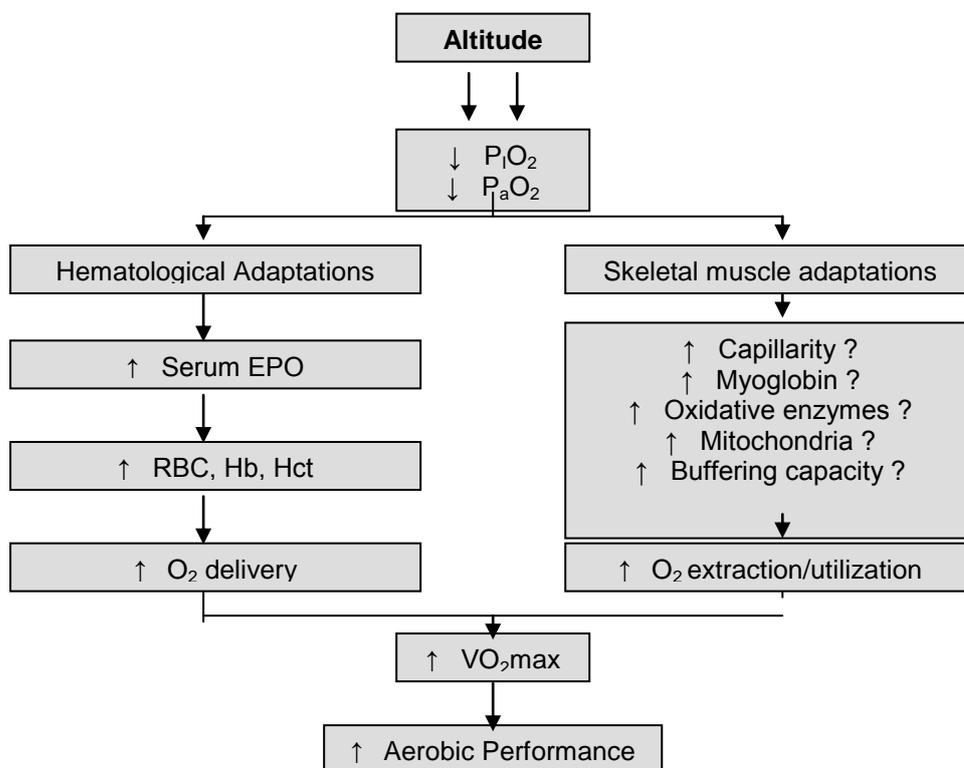


# Simulated Altitude Research Overview

## Benefits of Altitude Training

Altitude training has been integrated into athlete preparation and rehabilitation strategies comprehensively for the past five decades by elite endurance athletes, with the goal of improving performance (Gore, 2007). In general, the various systems of the human body – pulmonary, cardiovascular, endocrine, skeletal muscle – respond and adjust to normobaric (simulated) and hypobaric hypoxia (actual) altitude training in an effort to provide sufficient oxygen to survive in the hypoxic environment (Wilber 2004). Some mechanisms of physiological adaptation associated with simulated and actual altitude training have the potential to enhance athletic performance, particularly in endurance and repeated high intensity effort based sports and activities, including tactical and military environments. Figure 1 below, outlines the known physiological responses and subsequent performance benefits associated with simulated and real altitude training.



**Figure 1 Summary of physiological benefits of using altitude training for enhancement of aerobic performance. (Wilber 2004)**

↑ = increased or enhanced  
 ↓ = decreased  
 ? = potential adaptation  
 (research not conclusive)

EPO = erythropoietin  
 Hb = hemoglobin  
 Hct = hematocrit  
 RBC= red blood cells

P<sub>a</sub>O<sub>2</sub> = partial pressure of oxygen (arterial blood)  
 P<sub>I</sub>O<sub>2</sub> = partial pressure of inspired oxygen  
 VO<sub>2</sub>max = maximal oxygen consumption

