

Review

Hypoxic training methods for improving endurance exercise performance

Jacob A. Sinex, Robert F. Chapman *

School of Public Health, Department of Kinesiology, Human Performance Laboratory, Indiana University, Bloomington, IN 47401, USA

Received 17 March 2015; revised 15 June 2015; accepted 9 July 2015

Available online 23 July 2015

Abstract

Endurance athletic performance is highly related to a number of factors that can be altered through altitude and hypoxic training including increases in erythrocyte volume, maximal aerobic exercise capacity, capillary density, and economy. Physiological adaptations in response to acute and chronic exposure to hypoxic environments are well documented and range from short-term detrimental effects to longer-term adaptations that can improve performance at altitude and in sea-level competitions. Many altitude and hypoxic training protocols have been developed, employing various combinations of living and training at sea-level, low, moderate, and high altitudes and utilizing natural and artificial altitudes, with varying degrees of effectiveness. Several factors have been identified that are associated with individual responses to hypoxic training, and techniques for identifying those athletes most likely to benefit from hypoxic training continue to be investigated. Exposure to sufficiently high altitude (2000–3000 m) for more than 12 h/day, while training at lower altitudes, for a minimum of 21 days is recommended. Timing of altitude training related to competition remains under debate, although general recommendations can be considered.

© 2015 Production and hosting by Elsevier B.V. on behalf of Shanghai University of Sport.

Keywords: Altitude; Hypoxia; Performance; Training

1. Introduction

Altitude and hypoxic training is common among endurance athletes and recommended by many coaches for potential benefits during subsequent competition at or near sea-level. As altitude increases, atmospheric pressure decreases, and although the fractional concentration of oxygen remains the same (20.9%), the partial pressure of oxygen decreases, reducing the amount of oxygen available for delivery to exercising tissues. Altitude classifications have been developed (Table 1) to roughly delineate altitudes at which different physiological changes and stressors are observed.¹ Several aspects related to endurance performance may be altered by hypoxic exposure and training including increases in erythrocyte volume, maximal aerobic exercise capacity, capillary density, and economy. In the modern era of sport, increasingly sophisticated anti-doping controls, such as the World Anti-Doping Agency (WADA) biological passport program, leave elite athletes with few choices of legal ergogenic aids that have the potential to substantially improve performance, and altitude/hypoxic training is among them. The efficacy of altitude/hypoxic training and the best practices for its

use are still being debated in research circles, while athletes congregate in altitude training camps and use altitude simulation devices in the pursuit of improved exercise performance.

This review discusses some of the physiological adaptations to exposure to hypoxia, models that have been developed for hypoxic training to improve endurance exercise performance and considerations for optimizing altitude training in relation to individual response variation, determining how high to go and for how long and timing the return to sea-level.

2. Expected performance outcomes

While not all studies have demonstrated improved endurance exercise performance after exposure to hypoxia, altitude and hypoxic exposure, when appropriate protocols are used, do

Table 1
 Altitude classifications.

Classification	Altitude (m)	Altitude (ft)	Equivalent FiO ₂ (%)
Near sea-level	<500	<1640	19.8–20.9
Low altitude	500–2000	1640–6560	16.7–19.8
Moderate altitude	2000–3000	6560–9840	14.8–16.7
High altitude	3000–5500	9840–18,040	10.9–14.8
Extreme altitude	>5500	>18,040	≤10.9

Adapted from Bärtsch et al.¹ with permission.

Abbreviation: FiO₂ = fraction of inspired oxygen.

* Corresponding author.

E-mail address: rfchapma@indiana.edu (R.F. Chapman)

Peer review under responsibility of Shanghai University of Sport.

Table 2
Artificial hypoxic training protocols.

Protocol	Hypoxic duration (h/day)	Artificial altitude (m)	Hypoxic devices	Mean effect of protocol (effect probability)	
				Elite	Subelite
Long continuous LHTL	8–18	2200–3500	N ₂ house, N ₂ tent	-0.6 ± 2.0 (>5% ↑/↓)	1.4 ± 2.0 (≥50% ↑)
Short continuous LHTL	1.5–5.0	3650–5500	N ₂ tent, hypobaric chamber	—	-0.7 ± 2.5 (>5% ↑/↓)
Brief intermittent LHTL	0.5–1.5	3400–6000	Inhaler	-0.2 ± 1.8 (>5% ↑/↓)	2.6 ± 1.2 (≥50% ↑)
LLTH	0.2–2.0	2500–4500	Inhaler, hypobaric chamber, N ₂ house	—	-0.9 ± 2.4 (>5% ↑/↓)

Notes: Effect probability refers to “probabilistic outcomes with reference to the smallest important change of 1%”; a percent chance of enhancement (↑) and/or impairment (↓) of performance or (—) where sufficient data were not available. Adapted from Bonetti and Hopkins² with permission.

Abbreviations: LHTL = live-high train-low; LLTH = live-low train-high.

lead to improved performance in sea-level endurance exercise when training camp and group training effects are controlled.² In an extensive meta-analysis, Bonetti and Hopkins² concluded that artificial altitude protocols using long continuous exposure or intermittent exposure and training low (Table 2) improve endurance exercise performance in subelite athletes, while natural altitude protocols improve performance in both elite and subelite endurance athletes (Table 3) when a live-high train-low (LHTL) protocol is utilized.

