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The effects of reduced inspired oxygen fraction on the cardiorespiratory response to lower and upper body exercise

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Abstract.

Introduction: Exposure to acute hypoxia has been used as a tool to investigate the mechanisms limiting oxygen consumption ($\dot{V}O_2$) during predominately lower body (LB) exercise. However, the mechanisms limiting upper body (UB) exercise have been investigated to a lesser extent. **Aim:** To compare and contrast the cardiorespiratory responses to incremental LB and UB exercise to volitional exhaustion at three inspired oxygen fractions. **Participants:** Nine healthy, able bodied male participants (age 22 ± 2 years; height 180.6 ± 8.2 cm; body mass 78.7 ± 12.2 kg; estimated body fat 15.1 ± 6.3 %; estimated muscle mass 57.5 ± 6.5 %) gave their informed consent to participate in the study. **Methods:** In a counter balance designed study participants performed three LB and three UB incremental exercise tests to volitional exhaustion whilst breathing room air (N) or two levels of normobaric hypoxia (H_1 and H_2; F_IO_2 = 0.21, 0.15 and 0.13, respectively). Cycle ergometry (LB) and arm crank ergometry (UB) commenced at 70 and 35 W and were increased by 30 and 15 W every 3 min, respectively. Each workload was separated by 30 s passive recovery for the collection of bloods. Participants maintained a cadence of 70 rev.min^{-1}. Heart rate (HR), haemoglobin oxygen saturation (S_PO_2) and respiratory gases were collected in the final minute of each workload. **Results:** Peak power output (PPO) was reduced in both modes of exercise as F_IO_2 declined ($P<0.001$) and was highest during LB exercise in all conditions ($P<0.001$). During LB exercise peak oxygen consumption ($\dot{V}O_{2\ PEAK}$) declined with F_IO_2 (N 45 ± 7 *vs.* H_1 39 ± 6 mL·kg^{-1}·min^{-1}; $P<0.001$ and H_1 *vs.* H_2 34 ± 5 mL·kg^{-1}·min^{-1}; $P<0.05$). During UB exercise $\dot{V}O_{2\ PEAK}$ declined between N (32 ± 6 mL·kg^{-1}·min^{-1}) and H_1 (28 ± 5 mL·kg^{-1}·min^{-1}; $P<0.001$) and tended to be lower between H_1 and H_2 (26 ± 5 mL·kg^{-1}·min^{-1}; NS). During LB exercise 13 ± 8 and 24 ± 6 % reductions in $\dot{V}O_{2\ PEAK}$

were evident when F_IO_2 decreased from N to H_1 and from N to H_2, while during UB exercise 15 ± 7 and 19 ± 9 % reductions were observed from normoxic values for H_1 and H_2, respectively. During LB exercise estimated cardiac output ($\dot{Q}$) was reduced between each F_IO_2 (N, 25.9 ± 2.0 vs. H_1, 23.6 ± 1.8 L·min^{-1}; P<0.05 and H_1 vs. H_2, 21.1 ± 1.1 L·min^{-1}, P<0.05). During UB exercise $\dot{Q}$ declined between N (20.7 ± 3.0 L·min^{-1}) and H_1 (18.2 ± 3.2 L·min^{-1}; P<0.01) and tended to be lower between H_1 and H_2 (17.0 ± 2.8 L·min^{-1}; NS). S_PO_2 declined as F_IO_2 reduced in LB and UB exercise and was lower during LB exercise (P<0.001, main effect). At N, H_1 and H_2 S_PO_2 was (LB *vs.* UB) 96 ± 2 *vs.* 97 ± 1 (NS), 83 ± 4 *vs.* 88 ± 5 (NS) and 74 ± 6 *vs.* 82 ± 4 (P<0.01) %. Extraction increased as F_IO_2 decreased in both modes of exercise (P<0.001, main effect). At N, H_1 and H_2 extraction (E) was 10 ± 10 (NS), 12 ± 12 (P<0.05) and 13 ± 11 (P<0.01) % lower during UB compared to LB exercise, respectively. **Conclusions:** Both central and peripheral factors contribute to limiting $\dot{V}O_{2\ PEAK}$, however their extent differs between LB and UB exercise. As previously shown LB exercise is limited centrally by oxygen delivery. However, the present study shows that during UB exercise although $\dot{V}O_{2\ PEAK}$ declines as F_IO_2 is reduced this mode of exercise is limited by peripheral physiology.

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Abbreviations

LB – lower body

UB – upper body

VEX – volitional exhaustion

N - normoxia

H - hypoxia

NH – normobaric hypoxia

HH – hypobaric hypoxia

O_2 – oxygen

CO_2 – carbon dioxide

$\dot{V}_E$ – expired volume

$\dot{V}O_2$ – oxygen consumption

$\dot{V}CO_2$ - carbon dioxide production

$\dot{V}O_{2\ PEAK/MAX}$ – peak/maximal oxygen consumption

RER – respiratory exchange ratio

$\dot{V}_E/\dot{V}O_2$ – ventilatory equivalence for oxygen

$\dot{V}_E/\dot{V}CO_2$ – ventilatory equivalence for carbon dioxide

V_t – tidal volume

f – breathing frequency

[BLa] – blood lactate concentration

AT – anaerobic threshold

[Hb] – haemoglobin concentration

S_PO_2 – haemoglobin oxygen saturation

S_PO_{2VEX} – haemoglobin oxygen saturation at volitional exhaustion

SaO_2 – arterial oxygen saturation

CaO_2 – arterial oxygen content

$\dot{D}O_2$ – oxygen delivery

E – extraction

a-$\bar{v}$ O_2Diff. – arterial venous oxygen difference

HR – heart rate

SV – stroke volume

$\dot{Q}$ – cardiac output

PPO – peak power output

RPE – rate of perceived exertion

STPD – standard temperature and pressure dry

FO_2 – fraction of oxygen

FCO_2 – fraction of carbon dioxide

F_IO_2 – fraction of inspired oxygen

F_EO_2 – fraction of expired oxygen

F_ECO_2 – fraction of expired carbon dioxide

PO_2 – partial pressure of oxygen

PCO_2 – partial pressure of carbon dioxide

P_AO_2 – alveolar partial pressure of oxygen

PaO_2 – arterial partial pressure of oxygen

P_B – barometric pressure

HVR – hypoxic ventilatory response

EIAH – exercise-induced arterial hypoxemia

ATP – adenosine triphosphate

PTT – pulmonary transit time

ANS – autonomic nervous system

SNS – sympathetic nervous system

PNS – parasympathetic nervous system

ANOVA – analysis of variance

NS – not significant

n – number of subjects/data points

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CHAPTER 1

INTRODUCTION

1.0 Introduction.

Humans continually strive to overcome the physical challenges placed before them, whether the challenge comes from the natural environment or in pursuit of improved sporting performance. Altitude presents one of the most demanding natural challenges to physical performance and in the case of extreme altitude survival alone can be challenging. Early accounts of diminished physical capacity were reported among expeditions to high altitude. Upon ascent to 8,500 m without supplementary oxygen Norton (1924) reported being unable to achieve a target of 20 consecutive paces without stopping to rest (Ward *et al.,* 2000). The location of the 1968 Olympic Games (Mexico City) at an altitude of 2,240 m above sea level combined altitude and sporting competition and demonstrated how altitude can affect athletic performance positively or negatively. Those competing in endurance events found the environmental conditions detrimental to performance, while those competing in short duration, explosive events (e.g. sprints, jumping and throwing events) experienced improved performance due to reduced air resistance (Ward *et al.*, 2000).

In 1996 it was estimated that 140 million people reside at an altitude above 2,500 m (WHO, 1996) and these highlanders have undergone adaptations over years/generations that enable them to better transport oxygen in hypobaric conditions (Ward *et al.* 2000). Recently increasing numbers of lowlanders have been exposed to altitude, including those on occupational tasks (i.e. military operations and high altitude mines), those on recreational breaks such as skiing and climbing and athletes. Of these sports people have been reported exposing themselves to altitude to try and attain physiological adaptations that will benefit performance (Pugh, 1967; Shepard, 1973; Rusko *et al.* 2004).

Altitude reduces the transport of oxygen from ambient air to the mitochondria and therefore reduces the capacity for physical exercise. As a consequence of reduced blood oxygen content a series of acute or chronic adaptations (dependent on duration of exposure) occur in an attempt to maintain homeostasis. Those indigenous to high altitude (highlanders) experience a lesser decrement in exercise capacity at a given altitude, due to several physiological/genetic adaptations, while those who usually reside at sea level and rapidly ascend experience much greater disturbances in homeostasis and exercise capacity (Ward *et al.*, 2000; Mazzeo, 2005). This thesis focuses on acute exposure to highlight the mechanisms limiting exercise. The series of chronic adaptations to altitude is termed 'acclimatisation' but is beyond the scope of this thesis, for further reading on this subject see West (1993); Chapman *et al.* (1998) and Muza (2007).

Pulmonary diffusion, cardiac output, oxygen carrying capacity and metabolic factors are all involved in the transport of O_2 from the atmosphere to the cell and each of these stages has been investigated as a possible limitation to aerobic power. Research into the mechanisms limiting aerobic power concluded that peak oxygen consumption ($\dot{V}O_{2\ PEAK}$) is limited by the ability to transport O_2 to the muscle rather than pulmonary diffusion or metabolic factors at the muscle in healthy individuals during lower body (LB) exercise (Shepard *et al.*, 1988; Bassett and Howley, 2000). By removing blood, in turn reduced haemoglobin concentration and the content of O_2 carried by arterial blood (CaO_2), $\dot{V}O_{2\ PEAK}$ was reduced and subsequent reinfusion of the red blood cells increased CaO_2 and $\dot{V}O_{2\ PEAK}$ from control measures (Ekblom *et al.*, 1972; Ekblom *et al.*, 1976). At altitude the barometric pressure and partial pressure of O_2 decline which reduces the pressure gradient between the lung and blood. Though the capacity to carry O_2 is unchanged during acute exposure to hypoxia the saturation of haemoglobin with

O_2 (SaO_2) is reduced (Fig. 2.2) thus as with the above studies delivery of O_2 to the active tissue is reduced albeit by a different method. Several reviews have been published on the area of limitations to maximal aerobic power, though the literature tends to focus on LB exercise as this form of exercise elicits higher peak responses and is considered as representative of maximal whole body oxygen consumption in comparison to exercise using the upper extremities (Wagner, 1991; Sutton, 1992; Bassett and Howley, 2000).

The literature shows that the study of exercising in hypoxic conditions has been undertaken almost exclusively using LB exercise (Hammond *et al.*, 1986; Knight *et al.*, 1993; Ferretti *et al.*, 1997; Robergs *et al.*, 1998; Peltonen *et al.*, 2001a). Only a few studies appear to have examined the effects of breathing hypoxic gas during upper body (UB) exercise (Jansen-Urstad *et al.*, 1995; Hopman *et al.*, 2003; Hopman *et al.*, 2004). Two studies were found to investigate both LB and UB exercise in the same subject group in normoxic and hypoxic conditions (Shepard *et al.*, 1988; Angermann *et al.*, 2006). One of these studies used double pole ergometry which was highly specific to the subject group and therefore the results should be interpreted with caution in relation to other UB protocols (Nordic combined skiers; Angermann *et al.*, 2006). The second study focused on reducing the amount of muscle mass recruited during normoxic and hypoxic exercise employing two and one leg cycle ergometry and one arm crank ergometry with and without restraints (to stabilise the trunk during locomotion) finding that $\dot{V}O_{2\ PEAK}$ declined as active muscle mass was reduced (Shepard *et al.*, 1988).

Studies however, have compared LB and UB exercise in normoxic conditions (Bhambhani *et al.*, 1998; Schneider *et al.*, 2000; Schneider *et al.*, 2002; Gass and Gass, 1998). It has been shown that $\dot{V}O_{2\ PEAK}$ and peak power output (PPO) are lower when

exercising the UB (Bhambhani *et al.*, 1998; Muraki *et al.*, 2004). It is generally reported that UB exercise elicits $\dot{V}O_{2\ PEAK} \approx$ 60-80 % and PPO $\approx$ 50 % of that attained during LB exercise. These differences have been attributed to a smaller muscle mass and, unless specifically trained, a lower training status of the arm muscles in comparison to the legs.

There is a paucity of published work investigating the effects of hypoxia on UB exercise thus there is an absence of data illustrating whether the response to hypoxia is similar to that during LB exercise and whether maximal exercise capacity is limited by the same mechanisms during both forms of exercise. The amount of individuals exposed to altitude and the number of activities involving the UB (climbing, skiing, kayaking and rowing), not to mention exercise performed at altitude by those with spinal cord injury (Hopman *et al.*, 2003) warrants further investigation into the effect of hypoxia on UB exercise and the underlying mechanisms limiting aerobic power. Also clinical populations who are chronically hypoxic (patients with chronic obstructive pulmonary disease or heart disease) could benefit from a greater understanding of limitations to physical capacity and a greater understanding of exercising in these conditions could aid exercise prescription.

By assessing LB and UB exercise in identical conditions, in the same cohort of participants, limitations may be established in both modes of exercise. While the limitations to LB exercise have been well published, little work has been dedicated to finding what limits UB exercise (Sawka *et al.*, 1983). This study aims to establish whether UB exercise is limited in the same way and to the same extent as LB exercise by reducing oxygen delivery in both modes of exercise via hypoxia. Finally, it is hoped that by reporting the effect of reduced F_IO_2 on cardiorespiratory parameters at $\dot{V}O_{2\ PEAK}$

and LT that the mechanisms limiting both LB and UB exercise can be identified and that the above mentioned populations will benefit from a greater preparation and understanding of the physical stress undergone during these two exercise modes in normoxic and hypoxic environments.

CHAPTER 2

LITERATURE REVIEW

2.0 Literature review.

This thesis investigates the effect of acute hypoxia (simulating an altitude ≈ 2700 and 3700 m above sea level) on cardiorespiratory responses during incremental lower body (LB) and upper body (UB) exercise to volitional exhaustion. While a large body of literature is present on the effect of altitude on LB exercise and comparative data between LB and UB exercise in normoxia are available, research is limited regarding UB exercise under hypoxic conditions. Firstly, the environment at altitude is described before a review of acute physiological/cardiorespiratory responses to hypoxia and the consequent reductions in exercise capacity with increasing altitude. The use of Fick's principle to facilitate explaining the effect of hypoxia on the components of oxygen consumption is then discussed. Finally, differences between LB and UB exercise will be presented from normoxic exercise studies.

2.1 Atmosphere/environment at altitude.

The term hypobaria means reduced barometric pressure and refers to the ambient environment at altitude, while the term hypoxia meaning 'less than normal amount of oxygen' is often used at sea level to simulate conditions at altitude (Thake, 2006). Regardless of altitude the ambient air comprises 20.93 % oxygen (O_2), 0.03 % carbon dioxide (CO_2) and 79.04 % nitrogen, however the barometric pressure (P_B) decreases as altitude increases resulting in a lower partial pressure of these gases. At sea level the standard atmosphere is 760 mmHg resulting in a partial pressure of oxygen (PO_2) of 159 mmHg. At the summit of Mt. Everest (8,850 m) the P_B and PO_2 are 231 and 48 mmHg, respectively (Ward *et al.*, 2000). This results in a lower driving pressure of O_2 from the atmosphere to the cell (Fig. 2.4; West *et al.*, 1983) and represents a significant challenge to human performance at altitude.

Barometric pressure is not purely affected by altitude, at altitudes 6-16 km barometric pressure is greater around the equator. Prior to Messner and Habeler's ascent to the summit of Mt. Everest without supplementary O_2 (1978) it was thought to be beyond human capability, as extrapolated values from lower altitudes suggested that $\dot{V}O_{2\ PEAK}$ would be just sufficient to maintain basal metabolism towards the summit. However, as Everest is located 28°N of the equator a greater barometric pressure as well as seasonal variations in P_B result in a higher PO_2, making the summit of Everest just within the physiological limit of humans (Ward *et al.* 2000).

2.2 Simulating hypoxia.

Hypoxia can be split into two categories: hypobaric hypoxia (HH) and normobaric hypoxia (NH). HH can be induced either at altitude in the field (Pugh, 1967) or by using a hypobaric chamber (Robergs *et al.* 1998) whereby the barometric pressure is reduced leading to reduced PO_2. Alternatively the fraction of inspired oxygen (F_IO_2; NH) maybe reduced to lower PO_2 under constant P_B simulating altitude in a laboratory environment (Table 2.1; Richardson *et al.*, 1999b; Hopman *et al.*, 2003). This technique is used to simulate altitude in the study communicated in this thesis. Equation 2.1 shows the relationship between P_B, PO_2 and F_IO_2 and how to simulate the PO_2 of a given altitude by reducing the F_IO_2.

Equation 2.1 $$PO_2 = P_B \times F_IO_2$$

Therefore,

$$P_B = PO_2 / F_IO_2$$

When simulating altitude (NH),

$$F_IO_2 = PO_2 \text{ (at desired altitude)} / \text{Sea level } P_B \text{ (760 mmHg)}$$

Table 2.1 *Barometric pressure (P_B) and partial pressure of O_2 (PO_2) at altitude and the corresponding inspired O_2 fraction (F_IO_2) to simulate altitude at sea level (adapted from West et al., 2000).*

Altitude		Barometric Pressure	PO_2	Normobaric F_IO_2
m	ft	(mmHg)	(mmHg)	
0	0	760	159	0.209
1 000	3 281	674	141	0.186
2 000	6 562	596	125	0.164
3 000	9 843	526	110	0.145
4 000	13 123	462	97	0.127
5 000	16 404	405	85	0.112
6 000	19 685	354	74	0.097
7 000	22 966	308	64	0.085
8 000	26 274	267	56	0.074
9 000	29 258	231	48	0.064

2.3 Physiological/metabolic responses to acute hypoxia.

2.3.1 Ventilation.

One of the most apparent responses when acutely exposed to hypoxia is increased minute ventilation ($\dot{V}_E$), in an attempt to overcome the reduced PO_2 and maintain blood O_2 content. This increased $\dot{V}_E$ is termed the hypoxic ventilatory response (HVR) which varies between individuals (Fig. 2.1 B). Reductions in PO_2 are detected in the blood by peripheral chemoreceptors which result in the respiratory centres of the brain increasing the depth and frequency of breathing. An initial reduction in arterial oxygen tension (PaO_2) does not result in increased $\dot{V}_E$, however when PaO_2 reaches $\approx$ 60 mmHg ventilation rapidly increases. This is consistent with the start of the steep portion of the

O_2 dissociation curve (Fig. 2.2), thus in order to preserve blood O_2 content peripheral arterial chemoreceptors are stimulated at this threshold and increase respiratory drive. It can be seen that an initial reduction of PO_2 from 80 to 60 mmHg would cause≈ 8 % desaturation of the blood, while a further reduction from 60 to 40 mmHg would result in ≈ 15 % desaturation (Fig. 2.2). The response of $\dot{V}_E$ to reduced PaO_2 was demonstrated by Weil and co workers (1970) who recorded $\dot{V}_E$ whilst reducing inspired oxygen tension over a 15 – 20 min period (Fig.2.1 A).

Fig 2.1 *Ventilatory response as arterial oxygen tension is reduced in A) one subject with each point representing the mean of three successive breaths and B) ten participants (Weil et al., 1970).*

Gavin *et al.* (1998) investigated ventilation during acute exposure to hypoxia in two groups who were categorised by their normoxic ventilation response at $\dot{V}O_{2\ MAX}$. This study showed that at rest $\dot{V}_E$ increased from 8.4 ± 2.6 and 8.6 ± 1.8 $L \cdot min^{-1}$ to 9.8 ± 2.7 and 9.6 ± 2.24 $L \cdot min^{-1}$ when F_IO_2 = 0.133 (≈ 4000m) for those with low (≤ 27.7) and

high (≥ 30.2) $\dot{V}_E/\dot{V}O_2$ at maximal normoxic exercise, respectively. Maximal $\dot{V}_E$ was significantly higher in those participants with high respiratory responsiveness in both normoxic and hypoxic conditions, however neither group's maximal $\dot{V}_E$ differed between conditions. This concurs with the findings of Martin and O'Kroy (1993) who did not observe an increase in maximal ventilation between normoxia and hypoxia (F_IO_2 = 0.13) in trained ($\dot{V}O_{2\ MAX}$ = 67.2 ± 4.0 mL·kg^{-1}·min^{-1}) and untrained ($\dot{V}O_{2\ MAX}$ = 45.4 ± 5.5 mL·kg^{-1}·min^{-1}). While their findings were not significant the trained group's $\dot{V}_E$ at maximal exercise declined by 2.0 L·min^{-1} compared to an 8.2 L·min^{-1} increase for the untrained group on acute exposure to H compared to N. Lawler *et al.* (1988) found that maximal $\dot{V}_E$ was higher during H *vs.* N (150.9 ± 7.3 *vs.* 123.0 ± 3.6 L·min^{-1}) in a similarly untrained population ($\dot{V}O_{2\ MAX}$ = 45.0 ± 2.2 mL·kg^{-1}·min^{-1}) but no difference was observed for the trained group ($\dot{V}_E$ = 149.4 ± 6.8 *vs.* 147.4 ± 6.2 L·min^{-1}; $\dot{V}O_{2\ MAX}$ = 64.5 ± 2.4 mL·kg^{-1}·min^{-1}) when F_IO_2 = 0.14. Higher maximal $\dot{V}_E$ increases alveolar oxygen tension (P_AO_2) and arterial oxygen saturation (SaO_2; section 2.3.2; Gavin *et al.*, 1998).

Ventilation required per litre of O_2 consumed (ventilatory equivalent; $\dot{V}_E/\dot{V}O_2$) increases at maximal exercise during hypoxia in both trained and untrained participants, as although $\dot{V}_E$ may not alter, $\dot{V}O_2$ is reduced (Martin and O'Kroy, 1993; Zattara-Hartmann and James, 1996; Chapman *et al.*, 1999; Peltonen *et al.*, 2001a). Gavin *et al.* (1998) reported that $\dot{V}_E/\dot{V}O_2$ increased from to 26.4 ± 1.0 to 40.5 ± 4.7 and from 33.4 ± 2.7 to 46.5 ± 5.1 when reducing inspired O_2 fraction for participants with low and high $\dot{V}_E/\dot{V}O_2$ at maximal normoxic exercise, respectively.

When employing HH, at a simulated altitude of 2500 m above sea level maximal $\dot{V}_E$ was significantly higher during hypobaria compared to sea level (153 ± 4 *vs.* 147 ± 3 $L \cdot min^{-1}$; Ogawa *et al.*, 2007). While performing maximal exercise at sea level and at simulated altitudes (915, 1524 and 2439 m), Robergs *et al.* (1998) found that maximal $\dot{V}_E$ was higher at 2439 m and $\dot{V}_E/\dot{V}O_2$ was higher at 1524 and 2439 m compared to sea level. While both HH and NH reduce PO_2, $\dot{V}_E$ appears to respond differently under both conditions, possibly due to differences in gas density.

Comparing HH and NH at 1 min intervals, over a 40 min period at rest, showed that $\dot{V}_{EBTPS}$ and $\dot{V}_{ESTPD}$ were consistently higher during NH. This study found that while breathing frequency (*f*) was lower during NH, tidal volume (V_t) was higher so that $\dot{V}_E$ was higher at each 1 min stage (Savourey, *et al.*, 2003). Loeppky *et al.* (1996) reported that $\dot{V}_E$ was 20 and 14 % higher during NH and HH when compared to breathing air. Savourey *et al.* (2003) could not identify the mechanisms responsible but this study and a comparison of studies employing either NH or HH indicates that ventilatory response differs between NH and HH. As gas moves from high to low pressure during ventilation a reduced P_B during HH would reduce the flow from the atmosphere to the lung and a greater *f* would be required to maintain $\dot{V}_E$.

2.3.2 Arterial oxygen saturation.

Estimates of haemoglobin oxygen saturation (S_PO_2; section 2.3.3), as measured by pulse oximetry have been shown to have valid representations of functional arterial oxygen saturation (SaO_2) measured by arterial blood sampling (Mengelkoch *et al.* 1994), thus within this thesis S_PO_2 and SaO_2 are used interchangeably depending on the method of measurement used in the particular study discussed.

Decreased P_B at altitude or reduced F_IO_2 both reduce the inspired PO_2 in turn reducing alveolar oxygen tension (P_AO_2) lowering the pressure gradient between the lung and blood for gas exchange. Consequently SaO_2 is reduced at rest and during exercise and the extent of the reduction is dependent upon the altitude to which an individual is exposed and their HVR. At rest Gavin *et al.* (1998), Peltonen *et al.* (2001b) and Mollard *et al.* (2007) reported SaO_2 of 85.7 ± 3.0, 95.0 ± 1.0 and 90.0 ± 2.3 % using inspired O_2 fractions of, 0.133, 0.15 and 0.13, respectively. Upon the completion of maximal exercise the studies demonstrate further arterial desaturation compared to rest (SaO_2 = 71.5 ± 4.2, 84.0 ± 3.0 and 82.1 ± 3.3 %, respectively). Fig. 2.2 shows arterial desaturation in relation to PO_2 and its sigmoid shape allows for an initial fall in PO_2 without a large decrease in S_PO_2 although thereafter continuing reductions in PO_2 results in substantial decrements in S_PO_2.

Fig. 2.2 *Oxygen dissociation curve in human blood at 37^{O}C and pH 7.4 (West et al., 2000).*

Table 2.2 *Comparison of normoxic and hypoxic arterial saturation at rest and during maximal exercise. * significantly different from normoxia, † significantly different from rest (P<0.05), data presented to the decimal places as published in original articles.*

Study	Participants/methods	F_IO_2	S_PO_2 (%)	
			Rest	Maximal exercise
Calbet *et al.* (2003)	9 physically active participants	0.21	97.6 ± 0.1	96.1 ± 0.3
	5 male and 4 female	0.105	82.3 ± 3.1*	66.2 ± 2.7*
	Incremental cycle ergometry			
Peltonen *et al.* (2001)	6 male endurance athletes	0.32	99 ± 1*	97 ± 1
	Incremental cycle ergometry	0.21	97 ± 0	95 ± 1
		0.15	95 ± 1*	84 ± 3*
Gavin *et al.* (1998)	13 endurance trained male participants	0.21	L 96.0 ±1.2	92.6 ± 1.7
	6 = Low $\dot{V}_E / \dot{V}O_2$ (<27.7; L)		H 96.2 ± 1.2	93.7 ± 1.5
	7 = High $\dot{V}_E / \dot{V}O_2$ (>30.2; H)	0.133	L 85.7 ± 3.0	90.6 ± 7.9
	based on maximal normoxic $\dot{V}_E / \dot{V}O_2$		H 86.2 ± 2.8	71.5 ± 4.2
Zattara-Hartmann and Jammes (1996)	6 healthy male participants	0.21	89 ± 2	76 ± 2 †
	Incremental cycle ergometry	0.15	60 ± 2*	47 ± 1*†
	Measured **PaO_2** apposed to SaO_2	0.10	45 ± 1*	32 ± 1*†

At maximal exercise using F_IO_2s of 0.30, 0.21, 0.18, 0.16, 0.13 and 0.11 Ferretti and colleagues (1997) showed the influence of reducing PO_2 on saturation and $\dot{V}O_{2\ MAX}$. The levels of hypoxia resulted in SaO_2 of 98.2 ± 0.1, 95.8 ± 0.51, 94.0 ± 0.5, 87.6 ± 1.4, 80.2 ± 2.4, 66.2 ± 2.9 % and 96.8 ± 0.3, 93.0 ± 1.0, 90.0 ± 1.3, 83.6 ± 2.0, 66.8 ± 2.6, 53.8 ± 2.2 % for sedentary and endurance trained participants, respectively. These findings are comparable with those of Mollard *et al.* (2007) who found S_PO_2 to be lower at maximal exercise as F_IO_2 was reduced (F_IO_2 = 0.187, 0.173. 0.154, 0.13 and 0.117). Table 2.2 shows S_PO_2 reported for a selection of studies at rest and maximal exercise using different F_IO_2s.

As S_PO_2 affects oxygen delivery (Equation 2.4) and ultimately consumption, studying factors maintaining haemoglobin oxygen saturation could be beneficial to aerobic performance and research in this area has highlighted several factors affecting desaturation. One factor found to influence arterial desaturation is normoxic aerobic power. Those individuals with greater $\dot{V}O_{2\ MAX}$ at sea level experience greater desaturation upon exposure to altitude (Martin and O'Kroy, 1993; Ferretti *et al.*, 1997). Martin and O'Kroy (1993; LB exercise) reported S_PO_2 in trained ($\dot{V}O_{2\ MAX}$ = 67.2 ± 4.0 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$) and untrained ($\dot{V}O_{2\ MAX}$ = 45.4 ± 5.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$) participants, at rest and maximal exercise whilst breathing hypoxic gas (F_IO_2 = 0.13). At rest they reported S_PO_2 to be 84.0 ± 5.2 and 85.4 ± 5.4 % compared to 67.0 ± 7.1 and 77.5 ± 9.0 % at maximal exercise for trained and untrained participants, respectively. While no difference existed at rest S_PO_2 was significantly lower at maximal exercise indicating greater pulmonary diffusion limitation in trained athletes. A greater cardiac output in trained athletes (30-35 $L{\cdot}min^{-1}$ compared to 20 $L{\cdot}min^{-1}$ for untrained) results in reduced pulmonary transit time (PTT) thus reducing the time available for gaseous exchange. At rest PTT is ≈ 1 s while at maximal exercise blood spends ≈ 0.25 s in the lung

(Hopkins *et al.*, 1996). Lawler *et al.* (1988) reported normoxic $\dot{V}O_{2\ MAX}$ to be positively correlated with $\Delta\ \dot{V}O_{2\ MAX}$ upon exposure to hypoxia ($r = 0.94$, $P<0.05$), while $\Delta\ \dot{V}O_{2\ MAX}$ was negatively correlated with S_PO_2 at maximal exercise ($r = -0.84$, $P<0.05$). Therefore, although not presented, this data shows that a high normoxic $\dot{V}O_{2\ MAX}$ results in greater desaturation during hypoxia, which was reported by Mollard *et al.* (2007) in trained and untrained participants.

As stated in section 2.3.1 ventilation increases at the same point that arterial desaturation becomes more rapid (60 mmHg; Fig 2.2). Investigating the role of ventilation on arterial desaturation Gavin *et al.* (1998) found that resting hypoxic ventilatory response (rHVR) had no correlation with SaO_2 at maximal exercise in aerobically trained athletes. This study divided their participants dependent upon their normoxic $\dot{V}_E/\dot{V}O_2$ responsiveness ($\dot{V}_E/\dot{V}O_2$ <27.2 = LOW n = 6; $\dot{V}_E/\dot{V}O_2$ > 30.2 = HIGH, n = 7). For normoxia *vs.* hypoxia, SaO_2 at maximal exercise was 92.6 ± 1.7 *vs.* 60.6 ± 7.9 % for the LOW group and 93.7 ± 1.5 *vs.* 71.5 ± 4.2 % for the HIGH group. This represents a 31.9 ± 6.4 % desaturation compared to 22.1 ± 3.7 % in the HIGH compared to the LOW group at maximal exercise ($P<0.05$). They found that normoxic $\dot{V}_E/\dot{V}O_2$ response to maximal exercise was important in maintaining SaO_2 ($r = 0.6$, $P<0.05$) and aerobic power ($r = 0.62$, $P<0.05$) during maximal exercise when exposed to acute hypoxia. This study concluded that a low hyperventilatory response to maximal exercise results in greater desaturation associated with greater reduction in aerobic power.

