±33	±30	±5

Key: WR = work rate; VO_2 max = maximal oxygen consumption.

All subjects performed a series of pre-exercise 20 second maximal voluntary ventilation tests [MVV]. MVV is the maximal volume of gas in liters that a subject can ventilate over a given time. This test measures the endurance and force development of the ventilatory muscles [Belman MJ et al, 1980]. MVV is usually determined over 12s or 15s and the volume of expired gas in liters is multiplied by five or four to obtain the MVV in l/min [Taylor AE et al, 1989]. In this study, however, a more prolonged 20s MVV test was selected as being more appropriate for the high intensity exercise that was studied over 13 to 22 minutes. During the maximal voluntary ventilation test, the subjects were given verbal encouragement throughout. Tests were repeated on 3 different occasions and the highest value was taken as the maximum resting voluntary ventilation [MVVREST].

3.2 Measurement of maximal oxygen consumption [VO_2 max]:

Preliminary tests also included the measurement of each subject's maximal oxygen uptake [VO_2 max], peak ventilation [Vi max] and

maximum work rate [WR max] on an electronically braked cycle ergometer [Godart NV, Bilthoven, Holland]. In these tests, the initial work rate was 115 W, and, thereafter, the work rate was increased by 15 W every minute. The pedaling frequency was selected according to the preference of the subject and, in part, from recommendations of previous investigators [Hagberg JM et al, 1981].

During the VO_2 max tests, subjects cycled with a noseclip and inspired air from a Hans Rudolph 2700 [Vacumed, Ventura, CA] one-way valve connected to a Mijnhardt dry gas meter. Expired air was passed through a 15 l baffled mixing chamber and a condensation coil to Ametek N_2 - 22 M O_2 and CD - 3 A CO_2 gas analyzers [Thermox Instruments, Pittsburgh, P.A.]

Before each test the gasmeter was calibrated with a Hans Rudolph 5530 3l syringe and the analyzers were set with air and a 4% CO_2, 16% O_2, 80% N_2 mixture. Instrument outputs were processed by an on-line IBM PC computer which calculated the average Vi, VO_2 and VCO_2 each minute using conventional equations [McArdle WD, 1986]. Maximum VO_2 was achieved when the subject failed to continue exercising despite loud, verbal encouragement. The results of these tests were used to calculate

a workload which represented 70% and 80% of WR max for more continued exercise.

3.3 Measurement of blood lactate concentration:

For measurements of venous blood lactate concentrations, an Abbocath-T intravenous catheter unit [Abbott Ireland, Ltd., Sligo, Republic of Ireland] was fitted with a 3-way stopcock [Braun Melsungen AG D-3508, Melsungen, Germany] and inserted into a subcutaneous forearm vein. In order to keep the catheter and stopcock patent a sterile saline solution, $\pm$ 4 ml [Sabax Sodium Chloride 0.9%, Sabax Ltd., Johannesburg, South Africa] containing Sodium Heparin [5 U/ml] [Pularin, Allen & Hanburys, Wadeville, South Africa] was infused every one to two minutes.

Blood samples for lactate assays were collected every minute during exercise and a 0.5 ml aliquot was immediately added to tubes containing 1 ml of 0.6N perchloric acid [PCA] and stored on ice for the duration of the test. At the end of the test, the deproteinized samples were spun in a Sigma-302 K centrifuge [Sigma, West Germany] at 2200 rpm for 12 minutes and the supernatant was removed and frozen for later analysis of

the lactate concentration by standard enzymatic spectrophotometric procedures [HH Bergmeyer, 1974].

3.4 Heart rate measurement:

Prior to the VO_2 max tests disposable electrodes were placed on the chests of the subjects in a CM5 configuration, and heart rates were recorded every minute during exercise using a Life Tracer 12 monitor [M607 Lohmeier, Germany].

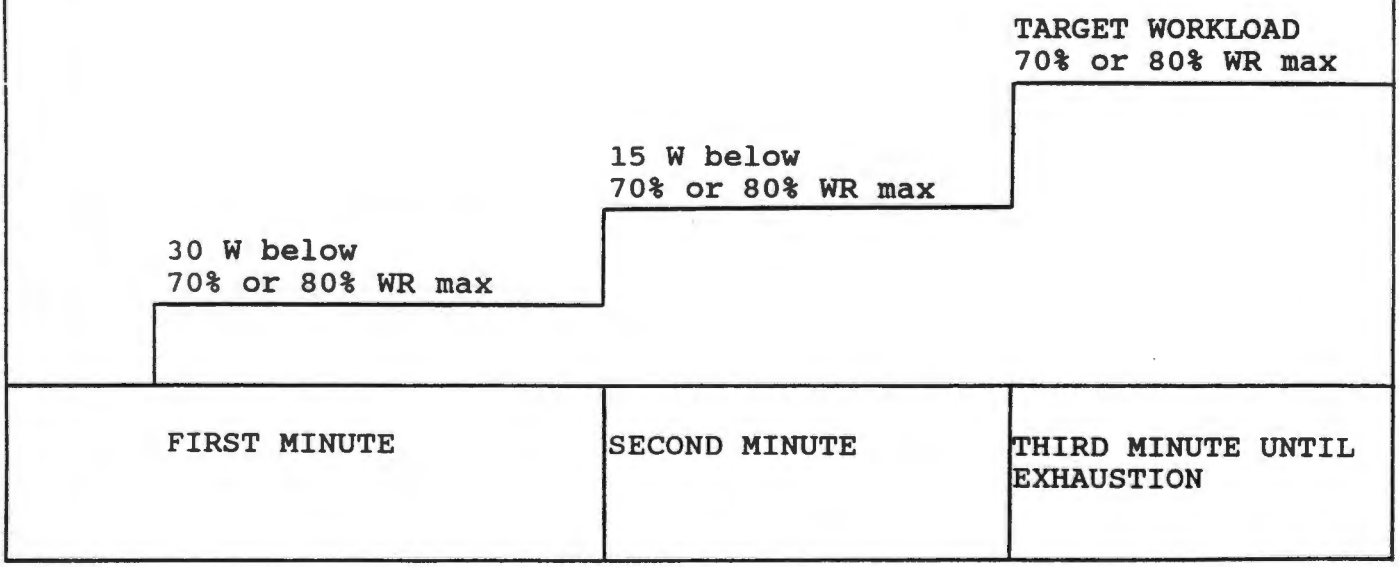
3.5 70% AND 80% WR max exercise tests:

Within 2 weeks of the VO_2 max tests, subjects rode at workloads corresponding to either 70% of WR max or 80% WR max on separate occasions. Five of the ten subjects completed the 70% WR max

exercise test, eight of the ten subjects completed the 80% WR max exercise test and three of the subjects completed both the 70% and 80% WR max exercise tests [Table 3.1].

The 70% and 80% WR max tests were started at 30 W below the target work rate. The work rate was then increased by 15 W per minute over the next two minutes until the target constant work rate of 70% and 80% WR max was reached in the third minute. Thereafter the work rate remained constant until the subject became exhausted [Figure 3.1].

Figure 3.1 Protocol for 70% or 80% WR max constant-load cycle ergometer exercise until exhaustion.



3.6 Ratings of perceived exertion for effort and for ventilatory effort:

Measurements of respiratory variables and heart rate during these tests were performed in the same way as described for the VO_2 max tests. In addition ratings of perceived exertion [RPE] and ratings of ventilatory effort [RVE] using the new category Borg scale [Borg GAV, 1982] were recorded every minute [Appendix 1]. The instructions for using the single numbered rating scale and signaling the value with fingers were explained prior to each exercise test.

3.7 Blood gas tensions and acid-base status:

In addition to the collection of venous blood lactate samples, as described previously, "arterialized" venous blood samples were also collected from a cannula in one of the superficial dorsal hand veins [near dorsal arch] every 5 minutes during the 70% WR max test and every minute during the 80% WR max test.

"Arterialized" venous blood was obtained by warming the arm and the sampling site for 10 minutes prior to and during exercise with a heating pad. This method of arterialization is reported to permit an accurate estimation of arterial carbon dioxide tension, pH and HCO_3^- ion concentrations [Forster HV, et al 1972].

Blood samples were drawn in 1 ml heparinized [B-D, Tuberculin] plastic syringes which were immediately sealed and stored on ice to minimize gas exchange with air. Within 15 - 30 minutes of the test, the samples were taken for measurements of arterialized venous carbon dioxide tension, pH, bicarbonate ion concentrations, buffer base [whole blood] and base excess [whole blood] using an Instrumentation Laboratories 11 System 1302 automated pH/blood gas analyzer [Protea Electro Medical, Cape Town]. This analyzer was calibrated automatically with pH, 7.284 - 7.484 and pH 6.740 - 6.940 buffers and, CO_2 4.5 - 5.5% / O_2 10.00% - 99.9% and CO_2 9.00% - 11.00% / O_2 0.00% - 3.00% gas mixtures.

Buffer base and base excess were measured as an index of the developing metabolic acidosis during both work rates. Reductions in buffer base [BB], base excess [BE] and bicarbonate ion concentration indicate metabolic acidosis [Murray JF et al, 1986].

Resting oxygenated whole blood buffer base values ranging between 46 - 54 mEq/l and are the sum of the HCO_3^- and protein buffering by principally hemoglobin. Equivalent base excess values range between 0 $\pm$ 2 mEq/l and are the difference between the observed total buffer base and the "normal" buffer base value taking into account the total hemoglobin content [Gardner MLG, 1978].

3.8 Methods for quantifying "excess" ventilation:

In an attempt to quantify the "excess" ventilation stimulated by metabolic acidosis the Vi/VCO_2 ratio was quantified during the two exercise tests. Vi/VCO_2 ratios were used in preference to the VE/VO_2 equivalent described by Koyal SN et al, [1976] as changes in ventilation follow changes in VCO_2 more closely than changes in VO_2 [Wasserman K et al, 1975; Walsh ML et al, 1988]. Minute ventilation is more or less linearly related to VCO_2 at work rates not associated with a significant ventilatory compensation for metabolic acidosis [Wasserman K, 1978; Wasserman K et al, 1990; Whipp BJ et al, 1980; Dempsey JA

et al, 1985]. Under these conditions, Vi/VCO_2 averages 26 units [Whipp BJ et al, 1984 and Flenley DC et al, 1983] and is termed the "predicted" ventilation.

Increases in the Vi/VCO_2 ratios above the "predicted" Vi/VCO_2 ratio of 26 at high work rates are thought to represent a respiratory compensation for the metabolic acidosis and an example of such data is given in Figure 3.2.

3.9 Post-exercise maximal voluntary ventilation test:

In the minute after exercise, post-exercise MVV [MVVPOST-EX] was recorded as described previously. In addition post-exercise MVV was measured on four separate occasions after completion of 4 different 80% WR max tests within one week of each other, first at 5 minutes, then 10, with the 15th and 20th minute values recorded during the 3rd and 4th trial respectively. Subjects were requested to perform these additional tests on separate occasions as MVV tests performed one after the other on the same day following a single 80% WR max test could result in lower recorded MVV values. Subjects may experience unpleasant symptoms as a result of decreases in $PaCO_2$ due to hyperventilation. The results of these tests were used to investigate whether maximal ventilation declines after high intensity exercise as a result of

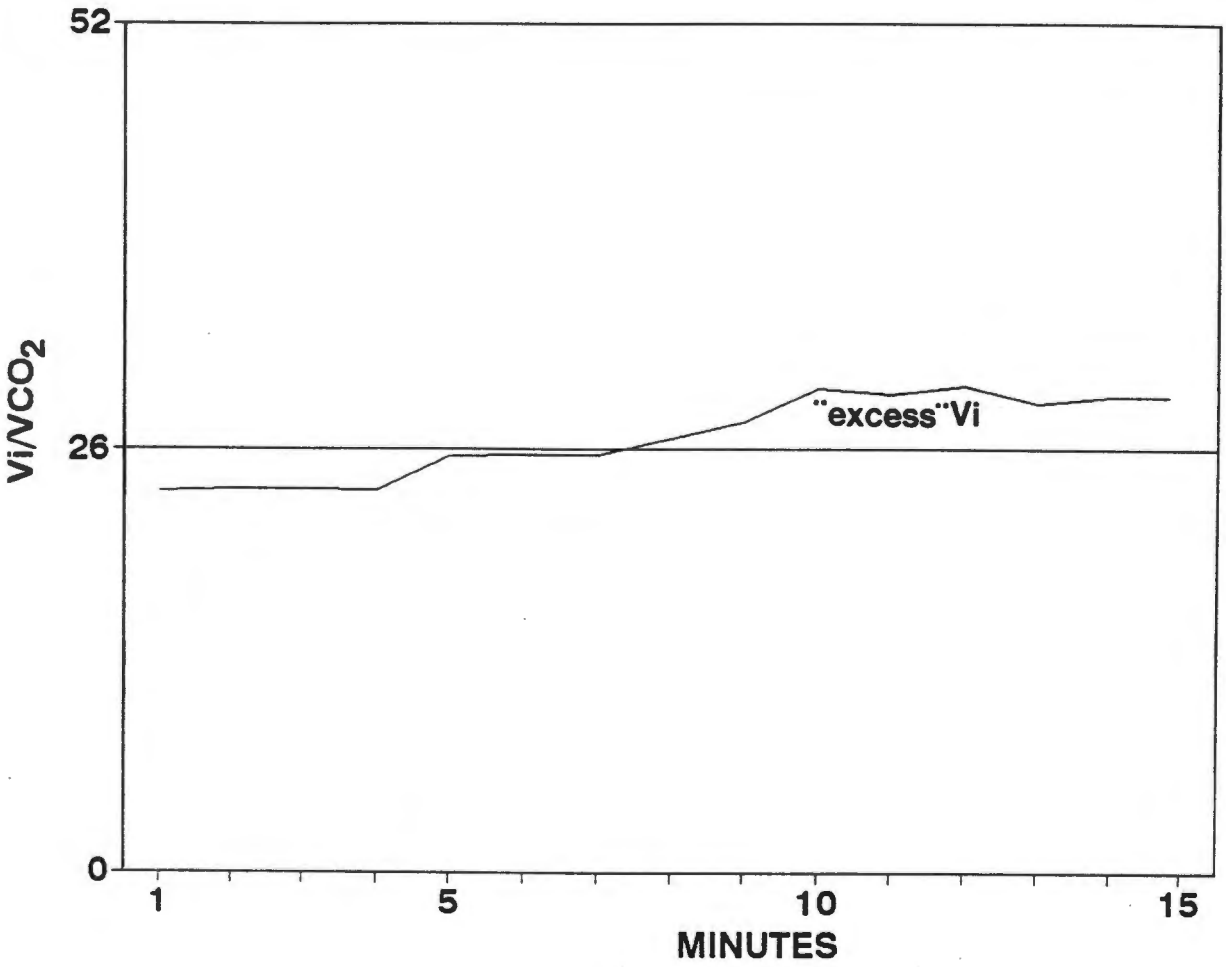


Figure 3.2 An example of "excess" Vi during constant-load cycling exercise at 80% WR max. "Excess" Vi is the difference between the measured Vi/VCO_2 ratio and that which would be predicted for a given VCO_2 at low work rates described in the text.

respiratory muscle fatigue. Only 4 of the 8 subjects participating in the 80% WR max test completed this time-consuming section of the study successfully as explained in Chapter Five [Section 5.7].

3.10 Reasons for stopping the exercise test:

Following the post-exercise maximal voluntary ventilation test, the subjects were asked in a non-leading fashion their reasons for stopping the test. Specifically the questions were:

1. Did you stop exercising because of shortness of breath?
2. Did you stop exercising because of generalized fatigue?
3. Did you stop exercising because of leg fatigue?

3.11 Statistical analysis:

Statistical significance over time ($P < 0.05$) was assessed by a one-way analysis of variance for repeated measures. Comparisons between 70% and 80% WR max tests were made with an unpaired Student's t test using two-tailed values of P.

CHAPTER 4

RESPIRATORY RESPONSES AND ACID-BASE BALANCE DURING HIGH INTENSITY CONSTANT-LOAD EXERCISE AT 70% WR max

4.1 Introduction:

This section of the study was undertaken to investigate whether pulmonary function becomes limiting during high intensity constant-load exercise corresponding to 70% WR max. In order to investigate whether the oxygen supply was sufficient and whether progressive dyspnoea could contribute to the termination of exercise, respiratory variables [Vi, VO_2, VCO_2] were measured throughout exercise. At 5 minute intervals, arterialized venous blood gas tensions and acid-base status were also measured to examine whether the increase in ventilation was adequate to cause a decline in $PaCO_2$ and to constrain a fall in pHa thereby ensuring full respiratory compensation for the developing metabolic acidosis associated with this intensity of exercise.

In order to establish whether respiratory muscle fatigue caused

the subjects to terminate exercise at this workload, maximal voluntary ventilation tests were performed before and after the completion of the exercise bouts.

4.2 Subjects:

Five of the ten subjects in the study exercised at a work rate representing 70% of the maximum work rate recorded during the preliminary VO_2 max test as described in Chapter Three. At this work rate, subjects were able to cycle for between 22 - 25 minutes.

These subjects' individual physiological characteristics and their physiological responses in the progressive VO_2 max tests and in the constant-load exercise at 70% WR max tests are listed in Table 4.1.

4.3 Results:

a. Respiratory variables:

Table 4.1 Physiological characteristics of 5 subjects measured at exhaustion during a maximal oxygen consumption [VO_2max] and a 70% WR max test.

Subject No.	Gender M/F	Age [yrs]	Weight [kg]	VO_2max [ml/kg/min]	VO_2 [l/min]	WR max [Watts]	Vi max [l/min]	70% VO_2 [ml/kg/min]	70% VO_2 [l/min]	70% WR max [Watts]	70% Vi [l/min]	Heart rate max [b/min]
3	M	33	77	58	4.5	360	113	48	3.7	250	82	193
5	F	30	50	60	3.0	310	115	48	2.4	220	78	195
7	M	33	67	57	3.8	290	123	51	3.4	210	94	194
9	M	27	68	63	4.3	355	126	53	3.6	250	93	187
10	M	36	73	53	3.9	340	113	52	3.8	240	105	191
Mean		32	67	58	3.9	330	118	51	3.4	234	90	192
S.D.		±3	±9	±3	±0.5	±30	±5	±2	±0.5	±18	±9	±2.9

Figure 4.1 shows that ventilation [Vi] increased fairly rapidly to 77.7 $\pm$ 5.6 l/min in the 5th minute and, thereafter, rose more gradually to 94.6 $\pm$ 8.8 l/min ($P < 0.05$) in the 22nd minute. At this point two of the five subjects could no longer continue exercising.

Measurements of VO_2, VCO_2 and RER during the 70% WR max exercise test are presented in Figure 4.2 and Table 4.2. At this workload VO_2 represented about 80 - 85% VO_2max and remained relatively constant throughout the exercise bout ranging from 3.1 $\pm$ 0.3 l/min in the 5th minute to 3.2 $\pm$ 0.4 l/min in the 20th minute. VCO_2 also remained constant after 5 minutes of exercise, ranging from 3.2 $\pm$ 0.3 l/min in the 5th minute to 3.1 $\pm$ 0.5 l/min in the 20th minute. RER rose to 0.98 $\pm$ 0.5 in the 10th minute and remained close to this value until the end of exercise. After 10 minutes, heart rates also remained steady and stayed close to the 10 minute value of 178 $\pm$ 9.9 beats/min.

The relationship between Vi and arterialized venous carbon dioxide tension [$PaCO_2$] is shown in Figure 4.3. The significant increase in ventilation in the first 10 minutes of exercise was associated with a decrease in $PaCO_2$ from a resting value of 46.0 $\pm$ 3.2 mmHg to 36.8 $\pm$ 4.7 mmHg within the first 10 minutes of exercise ($P < 0.05$).

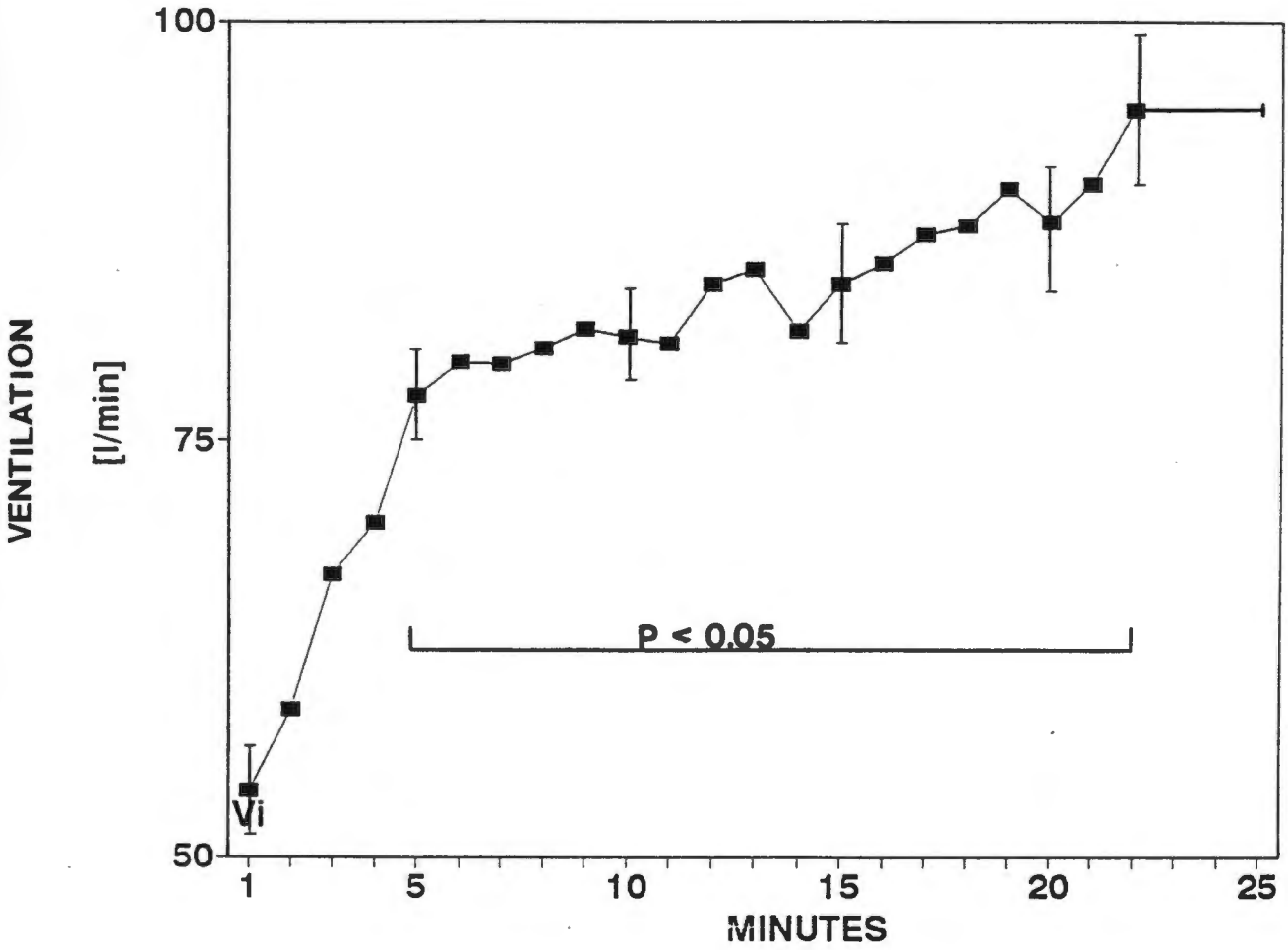


Figure 4.1 Changes in mean minute ventilation [Vi] with time during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

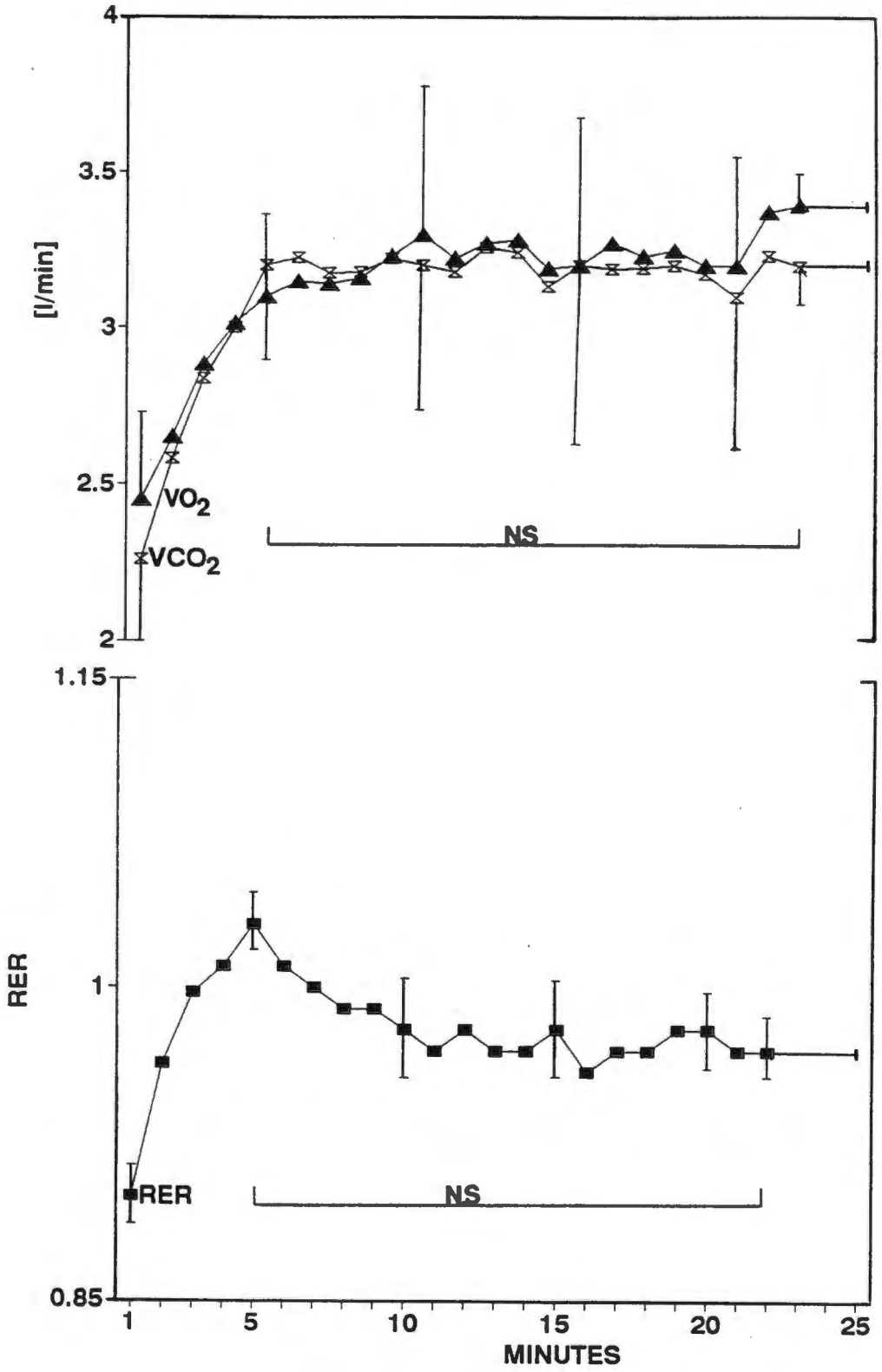


Figure 4.2 Changes in oxygen consumption [VO_2], carbon dioxide expiration [VCO_2] and respiratory exchange ratio [RER] with time during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

Table 4.2 Measures of ventilatory variables and heart rate during high intensity constant-load cycling exercise at 70% WR max until exhaustion

Time [minutes]	5	10	15	20	22
Vi [l/min]	77.7 ±5.6	81.1 ±5.6	84.2 ±7.4	87.9 ±7.2	94.6 ±8.8
RER	1.03 ±0.03	0.98 ±0.05	0.98 ±0.05	0.98 ±0.04	0.97 ±0.03
VO_2 [l/min]	3.1 ±0.3	3.3 ±0.5	3.2 ±0.5	3.2 ±0.4	3.4 ±0.1
VCO_2 [l/min]	3.2 ±0.3	3.2 ±0.5	3.2 ±0.6	3.1 ±0.5	3.2 ±0.1
Heart rate [Beats/min]	170 ±12.9	178 ±9.9	179 ±6.8	184 ±7.7	179 ±6.8

Values are means ± SD; n = 5; Vi, ventilation; RER, respiratory exchange ratio; VO_2, oxygen consumption; VCO_2, carbon dioxide expiration.