Further discussion of the factors that contribute to enhancements, impairments or insignificant changes in endurance performance at sea-level follows in this review. Briefly, red blood cell (RBC) and hemoglobin (Hb) content appear to be major factors contributing to (but probably not solely responsible for) increases in maximal oxygen uptake (VO_{2max}) observed after altitude training.^{3,4} Additional contributing factors to performance changes after altitude/hypoxic training include ventilation (or the perception of ventilation/dyspnea), the ability to train in hypoxia, timing of return from altitude training before primary performance measures, and the mode of exercise utilized (e.g., swimming, running, cycling).⁵

In addition to commonly discussed RBC and Hb mass changes, improved exercise economy has been argued as a potentially important mechanism contributing to performance improvements after altitude/hypoxic exposure. For example, running economy improved by ~3.3% at submaximal pace after 20 days of artificial LHTL conditions in a group of elite distance runners⁶ without substantial changes in Hb mass, suggesting that RBC production and Hb mass are not the only factors contributing to expected performance outcomes from altitude/hypoxic exposure. A subsequent study⁷ by the same group at the Australian Institute of Sport used a similar design with ~6–7 weeks of artificial LHTL and observed improved exercise

economy as well as increases in Hb mass, but the changes in Hb mass were not strongly correlated to changes in exercise economy. In contrast, 156 athletes studied by multiple research groups showed no changes in economy after altitude,⁸ demonstrating the complex nature of altitude training and potential performance improvements.

The focus of this review is sea-level performance improvements from altitude/hypoxic training, but it should be noted that hypoxic exposure can also be utilized to improve performance at altitude. In studies conducted by the United States Army Research Institute of Environmental Medicine,^{9,10} daily hypobaric hypoxic exposure for 7 and 15 days prior to exercise in hypobaric hypoxia improved performance at 4300 m by as much as ~21% during cycling exercise of ~25–30 min in duration. However, follow-up studies by the same group found no improvement in performance using similar treatments with normobaric hypoxic exposure,^{11,12} which may suggest that hypobaric and normobaric hypoxia do not induce the same adaptations or that “equivalent” protocols using each type of hypoxia are not equivalent in practice. Further discussion on the topic of hypobaric versus normobaric hypoxia is covered in detail in a 2012 issue of the *Journal of Applied Physiology*.^{13,14}

3. Physiological adaptations to hypoxic training

Physiological adaptations in response to acute and chronic exposure to hypoxic environments are well-documented and range from short-term detrimental effects necessitating reduced training loads to longer-term adaptations that can improve performance at altitude and in sea-level competitions. Balancing the positive adaptations that result from training in hypoxia while minimizing effects that can lead to detraining or maladaptation is key to obtaining the greatest benefit from hypoxic training.

Table 3
Natural altitude training protocols.

Protocol	Hypoxic duration (h/day)	“Live” altitude (m)	“Train” altitude (m)	Mean effect of protocol (effect probability)	
				Elite	Subelite
LHTH	24	1200–2700	1600–2400	-1.6 ± 2.7 (>5% ↑/↓)	-0.9 ± 3.4 (>5% ↑/↓)
LHTL	18–24	1800–2800	800–1250	4.0 ± 3.7 (≥50% ↑)	4.2 ± 2.9 (≥50% ↑)

Notes: Effect probability refers to “probabilistic outcomes with reference to the smallest important change of 1%”; a percent chance of enhancement (↑) and/or impairment (↓) performance. Adapted from Bonetti and Hopkins² with permission.

Abbreviations: LHTH = live-high train-high; LHTL = live-high train-low.

In the short-term, several physiological changes occur that may be disadvantageous to the endurance athlete. Immediate notable changes that may limit exercise performance include increased ventilatory work and dyspnea, increased oxidative stress, plasma volume loss and dehydration, possible jet lag due to travel, decreased training intensity, sunburn due to increased exposure to ultra-violet light, and decreased cardiac output.¹⁵ For these reasons, training volume and intensities may need to be reduced in the days immediately following travel to altitude.¹⁶

Almost immediately, peripheral chemoreceptor mediated increases in ventilation occur. The increase in ventilation causes expiration of larger than normal quantities of carbon dioxide, which results in hypocapnia and respiratory alkalosis. The effect of the shift toward alkalosis inhibits the central respiratory center, reducing the increase in ventilation to some extent. To compensate for the alkalosis, the kidney increases excretion of bicarbonate and reduces clearance of hydrogen ions, helping to lower pH and allowing ventilation to increase further.¹⁷

Within hours of arrival at high altitude, plasma volume begins to decrease, the extent to which depends on elevation. Athletes traveling to moderate altitude should expect a plasma volume loss of about 10%–15%, beginning within the first few hours at altitude. The reduced plasma volume results in less preload to the heart, maximum cardiac output is reduced and thermoregulation may be impaired.¹⁸ Plasma volume is lost in part to compensate for changes in acid/base balance but may also be influenced by increased erythropoietin (EPO) production.¹⁹ The overall effect is to increase hemoconcentration and help maintain arterial oxyhemoglobin saturation until RBC volume increases and plasma volume returns to normal or greater.

Longer-term adaptations to altitude are primarily more beneficial to the athlete. These adaptations include increased erythrocyte volume and hemoglobin content, increased oxidative enzyme activity, increased mitochondrial volume, increased free fatty acid substrate utilization and increased capillary density.¹⁵ The measurement of Hb content or mass is a primary outcome variable in many studies of altitude and hypoxic exposure and consideration should be given to the sensitivity, validity, and reproducibility of the protocol used for this measure. Radioactive labeling is considered the gold standard²⁰ against which more commonly used CO-rebreathing methods are compared.²¹ Many CO-rebreathing methods for estimating Hb mass have been described, with CO-rebreathing times ranging from 2 to ~20 min depending on the protocol.²¹ In general, Hb mass estimates using CO-rebreathing are reproducible (~1.7%–3.3% coefficient of variation) and able to detect small changes in Hb mass (~2% error) when conducted correctly. Since being described in 2005 by Schmidt and Prommer,²¹ the 2-min CO-rebreathing method appears to be the most reliable method and the default choice for measuring Hb mass in recently published literature.

