

# Application of altitude/hypoxic training by elite athletes

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## ABSTRACT

Wilber RL. Application of altitude/hypoxic training by elite athletes. *J. Hum. Sport Exerc.* Vol. 6, No. 2, 2011. At the Olympic level, differences in performance are typically less than 0.5%. This helps explain why many contemporary elite endurance athletes in summer and winter sport incorporate some form of altitude/hypoxic training within their year-round training plan, believing that it will provide the “competitive edge” to succeed at the Olympic level. The purpose of this paper is to describe the practical application of altitude/hypoxic training as utilized by elite athletes. Within the general framework of the paper, both anecdotal and scientific evidence will be presented relative to the efficacy of several contemporary altitude/hypoxic training models and devices currently used by Olympic-level athletes for the purpose of legally enhancing performance. These include the three primary altitude/hypoxic training models: 1) live high + train high (LH + TH), 2) live high + train low (LH + TL), and 3) live low + train high (LL + TH). The LH + TL model will be examined in detail and will include its various modifications: natural/terrestrial altitude, simulated altitude via nitrogen dilution or oxygen filtration, and normobaric normoxia via supplemental oxygen. A somewhat opposite approach to LH + TL is the altitude/hypoxic training strategy of LL + TH, and data regarding its efficacy will be presented. Recently, several of these altitude/hypoxic training strategies and devices underwent critical review by the World Anti-Doping Agency (WADA) for the purpose of potentially banning them as illegal performance-enhancing substances/methods. This paper will conclude with an update on the most recent statement from WADA regarding the use of simulated altitude devices. **Key words:** HYPOBARIC HYPOXIA, INTERMITTENT HYPOXIC TRAINING, LIVE HIGH-TRAIN LOW, NITROGEN DILUTION, NORMOBARIC HYPOXIA, SUPPLEMENTAL OXYGEN.

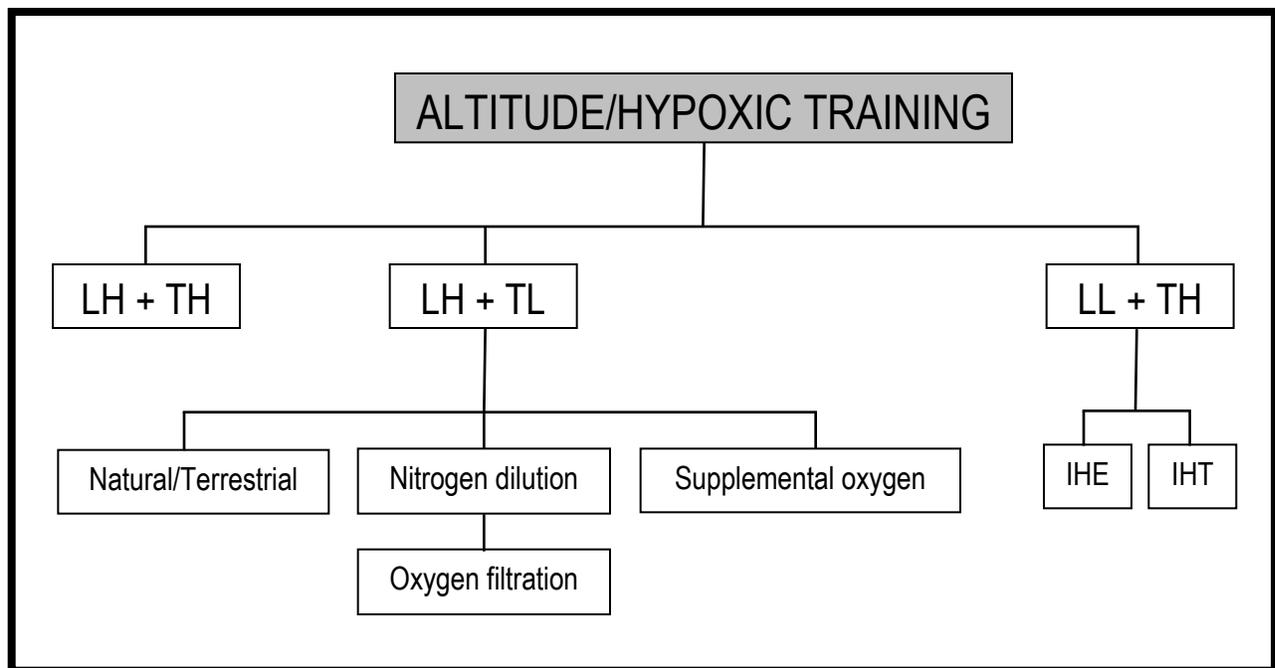
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**INTRODUCTION**