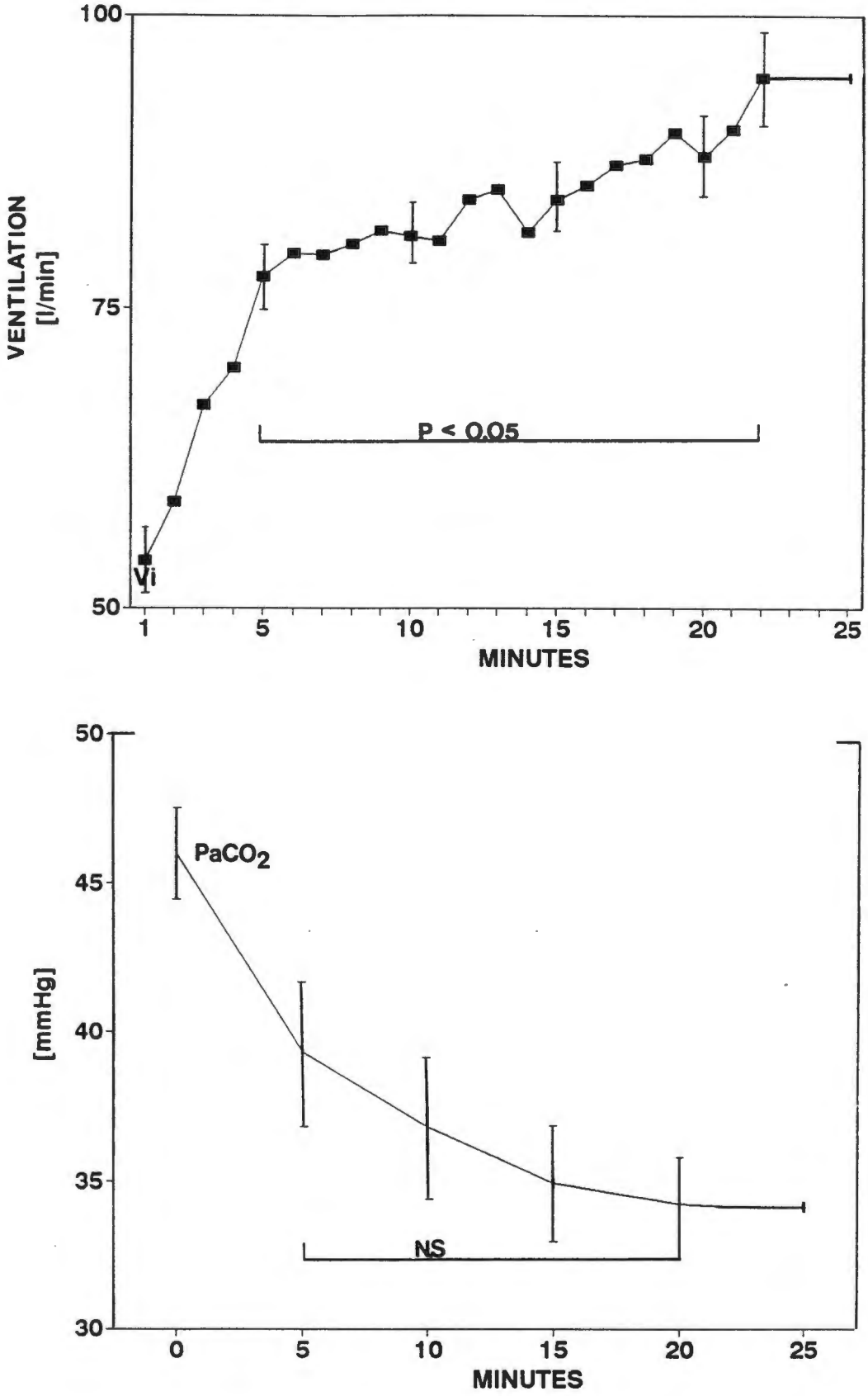


Figure 4.3 The reciprocal temporal relationship between mean minute ventilation [Vi] and arterialized venous carbon dioxide tension [$PaCO_2$] during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

Table 4.3 shows the changes in $Vi/PaCO_2$, Vi/VCO_2, Vi/VO_2 and Vi/HCO_3^- ratios. All ratios showed a steady increase from the 5th minute to the 20th minute of exercise. $Vi/PaCO_2$ and Vi/HCO_3^- ratios increased significantly during this time ($P < 0.05$). Changes in $PaCO_2$ and HCO_3^- concentrations are given in more detail later in Table 4.4.

Furthermore, Vi/VCO_2 values in excess of 26.0 ± 4.9 were recorded after the 10th minute of exercise and increased to values of 28.7 ± 4.1 in the 20th minute of exercise [Table 4.3]. This "excess" in ventilation indicated by Vi/VCO_2 values greater than the predicted value of 26, is explained in Chapter Three and shown in Figure 4.4.

b. Blood variables:

Again means and standard deviations of the blood measurements during the 20 - 25 minute cycle at 70% WR max to exhaustion are only reported until the 20th minute as [i] two of the five subjects stopped exercise at the beginning of the 23rd minute

Table 4.3 Changes in $Vi/PaCO_2$, Vi/VCO_2, Vi/VO_2 and Vi/HCO_3^- ratio with time during high intensity constant-load cycling exercise at 70% WR max until exhaustion.

Time [minutes]	5	10	15	20
$Vi/PaCO_2$ [l/min/mmHg]	2.0 ±0.3	2.3 ±0.3	2.5 ±0.3	2.6 ±0.3
Vi/VCO_2	24.0 ±4.4	26.2 ±4.9	27.2 ±4.1	28.7 ±4.1
Vi/VO_2	25.0 ±4.5	25.7 ±3.7	26.4 ±3.1	28.0 ±3.2
Vi/HCO_3^- [l^2/min/mmol]	3.8 ±0.5	4.5 ±0.8	4.9 ±0.3	5.1 ±0.3

Values are means ± SD; n = 5; Vi, ventilation volume; VCO_2 rates of carbon dioxide expiration; VO_2, rates of oxygen consumption; $PaCO_2$, arterialized venous carbon dioxide tension; HCO_3^-, arterialized venous bicarbonate ion concentration.

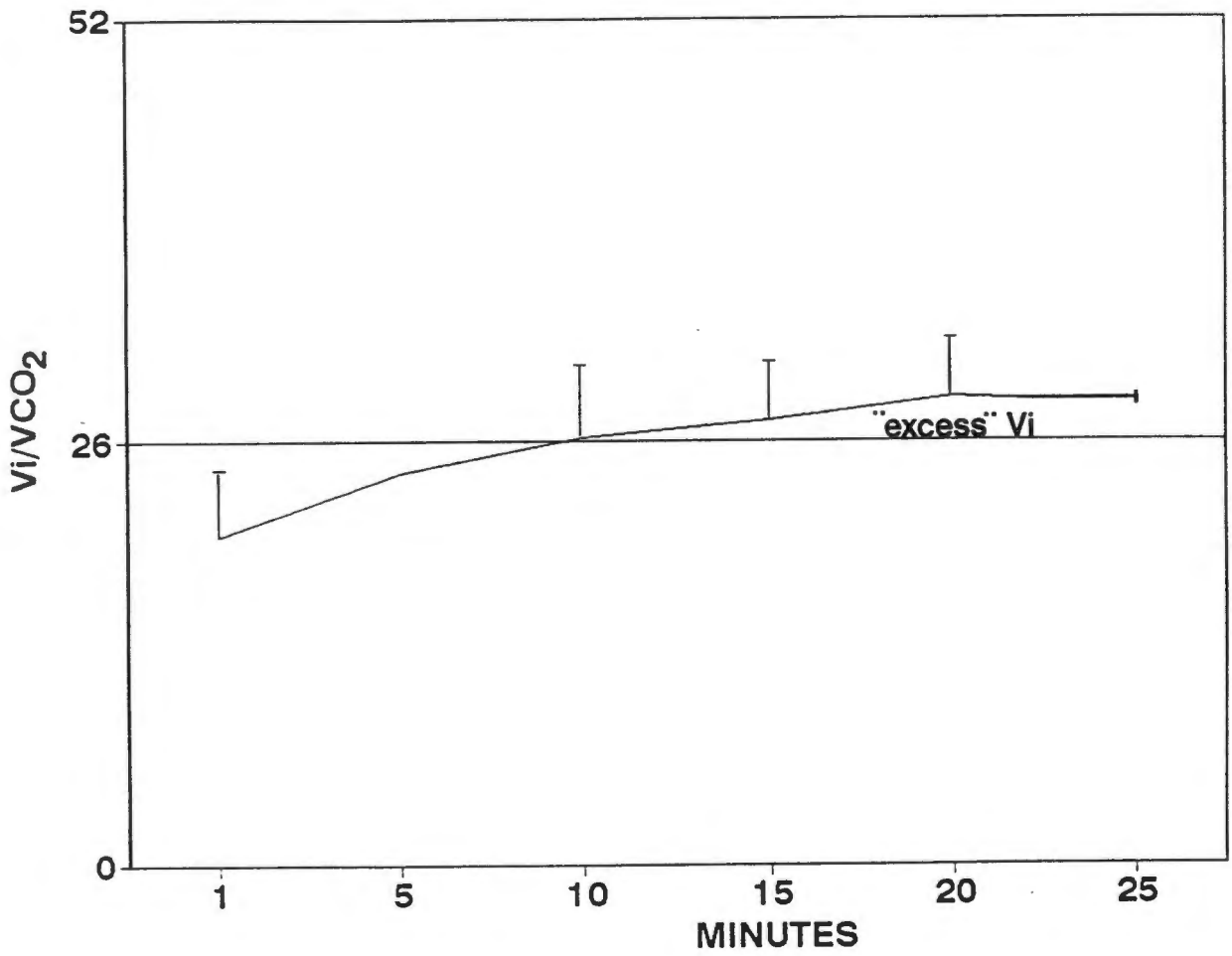


Figure 4.4 "Excess" ventilation during exercise at 70% WR max. Data are the differences between the measured ventilation ["actual" Vi] and that which would be predicted for normal gas exchange [predicted Vi] if the linear relationship between Vi and VCO_2 observed at lower work rates was maintained at higher work rates. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

and [ii] the 20th minute was the last time blood was taken from all the subjects. Blood measurements are summarized in Table 4.4.

i] Arterialized venous blood pH:

Arterialized venous pH fell from a resting value of 7.40 ± 0.02 to 7.32 ± 0.02 in the 5th minute of exercise. Thereafter it remained relatively constant throughout the exercise bout [Figure 4.5].

ii] Arterialized venous carbon dioxide tension:

Arterialized venous blood carbon dioxide tension decreased from a resting value of 46.0 ± 3.2 mmHg to 34.9 ± 4.0 mmHg in the first 15 minutes of exercise, after which it remained close to that value until the cessation of exercise [Figure 4.6].

Table 4.4 Measures of blood variables during high intensity constant-load cycling exercise at 70% WR max until exhaustion.

Time [minutes]	Rest	5	10	15	20
pHa	7.40 ±0.02	7.32 ±0.02	7.30 ±0.02	7.31 ±0.03	7.31 ±0.03
$PaCO_2$ [mmHg]	46.0 ±3.2	39.3 ±5.1	36.8 ±4.7	34.9 ±4.0	34.2 ±3.3
LACTATE [mmol/l]	1.8 ±0.6	4.7 ±0.8	6.7 ±0.9	7.1 ±0.6	7.6 ±0.9
$[HCO_3^-]$ [mmol/l]	24.3 ±1.7	20.6 ±2.0	18.3 ±2.1	17.2 ±1.2	17.2 ±1.5

Values are means ± SD; n = 5; pHa, arterialized venous pH; $PaCO_2$, arterialized venous carbon dioxide tension; $[HCO_3^-]$, arterialized venous bicarbonate ion concentration; LACTATE, venous blood lactate concentration.

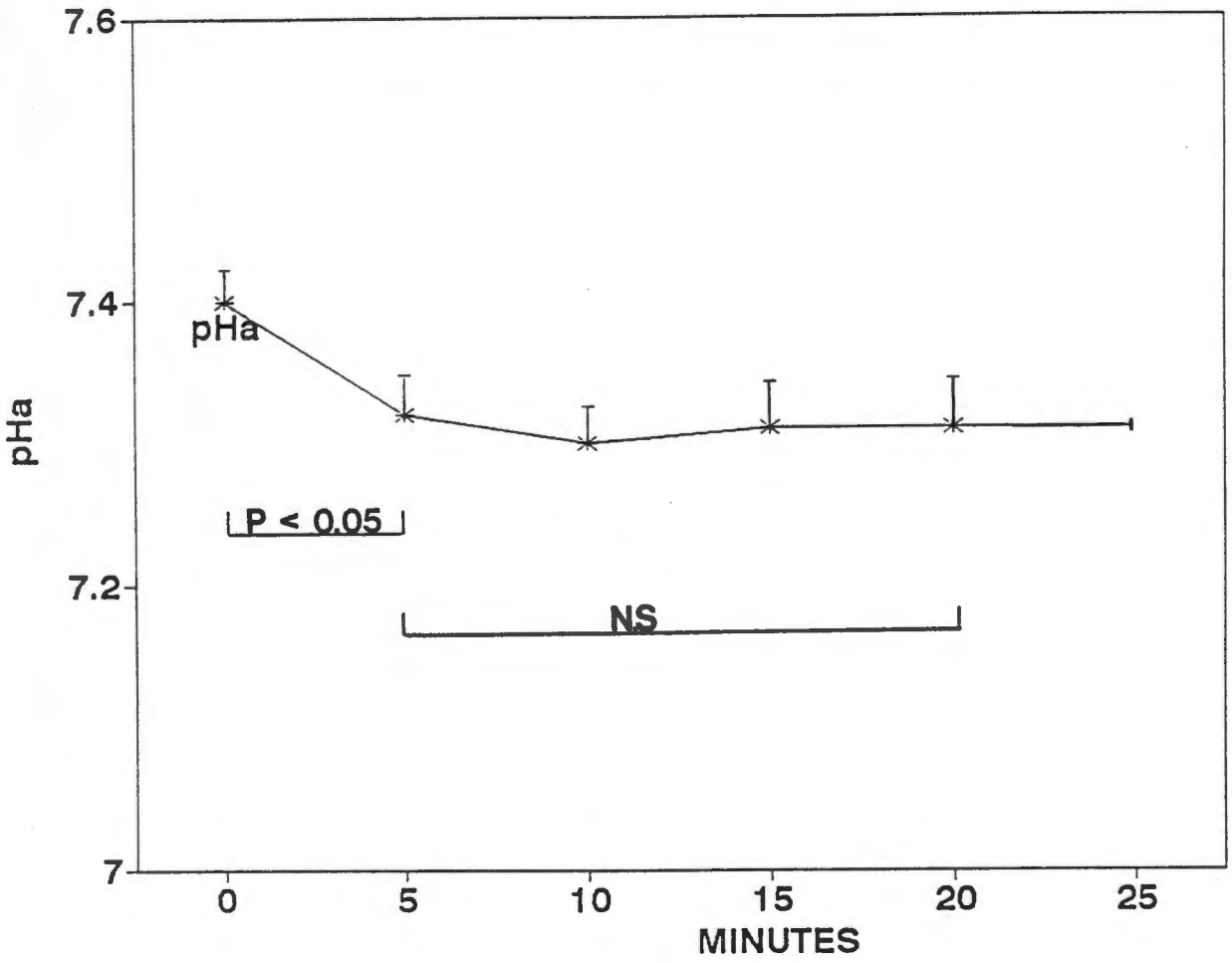


Figure 4.5 Changes in mean arterialized venous pH [pHa] with time during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

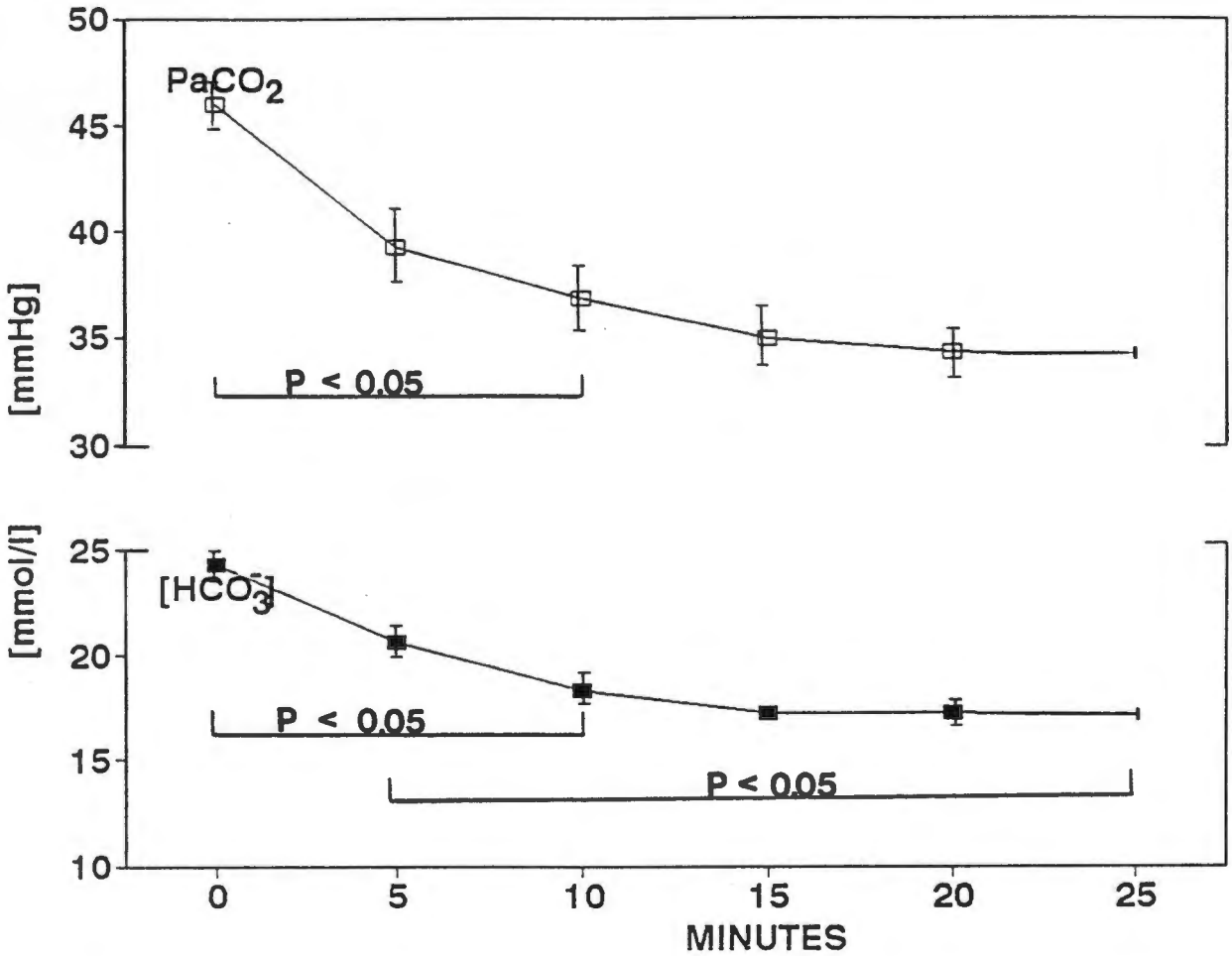


Figure 4.6 The temporal relationship between mean arterialized venous carbon dioxide tension [$PaCO_2$] and arterialized venous bicarbonate ion concentrations [HCO_3^-] during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

iii] Arterialized venous bicarbonate ion and venous blood lactate concentration:

Associated with the fall in $PaCO_2$, there was also a significant decrease in arterialized venous HCO_3^- ion concentration from a resting value of 24.3 $\pm$ 1.7 mmol/l to 17.2 $\pm$ 1.2 mmol/l in the first 15 minutes of exercise. The relationship between the fall in arterialized venous HCO_3^- concentration and arterialized venous $PaCO_2$ is shown in Figure 4.6.

The temporal relationship between the fall in arterialized venous HCO_3^- concentrations and the rise in venous blood lactate concentrations is shown in Figure 4.7. As lactate concentration rose from a resting value of 1.8 $\pm$ 0.6 mmol/l to 7.1 $\pm$ 0.6 mmol/l in the first 15 minutes of exercise, HCO_3^- concentration fell from 24.3 $\pm$ 1.7 to 17.2 $\pm$ 1.2 mmol/l. Thereafter both concentrations remained relatively constant.

4.4 Metabolic acidosis:

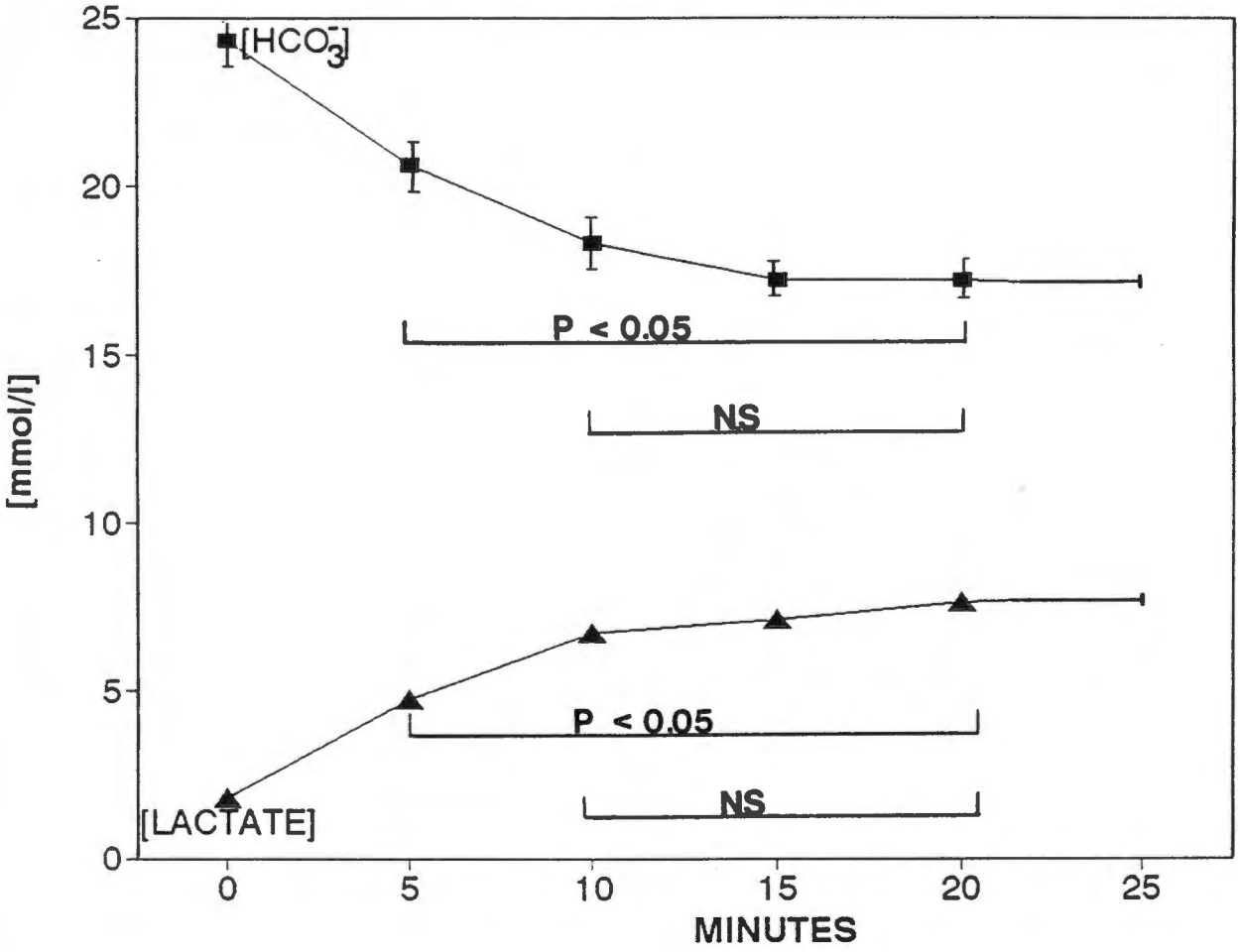


Figure 4.7 The reciprocal temporal relationship between mean arterialized venous bicarbonate [HCO_3^-] and venous blood lactate [LACTATE] concentrations during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

The values for base excess [BE], buffer base [BB] and arterialized venous HCO_3^- concentration are shown in Table 4.5. Base excess values decreased significantly from a 5th minute value of -4.2 ± 1.6 mEq/l to -7.7 ± 1.9 mEq/l in the 20th minute, whilst buffer base decreased ($P < 0.05$) from 43.8 ± 1.6 mEq/l to 40.3 ± 1.9 mEq/l and stayed close to these values until the end of exercise.