Exercise induced arterial hypoxemia (EIAH) is a phenomenon whereby desaturation occurs during normoxic exercise. This tends to happen in highly trained individuals with high cardiac outputs (Prefaut *et al.*, 2000; Galy *et al.*, 2005). During normoxic

maximal exercise highly trained participants desaturated to 90.6 ± 0.8 % compared to 94.1 ± 0.2 % in untrained participants (Powers *et al.*, 1989). When investigated during mild hypoxia (F_IO_2 = 0.187, ≈1000 m) those who demonstrated EIAH (SaO_2 <90 %) experienced greater desaturation and a significantly greater reduction in $\dot{V}O_{2\ MAX}$ opposed to non-EIAH (SaO_2 >92 %) whose $\dot{V}O_{2\ max}$ was not significantly reduced and did not desaturate to the same extent (Chapman *et al.*, 1999).

Several studies have employed hyperoxia (>21% O_2) in the assessment of blood oxygenation and aerobic power (Peltonen *et al.*, 2001a; Peltonen *et al.*, 2001b). While normoxic resting S_PO_2 is ≈ 97 % there is little room for improvement in saturation with increasing P_IO_2, as seen in Fig. 2.2. One such study showed that an 11 % increase in F_IO_2 (0.32) resulted in a 2% increase in S_PO_2 (99 ± 1), while 6 % reduction in F_IO_2 (0.15) resulted in a 2 % decrease in S_PO_2 (95 ± 1) compared to normoxic values at rest. This became more pronounced at maximal exercise when S_PO_2 was 97 ± 1, 95 ± 1 and 84 ± 3 % when F_IO_2 = 0.32, 0.21 and 0.15, respectively (Peltonen *et al.*, 2001b). These data further demonstrate the flat and steep portions of the O_2 dissociation curve, where increasing P_IO_2 has little effect on SaO_2 (flat portion) decreasing P_IO_2 below 60 mmHg results in rapid desaturation (steep portion; Fig. 2.2).

2.3.3 Validity and reliability of pulse oximetry.

Arterial haemoglobin oxygen saturation (S_PO_2) is commonly used as it offers a non-invasive means of assessing the degree of arterial hypoxemia in any given circumstance. As well as being an important physiological measure it is also essential in ensuring the safety of the subject so the oxygen saturation of the blood does not fall beyond safe limits (section 3.6). For these reasons it is important that the validity and reliability of pulse oximeters be known prior to their use. The ‘gold standard’ means to validate

pulse oximeters is to compare the S_PO_2 with haemoglobin oxygen saturations (SaO_2) directly from arterial blood sampling (Mengelkoch *et al.*, 1994). The validity of a wide range of pulse oximeters have been reported using ear, finger and forehead sensors at rest and during exercise in hypoxic and normoxic conditions (Martin *et al.*, 1992; Mengelkoch *et al.* 1992; Mengelkoch *et al.*, 1994; Benoit *et al.*, 1997; Yamaya *et al.*, 2002 Fernandez *et al.*, 2007).

Several methodological issues also need to be considered when using pulse oximetry, especially during exercise trials. Motion artefact results in increased signal noise/interference so the estimated SpO_2 is often inaccurate (Mengelkoch *et al.*, 1994). This becomes of particular concern during exercise trials as movement of some form is inevitable. Barker and Shah (1997) compared three different oximeters, attached to the 2nd, 3rd, and 4th fingers of the test hand and placed on a motion table. The same oximeters were attached to the same fingers on the control hand which remained motionless. While altering the F_IO_2 so saturation varied from 75 to 100% they measured the amount of time the test hand was within 7% of the control hand. While one oximeter remained with 7% of the control hand 97% of the time the other oximeters were only within 7% of the control hand 68 and 47% of the time. This shows the effect of motion on oximeter validity and also shows the oximetry chosen should be validated within the situation it is to be used. It should also be noted that 7% desaturation (limits used in the above study) would be sufficient to significantly reduce arterial oxygen content (CaO_2) which would dramatically reduce oxygen delivery ($\dot{D}O_2$) thus oximeters should be validated within tighter limits.

As pulse oximetry relies on the absorption of light by HbO_2 and the pulsatile component of blood, anything that reduces blood flow to the site of the pulse oximeter probe will

reduce the reliability of data gathered. Factors that affect peripheral perfusion include temperature, hypotension, hypovolemia and pharmacological agents thus where possible should be controlled during trials. While motion and perfusion are of considerable importance during exercise trials severity of hypoxia, skin pigmentation, ambient light, sensor site and whether the subject smokes can all affect the validity and reliability of pulse oximeters (Mengelkoch *et al.*, 1994; Benoit *et al.*, 1997; Fernandez *et al.*, 2007).

The pulse oximeter used in the present study (Nonin 8500, Nonin medical Inc, Minnesota, USA) used an ear sensor and had a reported accuracy of ± 4 digits (± 2 SD; manufacturers guide). Thake (2006) assessed the reliability of the Nonin 8500 oximeter during maximal exercise in normoxia and hypoxia in ten healthy male participants. A strong relationship was observed between test-retest data when normoxic and hypoxic data were considered together ($r = 0.979$, $n = 86$) and individually (normoxic $r = 0.762$, $n = 47$; hypoxic $r = 0.904$, $n = 39$; $P<0.001$).

As reported previously (Yamaya *et al.*, 2002) the results of the Thake (2006) show that as S_PO_2 decreases, variability increases (100-95% saturation ± 0.9%, n=39; 95-90% ± 2.7%, n = 9; 90-85% ± 2.6%, n = 4; 85-80% ± 2.6%, n = 15; 80-75% ± 2.0%, n = 11; 75-70% ± 3.0%, n = 8). This study showed only 3 (3.5%) points are outside ± 2SD of the mean, thus the reliability for the Nonin 8500 was deemed within acceptable limits. These papers suggest that despite several methodological issues, across a physiological range of 70-100%, S_PO_2 accurately estimates SaO_2. For further reading on the validity of pulse oximetry see Mengelkoch *et al.* (1994).

2.3.4 Blood lactate.

The intensity at which exercise is performed is a key factor determining how long it can be maintained. When exercising at low intensities ATP resynthesis can be met predominately by aerobic metabolism, however when exercise intensity increases, anaerobic resynthesis of ATP becomes progressively more prominent. Anaerobic ATP resynthesis promotes metabolic acidosis through the production of lactic acid and increasing acidosis affects the contractile proteins of the muscle. The point where lactic acid production in the muscle and subsequent lactate efflux into the blood accumulates exponentially from resting values is named the lactate threshold (LT).

Hypoxia reduces the amount of O_2 available to the muscle for metabolism thus an increased anaerobic component is evident during hypoxic exercise at the same absolute intensity. This is seen as BLa concentration ([BLa]) is higher at a given workload during incremental exercise during acute hypoxia. Friedmann and colleagues (2005) found higher [BLa] at 8, 10 and 12 $km.h^{-1}$ when investigating lactate threshold (LT) in hypoxia compared to normoxia in endurance trained males (68.0 ± 4.3 $mL \cdot kg^{-1} \cdot min^{-1}$). This study demonstrated that LT occurred at a slower running velocity in H with a lower HR and lower $\dot{V}O_2$ (57.3 ± 5.2 and 46.2 ± 3.4 $mL \cdot kg^{-1} \cdot min^{-1}$ for N and H, respectively) however when expressed relative to condition specific $\dot{V}O_{2\ MAX}$ LT was not significantly different (N = 84 ± 5 and H = 86 ± 6 %). In participants with a lower aerobic power (57.4 ± 7.1 $mL \cdot kg^{-1} \cdot min^{-1}$) using cycling ergometry $\dot{V}O_2$ at LT was significantly lower during hypoxic exercise but occurred at 76 and 78 % of $\dot{V}O_{2\ MAX}$ for normoxia and hypoxia respectively (Koistinen *et al.*, 1995). These two studies are representative of the literature where parameters are often lower at LT during hypoxic

exercise but when considered in relation to the maximal values in that condition there is little difference (Thake, 2006).

Maximal [BLa] is relatively unchanged during normoxic and acute hypoxic exercise (Kayser, 1996; Wagner and Lundby, 2007). Ekblom *et al.* (1975) reported higher maximal [BLa] when CaO_2 was reduced during treadmill running (13.0 ± 0.9 *vs.* 15.0 ± 0.8 $mmol \cdot L^{-1}$ for N and H, respectively) while the literature generally shows no difference during treadmill running (Friedmann *et al.*, 2005; Ogawa *et al.*, 2007) and cycle ergometry (Martin and O'Kroy, 1993; Calbet *et al.*, 2003; Mollard *et al.*, 2007).

A proposed mechanism for these adaptations is that hypoxemia detected by peripheral chemoreceptors increases sympathetic drive in turn increasing plasma catecholamines. In the presence of increased adrenaline levels phosphorylase *b* transforms to its active form phosphorylase *a*, which increases glycogenolysis leading to increased lactate production at a given exercise intensity. The metabolic cost of a given workload is the same in normoxia and hypoxia, however higher blood lactate concentration indicates a greater proportion of ATP resynthesis comes via anaerobic metabolism as a given workload represents a higher proportion of maximal exercise capacity in hypoxia (Kayser, 1996; Wagner and Lundby, 2007). It should be noted that the above mentioned BLa responses are associated with acute exposure to hypoxia as the responses seen during chronic exposure differ. The different response to acute and chronic hypoxic exposure is termed the 'lactate paradox'. Lowlanders acclimatised to high altitude accumulate lower [BLa] at maximal exercise compared to normoxic values. Those native to high altitude also present lower [BLa] at maximal exercise compared to sea level dwellers. However, when lowlanders return to sea level their BLa response to exercise returns to that observed prior to ascent to altitude, while high

altitude natives continue to accumulate lower [BLa] when at sea level (Hochachka *et al.*, 2002; Hochachka *et al.*, 1991).

2.4 Fick equation.

The Fick equation (below) states that oxygen consumption is a product of oxygen delivery via the blood and oxygen extraction at the muscle. Fig 2.3 shows the Fick equation and further divides its components to their constituent parts. By doing this it can be seen how changes in the stated physiological responses affect $\dot{V}O_2$. Within this section the components of the Fick equation, the effect that acute hypoxia has upon them and how this alters $\dot{V}O_2$ will be discussed.

Fick equation $\dot{V}O_2 = \dot{Q} \times a\text{-}\bar{v}\ O_2Diff.$

Where; $\dot{V}O_2$ *= Oxygen consumption,* $\dot{Q}$ *= Cardiac output, a-*$\bar{v}$ *O_2Diff. = Arterial – mixed venous oxygen difference.*

2.4.1 Oxygen consumption.

The volume of O_2 that can be consumed per minute ($\dot{V}O_2$) increases linearly with workload until maximal exercise. There has been much debate regarding the factors limiting $\dot{V}O_{2\ MAX}$, principally the contribution of central and peripheral factors. Ekblom *et al.*, (1976) found that by reducing the bloods capacity to carry O_2 $\dot{V}O_{2\ MAX}$ was reduced. When 800 ml of blood was removed (by venesection) $\dot{V}O_{2\ MAX}$ decreased from control (4.27 ± 0.4 to 4.03 ± 0.31 L·min^{-1}) while reinfusion of the red cells (30-35 days later) led to $\dot{V}O_{2\ MAX}$ increasing to 4.61 ± 0.38 L·min^{-1} ($P<0.05$) in normoxia. While $\dot{Q}$ and SaO_2 were not significantly different between control, postvenesection and postreinfusion, CaO_2 decreased after venesection and increased after reinfusion

(control = 19.94, venesection = 17.88 and reinfusion = 20.77 $mLO_2 \cdot L^{-1}$; $P<0.05$). The removal of blood resulted in a 10% reduction in CaO_2 which was accompanied by a 6 % reduction in $\dot{V}O_{2\,MAX}$. As discussed (section 2.4.3) a decrease in CaO_2 while $\dot{Q}$ remains unchanged would decrease $\dot{D}O_2$ leading to the conclusion that delivery of O_2 to the muscle limits maximal exercise capacity. Many consider these findings to be conclusive in the debate of central *vs.* peripheral limitation to exercise (Ekblom *et al.*, 1976; Ferretti, 2003).

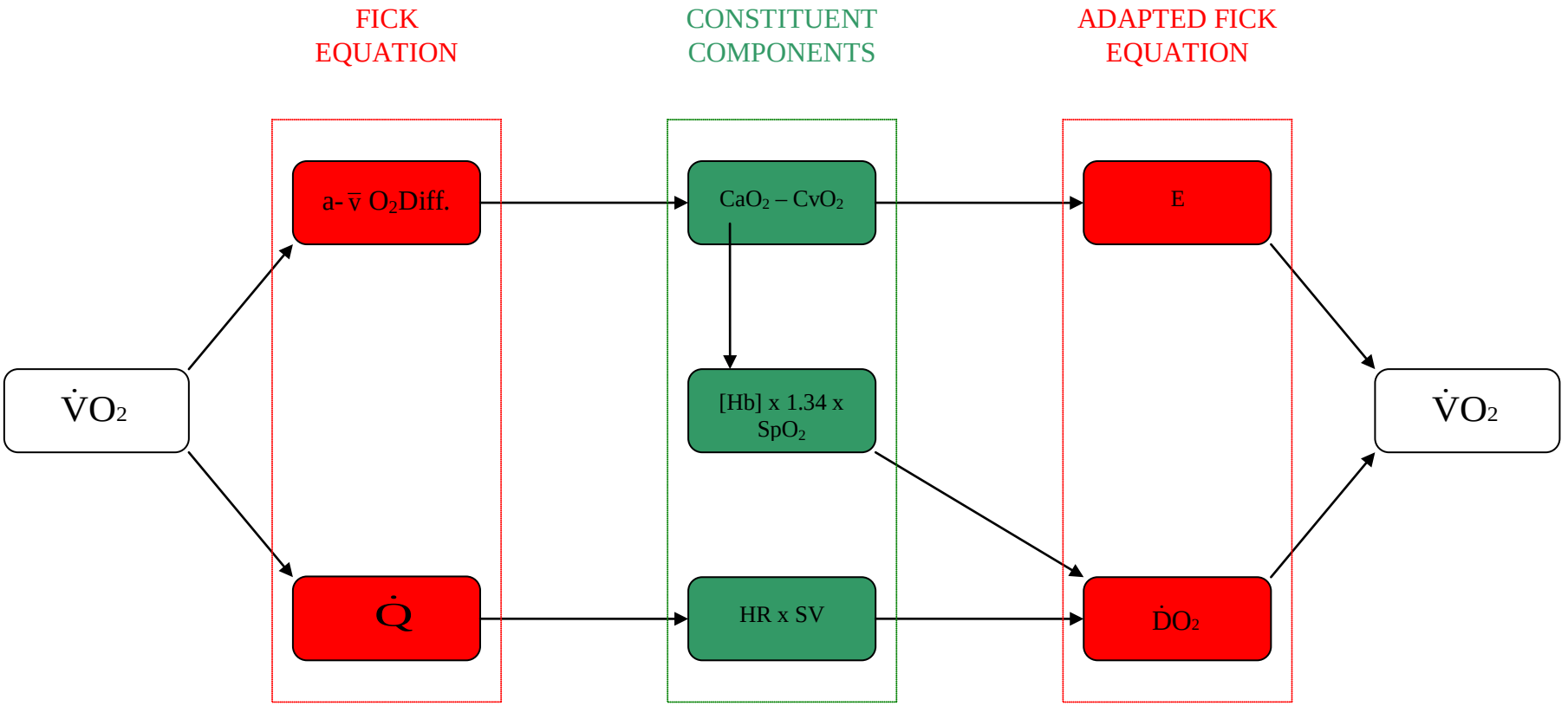


Fig 2.3 *Constituent components of the Fick equation and how they enable the calculation of oxygen consumption.* $\dot{V}O_2$ *= oxygen consumption,* $\dot{Q}$ *= cardiac output, HR = heart rate, SV = stroke volume, a-*$\bar{v}$ *O_2Diff. = arteriovenous oxygen difference,* CaO_2 *= arterial oxygen content,* CvO_2 *= venous oxygen content, [Hb] = haemoglobin concentration, 1.34 =* $mLO_2 \cdot gHb$ SpO_2 *= arterial haemoglobin oxygen saturation,* $\dot{D}O_2$ *= oxygen delivery and E = extraction ratio.*

$\dot{V}O_{2\ MAX}$ is significantly reduced upon exposure to altitude when compared to that attained at sea level (Knight *et al.*, 1993; Zattara-Hartmann and Jammes, 1996; Ferretti *et al.*, 1997; Cardus *et al.*, 1998; Richardson *et al.*, 1999a; Peltonen *et al.*, 2001a; Peltonen *et al.*, 2001b). Squires and Buskirk (1982) proposed there was little difference in aerobic power below an altitude of 1524 m, thereafter a decrease of 3.2 % could be seen every additional 305 m, however others have reported reductions $\leq$ 1000 m (Gore *et al.*, 1996; Mollard *et al.*, 2007). Dempsey and Wagner (1999) reported that for every 1 % reduction in arterial saturation below 95 %, $\dot{V}O_{2\ PEAK}$ was reduced by 1-2 %.

Hypoxia reduces SaO_2 (section 2.3.2), which in turn reduces CaO_2 and $\dot{D}O_2$ and as shown by Ekblom *et al.* (1976) a reduction in $\dot{D}O_2$ results in reduced $\dot{V}O_{2\ MAX}$. When breathing F_IO_2s of 0.3, 0.21, 0.18, 0.16, 0.13 and 0.11 $\dot{V}O_{2\ MAX}$ was 43.7 ± 4.0, 42.1 ± 2.6, 39.1 ± 2.3, 36.4 ± 2.4, 30.7 ± 3.1 and 26.5 ± 1.7 $mL \cdot kg^{-1} \cdot min^{-1}$ for sedentary participants and 66.3 ±3.2, 62.1 ± 1.8, 56.7 ± 2.4, 53.4 ± 1.7, 43.9 ± 0.8 and 35.6 ± 1.3 $mL \cdot kg^{-1} \cdot min^{-1}$ for trained participants, respectively. This study showed strong correlations between $\dot{V}O_{2\ MAX}$ as a % of that attained at F_IO_2 0.30 and SaO_2 for sedentary ($r = 0.87$; $P<0.001$) and trained ($r = 0.93$; $P<0.001$), respectively. These results show that the reduction in $\dot{V}O_{2\ MAX}$ during acute hypoxia to be dependent on the simulated altitude exposed to and the subsequent degree of arterial desaturation (Ferretti *et al.*, 1997). Agreeing with these findings are Mollard *et al.* (2007) when exposing sedentary and trained participants to simulated altitudes of 1000, 1500, 2500, 3500 and 4000 m. They found that as altitude increases the reduction in $\dot{V}O_{2\ MAX}$ becomes greater, being significantly reduced from 1000 m compared to sea level. This study showed that, in absolute terms from 1500 m the trained participants experienced greater reductions in $\dot{V}O_{2\ MAX}$ when compared to untrained. However, when $\Delta\ \dot{V}O_{2\ MAX}$ was

expressed as a % there was no difference between sedentary and trained participants at any altitude. Calbet *et al.* (2003) reported that two-thirds of the reduction in $\dot{V}O_{2\ MAX}$ could be accounted for by arterial desaturation with the remaining third a result of reduced cardiac output, both of which are components of oxygen delivery.

Lawler *et al.* (1988) and Martin and O'Kroy (1993) both investigated the effect of sea level $\dot{V}O_{2\ MAX}$ on aerobic performance at altitude and demonstrated similar findings. Lawler *et al.* (1988) found that when $F_IO_2 = 0.13$ $\dot{V}O_{2\ MAX}$ was reduced by 26 and 15 % for trained and untrained subject groups, respectively. Martin and O'Kroy (1993) found $\dot{V}O_{2\ MAX}$ declined by 26 and 12 % when $F_IO_2 = 0.14$ for trained and untrained, respectively. Both these papers demonstrated that trained individuals experience greater reduction in aerobic power at altitude and both suggested that an increased $\dot{Q}$ for trained participants would reduce the pulmonary transit time (PTT) resulting in arterial desaturation and therefore reduced $\dot{D}O_2$.

Few papers have investigated UB exercise whilst breathing hypoxic gas, however two such papers offer interesting findings. Hopman and co-workers (2003) compared hypoxia, normoxia and hyperoxia ($F_IO_2 = 0.15$, 0.21 and 0.50) during arm crank ergometry in healthy, but not UB trained male participants. Whilst finding no difference between hypoxia and normoxia, $\dot{V}O_{2\ MAX}$ was significantly higher during hyperoxia when compared to hypoxia (39.56 ± 7.04 *vs.* 36.00 ± 5.51 $mL \cdot kg^{-1} \cdot min^{-1}$; $P<0.05$). This study was the first to suggest that UB $\dot{V}O_{2\ MAX}$ was dependent on O_2 supply where it was previously assumed to be limited by factors at the muscle, however the reductions appear to be far smaller then those seen during LB exercise at the same F_IO_2 (Table 2.3).

Table 2.3 $\dot{V}O_{2\ PEAK}$ *during acute hypoxia and normoxia. T = trained ; S = sedentary; A = able-bodied; P = paraplegic; T = tetraplegic.* * *significantly different from normoxia (P<0.05).*

Study	Participants/methods	$\dot{V}O_{2\ PEAK}$		$\Delta\ \dot{V}O_{2\ MAX}$ (%)
		Normoxia	Hypoxia	
Angermann *et al.* (2007)	7 Nordic combined Skiers	LB 57.3 ± 3.7	52.5 ± 3.0*	8
	LB = Cycle ergometry	UB 53.6 ± 4.2	49.3 ± 3.4*	8
	UB = Double pole ergometry	$mL{\cdot}kg^{-1}{\cdot}min^{-1}$		
	Hypoxic F_IO_2 = 0.146			
Hopman *et al.* (2004)	10 able-bodied males	A 37.2 ± 7.3	36.0 ± 1.8	3
	6 paraplegic males	P 24.1 ± 1.6	23.1 ± 1.5*	4
	6 tetraplegic males	T 12.2 ± 1.8	12.7 ± 2.1	4
	Arm crank ergometry	$mL{\cdot}kg^{-1}{\cdot}min^{-1}$		
	Hypoxic F_IO_2 = 0.15			
Peltonen *et al.* (2001a)	11 male endurance athletes	59.8 ± 4.5	55.1 ± 4.8*	8
	Cycle ergometry	$mL{\cdot}kg^{-1}{\cdot}min^{-1}$		
	Hypoxic F_IO_2 = 16.6			
Peltonen *et al.* (2001b)	6 male endurance athletes	4.55 ± 0.32	3.58 ± 0.44*	21
	cycle ergometry	$L.min^{-1}$		
	Hypoxic F_IO_2 = 0.15			
Gavin *et al.* (1998)	13 endurance trained males	H 60.4 ± 4.8	43.8 ± 4.7	27
	6 high $\dot{V}_E / \dot{V}O_2$; 7 low $\dot{V}_E / \dot{V}O_2$	L 63.7 ± 3.7	42.1 ± 2.3	34
	Cycle ergometry	$mL{\cdot}kg^{-1}{\cdot}min^{-1}$		
	F_IO_2 = 0.133			

Table 2.3 *Continued.*

Study	Participants/methods	$\dot{V}O_{2\ PEAK}$ Normoxia	Hypoxia	$\Delta\ \dot{V}O_{2\ MAX}$ (%)
Ferretti *et al.* (1997)	5 trained participants	T 62.1 ± 1.8	35.6 ± 1.3*	43
	5 sedentary participants	S 42.1 ± 2.6	26.3 ±1.7*	38
	Cycle ergometry	$mL \cdot kg^{-1} \cdot min^{-1}$		
	Hypoxic $F_IO_2 = 0.11$			
Zattara-Hartmann	6 healthy male participants	3.60 ± 0.18	2.66 ± 0.12*	26
and Jammes (1996)	Cycle ergometry	$L \cdot min^{-1}$		
	Hypoxic $F_IO_2 = 0.10$			
Martin and O'Kroy	8 highly trained participants	T 5.53 ± 0.31	3.35 ± 0.23*	39
(1993)	8 sedentary participants	S 3.48 ± 0.58	2.90 ± 0.58*	17
	Cycle ergometry	$L \cdot min^{-1}$		
	Hypoxic $F_IO_2 = 0.13$			
Lawler *et al.* (1988)	7 trained participants	T 64.5 ± 2.4	51.1 ± 2.0*	21
	6 untrained participants	S 45.0 ± 2.2	40.4 ± 1.5*	10
	Cycle Ergometry	$mL \cdot kg^{-1} \cdot min^{-1}$		
	Hypoxic $F_IO_2 = 0.14$			

A study using participants who were highly UB trained (Nordic combined skiers) found that $\dot{V}O_{2\ MAX}$ was significantly reduced at a simulated altitude of 3200 m ($F_IO_2 = 0.146$) compared to normoxia (560 m; Angermann *et al.*, 2006). While at a slightly higher simulated altitude than Hopman *et al.* (2003), which could account for the significant reduction in $\dot{V}O_{2\ MAX}$, the difference in fitness between the participants should be considered. Where the UB elicits a $\dot{V}O_{2\ MAX}$ approximately 60-80% of that attained during LB exercise (section 2.5) in participants who are not specifically UB trained,

Angermann *et al.* (2006) found UB $\dot{V}O_{2\ MAX}$ was 93.5 ($P<0.05$) and 93.9 % (NS) of that reported for the LB for normoxia and hypoxia, respectively.

During LB exercise highly trained individuals experience reduced arterial saturation at maximal exercise due to a large cardiac output and reduced PTT, insufficient for complete pulmonary diffusion. Where $\dot{Q}$ is usually reduced during UB exercise those with highly trained UB musculature may provoke similar cardiovascular responses during both modes of exercise, thus it may be possible that they experience greater arterial desaturation and reduced oxygen delivery during UB exercise in hypoxia than those who are untrained. Angermann *et al.* (2006) did report higher HR_{MAX} *vs.* Hopman *et al.* (2003) for UB normoxic and hypoxic exercise (190 ± 10 and 192 ± 10 *vs.*176 ± 19 and 177 ± 16 $bt \cdot min^{-1}$, respectively) and the former study reported no significant difference for HR_{MAX} between UB and LB exercise. Neither of these studies reported $\dot{Q}$ during hypoxic or normoxic exercise. Angermann *et al.* (2006) reported arterial saturations of 93.2 ± 2.5 and 75.0 ± 5.9 % at maximal UB exercise for normoxia and hypoxia respectively. Galy *et al.* (2005) reported that from rest to maximal exercise arterial saturation fell from 99 ± 0.2 to 93.4 ± 1.4 % indicating EIAH during LB exercise. Though Angermann *et al.* (2006) did not report resting SaO_2 the low saturation at maximal exercise could indicate EIAH during UB exercise. While these two papers offer interesting comparisons it should be noted that all participants performed hypoxic exercise first in Angermann and colleagues (2006) study and different ergometers were used during UB exercise. Where Hopman *et al.* (2003) used an arm crank ergometer in the seated position, double poling ergometry (Angermann *et al.* 2006) may engage a greater muscle mass thus the two modes of UB exercise may elicit different maximal oxygen consumptions.

2.4.2 Cardiac output.

Cardiac output ($\dot{Q}$) is derived from heart rate (HR) and stroke volume (SV), a reduction in the maximal capacity of either would result in reduced maximal $\dot{Q}$. HR and SV respond differently to incremental exercise. HR increases progressively with workload until maximal exercise, while SV increases up to 40-60 % $\dot{V}O_{2\ MAX}$ (lactate threshold) where it plateaus until maximal exercise (Stringer *et al.*, 1997). Therefore, after lactate threshold an increase in $\dot{Q}$ is predominately due to increased HR.

Wagner (2000) reviewed the cardiovascular adaptations to exercise at altitude, briefly discussing the adaptations to acute exposure. It is generally accepted that when acutely exposed to altitudes below ≈ 4500 m $\dot{Q}$ is not reduced at maximal exercise, however $\dot{Q}$ is greater at a given $\dot{V}O_2$ (Wagner *et al.*, 1986). SV has been shown not to change up to an altitude of 4000 m (Stenberg *et al.*, 1966) thus if maximal HR and SV are unchanged during acute hypoxia then $\dot{Q}_{MAX}$ will not alter. However some studies have contradicted these findings demonstrating reduced HR and $\dot{Q}$ during acute hypoxic exercise. At a higher simulated altitude (F_IO_2 = 0.105; ≈ 5300 m) Calbet and colleagues (2003) found HR, SV and $\dot{Q}$ to be significantly reduced (8, 9 and 17%, respectively; $P<0.05$) at maximal exercise. Benoit *et al.* (2003) stated HR_{MAX} is reduced when altitude is greater then 4000 m while a later study found max HR to be significantly reduced from 1000 m above sea level in trained participants (65.5 ± 3.1 $mL \cdot kg^{-1} \cdot min^{-1}$) and from 2500 m in untrained participants (44.1 ± 5.3 $mL \cdot kg^{-1} \cdot min^{-1}$) with the trained participants experiencing greater reductions at all simulated altitudes (1000, 1500, 2500, 3500 and 4500 m; Mollard *et al.* 2007). Despite lower HR_{MAX} the observed reductions in $\dot{V}O_{2\ MAX}$ was attributed to arterial desaturation (r = 0.89 and 0.80 for trained and

untrained, respectively; $P<0.05$). Peltonen *et al.* (2001b) found that neither HR nor SV were significantly reduced during hypoxia, however both tended to be lower which resulted in $\dot{Q}$ being significantly reduced at maximal exercise (28.51 ± 2.36 *vs.* 25.99 ±3.37 $L \cdot min^{-1}$; $F_IO_2 = 0.15$).

Increased activity of the sympathetic nervous system (SNS) during acute hypoxia results in greater cardiovascular stress at rest and at a given workload/ $\dot{V}O_2$. Increased sympathetic activity and increased circulating adrenaline are the main contributors to the increased activity of the cardiovascular system (Hopkins *et al.,* 2003; Mazzeo, 2008). Calbet *et al.* (2003) reported significantly higher circulating concentrations of adrenaline and noradrenaline at a given workload during hypoxic cycling exercise, however there were no differences in these concentrations at maximal exercise. In spite of similar catecholamine concentrations at maximal exercise HR, SV and $\dot{Q}$ were significantly lower (182 *vs.* 167 $bt \cdot min^{-1}$; 128 *vs.* 116 $mL \cdot bt^{-1}$ and 23.2 *vs.* 19.4 $L \cdot min^{-1}$, respectively). This indicates that cardiovascular responses to hypoxia are not solely accountable for by catecholamine concentrations.

Hopkins and co-workers (2003) assessed heart rate and cardiac output during incremental exercise in normoxia and hypoxia ($F_IO_2 = 0.125$;≈ 4000 m) while separately blocking the β-sympathetic and parasympathetic arms of the autonomic nervous system (ANS). It was found that during the control trials (no pharmacological intervention) HR and $\dot{Q}$ were higher during submaximal and lower during maximal exercise in hypoxia, in agreement with the aforementioned papers (Calbet *et al.,* 2003; Mazzeo, 2008). If the observed difference between HR and $\dot{Q}$ during hypoxia was due to increased activity of the SNS then blocking the β-sympathetic arm of the ANS would

diminish the differences observed between normoxic and hypoxic exercise. This was not the case, β-sympathetic blockage resulted in significantly reduced HR and $\dot{Q}$ compared to control, however HR and $\dot{Q}$ were still higher at a given $\dot{V}O_2$ during hypoxia. It was hypothesised that the SNS and PNS may work reciprocally, i.e. when β-sympathetic receptors are blocked increased parasympathetic withdrawal occurs, however parasympathetic withdrawal only increases HR to 100-110 bt·min^{-1}. Alternatively α-adrenergic receptor excitation by noradrenaline would be unaffected by either of the drugs employed and may become prominent when other branches of the SNS are blocked (Hopkins *et al.*, 2003).