Among the first molecular and genetic changes that occur is increased activity of hypoxia inducible factor-1 (HIF-1), the master transcription factor regulator of oxygen homeostasis. HIF-1 has been identified as a key factor in the cascade of adaptations to hypoxic training. In normoxia, intracellular

levels of HIF-1 are low and HIF-1 is ubiquitinated and degraded, maintaining a steady-state activity level in the regulation of the genes that HIF-1 influences. In hypoxia, HIF-1 ubiquitination is inhibited which increases HIF-1 stability and its transactivation function, allowing HIF-1 to bind target genes and increase target gene transcription. HIF-1 targets a number of genes, including those involved in angiogenesis and upregulation of glycolysis.²² In the kidney, HIF-1 stimulates the specialized cells responsible for EPO production. HIF-1 is also involved in the coordination of iron uptake, delivery to bone marrow for Hb production and activating transcription of the EPO receptor,²³ all changes that lead to improved oxygen transport through the circulatory system.

Increased EPO production can be detected within a few hours of exposure to altitude and new erythrocytes are in circulation within 4–5 days.²⁴ Plasma EPO levels tend to peak within 48–72 h following initial exposure to altitude and slowly return to baseline in 2–4 weeks.²⁵ Within a few weeks, RBC volume and Hb content can increase substantially, while plasma volume remains depressed,²⁶ increasing the oxygen carrying capability of a given unit of blood. However, these hematological adaptations do not persist indefinitely. RBC volume is reduced fairly quickly upon return to sea-level, in a process called neocytolysis, which involves reducing RBC count primarily through the destruction of young RBCs.²⁷ In a group of world class biathletes, total Hb mass and RBC volume increased after 3 weeks of altitude training, with these parameters returning to baseline by the post-altitude test 16 days after return to sea-level.²⁸

4. Hypoxic training models

A number of different altitude and hypoxic training models have been developed, employing various combinations of living and training at sea-level, low, moderate, and high altitudes and utilizing natural/terrestrial and artificial altitudes. Further, within artificial altitude models, both normobaric hypoxia, where atmospheric pressure is unchanged but the fraction of inspired oxygen is decreased, and hypobaric hypoxia, where atmospheric pressure is decreased while fractional oxygen content is not manipulated, have been utilized in both research and training scenarios.

The classic model of altitude/hypoxic training is the live-high train-high (LHTH) approach, where athletes travel for 3–4 weeks to a moderate altitude (generally recommended to be between 2000 and 2500 m) and spend all of their time living and training at this altitude. Following the strong performances of East African runners at the 1968 Olympics in Mexico City (elevation 2250 m), Western athletes began to incorporate periods of living and training at moderate altitudes in the hopes of induce increasing RBC volume and training stress through increased tissue hypoxia compared to sea-level workouts. However, the results of early studies on the LHTH model were mixed with regard to effects on performance at sea-level.²⁹ A recent meta-analysis concluded that LHTH may have a positive effect on sea-level performance for both elite and subelite athletes.² Not many studies with adequate and strict controls have been conducted using this model, although it remains

probably the most commonly used in practice by endurance athletes, likely due to logistical issues involved with living at altitude and traveling to lower elevations to train. In a study using a crossover design, 12 middle-distance runners were divided into two groups and performed 3 weeks of training at either sea-level (760 mmHg) or altitude (2300 m, 586 mmHg), followed by 3 weeks of training in the opposite condition, at the same relative intensity. Overall, altitude training did not provide any benefit over sea-level training in terms of VO_{2max} , which was 2.8% lower than sea-level control, or 2 mile run performance, where both groups were similarly slower in the post-training trial at altitude. A delayed improvement in performance after altitude training has been reported for amateur runners, occurring approximately 2 weeks after return to sea-level,³⁰ while performance was found to be depressed for up to 3 weeks after LHTH altitude training in elite runners.³¹ Elite runners may be more susceptible to detraining effects from reduced training volume and intensity, so the LHTH model should be considered with caution for this population.

The natural altitude model that has received the most attention since being introduced is the LHTL model.³² In this model, athletes live at moderate altitude (2500 m) and train at lower altitudes (1250 m). The purpose of training at lower elevations is to enable athletes to maintain training intensity and capillary to mitochondria oxygen flux in the exercising muscle, while still being exposed to hypobaric hypoxia for a significant portion of the day to stimulate EPO production and physiological adaptations that accompany elevated plasma EPO levels. This model seeks to avoid the decrease in training intensity that can occur when training exclusively at moderate altitude and mitigate the chance of a detraining effect. In this initial study, 39 competitive runners (27 men, 12 women) completed 4 weeks of supervised training at sea-level, followed by 4 weeks in one of three conditions: a) sea-level living and training, b) moderate altitude living and training, or c) moderate altitude living and low altitude training. Both altitude groups increased VO_{2max} (5%) and RBC volume (9%), while these parameters were not changed in the control group. Performance in a 5000 m run time trial at sea-level following training was improved only in the group that lived at high altitude and trained at moderate altitude. This was a groundbreaking study that pointed toward a mixed model of altitude training being as or more effective than the traditional LHTH model, and several follow-up studies demonstrated largely similar results.^{25,33,34}

Other variations on the LHTL model have been developed, such as the high-high-low (HHL) model, where living and low intensity training occur at moderate altitude and only high intensity training takes place at low altitude or sea-level. In a similar design to the original LHTL study, 22 elite distance runners trained for 4 weeks and were tested in a 3000 m run following altitude training.²⁵ Overall, performance significantly improved by 5.8 ± 9.2 s ($\sim 1.1\%$), suggesting that using an HHL model for logistical or other reasons is a suitable altitude training model to improve endurance performance.