4.5 Ratings of perceived exertion for effort [RPE] and for ventilation [RVE]:

The means and standard deviations of the ratings of perceived exertion for effort and for ventilation are listed in Table 4.6.

Both RPE and RVE [Figure 4.8] increased progressively during exercise. RPE reached a maximum value of 9.6 ± 0.5 in the 22nd minute of exercise. At this stage RVE was 9.3 ± 1.0.

Table 4.6 also lists the measurements of the "dyspnoea index" described in Chapter Three. Those values rose from

Table 4.5 Changes in base excess, arterialized venous bicarbonate ion concentration and buffer base during high intensity constant-load cycling exercise at 70% WR max until exhaustion.

Time [minutes]	Rest	5	10	15	20
BE [mEq/l]	-0.6 ±0.6	-4.2 ±1.6	-6.7 ±1.7	-7.2 ±1.7	-7.7 ±1.9
$[HCO_3^-]$ [mmol/l]	24.3 ±1.7	20.6 ±2.0	18.3 ±2.1	17.2 ±1.2	17.2 ±1.2
BB [mEq/l]	47.3 ±0.6	43.8 ±1.6	41.3 ±1.7	40.3 ±1.7	40.3 ±1.9

Values are means ± SD; n = 5; BE, base excess; $[HCO_3^-]$, arterialized venous bicarbonate ion concentration; BB, buffer base.

Table 4.6 Measures of ratings of perceived exertion for effort [RPE], for ventilation [RVE] and the "dyspnoea index" recorded during high intensity constant-load cycling exercise at 70% WR max until exhaustion.

Time [minutes]	Rest	5	10	15	20	22
RPE	-	2.8 ±1.2	4.0 ±1.3	6.0 ±1.8	8.0 ±1.9	9.6 ±0.5
RVE	-	0.9 ±0.7	3.2 ±1.1	5.8 ±1.5	7.2 ±1.5	9.3 ±1.0
"dyspnoea index" [%]	3.0 ±0.4	47.0 ±4.1	51.0 ±4.6	51.0 ±5.5	54.0 ±4.6	54.0 ±5.0

Values are means ± SD; n = 5; RPE, ratings of perceived exertion for effort; RVE, ratings of perceived exertion for ventilation; "dyspnoea index", [Vi/MVVREST x 100].

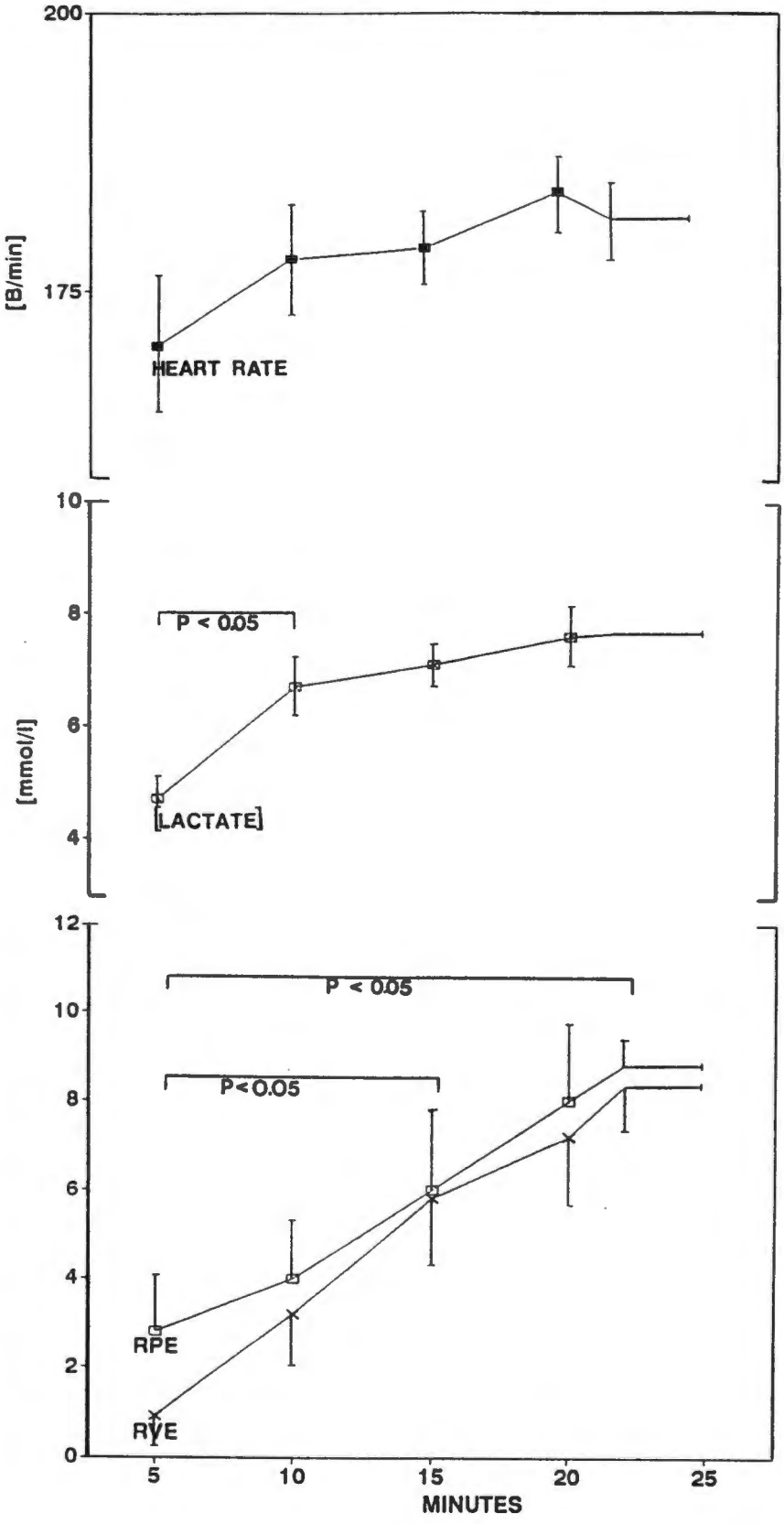


Figure 4.8 The temporal relationship between changes in mean venous blood lactate [LACTATE] concentrations, heart rate, ratings of perceived exertion for effort [RPE] and for ventilation [RVE] during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

resting values of 3.0 $\pm$ 0.4% to 47 $\pm$ 4.1% in the 5th minute of exercise and stayed close to the latter value until the end of exercise.

4.6 Variables that might influence RPE and RVE:

Increases in RPE and RVE were not related to rises in venous blood lactate concentrations or heart rate [Figure 4.8]. Both blood lactate concentrations and heart rate remained more or less constant from the 10th minute of exercise until exhaustion, whereas RPE and RVE showed a continuous increase throughout the exercise bout.

4.7 Reasons for stopping the exercise test:

All subjects indicated that leg fatigue rather than dyspnoea or general fatigue was the reason for terminating exercise.

4.8 Maximal voluntary ventilation [MVV]:

The values for MVV during the 20-s MVV test at rest [MVVREST] and after 70% WR max [MVVPOST-EX] are listed in Table 4.7 together with the maximum ventilation [Vi max] measured during the VO_2 max test and the final ventilation in the 70% WR max [70% Vi] exercise bout. The data show that both the incremental and the steady state exercise tests were conducted at minute ventilation volumes well below MVV values and that MVV was unaffected by 70% WR max exercise to exhaustion.

4.9 Summary:

The most relevant findings in this study were the following:

a. Ventilation continued to increase throughout the exercise period despite a metabolic steady state as shown by an unchanged VO_2 from the 5th minute until the end of exercise [Figure 4.2].

Table 4.7 Recorded values for resting maximal voluntary ventilation [MVVREST]; maximum ventilation during incremental exercise to exhaustion [Vi max]; final ventilation in the 70% WR max exercise bout [70% Vi] and maximal voluntary ventilation following cessation of exercise [MVVPOST-EX].

SUBJECT NO	MVVREST [l/min]	Vi max [l/min]	70% Vi [l/min]	MVVPOST-EX [l/min]
3	169	113	82	170
5	130	115	78	135
7	180	123	94	188
8	180	126	93	173
10	173	113	105	177
Means	176	118	90	177
S.D.	±5	±5	±9	±6
P Value		P < 0.05		
			P < 0.05	

b] Arterialized venous pH fell significantly from rest but remained in a steady state from the 5th minute until the end of exercise [Figure 4.5].

c] There was no significant difference between MVVREST values and MVVPOST-EX values and final ventilation [70% Vi] recorded at the end of 70% WR max did not reach values close to MVVREST [Table 4.7]. These findings indicate the absence of respiratory muscle fatigue.

d] Changes in blood lactate concentration and heart rate did not parallel changes in RVE and RPE [Figure 4.8].

e] Subjects stated that muscle fatigue was the reason why they stopped exercise at this work rate, despite RVE reaching values close to maximum.

The relevance of these findings are discussed in Chapter 6.

CHAPTER 5

RESPIRATORY RESPONSES AND ACID-BASE BALANCE DURING HIGH INTENSITY CONSTANT-LOAD EXERCISE AT 80% WR max

5.1 Introduction:

The results obtained from the 70% WR max study described in Chapter Four suggested that pulmonary fatigue did not limit endurance at an exercise intensity corresponding to 80 - 85% VO_2 max. Accordingly, in the study reported in this Chapter the same methods were used as in the previous study, except that the workload was increased to 80% WR max [85 - 90% VO_2 max] to determine whether the pulmonary system would continue to maintain an adequate oxygen supply and acid-base homeostasis at an even higher exercise intensity.

5.2 Subjects:

Eight of the ten subjects in the study exercised at a work rate representing 80% of their maximum work rate recorded during the preliminary VO_2 max test as described in Chapter Three. At this work rate, subjects were able to cycle between 12 - 15 minutes. These subjects' individual physiological characteristics and their physiological responses in the progressive VO_2 max tests and in the constant-load exercise at 80% WR max are given in Table 5.1.

5.3 Results:

a. Respiratory variables:

At 70% WR max, ventilation gradually increased from 77.7 $\pm$ 5.6 l/min in the 5th minute, to 94.6 $\pm$ 8.8 l/min in the 22nd minute of exercise at an average rate of $\pm$ 1.0 l/min . A much more rapid ventilation drift of $\pm$ 2.6 l/min was seen at 80% WR max. Figure 5.1 shows that ventilation increased ($P < 0.05$) from 91.4 $\pm$ 7.8 l/min in the 5th minute of exercise to 109.5 $\pm$ 8.6 l/min in the 12th minute of exercise. Mean ventilation

Table 5.1 Physiological characteristics of 8 subjects measured at exhaustion during a maximal oxygen consumption [VO_2max] and a 80% WR max test.

Subject No.	Gender M/F	Age [yrs]	Weight [kg]	VO_2max [ml/kg/min]	VO_2 [l/min]	WR max [Watts]	Vi max [l/min]	80% VO_2 [ml/kg/min]	80% VO_2 [l/min]	80% WR max [Watts]	80% Vi [l/min]	Heart rate max [b/min]
1	M	22	71	62	4.4	400	135	60	4.3	335	117	190
2	M	30	77	56	4.3	325	135	51	3.9	260	123	185
3	M	33	77	58	4.5	360	113	52	4.0	290	118	193
4	M	26	55	71	3.9	345	140	64	3.5	275	106	183
5	F	30	50	60	3.0	310	115	54	2.7	245	99	195
6	M	19	65	62	4.0	310	119	58	3.8	245	114	198
7	M	33	67	57	3.8	290	123	51	3.4	230	110	194
8	M	18	66	60	4.0	325	116	54	3.6	260	99	198
Mean		26	66	61	4.0	335	126	56	3.7	268	110	192
S.D.		±6	±9	±4	±0 4	±30	+9	±4	±0 4	±33	±3 0	±5 2

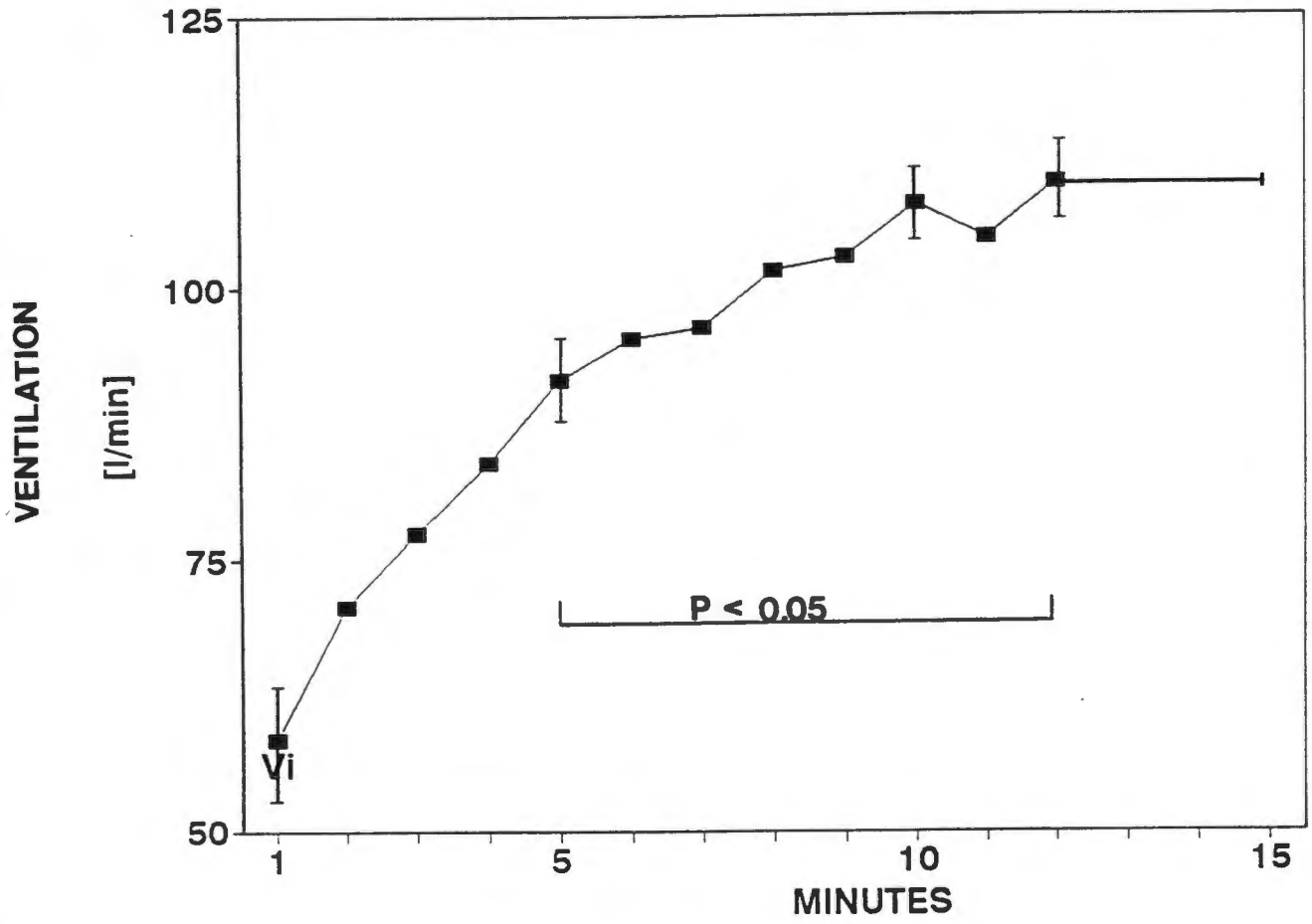


Figure 5.1 Changes in mean minute ventilation [Vi] with time during exercise at 80% WR max. [n =8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

recorded from the 5th minute of exercise until the end of exercise were significantly higher at 80% WR max than at 70% WR max ($P < 0.05$) [Table 5.2].

As had been found at 70% WR max, VO_2, VCO_2 and RER at 80% WR max also remained relatively constant ($P > 0.05$) from the 5th minute until the end of exercise [Figure 5.2]. Between 5 and 22 - 25 minutes at 70% WR max, subjects exercised at a mean VO_2 of 47.9 $\pm$ 1.9 ml/kg/min [$\pm$ 82% of VO_2 max] and at 80% WR max subjects maintained a mean VO_2 of 53.3 $\pm$ 5.2 ml/kg/min [$\pm$ 87% VO_2 max] from the 5th minute of exercise until the end of exercise at 12 - 15 minutes ($P < 0.05$) [Table 5.2].

Heart rates also remained relatively constant at around 180 beats/min after the first 5 minutes of exercise at 80% WR max until exhaustion [Table 5.3]. Surprisingly, the mean heart rate values recorded from the 5th minute of exercise until exhaustion at work rates of 70% and 80% WR max were similar [Table 5.2]. However, peak heart rates were greater at 80% WR max if compared to corresponding 70% WR max values [191.2 $\pm$ 3.8 vs 178.5 $\pm$ 8.5 beats/min ($P < 0.05$)].

The relationship between ventilation and arterialized venous $PaCO_2$ is shown in Figure 5.3. $PaCO_2$ showed a small non-

Table 5.2 Mean metabolic, cardiorespiratory and blood gas status recorded from the 5th minute until exhaustion during high intensity constant-load cycling exercise at 70% and 80% maximum work rate capacity [WR max].

Variable	70% WR max [Watts]	80% WR max [Watts]	P value
VO_2 [l/min]	3.2 ±0.4	3.4 ±0.4	NS
VO_2 max [ml/kg/min]	47.9 ±1.9	53.3 ±5.2	< 0.05
VCO_2 [l/min]	3.2 ±0.4	3.7 ±0.5	NS
VCO_2 max [ml/kg/min]	47.5 ±0.6	55.5 ±0.8	< 0.05
RER	0.98 ±0.04	1.03 ±0.03	< 0.05
[LACTATE] [mmol/l]	6.5 ±0.8	8.3 ±2.3	< 0.05
pHa	7.31 ±0.02	7.25 ±0.04	< 0.05
$PaCO_2$ [mmHg]	36.3 ±4.3	39.8 ±4.3	NS
Vi [l/min]	85.1 ±6.9	101.1 ±8.7	< 0.05
HR [Beats/min]	178 ±8.8	181 ±7.2	NS

Values are means ± S.D.; n = 5 at 70% WR max, n = 8 at 80% WR max; VO_2, oxygen consumption; VCO_2, carbon dioxide expiration; RER, respiratory exchange ratio; [LACTATE], venous blood lactate concentration; pHa, arterialized venous blood pH; $PaCO_2$, arterialized venous carbon dioxide tension; Vi, ventilation volumes; HR, heart rate; NS, not significant.

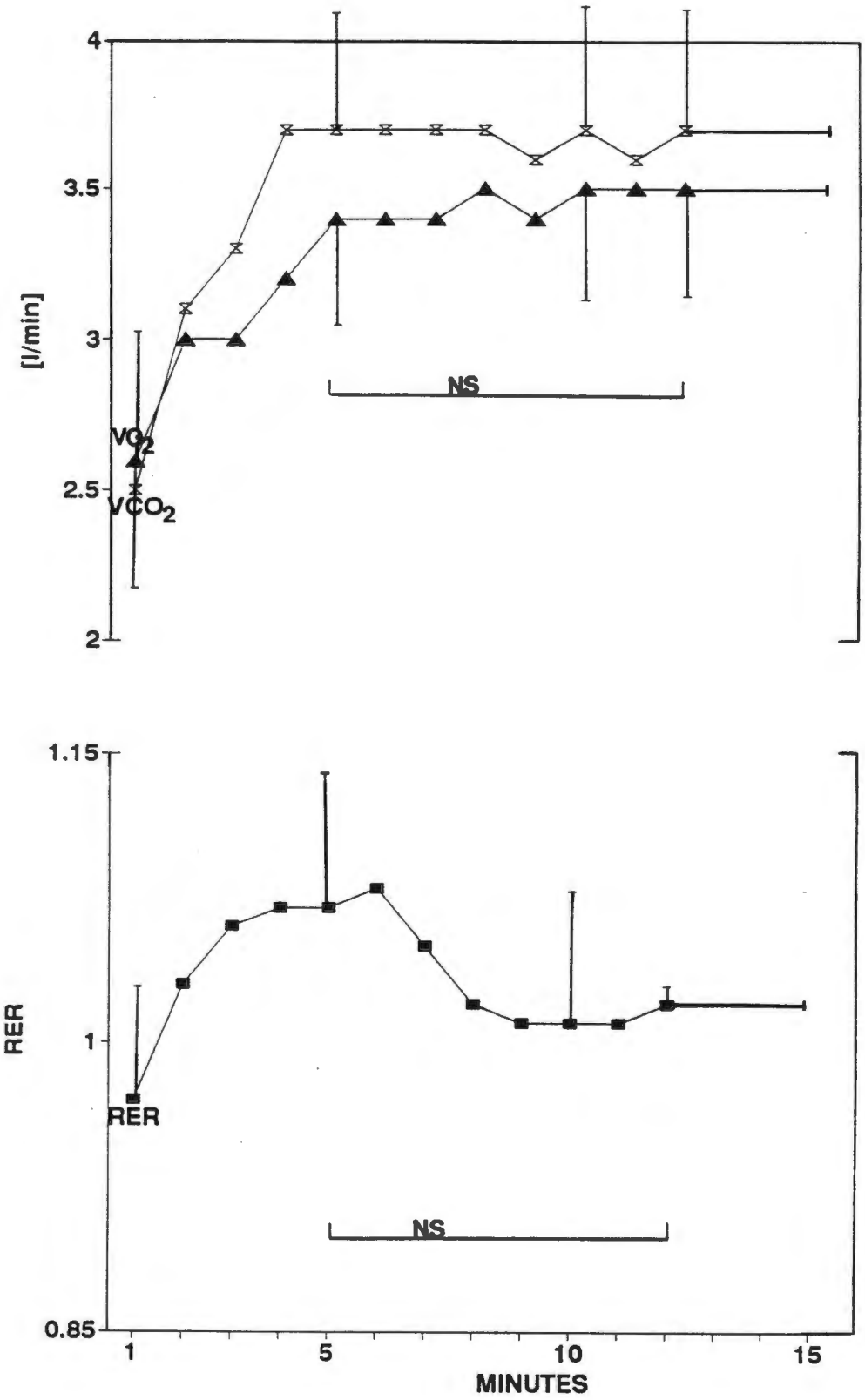


Figure 5.2 Changes in oxygen consumption [VO_2], carbon dioxide expiration [VCO_2] and respiratory exchange ratio [RER] with time during constant-load cycle ergometer exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

Table 5.3 Measures of ventilatory variables and heart rate during high intensity constant-load cycling exercise at 80% WR max until exhaustion.

Time [minutes]	1	2	3	4	5	6	7	8	9	10	11	12
Vi [l/min]	58.4 ±10.8	70.7 ±5.4	77.5 ±5.5	83.8 ±6.5	91.4 ±7.8	95.3 ±10.7	96.3 ±7.2	101.5 ±8.1	102.8 ±8.1	107.6 ±9.9	104.6 ±9.7	109.5 ±8.6
RER	0.97 ±0.08	1.03 ±0.04	1.06 ±0.03	1.07 ±0.04	1.07 ±0.05	1.08 ±0.05	1.05 ±0.04	1.02 ±0.03	1.01 ±0.02	1.01 ±0.02	1.01 ±0.02	1.02 ±1.01
VO_2 [l/min]	2.6 ±0.5	3.0 ±0.5	3.0 ±0.3	3.2 ±0.3	3.4 ±0.4	3.4 ±0.4	3.4 ±0.3	3.5 ±0.4	3.4 ±0.4	3.5 ±0.4	3.5 ±0.4	3.5 ±0.4
VCO_2 [l/min]	2.5 ±0.5	3.1 ±0.3	3.3 ±0.3	3.7 ±0.5	3.7 ±0.5	3.7 ±0.5	3.7 ±0.4	3.7 ±0.6	3.6 ±0.6	3.7 ±0.5	3.6 ±0.4	3.7 ±0.5
Heart rate [Beats/min]	150 ±20.4	162 ±13.5	167 ±14.7	173 ±11.7	176 ±11.1	177 ±9.2	179 ±8.9	181 ±0.3	183 ±7.3	185 ±7.3	185 ±7.5	187 ±6.7

Values are means ± SD; n = 8; Vi, ventilation; RER, respiratory exchange ratio; VO_2, oxygen consumption; VCO_2, carbon dioxide expiration.

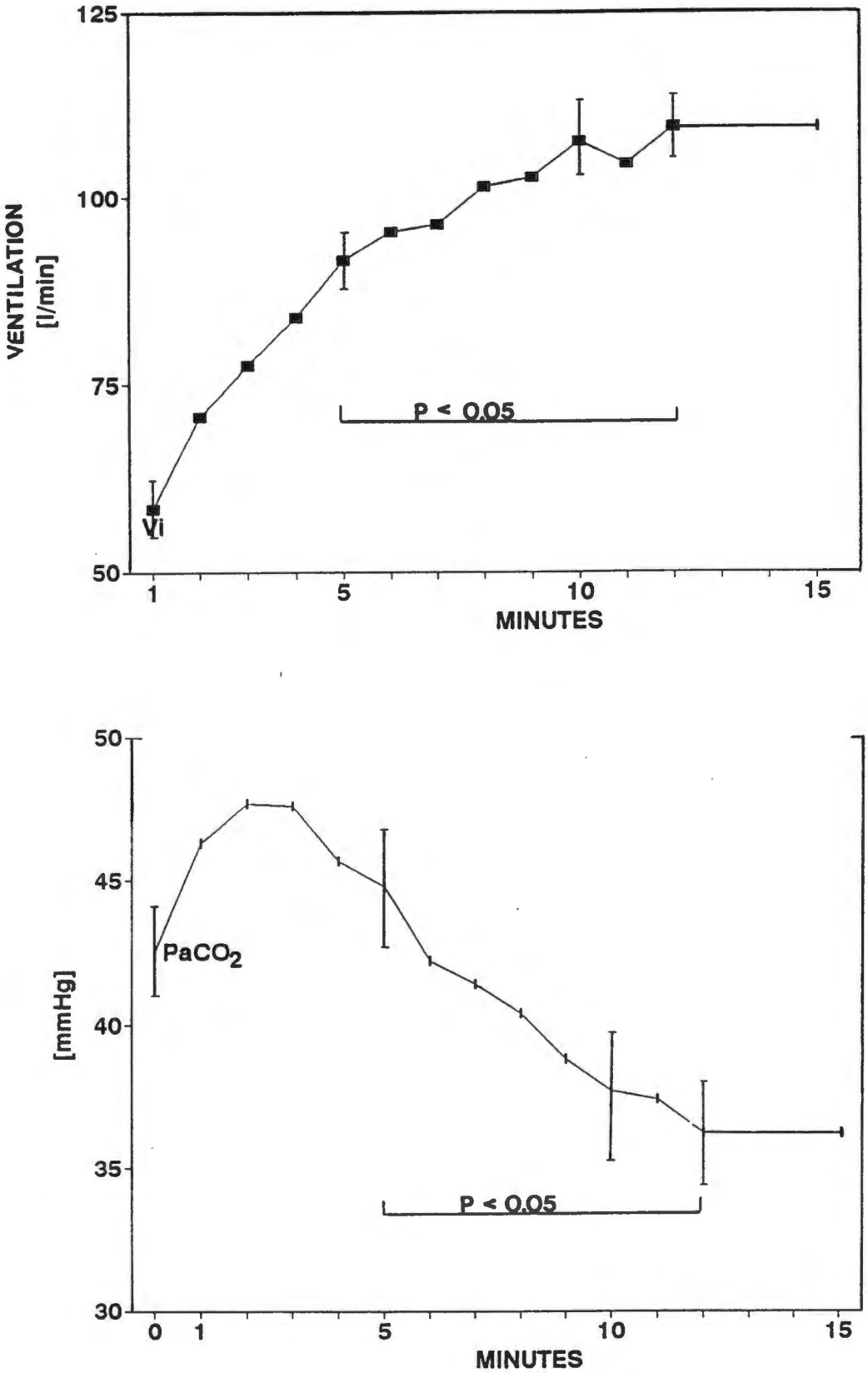


Figure 5.3 The reciprocal temporal relationship between mean minute ventilation [Vi] and arterialized venous carbon dioxide tension [$PaCO_2$] during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

significant increase from a first minute value of 46.3 ± 4.3 mmHg to 47.7 ± 4.1 mmHg in the second minute and thereafter, decreased with increasing ventilation to 44.8 ± 4.2 mmHg in the 5th minute and to 37.7 ± 4.6 mmHg in the 10th minute. There were no significant differences between the mean decreases in $PaCO_2$ from the 5 minute to exhaustion in the 70% and 80% WR max tests [Table 5.2].