Benoit and colleagues (2003) found that a higher $\dot{V}O_{2\ MAX}$ at sea level and low SaO_2 at maximal exercise were correlated with ΔHR_{MAX} in three groups, based on normoxic $\dot{V}O_{2\ MAX}$ (HIGH = 64.2 ± 3.3; MED = 50.8 ± 3.9 and LOW = 41.0 ± 1.9 mL·kg^{-1}·min^{-1}). They reported that HIGH experienced greater reduction in HR_{MAX} then MED and LOW ($P<0.05$ and $P<0.001$, respectively). Trained athletes have a greater $\dot{Q}_{MAX}$ than untrained and experience greater $\Delta \dot{V}O_{2\ MAX}$, ΔHR_{MAX} and desaturation during hypoxic exercise and are more likely to experience EIAH during normoxic exercise (Benoit *et al.*, 2003; Martin and O'Kroy, 1993; Lawler *et al.*, 1988). Benoit *et al.* (2003) also separated their participants with high normoxic $\dot{V}O_{2\ MAX}$ into those that experience EIAH (SaO_2 < 92 %) and those that did not. Those that experienced EIAH also experienced significantly greater ΔHR_{MAX} then those who did not (21 *vs.* 15 bt·min^{-1}, respectively). It may be that central chemoreceptors interpret larger arterial desaturation as potentially dangerous and by reducing HR_{MAX} and therefore $\dot{Q}_{MAX,}$ pulmonary transit time may increase, aiding gaseous exchange at the lung preventing further

desaturation. Also in the presence of reduced arterial oxygen content a reduced HR would ensure that myocardial O_2 demand is met.

Non-invasive techniques to measure/estimate $\dot{Q}$ have been developed to overcome the need for arterial blood sampling, however they often require sophisticated equipment, experimenter expertise and the participants to perform complicated manoeuvres which can be exaggerated by exercise such as CO_2 rebreathing (Stringer *et al.*, 1997). Two studies that identified simpler techniques for the estimation of $\dot{Q}$ during exercise have used oxygen pulse ($\dot{V}O_2$ /HR; Bhambhani, 1995) and by characterising the behaviour of arterial – mixed venous oxygen content (a-$\bar{v}$ O_2Diff.) as a percentage of $\dot{V}O_{2\ MAX}$ (Stringer *et al.*, 1997). Bhambhani (1995) reported significant correlation between $\dot{Q}$ estimated from CO_2 rebreathing and oxygen pulse for lower and upper body exercise in 25 males ($r = 0.76$ and 0.85, respectively; $P<0.01$) at lactate threshold (difference between LB and UB exercise for $\dot{Q}$, HR and SV are discussed in section 2.5). As SV remains unchanged from this point, if HR_{MAX} is recorded then $\dot{Q}_{MAX}$ can be calculated. Stringer and colleagues (1997) measured a-$\bar{v}$ O_2Diff. in five males via blood sampling during incremental exercise to exhaustion. As a-$\bar{v}$ O_2Diff. responds in a constant manner as a function of % $\dot{V}O_{2\ MAX}$ regression analysis allows for the estimation of $\dot{Q}$ and SV from the measurement of $\dot{V}O_2$ alone ($r = 0.94$, $P<0.0001$).

2.4.3 Arterial oxygen content/oxygen delivery.

CaO_2 is derived from the oxygen carry capacity of the blood and the extent to which the blood is saturated (S_PO_2). The bloods capacity for oxygen transport is dependant on haemoglobin concentration ([Hb]) as each gram of haemoglobin carries 1.34 mLO_2 (it should be noted that a nominal amount of O_2 is carried by plasma), therefore;

Equation 2.3 $CaO_2 = ([Hb] \times 1.34 \times SpO_2) + (0.003 \times PO_2)$

Oxygen delivery ($\dot{D}O_2$) is the CaO_2 and the rate at which blood is transported to the active tissues ($\dot{Q}$). $\dot{Q}$ increases linearly with workload, if CaO_2 remained constant $\dot{D}O_2$ would increase purely from the changes in $\dot{Q}$.

Equation 2.4 $\dot{D}O_2 = \dot{Q} \times CaO_2$

2.4.4 Arterial – mixed venous oxygen difference.

Arterial – mixed venous oxygen difference (a-$\bar{v}$ O_2Diff.) is the difference between the CaO_2 and the oxygen content of venous blood (CvO_2), in other words the amount of oxygen extracted from the blood. Fig 2.4 shows the partial pressure of oxygen (PO_2) as it is transported from the ambient air to the muscle and into the venous blood at rest and during exercise at sea level and at an altitude of 5800 m. It can be seen that there is a strong gradient between arterial and mixed venous PO_2 at sea level meaning that there is potential for more O_2 to be extracted from the blood by the muscle. At high altitude this gradient is diminished, the CaO_2 is reduced and less O_2 is available at the muscle for extraction, a situation further attenuated by exercise. It should be noted that as extraction (E) is a ratio between CaO_2 and CvO_2 the same ratio can represent two different amounts of O_2 extracted from the blood.

While O_2 tension was the same, Ekblom and co workers (1976) reduced arterial O_2 content (CaO_2) by reducing [Hb] and showed that by lowering CaO_2, a-$\bar{v}$ O_2Diff. decreased to 137.2 ± 13.0 from 149.0 ± 13.4 $mL \cdot L^{-1}$ in the control group. Exposure to a simulated altitude≈ 5300 m (F_IO_2 = 0.105) a-$\bar{v}$ O_2Diff. was 113 $mL \cdot L^{-1}$ compared to

174 $mL \cdot L^{-1}$ at sea level during maximal exercise which corresponded to extraction ratios of 0.89 and 0.92, respectively (Calbet *et al.*, 2003). Studies at simulated altitude show CaO_2 is reduced through desaturation which narrows the gradient between arterial and venous O_2 content and though extraction ratio tends to increase with altitude the absolute amount of oxygen extracted is reduced (Ekblom *et al.*, 1975; Richardson *et al.*, 1999b). Jansen-Urstad and colleagues (1995) found that during 10 mins of submaximal UB exercise (50 % of exercise-induced increase in $\dot{V}O_2$, i.e. $\dot{V}O_{2\ PEAK}$ - $\dot{V}O_{2\ REST}$) a-$\bar{v}\ O_2$Diff. was similar at rest during normoxia and hypoxia ($F_IO_2 = 0.12$) but was lower within 45s of commencing exercise during hypoxia compared to normoxia.

Fig. 2.4 *Partial pressure of oxygen from the atmosphere to the cell at sea level and an altitude of 5800 m during rest and exercise (taken from Ward et al., 2000).*

2.5 Lower vs. upper body exercise.

Where much debate and research has been directed towards the factors limiting $\dot{V}O_{2\ MAX}$ during lower body (LB) exercise (Ekblom *et al.,* 1976; Ferretti *et al.*, 1997) the limiting factors to upper body (UB) exercise are less conclusive. The realisation of the importance of UB musculature in recreational, military and exercise tasks and the increased research into the exercise capacity of those with spinal cord injury has led to a greater understanding of UB exercise (Sawka *et al.*, 1983; Hopman *et al.*, 2004). Where the differences between LB and UB exercise have been described, the underlying physiological mechanisms limiting exercise in the two modes of exercise have been studied to a lesser extent during UB exercise (Bar-Or and Zwiren, 1975; Sawka *et al.,* 1983; Bhambhani *et al.,* 1998; Mukari *et al.,* 2004).

Arm cranking elicited 62.5 ± 6.3 % of the $\dot{V}O_{2\ MAX}$ and 88.7 ± 4.9 % of the HR_{MAX} attained during treadmill running (Bar-Or and Zwiren, 1975) in 18 healthy male participants. UB exercise (arm crank ergometry) generally elicits 60-80 % of $\dot{V}O_{2\ MAX}$ achieved during cycling ergometry. The above study falls within the lower end of this range when using treadmill running for LB exercise, which itself elicits higher $\dot{V}O_{2\ MAX}$ compared to cycle ergometry (McKay and Banister, 1976). However, most studies comparing LB and UB exercise employ cyclical exercises (i.e. leg cycling ergometry *vs.* arm crank ergometry).

Using arm crank ergometry and cycling ergometry Bhambhani and colleagues (1998) found that $\dot{V}O_{2\ MAX}$ was significantly lower in males and females during arm crank ergometry. At a workload 56.7 and 58.1 % of that attained during LB exercise $\dot{V}O_{2\ MAX}$ was 68.5 and 70.2 % for males and females exercise, respectively. This was

only partially accounted for by HR_{MAX} which was reduced to 89.2 and 92.0 % of that seen whilst cycling for male and females, respectively. This is comparable with Mukari *et al.* (2004) who found $\dot{V}O_{2\ MAX}$ and HR_{MAX} to be 70.4 and 92.9 % of that attained during LB exercise when exercising the UB in females. Using untrained male participants Schneider *et al.* (2002) found $\dot{V}O_{2\ MAX}$ and HR_{MAX} to be 66.4 and 93.9 % during UB compared to LB exercise, respectively. This was similar to the findings of Bhambhani *et al.* (1998) whose participants had better aerobic conditioning ($\dot{V}O_{2\ MAX}$ = 39.0 ± 2.2 *vs.* 55.0 ± 13.1 $mL \cdot kg^{-1} \cdot min^{-1}$).

One study showed no difference in $\dot{V}O_{2\ MAX}$ between UB and LB exercise. Angermann and co-workers (2006) using Nordic combined skiers, reported $\dot{V}O_{2\ MAX}$ of 53.6 ± 4.2 and 57.3 ± 3.7 $mL \cdot kg^{-1} \cdot min^{-1}$ for UB and LB exercise, respectively. In contrast to other studies these participants were specifically UB trained and the UB ergometer was specific to cross country skiing (custom built double pole ergometer). Also, where continuous cycle ergometry was used during LB exercise the UB protocol was discontinuous. While no difference has been demonstrated in $\dot{V}O_{2\ MAX}$ between continuous and discontinuous protocols during cycle ergometry and arm crank ergometry (McArdle *et al.*, 1973; Stamford, 1976; Sawka *et al.*, 1983; Smith *et al.*, 2001) this may not be the case for double pole ergometry.

The reduced aerobic power of the UB has been attributed to several factors 1) upper body exercise uses a smaller muscle mass; 2) the majority of people have lesser training status in their arms; 3) different central responses to upper body exercise; 4) lower mechanical efficiency during upper body exercise and 5) a greater recruitment of type II muscle fibres (Johnson *et al.*, 1973; Sawka, 1983; Jansen-Urstad and Ahlborg, 1992;

Schneider *et al.*, 2002; Hopman *et al.*, 2003; Hopman *et al.*, 2004). While it had been assumed that UB exercise was limited peripherally Hopman *et al*. (2003) were the first to provide evidence that like the LB UB exercise is also limited centrally. Reducing the inspired O_2 fraction from 0.5 to 0.15 they found that $\dot{V}O_{2\,MAX}$ was significantly reduced. Unfortunately while increasing and decreasing the F_IO_2 from normoxia this study did not report SaO_2 data thus $\dot{V}O_{2\,MAX}$ could not be correlated with arterial desaturation or reduced $\dot{D}O_2$.

The cardiovascular response to exercise differs between LB and UB exercise, though the magnitude of the difference is dependant upon the training status of the UB. During both LB and UB exercise $\dot{Q}$ and HR increase linearly with $\dot{V}O_2$, however while the former is similar for LB and UB exercise HR is higher during UB exercise at a given oxygen consumption due to a lower SV (Pendergast, 1989; Tulppo *et al*, 1999). Bhambhani (1995) found HR_{MAX} was 170 ± 13 and 183 ± 10 bt·min^{-1} for males and 167 ± 16 and 183 ± 12 bt·min^{-1} for females during UB and LB exercise respectively ($P<0.05$). Schneider *et al.* (2002) also reported significantly lower HR_{MAX} for UB exercise compared to LB (181 ± 5 *vs.* 193 ± 2 bt·min^{-1}). The role of the autonomic nervous system differs between these two modes of exercise. Reviews by Miles *et al*. (1989) and Sawka (1986) stated that higher HR during UB exercise indicated greater sympathetic stimulation. While Tulppo *et al.* (1999) during submaximal exercise found HR to be higher during arm cranking due to a quicker withdrawal of the parasympathetic nervous system.

Table 2.4 *$\dot{V}O_{2\ PEAK}$ and peak power output (PPO) from selected studies comparing lower (LB) and upper body (UB) maximal exercise. M = males; F = females; ‡ = W.kg^{-1}; * significantly different from LB exercise (P<0.05).*

Study	Participants/methods	PPO (W)		$\dot{V}O_{2\ PEAK}$ (mL·kg^{-1}·min^{-1})	
		LB	UB	LB	UB
Angermann *et al.* (2006)	7 Nordic combined skiers Double pole *vs.* cycle ergometry	5.4 ± 0.2‡	3.4 ± 0.2*‡	57.3 ± 3.7	53.6 ± 4.2*
Mukari *et al.* (2004)	27 healthy females Arm crank *vs.* cycle ergometry	192 ± 35.7	81.2 ± 22.8*	44.4 ± 5.9	30.9 ± 6.5*
Schneider *et al.* (2002)	10 healthy male participants Arm crank *vs.* cycle ergometry	280.2 ± 14.9	128.6 ± 6.9*	39.0 ± 2.2	25.9 ± 1.6*
Bhambhani *et al.* (1998)	15 male participants 10 female participants Arm crank *vs.* cycle ergometry	M 268 ± 51 F 186 ± 29	152 ± 14* 108 ± 16*	55.0 ± 13.1 38.9 ± 10.4	37.7 ± 7.2* 27.3 ± 5.4*
Boileau *et al.* (1984)	40 healthy male participants Arm crank *vs.* cycle ergometry	-	-	47.6 ± 6.5	34.2 ± 5.4*
Davis *et al.* (1976)	39 healthy male participants Arm crank *vs.* cycle ergometry	-	-	48.8 ± 5.4	31.0 ± 4.2*
Bar-Or and Zwiren (1975)	18 healthy male participants Arm crank *vs.* treadmill	-	-	56.0 ± 6.5	34.6 ± 5.3*

SV is also lower during UB exercise which in turn reduces $\dot{Q}$ at a given HR in this mode of exercise. Stroke volume during UB exercise is ~20 % lower than during exercise with the LB, although individuals with highly trained UB musculature can have similar SV for LB and UB exercise (Pendergast, 1989). Bhambhani (1995) used the CO_2 rebreathing technique to measure $\dot{Q}$ at ventilatory threshold. Ventilatory thresholds offer non-invasive estimates of lactate threshold (LT; measured via arterial blood sampling) and previous investigations observed no difference between these two techniques during normoxic and hypoxic LB exercise (Thake, 2006). As SV plateaus after LT the measurement of $\dot{Q}$ and HR at LT means that SV and $\dot{Q}$ can be calculated and applied to all exercise intensities above LT, providing HR is known (section 2.4.2). In men and women SV was 19 and 22 % lower during UB compared with LB exercise, this was accompanied by a lower HR_{MAX} for both genders ($P<0.05$). It has been proposed that the use of the leg muscles during LB exercise aids venous return via the skeletal muscle pump, increasing ventricular filling and therefore stroke volume (Miles *et al.*, 1989; Sawka, 1986). Whilst it has been reported that systolic blood pressure was lower during UB exercise several other papers reviewed by Pendergast (1989) indicate that blood pressure is higher during UB exercise. As mentioned earlier $\dot{Q}$ is similar at a given workload for LB and UB exercise thus greater peripheral resistance during UB exercise increases blood pressure impeding SV due to increased afterload resulting in a greater HR at a given workload (Sawka, 1986; Miles *et al.* 1989).

Arteriovenous O_2 difference (a-$\bar{v}$ O_2Diff.) has been reported to be lower for arm cranking compared to cycle ergometry (Boileau *et al.*, 1984; Calbet *et al.*, 2005). Boileau *et al.* (1984) reported a-$\bar{v}$ O_2Diff. at peak exercise of 13.5 ± 2.6 and 15.0 ± 1.9 $mL \cdot 100mL^{-1}$ for UB and LB exercise, respectively. When participants were separated

into groups based on aerobic conditioning (high and low) during the respective mode of exercise a-$\bar{v}$ O_2Diff. was greater in the more highly conditioned group during both UB and LB exercise ($P<0.05$; Boileau *et al.*, 1984).

It has been well reported that [BLa] is significantly higher for a given exercise intensity using the UB (Ahlborg and Jansen-Urstad, 1991; Jansen-Urstad *et al.*, 1993; Bhambhani *et al.*, 1998) indicating an increased contribution of anaerobic metabolism for UB exercise. At 150 W Louhevaara and colleagues (1990) reported [BLa] of approximately 8 *vs.* 2 mmol·L^{-1} for UB *vs.* LB exercise respectively. This is due to a given workload representing a greater % of $\dot{V}O_{2\ PEAK}$ in the UB compared to the LB and an increased recruitment of type II fibres during UB exercise especially in those who are not specifically UB trained. While submaximal [BLa] is reported to be higher during UB exercise generally maximal [BLa] is higher during LB exercise as higher power outputs are achieved (Sawka, 1986; Miles, 1989; Schneider *et al.*, 2000; Angermann *et al.*, 2006). Louhevaara *et al.* (1990) found higher maximal BLa during UB *vs.* LB exercise (8.1 ± 1.3 *vs.* 5.9 ± 1.3 mmol·L^{-1}) although blood sampling was taken from the arm during both modes of exercise which represents blood directly from the active muscle during UB exercise.

Lactate threshold occurs at a lower absolute $\dot{V}O_2$ during UB exercise, however when expressed as a percentage of $\dot{V}O_{2\ MAX}$ LT occurs at the same point during UB and LB exercise in men (44.7 ± 10.1 and 43.2 ± 9.2%) and women (42.8 ± 10.2 and 44.8 ± 8.5 %; Bhambhani *et al.*, 1998). Davis *et al.* (1976) reported $\dot{V}O_2$ at LT of 1.22 ± 0.23, 2.61 ± 0.33 and 2.43 ± 0.29 L·min^{-1} which represented 46.5 ± 8.9, 63.8 ± 9.0 and 58.6 ± 5.8 % of $\dot{V}O_{2\ MAX}$ during arm cranking, cycling and running, respectively. This study

demonstrated that LT is found at a significantly higher % $\dot{V}O_{2\ PEAK}$ during cycling and running compared to arm cranking. Davis *et al.* (1976) used an arm cranking frequency of 50 rev.min^{-1} which has been shown not to elicit peak physiological responses (Sawka, 1983; Smith *et al.* 2001). Higher cadence during arm cranking increases $\dot{V}O_{2\ PEAK}$ and may increase efficiency so that $\dot{V}O_2$ at LT represents a greater % of peak oxygen consumption. Also this study measured LT using ventilatory thresholds whereas Bhambhani *et al.* (1998) used the v-slope method for determining LT from blood lactate concentrations.

2.6 Summary

Whether the experimenters have altered the O_2 carrying capacity of the blood (Ekblom *et al.*, 1976) or varied F_IO_2 (Ferretti *et al.*, 1997; Peltonen *et al.*, 2001a; Peltonen *et al.*, 2001b; Hopman *et al.*, 2003; Mollard *et al.*, 2007) the CaO_2 and $\dot{D}O_2$ to the exercising muscle has been manipulated either through [Hb] or SaO_2 resulting in reduced maximal aerobic power. Acute altitude/hypoxia reduces the P_IO_2 which in turn reduces P_AO_2; PaO_2 meaning less O_2 is available to the tissue per unit volume of blood for metabolism. Studies show that maximal aerobic power is dependant on the delivery of oxygen to the working muscle with theΔ $\dot{V}O_{2\ MAX}$ relative, but not exclusively due, to the severity of hypoxia experienced as training status and individual responses to acute hypoxia (HVR) also influence the effect of hypoxia on exercise (Lawler *et al.*, 1988; Ferretti *et al.*, 1997; Cardus *et al.*, 1998; Gavin *et al.*, 1998; Richardson *et al.*, 1999a). However much of the literature is based on LB exercise.

More recently UB exercise has been investigated as it cannot be assumed that the same mechanisms are at work for UB exercise. Recently Hopman and colleagues (2003; 2004) suggested that $\dot{V}O_{2\ PEAK}$ was limited by supply during UB exercise (F_IO_2 0.50 *vs.*

0.15 but no difference between F_IO_2 0.21 and 0.15), however these studies have only used 1 level of hypoxia, 1 protocol and special populations (spinal cord injury) have not been assessed using this mode of exercise (although Hopman *et al.*, 2004 compared able bodied people to participants with spinal cord injury). Clear differences have been demonstrated between hypoxic and normoxic exercise (Ferretti *et al.*, 1997; Calbet *et al.* 2003; Mollard *et al.* 2007) and between upper and lower body exercise (Sawka *et al.*, 1983; Bhambhani *et al.*, 1998; Mukari *et al.*, 2004), yet it is still to be shown what happens when these conditions are experienced together (i.e. is $\dot{V}O_{2\,MAX}$ during hypoxia the same as normoxia for LB compared to UB exercise).

Further research is therefore needed to assess the response of the UB to hypoxic exercise in the laboratory as well as field studies using UB exercise or comparing UB and LB responses. Research in this field will benefit those who are deployed on military operations at high altitude where physical activity often involves the UB. Furthering the understanding of the mechanisms limiting UB exercise will benefit athletes participating in events using the UB (rowers, cross-country skiers, climbers, athletes with spinal cord injury etc.). The use of acute hypoxia/altitude to determine alterations to UB exercise may provide the first step towards the development of altitude training protocols in order to prepare athletes for competition, which is already extensively used by endurance athletes (Wilber, 2007). Different levels of hypoxia as well as variation between different populations (i.e. training status or HVR) also require further research during UB exercise to assess whether the responses mirror those seen during LB hypoxic exercise.

Accordingly, the aim of this work is to compare and contrast the cardiorespiratory responses to incremental LB and UB exercise to volitional exhaustion at three inspired

oxygen fractions. It is hoped that this will identify the mechanisms which limit LB and UB exercise. It is hypothesised that UB $\dot{V}O_{2\ PEAK}$ will be approximately 70 % of that attained during LB exercise. In accordance with published literature, $\dot{V}O_{2\ PEAK}$ will decrease as F_IO_2 is reduced from 0.21 to 0.15 and from 0.15 to 0.13 during LB exercise. $\dot{V}O_{2\ PEAK}$ will not reduce to the same extent as F_IO_2 is reduced during UB compared to LB exercise. Accordingly, UB $\dot{V}O_{2\ PEAK}$ will represent a greater proportion of that achieved during LB exercise for hypoxic compared to normoxic exercise. Arterial desaturation will increase as F_IO_2 decreases in both LB and UB exercise. HR, SV and $\dot{Q}$ will be lower at maximal exercise during UB exercise but will not be significantly reduced as a result of hypoxia. $\dot{D}O_2$ will be lower during UB exercise and reduce as F_IO_2 decreases in proportion to the severity of arterial desaturation in both modes of exercise. Finally $\dot{V}O_{2\ PEAK}$ will correlate with $\dot{D}O_2$ at each F_IO_2 during LB and UB exercise andΔ $\dot{V}O_{2\ PEAK}$ will correlate to normoxic aerobic power for both modes of exercise.

CHAPTER 3

METHODOLOGY

3.0 Methodology.

3.1 Ethics.

Ethical approval for the present study was received from Coventry University's ethics committee. Healthy, non-smoking male participants free from any known cardiovascular, respiratory, nervous or skeletal/muscular disease and with normal haemoglobin concentrations ($>13 g \cdot dl^{-1}$) were recruited to participate in the study. The nature of the testing was communicated to the potential participants in verbal and written format and all participants completed informed consent forms (APPENDIX A) prior to any testing. Participants completed a physical activity readiness questionnaire (PAR-Q; APPENDIX B) on each laboratory visit. If any indication was given that participants were not in a suitable condition for testing (e.g. injury, respiratory illness etc.) the trial would be postponed.

To ensure subject safety, heart rate and oxygen saturation were continually monitored throughout pre-exercise, during exercise and recovery each trial. Participants were also continuously observed during all trials. If any of the following occurred exercise would be terminated and hypoxic gas replaced with room air:

- If it was requested by the subject
- If the subject exhibited symptoms or signs of dizziness, mental confusion, severe restlessness, vomiting or if the subject faints (subjectively assessed).
- If the subject reported chest pain or dyspnoea.
- If arterial oxygen saturation (SpO_2) fell below 70 % and is not immediately corrected.
- If a significant item of monitoring or measuring equipment failed/malfunctioned.

At the end of each trial participants were encouraged to cool down at a low workload until heart rate fell below 120 bt·min^{-1}. In hypoxic trials gas was immediately switched to room air (F_IO_2 = 0.21) at the cessation of exercise.

3.2 Subject information and preparation.

Nine healthy males, meeting all the inclusion criteria required for ethical approval, volunteered to participate in the present study. All participants were actively involved in sport and recreational fitness (≈ 4-6 hours per week) and eight participants exercised regularly for university sports teams (5 = Rugby; 2 = Athletics and 1 = Squash). One participant regularly undertook upper body exercise (indoor climbing) but none were specifically upper body trained. Table 3.2 shows participants' physiological characteristics.

Participants visited the laboratory on 7 occasions. On their first visit anthropometric data (section 3.3.1) and an earlobe capillary blood sample (to check haemoglobin concentration; section 3.9.3) were collected. Participants were habituated to the exercise ergometers and equipment/instruments to be used in all visits. Maximal exercise tests to volitional exhaustion were performed on each of the six subsequent visits. This consisted of 3 lower body (LB) and 3 upper body (UB) exercise trials whilst breathing varied F_IO_2s (0.21, 0.15 and 0.13) on separate occasions in a counterbalanced cross-over design. Prior to each trial participants were asked to refrain from strenuous exercise for 24hrs, consume a similar diet for 48hrs, fast for 4 hrs, and avoid caffeinated products and alcohol for 12 hrs. To avoid diurnal variations participants performed each of their 6 trials at the same time of day, individual trials were separated by at least 4 days.

3.3 Preliminary tests.

3.3.1 Anthropometric measurements.

Body mass and stature were measured using electronic scales (Tanita Corporation, Japan) and a stadiometer (SECA, Germany), respectively. Body fat was estimated using two methods: skinfolds (Harpenden skinfold callipers, Baty international, England) and volume displacement (BOD POD, Life measurement Inc., California, USA). Skinfolds were measured at the biceps and triceps (midway between the acromiale and the radiale), subscapular, suprailliac, anterior thigh (midway between the greater trochanter and lateral condyle) and medial calf (at the point of greatest girth). All measurements were taken from the right side of the body, in triplicate and the mean value used. Using Durnin and Womersley (1974) body fat percentage was estimated by measuring skinfolds at 4 sites (biceps, triceps, subscapular and suprailliac).

The volume displacement chamber (Fig. 3.1A and B) was calibrated according to manufacturer's instructions. In brief, calibration was performed when the chamber was empty and with a known volume canister (50.126 L) prior to each assessment. Participants wore tight shorts and a swim hat (as stated in the manufacturers instructions) and sat motionless whilst the BOD POD measured volume displacement. The participants then placed on a nose clip and inserted a mouthpiece and were asked to perform a respiratory manoeuvre to measure thoracic gas volume. This enables lung volume to be taken into account when estimating body volume.

Limb girths were measured at the thigh and calf at the same point as the skinfold and at the forearm around the greatest girth. Muscle mass was estimated using forearm girth, thigh girth, calf girth, thigh skinfold, calf skinfold, stature and body mass (Martin *et al.*, 1990).

3.3.2 Anthropometric results.

Table 3.1 *Comparison of two methods for estimating body fat percentage.*

Subject	% body fat (Durnin & Womersley, 1974)	% body fat (BOD POD)
1	11.8	13.4
2	25.3	22.0
3	16.7	14.2
4	26.7	25.1
5	17.0	14.6
6	09.5	10.0
7	21.7	17.8
8	11.1	03.5
9	11.7	15.0
Mean	**16.8**	**15.1**
SD	**6.4**	**6.3**

Table 3.1 presents individual and mean data for the two methods of estimating body fat. A strong correlation ($r = 0.87$; $P<0.01$) was evident between the two methods (Fig. 3.2). A Bland-Altman plot (Fig. 3.3) shows that all but 1 of the data plots fall within ±2 SD of the mean. The methods varied by 1.8 ± 3.2 % which was not significant ($P>0.05$). These data show that the BOD POD offers estimation of body composition in agreement with the method of Durnin & Womersley (1974). The 'gold standard' measure of body fat is dual-energy X-ray absorptiometry (DEXA). Strong correlations have been reported between this method and air-displacement plethysmography (BOD POD) however, BOD POD tends to underestimate body fat by≈ 2 – 3 % when compared to this method (Fields *et al.*, 2002).