### Maximum Oxygen Consumption (VO<sub>2</sub>max) and Lactate Threshold – Endurance Performance (Evidence)

- Increased maximal oxygen uptake (VO<sub>2</sub> Max) which is primarily as a result from the increased in red blood cells and increased ability to deliver oxygen.
- Anaerobic capacity and performances are enhanced as a result of using a hypoxic apartment (**Wilber, 2001; Roberts et al 2000**)
- Increases in VO<sub>2</sub>max (l.min<sup>-1</sup> and ml.kg.min<sup>-1</sup>), lactate threshold, simulated 30km time trial (TT) performance and mean power for the TT in trained male cyclists following 3wk of hypoxic training (**Czuba et al 2011**). Two groups of 10 male cyclists (VO<sub>2</sub>max = 67.7 and 67.8 ml.kg.min<sup>-1</sup>) completed identical training programme with the addition of 15.2% inspired oxygen concentration (approximately 2600m simulated altitude) to 3 x 1hr sessions per week, controls same training at 21% inspired oxygen concentration. SaO<sub>2</sub> 80-85% during hypoxic sessions and 94-95% in normoxia.
- **Rodriguez (1999)** compared an exercising vs non-exercising group over 9d at simulated altitude (4000m-5500m) for 3-5hrs/day. Significant increases in maximal exercise time and maximal pulmonary ventilation possibly as a result of improved haematological values and well as an increase in the lactate threshold.
- **Katayama (2003) and Roels (2005)** - increase in VO<sub>2</sub>max following hypoxic exposure (resting exposure and intermittent hypoxic interval training (IHIT) respectively) despite no change in haematological parameters.

### Haematological parameters (Evidence)

Increased red blood cells: body increases its number of red blood cells in response to the stimulus of training at altitude. As red blood cells carry oxygen to the working muscles, an increase in the number of red blood cells allows an increased work capacity as the working muscles are receiving more oxygen.

- **Rusko et al 1995; Laitenan et al 1995; Mattila and Rusko 1996** - Normobaric hypoxic apartment (simulated altitude) may produce beneficial changes in serum EPO levels, reticulocyte count and red blood cell mass, which in turn may lead to improvements in performance.
- **Rodriguez (1999)** - Significant increases in Hct, RBC count, reticulocyte count and Hb concentration (all associated with increased blood oxygen transport), yet no difference between groups- indicating that hypoxia alone was responsible for the changes.
  - Conclusion - very short term intermittent exposure to moderate hypoxia activates the erythropoietic response and improves endurance capacity in healthy subjects.
- **Eckhardt 1989** - An increase in EPO has also been found following 5.5hrs exposure to hypoxia (3000-400m) in a rested state
- **Levine et al. (1991)** found that levels of erythropoietin (EPO) almost doubled, and haemoglobin concentration (Hb) was increased, in elite athletes after 27 days of living at 2500m and training at 1250 m.
- **Stray-Gundersen et al. (1998)** investigated the effects of 27 days of living at moderate altitude of 2500 m, training intensively at 1250 m, and undergoing base training at both 1250 and 3000 m. They observed a 92% increase in EPO within the first 20 hours of exposure. After the 27 days of LHTL, Hb, haematocrit (Hct) and arterial O<sub>2</sub> saturation (SaO<sub>2</sub>) were increased. (**Millet et al 2010**)
- **Hamlin 2010** - duration of hypoxic exposure is the most important factor when considering the effects of erythropoietin release (Hamlin 2010).
- **Dehnert et al. (2002)** investigated the haematological acclimatization to intensive training at low altitude (800 m) and spending 13 h/day at moderate altitude (1960 m) in 15 male and six female triathletes over a period of 2 weeks. EPO increased significantly (30%) but temporarily in LHTL. Total Hb was unchanged in the LHTL group but showed a small significant decrease in the control sea-level group. Reticulocyte (Ret) count also showed a tendency to increase in the LHTL group, but was unchanged in the control group. Suggested that the observed EPO stimulation at altitude served to compensate for the exercise-induced destruction of red blood cells (RBCs).

- **Laitinen et al.(1995)** observed in seven male trained runners who lived 16–18 h/day at a simulated altitude of 2500m and lived and trained the other 6–8h/day at sea level, sEPO (84%) and RBC mass (7%) to be significantly increased (by 84% and 7% ,respectively) after 15 days of LHTL, and remain unchanged in the sea-level control group.

#### **Enhanced Mitochondrial function (Evidence)**

- **Ponsot (2006)**. After a 6 week training program, mitochondrial function was increased (through qualitative but not quantitative changes) demonstrated by an increase in Km for ADP. Represents a shift in mitochondrial respiration to a more oxidative state facilitating coupling between energy demand and supply resulting in an increase in time to exhaustion and VO<sub>2</sub>max. The results occurred with only 12-20mins of hypoxic exposure (14.5% O<sub>2</sub>) at VT<sub>2</sub>, twice a week.
- **Katayama (2004) and Serebrovskaya (2002)** both found a downward trend in the oxygen cost during submaximal power outputs suggesting an alteration in mitochondrial respiration, allowing it to be more economical and efficient in oxygen transport. I.e. This change may increase the amount of ATP produced per mole of oxygen consumed, resulting in less oxygen required for the same amount of energy produced. Katayama (2004) results occurred without the use of hypoxic training, instead using **passive hypoxic exposure** of 3hrs/day for 12days at 12.3% O<sub>2</sub>.