While it may be ideal to spend 3 or 4 weeks at an altitude training camp while following the LHTL model, many factors can limit travel for athletes. Family, work and other personal

commitments, and expenses associated with food and lodging for a long training camp, have led researchers, coaches, and athletes to seek alternative hypoxic training models with the goal of obtaining the same benefits of terrestrial altitude training. The use of artificial altitude simulation for improving endurance performance has been investigated by a number of research groups. The different types of protocols used can generally be grouped into artificial long continuous LHTL, artificial short continuous LHTL, artificial brief intermittent LHTL, and artificial live-low train-high (LLTH) (Table 2). A thorough meta-analysis by Bonetti and Hopkins² determined that improvements in power output were very likely with artificial brief intermittent LHTL and possible with artificial long continuous LHTL in subelite athletes but performance improvements were not likely in elite athletes.

In a study of male subelite competitive cyclists and triathletes, athletes were exposed to intermittent hypoxia (artificial brief intermittent LHTL) for 15 days over 3 weeks for 60 min per day with either 3 or 5 min periods of hypoxia followed by the same duration in normoxia. Cycling performance improved during incremental step exercise, including increases of $4.7\% \pm 3.1\%$ in peak aerobic power, $4.4\% \pm 3.0\%$ in lactate profile power, and $6.5\% \pm 5.3\%$ in heart rate profile power compared to control measured 3 days post-intervention.³⁵ Fourteen days after treatment, differences between the hypoxia groups were unclear, suggesting that intermittent hypoxia training should be timed for competitive events to take place within a few days following treatment. In a similar study, performance did not improve among elite athletes,³⁶ suggesting that artificial brief intermittent LHTL should be considered mainly by subelite athletes.

For athletes with sufficient time and resources to complete an altitude training camp, it is recommended that the LHTL model, with terrestrial altitude exposure, be used when the goal is to improve performance at sea-level (Table 3). This model of altitude training has been demonstrated to increase red cell mass and sea-level endurance performance in runners,^{25,32,34} orienteers,³⁷ and swimmers.³⁸

5. Individual variation in response to hypoxic training

Like many different training strategies, not all individuals are expected to respond equally to training at altitude. Considerable variation in the individual response to altitude training has been documented,^{25,39} both in terms of physiological variables such as red cell and Hb mass as well as endurance performance. Several factors have been identified that are associated with individual responses to hypoxic training, and techniques for identifying those athletes most likely to benefit from hypoxic training continue to be investigated. The benefit derived from hypoxic training depends on the balance of achieving hematological adaptations while achieving adequate training volume and intensity.⁴⁰

An important consideration before beginning altitude training is the normalization of iron status, since iron is needed for the production of Hb and erythrocytes. Iron deficiency is relatively common among endurance athletes⁴¹ and can limit the increases in erythrocyte volume increases and Hb content if not

treated before beginning hypoxic training. After 4 weeks of altitude training at 2500 m, athletes with pre-existing iron deficiency did not increase RBC volume,⁴² despite a significant and sustained increase in EPO production at altitude. Several studies of altitude training have since included a period of iron supplementation prior to altitude training to account for this factor.^{32,33}

Individual differences in EPO production play a role in determining how RBC volume and Hb mass change in response to altitude and hypoxic training. Plasma EPO concentration, increases in RBC mass and total blood volume were found to differ between athletes who improved their 5 km run performance versus those who did not in a retrospective analysis.²⁵ Responders ($n = 17$, athletes who improved run time by 14.1 s or more) still had significantly higher plasma EPO concentration after 14 days at altitude, while EPO levels among non-responders ($n = 15$, those who performed worse after altitude training) nearly returned to pre-altitude levels during the same time, and EPO concentration increased to a greater extent among responders during the first 30 h at altitude. Responders showed improvements in VO_{2max} (6.5%) and red cell mass (7.9%) while neither characteristic changed in non-responders. Considerable individual variation in EPO response was also reported for elite junior swimmers training at altitude for 3 weeks, and acute changes in EPO levels (after 1–2 days at altitude) were not correlated with Hb mass change,⁴³ which is common among altitude training studies. Pre-screening for acute EPO response may someday be a method to predict responsiveness to altitude training, but further research is needed to determine the individual factors that determine acute EPO and long-term Hb mass and RBC volume changes. An interesting recent finding is that illness, injury or systemic inflammation may inhibit the EPO response and hematological adaptations of altitude training,^{44,45} which suggests that athletes who are ill prior to or become ill during an altitude training camp should consider ending their altitude camp in favor of recovering from illness.