Elite athletes have utilized altitude/hypoxic training for several years. Although the efficacy of altitude/hypoxic training relative to sea level performance remains controversial from a research perspective, athletes continue to use it in preparation for elite level competition. Figure 1 outlines the different methods of altitude/hypoxic training currently used by elite athletes. The original method of altitude/hypoxic training was one in which athletes lived and trained at moderate altitude (1500-4000 m), for the purpose of increasing erythrocyte volume and ultimately enhancing sea level maximal oxygen uptake ( $VO_{2max}$ ) and endurance performance. Live high + train high (LH + TH) altitude training is still used today by sea level athletes who complete altitude training camps at specific times during the training year, and of course by altitude residents, such as the Kenyan and Ethiopian runners. It is not the purpose of this paper to review the extensive literature relative to LH + TH; however, the interested reader can access that information via comprehensive review articles (7,16,17,34,71).



*IHE (intermittent hypoxic exposure), IHT (intermittent hypoxic training), LH + TH (live high + train high), LH + TL (live high + train low), LL + TH (live low + train high)*

**Figure 1.** Contemporary altitude training models.

One major conclusion drawn from both the anecdotal and scientific evidence regarding LH + TH altitude training was that endurance athletes did not seem to be able to train at an equivalent of near-equivalent training intensity (e.g., running velocity) as compared with sea level training. Many runners and swimmers reported that they seemed to lose “race fitness/form” and “turnover” as a result of LH + TH altitude training. Indeed, in one of the original LH + TH altitude training studies conducted by Buskirk et al. (12), the results suggested that collegiate distance runners who completed 63 days of LH + TH (4000 m) returned to sea level in a *detrained* state, as evidenced by 3% to 8% decrements in time trial performance in the 880-yd, 1-

mile and 2-mile runs. More recently, it was demonstrated that absolute training intensity during “base” and “interval” workouts was significantly compromised at moderate altitude (2500 m) versus sea level in well-trained competitive distance runners (37,43).

## **LIVE HIGH + TRAIN LOW**

As a potential solution to the “training intensity” limitation that appears to be inherent in the LH + TH altitude training model, the live high + train low (LH + TL) model was developed in the early 1990s by Drs. Benjamin Levine and James Stray-Gundersen of the United States (34,36). Essentially, LH + TL is based on the premise that athletes can simultaneously experience the benefits of altitude/hypoxic acclimatization (i.e., increased erythrocyte volume) *and* sea level training (i.e., maintenance of sea level training intensity and oxygen flux), thereby resulting in positive hematological, metabolic and neuromuscular adaptations. Athletes who use LH + TL live and/or sleep at moderate altitude (2000-3000 m) and simultaneously train at low elevation (< 1500 m). This can be accomplished using a number of methods and devices.

### **LH + TL via Natural/Terrestrial Altitude**

Initial implementation and scientific evaluation of the LH + TL model was conducted in the “natural/terrestrial” altitude environment of the Wasatch Mountains in the state of Utah, United States. The seminal research study by Levine and Stray-Gundersen (37) evaluated the efficacy of LH + TL among 39 American female and male collegiate distance runners who were initially matched based on fitness level and then randomly assigned to one of three experimental groups (LL + TL, LH + TL, LH + TH). Following a 4-week baseline period at sea level (Dallas, Texas), the LH + TL runners ( $n = 13$ ) completed a 28-day training period in which they lived at 2500 m (Deer Valley, Utah) for approximately 22 hours per day, and trained at 1250 m (Salt Lake City, Utah) for approximately 2 hours per day. Training consisted of alternate workouts of base training and interval training. Thirteen fitness-matched female and male collegiate runners, serving as a control group (LL + TL), followed the same training program at sea level at 150 m (San Diego, California), as did another group of 13 female and male runners who followed a conventional LH + TH regimen at 2500 m (Deer Valley). Compared with pre-altitude values, post-altitude sea level tests conducted on the third day following altitude training indicated significant improvements in the LH + TL group for erythrocyte volume (5%), hemoglobin concentration (9%), and treadmill  $VO_{2max}$  (4%). Similar changes in erythrocyte volume, hemoglobin concentration and  $VO_{2max}$  were observed in the LH + TH runners, whereas no improvements in these parameters were seen in the sea level control group. In terms of running performance, an average 1% improvement ( $P < 0.05$ ) in post-altitude 5000-m run time was observed in the LH + TL group, an improvement that was equivalent to 13.4 seconds. Performance in the 5000-m run for the LH + TL runners was similar on days 7, 14 and 21 post-altitude compared with day 3 post-altitude, suggesting that the beneficial effects of LH + TL altitude training on running performance appear to last for up to 3 weeks post-altitude. In contrast, neither the sea level control group nor the conventional LH + TH group demonstrated any significant improvements in 5000-m run performance at any time following the 28-day altitude training period. Collectively, these results (37) suggested that living at moderate altitude (2500 m) resulted in significant increases in erythrocyte volume and hemoglobin concentration in both the LH + TH and LH + TL runners. However, simultaneous training at lower elevation (1250 m) allowed the LH + TL athletes to achieve running velocities and oxygen flux similar to sea level, thereby purportedly inducing beneficial metabolic and neuromuscular adaptations. When the runners returned to sea level, the LH + TL group was the only one that demonstrated significant improvements in both  $VO_{2max}$  and 5000-m run time. These results were attributed to positive hematological (“live high”), as well as metabolic and neuromuscular adaptations (“train low”) resulting exclusively from 4 weeks of LH + TL altitude training (37).