Ratios of $Vi/PaCO_2$ increased from 2.1 ± 0.3 l/min/mmHg in the 5th minute to 2.9 ± 0.2 l/min/mmHg in the 12th minute at 80% WR max [Table 5.4]. The 5 minute values at 80% WR max were similar to those at 70% WR max [2.1 ± 0.3 vs 2.0 ± 0.3 l/min/mmHg, N.S.], but, they were higher at 10 minutes [2.8 ± 0.3 vs 2.3 ± 0.3 l/min/mmHg, $P < 0.05$], when some subjects were 2 minutes from exhaustion. Close to exhaustion values after 20 minutes of exercise at 70% WR max were similar to the 10 minute values at 80% WR max [2.6 ± 0.3 vs 2.8 ± 0.3 l/min/mmHg, N.S.].

Vi/VO_2 values were 27.2 ± 2.4 in the 5th minute of exercise at 80% WR max and rose to 31.2 ± 3.4 in the 12th minute of exercise. Again, Vi/VO_2 values were higher at 80% WR max than at 70% WR max at 10 minutes [31.1 ± 3.2 vs 25.7 ± 3.7, $P < 0.05$], but, not at any other comparable time.

Table 5.4 Changes in $V_I/PaCO_2$, V_I/VCO_2, V_I/VO_2 and V_I/HCO_3^- ratio with time during high intensity constant-load cycling exercise at 80% WR max until exhaustion.

Time [minutes]	1	2	3	4	5	6	7	8	9	10	11	12
$V_I/PaCO_2$ [l/min/ mmHg]	1.3 ±0.3	1.5 ±0.2	1.6 ±0.2	1.8 ±0.2	2.1 ±0.3	2.3 ±0.3	2.4 ±0.2	2.5 ±0.2	2.6 ±0.3	2.8 ±0.3	2.8 ±0.3	2.9 ±0.2
V_I/VCO_2	23.4 ±3.8	23.6 ±3.2	23.6 ±3.4	23.5 ±3.1	25.5 ±3.2	25.6 ±3.7	25.6 ±3.7	26.6 ±3.6	27.6 ±3.6	29.6 ±3.2	29.3 ±3.2	29.8 ±2.9
V_I/VO_2	23.2 ±4.5	23.9 ±3.6	25.8 ±3.6	26.6 ±3.4	27.2 ±2.4	28.4 ±3.7	28.4 ±3.7	28.7 ±3.2	29.3 ±3.2	31.1 ±3.2	30.3 ±3.6	31.2 ±3.4
V_I/HCO_3^- [l^2/min/ mmol]	2.4 ±0.5	2.9 ±0.2	3.3 ±0.3	3.9 ±0.5	4.4 ±0.6	5.0 ±0.8	5.3 ±0.8	5.9 ±0.9	6.2 ±1.2	6.7 ±1.4	6.7 ±0.8	6.9 ±0.9

Values are means ± SD; n = 8; V_I, ventilation volume; VCO_2, rates of carbon dioxide expiration; VO_2, rates of oxygen consumption; $PaCO_2$, arterialized venous carbon dioxide tension; HCO_3^-, arterialized venous bicarbonate ion concentration.

After 10 minutes of exercise at 80% WR max, the Vi/HCO_3^- ratios were also greater than after 10 minutes of exercise at 70% WR max [6.7 $\pm$ 1.4 vs 4.5 $\pm$ 0.8 l /min/mmol, $P < 0.05$], as were the ratios close to exhaustion [6.9 $\pm$ 0.9 vs 5.1 $\pm$ 0.3 l /min/mmol, $P < 0.05$].

As the HCO_3^- ion concentrations were comparable near the end of the two trials [Table 4.4 and Table 5.5] the latter differences were largely due to higher ventilation volumes in 80% WR max exercise.

In contrast, rises in Vi/VCO_2 ratios were similar in exercise at 80% and 70% WR max [Table 4.3 and Table 5.4]. The only possible difference was that the subjects started to hyperventilate in the 8th minute with Vi/VCO_2 values of 26.6 $\pm$ 3.6 at 80% WR max exercise, whereas Vi/VCO_2 values in excess of 26 were only detected at 10 minutes during exercise at 70% WR max. This "excess" ventilation, indicated by Vi/VCO_2 values greater than the predicted value of 26 is explained in Chapter Three and shown in Figure 5.4.

b. Blood variables:

Again, the means and standard deviations of the blood

Table 5.5 Measures of blood variables during high intensity constant-load cycling exercise at 80% WR max until exhaustion.

Time [minutes]	Rest	1	2	3	4	5	6	7	8	9	10	11	12
pHa	7.37 ±0.02	7.34 ±0.03	7.30 ±0.02	7.30 ±0.02	7.29 ±0.03	7.28 ±0.04	7.27 ±0.04	7.25 ±0.05	7.24 ±0.05	7.24 ±0.05	7.25 ±0.06	7.24 ±0.03	7.23 ±0.03
[HCO_3^-] [mmol/l]	24.5 ±1.2	24.7 ±1.7	24.5 ±1.4	23.7 ±1.5	22.2 ±2.3	21.3 ±2.3	19.3 ±2.6	18.4 ±2.8	17.6 ±2.5	17.0 ±3.2	16.4 ±2.9	16.2 ±2.7	15.3 ±2.6
$PaCO_2$ [mmHg]	42.5 ±3.3	46.3 ±4.3	47.7 ±4.1	47.6 ±4.0	45.7 ±4.8	44.8 ±4.2	42.2 ±4.8	41.4 ±4.3	40.4 ±4.4	36.6 ±3.9	37.7 ±4.6	37.4 ±4.6	36.2 ±3.7
[LACTATE [mmol/l]	2.0 ±0.5	3.2 ±0.5	4.0 ±0.7	4.8 ±0.9	5.4 ±1.3	6.2 ±1.8	6.7 ±2.2	7.5 ±2.2	8.5 ±2.4	8.8 ±2.3	9.3 ±2.2	9.7 ±2.8	10.0 ±2.4

Values are means ± SD; n = 8; pHa, arterialized venous pH; HCO_3^-, arterialized venous bicarbonate ion concentration; $PaCO_2$, arterialized venous carbon dioxide tension; [LACTATE], venous blood lactate concentration

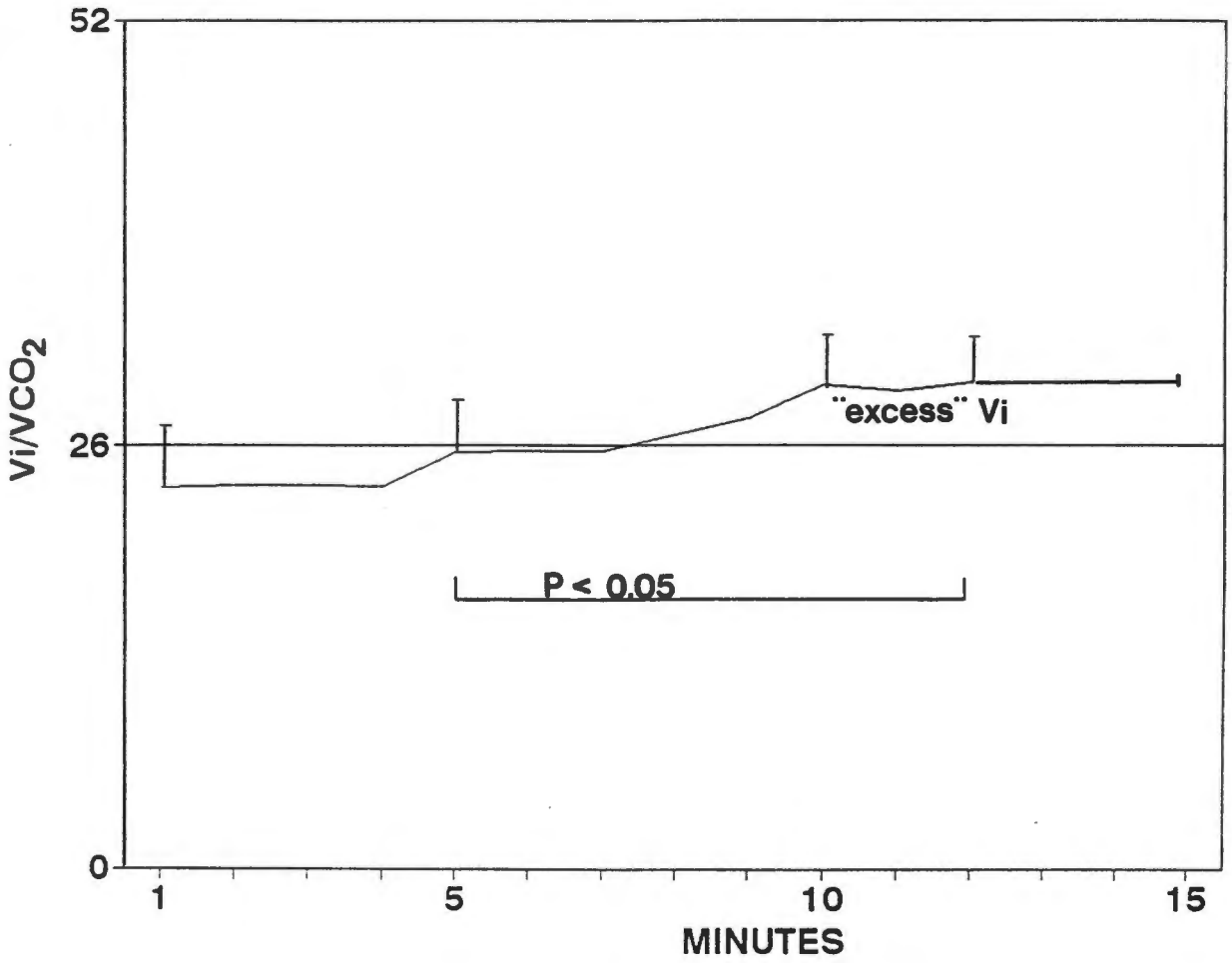


Figure 5.4 "Excess" ventilation during exercise at 80% WR max. Data are the differences between the measured ventilation ["actual" Vi] and that which would be predicted for normal gas exchange [predicted Vi] if the linear relationship between Vi and VCO_2 observed at lower work rates was maintained at higher work rates. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

measurements are reported until the 12th minute of a 12 - 15 minute cycle at 80% WR max to exhaustion as two of the eight subjects fatigued in the 13th minute of exercise [Table 5.5].

i] Arterialized venous blood pH:

During exercise at 80% WR max, a marked acidosis occurred. pHa declined ($P < 0.05$) from a resting value of 7.37 $\pm$ 0.02 to 7.28 $\pm$ 0.04 in the first 5 minutes of exercise and then slowly declined to 7.23 $\pm$ 0.03 over the next 7 minutes of exercise [Table 5.5, Figure 5.5].

These falls in pHa to 7.23 $\pm$ 0.03 with 12 minute of exercise at 80% WR max were greater than the falls in pHa to 7.31 $\pm$ 0.03 with 20 minutes of exercise at 70% WR max ($P < 0.05$) [Table 4.4].

ii] Arterialized venous carbon dioxide tension:

As mentioned earlier, $PaCO_2$ showed a transient rise ($P > 0.05$)

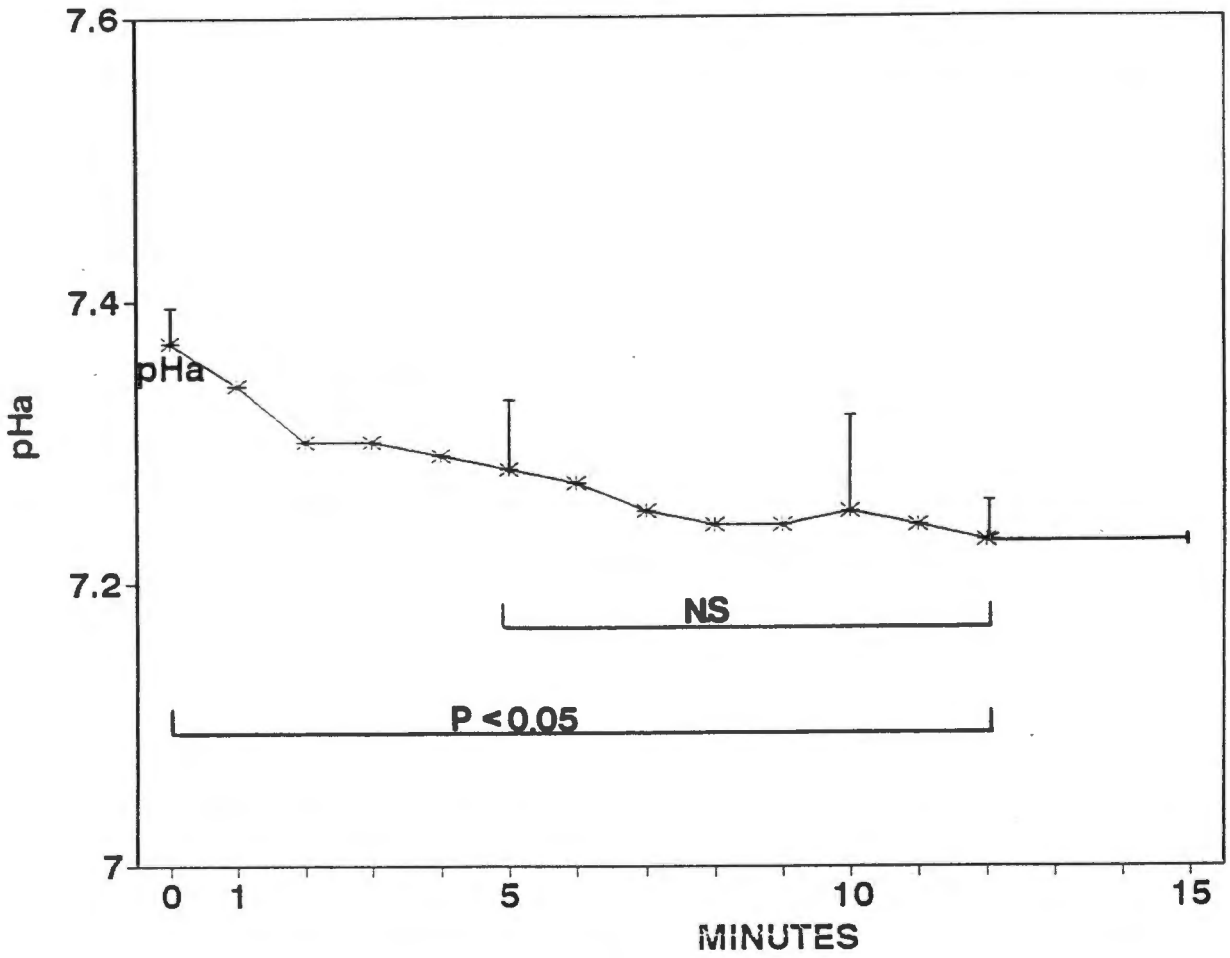


Figure 5.5 Changes in mean arterialized venous pH [pHa] with time during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

from a first minute value of 46.3 ± 4.3 mmHg to 47.7 ± 4.1 mmHg in the 2nd minute. Thereafter there was a decrease ($P < 0.05$) in arterialized venous $PaCO_2$ from a value of 44.8 ± 4.2 mmHg in the 5th minute to about 36.2 ± 3.7 mmHg at the end of exercise [Figure 5.6]. In contrast $PaCO_2$ fell to lower values of 39.3 ± 5.1 mmHg, after 5 minutes of exercise at 70% WR max and thereafter declined to 34.2 ± 3.3 mmHg at 20 minutes, but, the 5 minute differences were not quite significant ($P < 0.1$).

iii] Arterialized venous bicarbonate ion and venous blood lactate concentration:

Associated with the fall in $PaCO_2$, there was a significant decrease ($P < 0.05$) in HCO_3^- ion concentration from a resting value of 24.5 ± 1.2 mmol/l to the lowest value of 15.3 ± 2.6 mmol/l in the 12th minute of exercise [Figure 5.6]. Falls in HCO_3^- concentration in exercise at 80% WR max were similar to those found in 70% WR max exercise [Table 4.4 and Table 5.5].

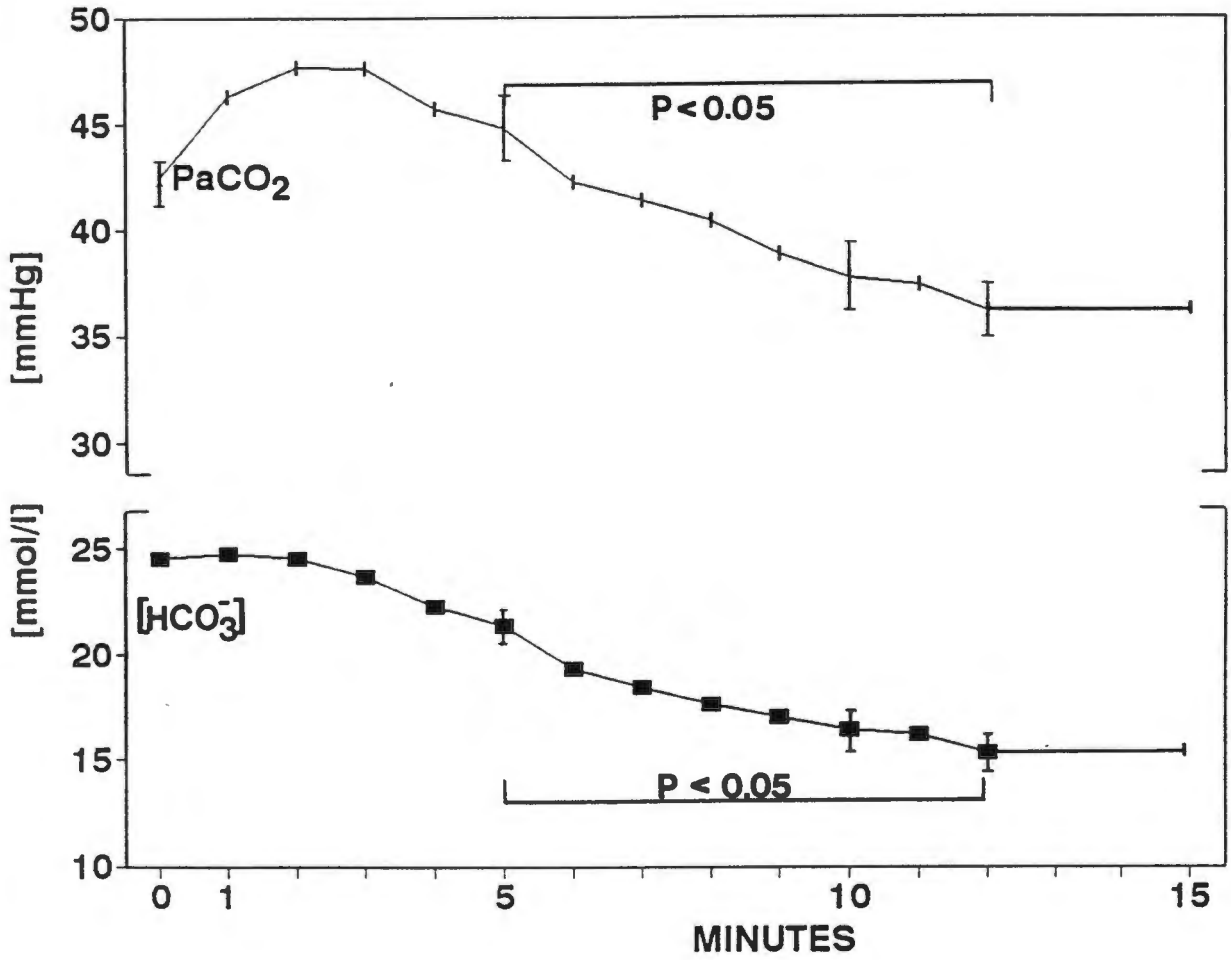


Figure 5.6 The temporal relationship between mean arterialized venous carbon dioxide tension [$PaCO_2$] and arterialized venous bicarbonate ion concentrations [HCO_3^-] during cycle exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute

The temporal relationship between the fall in arterialized venous HCO_3^- concentrations and the rise in venous lactate concentrations is shown in Figure 5.7. As lactate concentration rose from an initial value of 2.0 $\pm$ 0.5 mmol/l to 9.3 $\pm$ 2.2 mmol/l in the 10th minute of exercise, HCO_3^- concentration fell from 24.5 $\pm$ 1.2 mmol/l to 16.4 $\pm$ 2.9 mmol/l.

At 70% WR max, HCO_3^- ion concentrations fell from a resting value of 24.3 $\pm$ 1.7 mmol/l to 18.3 $\pm$ 2.1 mmol/l in the 10th minute and then, declined slowly to 17.2 $\pm$ 1.5 mmol/l at 20 minutes. There was no significant difference between the fall in HCO_3^- ion concentration from the 5th minute until the end of exercise at 70% and 80% WR max [Table 5.2], despite significantly greater rises in venous blood lactate concentrations at 80% WR max than at 70% WR max ($P < 0.05$), [Table 5.2].

5.4 Metabolic acidosis:

A marked metabolic acidosis during exercise at 80% WR max was demonstrated by significant ($P < 0.05$) decreases in buffer base,

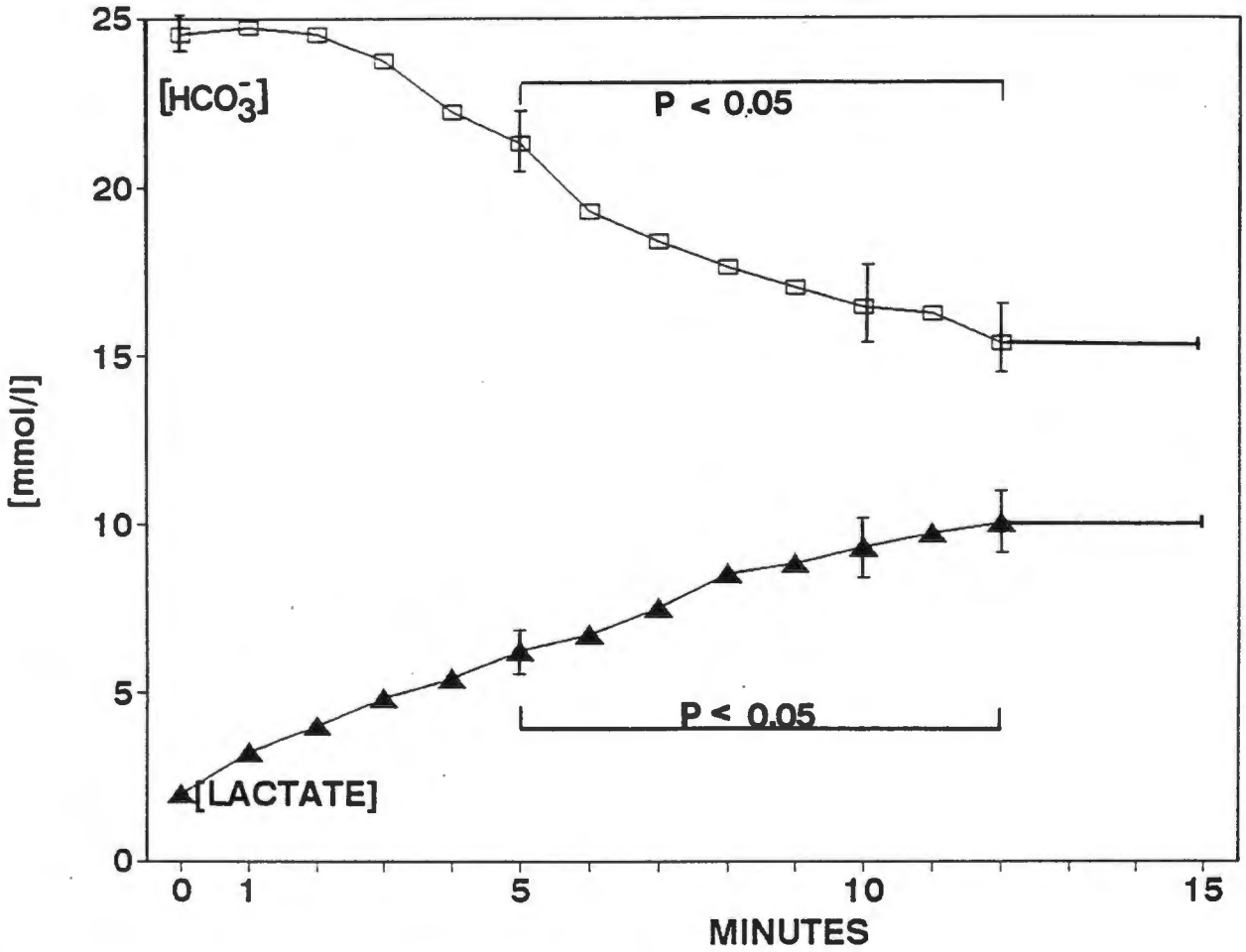


Figure 5.7 The reciprocal temporal relationship between mean arterialized venous bicarbonate [HCO_3^-] and venous blood lactate [LACTATE] concentrations during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

base excess and arterialized venous HCO_3^- ion concentrations as shown in Table 5.6. All concentrations were decreased more than in exercise at 70% WR max, but, none of the between work rate differences reached statistical significance.