A

B

Fig 3.1 A) *BOD POD, electronic scales, stadiometer, calibration weight (2* x *10kg) and calibration volume (50.126L)* ***B)*** *Participant appropriately dressed for body composition test with nose clip and mouth piece in place (as per respiratory manoeuvre).*

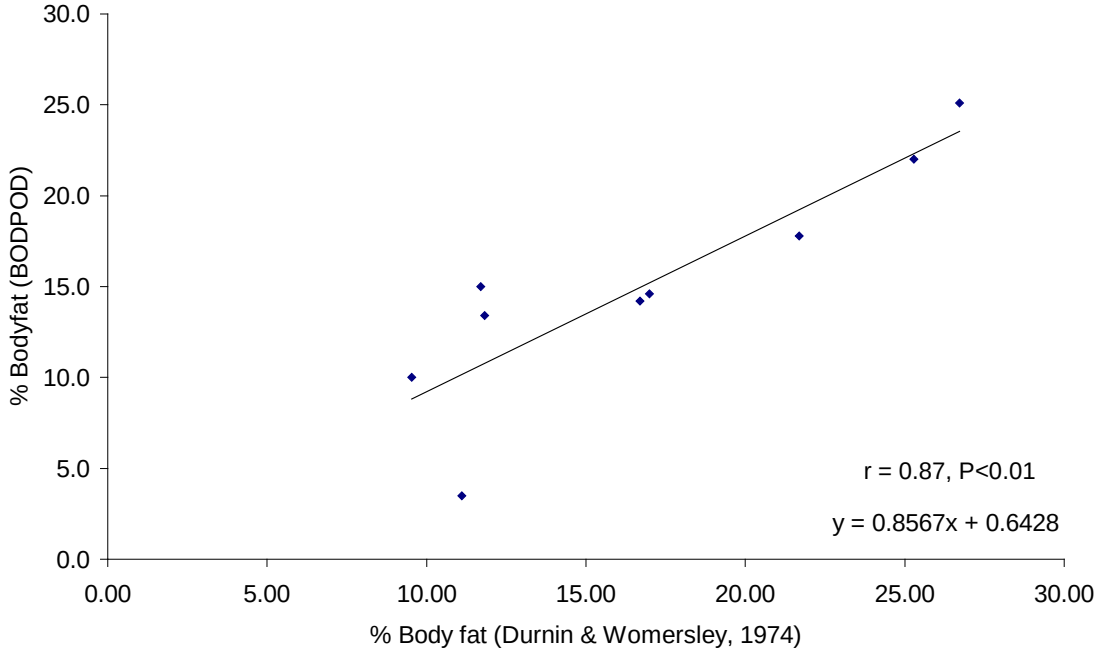


Fig. 3.2 *Correlation between body fat as measured by skinfold and BOD POD. Pearsons r = 0.87, P<0.01(n = 9).*

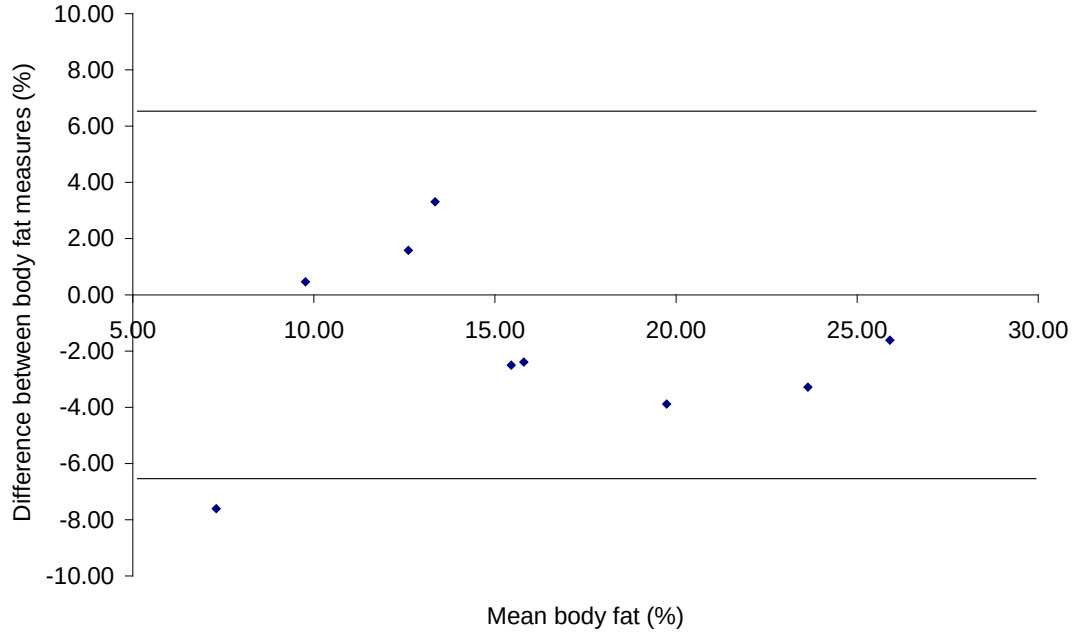


Fig. 3.3 *Bland-Altman plot for the difference in body fat percentage against mean body fat percentage (skinfold + BOD POD) for each subject, a comparison of skinfold measures and volume displacement (± 2 SD, n = 9).*

Table 3.2 *Anthropometric and physiological characteristics of subject group.* $\dot{V}O_{2\ PEAK}$ *from normoxic cycle ergometry; fat mass (%) taken from volume displacement method; FFM = fat free mass; MM = muscle mass.*

Subject No.	Age (yrs)	Height (cm)	Body mass (kg)	Fat mass (%)	Muscle mass (%)	$\dot{V}O_{2\ PEAK}$ ($L \cdot min^{-1}$)	$\dot{V}O_{2\ PEAK}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$\dot{V}O_{2\ PEAK}$ ($mL \cdot kgFFM^{-1} \cdot min^{-1}$)	$\dot{V}O_{2\ PEAK}$ ($mL \cdot kgMM^{-1} \cdot min^{-1}$)
1	21	162.2	57.5	13.4	58.3	2.67	47	54	80
2	21	178.1	89.5	22.0	48.7	3.55	39	51	81
3	22	186.7	79.1	14.2	58.7	4.00	50	59	86
4	21	188.8	101.9	25.1	48.1	3.50	33	46	72
5	18	174.4	73.7	14.6	57.2	2.86	38	45	68
6	24	181.9	74.8	10.0	61.9	3.49	47	52	75
7	24	183.4	82.3	17.8	53.8	3.87	47	57	87
8	26	185.5	73.1	3.5	67.1	4.20	57	60	86
9	22	184.0	76.3	15.0	63.9	3.55	45	55	73
Mean	**22**	**180.6**	**78.7**	**15.8**	**57.5**	**3.52**	**45**	**53**	**79**
SD	**2**	**8.2**	**12.2**	**6.4**	**6.5**	**0.50**	**7**	**5**	**7**

3.4 Delivery of inspired gas.

The inspired gas mixture was stored in a suspended 1000 L Douglas bag which was inflated using precision gasses (BOC, Gilford, Surrey). A constant flow of the respective F_IO_2 was fed into the Douglas bag so that the inspired gas reservoir was maintained. A face mask attached to a two-way valve was worn and the inspired side of the valve was connected to the gas reserve via polyvinyl tubing. During the normoxic trials the Douglas bag was maximally inflated, so to appear the same for every trial, but the valve remained closed and the participants breathed room air. Fig 3.4 and 3.5 show a schematic of the gas delivery and collection system used and figures of a subject attached to all instrumentation performing LB and UB exercise, respectively.

3.5 Protocol.

Discontinuous incremental lower body (LB) and upper body (UB) exercise to volitional exhaustion were performed on a mechanically braked cycle ergometer (Monark 824E) and an electronically braked arm crank ergometer (Lode Angio, Groningen, Holland), respectively. During cycle ergometry (Fig. 3.5 A and B) seat position was adjusted so that there was slight flexion in the knee when the pedal was at its lowest point. The arm crank ergometer (Fig. 3.5 C and D) used in the present study allows for reproducible positioning of seat height and distance from the ergometer so that: (1) the axis of rotation was at shoulder height, and (2) there was slight flexion in the elbow at the furthest point in the cycle. Ergometer set up was recorded on the participants' first visit and used on subsequent occasions.

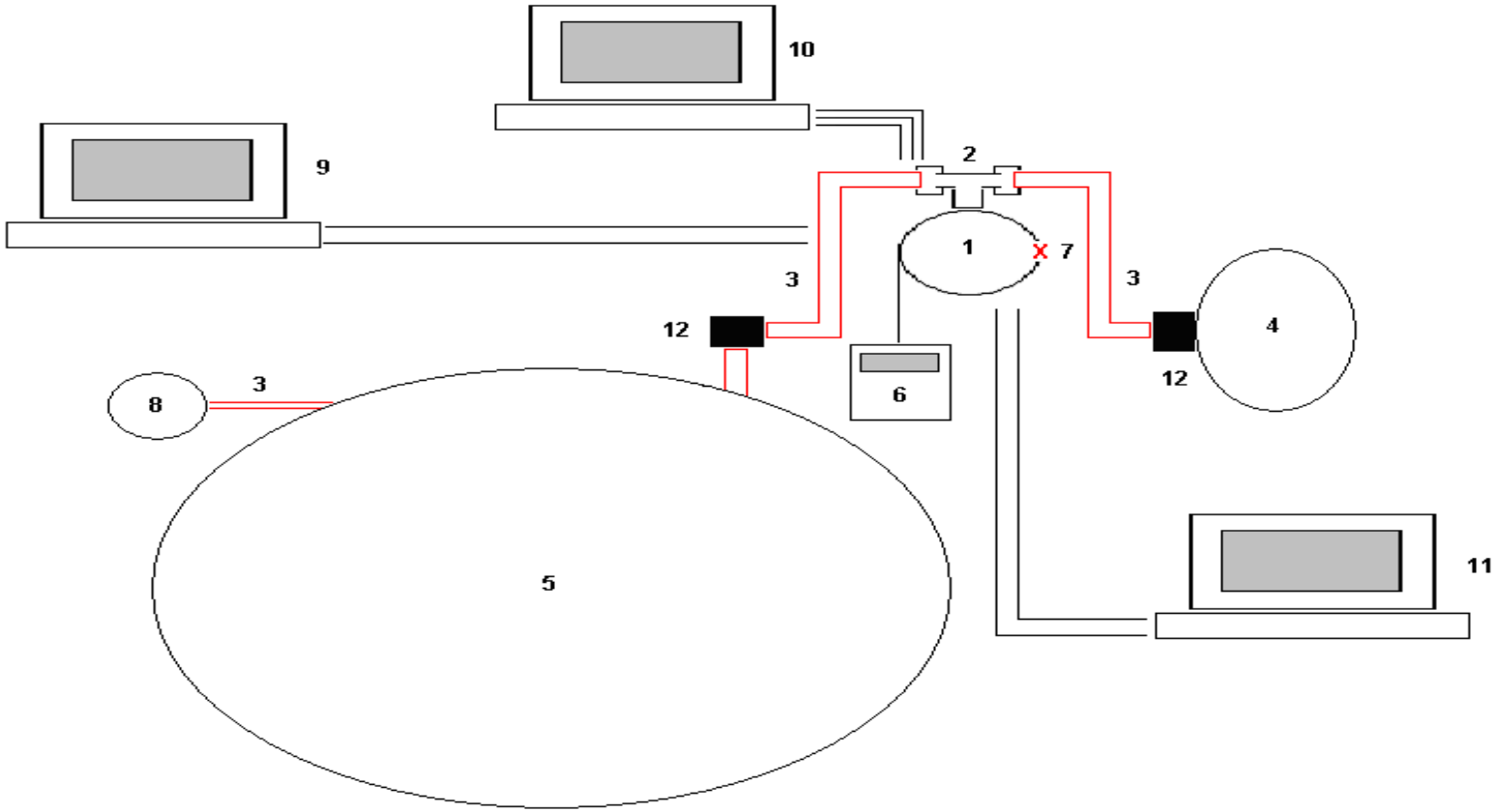
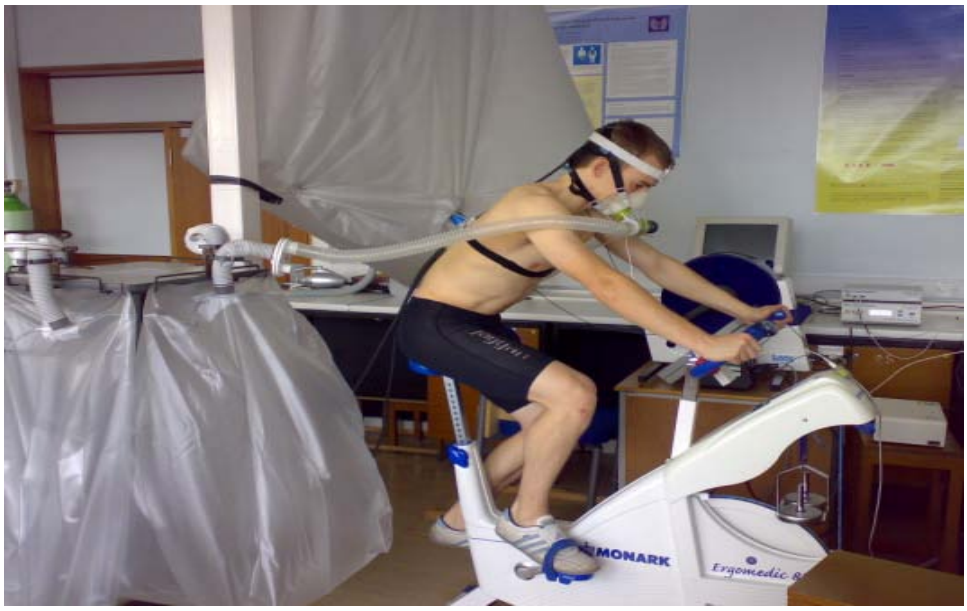


Fig. 3.4 *Schematic gas delivery/collection system and monitoring equipment. 1 = Subject; 2 = Two-way valve; 3 = Plastic tubing; 4 = 150 L Douglas Bag; 5 = 1000 L Douglas bag; 6 = Pulse oximeter; 7 = Blood sample site; 8 = Gas cylinder; 9 = Doppler Blood flow meter; 10 = Three lead ECG; 11 = Sweat rate meter; 12 = Sealable valves.*

A



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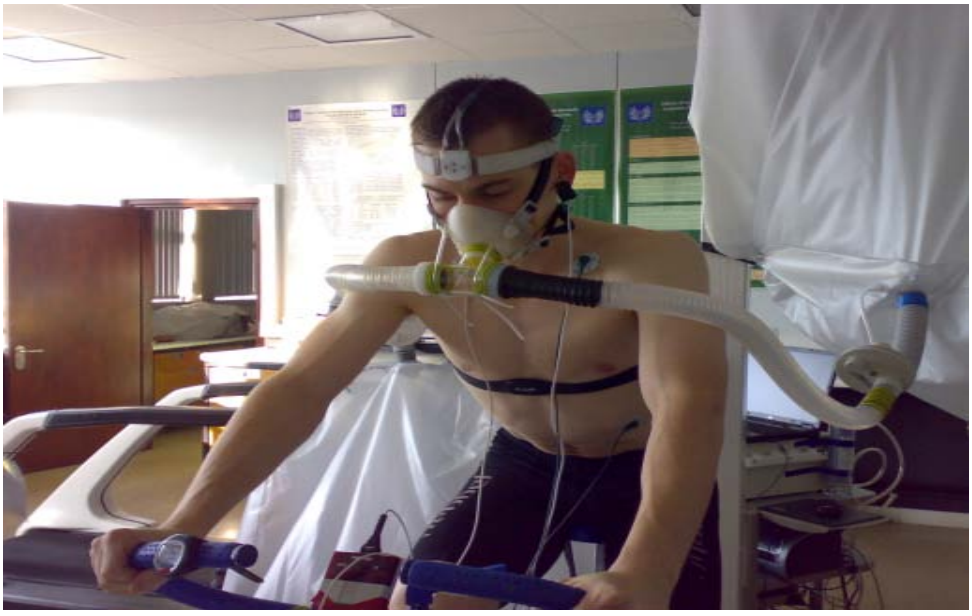
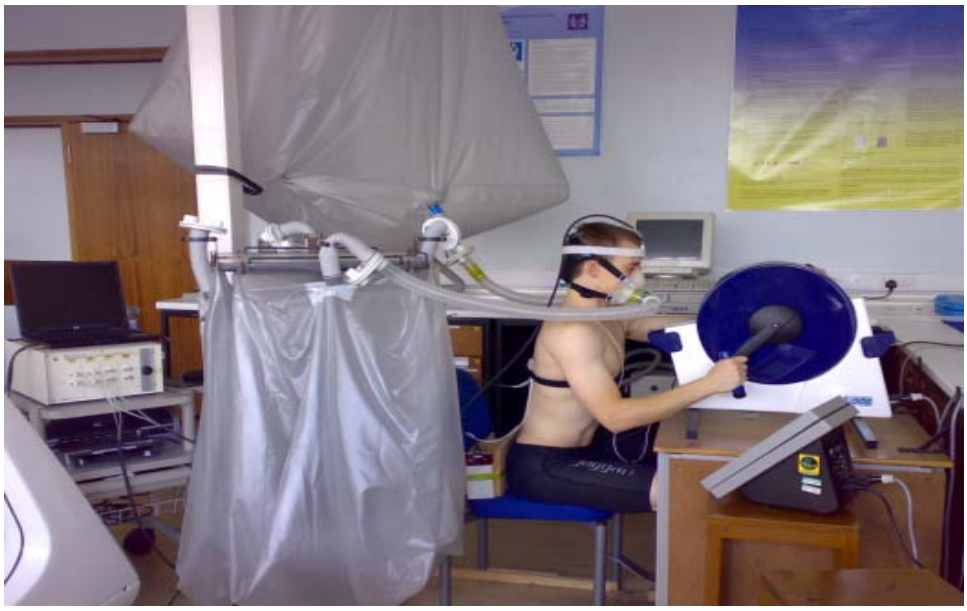


Fig 3.5 A and B *Subject performing LB exercise. Side and front profiles of laboratory setup and instrument placement.*

C



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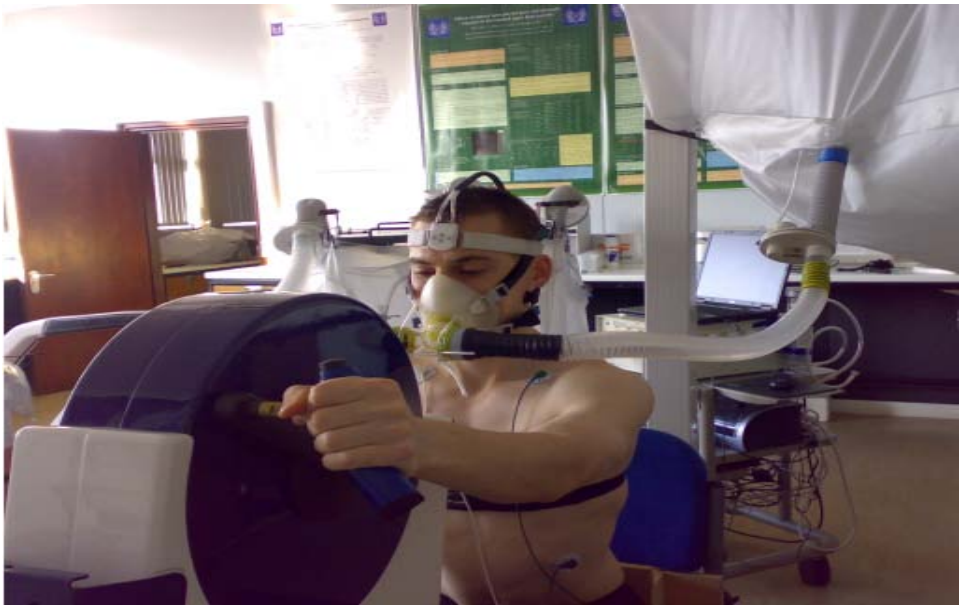

Fig 3.5 C and D *Subject performing UB exercise. Side and front profiles of laboratory setup and instrument placement.*

A 10 minute wash in period preceded the onset of exercise where the participants sat at rest whilst breathing the inspired gas fraction ($F_IO_2 \approx 0.21$, 0.15 or 0.13). At the end of this wash in period a resting blood sample was taken. Exercise commenced with a resistance of 70 W for cycle ergometry and 35W for arm ergometry and increased by 30 and 15 W every 3 mins thereafter, respectively. Participants maintained a cadence of 70 rev.min^{-1} until volitional exhaustion and were verbally encouraged throughout each trial. Central and local rating of perceived exertion (RPE; Appendix E) was collected 15 s prior to the collection of expired gas, SpO_2 and heart rate which was collected in the final minute of each stage of the test (2-3 mins). Earlobe capillary blood was collected during 30 s passive recovery between each exercise stage (Fig. 3.6).

Cycling trials were considered a maximal effort if 2 or more of the following criteria were met: (1) <100 mL increase in $\dot{V}O_2$ with increasing power output, (2) heart rate within 10 bt·min^{-1} of age predicted maximum (220-age), (3) respiratory exchange ratio (RER) >1.10, (4) central RPE > 18, and (5) blood lactate concentration > 8 mmol·L^{-1}. Arm cranking trials were considered a maximal effort if 2 or more of the following criteria were met: (1) <100 mL increase in $\dot{V}O_2$ with increasing power output, (2) heart rate within 10 bt·min^{-1} of age predicted maximum (200-age), (3) respiratory exchange ratio (RER) >1.10, (4) central RPE > 15 (local RPE > 18), and (5) blood lactate concentration > 8 mmol·L^{-1}.

The use of a discontinuous protocol in the present study was chosen primarily to aid the collection of blood during arm cranking and was used during the cycling trials for parity. However it has been previously reported that there is no statistical difference in $\dot{V}O_{2\ PEAK}$ values attained during continuous and discontinuous protocols for upper body (Sawka *et*

al., 1983; Smith *et al.*, 2001) and lower body exercise (McArdle *et al.*, 1973; Stamford, 1976). Also a cadence of 70 rev.min^{-1} has been shown to elicit statistically higher $\dot{V}O_{2\ PEAK}$ values when compared to slower cadences, however faster cadences had no significant effect on peak values during UB exercise (Price and Campbell, 1997; Smith *et al.*, 2001). During LB exercise McKay and Banister (1976) found that $\dot{V}O_{2\ PEAK}$ significantly increased from 60 to 80 rev.min^{-1} while cadences greater the 80 rev.min^{-1} resulted in reduced $\dot{V}O_{2\ PEAK}$.

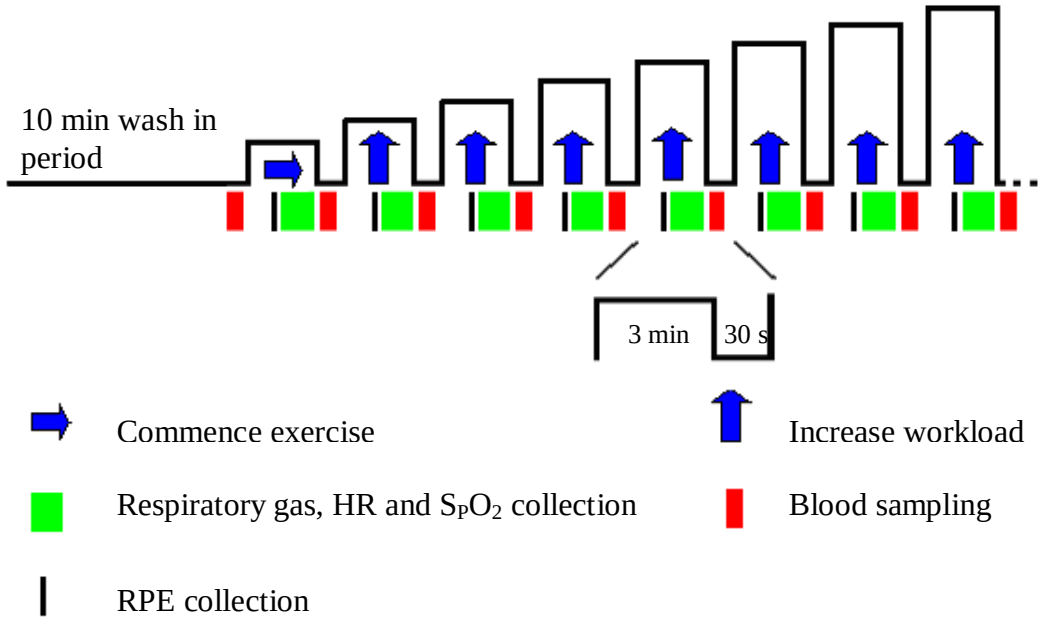

Fig. 3.6 *Breakdown of the discontinuous, incremental exercise protocol and collection points.*

3.6 Arterial haemoglobin oxygen saturation.

The pulse oximeter used in the present study (Nonin 8500, Nonin medical Inc, Minnesota, USA) used an ear sensor. Although it has been reported that the variability of ear sensor is

greater than that of finger sensors (Powers *et al.*, 1989) the reasons for this site are 1) As the present study required both upper and lower body exercise the ear lobe represents a relatively motionless site during both modes of exercise, thus reducing movement artefact (Barker and Shah, 1997; Kist *et al.*, 2002; Galy *et al.*, 2005); 2) Gripping of the handle bars, particularly during upper body exercise could interfere with blood flow to the fingers and reduce signal quality (Trivedi *et al.*, 1997).

The left earlobe was firstly cleaned with an alcohol wipe before being massaged with a vasodilating cream (Deep heat) to facilitate blood flow to the site and maintain signal quality. Any excess cream was removed prior to the placement of the ear sensor which was carefully placed so the LED was completely covered by the earlobe and that the skin pigmentation across the site was constant. The cable was then taped to the neck to further reduce and any movement artefact. If at any point during the trial the signal quality became compromised the sensor was removed, cleaned and the ear lobe massaged before being repositioned.

3.7 Expired gas analysis.

Expired gases were collected using the Douglas Bag method via polyvinyl tubing and a face mask. The face mask was attached tightly using a skull cap and adhesive sealant added to ensure an air tight seal so that inspired gas did not become contaminated with room air and that all expired gases were collected. Expired gases were analysed for fractions of O_2 and CO_2 (Servomex 1440, East Sussex, UK), volume (Harvard dry gas meter, Cranlea UK, Birmingham) and temperature (RS Supplies Thermocouple 206-3722, Corby, UK). Barometric pressure was measured using a mercury barometer (F. Darton and

Co Ltd, Watford, England). Oxygen and carbon dioxide samples were analysed over 1 and 2 minute periods, respectively. From this data $\dot{V}_{ESTPD}$, $\dot{V}O_2$, $\dot{V}CO_2$ and RER were calculated (APPENDIX C).

The Servomex 1440 gas analyser was calibrated using precision gases (BOC, Gilford, Surrey). O_2 and CO_2 used a 3 and 2 point calibration, respectively. The O_2 and CO_2 analysers were zeroed using nitrogen before being spanned with known gas concentrations. The O_2 analyser was spanned with the room air (FO_2 = 0.2093) during normoxic trials and precision gas (FO_2 = 0.15) during hypoxic trials. Finally a known concentration between zero and the spanned concentration was measured to ensure linearity (normoxic FO_2 = 0.15; hypoxic FO_2 = 0.12). The CO_2 analyser was spanned to FCO_2 = 0.05.

3.8 Bloods.

3.8.1 Blood lactate.

Blood samples (≈ 5 µl) where collected from the earlobe and analysed using a portable analyser (Lactate Pro, Arkray factory limited, Shiga, Japan) for blood lactate concentration between each exercise stage. This equipment displays blood lactate concentrations 60 s after sampling. The Lactate Pro measures blood lactate over a range of 0.8 – 23.3 mmol·L^{-1}, for statistical reasons when blood samples read *"Lo"* lactate was taken to be 0.5 mmol·L^{-1}. Lactate Pro function was checked prior to testing by ensuring the calibration strip measured within its defined range (2.1 – 2.6 mmol·L^{-1}). Blood samples were taken in duplicate and mean values used.

3.8.2 Lactate threshold.

Lactate threshold (LT) was identified using the Dmax method (Cheng *et al.* 1992; Fig. 3.7) by plotting blood lactate against $\dot{V}O_2$. In instances where LT could not be identified ventilation and/or ventilatory equivalent were plotted in place of lactate. No significant difference has been reported between these three methods of assessing LT in normoxic and hypoxic conditions (Thake, 2006).

When plotted and a trend line added (A) the first and last data points are joined with a linear line which represent the direction of change (B). A perpendicular line (C) joins lines A and B where their distance is greatest and the point were A and C join represents threshold (Fig. 3.7). The corresponding $\dot{V}O_2$ is then read from the x axis.

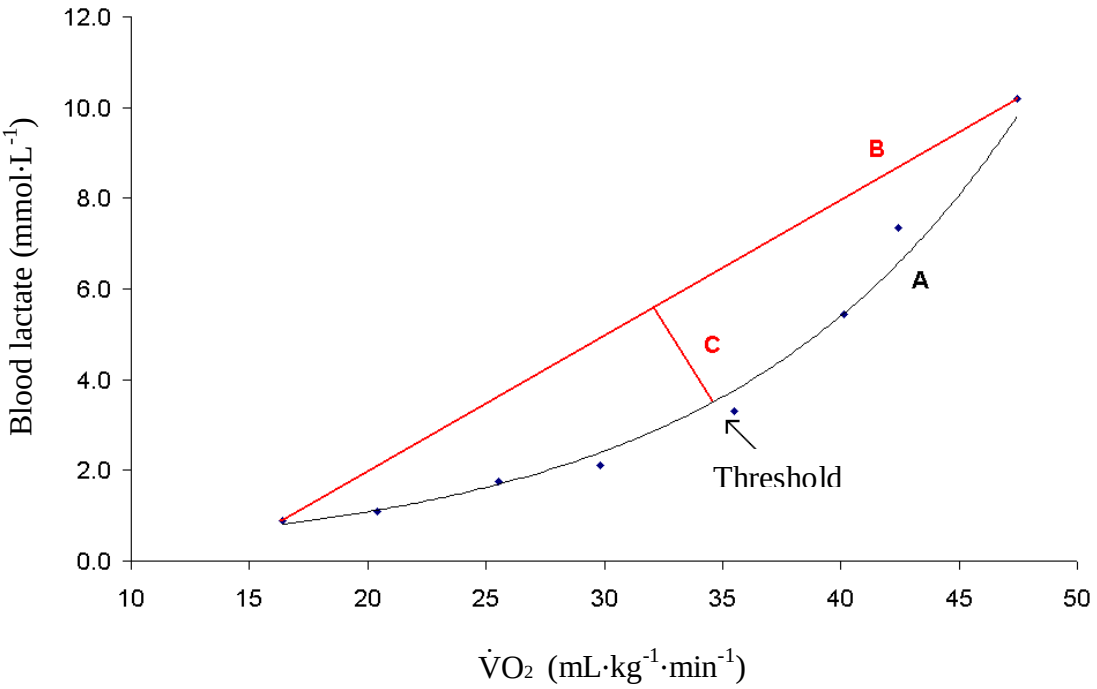

Fig. 3.7 *Example of Dmax method employed in the present study.*

3.8.3 Haemoglobin concentration.

During the 30 s recovery between stages a blood sample (≈ 20 -40 μL) was collected into an 80 μL heprinised capillary tube for the analysis of haemoglobin concentration. After being mixed in the capillary tube 10 μL of the blood was added to 2.5 mL of Drabkins reagent (cyanmethemoglobin). This was well mixed and left until the end of the trial at room temperature for analysis. A spectrophotometer (Cecil CE1010, Cecil instruments, Cambridge, England) set to 540 nm was zeroed using distilled water and used to read the absorbance. Haemoglobin concentration ($g \cdot dl^{-1}$) was then calculated by multiplying the absorbance reading by 37.66 (Boehringer Mannheim, Germany). Samples were measured in duplicate and the mean value recorded. Due to large intertrial variation a mean value of haemoglobin concentration at maximal exercise was calculated from end values of each trial and used in all trials (APPENDIX D).

3.9 Heart rate.

Heart rate (HR) was continuously monitored at rest and during exercise using a Polar heart rate monitor (Polar S120, Polar Electro Ltd, Finland) and a chest strap (Polar T31, Polar Electro Ltd, Finland). Heart rate was recorded at rest, 5 and 10 mins during the wash in period and an average HR calculated during each exercise stage from HR data collected every 15 s during the final minute of each stage.

3.10 RPE.

Participants were asked their central (cardiorespiratory stress) and local (either arms or legs depending on mode of exercise) RPE during each workload, 15 s prior to the collection of gas (Borg, 1970; APPENDIX E).

3.11 Estimation of cardiac output, oxygen delivery and extraction.

Stroke volume (SV) was estimated in the present study using the method of Bhambhani (1995) and as heart rate (HR) was continuously measured cardiac output ($\dot{Q}$) could be estimated. Oxygen pulse is the oxygen consumption per heart beat ($mL \cdot beat^{-1}$) and was used to estimate SV at lactate threshold using regression equations for LB and UB exercise at each F_IO_2 (equation 3.1). SV does not significantly alter after lactate threshold in LB and UB exercise (Sawka, 1986; Stringer *et al.*, 1997) and knowing maximal HR allows $\dot{Q}_{MAX}$ to be estimated. This method was developed during normoxic exercise and the present study has assumed that the same relationship is present upon acute exposure to hypoxia.

Equation 3.1 *LB – SV = 10.21* x *oxygen pulse – 1 (r = 0.76, P<0.01)*

UB – SV = 5.22 x *oxygen pulse + 53 (r = 0.85, P<0.01)*

Oxygen delivery ($\dot{D}O_2$) was calculated from $\dot{Q}$, and arterial O_2 content and extraction ratio (E) are calculated by dividing oxygen consumption by oxygen delivery. Arterial – mixed venous oxygen difference (a-$\bar{v}$ O_2Diff.) was calculated by rearranging the Fick equation (equation 3.5).