These initial findings by Levine and Stray-Gundersen (37) regarding LH + TL via natural/terrestrial altitude were subsequently supported in a similar study by Stray-Gundersen et al. (61) in elite athletes. American female and male national team distance runners demonstrated a significant 1% (5.8 second) pre-altitude to post-altitude improvement in 3000-m time trial performance following 28 days of LH + TL altitude training in Deer Valley (2500 m) and Salt Lake City (1250 m), although this performance test was not referenced against a control group. More recently, Wehrli et al. (69) evaluated the natural/terrestrial LH + TL model in conjunction with the training of Swiss national team orienteers. Compared with a fitness-matched control group, significant pre-altitude versus post-altitude increments in erythrocyte volume (5%) and hemoglobin mass (5%) were reported in the LH + TL athletes, who completed a 24-day period during which they lived at 2500 m and trained at 1000 m or 1800 m, depending on the goals of the specific training session. Although not referenced against a control group, significant pre-altitude versus post-altitude improvements in treadmill  $VO_{2max}$  (4%) and 5000-m run time trial performance (2%) were also reported in the LH + TL orienteers (69).

An example of LH + TL via natural/terrestrial altitude training in elite sport is the U.S. national team in long track speedskating, a group that initially used LH + TL in preparation for the 2002 Salt Lake City Winter Olympics. Three years before the Salt Lake City Olympics, the U.S. long track speedskaters began living in the Deer Valley/Park City area at approximately 2500 m for the purpose of enhancing erythrocyte volume and to acclimatize at an elevation markedly higher than the altitude of their competition venue (1425 m) in the Salt Lake City area. The speedskaters utilized a modified LH + TL regimen in which they performed moderate intensity, dry land training in Deer Valley/Park City (LH + TH *moderate* intensity) and completed high intensity workouts in Salt Lake City (LH + TL *high* intensity). This LH + TH *moderate* intensity + TL *high* intensity model of altitude training had been previously evaluated by Stray-Gundersen et al. (61) and found to be as effective as the basic LH + TL strategy in bringing about significant increases in erythropoietic markers and  $VO_{2max}$ , as well as improvements in 3000-m running performance in elite U.S. national team runners. During the year prior to the Salt Lake City Olympics, the speedskaters had access to the Olympic speedskating venue (Utah Olympic Oval; 1425 m), thereby gaining valuable experience and knowledge of the venue's ice conditions and aerodynamic characteristics. The U.S. long track speedskaters enjoyed unprecedented success in the 2002 Salt Lake City Winter Olympics, with six athletes winning eight medals, including three gold medals and two world records (68). The U.S. national long track speedskating team continued to use LH + TL via natural/terrestrial altitude in the quadrennium prior to the 2006 Torino Winter Olympics during which time they established themselves as one of the best and most consistent teams in the world based on World Cup and World Championship performances. Similar to the 2002 Salt Lake City Olympics, U.S. long track speedskaters performed very well in the 2006 Torino Olympics, capturing three gold, three silver and one bronze medal.