The only statistically significant differences ($P < 0.05$) to indicate a more marked metabolic acidosis during the 80% WR max test were the higher venous blood lactate concentrations [8.3 $\pm$ 2.3 mmol/l vs 6.5 $\pm$ 0.8 mmol/l] and the lower arterialized venous blood pH [7.25 $\pm$ 0.04 vs 7.31 $\pm$ 0.02] at 80% WR max than at 70% WR max [Table 5.2].

5.5 Ratings of perceived exertion for effort [RPE] and for ventilation [RVE]:

The means and standard deviations for RPE and RVE are shown in Table 5.7 and Figure 5.8. RPE and RVE increased continuously throughout exercise. RPE reached a value of 8.0 $\pm$ 1.8 and RVE reached a value of 6.7 $\pm$ 2.5 in the 12th minute of exercise.

Table 5.7 also shows the measurements of the "dyspnoea index" described in Chapter Three. Those values rose from resting

Table 5.6 Changes in base excess, arterialized venous bicarbonate ion concentration and buffer base during high intensity constant-load cycling exercise at 80% WR max until exhaustion.

Time [minutes]	Rest	1	2	3	4	5	6	7	8	9	10	11	12
BE [mEq/l]	-0.2 ±0.9	-0.6 ±1.6	-1.6 ±1.3	-2.4 ±1.4	-4.0 ±1.6	-4.8 ±1.9	-6.8 ±2.5	-7.8 ±2.7	-8.6 ±3.2	-9.3 ±3.3	-9.6 ±3.3	-9.8 ±2.9	-10.1 ±2.9
$[HCO_3^-]$ [mmol/l]	24.5 ±1.2	24.7 ±1.0	24.5 ±1.4	23.7 ±1.5	22.2 ±2.3	21.3 ±2.3	19.3 ±2.6	18.4 ±2.8	17.6 ±2.5	17.0 ±3.2	16.4 ±2.9	16.2 ±2.7	15.3 ±2.6
BB [mEq/l]	47.8 ±0.9	47.4 ±1.6	46.4 ±1.3	45.6 ±1.4	44.0 ±1.6	43.2 ±1.9	41.2 ±2.5	40.2 ±2.7	39.4 ±3.2	38.7 ±3.3	38.4 ±3.3	38.2 ±2.9	37.9 ±2.9

Values are means ± SD; n = 8; BE, Base Excess; $[HCO_3^-]$, arterialized venous bicarbonate ion concentration; BB; Buffer Base.

Table 5.7 Measures of ratings of perceived exertion for effort [RPE], for ventilation [RVE] and the "dyspnoea index" recorded during high intensity constant-load cycling exercise at 80% WR max until exhaustion.

Time [minutes]	Rest	1	2	3	4	5	6	7	8	9	10	11	12
RPE	-	0.7 ±0.6	1.3 ±1.0	2.0 ±1.2	2.6 ±1.6	3.4 ±1.3	3.9 ±1.0	4.6 ±1.2	5.0 ±1.2	5.7 ±1.6	6.6 ±2.0	7.1 ±1.9	8.0 ±1.8
RVE	-	0.7 ±0.8	0.9 ±0.7	1.4 ±0.9	1.7 ±0.8	3.0 ±1.5	3.0 ±1.5	3.6 ±1.5	4.0 ±1.6	5.0 ±2.1	5.6 ±2.4	6.0 ±2.5	6.7 ±2.5
"Dyspnoea index" [%]	3.3 ±0.1	33 ±4.1	37 ±3.1	44 ±3.1	48 ±3.9	52 ±4.3	54 ±4.1	55 ±4.2	58 ±4.6	59 ±4.7	61 ±5.6	60 ±5.5	63 ±5.1

Values are means ± SD; n = 8; RPE, ratings of perceived exertion for effort; RVE, ratings of perceived exertion for ventilation; "dyspnoea index", [Vi/MVVREST x 100].

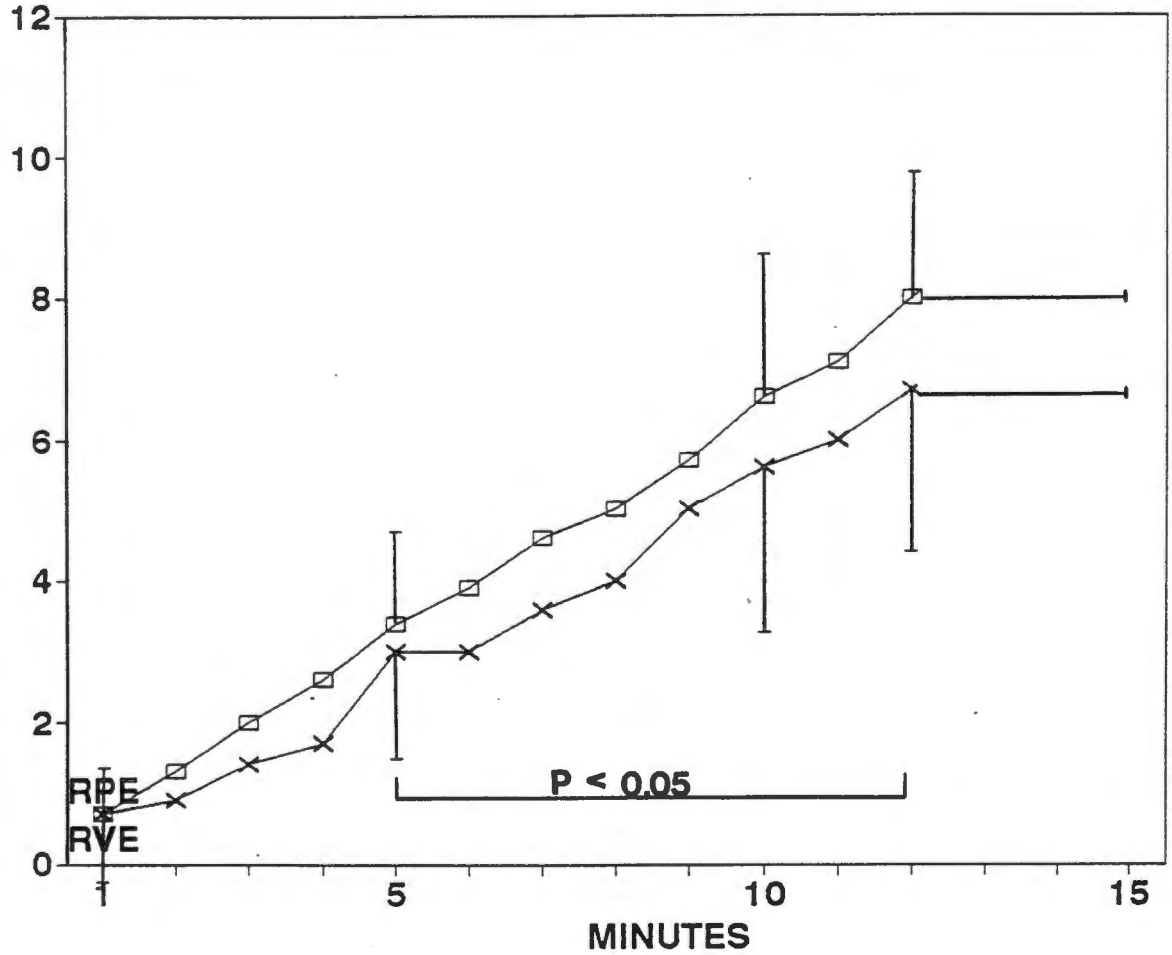


Figure 5.8 Changes in mean ratings of perceived exertion for effort [RPE] and for ventilation [RVE] with time during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

values of 3.3 ± 0.1% to 52.0 ± 4.3% in the first 5 minutes of exercise and, thereafter, rose more gradually ($P < 0.05$) to 63.0 ± 5.1% at the end of exercise.

5.6 Reasons for stopping the exercise test:

Seven of the eight subjects reported the feeling of muscular fatigue in the exercising quadriceps muscles as the reason for ending the exercise. The other subject indicated general fatigue as the reason for terminating exercise at 80% WR max.

5.7 Maximal Voluntary Ventilation [MVV]:

MVV values during the pre-exercise 20-s test at rest and after 80% WR max [MVVPOST-EX] are listed in Table 5.8, together with the maximum ventilation [Vi max] recorded during the VO_2 max test. These data show that the resting MVV values [MVVREST] were significantly higher ($P < 0.05$) for all subjects compared

Table 5.8 Recorded values for resting maximal voluntary ventilation [MVVREST]; maximum ventilation during incremental exercise to exhaustion [Vi max]; final ventilation in the 80% WR max exercise bout [80% Vi] and maximal voluntary ventilation following cessation of exercise [MVVPOST-EX].

Subject No	MVVREST [l/min]	80% Vi [l/min]	Vi max [l/min]	MVVPOST-EX [l/min]
1	182	117	135	179
2	167	123	135	183
3	169	118	113	177
4	162	106	140	187
5	130	99	115	114
6	180	114	119	195
7	180	110	123	193
8	165	99	116	185
Means	174	110	126	186
S.D.	±7	±3	±9	±6
P Value		P < 0.05		
		P < 0.05		
		P < 0.05		

to either their Vi max obtained during the incremental test or the exercise at 80% WR max.

Figure 5.9 shows that 13 - 15 minutes of exercise at 80% WR max to exhaustion not only caused changes ($P < 0.05$) in the 20-s MVV test performed immediately after exercise [MVVPOST-EX] but also during a 20 minute recovery period [MVVR5 - MVVR20]. MVVR 5 - 20 minute values were only obtained in 4 of the 8 subjects. Subjects were required to complete another 4 tests each on 4 separate occasions and as mentioned in Chapter Three, not all subjects were willing to complete this time-consuming section of the test.

MVVPOST-EX in the 30s immediately following exhaustive exercise 186 $\pm$ 6 l/min was significantly higher from MVVREST 174 $\pm$ 7 l/min. In contrast, the MVV values after a 10, 15 and 20 minute period of recovery following exhaustive exercise were significantly lower than resting values. Those values [MVVR10, MVVR15 and MVVR20] fell to 158 $\pm$ 10 l/min, 157 $\pm$ 6 l/min and 159 $\pm$ 10 l/min respectively [Table 5.9, Figure 5.9].

5.8 Summary:

The most relevant findings of this study were the following:

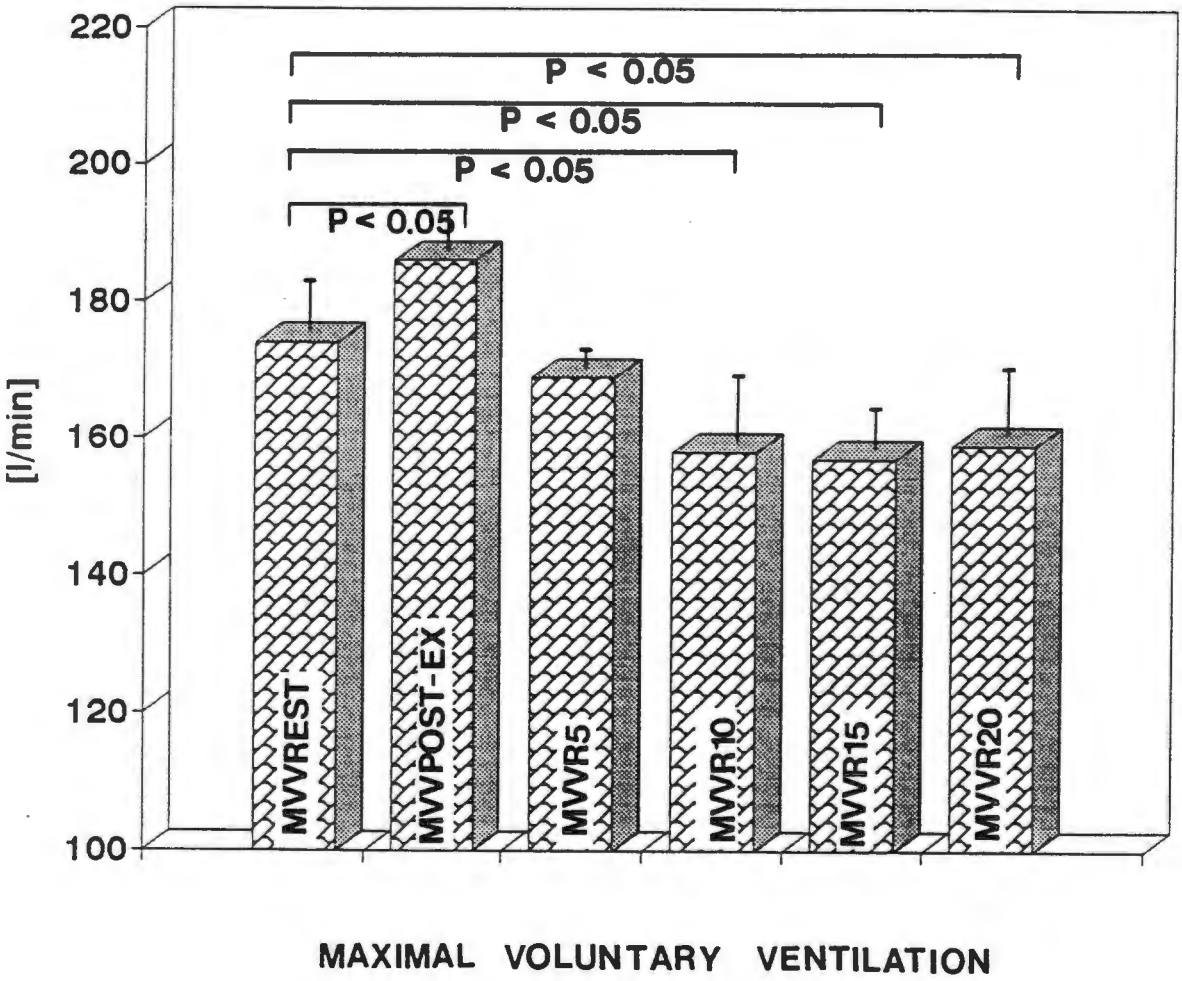


Figure 5.9 Resting [MVVREST], immediate 30 s post 80% WR max exercise maximal voluntary ventilation [MVVPOST-EX] and recovery maximal voluntary ventilation [MVVR] performed after 5 minutes [MVVR5], 10 minutes [MVVR10], 15 minutes [MVVR15] and 20 minutes [MVVR20] of rest after exercise. [n = 4].

Table 5.9 Resting maximal voluntary ventilation [MVVREST]; maximal voluntary ventilation following cessation of exercise [MVVPOST-EX] and maximal voluntary ventilation recorded every 5 minutes [MVVR5-MVVR20] after cessation of high intensity constant-load cycling exercise to exhaustion at 80% WR max.

SUBJECT NO	MVVREST [l/min]	MVVPOST-EX [l/min]	MVVR5 [l/min]	MVVR10 [l/min]	MVVR15 [l/min]	MVV20 [l/min]
1	182	179	173	176	166	175
2	167	183	169	151	154	151
6	180	195	165	150	152	150
8	165	185	167	157	153	161
Means	174	186	169	158	157	159
S.D.	±7	±6	±3	±10	±6	±10
P Value	└P < 0.05┘					
	└──P < 0.05──┘					
	└──P < 0.05──┘					
	└──P < 0.05──┘					

a] There was a continuous rise in ventilation [Figure 5.1] despite the steady state gas exchange VO_2 from the 5th minute until the end of exercise [Figure 5.2], which was greater at 80% WR max than at 70% WR max [Table 5.2].

b] VO_2 and VCO_2 values in ml/min/kg body mass terms were also higher at 80% WR max than at 70% WR max. Furthermore, peak heart rates were also greater at 80% WR max compared to peak heart rates at 70% WR max.

c] Falls in pHa [Figure 5.5] and rises in venous blood lactate [Figure 5.7] concentrations were also greater at 80% WR max than at 70% WR max.

d] Despite the greater acidosis as shown by lower pHa values and higher blood lactate concentrations at 80% WR max than at 70% WR max, decreases in HCO_3^- ion concentration and $PaCO_2$ were not significantly different.

e] Maximum ventilation recorded at the end of 80% WR max were far below MVVREST values [Table 5.8]. Further, immediately post-exercise MVV values [MVVPOST-EX] were significantly

higher compared with MVVREST values [Table 5.8]. These data suggest the absence of respiratory muscle fatigue.

f] There was, however, a small but significant difference between MVVREST values and MVVR10, MVVR15 and MVVR20 values. MVVR10, MVVR15 and MVVR20 values were slightly lower than MVVREST values [Table 5.9].

g] Subjects stated that muscle fatigue was the major reason for terminating exercise.

The relevance of these findings are discussed in Chapter 7.

CHAPTER 6

DISCUSSION OF RESPIRATORY RESPONSES AND ACID-BASE BALANCE DURING HIGH INTENSITY CONSTANT-LOAD EXERCISE AT 70% WR max

There were several important findings from the study reported in Chapter Four. The most important of these were the following:

1. During exercise, there was a continuous increase in ventilation with a relative steady state in VO_2. This is shown in Figure 6.1 which indicates that VO_2 at 5, 10 and 22 minutes was not significantly different. Hence there was no evidence for a drift in VO_2 in this study after the 5th minute.

To our knowledge this is one of the first studies to use this type of exercise protocol and to monitor ventilatory changes continuously until the subjects terminated exercise due to

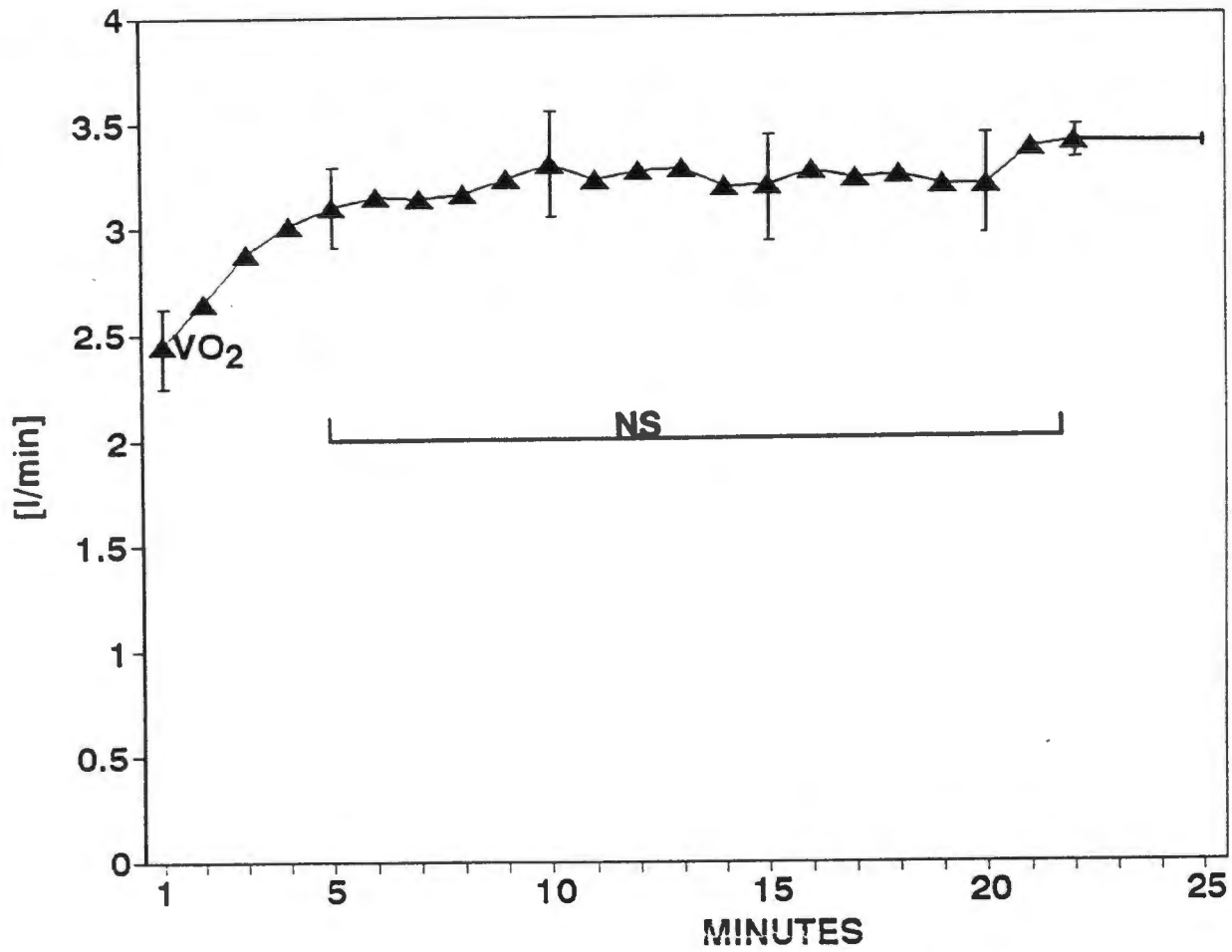


Figure 6.1 Changes in oxygen consumption [VO_2] with time during exercise at 70% WR max. [n = 5].
Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22nd minute.

exhaustion. Previous measurements of ventilatory changes during exercise of high intensity have usually used progressive incremental exercise tests in which no steady state was attained and VO_2 continued to rise progressively until the maximum VO_2 was attained [Roth DA et al, 1988; Whipp BJ et al, 1987].

Alternatively constant-load high intensity exercise tests lasting 8 minutes or less have been studied [Linnarson D, 1974; Roston WL et al, 1987; Casaburi R et al, 1987; Poole DC et al, 1988; Hagberg JM et al, 1978]. These constant-load exercise studies have all reported a slow rise in VO_2 to the point of fatigue. The slow kinetic phase of this VO_2 drift was measured as the increase occurring between the third minute of exercise and the termination of exercise [Roston WL et al, 1987; Casaburi R et al, 1987; Barstow TJ et al, 1991]. The magnitude of this "excess" VO_2 was reported to correlate highly with blood lactate concentrations [BJ Whipp, 1987; Poole DC, 1988; Wasserman K et al, 1975].

But the relevance of the above studies is difficult to determine as a true VO_2 steady state might have been expected to occur if the exercise lasted longer [Hickson RC et al, 1978]. These studies have used VO_2 values at 3 and 6 minutes and the end of

exercise to determine whether a steady state VO_2 was reached. A number of studies have shown that the time required to attain steady state VO_2 is longer, the heavier the work rate [Linnarsson D, 1974; Whipp BJ, 1972].

Accordingly, we chose VO_2 values at 5 and 10 minutes and at the end of exercise to quantify the slow kinetic phase of any VO_2 drift in this study [Figure 6.1]. This was necessary because our subjects exercised for a longer period at a higher work rate and took 5 minutes to reach steady state VO_2 values rather than 3 minutes, as reported in the previous studies. The reason for this discrepancy is that the work rate was only achieved in the 3rd minute of exercise. In minutes 1 and 2 work rates were 30 and 15 W below the target work rate. There are several interesting possibilities to explain the absence of a slow VO_2 drift [Figure 6.1] in this study:

a] One possible explanation is, the physical fitness of our subjects [Table 4.1], as demonstrated by the high work rates [$\pm$ 234 W] at which they exercised as well as the high blood lactate concentrations that were tolerated for an extended period of time [Figure 4.7].

It has been demonstrated that the pattern of VO_2 during the slow kinetic phase of the VO_2 drift is dependent on both the work rate and the physical fitness of the subject [Wasserman K et al, 1967].

In addition Yoshida T et al, [1982] observed that endurance training can lower the extent of the VO_2 drift at any given work rate. Åstrand PO et al, [1977] have also reported that highly conditioned endurance athletes were able to maintain a greater steady state VO_2 expressed as a % VO_2 max, than less-fit subjects, before a slow VO_2 drift occurred.

b] Another possibility is that the subjects used in this study exercised at a similar work rate but for much longer than previous studies.

The absence of any steady state VO_2 in studies by Linnarson D, [1974] and Roston WL et al, [1987] could perhaps be explained by the fact that the exercise bout was terminated before a true steady state could be reached. Roston WL et al, [1987] noted that the rate of change of the slow component of the VO_2 kinetics decreases with the duration of the exercise.

c] Thirdly, the type of exercise test used to study VO_2 kinetics of heavy exercise differed from previous studies.

Our study used a constant-load exercise test whilst other studies [Poole DC et al, 1988; Roth DA et al, 1988 and Whipp BJ, 1987] reporting VO_2 kinetics used progressive exercise tests to exhaustion.

The obvious explanation would be that these repetitive increments in work rate caused a continuous increase in VO_2 which was absent in our study in which a constant work rate was used from the 3rd minute until exhaustion.

The absence of VO_2 drift in this study indicates that oxygen supply to the active muscles was adequate from the 5th minute of exercise. Hence any change in ventilation that may have occurred during this study was clearly not to increase oxygen supply to the active muscles. The data also suggest that the oxygen cost of rising ventilation is probably trivial compared to the oxygen cost of skeletal muscle exercise.

A critical question that needs to be addressed is the underlying reason [s] or predominant mediator[s] of the ventilatory drift identified during constant-load, high intensity exercise.

The results of this study appear to shed some light on this controversy. In particular, they suggest that under the conditions of this study, the continual increase in ventilation was partly a response to a progressively increasing metabolic acidosis.