Athletes who are able to maintain training intensity at altitude may benefit more from altitude training than those who have to reduce training intensity. While a number of factors are involved, the degree to which pulmonary gas exchange is limited during acute altitude exposure seems to be a primary factor that impacts performance at altitude. Trained athletes tend to show a greater impairment in performance compared to untrained individuals.⁴⁶ Within the trained athlete population, greater declines in VO_{2max} in hypoxia have been found in athletes who substantially decrease arterial oxyhemoglobin saturation (SaO_2) during high intensity exercise in normoxia.^{47,48} Additionally, running time trial performance is impaired to a greater extent among athletes who operate at a lower SaO_2 (less than approximately 92% at VO_{2max} in normoxia) compared to athletes who maintain SaO_2 (Fig. 1).⁴⁹ It may be worthwhile to prescreen SaO_2 levels at high intensity training workloads prior to sending athletes to altitude training. It should be noted that measurement of SaO_2 during exercise can be unreliable, especially when using many forms of commercially available pulse oximetry equipment.⁵⁰ Commercial pulse oximeters, such as

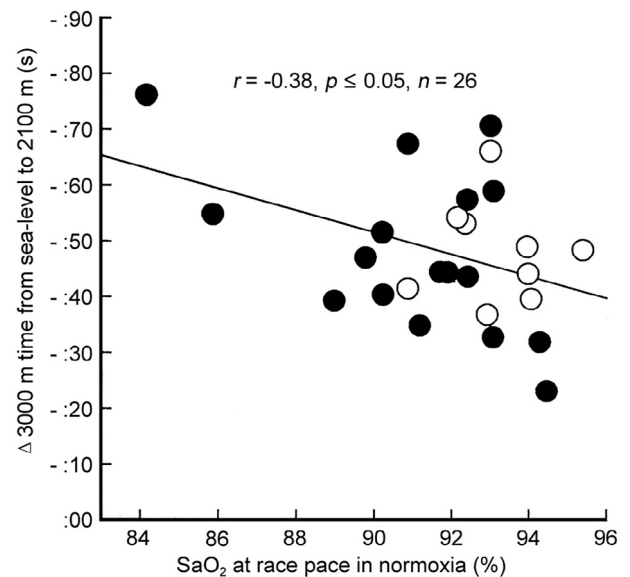


Fig. 1. Relationship between SaO_2 during race pace running in normoxia and the change in 3000 m race time from sea-level to an altitude of 2100 m. Closed circles indicate men; open circles, women. Reused with permission.⁴⁹

those used in hospitals, may not perform well during exercise, given increased blood flow, movement and vibration, and may not achieve high enough accuracy for reliably identifying athletes who desaturate during maximal exercise.⁵⁰ Athletes who do not adequately maintain SaO_2 during high intensity exercise would be advised to follow the LHTL model, especially when performing their highest intensity training sessions, and to seek the lowest possible altitude during those training sessions.

6. How high and how long

The selection of an appropriate altitude for training, the daily exposure to moderate altitude and the altitude at which training should occur are all important considerations. A number of factors influence these decisions including the time course of EPO response and RBC production, potential changes in exercise economy, desired training intensity and volume, as well as logistical concerns such as available time and financial costs. In general, living at 2000–2500 m while training at 1250 m or lower for 3–4 weeks with over 12 h of continuous altitude exposure per day appears to be sufficient to improve sea-level performance in most athletes.

The reduction in inspired oxygen partial pressure (PiO_2) that occurs with altitude ascent (or exposure to hypoxia) is the stimulus for increased EPO production, with greater increases in EPO production expected at increasing altitudes.⁵¹ The individual variability in EPO response increases from the low to moderate altitudes (1800–3000 m) where most altitude training camps are held. EPO concentrations were found to increase to a modest extent (24%–30%) at 1780 m and 2085 m, with peaks at 6 h after exposure, while 2454 m and 2805 m induced more substantial changes (77%–92%) that continued to rise through 24 h post-exposure.⁵² Additionally, some individuals displayed

remarkably greater EPO responsiveness to altitude exposure increasing EPO concentrations up to about 400% of baseline levels at the two higher altitudes. These data suggest that for sustained EPO production to be achieved, altitudes from around 2500 to 3000 m are probably more effective than lower altitudes. However, training at 2500–3000 m is difficult and training intensity and volume should probably be reduced if training has to take place at these altitudes.

The degree to which RBC volume and Hb mass increase is related to the number of hours in hypoxia,⁵³ and there appears to be a minimum threshold of about 12–13 h/day exposure to altitude/hypoxia needed to increase RBC volume and Hb mass substantially. The time spent at altitude in the LHTL studies conducted by the Levine and Stray-Gundersen group³² was about 20–24 h/day at 2500 m which achieved an increase in RBC mass of 9%. Rusko et al.⁵⁴ reported an increase of 5% RBC mass after athletes lived at a simulated altitude of 2500 m for 12–16 h/day. In contrast, 23 nights (8–10 h/night) in a nitrogen house with a simulated altitude of 3000 m were not sufficient stimulus to increase RBC production.⁵⁵ These data suggest that for hematological adaptations to occur, athletes should spend at least 12 h/day at altitude or in hypoxic conditions. However, athletes should be careful to avoid being sedentary outside of training, which is especially a concern if artificial hypoxia is utilized and athletes are confined to a bedroom or small apartment, as losses of plasma volume may result.⁵⁶

7. Timing altitude training to improve sea-level performance

Improving performance in the next competitive event or series of future events is the primary goal of many athletes who undertake altitude and hypoxic training. Timing the return to sea-level relative to competition can play a substantial role in the outcome of sport performance. Conventional wisdom for the time course of performance after altitude training includes several phases including initial improvements in performance (days 1–7), decrements in performance and reducing training capability (days 3–14) and a higher plateau in performance (days 14 to 18–20 or more),^{16,57} plus possible benefits from about 36 to 46 days after return to sea-level.¹⁶ There is some overlap in these blocks of time, indicating variability among athletes and sports and insufficient evidence to support more specific guidelines.