Equation 3.2 $\dot{D}O_2 = \dot{Q}$ x CaO_2

Were,

Equation 3.3 $CaO_2 = 1.34$ x $[Hb]$ x S_PO_2

Equation 3.4 $E = \dot{V}O_2 / \dot{D}O_2$

Equation 3.5 a-$\bar{v}$ O_2Diff. = $\dot{V}O_2 / \dot{Q}$

3.12 Data presentation and statistical analysis.

Data were analysed at maximal exercise and lactate threshold. Values referred to as 'peak' are those collected at volitional exhaustion (VEX). All data are presented as mean ± SD and significance was accepted at 5 % ($P < 0.05$). All participants completed all trial thus n = 9 for all data points. The two modes of exercise, lower and upper body will be referred to as LB and UB, respectively. The three experimental conditions will be referred to as N ($F_IO_2 \approx 0.21$), H_1 ($F_IO_2 \approx 0.15$) and H_2 ($F_IO_2 \approx 0.13$) in the text but as their oxygen fractions in tables and figures from this point. Differences were analysed between exercise modes within the same condition and between conditions within the same mode of exercise, where condition is inspired oxygen fraction.

Table 3.3 *Symbols used to identify level of significance on figures. LB vs. UB = within condition, N vs. H_1, N vs. H_2 and H_1 vs. H_2 = within exercise mode.*

	P<0.05	P<0.01	P<0.001
LB *vs.* UB	*	**	***
N *vs.* H_1	‡	‡‡	‡‡‡
N *vs.* H_2	σ	σσ	σσσ
H_1 *vs.* H_2	$	$$	$$$

Analysis of variance (ANOVA) general linear model was used to analyse main effects for exercise mode (LB and UB), condition (N, H_1 and H_2) and interaction (exercise x condition). Post hoc analysis was performed using Tukey pairwise comparisons. Correlation analysis was performed using Pearson's correlation coefficient. When viewing tables in Chapter 4 # = main effect for exercise, † = main effect for condition and Φ = interaction between exercise and condition (P<0.05). Table 3.3 displays the symbols used

to identify significance on figures within Chapter 4. All data were processed using Microsoft Excel (2003) and statistical analysis performed using Minitab statistical software release 15.0 (Minitab Inc.).

CHAPTER 4

RESULTS

4.0 Results.

4.1 Performance variables.

Peak power output (PPO) was reduced in both modes of exercise as F_IO_2 declined ($P<0.001$) and was highest during LB exercise in all conditions ($P<0.001$). A greater reduction in PPO as a consequence of reduced F_IO_2 was present during LB exercise ($P<0.01$). PPO was 273 ± 49 *vs.* 135 ± 27, 250 ± 37 *vs.* 127 ± 20 and 223 ± 28 *vs.* 123 ±18 W for LB *vs.* UB during N, H_1 and H_2, respectively. PPO at H_1 and H_2 were 23 ± 20 and 50 ± 26 W lower than N in LB exercise ($P<0.05$), although there was no difference between H_1 and H_2 ($P=0.053$). UB exercise showed PPO to fall by 8 ± 11 W from N to H_1 and by 12 ± 15 W between N and H_2 (NS).

Exercise duration was reduced in both modes of exercise as F_IO_2 decreased ($P<0.001$). Exercise duration (decimal time) was 27.11 ± 5.74 *vs.* 26.58 ± 6.61, 24.06 ± 4.21 *vs.* 24.53 ± 4.98 and 21.22 ± 3.31 *vs.* 23.56 ± 4.27 min for LB *vs.* UB for N, H_1 and H_2, respectively. As seen in PPO a reduction was present from N to H_1 ($P<0.05$) and H_2 (0.001) but there was no difference between H_1 and H_2 during LB exercise. In UB exercise, duration was reduced between N and H_2 ($P<0.05$) despite no difference in PPO between the two conditions.

4.2 Cardiorespiratory variables at $\dot{V}O_{2\ PEAK}$.

4.2.1 Ventilation.

Pulmonary ventilation ($\dot{V}_E$; Table 4.1) did not vary between F_IO_2, however $\dot{V}_E$ was higher during LB compared to UB exercise at each F_IO_2 ($P<0.001$). During N and H_2 $\dot{V}_E$ was 20.8 ± 10.6 and 17.0 ± 18.4 L higher during LB compared to UB exercise, respectively (N,

P<0.01 and H_2, P<0.05). A 15.9 ± 19.7 L difference between LB and UB exercise for H_1 was not significant (P=0.09).

4.2.2 Oxygen consumption.

Table 4.1 shows $\dot{V}O_{2\ PEAK}$ in absolute terms ($L \cdot min^{-1}$; Fig 4.1) and relative to body mass ($mL \cdot kg^{-1} \cdot min^{-1}$) and muscle mass ($mL \cdot kgMM^{-1} \cdot min^{-1}$). When viewed in absolute terms $\dot{V}O_{2\ PEAK}$ significantly declined as F_IO_2 decreased (P<0.001) and was greater during LB compared to UB exercise in all F_IO_2s (P<0.001). Reductions in $\dot{V}O_{2\ PEAK}$ were greater for LB exercise as F_IO_2 decreased (P<0.05). The same level of significance was present when relative to muscle mass however, when expressed relative to body mass interaction was not significant (P=0.07). LB exercise experienced reductions between each F_IO_2 (N *vs.* H_1 p<0.001; N *vs.* H_2 P<0.001 and H_1 *vs.* H_2 P<0.05), while during UB exercise the reduction between H_1 and H_2 was not significant (N *vs.* H_1 p<0.001 and N *vs.* H_2 P<0.001). When expressed relative to normoxic values, during LB exercise a 13 ± 8 and 24 ± 6 % reduction was evident when F_IO_2 decreased from N to H_1 and from N to H_2 (P=0.07), respectively. During UB exercise a 15 ± 7 and 19 ± 9 % reduction was observed from normoxic values for H_1 and H_2, respectively (Fig. 4.2.). During N, H_1 and H_2 $\dot{V}O_{2\ PEAK}$ was 28 ± 3, 29 ± 10 and 24 ± 8 % lower for UB *vs.* LB exercise, respectively.

4.2.3 Respiratory exchange ratio.

In both LB and UB exercise respiratory exchange ratio (RER) increased as F_IO_2 decreased (P<0.01) and RER was highest during UB exercise in all conditions (P<0.01). During LB exercise RER increased from 1.19 ± 0.04 to 1.21 ± 0.06 and 1.27 ±0.04, while UB exercise elicited an RER of 1.18 ± 0.08, 1.28 ± 0.10 and 1.34 ±0.11 for N to H_1 and H_2, respectively.

Table 4.1 *Respiratory variables at peak exercise (mean ± SD). # = main effect for exercise, P<0.05; † = main effect for condition, P<0.05; Φ = interaction between exercise and condition, P<0.05 and mL·kgMM^{-1}·min^{-1} = relative to muscle mass.*

		LB			UB		
F_IO_2		0.21	0.15	0.13	0.21	0.15	0.13
$\dot{V}_{ESTPD}$ (L·min^{-1})	#	116.6 ± 22.5	111.3 ± 23.9	109.1 ± 22.2	95.8 ± 22.2	95.4 ± 24.5	92.2 ± 19.8
$\dot{V}O_{2\ PEAK}$ (L·min^{-1})	# † Φ	3.52 ± 0.5	3.04 ± 0.46	2.68 ± 0.27	2.53 ± 0.35	2.15 ± 0.40	2.04 ± 0.34
$\dot{V}O_{2\ PEAK}$ (mL·kg^{-1}·min^{-1})	# †	45 ± 7	39 ± 6	34 ± 5	32 ± 6	28 ± 5	26 ± 4
$\dot{V}O_{2\ PEAK}$ (mL·kgMM^{-1}·min^{-1})	# † Φ	79 ± 7	68 ± 6	60 ± 5	57 ± 6	48 ± 6	46 ± 6
RER	# †	1.18 ± 0.04	1.21 ± 0.07	1.27 ± 0.04	1.21 ± 0.08	1.28 ± 0.10	1.34 ± 0.11
$\dot{V}_E / \dot{V}O_2$	# †	36.93 ± 5.65	40.64 ± 4.50	44.03 ± 5.59	42.45 ± 8.98	47.34 ± 9.84	50.75 ± 9.57
$\dot{V}_E / \dot{V}CO_2$	# †	31.28 ± 4.72	33.74 ± 4.55	34.49 ± 3.86	34.94 ± 6.56	36.70 ± 6.18	37.84 ± 5.68

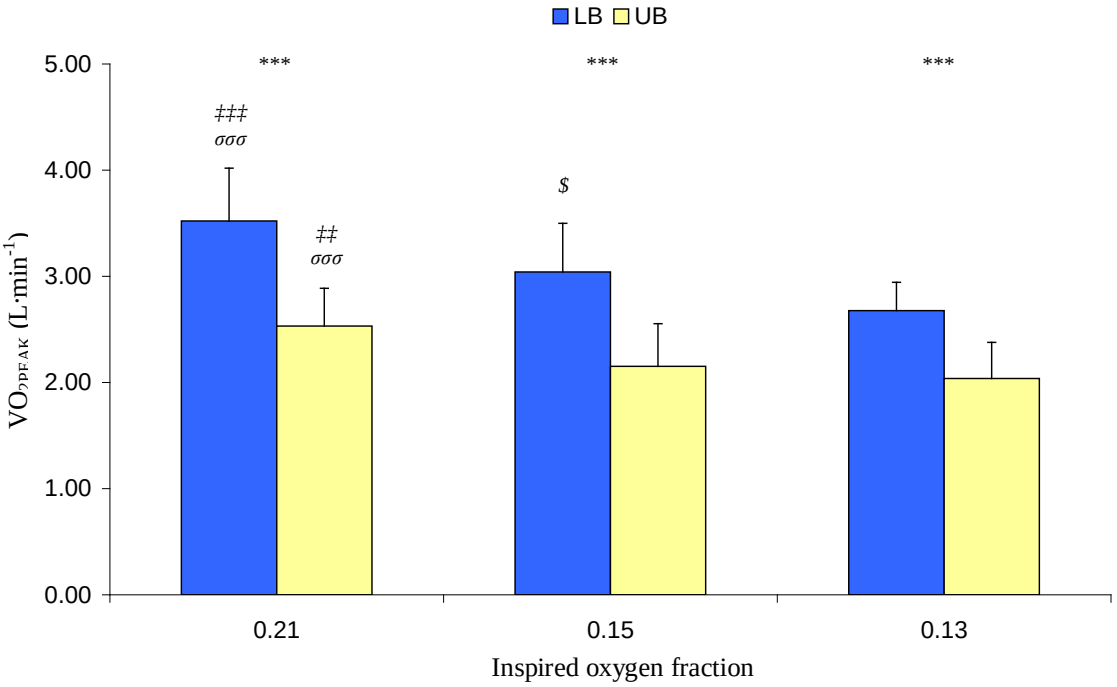

Fig 4.1 *$\dot{V}O_{2\ PEAK}$ (mean ± SD) during LB and UB exercise. LB vs. UB ***P<0.001; N vs. H_1 ‡‡P<0.01, ‡‡‡P<0.001; N vs. H_2 σσσP<0.001 and H_1 vs. H_2 $P<0.05.*

4.2.4 Ventilatory equivalent.

Ventilatory equivalent (Table 4.1) for O_2 ($\dot{V}_E/\dot{V}O_2$) and CO_2 ($\dot{V}_E/\dot{V}CO_2$) increased as F_IO_2 decreased during LB and UB exercise ($\dot{V}_E/\dot{V}O_2$ P<0.01 and $\dot{V}_E/\dot{V}CO_2$ P<0.05). $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ was highest during UB compared to LB exercise at all F_IO_2s (P<0.001). $\dot{V}_E/\dot{V}O_2$ increased significantly during LB and UB exercise between N and H_2 (LB = 36.93 ± 5.65 and 44.03 ± 5.59; UB = 42.45 ± 8.98 and 50.75 ± 9.57, respectively; P<0.05). Post hoc analysis for $\dot{V}_E/\dot{V}CO_2$ shows no difference between F_IO_2 within exercise mode or between exercise modes at a given F_IO_2.

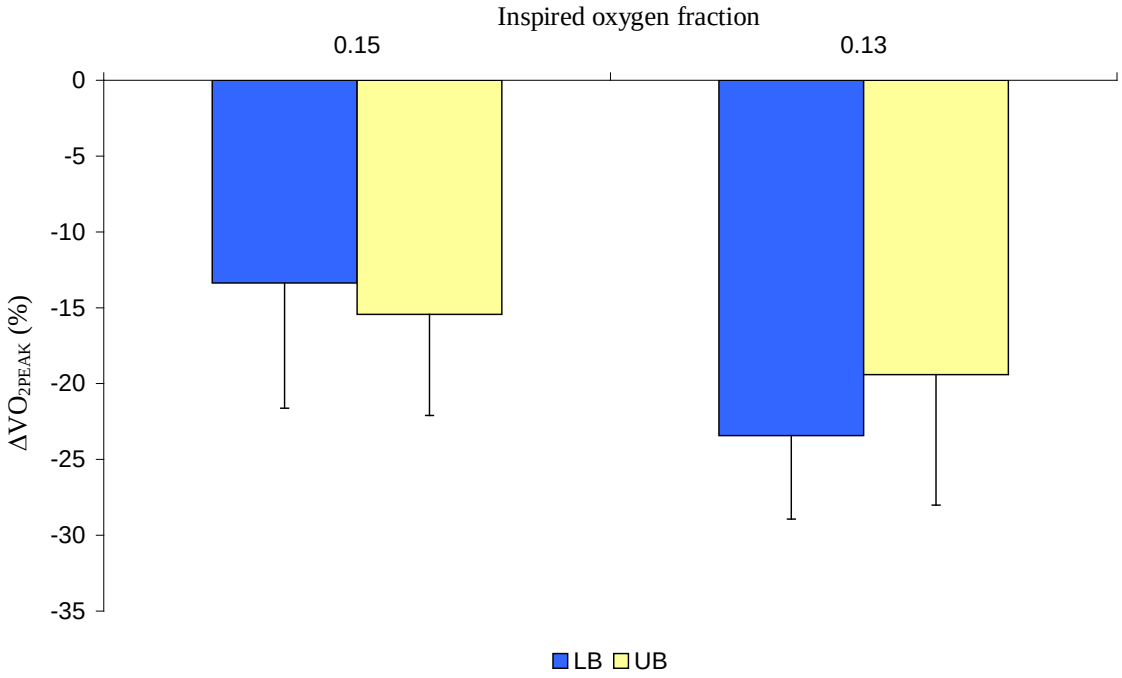

Fig 4.2 *Δ $\dot{V}O_{2\ PEAK}$ (mean ± SD) when expressed as a percentage of normoxic $\dot{V}O_{2\ PEAK}$ values. LB H_1 vs. H_2 P=0.07, UB H_1 vs. H_2 P>0.1.*

4.2.5 Stroke volume, heart rate and cardiac output.

Stroke volume (SV) decreased as F_IO_2 decreased (P<0.001) and was higher during LB compared to UB exercise at each F_IO_2 (P<0.001). During LB and UB exercise SV was significantly reduced during H_1 and H_2 compared to N (P<0.05) but there was no statistical difference between H_1 and H_2 (Table 4.4). HR (Fig. 4.3) declined as F_IO_2 was reduced (P<0.01) and was highest during LB exercise (P<0.001). At N and H_1 HR was higher during LB *vs.* UB exercise (189 ± 12 *vs.* 180 ± 12 bt·min^{-1}, P<0.01 and 188 ± 12 *vs.* 180 ± 13 bt·min^{-1}, P<0.05, respectively) no significant difference was present between LB and UB exercise during H_2 (183 ± 13 *vs.* 176 ± 14 bt·min^{-1}; P=0.07).

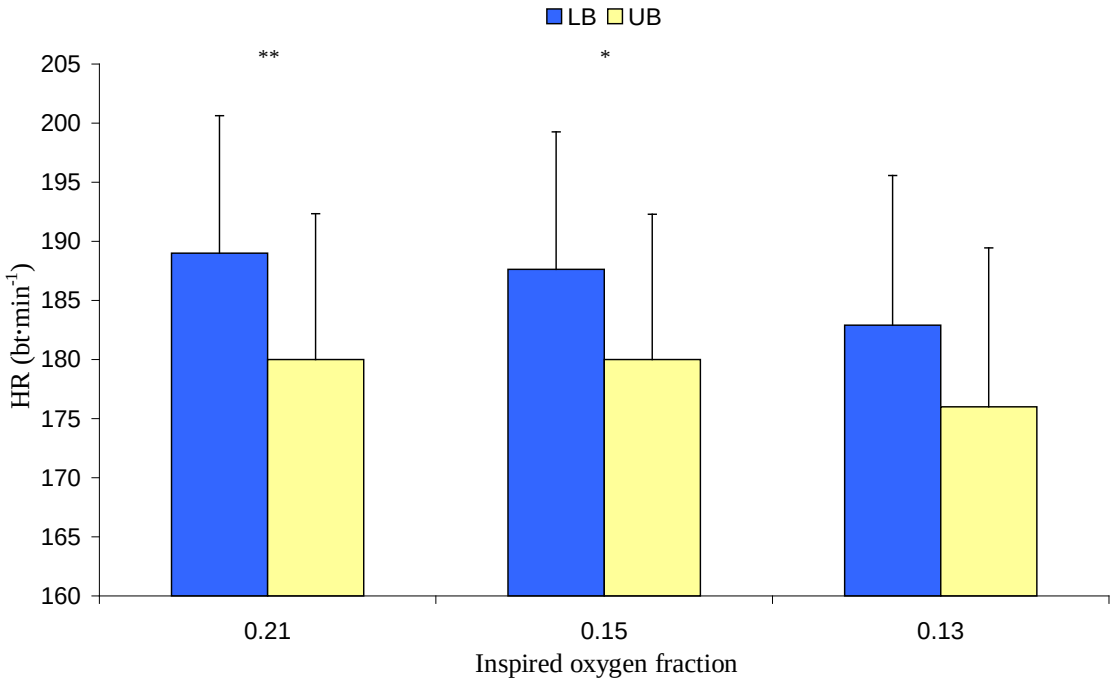

Fig. 4.3 *HR (mean ± SD) at peak exercise during LB and UB exercise. LB vs. UB **P<0.01 and *P<0.05.*

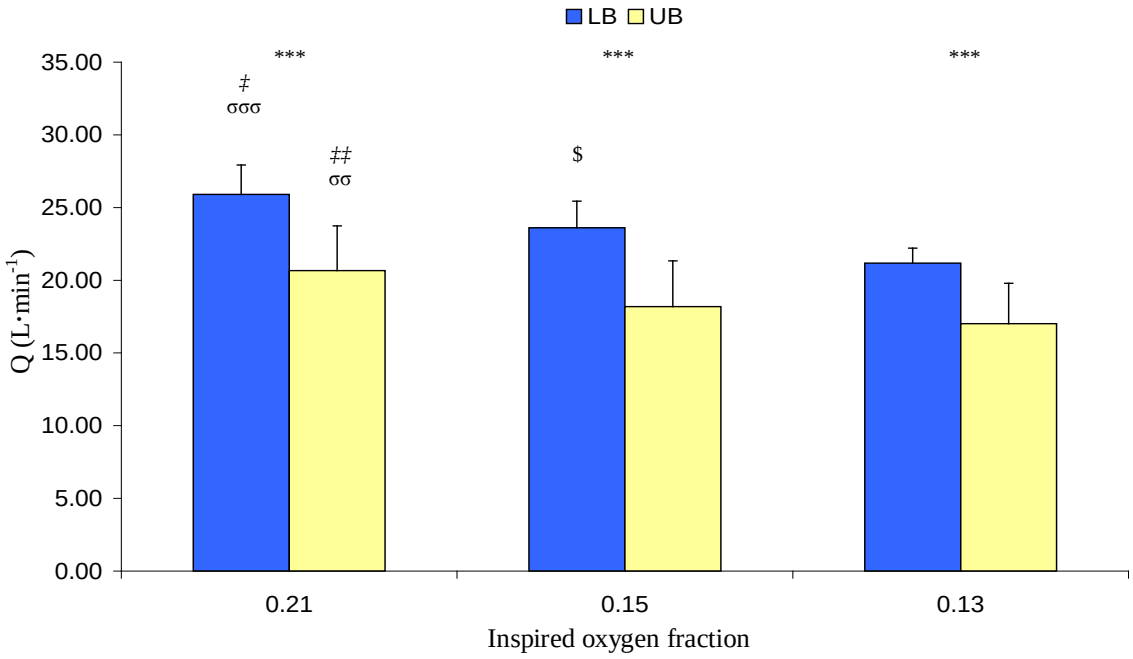

Fig. 4.4 $\dot{Q}$ *(mean ± SD) at peak exercise during LB and UB exercise. LB vs. UB ***P<0.001; N vs. H_1, ‡P<0.05 and ‡‡P<0.01; N vs. H_2 ^{σσ}P<0.01 and ^{σσσ}P<0.001 and H_1 vs. H_2 $^{\$}$P<0.05.*

$\dot{Q}$ (Fig 4.4) was reduced as F_IO_2 declined in both modes of exercise ($P<0.001$) and was higher during LB exercise at each F_IO_2 ($P<0.001$). At H_1 and H_2 $\dot{Q}$ was reduced by 9 ± 4 and 18 ± 4 % during LB exercise (N *vs.* H_1, $P<0.05$; N *vs.* H_2, $P<0.01$ H_1 *vs.* H_2, $P<0.05$) and by 12 ± 10 and 18 ± 9 % during UB exercise (N *vs.* H_1, $P<0.01$; N *vs.* H_2, $P<0.01$ H_1 *vs.* H_2, NS) when compared to N, respectively. $\dot{Q}$ was 21 ± 7, 23 ± 10 and 20 ± 10 % lower during UB compared to LB exercise for N, H_1 and H_2, respectively.

4.3 Haemodynamic variables at $\dot{V}O_{2\ PEAK}$ and lactate threshold (LT).

Blood lactate (BLa; Table 4.2) at maximal exercise showed no difference with F_IO_2 for either LB or UB exercise but was highest during LB exercise in all F_IO_2s ($P<0.01$). No difference was observed for BLa concentration at LT for both LB and UB exercise. BLa at LT tended to increase as F_IO_2 decreased from N to H_2 in both modes of exercise (NS).

The $\dot{V}O_2$ that elicited LT declined as F_IO_2 was reduced ($P<0.001$) and was highest during LB *vs.* UB exercise in all conditions (N= 32 ± 6 *vs.* 20 ± 4, H_1 = 29 ± 5 *vs.* 19 ± 3 and H_2 = 25 ± 4 *vs.* 18 ± 3 $mL \cdot kg \cdot min^{-1}$; $P<0.001$). During LB compared to UB exercise the $\dot{V}O_2$ at LT tended to decline by a greater amount ($P=0.54$). LT as a % $\dot{V}O_{2\ PEAK}$ increased as F_IO_2 decreased in both modes of exercise ($P<0.05$) and occurred at a greater % $\dot{V}O_{2\ PEAK}$ during LB exercise ($P<0.001$). During LB exercise $\dot{V}O_2$ at LT was reduced by 3 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$ from N to H_1 ($P<0.01$) and by 4 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$ between H_1 and H_2 ($P<0.05$). During UB exercise there was a 2 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$ reduction between N and H_1 (NS) and a further 3 ± 3 $mL \cdot kg^{-1} \cdot min^{-1}$ reduction between N and H_2 ($P<0.05$). When $\dot{V}O_2$ at LT was expressed as a percentage of $\dot{V}O_{2\ PEAK}$, LB LT was 8 ± 5 % higher than UB during N

($P<0.05$). All other significant differences observed in absolute terms were not present when LT is expressed relative to $\dot{V}O_{2\ PEAK}$ in each F_IO_2 (Table 4.2).

Table 4.2 *Peak blood lactate (BLa), blood lactate at LT, $\dot{V}O_2$ at LT and % $\dot{V}O_{2\ PEAK}$ at LT (mean ± SD). # = main effect for exercise, P<0.05; † = main effect for condition, P<0.05 and Φ = interaction between exercise and condition, P<0.05.*

		LB			UB		
F_IO_2		0.21	0.15	0.13	0.21	0.15	0.13
Peak BLa ($mmol \cdot L^{-1}$)	#	11.5 ± 2.4	12.3 ± 2.5	11.5 ± 2.4	10.8 ± 2.0	10.7 ± 1.7	10.6 ± 2.1
BLa @ LT ($mmol \cdot L^{-1}$)		4.7 ± 1.0	5.3 ± 1.2	5.4 ± 1.1	5.0 ± 0.6	5.0 ± 1.0	5.5 ± 1.1
$\dot{V}O_2$ ($mL \cdot kg^{-1} \cdot min^{-1}$) @ LT	# †	32 ± 6	29 ± 5	25 ± 4	20 ± 4	19 ± 3	18 ± 3
% $\dot{V}O_{2\ PEAK}$ @ LT	# †	71 ± 3	74 ± 6	73 ± 3	63 ± 9	67 ± 6	68 ± 6

Table 4.3 *Central and local RPE (mean ± SD) at peak exercise. # = main effect for exercise, P<0.05.*

		LB			UB		
F_IO_2		0.21	0.15	0.13	0.21	0.15	0.13
RPE – Central	#	18 ± 1	18 ± 2	17 ± 2	17 ± 2	17 ± 2	16 ± 2
RPE – Local		19 ± 1	19 ± 1	19 ± 0	19 ± 1	19 ± 1	19 ± 1

4.4 Oxygen delivery and the Fick equation.

Tables 4.4 and 4.5 present the components of the Fick equation and arterial oxygen saturation (SpO_2), respectively. SV was estimated using the method of Bhambhani (1995) according to O_2 pulse, where all other variables were directly measured or calculated from direct measurements (section 3.12). It can be seen from table 4.5 that reduced $\dot{V}O_{2\ PEAK}$ as F_IO_2 declines is accompanied with reductions in $\dot{Q}$, CaO_2 and $\dot{D}O_2$ while E increased ($P<0.05$, main effect). In addition $\dot{V}O_{2\ PEAK}$, $\dot{Q}$, a-$\bar{v}$ O_2Diff., CaO_2, $\dot{D}O_2$ and E were all highest during LB compared to UB exercise ($P<0.05$, main effect).

4.4.1 Arterial oxygen saturation.

Arterial oxygen saturation (S_PO_2) are presented as both lowest recorded in each trial (Lowest S_PO_2) and values at volitional exhaustion (S_PO_{2VEX}; Table 4.5). Lowest S_PO_2 values were lower in all conditions during LB exercise ($P<0.01$) and declined as F_IO_2 decreased during both modes of exercise ($P<0.001$). Reduction in S_PO_2 also occurred to a greater extent during LB exercise ($P<0.05$). During LB and UB exercise lowest S_PO_2 declined between N and H_1 (LB+UB, $P<0.001$) and between H_1 and H_2 (LB $P<0.001$; UB $P<0.01$). Arterial desaturation occurred to a lesser extent during UB compared to LB exercise at H_2 (73 ± 4 *vs.* 79 ± 4 %; $P<0.01$). S_PO_{2VEX} declined as F_IO_2 reduced in LB and UB exercise ($P<0.001$) and was lower during LB exercise in all conditions ($P<0.001$) however, interaction between exercise and condition was close to significance ($P=0.075$). As with lowest S_PO_2 only H_2 was significantly different as a result of exercise (LB *vs.* UB = 74 ± 6 *vs.* 82 ± 4 %; $P<0.01$). S_PO_{2VEX} during LB and UB exercise experienced a 13 ± 5 and 9 ± 5 % reduction when F_IO_2 reduced from N to H_1 (LB+UB $P<0.001$) and a 9 ± 4 and 6 ± 5 % reduction between H_1 and H_2,

respectively (LB P<0.001; UB P<0.01). Arterial desaturation was greatest during LB exercise in H_2, being significantly lower than all other trials (P<0.001).

4.4.2 Arterial oxygen content.

As the present study used a constant haemoglobin concentration (14.9 ± 0.1g·dL^{-1}; section 3.8.3) and the capacity for haemoglobin to transport oxygen is fixed (1.34 mLO_2·g^{-1}) the only factor able to alter CaO_2 is S_PO_2. For this reason the statistical significance mimics that observed for S_PO_2 at maximal exercise. CaO_2 (Table 4.4) was higher during UB exercise in all conditions (P<0.001) and reduces as a result of condition from N to H_1 and from H_1 to H_2 (P<0.001), whist interaction between exercise and F_IO_2 was not significant (P=0.075).

4.4.3 Oxygen delivery.

Oxygen delivery ($\dot{D}O_2$; Table 4.4) was reduced in both modes of exercise as F_IO_2 declined (P<0.001) and was higher during LB exercise during each condition (P<0.001). The observed reduction in $\dot{D}O_2$ tended to be greater during LB compared to UB exercise (P=0.064). During LB and UB exercise $\dot{D}O_2$ reduced from N to H_1 (LB = P<0.001; UB = P<0.001) and from H_1 to H_2 (LB = P<0.001; UB = P=0.68). LB exercise experienced 21 ± 6 and 37 ± 6 % reductions in $\dot{D}O_2$ during H_1 and H_2 compared to N, respectively. During H_1 and H_2 $\dot{D}O_2$ was reduced by 20 ± 12 and 30 ± 9 % when exercising the UB when compared to N (Fig. 4.5). $\dot{D}O_2$ was 20 ± 8, 18 ± 14 and 11 ± 14 % lower during UB exercise for N, H_1 and H_2 compared to LB exercise, respectively.