2. <u>This study indicates a possible relationship between the metabolic acidosis and hyperventilation during heavy exercise.</u>

There was an almost "mirror image" appearance of ventilatory increases and arterialized venous bicarbonate ion decreases in the first 10 minutes of exercise [Figure 6.2]. Koyal SN et al, [1976] plotted the decrease in bicarbonate ion concentration from the resting value and the "excess" ventilation as described in Chapter Three in order to determine the extent to which the "excess" ventilation may be related to the metabolic acidosis that develops during intense exercise. They concluded that "excess" ventilation was closely related to the metabolic

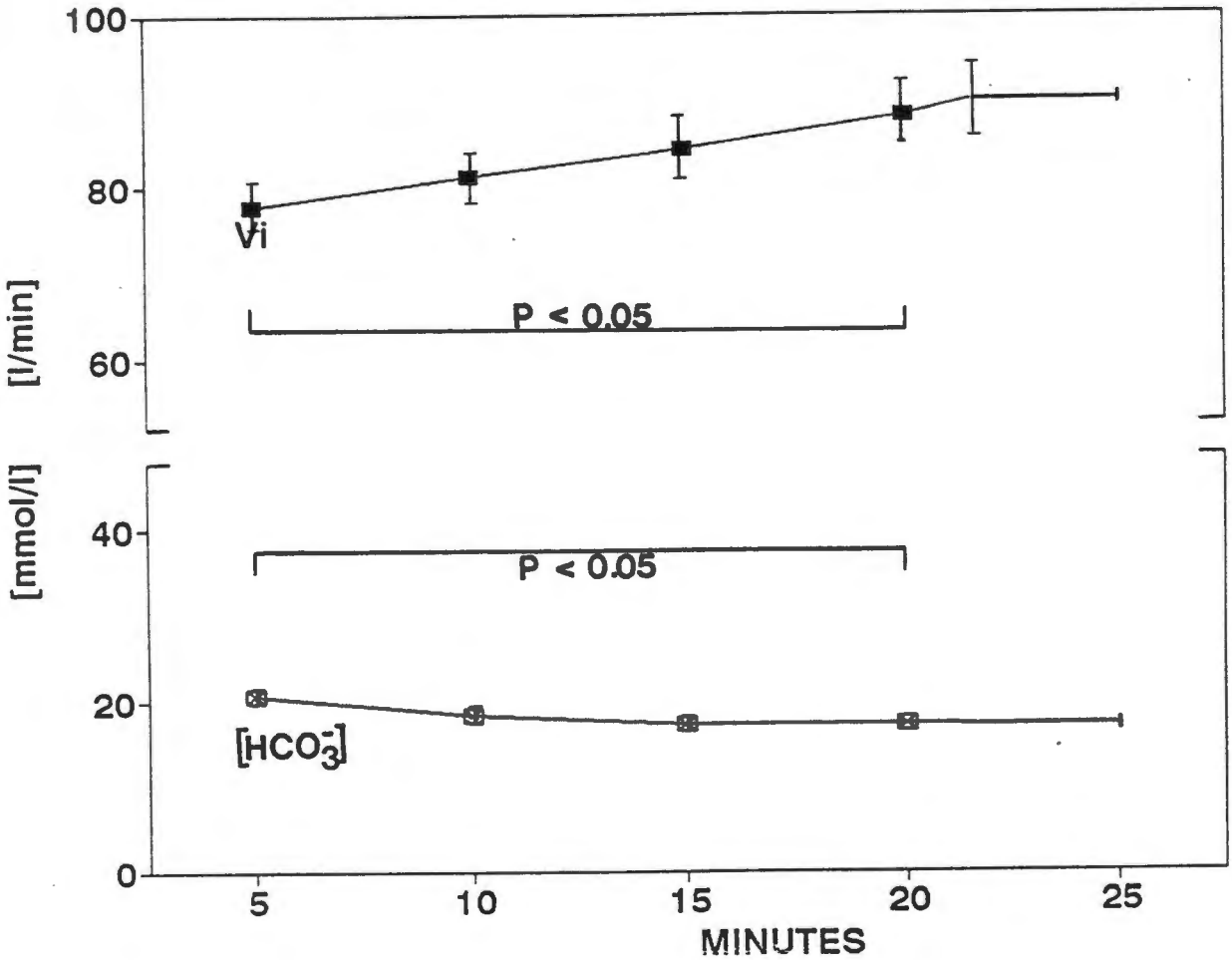


Figure 6.2 The temporal relationship between mean minute ventilation [Vi] and arterialized venous bicarbonate ion concentrations [HCO_3^-] during exercise at 70% WR max. [n = 5].

Horizontal error bar indicates that 2 of the 5 subjects stopped exercise at the end of the 22th minute.

acidosis so that ventilation increased about 4 l/min for every 1 mmHg drop in bicarbonate ion concentration.

Our results [Table 4.3] are similar to those of Koyal SN et al, [1976] and indicate that the added increment in ventilation [Figure 4.4] could possibly be linked to the maintenance of acid base balance. Ventilation increased 5 l/min for every 1 mmHg drop in bicarbonate ion concentration from the 15th minute and stayed close to that value until the end of exercise [Table 4.3].

3. Respiratory compensation for metabolic acidosis was adequate, but incomplete, as pH fell from rest to exercise, but remained reasonably constant during exercise.

Our results agree with those of Wasserman K et al, [1984] as the plasma bicarbonate ion concentration decreased almost stoichiometrically with the increase in blood lactate concentration as shown in Figure 4.7.

This apparent association between increases in blood lactate concentration and decreases in HCO_3^- concentration is due to both changes being indirectly related to excessive H^+ ion production.

Many investigators assumed lactate to be the source of H^+ generated during exercise [Wasserman K et al, 1973; Whipp BJ, 1977; Davies JA, 1985]. However, other studies have indicated that protons are generated as a result of glycolytically produced ATP [Gevers W, 1977; Alberti KGMM et al, 1982; Hochachka PW et al, 1983] and that the increase in lactate production is more a consequence than a cause of the developing metabolic acidosis [Dennis SC et al, 1991].

The apparent association between blood lactate concentration and bicarbonate ion concentration is presumed to reflect the possibility that some lactate anions may combine with H^+ ions before passing through the sarcolemmal membrane after which they dissociate in the blood [Walsh ML et al, 1988].

There would be a substantial decrease in arterial blood pH during periods when the rate of H^+ ion production is increased, such as in high intensity exercise above the "second ventilatory threshold" were it not for the bicarbonate buffering system.

Recent studies by Wasserman K et al, [1986] suggest that as much as 94% of the hydrogen ion load produced during high intensity exercise is buffered by the bicarbonate system. H^+ ions combine with bicarbonate ions to form carbonic acid which dissociates to form carbon dioxide and water. The added increment in ventilation then clears the blood of the excess carbon dioxide formed by this dissociation [Murray JF, 1986].

It is therefore probable that blood bicarbonate ion changes are not necessarily caused by an increase in lactate turnover but rather by an increase in proton generation through glycolysis that could also cause an increase in lactate turnover [Issekutz B, 1984; Stainsby WN et al, 1987 and Brooks GA et al, 1991]. This explains the apparent association between bicarbonate ion decreases and lactate increases [Figure 4.7] observed in this study.

It therefore appears that the added increment in ventilation [Figure 4.4] eliminates the carbon dioxide liberated in the reaction between protons and bicarbonate ions and as a consequence pH remained virtually normal.

4. There was no retention of carbon dioxide as arterialized venous carbon dioxide tension did not increase. Instead arterialized venous carbon dioxide tension decreased ($P < 0.05$) from a resting value of 46.0 ± 3.2 mmHg to 34.9 ± 4.0 mmHg in the 15th minute of exercise after which it remained close ($P > 0.05$) to that value until the end of exercise [Figure 4.6].

$PaCO_2$ is an accepted indicator of the adequacy of ventilation [Severinghaus JW, 1965] in meeting the body's metabolic requirements. A reduced $PaCO_2$ may indicate hyperventilation due to neurogenic drive [Rybicki KJ et al, 1985; Walsh ML et al, 1988]. Alternatively $PaCO_2$ must fall if the HCO_3^- concentration falls to keep pH constant.

The ventilatory response to the metabolic acidosis induced by exercise was therefore to reduce $PaCO_2$. The increase in ventilation exceeds the rise in carbon dioxide expiration [VCO_2] [Whipp BJ et al, 1984] [Table 4.3]. The Vi/VCO_2 ratio showed a steady increase and values of 28.7 ± 4.1 were recorded in the 20th minute of exercise. This caused a decrease in $PaCO_2$ and the pH fall was constrained [Wasserman K, 1984].

Therefore, in this study, the less severe acidosis was a result of the added increment of ventilation with a fall in arterial carbon dioxide tension which was sufficient to prevent pH falling continuously during the exercise period [Figure 4.5].

5. The ability to ventilate maximally after severe exercise was not impaired but was, in fact, increased [Table 4.7]. This was shown by the insignificant difference ($P > 0.05$) between MVVREST values and MVVPOST-EX values recorded in the 30 s immediately following exercise at 70% WR max.

Several authors have used the MVV manoeuvre to evaluate respiratory muscle fatigue which could reduce ventilatory capacity during and after severe exercise [Martin BJ et al, 1984; Bender PR et al, 1985; Loke J et al, 1982; Anholm JD et al, 1989; Warren GL, 1989].

These results therefore indicate that it is unlikely that fatigue of the respiratory muscles could have contributed to the termination of exercise at 70% WR max in these subjects.

6. Peak rates of ventilation measured during the prolonged exercise at 70% WR max did not reach values close to MVVREST or to maximum values measured during the VO_2 max test.

Subjects ventilated at about 72% of the Vi max achieved during an incremental test to exhaustion and at about 50% of their MVV recorded during sustained voluntary hyperventilation at rest. Data from Freedman S, [1970], Tenney SM et al, [1968], and Zocche GP et al, [1960] indicate that a ventilation rate equivalent to about 50 - 60% of MVV can be maintained for 15 minutes. The subjects in this study were able to sustain 50% of MVV for approximately 22 minutes of exercise at 70% WR max.

Thus, this study suggests that the maximum rate of ventilation achieved during an incremental test to exhaustion is a more realistic measure of the true maximum ventilatory capacity as it simulates the normal exercise response more closely.

If the maximum ventilation achieved during an incremental test to exhaustion is interpreted as the real maximum, then during prolonged exercise, the subjects maintained about 72% of their maximum ventilation for 22 minutes.

These high levels of ventilation may have contributed to the feeling of breathlessness towards the end of exercise as reflected by the increasing perception of ventilatory effort [Figure 4.8] as well as by the increase in the "dyspnoea index" reaching a value of 54 $\pm$ 5.0% [Table 4.6] in the 22nd minute of exercise.

The "dyspnoea index" has been used to assess the intensity of breathlessness and often approximates 100% in patients with chronic obstructive pulmonary disease [Gandevia B, 1963]. These patients normally attribute their exercise intolerance exclusively to the discomfort associated with the act of breathing [Cotes JE, 1979; Roussos C, 1982; Jones NL et al, 1990]. At the end of maximal exercise the "dyspnoea index" in healthy subjects is usually in the range of 70 - 90% but often higher in athletes [Cotes JE, 1979]. Therefore, the intensity of breathlessness as measured by the "dyspnoea index" [Table 4.6] would seem to have been an unlikely cause of the termination of exercise at 70% WR max.

In contrast, ventilation [Figure 4.1] and RVE [Figure 4.8] showed a continuous rise from the first minute until the end of exercise. The similarity of ratings of perceived exertion

for ventilation and changes in ventilation under these conditions suggests that these two variables are related to each other at work rates above the "second ventilatory threshold".

Most investigations have found a relationship between RPE and ventilation during high intensity exercise [Borg GAV et al, 1976; Kamon E et al, 1974; Noble B et al, 1973 and Pandolf K, 1977; Robertson RJ, 1982], whilst other studies [Stamford BA et al, 1974; Edwards RHT et al, 1972] concluded that ventilation was relatively unimportant as a cue for the effort sense at moderate intensity exercise.

The ventilatory signal is hypothesized to be strong during respiratory compensation for the developing metabolic acidosis [Jones NL, 1984; Demello JJ et al, 1987], although the exact aspect[s] of ventilation that is sensed remains unclear [Demello JJ et al, 1987].

Results of this study support the hypothesis that ventilation is a relatively important cue for effort sense [Borg GAV et al, 1976; Noble B et al, 1973; Pandolf K, 1977; Robertson RJ, 1982] at work rates associated with a progressive developing metabolic acidosis [Jones NL, 1984; Demello JJ et al, 1987].

This study therefore suggests that the high levels of ventilation [Figure 4.1] maintained during this work rate contributed towards the continuous increase in the perception of ventilatory effort [Figure 4.8]. However, it is unlikely that the subjects terminated exercise at 70% WR max because of the feeling of breathlessness. The basis for this conclusion is the following:

i] Final ventilation recorded [70% Vi] at the end of 70% WR exercise [Table 4.1] did not reach values close to maximal voluntary ventilation [MVVREST] or maximum ventilation [Vi max] recorded during incremental exercise to exhaustion [Table 4.7].

ii] Subjects stated that leg muscle fatigue rather than dyspnoea was the reason why they terminated the exercise.

iii] The "dyspnoea index" did not reach values close to maximum values used to assess breathlessness [Gandevia B, 1963]. However, this study questions the use of the "dyspnoea index" as a method to assess breathlessness as the index is not a true measure of a sensation [dyspnoea] but rather expresses ventilation as a percentage of MVV.

7. Changes in blood lactate concentration and heart rate did not parallel changes in RVE and RPE [Figure 4.8].

This study showed that whereas blood lactate concentrations and heart rates reached steady states after 10 minutes at this work rate [Figure 4.8], the perception of effort continued to increase throughout the exercise bout.

While some investigators have concluded that blood lactate concentration is the factor determining the ratings of perceived exertion [Edwards RHT et al, 1972; Demello JJ et al, 1987; Horstman DH 1977; Ekblom B et al, 1971; Gamberale B, 1972; Borg G, 1962], others have furnished evidence which disputes the central importance of lactate as a perceptual cue [Kay C et al, 1969; Lollgen H et al, 1980].

It appears as if blood [or muscle] lactate concentrations could possibly influence perception of effort at higher exercise intensities in which there is a continuous increase in blood lactate concentration. But its contribution at lower exercise intensities would be minimal because blood lactate concentrations do not increase appreciably below exercise intensities of 65% VO_2 max [Mihevic PM, 1981].

Although our study involved high intensity exercise [more than 80% VO_2 max], blood lactate concentrations did not change significantly ($P > 0.05$) after the first 10 minutes of constant-load work [Figure 4.7].

It appears that the dissociation between blood lactate concentration and perception of effort reported in this study [70% WR max] and by Kay C et al, [1969] [80% MAP], shows that the blood lactate concentration can be excluded as the most important factor determining the RPE during high intensity constant-load exercise.

Others have also suggested a relationship between heart rate and the perception of effort during exercise. A strong linear relationship between heart rate and perceived exertion during progressive exercise to exhaustion has been reported by several investigators [Skinner JS et al, 1973; Stamford BA, 1976; Edwards RHT et al, 1972; Gamberale B, 1972]. But there seems to be a dissociation between heart rate and perception of effort during constant-load exercise [Borg G, 1962].

Results from other studies have suggested that heart rate is not a factor determining the rating of perceived exertion during exercise [Kamon E et al, 1974; Ekblom B et al, 1971; Pandolf KB et al, 1972 and Noble BJ et al, 1983].

Perhaps the dissociation between heart rate and perception of effort found in this study is due to the fact that the RPE scale was designed to follow the heart rate response to exercise in which the intensity increases progressively [Borg G, 1962]. Other studies using constant-load work showed that heart rate remained in a steady state whilst ratings of perceived exertion for effort showed a progressive increase with time [Stamford BA, 1976; Noble BJ et al, 1979].

8. Causes of fatigue at this exercise intensity:

Subjects participating in this study complained primarily of severe fatigue of the quadriceps muscle and stated that muscle fatigue was the reason why they stopped exercise at this work rate.

The cause of the muscle fatigue at this work rate is uncertain. Factors that can be excluded are the following: a decreased oxygen supply to the working muscles, severe systemic acidosis and high blood lactate concentrations.

9. Summary:

The most important conclusion from this study was that pulmonary function can be excluded as a limiting factor for performance of high intensity exercise at a workload corresponding to 70% WR max. The basis for this conclusion is the following:

a] VO_2 remained constant throughout the exercise period [Figure 6.1] indicating that the oxygen supply to the muscles was adequate.

b] There was an effective respiratory compensation for the less severe metabolic acidosis that occurred at this work rate. This was shown as the added increment in ventilation which caused a progressive fall in arterial carbon dioxide tension [Figure 4.3] which in turn was sufficient to prevent pHa falling continuously during the exercise period [Figure 4.5].

c] The "dyspnoea index" did not reach values close to maximum [Table 4.6]. Similarly, peak ventilation did not reach values close to maximal voluntary ventilation.

d] There was no evidence of respiratory muscle fatigue as MVVREST and MVVPOST-EX values were not significantly different [Table 4.7].

Despite the relative constancy of these variables, the perception of effort rose to high values at exhaustion. Similarly, subjects complained that muscle fatigue terminated exercise. Hence the increase in perception of effort cannot be explained on the basis of the measurements made in this study.

CHAPTER 7

DISCUSSION OF RESPIRATORY RESPONSES AND ACID-BASE BALANCE DURING HIGH INTENSITY CONSTANT-LOAD EXERCISE AT 80% WR max

The data reported in Chapter Five provide evidence which convincingly eliminate the pulmonary system as a possible factor limiting performance during high intensity exercise at 80% WR max. The major findings in that investigation, which were similar to those measured at 70% WR max, were the following:

1. The VO_2 response at 80% WR max was similar to that at 70% WR max as reported in Chapter Four. In particular, VO_2 was in steady state [Figure 7.1] despite a continuous increase in ventilation ($P < 0.05$).

The steady state in VO_2 reported in this section of the study indicates that, as was the case during exercise at 70% WR

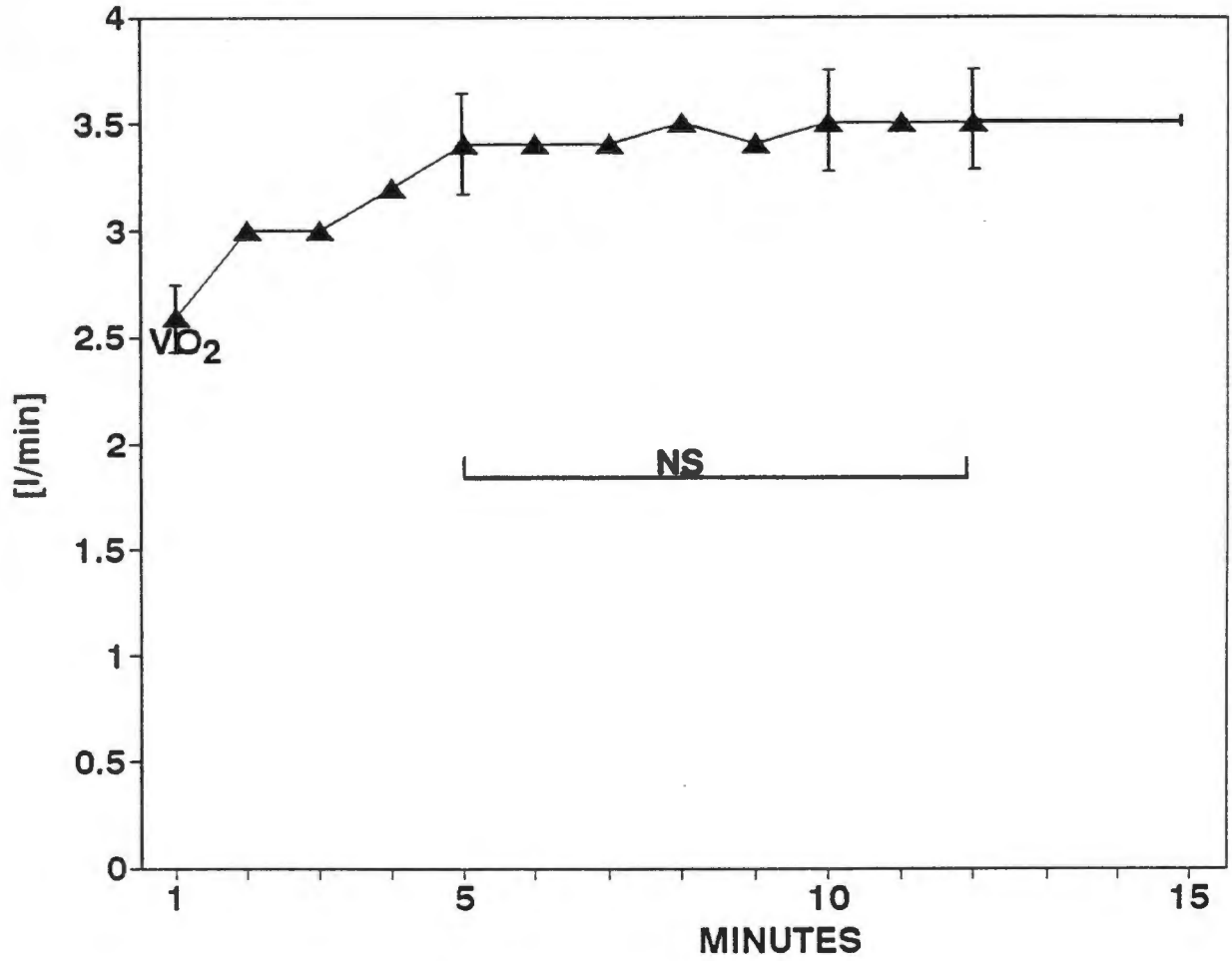


Figure 7.1 Changes in oxygen consumption [VO_2] with time during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise in the 12th minute.

max, the ventilatory response at this high work rate was adequate to maintain oxygen delivery to the tissues.

It was clear that the steady state oxygen consumption between the 5th minute and end of exercise could not account for the ventilatory drift [Figure 5.1] observed at 80% WR max, in these subjects.

2. As argued in Chapter Six, evidence in this study does suggest that the continuous ($P < 0.05$) rise in ventilation must be in part due to the respiratory compensation for the metabolic acidosis.

This is reflected in the almost "mirror image" appearance of the increase in ventilation and the reduction in arterial bicarbonate ion concentration [Figure 7.2].

Furthermore, the "excess" ventilation as described in Chapter Three [Figure 5.4] appears to be an attempt to compensate for the progressively developing metabolic acidosis as illustrated by an

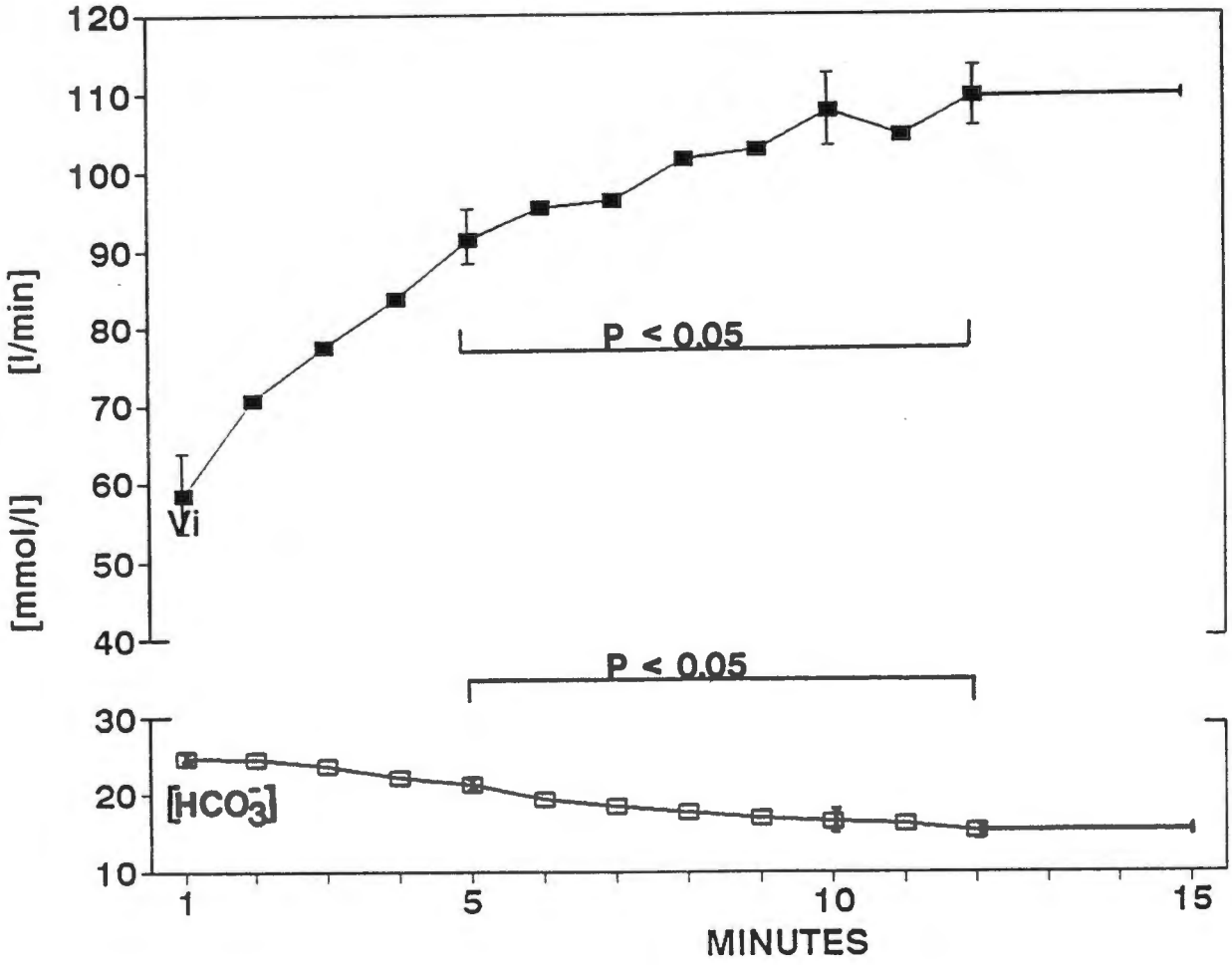


Figure 7.2 The temporal relationship between mean minute ventilation [Vi] and arterialized venous bicarbonate ion concentrations [HCO_3^-] during exercise at 80% WR max. [n = 8].

Horizontal error bar indicates that 2 of the 8 subjects stopped exercise at the end of the 12th minute.

increase of over 6 l/min in ventilation with every 1 mmol/l decrease in bicarbonate ion concentration [Table 5.4]. These increases in ventilation were higher for every 1 mmol/l decrease in bicarbonate ion concentration than those reported in Chapter Six. This might indicate a greater ventilatory response to the more marked metabolic acidosis at 80% WR max compared to 70% WR max.

3. Respiratory compensation for the marked metabolic acidosis was appropriate as shown by a low but constant pHa which remained in a steady state from the 5th minute until the end of exercise [Figure 5.5].

4. Furthermore, there was no retention of carbon dioxide tension [greater than resting values] [Figure 5.6].

Arterialized venous carbon dioxide tension decreased from a resting value of 42.5 $\pm$ 3.3 mmHg to 36.2 $\pm$ 3.7 mmHg in the

12th minute of exercise. In addition, the ventilatory equivalent for arterial carbon dioxide [$Vi/PaCO_2$] showed a steady increase from 2.1 $\pm$ 0.3 l/min/mmHg in the 5th minute to 2.9 $\pm$ 0.2 l/min/mmHg in the 12th minute of exercise [Table 5.4]

This reflects an adequate ventilatory response to the metabolic acidosis of exercise. As was the case at 70% WR max, $PaCO_2$ values were reduced by the added increment of ventilation which was greater than the increase in the rate of carbon dioxide production. The Vi/VCO_2 ratio therefore showed a steady increase and values of 29.8 $\pm$ 2.9 were recorded in the 12th minute of exercise [Table 5.4].