Performance has been reported to improve among subelite and elite endurance runners in the first few days after return to sea-level following training at altitude using the LHTL model. Levine and Stray-Gundersen³² reported that 5000 m run performance improved by an average of 13.4 ± 10.0 s ($\sim 1.5\%$) in their LHTL group of competitive (subelite) runners immediately upon return from sea-level. In a subsequent study with elite athletes and the same altitude protocol, elite runners were able to improve their 3000 m run performance by 5.8 s ($\sim 1.1\%$).³³ However, Levine and Stray-Gundersen³² also found that performance in the LHTH group did not improve from pre-altitude training to post-altitude training, suggesting that LHTL may be more effective than LHTH, at least when performance immediately after return to sea-level is the primary concern.

Robertson et al.⁵⁸ reported similar $1.1\% \pm 1.0\%$ improvements in 3000 m run performance in their artificial normobaric hypoxia LHTL + IHT (intermittent hypoxic training) group.

In the weeks following altitude training, performance changes are less clear and possibly more variable than immediately after altitude training. Many altitude studies have not included performance trials in the weeks after return to sea-level, and among those that have, it can be difficult to determine if training and other factors were controlled after altitude training. Levine and Stray-Gundersen³² tested competitive runners in each of the 3 weeks after returning from altitude training. Running performance remained improved from pre-altitude baseline in their LHTL group during the three trials. These results are somewhat in contrast to other research, where 5000 m run performance had returned to pre-altitude baseline 2 weeks following a 4-week altitude training camp.⁵⁹ Robertson et al.⁵⁸ also noted that performance had reverted to pre-altitude training levels at 2 weeks in the LHTL + IHT group.

Additionally, optimal timing of altitude training may depend on the endurance event, such as in swimming, where performance may be impaired in the short term after altitude training and improve in the following weeks. Wachsmuth et al.⁶⁰ tracked 45 top German swimmers through several LHTH altitude training camps over the course of 2 years and compared swimming performance according to the German point system, where the world record as of the most recent Olympic Games is assigned 1000 points. Swimming performance decreased by 11 points on average up to 14 days after return from altitude training, was similar to baseline during the next 10 days, and improved by 23 points during the 25–35 days after altitude training.

While general guidelines are available, further research is needed to determine optimal timing for sea-level competition after altitude training, especially considering possible differences among athletic disciplines. Also, relatively little is known about transitioning from altitude to sea-level training to maximize training effectiveness, how to manage multiple altitude training camps during a competitive season, and how long-term sea-level performance may be affected by periodic altitude training. These issues should provide altitude training researchers with numerous questions to answer with future research.

8. Conclusion and summary of recommendations

Altitude training, both in natural/terrestrial and artificial conditions, has been established as an effective means to improve oxygen transport, RBC volume, and VO_{2max} , given sufficiently high “doses” of elevation and exposure duration. A number of different models for altitude training have been investigated, with LHTL being found to consistently improve hematological parameters and provide meaningful performance improvements in both elite and subelite athletes. Other altitude training models may be effective for certain groups of athletes as well, and are worth considering if an LHTL training camp is not an available option for a given athlete. Future advancements in altitude and hypoxic training research will likely include the improvement of LHTL through modifications and enhancements borrowed from other altitude models, and additional investigation of LHTL in non-running disciplines.

Individual variation in the response to altitude training is not yet fully understood. Future additions to the altitude and hypoxic training literature may include identification of the underlying causes of individual variation, techniques to identify responders and non-responders and strategies to improve adaptations among non-responders. Until such information is available, coaches and athletes should consider that altitude training will be effective for many, but not all participants, and perhaps experiment with altitude training at non-critical periods of the competitive season to determine how the individual responds. When using altitude training, coaches and athletes should follow generally established recommendations, such as easing into training after traveling to higher elevations and making concerted efforts to maintain hydration and nutrition status while initial acclimatization takes place.