Table 4.4 *The Fick equation, arterial oxygen content (CaO_2), oxygen delivery ($\dot{D}O_2$) and extraction (E) at maximal exercise (mean ± SD). # = main effect for exercise, P<0.05; † = main effect for condition, P<0.05 and Φ = interaction between exercise and condition, P<0.05.*

Exercise	F_IO_2	$\dot{V}O_2$ (L·min^{-1})	=	HR (bt·min^{-1}) x SV (mL·beat^{-1})	x	a-$\bar{v}$ O_2Diff. (mL·dL^{-1})		CaO_2 (mL·dL^{-1})	$\dot{D}O_2$ (L·min^{-1})	E
		# † Φ		# †		#		# †	†	# †
	0.21	3.41 ± 0.58	=	(189 ± 12 x 137 ± 15)	x	13.54 ± 1.06		19.2 ± 1.0	4.98 ± 0.43	0.71 ± 0.07
LB	0.15	2.97 ± 0.48	=	(188 ± 12 x 126 ± 13)	x	12.83 ± 1.09		16.7 ± 1.3	3.94 ± 0.42	0.77 ± 0.06
	0.13	2.65 ± 0.26	=	(183 ± 13 x 116 ± 12)	x	12.61 ± 0.68		14.9 ± 1.3	3.15 ± 0.33	0.85 ± 0.09
	0.21	2.48 ± 0.38	=	(180 ± 13 x 115 ± 20)	x	12.29 ± 0.81		19.4 ± 0.8	4.01 ± 0.58	0.63 ± 0.04
UB	0.15	2.10 ± 0.41	=	(180 ± 13 x 102 ± 21)	x	11.83 ± 0.85		17.7 ± 1.4	3.23 ± 0.66	0.68 ± 0.08
	0.13	1.97 ± 0.38	=	(176 ± 14 x 97 ± 20)	x	12.01 ± 0.87		16.4 ± 1.0	2.78 ± 0.45	0.73 ± 0.06

Table 4.5 *Lowest arterial oxygen saturation recorded in each trial (Lowest S_PO_2) and volitional exhaustion (S_PO_{2VEX}; mean ± SD). # = main effect for exercise, P<0.05; † = main effect for condition, P<0.05 and Φ = interaction between exercise and condition, P<0.05.*

		LB			UB		
F_IO_2		0.21	0.15	0.13	0.21	0.15	0.13
Lowest SpO_2 (%)	#, †, Φ	96 ± 2	83 ± 4	73 ± 4	96 ± 2	85 ± 5	79 ± 4
SpO_{2VEX} (%)	#, †	96 ± 2	83 ± 4	74 ± 6	97 ± 1	88 ± 5	82 ± 4

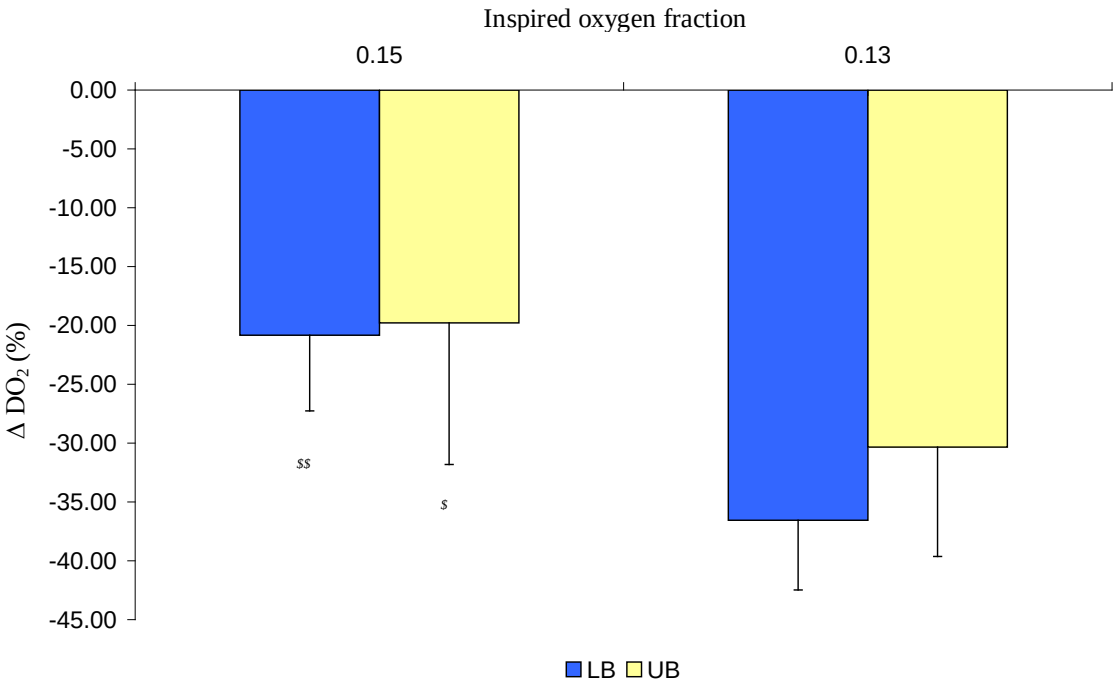

Fig 4.5 *Reduction in oxygen delivery (mean ± SD) during hypoxic exercise relative to normoxic values. H1 vs. H_2 $^{\$}P<0.05$, $^{\$\$}P<0.01$.*

4.4.4 Arterial – mixed venous oxygen difference and extraction.

Arterial – mixed venous oxygen difference (a-$\bar{v}$ O_2Diff.; Table 4.4) was higher during LB exercise compared to the UB ($P<0.001$), and tended to decrease as F_IO_2 was reduced ($P=0.062$). During LB exercise a-$\bar{v}$ O_2Diff. decreased from 13.54 ± 1.06 mL·dL^{-1} during N to 12.83 ± 1.09 and 12.61 ± 0.68 mL·dL^{-1} for H_1 and H_2, respectively. UB exercise resulted in a-$\bar{v}$ O_2Diff. decreasing between N and H_1 from 12.29 ± 0.81 to 11.83 ± 0.85 mL·dL^{-1} before increasing to 12.01 ± 0.87 mL·dL^{-1} during H_2.

Extraction (E; Table 4.4) increased as F_IO_2 decreased in both modes of exercise ($P<0.001$) and E was highest during LB exercise ($P<0.001$). At N, H_1 and H_2 E was 10 ± 10 (NS), 12 ± 12 ($P<0.05$) and 13 ± 11 ($P<0.01$) % lower during UB compared to LB exercise, respectively.

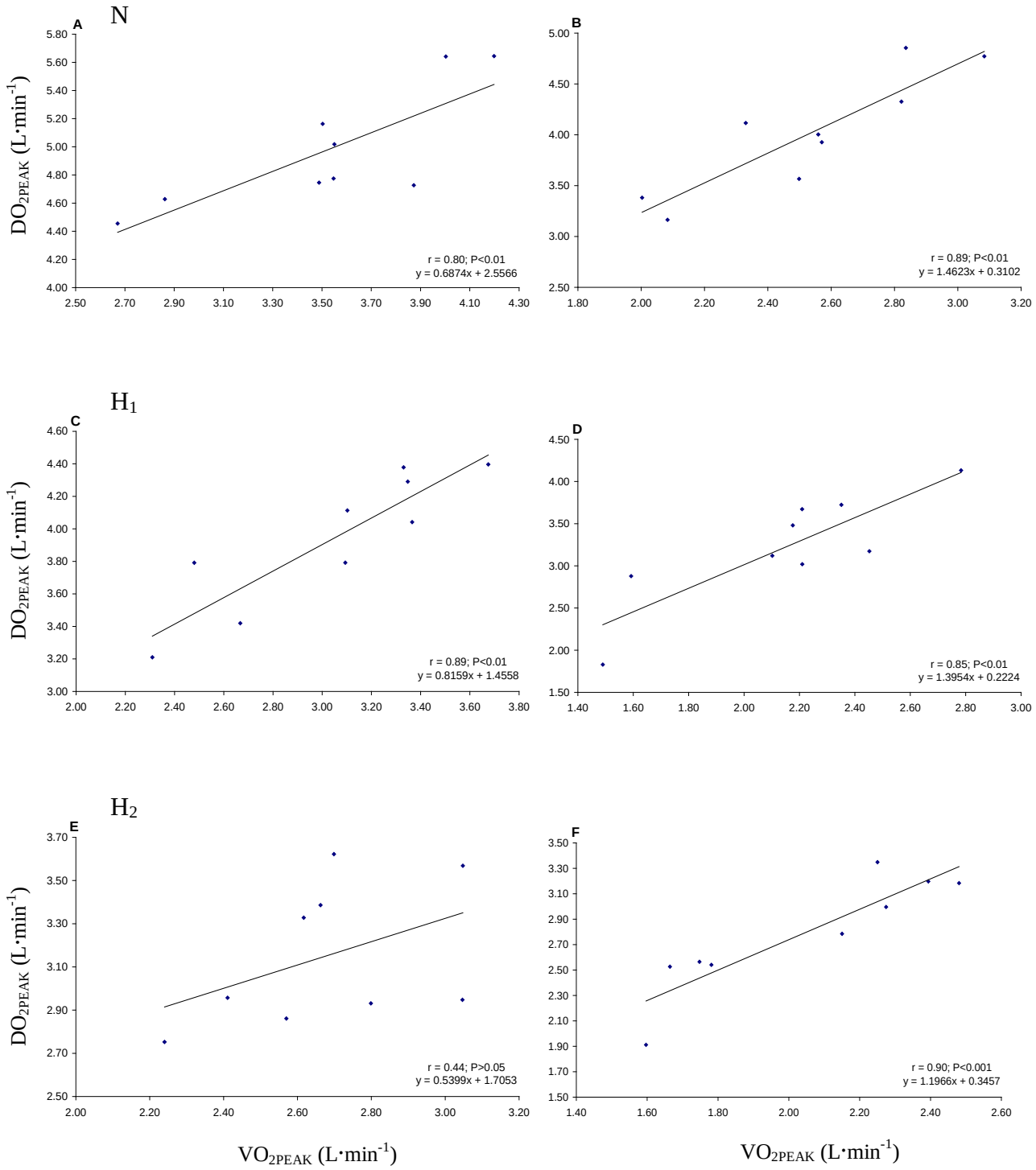

Fig. 4.6 *Correlation between oxygen delivery ($\dot{D}O_2$) and oxygen consumption ($\dot{V}O_2$) at maximal exercise (Individual subject data, n = 9). A = LB 0.21, r = 0.80, P<0.01, B = UB 0.21, r = 0.89, P<0.01; C = LB 0.15, r = 0.89, P<0.01; D = UB 0.15, r = 0.85, P<0.01; E = LB 0.13, r = 0.44, P>0.05; F = UB 0.13, r = 0.90, P<0.001.*

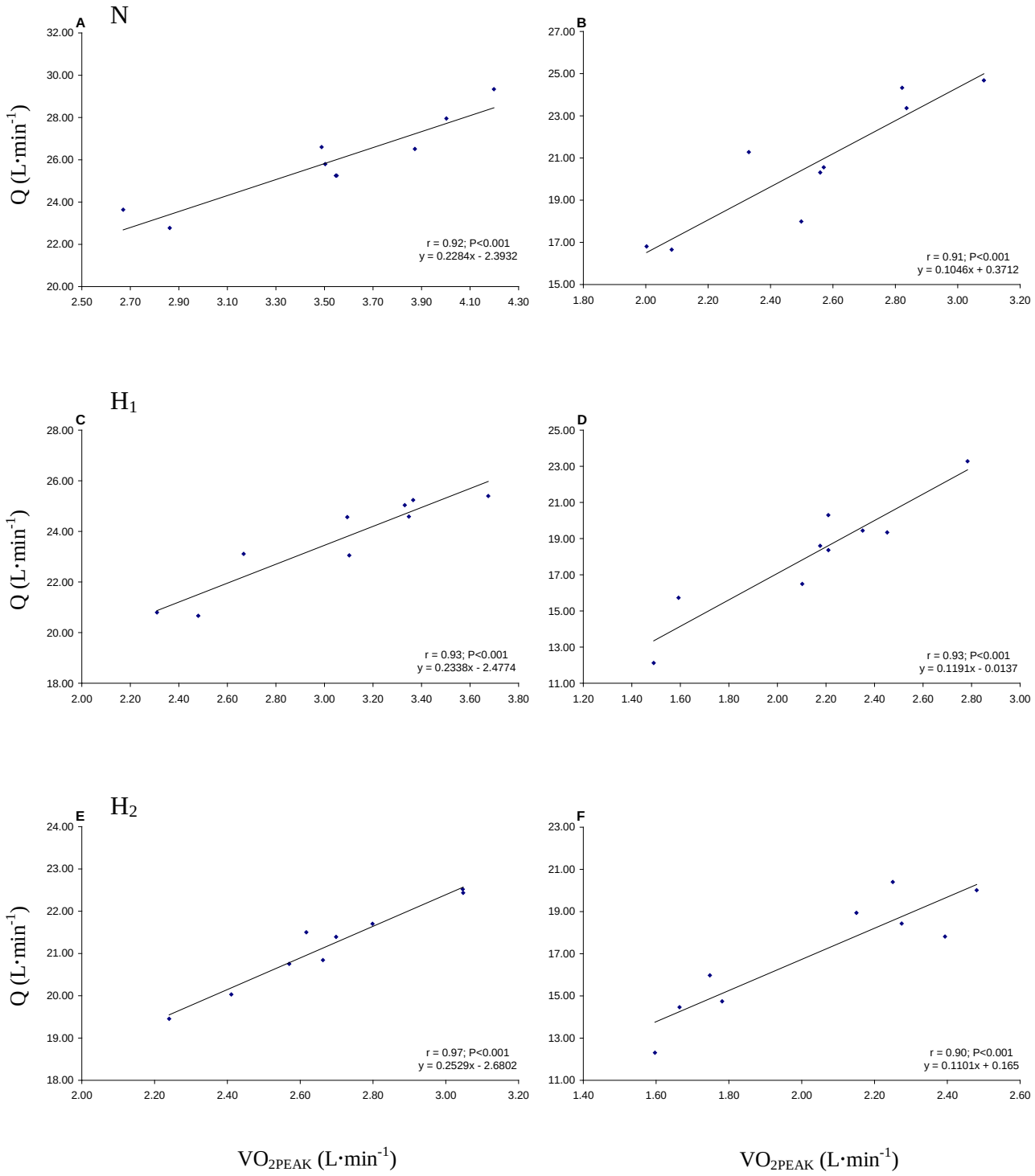

Fig. 4.7 *Correlation between cardiac output ($\dot{Q}$) and oxygen consumption ($\dot{V}O_2$) at maximal exercise (Individual subject data, n = 9). A = LB 0.21, r = 0.92, P<0.001, B = UB 0.21, r = 0.91, P<0.001; C = LB 0.15, r = 0.93, P<0.001; D = UB 0.15, r = 0.93, P<0.001; E = LB 0.13, r = 0.97, P<0.001; F = UB 0.13, r = 0.90, P<0.001.*

4.5 Oxygen delivery and cardiac output vs. oxygen consumption.

Fig 4.8 and 4.9 show the correlation between $\dot{D}O_2$, $\dot{Q}$ and $\dot{V}O_2$ at peak exercise in each experimental condition, respectively. Significant positive correlations were present for $\dot{D}O_2$ *vs.* $\dot{V}O_2$ ($r = 0.86$, $P<0.001$; $n = 54$) and for $\dot{Q}$ *vs.* $\dot{V}O_2$ ($r = 0.95$, $P<0.001$; $n = 54$). Correlations were stronger for $\dot{Q}$ compared to $\dot{D}O_2$ during each experimental condition.

4.6 Aerobic power and severity of exposure to acute hypoxia.

When $\dot{V}O_{2\ PEAK}$ was plotted against reduction in $\dot{V}O_{2\ PEAK}$ a negative correlation was present in all conditions (Fig. 4.8). Correlations tended to be stronger during LB exercise and in both LB and UB exercise the strongest correlations were seen during H_2, $r = 0.73$ ($P<0.05$) and 0.56 (NS), respectively. H_1 resulted in correlations between $\dot{V}O_{2\ PEAK}$ and reduction in $\dot{V}O_{2\ PEAK}$ of $r = 0.54$ and 0.21 (NS) for LB and UB, respectively. When $\dot{V}O_{2\ PEAK}$ is expressed relative to muscle mass then $r = 0.62$ ($P=0.07$), 0.73 ($P<0.05$), 0.36 (NS) and 0.41 (NS) for LB H_1, LB H_2, UB H_1 and UB H_2, respectively.

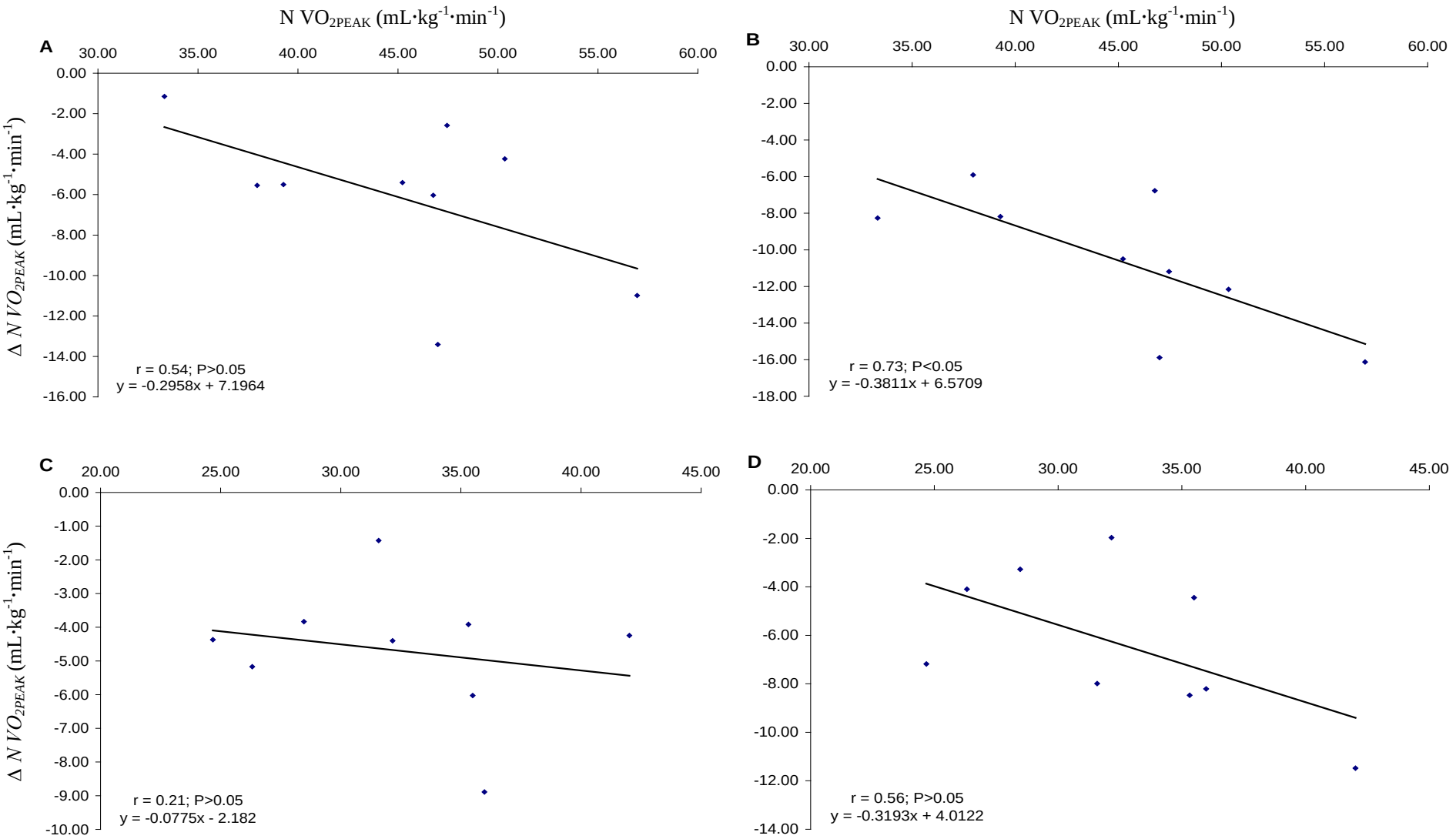

Fig 4.8 *Relationship between aerobic fitness and the Δ from normoxic* $\dot{V}O_{2\ PEAK}$ *during hypoxic exercise (individual subject data, n = 9). A = LB* H_1*, r = 0.54 (NS); B = LB* H_2*, r = 0.73, P<0.05; C = UB* H_1*, r = 0.21 (NS); D = UB* H_2*, r = 0.56(NS).*

4.7 Rating of perceived exertion.

Central and local rating of perceived exertion (RPE; Table 4.3) did not vary between F_IO_2. Central RPE was highest during LB exercise in all conditions ($P<0.01$), while local RPE did not differ between LB and UB exercise. ΔRPE (central RPE – local RPE) was higher in UB exercise ($P<0.001$). For N, H_1 and H_2 ΔRPE (Fig. 4.9) was 1 ± 2, 1 ± 1 and 2 ± 2 for LB exercise and 3 ± 2, 3 ± 2 and 3 ± 2 during UB exercise, respectively.

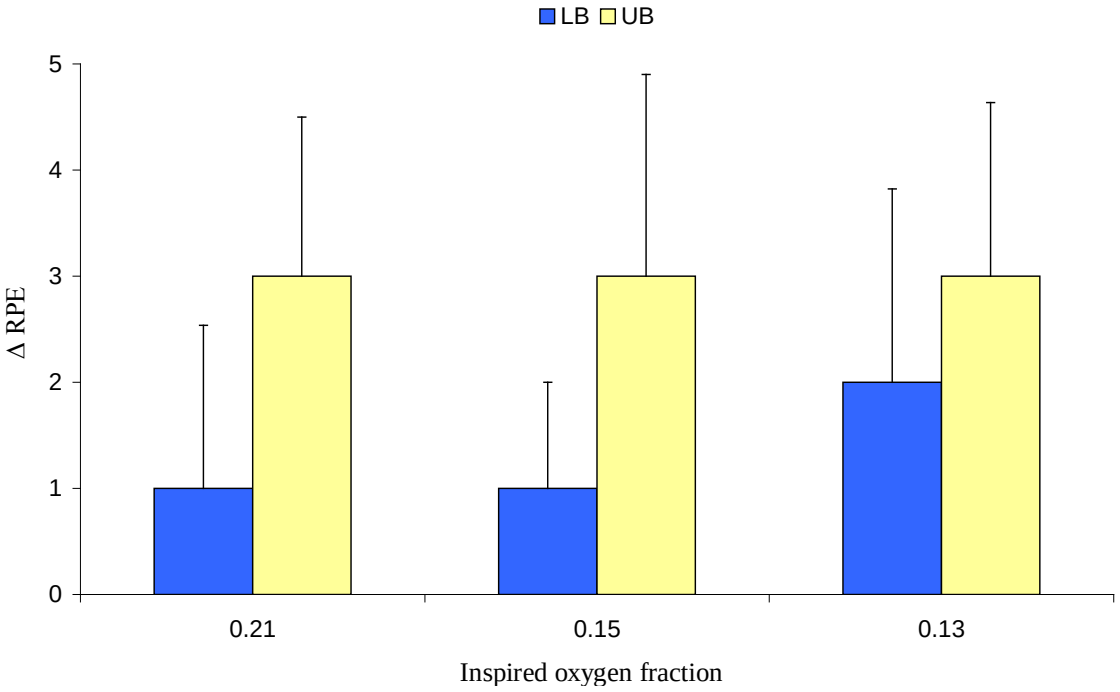

Fig. 4.9 *ΔRPE at peak exercise during LB and UB exercise (mean ± SD). LB vs. UB for H_2 P=0.087.*

4.8 Results summary.

Peak power output declined as F_IO_2 was reduced during LB and UB exercise but this reduction was greater during LB exercise. Ventilation was highest during LB compared to UB exercise but no difference was observed as F_IO_2 was reduced. The present study has shown that $\dot{V}O_{2\ PEAK}$ decreased from N to H_1 in LB and UB exercise and from H_1 to H_2 in LB exercise. RER increased as F_IO_2 decreased in both modes of exercise and was

highest while exercising the UB. HR and $\dot{Q}$ were highest during LB exercise for N and H_1 but no difference was apparent for H_2 and $\dot{Q}$ was higher in N compared to H_2 in LB exercise.

BLa concentration was highest during LB exercise at volitional exhaustion, while at LT there was no difference in BLa concentration for exercise or condition. $\dot{V}O_2$ at LT decreased between N and H_1 and from H_1 to H_2 during LB exercise. During UB exercise $\dot{V}O_2$ at LT decreased between N and H_2. When expressed as a % of $\dot{V}O_{2\ PEAK}$ LT was higher during LB exercise during N.

During LB and UB exercise S_PO_{2VEX} decreased from N to H_1, however a further decrease between H_1 and H_2 only occurred during LB exercise. $\dot{D}O_2$ decreased as F_IO_2 declined in both modes of exercise but there were no differences in $\dot{D}O_2$ between LB and UB exercise at any F_IO_2. CaO_2 mimics that that of S_PO_{2VEX}. Extraction was highest during LB exercise at each F_IO_2. As F_IO_2 decreased a-$\bar{v}$ O_2Diff. was reduced in both modes of exercise, however it reduced to a greater extent during LB exercise. Participants RPE was higher locally (i.e. arms or legs) than centrally during LB and UB exercise and this ΔRPE tended to be greater during UB exercise (NS).

Significant correlations were present between $\dot{D}O_2$, $\dot{Q}$ and $\dot{V}O_2$ at maximal exercise during LB and UB exercise for N, H_1 and H_2 (F_IO_2 = 0.21, 0.15 and 0.13, respectively). At H_2 during LB exercise participants with the greatest $\dot{V}O_{2\ PEAK}$ during N experienced the greatest reduction in aerobic power.

CHAPTER 5

DISCUSSION

5.0 Discussion.

The present study shows that $\dot{V}O_{2\ PEAK}$ is reduced when an individual is acutely exposed to normobaric hypoxia when compared to normoxia during both LB and UB exercise. This supports the tendency observed by others who suggested the reduced $\dot{V}O_{2\ PEAK}$ as F_IO_2 declined during UB exercise to be indicative of central limitation (Hopman *et al.*, 2003; 2004). The present study demonstrated that $\dot{V}O_{2\ PEAK}$ declined by 13 ± 8 and 23 ± 6 % during LB exercise and 15 ± 7 and 19 ± 9 % during UB exercise for H_1 and H_2, respectively. Evidence is presented for different mechanisms limiting aerobic power in the two modes of exercise. The Fick equation states that $\dot{V}O_2$ is dependent on the delivery of O_2 to the active tissue ($\dot{D}O_2$) and the ability of that tissue to extract that O_2 (E). The present study shows that during LB exercise $\dot{V}O_{2\ PEAK}$ is predominately limited centrally by $\dot{D}O_2$ whilst during UB exercise peripheral factors (E) predominately limit aerobic power (Fig. 5.1).

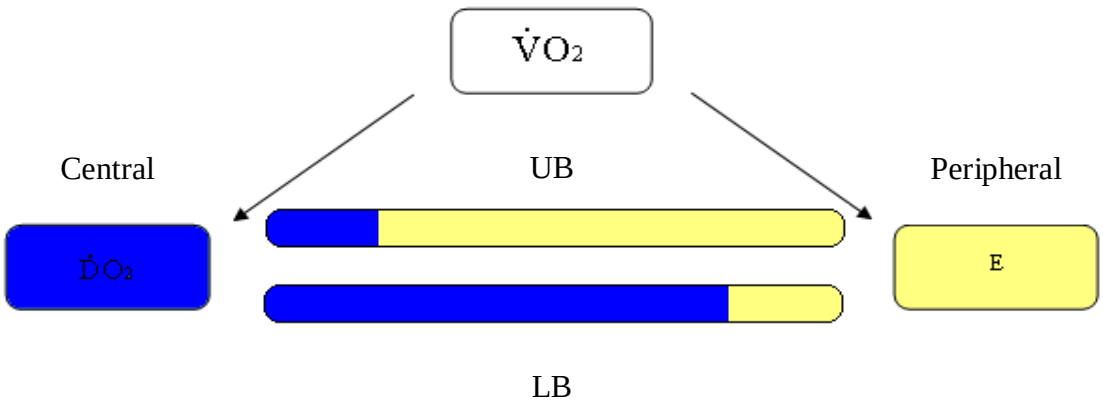

Fig 5.1 *Adapted Fick equation and the prominence of central vs. peripheral limitation to aerobic power during LB and UB exercise.*

5.1 Oxygen consumption.

Sawka (1986) reported UB $\dot{V}O_{2\ PEAK}$ to be 60-80 % of that attained during LB exercise which is in agreement with the present study where UB $\dot{V}O_{2\ PEAK}$ was 72 ± 3 % compared to LB exercise during N. The present study is the first to show that the relationship between UB and LB $\dot{V}O_{2\ PEAK}$ remains evident in H where UB $\dot{V}O_{2\ PEAK}$ was 71 ± 10 and 76 ± 8 % of that attained for LB exercise during H_1 and H_2, respectively. Although the absolute $\Delta\ \dot{V}O_{2\ PEAK}$ was greater during LB exercise with reduced F_IO_2 (Fig. 4.1) the relative $\Delta\ \dot{V}O_{2\ PEAK}$ was similar for LB and UB exercise (Fig. 4.2) hence the relationship between LB and UB exercise holds true at simulated altitude. Peak power output (PPO) attained during UB exercise was 50 ± 6, 49 ± 5 and 45 ± 3 % of that attained during LB exercise for N, H_1 and H_2 respectively. PPO is reduced by a greater relative amount than $\dot{V}O_{2\ PEAK}$ indicating reduced mechanical efficiency during UB compared to LB exercise. These findings are in agreement with previous authors when using sedentary participants with little experience of UB exercise (Sawka, 1986; Bhambhani *et al.*, 1998; Schneider *et al.*, 2002; Mukari, 2002; Mukari *et al.*, 2004). However, participants with highly trained UB musculature may elicit PPO and $\dot{V}O_{2\ PEAK}$ during UB exercise similar to that during LB exercise (Angermann *et al.*, 2006; Table 2.4).

The $\Delta\ \dot{V}O_{2\ PEAK}$ when acutely exposed to hypoxia during LB exercise is in agreement with a range of F_IO_2s previously reported (Ekblom *et al.*, 1975; Ferretti *et al.*, 1997; Cardus *et al.*, 1998; Peltonen *et al.*, 2001a; Mollard *et al.*, 2007; Table 2.3). In the present study during LB exercise as F_IO_2 was reduced aerobic power declined ($\Delta\ \dot{V}O_{2\ PEAK}$ = 13 ± 8 and 23 ± 6 % for H_1 and H_2, respectively) though the magnitude of the reduction was greater than previously reported in sedentary participants when

F_IO_2 = 0.13. Investigating the effect of hypoxia (F_IO_2 = 0.13) on $\dot{V}O_{2\ PEAK}$ in trained (Normoxic $\dot{V}O_{2\ PEAK}$ = 67.2 ± 4.0 mL·kg^{-1}·min^{-1}) and untrained (Normoxic $\dot{V}O_{2\ PEAK}$ = 45.4 ± 5.5 mL·kg^{-1}·min^{-1}) participants Martin and O'Kroy (1993) reported $\Delta\ \dot{V}O_{2\ PEAK}$ of 26.2 ± 2.3 and 14.9 ± 5.1 %, respectively in hypoxia. Similar findings were observed by Lawler *et al.* (1988) using F_IO_2 = 0.14 in trained and untrained participants. The present study used untrained participants ($\dot{V}O_{2\ PEAK}$ = 45 ± 7 mL·kg^{-1}·min^{-1}) similar to those used in the above study however, the $\Delta\ \dot{V}O_{2\ PEAK}$ was higher in the present study and similar to the trained participants. In the untrained participants Martin and O'Kroy (1993; F_IO_2 = 0.13) reported higher HR and S_PO_2 at maximal exercise when compared to the present study (189 ± 4 *vs.* 183 ± 13 bt·min^{-1} and 78 ± 9 *vs.* 74 ± 6 % at the same simulated altitude, respectively). In addition Martin and O'Kroy (1993) reported higher $\dot{V}_E/\dot{V}O_2$ during hypoxic exercise than the present study (55.1 ± 5.4 *vs.* 44.0 ± 5.6) indicating greater hyperventilation at maximal exercise which has been shown to reduce arterial desaturation, all of which are beneficial in maintaining $\dot{V}O_{2\ PEAK}$ (Gavin *et al.*, 1998).

Reduced $\dot{V}O_{2\ PEAK}$ during acute normobaric hypoxia in the present study supports the tendency observed by Hopman *et al.* (2003; 2004) in able bodied participants. They reported that $\dot{V}O_{2\ PEAK}$ was reduced significantly from hyperoxia (F_IO_2 = 0.5) to hypoxia (F_IO_2 = 0.15) but did not vary between normoxia and hypoxia. They suggested that $\dot{V}O_{2\ PEAK}$ during UB exercise is limited centrally by oxygen supply but only reported a 3 % reduction in $\dot{V}O_{2\ PEAK}$ between normoxia and hypoxia compared to 13 ± 8 % in the present study at the same simulated altitude (F_IO_2 = 0.15). Hopman *et al.*'s (2003; 2004) participants (n = 10) were of similar age, mass, stature and UB $\dot{V}O_{2\ PEAK}$ in normoxia as the present study but used a continuous ramp protocol compared to the

discontinuous step protocol in the present study. If the exercise increments were smaller in the present study then participants may have been able to progress further; however, secondary data indicate that maximal effort was attained in each trial in the present investigation. Although Hopman and colleagues (2003; 2004) reported the $\dot{V}O_{2\ PEAK}$ to be limited centrally the mechanism were not explored as S_PO_2, CaO_2 or $\dot{D}O_2$ were not reported and it is therefore difficult to identify why the present results differ from those reported by Hopman *et al.* (2003; 2004).