#### **pH Regulation and Muscle Buffering Capacity (Evidence)**

Lactate buffering: increased number of red blood cells then allows lactate buffering to occur (through increased bicarbonate and haemoglobin levels) and the muscles can produce a higher amount of work and produce less lactic acid. Altitude-induced increase in the co-transport of lactate is related to the increase in the content of the relevant transporters (i.e. monocarboxylate MCT1 and MCT4). May facilitate lactate exchange and removal and a slower pH decrease within 'glycolytic' exercise. (**Zoll et al 2006**).

- **Juel et al (2003), Gore et al (2007), Gore et al (2001) & Mizuno et al (1990) (Millet et al 2010)** altitude acclimatization induces an increase in isoforms of carbonic anhydrase (CA) that influence both H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup> regulation = likely to improve muscle buffering capacity, and may be important in the explanation of post-altitude improvement in performance.
- **Taylor et al. 2010** - An increase in heat shock protein (HSP), one of the hydrogen ion buffering proteins, has been reported in response to exposure to hypoxia. Increases in the concentration of this protein and other proteins can contribute to an improved tolerance to the anaerobic component of intense exercise.
- **Taylor et al (2011)** - sought to use a hypoxic stimulus to elicit increases in HSP72 and HSP32 in an attempt to confer protection to the oxidative rigours of sub-maximal aerobic exercise. Eight healthy recreationally active male subjects performed 60 min cycling on a cycle ergometer prior to (EXB1) and following (EXB2) five consecutive days of once daily hypoxia (2980 m, 75 min). Significant increases were found in HSP72, HSP32, oxidised glutathione and TBARS in response to the 5 day hypoxic intervention. Exercise induced significant increases in HSP72 and HSP32 post exercise in EXB1, this response was absent for post EXB2. The hypoxia mediated increased bio-available HSP32 and HSP72 prior to exercise commencing in EXB2 compared to EXB1. Furthermore, the favourable alterations in glutathione redox, before commencement of EXB2 compared to EXB1, may also contribute to this reduction in the oxidative cost of this sub-maximal aerobic exercise.
- **Abellan et al (2005)** 16 male triathletes who were exposed 3 hours a day for 5 days a week over 4 week to a progressively increased simulated altitude (4000–5000 m), observed significant 100% and 440% increases in sEPO 3 hours after the first and last IHE sessions, respectively.
- **Hellemans (1999)** investigated the effects of a different IHE method that consisted of alternating 5 minutes of inhaling low O<sub>2</sub> gas mixture with 5 minutes of ambient air during 60 minutes. The protocol was two IHE sessions a day during 20 days in ten elite endurance athletes. The FIO<sub>2</sub> was ~10% (5800 m) for the first 10 days and then ~9% (6400 m) for the last 10 days. Significant increases in Ret count (29%), Hb (4%)and Hct (5%) were reported.

### Physiological responses to exercise at altitude

The extent to which individuals adjust and adapt to the stress imposed by exposure to high altitude. Included among these are:

- the degree of hypoxia
- the duration of exposure to hypoxic conditions
- the exercise intensity (absolute vs relative workload)
- the inter-individual variability in adapting to hypoxic environments ('responders' vs 'non-responders').

Decrease in inspired O<sub>2</sub> and resulting drop in SaO<sub>2</sub> with high altitude exposure represents significant disruption in resting homeostasis. A number of essential physiological and metabolic adjustments are required to ensure proper tissue oxygenation in response to imposed stress d/t hypoxia (**Mazzeo 2008**).

### Acute responses: cardiovascular

- $VO_2 = Q \times (a-v)O_2$  difference
- $VO_2 =$  function of blood flow (Q) and O<sub>2</sub> utilisation (a-v)O<sub>2</sub> dif
- $Q = HR \times SV$
- Initial exposure =  $\uparrow HR$  & Q to compensate  $\downarrow$  O<sub>2</sub> content of blood. (**Mazzeo 2008**).

### Heart Rate

- $\uparrow Q$  results from stim of cardiac  $\beta$ -adrenergic receptors by cardiac sympathetic nerves and circulating adrenaline
- SNS activated by short and long term exposure to high altitude (arterial adrenaline and nor-adrenaline levels) (**Mazzeo 2008**).