References

- Bärtsch P, Saltin B, Dvorak J. Consensus statement on playing football at different altitude. *Scand J Med Sci Sports* 2008;**18**:96–9.
- Bonetti DL, Hopkins WG. Sea-level exercise performance following adaptation to hypoxia: a meta-analysis. *Sports Med* 2009;**39**:107–27.
- Levine BD, Stray-Gundersen J. Point: positive effects of intermittent hypoxia (live high: train low) on exercise performance are mediated primarily by augmented red cell volume. *J Appl Physiol* 2005;**99**:2053–5.
- Gore CJ, Hopkins WG. Counterpoint: positive effects of intermittent hypoxia (live high: train low) on exercise performance are not mediated primarily by augmented red cell volume. *J Appl Physiol* 2005;**99**:2055–7.
- Chapman RF, Stickford ASL, Lundby C, Levine BD. Timing of return from altitude training for optimal sea level performance. *J Appl Physiol* 2014;**116**:837–43.
- Saunders PU, Telford RD, Pyne DB, Cunningham R, Gore CJ, Hahn AG, et al. Improved running economy in elite runners after 20 days of simulated moderate-altitude exposure. *J Appl Physiol* 2004;**96**:931–7.
- Saunders P, Telford R, Pyne D, Hahn A, Gore C. Improved running economy and increased hemoglobin mass in elite runners after extended moderate altitude exposure. *J Sci Med Sport* 2009;**12**:67–72.
- Lundby C, Calbet J, Sander M, Van Hall G, Mazzeo R, Stray-Gundersen J, et al. Exercise economy does not change after acclimatization to moderate to very high altitude. *Scand J Med Sci Sports* 2007;**17**:281–91.
- Beidleman BA, Muza SR, Fulco CS, Cymerman A, Ditzler DT, Stulz D, et al. Intermittent altitude exposures improve muscular performance at 4300 m. *J Appl Physiol* 2003;**95**:1824–32.
- Beidleman BA, Muza SR, Fulco CS, Cymerman A, Sawka MN, Lewis SF, et al. Seven intermittent exposures to altitude improves exercise performance at 4300 m. *Med Sci Sports Exerc* 2008;**40**:141–8.
- Beidleman BA, Muza SR, Fulco CS, Jones JE, Lammi E, Staab JE, et al. Intermittent hypoxic exposure does not improve endurance performance at altitude. *Med Sci Sports Exerc* 2009;**41**:1317–25.
- Fulco CS, Beidleman BA, Muza SR. Effectiveness of preacclimatization strategies for high-altitude exposure. *Exerc Sport Sci Rev* 2013;**41**:55–63.
- Millet GP, Faiss R, Pialoux V. Point: counterpoint: hypobaric hypoxia induces/does not induce different responses from normobaric hypoxia. *J Appl Physiol* 2012;**112**:1783–4.
- Mounier R, Brugniaux JV. Counterpoint: hypobaric hypoxia does not induce different responses from normobaric hypoxia. *J Appl Physiol* 2012;**112**:1784–6.
- Bailey DM, Davies B. Physiological implications of altitude training for endurance performance at sea level: a review. *Br J Sports Med* 1997;**31**:183–90.
- Issurin V. Altitude training: an up-to-date approach and implementation in practice. *Sporto Mokslas* 2007;**1**:12–9.
- Boron WF, Boulpaep EL. *Medical physiology*. 2nd ed. Philadelphia, PA: Elsevier Health Sciences; 2012.
- Sawka MN, Convertino VA, Eichner ER, Schnieder SM, Young AJ. Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. *Med Sci Sports Exerc* 2000;**32**:332–48.
- Lundby C, Thomsen JJ, Boushel R, Koskolou M, Warberg J, Calbet JA, et al. Erythropoietin treatment elevates haemoglobin concentration by increasing red cell volume and depressing plasma volume. *J Physiol* 2007;**578**:309–14.
- Petit JE. Recommended methods for measurement of red cell and plasma volume. *J Nucl Med* 1980;**21**:793–800.
- Schmidt W, Prommer N. The optimised CO-rebreathing method: a new tool to determine total haemoglobin mass routinely. *Eur J Appl Physiol* 2005;**95**:486–95.
- Semenza GL. Regulation of oxygen homeostasis by hypoxia-inducible factor 1. *Physiology (Bethesda)* 2009;**24**:97–106.
- Manalo DJ, Rowan A, Lavoie T, Natarajan L, Kelly BD, Ye SQ, et al. Transcriptional regulation of vascular endothelial cell responses to hypoxia by HIF-1. *Blood* 2005;**105**:659–69.
- Paralikalr SJ, Paralikalr JH. High-altitude medicine. *Indian J Occup Environ Med* 2010;**14**:6.
- Chapman RF, Stray-Gundersen J, Levine BD. Individual variation in response to altitude training. *J Appl Physiol (1985)* 1998;**85**:1448–56.
- Merino CF. Studies on blood formation and destruction in the polycythemia of high altitude. *Blood* 1950;**5**:1–31.
- Risso A, Ciana A, Achilli C, Antonutto G, Minetti G. Neocytolysis: none, one or many? A reappraisal and future perspectives. *Front Physiol* 2014;**5**:54.
- Heinicke K, Heinicke I, Schmidt W, Wolfarth B. A three-week traditional altitude training increases hemoglobin mass and red cell volume in elite biathlon athletes. *Int J Sports Med* 2005;**26**:350–5.
- Svedenhag J, Saltin B, Johansson C, Kaijser L. Aerobic and anaerobic exercise capacities of elite middle-distance runners after two weeks of training at moderate altitude. *Scand J Med Sci Sports* 1991;**1**:205–14.
- Burtscher M, Nachbauer W, Baumgartl P, Philadelphy M. Benefits of training at moderate altitude versus sea level training in amateur runners. *Eur J Appl Physiol* 1996;**74**:558–63.
- Bailey DM, Davies B, Romer L, Castell L, Newsholme E, Gandy G. Implications of moderate altitude training for sea-level endurance in elite distance runners. *Eur J Appl Physiol* 1998;**78**:360–8.
- Levine BD, Stray-Gundersen J. “Living high-training low”: effect of moderate-altitude acclimatization with low-altitude training on performance. *J Appl Physiol* 1997;**83**:102–12.
- Stray-Gundersen J, Chapman RF, Levine BD. “Living high-training low” altitude training improves sea level performance in male and female elite runners. *J Appl Physiol (1985)* 2001;**91**:1113–20.
- Chapman RF, Karlsen T, Resaland GK, Ge R-L, Harber MP, Witkowski S, et al. Defining the “dose” of altitude training: how high to live for optimal sea level performance enhancement. *J Appl Physiol* 2014;**116**:595–603.
- Bonetti DL, Hopkins WG, Lowe TE, Boussana A, Kilding A. Cycling performance following adaptation to two protocols of acutely intermittent hypoxia. *Int J Sports Physiol Perform* 2009;**4**:68–83.
- Julian CG, Gore CJ, Wilber RL, Daniels JT, Fredericson M, Stray-Gundersen J, et al. Intermittent normobaric hypoxia does not alter performance or erythropoietic markers in highly trained distance runners. *J Appl Physiol* 2004;**96**:1800–7.
- Wehrin JP, Zuest P, Hallén J, Marti B. Live high-train low for 24 days increases hemoglobin mass and red cell volume in elite endurance athletes. *J Appl Physiol* 2006;**100**:1938–45.
- Rodríguez FA, Iglesias X, Feriche B, Calderón-Soto C, Chaverri D, Wachsmuth NB, et al. Altitude training in elite swimmers for sea level performance (altitude project). *Med Sci Sports Exerc* 2015;**47**:1965–78.
- Chapman RF. The individual response to training and competition at altitude. *Br J Sports Med* 2013;**47**(Suppl. 1):i40–4.
- Chapman RF, Levine BD. *The effect of hypo and hyperbaria on performance*. Exercise and sport science. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.p.447–58.