Previous papers have reported that those with a greater $\dot{V}O_{2\ PEAK}$ during normoxia experience greater reduction in aerobic power when exposed to simulated altitude (Lawler *et al.*, 1988; Martin and O'Kroy, 1993; Mollard *et al.*, 2007). When the reduced aerobic power is expressed relative to normoxic $\dot{V}O_{2\ PEAK}$ Mollard *et al.* (2007) observed no difference between trained and untrained while others observed greater reductions in aerobic power in trained athletes (Lawler *et al.*, 1988; Martin and O'Kroy, 1993). In H_2 $\Delta\dot{V}O_{2\ PEAK}$ was correlated with normoxic $\dot{V}O_{2\ PEAK}$ during LB exercise ($r = 0.73$, $P<0.05$; Fig. 4.8) as was reported previously when using F_IO_2s of 0.14 ($r = 0.94$, $P<0.05$) and 0.13 ($r = -0.91$, $P<0.01$; Lawler *et al.*, 1988; Martin and O'Kroy, 1993, respectively) but were not significantly correlated during H_1. The present study only used sedentary participants while the above mentioned studies had a greater number of participants and compared both sedentary and aerobically trained individuals thus had data across a greater physiological range which may have added to the strength of their correlations. During UB exercise weak correlations ($r = 0.21$ and $r = 0.56$, $P>0.05$ for H_1 and H_2, respectively) were present for normoxic $\dot{V}O_{2\ PEAK}$ *vs.* $\Delta\dot{V}O_{2\ PEAK}$ indicating that in sedentary participants normoxic $\dot{V}O_{2\ PEAK}$ is not an indication of $\Delta\dot{V}O_{2\ PEAK}$

however the addition of data from UB trained individuals may increase the strength of these correlations.

5.2 Ventilation.

$\dot{V}_E$ was higher during LB exercise at each F_IO_2. $\dot{V}_E$ has been reported≈ 20 % lower during normoxic UB exercise in men and women (Bhambhani *et al.,* 1998; Mukari *et al.,* 2004; Angermann *et al.,* 2006). Angermann and colleagues (2006) reported $\dot{V}_E$ to be 21.1 and 14.9 % lower during UB compared to LB exercise in N and H (F_IO_2 = 0.146), respectively. This is in agreement with those reported in the present study (N = 18 ± 9, H_1 = 14 ± 17 and H_2 = 15 ± 17 % lower during UB exercise). UB exercise should not be viewed solely as arm exercise, especially at higher workloads as movement of the torso increases to aid performance. Muscles that usually assist ventilation may be recruited to aid locomotion during UB exercise, therefore reducing the musculature recruited for ventilation itself. However, when restraints were used during UB exercise in an attempt to reduce torso movement $\dot{V}_E$ was 18 % lower than LB exercise (Boileau *et al.,* 1984) suggesting that torso movement does not impede recruitment for ventilation or that other mechanisms are responsible. $\dot{V}_E$ requires a pressure gradient between the lung and the environment; if this gradient was altered it could subsequently affect tidal volume (V_t). Increased intrathoracic pressure during UB exercise has been reported previously with regards its effect on SV (Sawka, 1986), however it may reduce the pressure gradient between lung and environment in turn impeding the flow of gas and reducing V_t.

In the present study $\dot{V}_E$ was unchanged as F_IO_2 was reduced, however $\dot{V}_E$ tended to decrease as F_IO_2 declines. It is generally seen that $\dot{V}_E$ is unchanged (Martin and O'Kroy, 1993; Zattara-Hartmann and Jammes, 1996) or increased (Lawler *et al.,* 1988;

Gavin *et al.,* 1998; Ogawa *et al.,* 2007) when acutely exposed to hypoxia, however the ventilatory response is also associated with training status and hypoxic ventilatory response (HVR), which itself has a great deal of individual variability. Lawler *et al.* (1988) found that $\dot{V}_E$ at maximal exercise increased significantly during hypoxic exercise in untrained males (123.0 ± 3.6 *vs.* 150.9 ± 7.3 $L \cdot min^{-1}$), whereas trained participants maximal $\dot{V}_E$ was unchanged (147.4 ± 6.2 *vs.* 149.4 ± 6.8 $L \cdot min^{-1}$). Exercising at a higher simulated altitude than Lawler *et al.* (1988; F_IO_2 = 0.13 *vs.* 0.14) Martin and O'Kroy (1993) found that maximal $\dot{V}_E$ was not significantly different between normoxic and hypoxic exercise in trained and untrained participants.

During maximal exercise 10-15% of $\dot{Q}$ is directed to the respiratory muscles for ventilation (Harms *et al.*, 1998). If it is assumed that the same occurs during acute hypoxia the reduced $\dot{V}_E$ as F_IO_2 declines could be a result of reduced CaO_2 and therefore oxygen delivery to the respiratory muscles at maximal exercise. In addition the hyperventilatory response to hypoxic exercise may reduce the CO_2 concentrations in the blood (Hypocapnia) in turn blunting the drive to ventilate (Ward *et al.,* 2000). This possibility is supported by ventilatory equivalent for CO_2 which increases as F_IO_2 decreases. Diaphragmatic fatigue in resting humans results in increased vascular resistance in the limbs as blood flow is directed to the diaphragm, this reflex may also be present during intense exercise (Dempsey *et al.,* 2006). The greater $\dot{V}_E$ observed during LB compared to UB exercise may have induced greater diaphragmatic fatigue therefore increasing the blood flow to the diaphragm and increased vascular resistance at the exercising muscle. This may contribute to the greater reductions in performance and $\dot{V}O_{2\ PEAK}$ observed during LB exercise. With the measurement of breathing

frequency and/or tidal volume it may have been possible to identify why $\dot{V}_E$ responds differently at different F_IO_2s.

Ventilatory equivalent ($\dot{V}_E/\dot{V}O_2$) in the present study increased in both LB and UB exercise as F_IO_2 was reduced. This is in agreement with other studies when acutely exposed to hypoxia where $\dot{V}_E$ is higher at a given oxygen consumption (Lawler *et al.*, 1988; Mollard *et al.*, 2007; Ogawa *et al.*, 2007). Higher $\dot{V}_E$ increases alveolar oxygen tension (P_AO_2) which increases haemoglobin oxygen saturation (SaO_2) and CaO_2 in turn benefiting oxygen delivery. Arterial desaturation and $\dot{V}O_{2\,MAX}$ are reduced less in those who have greater normoxic $\dot{V}_E/\dot{V}O_2$ (Gavin *et al.*, 1998). In the present study during H_1 and H_2 $\dot{V}_E/\dot{V}O_2$ was highest during UB exercise ($P = 0.054$ and $P<0.05$, respectively) as was S_PO_2 ($P = 0.051$ and $P<0.05$, respectively). These data indicate that a hyperventilatory response at a given $\dot{V}O_2$ maintains S_PO_2 during hypoxic exercise.

5.3 Metabolic factors.

No significant difference was observed for maximal blood lactate concentration ([BLa]) between LB and UB exercise at N, H_1 and H_2 in the present study. This indicates a similar contribution of anaerobic metabolism at maximal exercise across the three conditions, however significantly higher workloads achieved during LB compared to UB exercise at each F_IO_2. These findings concur with others who have shown BLa and the anaerobic contribution to exercise is higher at a given exercise intensity during UB exercise (Louhevaara *et al.*, 1990; Ahlborg and Jansen-Urstad, 1991; Jansen-Urstad *et al.*, 1993; Bhambhani *et al.*, 1998). Unless specifically trained, the UB musculature is used to a lesser extent than that of the LB which is used in daily locomotion and the

majority of athletic events in healthy individuals. Due to this relative inactivity of the UB a higher proportion of type II fibres are present compared to LB muscles (Johnson *et al.*, 1978), however athletes with trained UB musculature display higher proportion of type I fibres (Angermann *et al.*, 2006). A greater proportion and recruitment of type II fibres during UB exercise elicits greater BLa concentrations at a given exercise intensity due to the reduced aerobic capacity of these fibres (Sawka, 1986; Hopman *et al.*, 2003). Angermann and colleagues (2006) reported that the *medial deltoideus* muscle comprised 69 ± 11, 23 ± 9 and 8 ± 12 % type I, IIa and IIx, respectively in cross country skiers who are highly UB trained and have aerobic power similar to that observed in the LB. In untrained participants Johnson *et al.* (1978) reported the superficial deltoid consisted of 53.3 % type I fibres and 46.7 % type II fibres. Angermann *et al.* (2006) reported that at maximal exercise PPO was lower during UB exercise as was [BLa] where previously [BLa] was found to be unchanged while PPO was lower during UB compared to LB exercise (Sawka, 1986). A higher proportion of type I fibres in the trained participants would result in a greater contribution of aerobic metabolism to exercise thus reducing the [BLa] at a given exercise intensity and at maximal exercise.

PPO is greater when the exercising muscle mass is increased, as observed in the present study where the smaller muscle mass of the UB elicited a lower PPO. Shepard (1988) found that as active muscle mass was reduced (2 leg cycle ergometry; 1 leg cycle ergometry; 1 arm ergometry without restraints; 1 arm ergometry with restraints) PPO and $\dot{V}O_{2\ MAX}$ declined. These findings should be interpreted with caution as the slow cadences employed (LB = 50 rev.min^{-1}; UB = 40 thrusts·min^{-1}) have been subsequently shown not to elicit peak physiological responses (McKay and Banister, 1976; Smith *et al.*, 2001) and affects economy at lower exercise intensities. This is further supported by the low heart rates reported at maximal exercise.

RER at maximal exercise was highest during UB exercise, reflecting the higher $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ in this mode of exercise. This adds further evidence that anaerobic metabolism is higher at a given exercise intensity/$\dot{V}O_2$ during UB exercise as the same [BLa] and higher RER are accompanied by lower $\dot{V}O_2$ at maximal exercise. In addition the same workload represents a greater proportion of maximal exercise capacity during UB exercise (Bhambhani *et al.*, 1998; Mukari *et al.*, 2004). The same $\dot{V}CO_2$ at maximal exercise in hypoxia when accompanied with a lower $\dot{V}O_2$ will result in an increased RER, as seen in the present study and by others (Knight *et al.*, 1993; Martin and O'Kroy, 1993; Gavin *et al.*, 1998).

[BLa] at lactate threshold (LT) did not differ between LB and UB exercise or between F_IO_2 as this is a physiological fixed point. However, the $\dot{V}O_2$ at LT was lower during UB exercise at each F_IO_2 and decreased from N to H_1 and from H_1 to H_2 during LB exercise and from N to H_2 during UB exercise. Koistinen *et al.* (1995) found BLa concentrations at LT to be unchanged when acutely exposed to 3000 m but the corresponding $\dot{V}O_2$ was significantly lower during hypoxic LB exercise. Koistinen and colleagues (1995) reported LT to occur at 76 and 78 % $\dot{V}O_{2\ PEAK}$ for normoxia and hypoxia compared to 71 ± 3 and 74 ± 5 % during N and H_1 (≈ 2700 m) in the present study, respectively. This is supported by others who found no difference in % $\dot{V}O_{2\ PEAK}$ at LT during LB exercise as F_IO_2 is reduced (Freidmann *et al.*, 2005; Thake, 2006). Comparing three exercise modes (arm crank ergometry, cycle ergometry and treadmill running) LT occurred at 46.5, 63.8 and 58.6 % $\dot{V}O_{2\ PEAK}$, respectively (Davis *et al.* 1976). While lower than that observed in the present study, possibly due to lower cadences employed, this study showed that LT occurs at a lower % $\dot{V}O_{2\ PEAK}$ during UB compared to LB exercise. Our findings indicate that LT as a % $\dot{V}O_{2\ PEAK}$ responds

similarly during LB and UB exercise (tending to occur at a higher $\%\dot{V}O_{2\ PEAK}$ as F_IO_2 decreases) however, there is a lack of literature assessing LT during acute hypoxic UB exercise.

5.4 Oxygen delivery.

$\dot{V}O_{2\ PEAK}$ is limited centrally by oxygen delivery ($\dot{D}O_2$; Equation 2.4) during LB exercise (Ekblom *et al.*, 1976; Ferretti *et al.*, 1997; Peltonen *et al.*, 2001a) and central physiology has been suggested to be a key factor during UB exercise (Hopman *et al.*, 2003). Consideration of the factors determining $\dot{D}O_2$ and any differences that exist between LB and UB exercise will provide an insight into the differences observed in $\Delta\dot{V}O_{2\ PEAK}$ between LB and UB exercise. The following discusses the components of and their subsequent effect on $\dot{D}O_2$ during LB and UB exercise.

5.4.1 SV, HR and $\dot{Q}$.

Mollard and co workers (2007) found that HR_{MAX} was reduced in untrained participants from 2500 m (F_IO_2 = 0.154) during cycle ergometry whilst it was previously thought that for HR_{MAX} to be reduced during acute hypoxia the simulated altitude must be greater than $\approx$ 3800 m (Benoit *et al.*, 2003; Calbet *et al.*, 2003). The present study found that HR_{MAX} tended to decrease as F_IO_2 was reduced between sea level and simulated altitude$\approx$ 3700 m (N *vs.* H_2 P = 0.06) during LB exercise, however HR_{MAX} did not vary during UB exercise. During LB exercise greater aerobic power has been associated with a greaterΔHR_{MAX} (Benoit *et al.*, 2003) with reduced HR_{MAX} occurring at a lower simulated altitude (1000 m; Mollard *et al.*, 2007). Studies at similar simulated altitudes and exercise protocols in untrained participants as the present study

have shown HR_{MAX} to be unchanged (Lawler *et al.*, 1988; Martin O'Kroy, 1993; Peltonen *et al.*, 2001) but the tendency is for HR_{MAX} to decline.

HR is higher at a given $\dot{V}O_2$ during hypoxic exercise but is unchanged or reduced at maximal exercise. This was thought to be due to increased sympathetic drive during hypoxic exercise, supported by increased circulating catecholamines (Calbet *et al.*, 2003). However, when the sympathetic pathways were blocked HR remained higher during hypoxia at a given $\dot{V}O_2$ indicating other mechanisms to be responsible for the observed differences (Hopkins *et al.*, 2003). Benoit *et al.*, (2003) highlighted two mechanisms by which HR_{MAX} may be reduced during acute hypoxic exercise; 1) reduced F_IO_2 has a direct effect on myocardial physiology including repolarisation length and transmission time at the AV node (Roach *et al.*, 2003) and 2) that skeletal muscle $\dot{V}O_2$ dictates $\dot{Q}$ during hypoxic exercise and if it is assumed the SV is constant HR would be reduced (Wagner, 2000). It has also been proposed that the central nervous system ("central governor") could limit the muscle mass recruited in order to maintain the supply of O_2 to the heart (Mollard *et al.*, 2007).

HR_{MAX} is lower during UB compared to LB exercise (Bhambhani, 1995; Schneider *et al.*, 2002) but is higher at a given $\dot{V}O_2$. HR_{MAX} during UB exercise in the present study was 95 ± 4, 96 ± 3 and 97 ± 4 % whilst $\dot{V}O_{2\ PEAK}$ was 72 ± 3, 71 ± 10 and 76 ± 8 % of that attained during LB exercise for N, H_1 and H_2, respectively. While HR_{MAX} was lower during UB exercise it was higher for the aerobic output achieved. At a given $\dot{V}O_2$ $\dot{Q}$ has been reported to be similar for LB and UB exercise, however to maintain $\dot{Q}$ HR is higher due to ≈ 20 % lower stroke volume in UB exercise (Sawka, 1986; Miles *et al.*, 1989; Bhambhani, 1995). Angermann *et al.* (2006) reported no difference

in HR_{MAX} between LB and UB exercise however this study used double pole ergometry which may recruit a greater muscle mass than arm crank ergometry. In addition individuals with highly trained UB musculature were used whose SV_{MAX} is similar during LB and UB exercise thus maintaining $\dot{Q}$ at a similar HR (Pendergast, 1989).

Bhambhani *et al.* (1995) found using the CO_2 rebreathing technique that SV was 19 % higher during cycling compared to arm crank ergometry in healthy males when breathing room air. Using the method of Bhambhani *et al.* (1995; section 3.11) to estimate SV using O_2 pulse SV was 16 ± 8, 20 ± 11 and 17 ± 9 % lower for UB exercise during N ($P<0.01$), H_1 ($P<0.05$) and H_2 ($P=0.07$) respectively. The reduced SV during UB exercise may be due to the absence of the skeletal muscle pump of the inactive legs, which during LB exercise increases venous return, end diastolic volume and therefore SV. Also increased intrathoracic pressure during UB exercise increases afterload and therefore reduces the ejection fraction (Sawka, 1986; Miles *et al.*, 1989).

SV was lower during H_1 and H_2 compared to N ($P<0.05$) however while lower, no significant difference was observed between H_1 and H_2 for LB and UB exercise. At ≈ 4,000 m SV has been shown to decrease (Hopkins *et al.*, 2003) or remain unchanged (Stenberg *et al.*, 1966) however, at higher altitudes (5,260 m) SV has been shown to decrease (Calbet *et al.*, 2003). At 5,260 m (F_IO_2 = 0.105) SV was 116 mL·beat^{-1} compared to 128 mL·beat^{-1} during normoxia (Calbet *et al.*, 2003) while in the present study SV was reduced from a simulated altitude of ≈ 2,700 m (Table 4.4), lower than previously reported. The above studies have directly measured SV while the present study estimated SV from O_2 pulse at LT based on methods validated during normoxic exercise. At LT during hypoxic exercise $\dot{V}O_2$ decreased (Table 4.2) and HR increased (LB *vs.* UB = 150 ± 16 *vs.* 140 ± 12; 160 ± 15 *vs.* 144 ± 14 and 160 ± 13 *vs.* 144 ± 16

$bt \cdot min^{-1}$ for N, H_1 and H_2, respectively) resulting in lower O_2 pulse at LT which could cause SV to be underestimated during hypoxic exercise.

$\dot{Q}$ and SV were lower during UB exercise at each F_IO_2 and HR was lower during N and H_1 and tended to be lower during H_2 ($P<0.07$; Table 4.4) compared to LB exercise. This is in accordance with the literature where even if HR and SV are not significantly reduced but tend to be lower, $\dot{Q}$ can be significantly reduced (Peltonen *et al.*, 2001b). As reported previously $\dot{Q}$ was reduced on acute exposure during LB exercise and was reduced further as severity of hypoxia increased; however, the present study used lower simulated altitudes (Calbet *et al.*, 2003; Hopkins *et al.*, 2003). During UB exercise $\dot{Q}$ was reduced from N to H_1 in the presence of reduced SV without a reduction in HR, while from H_1 to H_2 $\dot{Q}$ was unchanged as neither HR nor SV were significantly changed. To date no literature is available regarding the response of $\dot{Q}$ to hypoxia during UB exercise and the present study suggests that $\dot{Q}$ seems to respond in a similar fashion to LB exercise. During LB exercise $\dot{Q}$ was reduced by 9 ± 4 and 18 ± 4 % and during UB exercise by 12 ± 10 and 18 ± 9 % for H_1 and H_2, respectively compared to N. However the greater intersubject variation during UB exercise weakens the statistical power.

The above findings should be interpreted with caution as the method used to estimate SV and therefore $\dot{Q}$ has potential for error and has not been validated during hypoxic exercise. Bhambhani (1995) estimated $\dot{Q}$ at 7 and 10 mins of submaximal exercise, equivalent to LT using the CO_2 rebreathing technique and derived regression equations to estimate SV from O_2 pulse. The CO_2 rebreathing technique is an indirect estimate

thus Bhambhanis' method (1995) is an estimation based on an estimation therefore, the potential for error is increased. In addition during CO_2 rebreathing a theoretical [Hb] concentration of 15.8 g·dL (so that testing remained non-invasive) was used to estimate the arterial/venous CO_2 content and used in the calculation of $\dot{Q}$, furthering the potential for error. While Bhambhani (1995) reported significant correlation between SV and O_2 pulse for LB and UB exercise,≈ 50 % of the data points lie outside the 95 % confidence intervals. Despite their mathematical connection, significant correlations were not present for O_2 pulse and a-$\bar{v}$ O_2Diff. during LB and UB exercise (Equation 5.1). Comparisons between the CO_2 rebreathing technique and direct measurements of $\dot{Q}$ have reported on average ≈ 12 % error (Marks *et al.*, 1985; Bhambhani, 1995). When Bhambhani's (1995) equations were retrospectively applied to studies SV was within 10 % of the value reported in the respective study, whether direct or indirect measures for SV where used.

Equation 5.1 O_2 *pulse* = *SV* x *a-*$\bar{v}$ O_2*Diff.*

In the present study HR was higher and $\dot{V}O_2$ lower at LT during hypoxia, causing O_2 pulse to decline, in turn estimations of SV declined as F_IO_2 was reduced. This is a contentious area during LB exercise as studies have reported SV during acute hypoxia to be unchanged (Stenberg *et al.*, 1966) or reduced (Calbet *et al.*, 2003) albeit at higher simulated altitudes than the present study. Bhambhani (1995) compared upright cycle and arm crank ergometry and the participants LB and UB $\dot{V}O_{2\ PEAK}$ were similar to those reported in the present study (LB = 43.9 ± 6.3 and UB = 30.3 ± 6.6 mL·kg·min^{-1}). Their method predicts SV from O_2 pulse at LT assuming that SV remains unchanged after this point. SV was thought to plateau at ≈ 40-50 % $\dot{V}O_{2\ PEAK}$ however, different

populations respond differently during incremental exercise. Where endurance athletes SV can continually increase until maximal exercise, untrained populations SV response can vary between individuals and may increase/decrease when approaching maximal workload after an initial plateau during submaximal work (Gonzalez-Alonso, 2008). If this is the case in the present study, estimates of SV at LT cannot be used to accurately estimate SV/$\dot{Q}$ at maximal exercise.

The method used in the present study (Bhambhani, 1995) offers estimates of SV during LB and UB exercise in a similar population. While this allows the possible mechanisms limiting aerobic power to be explored, there is potential for error in the estimation of SV and subsequent estimates of $\dot{Q}$, $\dot{D}O_2$, a-$\bar{v}$ O_2Diff. and E.

5.4.2 CaO_2/S_PO_2.

Arterial desaturation occurred to a greater extent during LB exercise compared to UB exercise (Table 4.5). S_PO_2 reduced from N to H_1 and from H_1 to H_2 in both LB and UB exercise. This is in agreement with studies using similar F_IO_2s during LB exercise (Lawler *et al*, 1988; Martin and O'Kroy, 1993; Ferretti *et al.*, 1997; Mollard *et al*, 2007), while there are no reports of S_PO_2 during arm crank ergometry in hypoxia. Angermann and co workers (2006) using double pole ergometry (UB exercise) reported SaO_2 of 93.2 ± 2.5 and 75.0 ± 5.9 % for normoxia and hypoxia (F_IO_2 = 0.146), respectively during maximal UB exercise. At a simulated altitude of 3,200 m Angermann *et al.* (2006) reported lower SaO_2 than observed in the present study which simulated a higher altitude (≈ 3,700 m; S_PO_2 = 82 ± 4 %). There are three possible explanations for these differences; 1) double pole ergometry elicits more of a whole body response compared to arm crank ergometry thus higher $\dot{Q}$ and reduced pulmonary transit time (PTT) may cause greater desaturation similar to those observed during LB

exercise. Angermann *et al.*'s (2006) study there was no difference in HR_{MAX} between double pole and cycle ergometry in normoxia and hypoxia indicating a similar whole body response, 2) recruitment of greater muscle mass during LB exercise would extract more O_2 from the blood in turn reducing the oxygen content of venous blood (CvO_2) and greater saturation of the blood would be required in the lung compared to arm crank ergometry, and 3) the participants were of a higher training status then those in the present study and normoxic S_PO_2 was 92.8 ± 1.4 and 93.2 ± 2.5 % for LB and UB exercise, respectively which is indicative of exercise induced arterial hypoxemia (EIAH; Prefaut *et al.*, 2000; Galy *et al.,* 2005). EIAH occurs in trained athletes with high $\dot{Q}$ and has been associated with greater desaturation during hypoxic maximal exercise (Chapman *et al.*, 1999; Mollard *et al*., 2007).

During LB and UB exercise S_PO_2 decreased with F_IO_2 as does $\dot{Q}$ during LB exercise, however during UB exercise $\dot{Q}$ was not reduced at H_2 from H_1. During N and H_1 S_PO_2 was not different between LB and UB exercise, while at H_2 S_PO_2 was significantly higher during UB compared to LB exercise. This indicates that at simulated altitudes above ≈ 2,700 m arterial desaturation is due to a combination of reduced P_IO_2 and $\dot{Q}$ which dictates PTT as when $\dot{Q}$ is unchanged from H_1 to H_2 in UB exercise S_PO_2 remains significantly higher than that seen during LB exercise. This may be due to reduced consumption at the muscle resulting in higher oxygenation of venous blood returning to the lungs. This is of interest as reduced PTT is generally only seen in highly trained athletes with large $\dot{Q}$, however the present study shows that when F_IO_2 = 0.13 reduced $\dot{Q}$ and therefore increased PTT is beneficial to S_PO_2 in untrained participants with lower $\dot{Q}$. Due to methodological issues (section 3.8.3) a constant

haemoglobin concentration ([Hb]) was used in the present study thus arterial oxygen content (CaO_2) showed the same response as S_PO_2.

5.4.3 Effect on delivery

As both maximal $\dot{Q}$ and CaO_2 are reduced as F_IO_2 declines during LB exercise, $\dot{D}O_{2\ PEAK}$ is reduced at H_1 and H_2 from N as was $\dot{V}O_{2\ PEAK}$. UB exercise did not respond in the same manor as although CaO_2 was reduced and $\dot{Q}$ tended to be lower between H_1 and H_2 $\dot{D}O_{2\ PEAK}$ and $\dot{V}O_{2\ PEAK}$ tended to be lower (NS). $\dot{D}O_{2\ PEAK}$ was not different between LB and UB exercise during H_2 due to greater SaO_2 and therefore CaO_2 while $\dot{D}O_2$ was significantly higher during LB exercise in all other conditions due to higher flow ($\dot{Q}$). During H_2 where $\dot{D}O_{2\ PEAK}$ was not reduced during UB exercise from H_1 no further reduction was present for $\dot{V}O_{2\ PEAK}$ while during LB exercise $\dot{D}O_{2\ PEAK}$ and $\dot{V}O_{2\ PEAK}$ decreased further between H_1 and H_2 ($P<0.05$).

5.5 Extraction.

Arterial – mixed venous oxygen difference (a-$\bar{v}$ O_2Diff.) was higher during LB exercise in normoxia compared to UB exercise, which is in agreement with a previous study despite using different ergometers and participants who were both LB and UB trained (Calbet *et al.*, 2005). a-$\bar{v}$ O_2Diff. did not vary between LB and UB hypoxic exercise however tended to be lower during UB exercise. Sawka (1986) reported that for a given $\dot{V}O_2$ muscle blood flow is similar in LB and UB exercise. Greater capillary density reduces diffusion distance and is beneficial to extraction at the muscle. Type II muscle fibres have a reduced fibre capillary ratio than type I, and type II fibres are prominent in the UB musculature of the untrained population. This would result in increased diffusion distance for O_2 during UB exercise thus reducing the extraction

capacity of the muscle, as seen in the present study as E was lower at each F_IO_2 during UB exercise. $\dot{V}O_2$ has been reported higher in some studies during UB exercise and unchanged in others at a given power output with some authors highlighting that UB exercise is less efficient than LB (Sawka, 1986). Extraction of O_2 at the muscle is dependent on a concentration gradient between the blood (PaO_2) and muscle, the greater the gradient the greater the potential for E. Hypoxia reduces the concentration gradient and therefore a-$\bar{v}$ O_2Diff. is lower, as seen in the present study.

Several reasons could explain the differences observed for E between LB and UB exercise. $\dot{D}O_2$ can be maintained either through an increased blood flow or by an increased CaO_2, however the latter of these components would be more beneficial to the concentration gradient between the blood and the muscle. That is to say, a low CaO_2 rapidly delivered to the muscle will maintain delivery but compromise the extraction. While a-$\bar{v}$ O_2Diff. declines during hypoxia, extraction ratio (E) increases as the absolute amount of O_2 consumed by the muscle declines to a lesser extent than the amount of O_2 delivered to the muscle ($\dot{D}O_2$). However it has been commented that the muscles' ability to extract O_2 is not fully taxed during maximal exercise (Calbet *et al.*, 2005) as studies have shown that hyperoxia increases $\dot{V}O_{2\ PEAK}$ from normoxia during LB exercise. S_PO_2 and $\dot{Q}$ tended to be higher thus increasing CaO_2 and the O_2 concentration gradient between blood and muscle (Peltonen *et al.*, 2001b). During UB exercise $\dot{V}O_{2\ PEAK}$ only increased by 3 % (NS) from normoxia when acutely exposed to hyperoxia (F_IO_2 = 0.5) which may indicate that extraction is fully taxed in this mode of exercise, however delivery and extraction were not reported in this study (Hopman *et al.*, 2003).

5.6 Limitations to aerobic power.

The present study supports those previously published using LB exercise (Ekblom *et al.* 1976; Wagner, 1991; Ferretti *et al.*, 1997; Bassett and Howley, 2000) where $\dot{V}O_{2\ PEAK}$ has been suggested to be limited centrally. Ekblom and colleagues (1976) found that when CaO_2 was reduced by 10 % $\dot{V}O_{2\ PEAK}$ was reduced by 6 %. The present study found that at H_1 and H_2 $\dot{V}O_2$ *vs.* CaO_2 was reduced by 13 ± 8 *vs.* 13 ± 5 and 23 ± 6 *vs.* 23 ± 7 %, respectively. $\dot{V}O_2$ *vs.* $\dot{D}O_2$ in the present study was reduced by 13 ± 8 *vs.* 21 ± 6 and 23 ± 6 *vs.* 37 ± 6 % for H_1 and H_2 from N, respectively.

Significant correlations were observed for $\dot{V}O_2$ and $\dot{D}O_2$ during LB exercise in N and H_1 but not H_2 (Fig. 4.6). The difference at H_2 may be due to greater arterial desaturation and therefore reduced CaO_2 rather than reduced $\dot{Q}$ from normoxia. Thus the arterial - tissue PO_2 gradient would be reduced, which is detrimental to O_2 diffusion and $\dot{D}O_2$ would be maintained via flow rather than content. Also the pulse oximeter used in the present study has been validated across a physiological range of 70 – 100 % and when F_IO_2 = 0.13 arterial saturation fell to the lower end of the range (mean 74 ± 6 %; range 66 – 84 %) where there may be more error (section 2.3.3). When combined with the estimated $\dot{Q}$ the multiplication of error may weaken the correlation in this condition.

UB exercise has much less literature published on the mechanisms limiting maximal exercise capacity and the data in the present study offer arguments for both central and peripheral limitation. Hopman *et al.* (2003) found no difference for $\dot{V}O_{2\ PEAK}$ between F_IO_2 0.21 and 0.15 while the present study found a significant reduction (15 ± 6 %) between these two inspired O_2 fractions. Hopman and co-workers (2003) used a

continuous exercise protocol with smaller increments in exercise intensity which may have facilitated the high workloads achieved. However Hopman *et al.* (2003) reported that $\dot{V}O_{2\ PEAK}$ reduced from hyperoxia ($F_IO_2 = 0.5$) to hypoxia ($F_IO_2 = 0.15$) suggesting that this F_IO_2 dependency indicates that UB aerobic power was limited centrally. While suggesting that this reduction in $\dot{V}O_{2\ PEAK}$ as inspired O_2 tension was reduced resulted in reduced $\dot{D}O_2$ they could not discount the possibility that peripheral factors limited exercise as SaO_2, $\dot{Q}$, $\dot{D}O_2$ and E were not reported.