### Stroke Volume

- SV is the other factor contributing to Q
- Initial exposure to high altitude, SV appears to be only marginally affected (lower compared with sea level) during submaximal exercise. (**Grover et al 1986**)
- With a more prolonged exposure to altitude, SV clearly declines over time, stabilising after 1–2 weeks.
- While the factors responsible for this alteration in SV are unknown, loss of plasma volume, a well-documented adaptation associated with high-altitude exposure, may play a role.
- A loss in plasma volume will result in a reduction in venous return and, consequently, left ventricular filling thereby yielding a lower SV. (Frank Starling effect) (**Mazzeo 2008**).
- Possible increase in afterload may also contribute to reduction in SV over time.
- Elevated SNS activity initially results in  $\uparrow$ system vascular resistance & mean arterial BP.
- With acclimatisation (1-3wks) for given power output there is a  $\downarrow Q$  d/t  $\downarrow SV$  d/t  $\downarrow$ venous filling and  $\downarrow HR$  linked with attenuation of cardiac responsiveness to  $\beta$ -adrenergic stimulation (**Roach et al 1999, Wagner 2000**)

### Muscle energetics and substrate utilisation

- Generally accepted that exposure to hypoxia results in alteration in substrate utilisation at rest and during ex (**Braun et al 2000, Brooks et al 1991**).
- $VO_2$  max declines progressively with increasing altitude.
- Resultant similar absolute workload performance at sea level represents greater relative exercise intensity when performed at altitude.
- Reliance to CHO as fuel source known to increase with increased intensity (**Brooks et al 1994**).

### Hypoxia inducible factor (HIF-1)

Hypoxia inducible factor (HIF-1) is a specific oxygen-sensing transcription factor that plays pivotal role for the functional adaptations to hypoxic training.

- **Clerici et al 2000** - HIF-1 stimulates angiogenesis and glycolytic enzyme activity, cell glucose transporters, muscle lactate metabolism, carbonic anhydrase for enzymes that regulate pH and others that produce vasodilators such as nitric oxide .

- **Levine et al 1997** - hypoxia causes a multitude of responses in the human body including but not limited to changes in red cell mass, angiogenesis, glucose transport, glycolysis, pH regulation, and changes in the efficiency of energy production at the mitochondrial level which could all potentially have a positive impact on exercise performance, potentially all of these mechanisms either solely or combined could be the cause of enhanced sea-level performance after altitude training
- **Vogt (2001)** studied 4 groups of subjects who trained 5 days a week for 6 weeks. Subjects were divided into hypoxia (3580m) and normoxia as well as high (Blood lactate=4-6mM) and low intensity (2-3mM) training. The level of HIF-1a mRNA increased after training under hypoxic conditions, irrespective of the level of training intensity. Myoglobin and VEGF (vascular endothelial growth factor) were also increased but only after the high intensity hypoxia protocol, concluding that high-intensity training in hypoxia elicits molecular and structural adaptations favouring oxygen transport and utilization in human skeletal muscle under oxygen-restricted conditions and may result in enhanced exercise performance at altitude.
- **Dufour (2006)** has expressed the importance of sufficient hypoxic exercise intensity and duration within intermittent hypoxic training (IHT) programs in order to reduce oxygen pressure in the active muscle and achieve a substantial HIF-1 in order to obtain significant performance improvements in already trained athletes.

### **Non-Haematological Adaptations**

#### **Economy**

- Schmitt et al (2006), Gore et al (2001), Gore et al (2007), Saunders et al (2004), Neya et al (2007) have demonstrated 3–10% improvements in exercise economy with altitude training that may be associated with a decreased cost of ventilation, greater carbohydrate (CHO) use for phosphorylation, or, more likely, from improved mitochondrial efficiency (as denoted by P/O ratio or an increase in ATP production per mole of oxygen used).

### **Simulated Live Low / Train High (Intermittent Hypoxic Exposure)**

Simulated altitude affords athletes with the ability to live low (sea level) and train high (completing training sessions at altitude) to enable an intermittent hypoxic exposure (IHE) training paradigm to optimise adaptation and performance.

Intermittent Hypoxic Exposure (IHE) is based on the concept of repetitive brief exposure to hypoxia (1.5 to 2.0) hrs to stimulate EPO (**Wilber 2001**). Based on these findings, it is assumed IHE will be sufficient to bring about significant increments in serum EPO levels and RBC concentration and therefore, ultimately enhance VO<sub>2</sub> max and endurance performance (**Wilber 2001**).