41. Chatard JC, Mujika I, Guy C, Lacour JR. Anaemia and iron deficiency in athletes. Practical recommendations for treatment. *Sports Med* 1999;**27**:229–40.
42. Stray-Gundersen J, Alexander C, Hochstein A, DeLemos D, Levine BD. Failure of red cell volume to increase to altitude exposure in iron deficient runners: 540. *Med Sci Sports Exerc* 1992;**24**:S90.
43. Friedmann B, Frese F, Menold E, Kauper F, Jost J, Bartsch P. Individual variation in the erythropoietic response to altitude training in elite junior swimmers. *Br J Sports Med* 2005;**39**:148–53.
44. Wachsmuth N, Völzke C, Prommer N, Schmidt-Trucksäss A, Frese F, Spahl O, et al. The effects of classic altitude training on hemoglobin mass in swimmers. *Eur J Appl Physiol* 2013;**113**:1199–211.
45. Morceau F, Dicato M, Diederich M. Pro-inflammatory cytokine-mediated anemia: regarding molecular mechanisms of erythropoiesis. *Mediators Inflamm* 2010;**2009**:405016. doi:10.1155/2009/405016
46. Dill DB, Adams WC. Maximal oxygen uptake at sea level and at 3090-m altitude in high school champion runners. *J Appl Physiol* 1971;**30**:854–9.
47. Chapman RF, Emery M, Stager JM. Degree of arterial desaturation in normoxia influences $\text{VO}_{2\text{max}}$ decline in mild hypoxia. *Med Sci Sports Exerc* 1999;**31**:658–63.
48. Gavin TP, Derchak PA, Stager JM. Ventilation's role in the decline in $\text{VO}_{2\text{max}}$ and SaO_2 in acute hypoxic exercise. *Med Sci Sports Exerc* 1998;**30**:195–9.
49. Chapman RF, Stager JM, Tanner DA, Stray-Gundersen J, Levine BD. Impairment of 3000-m run time at altitude is influenced by arterial oxyhemoglobin saturation. *Med Sci Sports Exerc* 2011;**43**:1649–56.
50. Yamaya Y, Bogaard HJ, Wagner PD, Niizeki K, Hopkins SR. Validity of pulse oximetry during maximal exercise in normoxia, hypoxia, and hyperoxia. *J Appl Physiol* 2002;**92**:162–8.
51. Levine BD, Stray-Gundersen J. *Dose-response of altitude training: how much altitude is enough? Hypoxia and exercise*. New York, NY: Springer; 2007.p.233–47.
52. Ge R-L, Witkowski S, Zhang Y, Alfrey C, Sivieri M, Karlsen T, et al. Determinants of erythropoietin release in response to short-term hypobaric hypoxia. *J Appl Physiol* 2002;**92**:2361–7.
53. Rusko HK, Tikkanen HO, Peltonen JE. Oxygen manipulation as an ergogenic aid. *Curr Sports Med Rep* 2003;**2**:233–8.
54. Rusko H, Tikkanen H, Paavolainen L, Hämmäläinen I, Kalliokoski K, Puranen A. Effect of living in hypoxia and training in normoxia on sea level $\text{VO}_{2\text{max}}$ and red cell mass. *Med Sci Sports Exerc* 1999;**31**:S86.
55. Ashenden MJ, Gore CJ, Dobson GP, Hahn AG. “Live high, train low” does not change the total haemoglobin mass of male endurance athletes sleeping at a simulated altitude of 3000 m for 23 nights. *Eur J Appl Physiol* 1999;**80**:479–84.
56. Siebenmann C, Robach P, Jacobs RA, Rasmussen P, Nordsborg N, Diaz V, et al. “Live high-train low” using normobaric hypoxia: a double-blinded, placebo-controlled study. *J Appl Physiol* 2012;**112**:106–17.
57. Millet GP, Roels B, Schmitt L, Woorons X, Richalet J. Combining hypoxic methods for peak performance. *Sports Med* 2010;**40**:1–25.
58. Robertson EY, Saunders PU, Pyne DB, Gore CJ, Anson JM. Effectiveness of intermittent training in hypoxia combined with live high/train low. *Eur J Appl Physiol* 2010;**110**:379–87.
59. Stray-Gundersen J, Levine BD. Altitude acclimatization/normoxic training (high/low) improves sea level endurance immediately on descent from altitude. *Med Sci Sports Exerc* 1994;**26**:S64 [Abstract].
60. Wachsmuth NB, Völzke C, Prommer N, Schmidt-Trucksäss A, Frese F, Spahl O, et al. The effects of classic altitude training on hemoglobin mass in swimmers. *Eur J Appl Physiol* 2013;**113**:1199–211.