The present study as with Hopman and colleagues (2003; 2004) observed that $\dot{V}O_{2\ PEAK}$ reduced as F_IO_2 declined during UB exercise. At H_1 and H_2 $\Delta\dot{V}O_{2\ PEAK}$ *vs.* $\Delta\dot{D}O_2$ was 15 ± 6 *vs.* 20 ± 12 and 19 ± 8 *vs.* 30 ± 9 %, respectively. The data so far indicate that LB and UB exercise respond similarly during exposure to acute hypoxia, however when the components of oxygen consumption (Table 4.4) are assessed differences are apparent. During LB exercise the normoxic $\dot{V}O_{2\ PEAK}$ of 3.41 ± 0.58 $L \cdot min^{-1}$ cannot be met at H_2 as $\dot{D}O_2$ is only 3.15 ± 0.33 $L \cdot min^{-1}$. However during UB exercise $\dot{D}O_2$ at H_2 (2.78 ± 0.45 $L \cdot min^{-1}$) is sufficient to sustain normoxic $\dot{V}O_{2\ PEAK}$ (2.48 ± 0.33 $L \cdot min^{-1}$) if E could reach 0.89. Also, although $\dot{D}O_2$ is higher during LB exercise in each condition CaO_2 is lower thus delivery is maintained via flow rather than content. Assuming the active tissue PO_2 is the same in LB and UB exercise the concentration gradient for O_2 diffusion at the muscle would be greater during UB exercise, which should aid E.

The peripheral limitations to $\dot{V}O_{2\ PEAK}$ during UB exercise could be attributed to several factors; 1) reduced muscle mass recruited, 2) inadequate perfusion of the active tissue bed, 3) reduced O_2 transit time within the muscle and 4) lower oxidative capacity of the muscles used during UB exercise. At a given power output a smaller muscle

mass would operate at a higher percentage of its peak tension, increasing intramuscular tension and impeding blood flow (Sawka *et al.*, 1983). Also a smaller muscle mass with reduced capillary network (compared to the leg muscles) would reduce the time oxygenated blood spends in the muscle and therefore the time available for O_2 to transfer from erythrocytes to mitochondria (Calbet *et al.*, 2005). This is further supported in the present study as S_PO_2 and CaO_2 were higher but E was lower during UB exercise in H_2. Reduced offloading of O_2 at the muscle would result in increased oxygenated blood returning to the lungs and enabling greater saturation when compared to LB exercise where greater amounts of O_2 are consumed for metabolism as it seems in the present study. Finally the musculature of the UB, especially in those who are not UB trained, has a greater proportion of type II muscle fibres, thus these fibres with reduced oxidative capacity are recruited more during UB exercise (Johnson *et al.*, 1973; Sawka, 1983; Jansen-Urstad and Ahlborg, 1992; Schneider *et al.*, 2002; Hopman *et al.*, 2003; Angermann *et al.*, 2006).

Calbet and colleagues (2005) when using participants who were highly UB trained found that extraction was higher during LB compared to UB exercise. This study compared diagonal stride (whole body), double poling (UB) and leg skiing (LB) in cross country skiers while the present study used cycle and arm crank ergometry in an untrained population but also found that extraction was lower during UB compared to LB exercise. This is supported further by considering the Fick equation (Fig. 2.3); to maintain $\dot{V}O_2$ when extraction is lower cardiovascular stress must be increased, as is the case during UB exercise (Sawka *et al.*, 1986; Calbet *et al.*, 2005).

5.7 Summary/applications.

The present study confirms that both LB and UB $\dot{V}O_{2\ PEAK}$ is reduced when acutely exposed to simulated altitude but offers evidence that different mechanisms are responsible for these reductions. The present study is in agreement with the large body of literature investigating the effects of acute hypoxia during LB exercise with reduced oxygen delivery insufficient to maintain previously attained $\dot{V}O_{2\ PEAK}$ during normoxia (Ferretti *et al.*, 1997; Cardus *et al.*, 1998; Peltonen *et al.*, 2001a; Mollard *et al.*, 2007). Recently Hopman and colleagues (2003) proposed that UB exercise is also limited centrally however it has also been suggested that peripheral factors limit UB exercise (Calbet *et al.*, 2005). During LB exercise studies have shown that $\dot{V}O_{2\ PEAK}$ is increased from normoxia to hyperoxia (Peltonen *et al.*, 2001b) indicating that extraction is not fully taxed in this mode of exercise while this does not occur during UB exercise (Hopman *et al.*, 2003). The present study shows that $\dot{D}O_2$ is sufficient to maintain $\dot{V}O_{2\ PEAK}$ if extraction were able to increase during UB exercise at ≈ 3700 m, thus indicating peripheral limitation. The observed reduction in CaO_2 during acute hypoxia would reduce the O_2 concentration gradient between the blood and the active tissue bed creating an environment detrimental to extraction causing $\dot{V}O_{2\ PEAK}$ to decline during UB exercise.

The present study simulated altitudes commonly used by athletes during training or competitions and it is hoped the improved knowledge of the physiological consequences will enable better preparation and ultimately performance in these conditions. Knowledge of the mechanisms limiting LB exercise have been used during exercise prescription to maximise the physiological/performance adaptations. The present study offers evidence that UB exercise is limited peripherally, therefore training programmes that elicit peripheral adaptations may aid performance during UB aerobic exercise more

than those eliciting central adaptations. Indeed Angermann and co workers (2006) reported a higher proportion of type I fibres in the UB musculature in cross country skiers. This was accompanied by an UB $\dot{V}O_{2\ PEAK}$ of 94 % of that attained for LB exercise, dramatically higher than typically reported in untrained populations (60-80 %). This information has been commonly used during LB exercise but may now be applied to UB exercise which will benefit cross country skiers, rowers, wheel chair athletes and other activities involving the UB undertaken at altitude. Arm crank ergometry is a commonly used mode of exercise to test UB $\dot{V}O_{2\ PEAK}$ but may be applicable to one event more than another (i.e. wheelchair athletes *vs.* cross country skiers) and it has yet to be shown whether different populations (aerobically trained athletes) respond in the same manner during hypoxic UB exercise as differences are apparent during LB exercise.

CHAPTER 6

LIMITLTIONS AND FUTURE RESEARCH

6.0 Limitations and future research.

6.1 Limitations.

The present study estimated stroke volume (SV) based on the method of Bhambhani (1995) which uses O_2 pulse at lactate threshold (SV remains consistent post threshold) during cycle and arm crank ergometry in normoxia. No studies have yet assessed the validity and reliability of this or any other method of estimating SV/$\dot{Q}$ during hypoxic exercise. When exercising under hypoxic conditions HR was slightly increased and $\dot{V}O_2$ decreased at LT compared to normoxia resulting in reduced O_2 pulse. This would result in the underestimation of SV as severity of hypoxia increased in both modes of exercise. This is a contentious issue in LB exercise as SV has been reported to be reduced (Calbet *et al.*, 2003) or unchanged (Stenberg *et al.*, 1966) when acutely exposed to hypoxia (at greater simulated altitudes than employed in the present study) and has yet to be reported during UB exercise. If these assumptions were incorrect and SV was underestimated, this would subsequently result in underestimation of $\dot{Q}$ and $\dot{D}O_2$ and the overestimation of $a\text{-}\bar{v}$ O_2*Diff.* and extraction. The rationale for using this method was based on the model observed during LB exercise. During LB exercise in hypoxia extraction ratio increases as the same quantity of O_2 is utilised from a reduced content (CaO_2) and this was apparent when using the above mentioned assumptions. These assumptions were also applied to UB exercise.

Due to large intertrial variation for haemoglobin concentration ([Hb]) a mean value (calculated as the mean of the [Hb] at maximal exercise in each trial) was used for the calculation of CaO_2. When [Hb] is not measured a fixed concentration of 15 $g.dL^{-1}$ can be assumed, the mean [Hb] for all participants in the present study was 14.9 ± 0.7 $g.dL^{-1}$ (range 13.7 – 16.2 $g.dL^{-1}$). Thus it was considered better to use the mean of a measured variable rather than a hypothetical fixed concentration despite the observed variation.

This may have resulted in errors when calculating CaO_2 from [Hb] and SpO_2 leading to possible errors in $\dot{D}O_2$ (further compounded by possible error when estimating $\dot{Q}$). As the interassay variability was within acceptable limits (coefficient of variation = 2.9 %). The discrepancies between trials may be due to differences between different mixtures of reagent increasing possible measurement error between trials.

The assumptions enable the most accurate estimations of SV, $\dot{Q}$, CaO_2, $\dot{D}O_2$ and E from the data collected and offer the reader possible correlations to $\Delta\dot{V}O_{2\ PEAK}$. This said there is possibility of error in these estimations and therefore should be interpreted with caution.

The present study used moderate – high simulated altitudes (F_IO_2s 0.15 and 0.13 equivalent to≈ 2700 and 3700, respe ctively; Barry and Pollard, 2005) where others when investigating LB exercise have used higher simulated altitude (Benoit *et al.*, 2003; Calbet *et al.*, 2003; Mollard *et al.*, 2007). Ferretti and co-workers (1997) found that when using F_IO_2s from 0.3 to 0.11 that the reduction in $\dot{V}O_{2\ PEAK}$ as F_IO_2 was reduced is dictated by the shape of the O_2 dissociation curve (sigmoid). The comparison of LB and UB exercise at greater simulated altitudes may identify different responses during extreme simulated altitudes, as in the present study the significant reduction in $\dot{V}O_{2\ PEAK}$ between F_IO_2 0.15 – 0.13 during LB exercise was not observed during UB exercise.

The present study used sedentary participants none of whom undertook regular UB exercise. While from a mechanistic approach this population provides useful information regarding the limiting factors in the two mode of exercise, from an

application viewpoint the data can only be applied to a similar cohort. The findings of the present study would benefit athletes participating in events using the UB (rowers, cross-country skiers, climbers, athletes with spinal cord injury etc.) who will be specifically UB trained and therefore may respond differently to the untrained population used in the present study as seen during LB exercise (Lawler *et al.,* 1988; Martin and O'Kroy, 1993; Mollard *et al.*, 2007).

6.2 Future research.

First it is recommended that future research should be directed towards addressing the limitations of the present study. The use of different subject population (i.e. trained *vs.* untrained, wheelchair athletes) would identify if the differences observed between populations for LB exercise were still present during UB exercise and when combined with the finding of the present study enable the application of the data in better context. The present study used cycle and arm crank ergometry as these two forms of cyclical exercise offer good comparisons. Recently other studies have used double pole ergometry (Calbet *et al.* 2005; Angermann *et al.* 2006). Using exercise protocols similar to the activities undertake at altitude (i.e. skiing, rowing, wheelchair ergometry) or field studies at altitude would enable better application of these data. Further research should also investigate more severe hypoxia as well as hyperoxia during UB exercise and their effect on aerobic power as this would further the understanding of the mechanisms limiting exercise and highlight whether the LB and UB respond similarly at different F_IO_2s. The model of Ekblom *et al.* (1976) may also be beneficial when applied to UB exercise as this offers a different means of reducing $\dot{D}O_2$. Ekblom *et al.* (1976) reduced and enhanced [Hb] from control thus altering the capacity of blood to transport O_2 and would add further evidence to the mechanisms limiting UB exercise.

This protocol would reduce the ability of blood to transport O_2 by the same amount for both modes of exercise whereas with hypoxia, desaturation occurs to different extents.

A model is required for the non-invasive estimation of $SV/\dot{Q}$ during hypoxia for both LB and UB exercise. Methods have been developed that accurately estimate $\dot{Q}$ non-invasively during normoxia for LB (Stringer *et al.* 1997) and LB and UB exercise (Bhambhani, 1995). To this author's knowledge these methods have not been validated during hypoxia, thus future studies should be directed towards either validating the above mentioned methods in hypoxia or develop new methods that offer accurate and reliable estimates of $SV/\dot{Q}$ from non-invasive measures in hypoxia.

Hypoxic studies using LB exercise have identified that $\Delta \dot{V}O_{2\ PEAK}$ to be closely related to arterial desaturation and factors that reduce arterial desaturation also reduce $\Delta \dot{V}O_{2\ PEAK}$ (Gavin *et al.* 1998). Also those that experience exercise induced arterial hypoxemia (EIAH) during normoxia experience greater desaturation and $\Delta \dot{V}O_{2\ PEAK}$ upon exposure to hypoxia (Chapman *et al.* 1999). Research could now attempt to establish characteristics that maintain saturation and therefore $\dot{V}O_{2\ PEAK}$ during UB exercise when exposed to hypoxia/altitude. Further studies could also investigate which peripheral factors are responsible for reduced extraction during UB exercise (i.e. capillary transit time, O_2 off-loading or oxidative capacity of the muscle) and the use of training studies could identify which peripheral factors are associated with $\dot{V}O_{2\ PEAK}$.

To date all studies investigating hypoxia and UB exercise have used normobaric hypoxia but with athletic activities using the UB taking place at altitude more field studies may be advantageous. These studies could progress the work already

undertaken during LB exercise and apply them to the UB exercise (i.e. acclimatisation and its effects on UB exercise). Athletes also use altitude as part of their training programme as preparation for an upcoming event and much research has been directed at what altitude training programme is most beneficial (i.e. live hi – train low). This should now be applied to UB exercise to see whether altitude training invokes similar responses as those seen in LB exercise. Further research should also investigate which peripheral factors limit exercise capacity then exercise programmes can be specifically designed to improve these aspects of physiology.

Hypoxia during UB exercise is still a relatively new area of investigation with many questions to be answered. Much of the research that has been undertaken using LB exercise should now be replicated using UB exercise to establish whether the responses are the same and this will inevitably raise more points for investigation in the future.

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Appendices.

APPENDIX A. Informed consent form.

TITLE: The effect of reduced inspired oxygen fraction on the cardiorespiratory response to upper and lower body exercise.

1. I have read the subject information form and I am aware what is required of me before the test.

2. I understand the protocol of the test which I am participating in and understand what is required of me.

3. I am aware that the study consists of 6 separate trials each requiring physical exercise and that there may be some risks associated with exercise at that intensity such as fainting, light headiness and nausea.

4. I understand that the research staff will take the appropriate action if any of the above risks occur, and will fully assume that risk.

5. I understand that the side effects that could manifest as a result of hypoxia (see subject information) may continue for several hours after the experiment.

6. I understand that I have the right to withdraw myself from the study, without explanation, at anytime before, during or after testing.

7. I understand that the information gathered as a result of the study will be kept confidential and not be disclosed to anyone else other then the research staff.

8. I release the laboratory and its employees from any liability for any injury or illness that may occur either directly or indirectly as a result of this study.

9. I agree to abide by the guidelines stated in the subject information form and present myself in a suitable condition for testing.

Signed …….. Date …/…/…

Print Name …….

Investigator's Statement

I confirm that I have explained the nature, demands and possible risks associated with the present study to the volunteer prior to the testing.

Signed …….. Date …/…/…

Print Name …….

APPENDIX B. Physical activity readiness questionnaire (PAR-Q).

NAME _____

DATE OF BIRTH _____ **AGE** _____

TEST PLANNED FOR TODAY (TO BE COMPLETED BY THE EXPERIMENTER)

_____

_____

GENERAL PHYSICAL FITNESS

HOW OFTEN DO YOU TAKE REGULAR PHYSICAL EXERCISE?

- LESS THEN ONCE A WEEK
- ONCE A WEEK
- TWO TO THREE TIMES A WEEK
- MORE THEN THREE TIMES A WEEK

HOW LONG HAVE YOU BEEN EXERISING AT THIS FREQUENCY?

- LESS THEN 1 MONTH
- 1-6 MONTHS
- MORE THEN 6 MONTHS

IS YOUR CURRENT BODYWEIGHT

- NORMAL RANGE
- OVERWEIGHT
- UNDERWEIGHT

SMOKING HABITS (TICK ALL THAT APPLY)

- NEVER SMOKED
- GAVEN UP MORE THEN 1 MONTH
- TOTAL YEARS SMOKED FOR
- SMOKE/USED TO SMOKE LESS THEN 20 CIGARETTES PER DAY
- SMOKE/USED TO SMOKE MORE THEN 20 CIGARETTES PER DAY

GENERAL HEALTH

DO YOU SUFFER OR HAVE YOU EVER SUFFERED FROM THE CONDITIONS BELOW? (GIVE DETAILS IF YES)

- HEART DISEASE AND/OR CIRCULATORY PROBLEMS
- DIABETES
- HIGH BLOOD PRESSURE
- HIGH CHOLESTEROL
- ASTHMA OR ANY OTHER LUNG DISEASE
- KIDNEY DISEASE
- CLOTTING DISORDERS
- ANEMIA OR OTHER BLOOD DISORDERS
- ANY OTHER LONG TERM MEDICAL CONDITION

DETAILS _____

_____

DO YOU REGULARY TAKE

- ANY PERSCRIBED MEDICINES
- ANY OVER THE COUNTER MEDICINES
- ANY OTHER DRUGS
- ANY SUPPLEMENTS

DETAILS_____

_____

HAVE YOU EVER HAD ANY PAST INJURIES THAT MIGHT BE AFFECTED BY THE TEST PLANNED FOR TODAY?

IS THERE ANY OTHER INFORMATION THAT MIGHT AFFECT YOUR SAFTY/HEALTH IN CARRYING OUT THESE TESTS?

_____

YOUR HEALTH TODAY

HAVE YOU HAD ANY OF THE FOLLOWING HEALTH PROBLEMS IN THE LAST FEW DAYS?

- COUGHS/COLDS
- HEADACHES
- SHORTNESS OF BREATH
- MUSCLE/JOINT PAIN
- ANY OTHER HEALTH PROBLEMS

DETAILS_____
_____

DO YOU CURRENTLY HAVE ANY OF THE FOLLOWING SYMPTOMS?

- SORE THROAT OR BLOCKED NOSE
- SHORTNESS OF BREATH
- HEADACHE AND/OR DIZZINESS
- NAUSEA
- PAIN IN MUSCLES/TENDONS/BONES
- ANY OTHER FEELINGS/PAINS THAT YOU DO NOT NORMALLY HAVE

DETAILS_____
_____

ARE YOU PREGNANT?

_____

IS THERE ANY OTHER INFORMATION THAT MIGHT AFFECT YOUR SAFETY/ HEALTH IN CARRYING OUT THE TESTS TODAY?

_____
_____

I CONFIRM THAT I HAVE GIVEN DETAILS OF ANY INFORMATION THAT MAT AFFECT MY SUITIBILITY TO PARTICIPATE AS A SUBJECT TODAY. I HAVE ALSO READ AND SIGNED THE SUBJECT INFORMATION AND INFORMED CONSENT FORMS FOR TODAYS TEST.

SIGNATURE OF SUBJECT _____

AUTHORISED BY (PRINT NAME) _____

(SIGNATURE) _____

DATE_____

APPENDIX C. Respiratory gas calculations.

Expired volume correction to standard temperature pressure dry (STPD).

$$V_{ESTPD} = V_{EATPS} \left[\frac{273^{O}}{273^{O} + Ta} \right] \left[\frac{P_I - PH_2O}{760 \text{ mm Hg}} \right]$$

V_{ESTPD} = Expired volume standard temperature pressure dry

V_{EATPS} = Expired volume ambient temperature pressure and saturated

Ta = Temperature of expired gas

P_I = Barometric pressure of inspired gas

PH_2O = Partial pressure of water vapour at ambient temperature

Oxygen consumption.

$$\dot{V}O_2 = (\dot{V}_I \times F_IO_2) - (\dot{V}_E \times F_EO_2)$$

$$\dot{V}_I \times F_IN_2 = \dot{V}_E \times F_EN_2$$

$$F_EN_2 = 1 - (F_EO_2 + F_ECO_2)$$

$\dot{V}O_2$ = Oxygen consumption

$\dot{V}_I$ = Inspired gas volume

$\dot{V}_E$ = Expired gas volume

F_IO_2 = Inspired oxygen fraction

F_EO_2 = expired oxygen fraction

F_ECO2 = expired carbon dioxide fraction

F_IN_2 = Inspired nitrogen fraction

F_EN_2 = Expired nitrogen fraction

Respiratory exchange ratio (RER).

$$RER = \dot{V}CO_2 / \dot{V}O_2$$

APPENDIX D. Interassay/intertrial variability.

Coefficient of variation between duplicate haemoglobin measurements collected in the present study. Total number of data sets = 353.

Sample 1 (A)	Sample 2 (B)	Difference (C)	Square route of the difference squared (D)
Eg.		A – B	$\sqrt{(C^2)}$
15.1	15.4	-0.3	0.3
Mean of "D"			0.87
Sum of "D"			307.12
Square route of the sum of the difference divided by number of samples		$\sqrt{\frac{307.12}{706}}$	0.02
CV		$\left(\frac{0.02}{0.87}\right) * 100$	2.86

Coefficient of variation for haemoglobin concentration ($g \cdot dl^{-1}$) at rest between experimental trials.

		Subject								
Exercise	F_IO_2	1	2	3	4	5	6	7	8	9
	0.21	14.4	14.0	14.9	14.6	13.7	15.7	11.4	14.7	14.9
LB	0.15	15.2	13.9	15.7	15.5	15.1	13.6	11.9	13.7	12.7
	0.13	13.0	18.2	15.5	14.8	15.1	13.7	14.5	13.3	15.1
	0.21	11.9	14.1	14.6	14.7	15.8	12.8	13.3	16.6	14.9
UB	0.15	14.0	13.7	15.9	15.3	14.7	11.5	14.8	13.6	14.0
	0.13	13.8	14.3	14.8	13.7	12.3	13.5	15.9	11.9	13.2
Mean		13.7	14.7	15.2	14.8	14.4	13.5	13.6	14.0	14.1
SD		1.2	1.7	0.5	0.6	1.3	1.4	1.8	1.6	1.0
CV		8.4	11.6	3.5	4.3	8.7	10.2	13.1	11.2	7.1

Coefficient of variation for haemoglobin concentration ($g \cdot dl^{-1}$) at maximal exercise between experimental trials.

		Subject								
Exercise	F_IO_2	1	2	3	4	5	6	7	8	9
	0.21	15.9	13.7	15.8	16.1	16.2	16.9	12.3	13.4	16.0
LB	0.15	15.1	14.5	15.9	16.8	16.1	13.6	14.4	15.8	12.5
	0.13	13.2	13.0	17.2	14.6	14.3	14.6	12.8	14.5	16.1
	0.21	14.1	14.5	15.6	15.9	16.0	14.6	13.6	16.0	16.5
UB	0.15	15.9	15.9	15.9	15.4	16.3	13.2	15.2	15.2	15.4
	0.13	14.4	14.8	16.5	13.6	14.2	13.7	14.0	13.9	14.3
Mean		14.8	14.4	16.2	15.4	15.5	14.4	13.7	14.8	15.1
SD		1.1	1.0	0.6	1.1	1.0	1.3	1.1	1.0	1.5
CV		7.2	6.9	3.7	7.4	6.4	9.2	7.7	7.1	9.9

APPENDIX E. Borg rating of perceived exertion (RPE) scale.

6 NO EXERTION AT ALL

7 EXTREMELY LIGHT

8

9 VERY LIGHT

10

11 LIGHT

12

13 SOMEWHAT HARD

14

15 HARD (HEAVY)

16

17 VERY HARD

18

19 EXTREMELY HARD

20 MAXIMAL EXERTION

APPENDIX F. British Association of Sport and Exercise Science (BASES) abstract 2008.

The effect of acute hypoxia on peak oxygen consumption during upper compared to lower body exercise.

C.D. Thake, C. Simons, & M.J. Price

Coventry University, UK

At sea level upper body exercise elicits approximately 70% $\dot{V}O_2$ peak of that attained during lower body exercise (Sawka *et al.*, 1983: *Journal of Applied Physiology*, 54, 113-117). Although it is well established that exposure to altitude results in reduced $\dot{V}O_2$ peak these data are almost exclusively from lower body exercise studies. Therefore we examined the effect of reduced F_IO_2 and the magnitude of reduction in $\dot{V}O_2$ peak in upper compared to lower body exercise.

With local ethical committee approval nine healthy male participants (age mean 22, *s* = 2 years) undertook three upper and three lower body discontinuous (30 sec intervals) incremental exercise (UBX; LBX) tests to volitional exhaustion whilst breathing either normoxia (N) or normobaric hypoxia (H_1 and H_2); F_IO_2s ≈ 0.21, 0.15 and 0.13 respectively. Exercise commenced with a resistance of 70 W for cycle ergometry and 35 W arm cranking and was increased by 30 and 15 W respectively every 3 min thereafter; cadence was maintained at 70 rpm throughout. Heart rate (HR) and arterial haemoglobin oxygen saturation (SpO_2) were monitored continually. Data were examined using general linear model analysis of variance.

Physiological responses are given in Table I. UBX $\dot{V}O_2$ peak was 71 ± 10 and 76 ± 8% of that in LBX at H_1 and H_2 respectively. Peak blood lactate was >10 mmol.L^{-1} in UBX and LBX and did not vary with F_IO_2.

Table 1: Physiological variables at peak exercise (mean ± *s*).

		LBX			UBX		
		N	H_1	H_2	N	H_1	H_2
Peak Power output (W)	#, †	273 ± 49	250 ± 37	223 ± 28	135 ± 27	127 ± 20	123 ±18
$\dot{V}O_2$ peak ($L.min^{-1}$)	#, †, Φ	3.52 ± 0.50	3.04 ± 0.46	2.68 ± 0.27	2.53 ± 0.35	2.15 ± 0.40	2.04 ± 0.34
HR ($bt.min^{-1}$)	#, δ	189 ± 12	188 ± 12	183 ± 13	180 ± 13	180 ± 13	176 ± 14
SpO_2 (%)	#, †, Φ	96 ± 2	83 ± 4	73 ± 4	96 ± 2	85 ± 5	79 ± 4

#P<0.001 exercise mode; †P<0.001, δP<0.01 F_IO_2; ΦP<0.05 exercise mode × F_IO_2; effect size eta^2 = 0.03 to 0.80

To conclude, the reduction in $\dot{V}O_2$ peak appears to be less in UBX compared to LBX at the lowest F_IO_2. This is potentially relevant to athletes conducting UBX at altitude.

Reference: Thake, C. D., Simons, C and Price, M. J. (2008). The effect of reduced inspired oxygen fraction on the VO_2 peak during upper compared to lower body exercise. *Submitted to British Association of Sport and Exercise Annual Conference*, Brunel University In press

APPENDIX G. British Paralympic Association (BPA) abstract 2008.

***The effect of acute hypoxia on the VO_2 peak during upper compared to lower body exercise*.**

C D Thake, C Simons and M J Price

Faculty of Health and Life Sciences, Coventry University, Coventry, CV1 5FB.

Introduction: At sea level upper body exercise elicits approximately 70% $\dot{V}O_2$ peak of that attained during lower body exercise (Sawka *et al.*, 1983, *Journal of Applied Physiology* (54) 113-117). Although it is well established that exposure to altitude results in reduced $\dot{V}O_2$ peak these data are almost exclusively from lower body exercise studies (Martin and O'Kroy, 1993, *Journal of Sport Sciences, (*11) 37-42).

Aim: To examine the relationship between reduced F_IO_2 and the magnitude of reduction in VO_{2peak} during upper compared to lower body exercise.

Patricipants: In accordance with ethical approval from Coventry University Ethics committee nine healthy able bodied male participants (age 22±2 years; height 180.6±8.2 cm; body mass 78.7±12.2 kg; estimated body fat 15.8±12.4%; estimated muscle mass 57.5±6.5 %; haemoglobin 15.1±0.6 $g.dl^{-1}$; n=9) gave their informed consent to participate in the study.

Methods: Using a crossover type design participants undertook three upper and three lower body discontuous incremental exercise (UBX; LBX) tests to volitional exhaustion (VEX) whilst breathing either normoxia (N) or normobaric hypoxia (H_1 and H_2); F_IO_2s ≈ 0.21, 0.15 and 0.13 respectively. Exercise commenced with a resistance of 70W for cycle ergometry (Monark 824E) and 35W arm cranking (Lode Angio, Groningen, Holland) and was increased by 30 and 15W respectively every 3 min thereafter. A cadence of 70rpm was maintained throughout. Heart rate (HR) and arterial haemoglobin oxygen satuation (SpO_2)

were continually monitored. A 30 sec interval between work stages enabled the collection of earlobe capillary blood for lactate (BLa) analysis.

Statistical analysis: General linear model analysis of variance (ANOVA) was used to examine differences between upper and lower body exercise and between F_IO_2s (level of hypoxia). Significant main effects were further investigated with Tukey post-hoc tests.

Results: Peak power output declined with reduced F_IO_2 and was higher during LBX compared to UBX (N, 273 ± 49 *vs.* 135 ± 27; H_1, 250 ± 37 *vs.* 127 ± 20 and H_2, 223 ± 28 *vs.* 123 ±18 W; $P<0.001$, main effects for exercise mode and F_IO_2). In accord $\dot{V}O_2$ peak decreased with F_IO_2 ($P<0.001$, main effect). The reduction in $\dot{V}O_2$ peak from N was lower in UBX compared to LBX ($P<0.05$, mode × F_IO_2). Post hoc tests revealed reductions between each F_IO_2 in LBX (N, 3.52 ± 0.50 *vs.* H_1, 3.04 ± 0.46 L.min^{-1}, $P<0.001$; H_1 *vs.* H_2, 2.68 ± 0.27 L.min^{-1}, $P<0.05$). Whereas significant reductions were not evident between each F_IO_2 in UBX (N, 2.53 ± 0.35 *vs.* H_1, 2.15 ± 0.40 L.min^{-1}, $P<0.001$; H_1 *vs.* H_2, 2.04 ± 0.34 L.min^{-1}, NS). The relative reduction in $\dot{V}O_2$ peak from that at N being similar between exercise modes (H_1, 13 ± 8 and 15 ± 6; H_2 23 ± 6 and 19 ± 8 % for LBX and UBX respectively). Peak BLa did not vary with F_IO_2 and was highest during LBX exercise e.g. H_2, LBX 11.5 ± 2.4 vs. UBX, 10.6 ± 2.1 mmol ($P<0.01$, main effect). The lowest SpO_2 recorded in the final work stage declined between N (LBX and UBX, 96 ± 2%) and H_1 (LBX, 83 ± 4 % and UBX, 85 ± 5 %, $P<0.001$) and H_2 (LBX, 73 ± 4 %, $P<0.001$; UB 79 ± 4 %, $P<0.01$); with the magnitude of reduction being greater in LBX compared to UBX at H_2 ($P<0.01$). Whereas peak HR declined with F_IO_2 ($P<0.01$, main effect) and was lower in UBX at each F_IO_2 e.g. H_2 UBX, 176 ± 14 vs. LBX, 183 ± 13 bt. min^{-1} ($P<0.001$, main effect). Further analyses estimated that oxygen extraction ($\dot{V}O_2$/ O_2 delivery) during the last minute of exercise did not vary with F_IO_2 and was lower in UBX (0.61 ± 0.05) compared to LBX (0.85 ± 0.07; $P<0.05$) at volitional exhaustion.

Conclusions: These data indicate that the relationship between F_IO_2 and $\dot{V}O_2$ peak varies between LBX and UBX in the same subjects. The F_IO_2s used are representative of terrestrial altitudes often used for training and competition. Such findings are potentially relevant to both able bodied and paralympic athletes conducting predominantly UBX at altitude and form the basis for further study.

Reference: Thake, C. D., Simons, C and Price, M. J. (2008). The effect of acute hypoxia on the VO_2 peak during upper compared to lower body exercise. *Proceedings of the British Paralympic Association Conference*, Loughborough, March 2008.

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