- **Rodriguez et al (2000)** - After IHE in progressively increased hypobaric hypoxia (4000–5500 m) for 90 minutes three times a week for 3 weeks, reported a significant increase in Ret count (180%), RBCs (7%), Hb (13%) and Hct (6%) - demonstrated that 90 minutes of passive hypoxic exposure was sufficient to obtain significant changes in haematological parameters.
- **Terrados et al (1988)** investigated 8 elite male cyclists, splitting them into two groups. One group trained at sea level whilst the other group trained in a hypobaric chamber at a simulated altitude of 2300m. The group exposed to the simulated altitude training demonstrated significant improvements in total work capacity (33%) and maximal power output (12%) during an exhaustive cycling test.
- **Meeuwssen (2000)** undertook additional research involving triathletes and IHE and demonstrated significant improvements in anaerobic power and anaerobic capacity
- **Dufour et al (2006)** - found significant improvements of several indexes of aerobic performance capacity, not only at altitude, but also at sea level; these include VO<sub>2</sub> max and time to exhaustion - suggests enhanced endurance performance capacity obtained with IHE might be due to specific muscle adaptations to hypoxic training.

IHT may be more efficient at improving haematological parameters if combine with IHE.

- **Rodriguez et al.(1999)** examined the combined effects of IHE and IHT in 17 subjects who conducted a high-altitude expedition. IHE consisted in an exposure of 3–5h/day for 9 days at altitudes that progressively increased (from 4000m to 5500 m). In addition, the subjects had to perform three to five training sessions a week (30–75 minutes each) at low intensity. The authors observed a significantly increased RBC (+12%), Ret (+54%), Hb (+18%) and Hct (+11%) when the data of both groups were combined. These authors concluded that IHE in hypobaric hypoxia could stimulate the erythropoietic response.
- **Casas et al (2000)** using the same protocol as Rodriguez et al (1999) for 17 days, found significant increases in packed cell volume from 41% to 44.6%, in RBC from 4.61 to 4.97 10<sup>6</sup> cells/mL and in Hb from 14.8 to 16.4 g/dL. authors suggested that short-term hypobaric hypoxia with low-intensity training induced an improvement in the blood oxygen transport capacity

### Sprint performance

- **Meeuwssen (2001) and Hendrickson (2003)** - found that 10 consecutive days of 2hrs cycling at 60-70% HRR (heart rate reserve) at 2500m (simulated altitude) provided an additional effect on the anaerobic system vs sea level as a result of an enhanced stimulus for adaptation demonstrating that low intensity training during intermittent exposure to hypoxia can improve aerobic and anaerobic systems. Hypoxic training resulted in an increase in maximal power output, anaerobic mean power and aerobic peak power.
- **Hamlin (2010)** - 10 consecutive days of IHT substantially enhanced anaerobic power during a 30s Wingate cycle test - subjects only completed 90mins (vs 2hrs) of training at 60-70% HRR but had the addition of 2x30s all out sprints at the end of each session as well as decreasing oxygen concentration over the 10days to allow for adaptation (simulated equivalent of 3200m-4400m). 30s Wingate test performance improved by 3% and mean 30s power increased.

### Resistance training.

- **Nishimura et al (2010)**. Resistance training during acute exposure to hypoxia before returning to normal air conditions demonstrated a positive impact on the training and adaptive response.
- **Kon et al (2010)** showed that resistance training in hypoxia (13% O<sub>2</sub>) caused greater increases in lactate (an indication of exercise intensity), epinephrine, norepinephrine and growth hormone. Both the intensity of the exercise and GH are highly correlated with the level of hypertrophy and strength gains. This study demonstrated that resistance exercise under hypoxia induces a greater anabolic hormone response than that under normoxia.
- **Kon (2011)** - determine the effects of resistance exercise training under systemic hypoxia on hormonal responses and muscular adaptations. 8weeks of resistance training in normoxia or hypoxia (14.4 %), muscle CSA of the femoral region and 1RM in bench and leg press were increased. However there was no significant difference between groups. Following hypoxic resistance training (but not normoxia) there was an increase in exercise volume, testosterone/cortisol ratio and plasma vascular endothelial growth factor (VEGF). The findings suggest that resistance exercise training under systemic hypoxia caused greater hormonal responses and greater increases in muscular endurance than that under normoxic conditions

### Body Composition

- **Haufe (2008)** identified a reduction in triglyceride (representing greater lipid oxidation) and body fat levels following 3/wk x 60mins x 4weeks at 15%O<sub>2</sub> at a moderate intensity despite exercising at a lower workload (but same cardiovascular intensity) than the normoxic group.
- **Burtscher (2010)**. Body mass decreased following the first 5 weeks of hypoxic exposure (2hrsx 3/wk resting exposure at 15-11% O<sub>2</sub>)

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