As argued in Chapter Six, the pulmonary system seems to have functioned perfectly under these conditions, maintaining acid-base balance through a full respiratory compensation for the marked acidosis.

5. <u>MVVPOST-EX increased after exercise indicating that the ability to ventilate following heavy exercise was in fact increased. [Figure 5.9].</u>

All subjects increased their maximal voluntary ventilation ($P < 0.05$) in the minute immediately following exhaustive exercise at 80% WR max.

However, there was a small but significant drop ($P < 0.05$) in MVV values recorded after a 10, 15 and 20 minute recovery period [MVVR10 , MVVR15 and MVVR20] if compared to MVVREST values [Figure 5.9]. This finding is consistent with the studies of Bender PR et al, [1985] who observed that the largest decreases in the MVV value occurred 10 minutes after long-term exercise.

One explanation for the lower MVV values recorded after a 10 minute recovery period is that exercise-induced bronchodilation and improved contractility of the respiratory muscles could have masked respiratory muscle fatigue. Catecholamine concentrations rise sharply at work rates above 50 - 70% VO_2 max [Banister EW et al, 1972]. It has been reported that catecholamines cause an improved contractility of skeletal muscles, resulting from improvement in excitation-contraction coupling [Gross D et al, 1988]. Furthermore, bronchodilation associated with exhaustive exercise may lower the work of

breathing sufficiently [Anholm JD et al, 1989]. This could account for the increased MVVPOST-EX ($P < 0.05$) values recorded by this study in the minute immediately following exercise. The lower MVVR10, MVVR15 and MVVR20 values could be interpreted as an indication of respiratory muscle fatigue which became apparent only after a recovery period of 10 minutes due to a possible fall in catecholamine levels, thereby reversing exercise-induced bronchodilation and the improved contractility of respiratory muscles after a period of rest following exhaustive exercise.

Unfortunately, this study did not measure serum catecholamine concentrations during exercise and the recovery period following exhaustive exercise and can therefore only speculate about the reasons for [i] the increased MVVPOST-EX values recorded immediately after exercise and [ii] the significant decrease in MVV values recorded after a 10, 15 and 20 minute recovery period.

A critical question that remains unanswered is whether respiratory muscle fatigue occurred prior to, or coincidental

with the termination of exhaustive constant-load exercise at 80% WR max and whether it limits exercise performance at this work rate.

According to Roussos C et al, [1982], the identification of respiratory muscle fatigue ultimately depends on the demonstration of a decrease in force development by the respiratory muscles which could lead to a decreased capacity to maintain or increase alveolar ventilation appropriately. Hence, the pulmonary system fails to increase alveolar ventilation sufficiently causing incomplete respiratory compensation for the developing metabolic acidosis [Inbar O et al, 1987; Hopkins SR et al, 1989; Dempsey JA et al, 1990] and hypercapnia [Roussos C et al, 1982].

To our knowledge, this is the first study into the effects of high intensity constant-load exercise on the endurance of respiratory muscles that also measured blood gas tensions and acid-base balance during the exercise bout. As reported earlier, the pulmonary system performed perfectly, maintaining acid-base balance. Respiratory compensation for the developing metabolic acidosis was appropriate at 80% WR max as shown by the following:

i] a low but consistent arterialized venous pH which remained in a steady state from the 5th minute until the end of exercise [Figure 5.5].

ii] the absence of hypercapnia as there was no increase in arterialized venous carbon dioxide tension [Figure 5.6]. Rather, $PaCO_2$ continued to decrease throughout the exercise period.

Thus, this study therefore proposes that the reversal of exercise-induced bronchodilation and decreased contractility and not respiratory muscle fatigue are possibly the reasons for the lower recorded MVV values after a 10, 15 and 20 minute recovery period. Previous studies [Bender PL et al, 1985] showing decrements in the MVV values recorded after prolonged high intensity and marathon running [Loke J et al, 1982] have attributed the fall to respiratory muscle fatigue. These investigators have not included gas measurements as a further measure of the adequacy of pulmonary function. The absence of respiratory muscle fatigue in this study was further supported by the following findings:

i] There was a sufficient increase in alveolar ventilation, ensuring a complete respiratory compensation for the developing metabolic acidosis at 80% WR max.

ii] The absence of hypercapnia at this level of ergometer work.

6. Peak ventilation did not reach values close to MVVREST.

Subjects in this study ventilated at about 54% of their recorded MVVREST values during exercise and at about 80% of the maximum ventilation [Vi max] achieved during the incremental test to exhaustion.

As argued in Chapter Six, these high levels of ventilation may have contributed to the feeling of breathlessness at the highest work rates as reflected by the increasing perception of ventilatory effort [Figure 5.8] as well as by the increased "dyspnoea index" [Table 5.7].

However, the "dyspnoea index" did not reach values close to maximum as explained in Chapter Five. Values of 61 $\pm$ 5.6% were recorded in the 10th minute and stayed close to that value until the end of exercise [Table 5.7]. Recorded values indicate that the feeling of breathlessness did not reach values close to maximum and did not show any significant increase in the last five minutes of exercise.

The intensity of breathlessness can be excluded as a factor limiting exercise at 80% WR max for the following reasons:

i] The final rates of ventilation recorded at the end of 80% WR max exercise [80% Vi] did not reach values close to maximal voluntary ventilation [MVVREST] or maximum ventilation [Vi max] recorded during the incremental exercise to exhaustion [Table 5.8].

ii] Subjects stated leg muscle fatigue rather than dyspnoea as the reason why they terminated the exercise.

iii] The "dyspnoea index" did not reach values close to the maximum values usually considered to indicate severe breathlessness [Gandevia B, 1963].

7. Causes of fatigue at this exercise intensity:

As was the case at 70% WR max, subjects complained primarily of severe fatigue of the quadriceps muscle and listed muscle fatigue as the most dominant subjective sensation limiting further exercise.

Results collected under these conditions do not indicate the cause of muscle fatigue but certain factors can be excluded: a decreased oxygen supply to the working muscles and elevated blood lactate concentrations.

8. Summary:

The results of this study indicate that the pulmonary system responded adequately and can therefore be excluded as a limiting factor for performance at this exercise intensity. The basis for this conclusion is the following:

a] The steady state VO_2 kinetics at 80% WR max [Figure 7.1] indicates that the ventilatory response was adequate to maintain oxygen delivery to the working muscles.

b] There was a full respiratory compensation for the marked metabolic acidosis that occurred at this work rate. This was shown by an increased ventilation which caused a progressive fall in arterialized carbon dioxide tension [Figure 5.3]. Although a low pHa was recorded throughout the exercise, the respiratory compensation was sufficient to prevent pHa from falling continuously during the exercise period [Figure 5.5].

c] The "dyspnoea index" did not reach values close to maximum [Table 5.7]. Similarly, final ventilation [80% Vi] did not reach values close to the maximal voluntary ventilation [Table 5.8].

d] There was no evidence of respiratory muscle fatigue as MVVPOST-EX values were increased if compared with MVVREST values [Figure 5.9].

The perception of effort rose to high values reaching almost maximum values at exhaustion [Table 5.7] despite the relative constancy of these variables. Similarly, subjects complained that muscle fatigue caused the cessation of the exercise bout. Hence the measurements made in this study cannot explain the increase in perception of effort.

7.1 A comparison between the variables measured during high intensity constant-load exercise at 70% and 80% WR max from the 5th minute of exercise until the end of exercise:

Data obtained in this study from the 5th minute of exercise until the end of exhaustive high intensity constant-load exercise at 70% and 80% WR max clearly show that the only significant difference in measured variables were for ventilation, arterialized venous pH, venous blood lactate concentrations, VO_2 and VCO_2 in ml/kg/min [Table 5.2].

The difference between variables measured at the two constant-load work rates appears to be related to the more marked

metabolic acidosis observed during 80% WR max [Table 5.6] cycle ergometer work compared to 70% WR max [Table 4.5].

Evidence for this conclusion is supplied by the progressive increase in the blood lactate concentration reported at 80% WR max as a consequence of the increasing metabolic acidosis [Table 5.5]. In contrast lactate turnover at 70% WR max seems to be in an apparent steady state [Table 4.4] showing a less marked metabolic acidosis.

Furthermore, pHa decreased progressively in the first 3 minutes of exercise at 80% WR max but then remained at a low but steady state level from the 5th minute until the end of exercise [Table 5.5], whilst pHa was maintained at a higher steady state level during 70% WR max exercise [Table 4.4].

This indicates a less marked metabolic acidosis at this level of ergometer work. Subjects at both work rates were able to maintain acid-base homeostasis during the exercise period by an appropriate hyperventilation [Figure 4.1 and Figure 5.1]. This respiratory compensation which produced a progressive fall in $PaCO_2$ [Figure 4.3 and Figure 5.3] was sufficient to prevent pHa from falling continuously during either exercise periods [Figure 4.5 and Figure 5.5].

7.2 Reasons for fatigue at 70% and 80% WR max:

This study suggests that subjects participating at both 70% and 80% WR max became exhausted for reasons other than failure of acid-base homeostasis. Subjects complained primarily of severe fatigue of the quadriceps muscle and stated muscle fatigue as the most dominant subjective sensation limiting further exercise.

In conclusion, muscle fatigue seems to be the factor limiting exercise under these conditions but the reason for the onset of muscle fatigue remains uncertain. The higher work rates at 80% WR max caused muscle fatigue to develop more rapidly as subjects exercised for a shorter time period at 80% than at 70% WR max.

CHAPTER 8

CONCLUSIONS AND RECOMMENDATIONS

8.1 Conclusions:

This thesis set out to investigate whether or not the pulmonary system may limit performance during high intensity constant-load exercise, ultimately causing the termination of exercise. The question of pulmonary function limiting exercise was examined in terms of a possible limitation arising from VO_2 kinetics, acid-base balance, development of progressive dyspnoea and respiratory muscle fatigue.

In conclusion, the results from this study indicate that the pulmonary system can be excluded as a factor limiting exercise during high intensity constant-load exercise at 70% and 80% WR max, work rates above the "second ventilatory threshold".

The basis for this conclusion is the following:

1. The ventilatory response at 70% and 80% WR max was adequate to maintain oxygen delivery to the tissues. The steady

state VO_2 [Figure 6.1 and Figure 7.1] indicates adequacy of tissue oxygenation.

2. The pulmonary system performed perfectly, maintaining acid-base balance. Respiratory compensation for the progressive metabolic acidosis was appropriate during both work rates. This is shown by the following:

a] 70% WR max:

i] Arterialized venous pH remained in a steady state and virtually unchanged from the resting value [Figure 4.5].

ii] Alveolar ventilation could be increased to cause a progressive decrease in $PaCO_2$ during the exercise period [Figure 4.6].

iii] There was a continuous increase in the following ratio's indicating an adequate respiratory compensation: $Vi/PaCO_2$, Vi/VCO_2 and Vi/VO_2 [Table 4.3].

b] 80% WR max:

i] A low but constant arterialized venous pH remained in a steady state from the 5th minute until the end of exercise [Figure 5.5].

ii] Alveolar ventilation could be increased to cause a progressive decrease in $PaCO_2$ during the exercise period [Figure 5.6].

iii] There was a continuous increase in the $Vi/PaCO_2$, Vi/VCO_2 and Vi/VO_2 ratio's [Table 5.4].

3. The "dyspnoea index" did not reach values close to maximum. The index showed a continuous increase until the 10th minute at 80% WR max after which it did not show any further increase [Table 5.7].

4. A further argument against the pulmonary system limiting exercise during both work rates was that ventilation recorded in the final minute [80% Vi] did not reach values

close to MVVREST [Table 5.8]. The ventilation capacity under these exercise conditions was in fact increased after exercise.

5. There was no evidence of respiratory muscle fatigue as shown by the following:

a] 70% WR max:

i] Subjects increased their MVVPOST-EX ventilation in 30 s immediately following exercise [Table 4.7].

b] 80% WR max:

i] All subjects increased ($P < 0.05$) their MVVPOST-EX values in in the 30 s following exercise [Table 5.8].

ii] This study proposes that the reversal of exercise-induced bronchodilation and decreased contractility and not respiratory fatigue were possibly the reasons for the lower

MVV values recorded after 10, 15 and 20 minute recovery periods [Figure 5.9]. The absence of respiratory muscle fatigue was supported by [i] a sufficient increase in alveolar ventilation ensuring a complete respiratory compensation for the metabolic acidosis and [ii] the absence of hypercapnia in arterialized venous blood [Figure 5.6].

6. Muscle fatigue seems to be the reason why subjects stopped exercise at both work rates. Subjects complained primarily of severe fatigue of the quadriceps muscle and stated muscle fatigue as the dominant sensation limiting further exercise. The cause of muscle fatigue at this work rate is uncertain and factors that were not directly considered in this study seem to have been involved. However, certain factors can be excluded:

a] a decreased oxygen supply to the working muscles.

b] rising blood lactate concentrations.

Although this study did not set out to examine the following factors, it provides evidence that:

a] the oxygen cost of breathing can be excluded as one of the factors contributing to a limitation of oxygen delivery. This was shown by the steady state VO_2 at both work rates indicating adequate oxygen delivery to the working tissues [Figure 6.1 and Figure 7.1] and excluding the metabolic cost of ventilation "stealing" oxygen from the working skeletal muscles.

b] the rise in blood lactate concentrations during exercise at 80% WR max was not caused by an inadequate oxygen delivery to the active muscles. Similarly, increasing blood lactate concentrations did not cause the slow rise in VO_2 normally associated with work rates above the "second ventilatory threshold". This was shown by the absence of a VO_2 drift at 80% WR max in the face of an increasing blood lactate concentration [Figure 5.7].

c] In addition, the results of this study contrast with those of Reybrouck T et al, [1983] who have described a ventilatory threshold for long-term exercise at about 73% VO_2 max ["second ventilatory threshold"]. During work at the

"second ventilatory threshold" for long-term exercise, ventilation, VO_2 and blood lactate concentrations remain in steady state whereas above the "second ventilatory threshold" each of these variables is said to increase continuously.

However, this study reported another work rate above the "second ventilatory threshold" during which there was a continuous increase in ventilation [Figure 4.1] BUT with steady state VO_2 [Figure 4.2] and blood lactate [Figure 4.7] concentrations. This work rate at 70% WR max corresponded to 80 - 85% VO_2 max and was maintained for between 22 - 25 minutes by the subjects participating in this study.

A possible reason for the difference between our study and that of Reybrouck T et al, [1983] is that they used data collected during cycle ergometer tests to describe the "second ventilatory threshold", whereas a 12 minute running test to exhaustion was used to describe the work rate above the "second ventilatory threshold".

Secondly, the superior condition of our subjects might have accounted for the difference between these two studies. However, the behaviour of ventilation, VO_2 and blood lactate

concentration during exercise at 80% WR max was similar to that reported by Reybrouck T et al, [1983] at work rates above the "second ventilatory threshold" corresponding to 85 - 90% VO_2 max.

8.2 Recommendations:

This study recommends that any further research attempting to evaluate the adequacy of pulmonary function at constant-load work rates above 80% VO_2 max should include the following:

i] Measurements of muscle pH to establish whether acidosis in the working tissue could account for the termination of exercise at that work rate.

ii] Measurements of catecholamine concentrations accompanying MVV tests before, after exercise and during a recovery period to establish whether there is a significant relationship between the two variables.

iii] Spirometry measurements before and after exercise, P_I (max) and P_E (max), respiratory rate, rectal temperatures, and V_d/V_t ratios.

REFERENCES

* ALBERTI, KGMM. and C. CUTHBERT. The hydrogen ion in normal metabolism: a review. In. Metabolic acidosis. Ciba Foundation Symposium. 87:1 - 19, 1982.

* ANHOLM, J.D., J. STRAY-GUNDERSEN, M RAMANATHAN, and R.L. JOHNSON Jr. Sustained maximal ventilation after endurance exercise in athletes. J. Appl. Physiol. 67:1759-1763, 1989.

* ANHOLM, J.D., R.L. JOHNSON, and M RAMANATHAN. Changes in cardiac output during sustained maximal ventilation in humans. J. Appl. Physiol. 63:181-187, 1987.

* ASMUSSEN, E. Muscular Exercise. In: Handbook of Physiology Respiration. Ed. Washington DC: W.O. Fenn and H. Rahn. Am. Physiol Soc, 1965, Sect. 3, Vol II, Chapt. 36, pp 939-978.

* ÅSTRAND, P-O. and K. RODAHL. Textbook of Work Physiology. Physiological Basis of Exercise, 2nd Ed. New York: McGraw-Hill Book Company, 1977, pp. 235-236.

* AUBIER, M., N VIIRES, D MURCIANO, J.P. SETA, and R. PARIENTE. Effects of digoxin on diaphragmatic strength generation. J. Appl. Physiol. 61:1767-1774, 1986.

* AUBIER, M., N VIIRES, J. PIQUET, D. MURCIANO, F. BLANCHET, C. MARTY, R. GHERARDI, and R. PARIENTE. Effects of hypocalcemia on diaphragmatic strength generation. J. Appl. Physiol. 58:2054-2061, 1985.

* BAI, T.R., B.J. RABINOVITCH, and R.I. PARDY. Near-maximal voluntary hyperpnea and ventilatory muscle function. J. Appl. Physiol. 57:1742 - 1748, 1984.

* BANISTER, E.W., J. GRIFFITHS. Blood levels of adrenergic amines during exercise. J. Appl. Physiol. 33:674-676, 1972.

* BARSTOW, T.J. and P.A. MOLE. Linear and nonlinear characteristics of oxygen uptake kinetics during heavy exercise. J. Appl. Physiol. 71:2099 - 2106, 1991.

* BELMAN, M.J. and C. MITTMAN. Ventilatory muscle training improves exercise capacity in chronic obstructive pulmonary disease patients. Am. Rev. Respir. Dis. 121:273-280, 1980.

* BELMAN, M.J. and R. SHADMEHR. Targeted resistive ventilatory muscle training in chronic obstructive pulmonary disease. J. Appl. Physiol. 65:2726-2735, 1988.

* BENDER, P.R. and B.J. MARTIN. Maximal ventilation after exhausting exercise. Med. Sci. Sports Exerc. 17:164-167, 1985.

* BERGMEYER, H.H. Methods of Enzymatic Analysis. Vol. III, 2nd Ed. New York: Academic Press, 1974, pp 1464 - 1472.

* BORG, G.A.V. Physical performance and perceived exertion. Lund, Sweden, Gleerup, 1962, pp 1 - 62.

* BORG, G.A.V. Psychological bases of perceived exertion. Med. Sci. Sports Exerc. 14:377-381, 1982.

* BORG, G., J. KARLSSON, and I. LINDBLAD. Quantitative variation of subjective symptoms during ergometer work. In: Reports from the Institute of Applied Physiology. Stockholm The University of Stockholm. 72:1 - 12, 1976.

* BRADLEY, M.E. and D.E. LEITH. Ventilatory muscle training and oxygen cost of sustained hyperpnea. J. Appl. Physiol. 45:858 - 892, 1978.

* BROOKS, G.A. Anaerobic threshold: A review of the concept and directions of future research. Med. Sci. Sports Exerc. 17:22-31, 1985.

* BROOKS, G.A., G.E. BUTTERFIELD, R.R. WOLFE, B.M. GROVES, and R.S. MAZZEO. Decreased reliance on lactate during exercise after acclimatization to 4300m. J. Appl. Physiol. 71:333 - 341, 1991.

* BROOKS, G.A., R.S. MAZZEO, D.A. SCHOELLER, and T.F. BUDINGER. Lactate turnover in man during rest and graded exercise. Med. Sci. Sports Exerc. 16:121, 1984.

* BROOKS, G.A. and T.D. FAHEY. Exercise Physiology: Human Bioenergetics and its applications. Ed. New York: John Wiley and Sons, 1984, pp. 270 - 274.

* BYE, P.T.P., G.A. FARKAS, and C.H. ROUSSOS. Respiratory factors limiting exercise. Ann. Rev. Physiol. 45:439 - 451, 1983.

* BYE, P.T.P., S.A. ESAU, K.R. WALLEY, P.T. MACKLEM, and R.L. PARDY. Ventilatory muscles during exercise in air and oxygen in normal men. J. Appl. Physiol 56: 464 - 471, 1984.

* BYRD, S.K., L.J. McCUTLHEON, D.R. HODGSON, and P.D. GOLLNICK. Altered sarcoplasmic reticulum function after high-intensity exercise. J. Appl. Physiol. 67:2072 - 2077, 1989.

* CAIOZZO, V.J., J.A. DAVIS, J.F. ELLIS, J.L. AZUS, R. VANDAGRIFF, C.A. PRIETTO, and W.C. McMASTER. A comparison of gas exchange indices used to detect the Anaerobic Threshold. J. Appl. Physiol. 53:1184-1189, 1982.

* CAMPBELL, E.J.M., E. AGOSTONI, and J.N. DAVIS. The respiratory muscles. Mechanics and neural control. Ed. London: Medical Books., 1970, pp. 128 - 134.

* CAMPBELL, M.E., R.L. HUGHSON, and H.J. GREEN. Continuous increase in blood lactate concentration during different ramp exercise protocols. J. Appl. Physiol. 66:1104 - 1107, 1989.

* CASABURI, R., T.W. STORER, I. BEN-DOV, and K. WASSERMAN. Effect of endurance training on possible determinants of VO_2 during heavy exercise. J. Appl. Physiol. 62:199 - 207, 1987.

* CHANCE, B. and B. QUISTORFF. Study of tissue O_2 gradients by single and multiple indicators. Advances in Experimental Medicine and Biology. 94:331 - 338, 1978.

* COAST, J.R., P.S. CLIFFORD, T.W. HENRICH, J. STRAY-GUNDERSEN, and R.L. JOHNSON Jr. Inspiratory muscle fatigue following maximal exercise. Med. Sci. Sports Exerc. 19:(Suppl)S1, 1987.

* COAST, J.R., P.S. CLIFFORD, T.W. HENRICH, J. STRAY-GUNDERSEN, and R.L. JOHNSON Jr. Maximal inspiratory pressure following maximal exercise in trained and untrained subjects. Med. Sci. Sports Exerc. 22:811 - 815, 1990.

* CONNETT, R.J., T.E.J. GAYESKI, and C.R. HONIG. Lactate accumulation in fully aerobic, working, dog gracilis muscle. Am. J. Physiol 246:H120 - H128, 1984.

* CONNETT, R.J., T.E.J. GAYESKI, and C.R. HONIG. Lactate efflux is unrelated to intracellular PO_2 in working red muscle in situ. J. Appl. Physiol. 61:402 - 407, 1986.

* COTES, J.E. Lung Function: Assessment and Application in Medicine. 4th Ed. London: Blackwell Scientific Publications, 1979, p. 265.

* DAVIS, J.A., M.H. FRANK, B.J. WHIPP, and K. WASSERMAN. Anaerobic Threshold alterations caused by endurance training in middle-aged men. J. Appl. Physiol. 46:1039 - 1046, 1979.

* DAVIS, J.A., P. VODAK, J.H. WILMORE, J. VODAK, and P. KURTZ. Anaerobic threshold and maximal aerobic power for three modes of exercise. J. Appl. Physiol. 41:544 - 550, 1976.

* DEMELLO, J.J., K.J. CURETON, R.E. BOINEAU, and M.M. SINGH. Ratings of perceived exertion at the lactate threshold in trained and untrained men and women. Med. Sci. Sports Exerc. 19:354 - 362, 1987.

* DEMPSEY, J.A., E.H. VIDRUK, and G.S. MITCHELL. Pulmonary control systems: update. Fed. Proc. 44:2260 - 2270, 1985.

* DEMPSEY, J.A. Is the lung built for exercise. Med. Sci. Sports Exerc. 18:143 - 155, 1986.

* DEMPSEY, J.A., E.H. VIDRUK, and S.M. MASTENBROOK. Pulmonary control systems in exercise. Fed. Proc. 39:1498 - 1505, 1980.

* DEMPSEY, J.A., G.S. MITCHELL, and G.A. SMITH. Exercise and chemoreception. Am. Rev. Respir. Dis. 129:[Suppl) S31 -S34, 1984.

* DEMPSEY, J.A., P.E. HANSON, S.M. MASTENBROOK. Arterial hypoxemia during exercise in highly trained runners. [Abstract] Fed. Proc. 40:396, 1981.

* DEMPSEY, J.A., P.E. HANSON, and K.S. HENDERSON. Exercise-induced arterial hypoxemia in healthy humans at sea-level. J. Physiol. [London]. 355:161 - 175, 1984.

* DEMPSEY, J.A., S.K. POWERS, and N. GLEDHILL. Discussion: Cardiovascular and Pulmonary Adaptation Physical Activity. In: Exercise, Fitness, and Health. A Consensus on current knowledge. Ed. Champaign, Illinois: Human Kinetics Books., 1990, pp. 205 -215.

* DENNIG, H., J.H. TALBOT, H.T. EDWARDS, and D. DILL. Effect of acidosis and alkalosis upon capacity for work. J. Clin. Invest. 9:601 - 613, 1931.

* DENNIS, S.C., M.C. KOHN, M.C. ANDERSON, and D GARFINKEL. Kinetic analysis of monocarboxylate uptake into perfused rat hearts. J. Mol. Cell. Cardiol. 17:987 - 995, 1985.

* DENNIS, S.C., W. GEVERS, and L.H. OPIE. Protons in Ischemia: Where do they come from; where do they go to? J. Mol. Cell Cardiol. 23:1077 - 1086, 1991.

* DENNIS, S.C., T.D. NOAKES, and A.N. BOSCH. Ventilation and blood lactate increase exponentially during incremental exercise. J. Sports Sciences. 10:437 - 449, 1992.

* DERENNE, J.P., P.T. MACKLEM, and C. ROUSSOS. The respiratory muscles: Mechanics, control and pathophysiology. Parts I, II, IV. Am. Rev. Respir. Dis. 118, 119 - 133, 373 - 390, 581 - 601, 1978.

* DOCKTER, R. and B.J. SHARKEY. Notes on some physiological and subjective reactions to exercise and training. Percept. Mot. Skills. 32:233 - 234, 1971.

* DONALDSON, S.K.B. and L. HERMANSEN. Differential direct effects of H^+ion and Ca^{++}- activated force of skinned fibers from the soleus, cardiac, and adductor magnus muscles of rabbits. Pfluegers Arch. 376:55 - 65, 1978.