LH + TL via natural/terrestrial altitude was also utilized effectively by U.S. national team marathon runners in preparation for the 2004 Athens Olympics. These athletes employed a LH + TH *moderate* intensity + TL *high* intensity model similar to the one used by the U.S. national long track speedskaters. The marathon runners lived and completed their moderate intensity training at 2440 m (Mammoth Lakes, California), whereas high intensity workouts were done at 1260 m (Bishop, California). The marathoners also employed heat/humidity pre-acclimatization strategies while living and training in the relatively moderate temperature, low humidity environment of the Sierra Nevada mountains. These pre-acclimatization strategies served to prepare them very effectively for the harsh environmental conditions (30-35°C; 30-40% relative humidity) they eventually faced in Athens during the Olympics. U.S. Olympic team marathon runners enjoyed unprecedented success at the Athens Olympics, winning a bronze medal in the women's event and a silver medal in the men's race.

**LH + TL via Nitrogen Dilution**

“Nitrogen apartment/house” is a term used to describe a normobaric hypoxic apartment that simulates an altitude environment. The nitrogen apartment was developed by Dr. Heikki Rusko in Finland in the early 1990s for the purpose of simulating an altitude environment in relatively low-elevation Finland, thereby allowing Finnish elite athletes to LH + TL without having to travel abroad to do so. The nitrogen apartment simulates elevations equivalent to approximately 2000 m to 3000 m via dilution of the oxygen concentration within the apartment. A ventilation system pulls in ambient air (~20.9% oxygen, ~79.0% nitrogen), and a gas composed of 100% nitrogen is simultaneously introduced into the ventilation system, resulting in an internal gas composition of approximately 15.3% oxygen and 84.7% nitrogen. This normobaric hypoxic environment simulates an altitude of approximately 2500 m.

Since the development of the nitrogen apartment by the Finns in the early 1990s, elite athletes in other Scandinavian countries, as well as Australian elite athletes have utilized nitrogen apartments in conjunction with LH + TL altitude training. Typically, these athletes live/sleep in the simulated altitude environment of the nitrogen apartment for  $\geq 12$  hours per day for  $\geq 4$  weeks, and perform their training in natural/terrestrial sea level, or near sea level conditions.

Several studies have evaluated the efficacy of the nitrogen apartment on endurance athletes in Australia (2,6,14,19,30,31,39,51,56,64), Finland (33,40,44,54,55), and Sweden (46). The details of these investigations can be reviewed elsewhere (70,72). Within this group of studies, a more limited number were conducted on elite athletes from the Australian national team (3,39,56) and Finnish national team (44,54). The results of this limited number of studies on elite athletes have been equivocal. Whereas some researchers have reported significant increases in erythropoietic indices (54), others have not been able to replicate those results (3,56), or did not report erythropoietic data (39,44). However, several of these investigations on national team athletes reported significant improvements in sea level performance following various “doses” of LH + TL via nitrogen dilution (39,44,56).

Thus, although limited, the empirical evidence suggests that LH + TL via nitrogen dilution may enhance sea level performance in elite athletes, provided a sufficient “dose” of simulated altitude is applied, i.e.,  $\geq 12$  to 16 hours per day for  $\geq 4$  weeks at an elevation of 2500 m to 3000 m. It is not clear, however, whether the performance-enhancing effects of LH + TL via nitrogen dilution are due to accelerated erythropoiesis (54), or may be due to beneficial changes in running economy (56), skeletal muscle buffering capacity (19), hypoxic ventilatory response (64), and/or skeletal muscle Na<sup>+</sup>-K<sup>+</sup>-ATPase activity (5,6).

**LH + TL via Oxygen Filtration**

Similar to the method of nitrogen dilution, a normobaric hypoxic environment can also be simulated via oxygen filtration. This method of LH + TL via oxygen filtration can take the form of an apartment/house, or a commercially-available “hypoxic tent”. LH + TL via oxygen filtration utilizes an oxygen-filtration membrane that reduces the molecular concentration of oxygen in ambient air drawn from outside the apartment/tent. The oxygen-reduced air is pumped by generator into the apartment/tent, resulting in a normobaric hypoxic living and sleeping environment. There are several sites worldwide that employ LH + TL via oxygen filtration in conjunction with the training of elite athletes. These include the U.S. Olympic Training Center (Chula Vista, California, USA), Nike® Oregon Project (Portland, Oregon, USA), Pettit National Ice Center (Milwaukee, Wisconsin, USA), Japan Institute of Sport (Tokyo, Japan), Centre National de Ski Nordique (Premanon, Jura, France), English Institute of Sport (Twickenham, UK), New Zealand Institute of Sport (Auckland, New Zealand), Canadian Sport Centre (Calgary, Alberta, Canada), and Aspire Dome (Doha, Qatar).