* EDWARDS, R.H.T., A. MELCHER, C.M. HESSER, O. WIGERTZ, and L.G. EKELUND. Physiological correlates of perceived exertion in continuous and intermittent exercise with the same average power output. Eur. J. Clin. Invest. 2:108 - 114, 1972.

* EKBLOM, B. and A.N. GOLDBARG. The influence of physical training and other factors on the subjective ratings of perceived exertion. Acta. Physiol. Scand. 83:399 - 406, 1971.

* EL-MANSHAWI, A., K.J. KILLIAN, E. SUMMERS, and N.L. JONES. Breathlessness during exercise with and without resistive loading. J. Appl. Physiol. 61:896 - 905, 1986.

* FABIATO, A. and F. FABIATO. Effects of pH on the myofilaments and the sarcoplasmic reticulum of skinned cells from cardiac and skeletal muscles. J. Physiol. Lond. 276:233 - 255, 1978.

* FELLOWS, I.W., T. BENNETT, and I.A. MacDONALD. The effect of adrenaline upon cardiovascular and metabolic functions in man. Clin. Sc. Lond. 69:215 - 222, 1985.

* FIITS, R.H. and J.O. HOLLOSZY. Lactate and contractile force in frog muscle during development of fatigue and recovery. Am. J. Physiol. 231:430 - 433, 1976.

* FLENLEY, D.C. and P.M. WARREN. Ventilatory responses to O_2 and CO_2 during exercise. Ann. Rev. Physiol. 45:415-426, 1983.

* FORSTER, H.V., J.A. DEMPSEY, J. THOMSON, E. VIDRUK, and G.A. DOPICO. Estimation of arterial PO_2, PCO_2, pH and Lactate from arterialized venous blood. J. Appl. Physiol. 32:134 - 137, 1972.

* FREEDMAN, S. Sustained maximum voluntary ventilation. Respir. Physiol. 8:230 -244, 1970.

* FREGOSI, R.F. and J.A. DEMPSEY. Arterial blood acid-base regulation during exercise in rats. J. Appl. Physiol. 57:396 - 402, 1984.

* GAESSER, G.A. and D.C. POOLE. Lactate and ventilatory threshold: disparity in time course of adaptations to training. J. Appl. Physiol. 61:999 - 1004, 1986.

* GAESSER, G.A., D.C. POOLE, and B.P. GARDNER. Dissociation between VO_2 max and ventilatory responses to endurance training. Eur. J. Appl. Phys. 53:242 - 247, 1984.

* GALBO H. Hormonal and Metabolic Adaptations to Exercise. New York: Thieme-Stratton, 1983

* GAMBERALE, F. Perceived exertion, heart rate, oxygen uptake and blood lactate in different work operations. Ergonomics 15:545 - 554, 1972.

* GANDEVIA, B. Ventilatory response to exercise and the results of a standardized exercise test in chronic obstructive lung disease. Am. Rev. Resp. Dis. 88:406 - 408, 1963.

* GARDNER M.L.G. Medical Acid-base Balance. The basic principles. Cassell Ltd, London, 1978, p 53.

* GAUTIER, H., D. MAILLARD, J. VINCENT, and D ZAOUI. Gas exchange during exercise in normoxia and hyperoxia. Resp. Physiol. 33:199 -211, 1978.

* GEVERS, W. Generation of protons by metabolic processes in the heart cells. J. Mol. Cell. Cardiol. 9:867 - 874, 1977.

* GOSSELIN, L.E., J.T. BOHLMANN, and D.P. THOMAS. Effect of endurance training and age on rat diaphragm. Med. Sci. Sports Exerc. 20:(Suppl)S9, 1988.

* GRAHAM, T.E., J.K. BARCLAY, and B.A. WILSON. Skeletal muscle lactate release and glycolytic intermediates during hypercapnia. J. Appl. Physiol. 60:568 - 575, 1986.

* GREEN, H.J., R.L. HUGHSON, G.W. ORR, and D.A. RANNY. Anaerobic threshold, blood lactate and muscle metabolites in progressive exercise. J. Appl. Physiol. 54:1032 - 1038, 1983.

* GREGG, S.G., R.S. MAZZEO, T.F. BUDINGER, and G.A. BROOKS. Acute anemia increases lactate production and decreases clearance during exercise. J. Appl. Physiol 67:756 - 764, 1989.

* GROSS, D., H.W. LADD, E.J. RILEY, P.T. MACKLEM, and A. GRASSINO. The effect of training on strength and endurance of the diaphragm in quadriplegia. Am. J. Med. 68: 27 - 35, 1988.

* HAGBERG, J.M., E.F. COYLE, J.E. CARROLL, J.M. MILLER, W.H. MARTIN, and M.H. BROOKS. Exercise hyperventilation in patients with McArdle's disease. J. Appl. Physiol. 52: 991 -994, 1982.

* HAGBERG, J.M. Effect of pedaling rate on submaximal exercise responses of competitive cyclists. J. Appl. Physiol. 51:447 - 451, 1981.

* HAGBERG, J.M., J.P. MULLIN, and F.J. NAGLE. O_2 consumption during constant-load exercise. J. Appl. Physiol. 45:381 - 384, 1978.

* HEIGENHAUSER, G.J.F., J.R. SUTTON, and N.L. JONES. Effect of glycogen depletion on the ventilatory response to exercise. J. Appl. Physiol. 54:470 - 474, 1983.

* HANSON, P., A. CLAREMONT, J. DEMPSEY, and W. REDDAN. Determinants and consequences of ventilatory responses to competitive endurance running. J. Appl. Physiol. 52:615 - 623, 1982.

* HENRY, F.M. Aerobic oxygen consumption and alactic debt in muscular work. J. Appl. Physiol. 3:427 - 438, 1951.

* HERMANSEN, L., and J.B. OSNES. Blood and muscle pH after maximal exercise in man. J. Appl. Physiol. 32:304 - 305, 1972.

* HICKSON, R.C., H.A. BOMZE, and J.O. HOLLOSZY. Faster adjustment of O_2 uptake to the energy requirement of exercise in the trained state. J. Appl. Physiol 44:877 - 881, 1978.

* HOCHACHKA, P.W. and T.P. MOMMSEN. Protons and anaerobiosis. Science 210:1391 - 1397, 1983.

* HOLLOSZY, J.O. Adaptations of muscular tissue in training. Progress in Cardiovascular Disease. 18:445 - 458, 1976.

* HOLLOSZY, J.O. Biochemical adaptations to exercise. Aerobic metabolism. In: Exercise and Sport Sciences. Ed. New York: JH Wilmore, Academic Press, 1973, 1: pp 45 - 71.

* HOPKINS, S.R. and D.C. McKENZIE. Hypoxic ventilatory response and arterial desaturation during heavy work. J. Appl. Physiol. 67:1119 - 1124, 1989.

* HORSTMAN, D.H. Exercise performance at 5°C. [abstract] Med. Sci. Sports Exerc. 9:52, 1977.

* HUGHES, E.F., S.C. TURNER, and G.A. BROOKS. Effects of glycogen depletion and pedaling speed on "anaerobic threshold". J. Appl. Physiol. 52:1598 - 1607, 1982.

* HUGHES, R.L., C.J. ORAK, and LE STAUDT. A high velocity treadmill running test to assess endurance running potential. Int. J. Sports. Med. 5:23 - 25, 1984.

* HUGHES, R.L., M. CLODE, R.H.T. EDWARDS, T.J. GOODWIN, and N.L. JONES. Effect of inspired O_2 on cardiopulmonary and metabolic responses to exercise in man. J. Appl. Physiol. 24:336 - 347, 1968.

* HUGHSON, R.L. and H.J. GREEN. Blood acid-base and lactate relationships studied by ramp work tests. Med. Sci. Sports Exerc. 14:297 - 302, 1982.

* INBAR, O., A. KOWALSKI, S. EPSTEIN, Y. WEINSTEIN. Possible ventilatory limitations to maximal aerobic exercise. J. Appl. Physiol 63:(Suppl) R35, 1987.

* ISSEKUTZ, B. Effect of beta-adrenergic blockade on lactate turnover in exercising dogs. J. Appl. Physiol. 57:1754 - 1759, 1984.

* JACOBS, I. Blood lactate: Implications for training and sport performance. Sport Medicine. 3:10 -25, 1986.

* JOBSIS, F.F. and W.N. STAINSBY. Oxidation of NADH during contractions of circulated mammalian skeletal muscle. Resp. Physiol. 4:292 - 300, 1968.

* JONES, N.L. and K.J. KILLIAN. Exercise in Chronic Airway obstruction. In: Exercise, Fitness, and Health. A Consensus on current knowledge. Ed. Champaign, Illinois: Human Kinetics Books., 1990, pp. 547 - 559.

* JONES, J.L. Dyspnea in exercise. Med. Sci. Sports Exerc. 16:14 - 19, 1984.

* JONES, N.L. Hydrogen ion balance during exercise. Clin. Sci. 59:85 - 91, 1980.

* JONES, N.L., J.R. SUTTON, R. TAYLOR, and C.J. TOEWS. Effect of pH on cardiorespiratory and metabolic responses to exercise. J. Appl. Physiol. 43:959 - 964, 1977.

* KAMON, E., K. PANDOLF, and E. CAFARELLI. The relationship between perceptual information and physiological responses to exercise in the heat. J. Hum. Ergol. 3:45 - 54, 1974.

* KARLSSON, J. Lactate and phosphagen concentration in working muscle of man. Acta. Physiol. Scand. 358:(Suppl) 70 - 72, 1971.

* KAY, C. and R.J. SHEPHARD. On muscle strength and the threshold of anaerobic work. Int. Z. Angew. Physiol. 27:311 - 328, 1969.

* KILLIAN, K.J., D.D. BIRENS, and E.J.M. CAMPBELL. Effect of breathing patterns on the perceived magnitude of added loads to breathing. J. Appl. Physiol. 52:578 - 584, 1982.

* KOYAL, S.N., B.J. WHIPP, D. HUNTSMAN, G.A. BRAY, and K WASSERMAN. Ventilatory responses to the metabolic acidosis of treadmill and cycle ergometry. J. Appl. Physiol. 40:864 - 867, 1976.

* LEITH, D.E. and M. BRADLEY. Ventilatory muscle strength and endurance training. J. Appl. Physiol 41:508 - 516, 1976.

* LINNARSSON, D. Dynamics of pulmonary gas exchange and heart rate changes at start and end of exercise. Acta. Physiol. Scand. 415:(Suppl) 1 - 65, 1974.

* LOKE, J., D.A. MAHLER, and J.A. VIRGULTO. Respiratory muscle fatigue after marathon running. J. Appl. Physiol. 52:821 - 824, 1982.

* LOLLGEN, H., T. GRAHAM, and G. SJOGAARD. Muscle metabolites, force, and perceived exertion bicycling at varying pedal rates. Med. Sci. Sports Exerc. 12:345 - 351, 1980.

* MAINWOOD, G.W. and J.M. RENAUD. The effect of acid-base balance on fatigue of skeletal muscle. Can. J. Physiol. Pharm. 63:403 - 416, 1985.

* MANDEL, F., E.G. KRANIAS, A.C. DE GENDE, M. SUMIDA, and A. SCHWARTZ. The effect of pH on the transient-state kinetics of Ca^{++}- Mg^{++}- ATPase of cardiac sarcoplasmic reticulum. A comparison with skeletal sarcoplasmic reticulum. Circ. Res. 50:310 - 317, 1982.

* MARTIN, B.J., and J.M. STAGER. Ventilatory endurance in athletes and non-athletes. Med. Sci. Sports Exerc. 13:21 - 26, 1981.

* MARTIN, B.J., H. CHEN, and M.A. KOLKA. Anaerobic Metabolism of the respiratory muscles during exercise. Med. Sci. Sports Exerc. 16:82 - 86, 1984.

* MARTIN, B., M. HEINTZELMAN, and H. CHEN. Exercise performance after ventilatory work. J. Appl. Physiol. 52: 1581 - 1585, 1982.

* MAZZEO, R.S., G.A. BROOKS, D.A. SCHOELLER, and D.F. BUDINGER. Disposal of blood [1 - ^{13}C] lactate in humans during rest and exercise. J. Appl. Physiol. 60:232 - 241, 1986.

* McARDLE, W.D., F.I. KATCH, and V.L. KATCH. Exercise Physiology. Energy, Nutrition, and Human Performance. Ed. Philadelphia: Lea & Febiger, 1981, pp 180 - 185.

* MICKELSON, T.C. and F.C. HAGERMAN. Anaerobic threshold measurements of elite oarsmen. Med. Sci. Sports Exerc. 14: 440 - 444, 1982.

* MIHEVIC, P.M. Sensory cues for perceived exertion. A review. Med. Sci. Sports Exerc. 13:150 - 163, 1981.

* MOLE, P.A. and R.L. COULSON. Energetics of myocardial function. Med. Sci. Sports Exerc. 17:538 - 545, 1985.

* MORITANI, T., A. NAGATA, H.A. DE VRIES, and M. MURO. Critical power as a measure of physical work capacity and anaerobic threshold. Ergonomics. 24:339 - 350, 1981.

* MURRAY, J.F. The normal lung. The basis for diagnosis and treatment of pulmonary disease. 2nd Ed. Philadelphia: W.B. Saunders Company, 1986, pp 122 - 137.

* NAKAMARU, Y. and A. SCHWARTZ. The influence of hydrogen ion concentration on calcium binding and release by skeletal muscle sarcoplasmic reticulum. J. Gen. Physiol. 59:22 - 23, 1972.

* NEWSHOLME, E.A. and C.M. START. Regulation in Metabolism. London: John Wiley, 1973, pp 148 - 152.

* NOBLE, B.J., C.M. MARESH, T.G. ALLISON, and A. DRASH. Cardiorespiratory and perceptual recovery from a marathon run. Med. Sci. Sports Exerc. 11:239 - 243, 1979.

* NOBLE, B.J., G.A.V. BORG, I. JACOBS, R. CECI, and P. KAISER. A category-ratio perceived exertion scale: relationship to blood and muscle lactates and heart rate. Med. Sci. Sports Exerc. 15:523 - 528, 1983.

* NOBLE, B.J., K. METZ, K. PANDOLF, and E CAFARELLI. Perceptual responses to exercise: a multiple regression study. Med. Sci. Sports Exerc. 5:104 - 109, 1973.

* OLAFSSON, S. and R.E. HYATT. Ventilatory mechanics and expiratory flow limitations during exercise in normal subjects. J. Clin. Invest. 48:564 - 573, 1969.

* PANDOLF, K.B., E. CAFARELLI, B.J. NOBLE, and K.F. METZ. Perceptual responses during prolonged work. Percept. Mot. Skills 35:975 - 985, 1972.

* PANDOLF, K. Psychological and physiological factors influencing perceived exertion. In: Physical Work and Effort. Ed. Oxford: Pergamon, 1977, pp 371 - 383.

* PARDY, R.L., R.N. RIVINGTON, P.J. DESPAS, and P.T. MACKLEM. The effects of inspiratory muscle training on exercise performance in chronic airflow limitations. Am. Rev. Respir. Dis. 123:426 - 433, 1981.

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

* POON, C. Ventilatory control in hypercapnia and exercise optimization hypothesis. J. Appl. Physiol. 62:2447 - 2459, 1987.

* POWERS, S.K. and R.E. BEADLE. Onset of hyperventilation during incremental exercise. A brief review. Research Quart. Exerc and Sport. 56:352 - 360, 1985.

* POWERS, S.K., S. DODD, and R. GARNER. Precision of ventilatory and gas exchange alterations as a predictor of the anaerobic threshold. Eur. J. Appl. Physiol. 52:173 - 177, 1984.

* REINHARD, U., P.H. MULLER, and R. SCHMULLING. Determination of anaerobic threshold by the ventilation equivalent in normal individuals. Resp. 38:36 - 42, 1979.

* REYBROUCK, R., J. GHESQUIERE, A. CATTAERT, R. FAGARD, and A. AMERY. Ventilatory thresholds during short- and long-duration exercise. J. Appl. Physiol 55:1694 - 1700, 1983.

* ROBERTSON, R.J. Central signals of perceived exertion during dynamic exercise. Med. Sci. Sports Exerc 14:390 - 396, 1982.

* ROCHESTER, D.F., N.S. ARORA, N.M.T. BRAUN, and S.K. GOLDBERG. The respiratory muscles in chronic obstructive pulmonary disease [COPD]. Bull. Eur. Physiol-path. Respir. 15:951 - 975, 1979.

* ROBINSON, E.P. and J.M. KJELDGAARD. Improvement in ventilatory muscle function with running. J. Appl. Physiol 52:1400 - 1406, 1982.

* ROSTON, W.L., B.J. WHIPP, J.A. DAVIS, D.A. CUNNINGHAM, R.M. EFFROS, and K. WASSERMAN. Oxygen uptake kinetics and lactate concentration during exercise in humans. Am. Rev. Respir. Dis. 135:1080 - 1084, 1987.

* ROTH, D.A., W.C. STANLEY, and G.A. BROOKS. Induced lactacidemia does not affect post-exercise O_2 consumption. J. Appl. Physiol 65:1045 - 1049, 1988.

* ROUSSOS, C. and P.T. MACKLEM. The respiratory muscles. New. Eng. J. Med. 307:786 - 797, 1982.

* ROUSSOS, C.M., M. FIXLEY, D. GROSS, and P.T. MACKLEM. Fatigue of inspiratory muscles and their synergic behavior. J. Appl. Physiol 46:897 - 904, 1979.

* ROUSSOS, C. Respiratory muscle fatigue and ventilatory failure. Chest. 97:(Suppl) S89 - S96, 1990.

* RYBICKI, K.J. and M.P. KAUFMAN. Stimulation of group III and IV muscle afferents reflexly decreases total pulmonary resistance in dogs. Resp. Phys. 59:185 - 195, 1985.

* SAHLIN, K. Intracellular pH and energy metabolism in skeletal muscle of man. Acta. Physiol. Scand. 455:(Suppl) 1 - 56, 1978.

* SALTIN, B. and P.D. GOLLNICK. Skeletal muscle adaptability. Significance for metabolism and performance. In: Handbook of Physiology, Am. Phys. Soc., Sect 10, Vol II, part 1, Chapt 19, 1983, pp 551 - 631.

* SCHARF, S., P. BYE, R. PARDY, and P.T. MACKLEM. Dyspnea, Fatigue and Second Wind. Am. Rev. Respir. Dis. 129:(Suppl) S88 - S89, 1984.

* SEVERINGHAUS, J.W. Blood gas concentration. In: Handbook of Physiology Respiration, 1965, Sect. 3, Vol II, Chapt. 61, pp 1474 - 1479.

* SHEPHARD, R.J. O_2 cost of breathing during vigorous exercise. Q. J. Exp. Physiol. 51:330 - 350, 1966.

* SKINNER, J.S., R. HUSTLER, V. BERGSTEINOVA, and E.R BUSKIRK. Perception of effort during different types of exercise and under different environmental conditions. Med. Sci. Sports Exerc. 5:110 - 115, 1973.

* SONNE, L.J. and J.A. DAVIS. Increased exercise performance in patients with severe COPD following inspiratory muscle resistive training. Chest. 81:436 - 439, 1982.

* STAINSBY, W.N., C. SUMNERS, and P.D. EITZMAN. Effects of adrenergic agonists and antagonists on muscle O_2 uptake and lactate metabolism. J. Appl. Physiol. 62:1845 - 1851, 1987.

* STAINSBY, W.N., G.A. BROOKS. Control of lactate metabolism in contracting muscles and during exercise. In. Exerc and Sport Sci. Reviews. Ed. Baltimore: Williams and Wilkens, 1990, pp 29 - 63.

* STAMFORD, B.A. and B.J. NOBLE. Metabolic cost and perception of effort during bicycle ergometer work performance. Med. Sci. Sports 6:226 - 231, 1974.

* STAMFORD, B.A., A. WELTMAN and C. FULCO. Anaerobic threshold and cardiovascular responses during one-versus two-legged cycling. Research Quarterly 49:351 - 362, 1978.

* STAMFORD, B.A. Validity and reliability of subjective rating of perceived exertion during work. Ergonomics 19:53 - 60, 1976.

* STEVENS, E.D. Effect of pH on muscle fatigue in isolated frog sartorius muscle. Can. J. Physiol. Pharmacol. 58:568 - 570, 1980.

* SUTTON, J.R., N.L. JONES, and C.J. TOEWS. Effect of pH on muscle glycolysis during exercise. Clin. Sci. 61:331 - 338, 1981.

* TAYLOR, A.E., K. REHDER, R.T. HYATT, and J.C. PARKER. Clinical Respiratory Physiology. Philadelphia: WB Saunders Company, 1989, pp 160; 193 - 215.

* TENNEY, S.M. and R.E. REESE. The ability to sustain great breathing efforts. Respir. Physiol. 5:187 - 201, 1968.

* VOLKOV, N.I., V.N. CHEREMISINOV, and E.M. RAZUMOVSKII. Oxygen exchange in man during muscular activity. In: The oxygen regime of the organism and its regulation. Ed. N.L. Lauer and A.Z. Kolchinskaya. NASA Technical Translation, 1969.

* VIIRES, N., D. MURCIANO, J.P. SETA, B. DURCEUIL, R. PARIENTE, and M. AUBIER. Effects of Ca^{++}withdrawal on diaphragmatic fiber tension generation. J. Appl. Physiol. 64:26 - 30, 1988.

* WALSH, M.L. and E.W. BANISTER. Possible mechanisms of the anaerobic threshold. A review. Sports Medicine. 5:269 - 302, 1988.

* WARREN, G.L., K.J. CURETON, and P.B. SPARLING. Does lung function limit performance in a 24-hour marathon? Resp. Physiol. 78:253 - 264, 1989.

* WASSERMAN, K., A.L. VAN KESSEL, AND G.G. BURTON. Interaction of physiological mechanisms during exercise. J. Appl. Physiol 22:71 - 85, 1967.

* WASSERMAN, K. and B.J. WHIPP. Exercise Physiology in health and disease. Am. Rev. Respir. Dis. 112:219 - 249, 1975.

* WASSERMAN, K. and M.B. McILROY. Detecting the threshold of anaerobic metabolism in cardiac patients during exercise. Am. J. Cardiol. 14:844 - 852, 1964.

* WASSERMAN, K., B.J. WHIPP, P. CASABURI, W. BEAVER, and H. BROWN. CO_2 flow to the lungs and ventilatory control. In: Wisconsin Press, 1977, pp 103 - 136.

* WASSERMAN, K., B.J. WHIPP, S.N. KOYAL, and M.G. CLEARY. Effect of carotid body resection on ventilatory and acid-base control during exercise. J. Appl. Physiol 39:354, 1975.

* WASSERMAN, K., B.J. WHIPP, S.N. KOYAL, and W.L. BEAVER. Anaerobic threshold and respiratory gas exchange during exercise. J. Appl. Physiol 35:236 - 243, 1973.

* WASSERMAN, K. Breathing during exercise. New Engl. J. Med. 298:780 - 785, 1978.

* WASSERMAN, K. Coupling of External to Internal Respiration. Am. Rev. Resp. Dis. 129(Suppl) S21 - S24, 1984 [b].

* WASSERMAN, K. Physiology of gas exchange and external dyspnoea. Clin. Sci. 61:7 - 13, 1981.

* WASSERMAN, K. The Anaerobic Threshold Measurements to Evaluate Exercise Performance. Am. Rev. Resp. Dis. 129:(Suppl) S35 - S40, 1984 [a].

* WASSERMAN, K., W.L. BEAVER, and B.J. WHIPP. Gas exchange theory and the lactic acidosis [anaerobic] threshold. Circulation. 8:(Suppl)14 - 27, 1990.

* WASSERMAN, K., W.L. BEAVER, and B.J. WHIPP. Mechanics and patterns of blood lactate increase during exercise in man. Med. Sci. Sports Exerc. 18:344 - 352, 1986.

* WENGER, H.A. and A.T. REED. Metabolic factors associated with muscular fatigue during aerobic and anaerobic work. Can. J. Appl. Sports Science. 1:43 - 48, 1976.

* WHIPP, B.J. and K. WASSERMAN. Oxygen uptake kinetics for various intensities of constant-load work. J. Appl. Physiol. 33:351 - 356, 1972.

* WHIPP, B.J. and S.A. WARD. Ventilatory control dynamics during muscular exercise in man. Int. J. Sports Med. 1:146 - 159, 1980.

* WHIPP, B.J. and S.A. WARD. Physiological determinants of pulmonary gas exchange kinetics during exercise. Med. Sc. Sports Exerc. 22:62 - 71, 1990.

* WHIPP, B.J. Dynamics of pulmonary gas exchange. Circulation 76: VI - 18 - VI - 28, 1987.

* WHIPP, B.J. S.A. WARD, and K. WASSERMAN. Ventilatory responses to exercise and their control in man. Am. Rev. Resp. Dis. 129 (Suppl) S17 - S20, 1984.

* WHIPP, B.J. The control of breathing in man. Physiological Society Study Guide. No. 3. Manchester: Manchester Univ. Press, 1987, pp 88, 94.

* WHIPP, B.J. The hyperpnea of dynamic muscular exercise. In: Exercise and Sport Reviews, Ed. Santa Barbara: R.S. Hutton, 1977, 5:295 - 311.

* WILSON, S.H., N.T. COOK, J. MOXHAM, and S.G. SPIRO. Sternomastoid muscle function and fatigue in normal subjects and in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 129:460 - 464, 1984.

* YAMAMOTO, Y. and R.L. HUGHSON. Letter to the editor. J. Appl. Physiol. 67:2641, 1989.

* YOSHIDA, T., Y. SUDA and T. TAKEUCHI. Endurance training regimen based upon arterial blood lactate: Effects on Anaerobic Threshold. Eur. J. Appl. Physiol. Occup. Physiol. 41:223 - 230, 1982.

* ZECHMAN, F.W. Jr., and R.L. WILEY. Afferent inputs to breathing: respiratory sensation. In: Handbook of Physiology, Am. Phys. Soc., Sect 3, Vol II, part 1, Chapt 14, 1986, pp 449 - 474.

* ZOCCHE, G.P., H.W. FRITTS, and A. COURNAND. Fraction of maximum breathing capacity available for prolonged hyperventilation. J. Appl. Physiol. 15:1073 - 1074, 1960.

Appendix 1. The new rating scale constructed as a category scale with ratio properties [Borg GAV, 1982].

0	Nothing at all	(just noticeable)
0.5	Very, very weak	
1	Very weak	
2	Weak	(light)
3	Moderate	
4	Somewhat strong	
5	Strong	(heavy)
6		
7	Very strong	
8		
9		
10	Very, very strong	(almost maximal)
*	maximal	