The key research findings relative to the efficacy of LH + TL via oxygen filtration can be organized based on studies that have evaluated hypoxic apartments and hypoxic tents. All of the hypoxic apartment investigations were conducted on elite endurance athletes from the French national team (athletics, biathlon, Nordic ski, swimming), whereas none of the hypoxic tent studies evaluated elite athletes. Collectively, the research findings regarding LH + TL via oxygen filtration are equivocal regarding erythropoietic effect, with two studies (10,49) reporting significant increases in erythrocyte volume and/or total hemoglobin mass, whereas others (24,25,41,50) found no significant erythropoietic response following LH + TL via oxygen filtration. In addition, the effect of LH + TL via oxygen filtration on performance is unclear. Significant post-altitude improvements have been reported in  $VO_{2max}$  (10), cycling peak power output (60), cycling power output at the respiratory compensation point (60), and 800-m to 3000-m run time (24). In contrast, no significant enhancement of  $VO_{2max}$  (50,60), treadmill run time to exhaustion (50), or 2000-m swim time (49) have been demonstrated following LH + TL via oxygen filtration. Thus, although elite athletes continue to use LH + TL via oxygen filtration to enhance performance, it appears to be supported as much by anecdotal versus empirical evidence based on the current literature.

A final note regarding the potential negative effects of utilizing LH + TL via oxygen filtration. Brugniaux et al. (11) recently evaluated the safety and efficacy of oxygen filtration technology in elite athletes (5-6 days at 2500 m + 8-12 days at 3000-3500 m;  $\geq 11$  hours per day). Although they reported that cardiac function and symptoms of acute mountain sickness were not negatively affected at any elevation, immune status was compromised at 3500 m, as evidenced by a significant decrease in leukocyte count (11). Similar results were demonstrated by Tiollier et al. (63) who reported a significant depletion of secretory immunoglobulin A (sIgA) in French national team athletes living at a simulated altitude of 3500 m. These investigations (11,63) were taken into consideration by the World Anti-Doping Agency (WADA) in their recent evaluation of simulated altitude devices. Based on the findings of these studies, WADA concluded that there were potential negative health effects associated with the use of simulated altitude (<<http://altitudeforall.info/index.html>). However, WADA's conclusion was subsequently challenged by the research group that conducted these investigations (11,63), in which they argued that their findings had been misinterpreted by WADA, and that there were minimal and physiologically insignificant health effects resulting from the use of simulated altitude via oxygen filtration (<<http://altitudeforall.info/index.html>).

### **LH + TL via Supplemental Oxygen**

Another modification of LH + TL altitude training is one in which athletes live in a natural, hypobaric hypoxic environment but train at simulated "sea level" with the aid of supplemental oxygen (LH + TLO<sub>2</sub>). LH + TLO<sub>2</sub> is used effectively at the U.S. Olympic Training Center in Colorado Springs, Colorado, USA, where U.S. national team athletes live at approximately 2000 m to 3000 m in the foothills of the Rocky Mountain range. The average barometric pressure ( $P_B$ ) in Colorado Springs is approximately 610 Torr, which yields a partial pressure of inspired oxygen ( $P_{iO_2}$ ) of approximately 128 Torr. By inspiring a certified medical grade gas with a fraction of inspired oxygen ( $F_{iO_2}$ ) approximately 0.26, athletes can complete high-intensity training sessions in a simulated "sea level" environment at a  $P_{iO_2}$  equivalent to approximately 150 Torr. In addition to U.S. national team athletes at the U.S. Olympic Training Center in Colorado Springs, the previously mentioned U.S. long track speedskating team utilizes LH + TLO<sub>2</sub> in conjunction with high-intensity training sessions done at the Utah Olympic Oval (1425 m) in Salt Lake City.

Only a few studies have evaluated the efficacy of LH + TLO<sub>2</sub> on athletic performance (13,42,73-75). Wilber et al. (73) evaluated the acute effects of supplemental oxygen on physiological responses and exercise performance during a high-intensity cycling interval workout (6 x 100 kilojoules [kJ]; work:recovery ratio = 1:1.5) in trained endurance athletes who were altitude residents (1800-1900 m). Compared with a control

trial ( $F_{I}O_2$  0.21), average total time for the 100-kJ work interval was 5% and 8% ( $P < 0.05$ ) faster in the  $F_{I}O_2$  0.26 and  $F_{I}O_2$  0.60 trials, respectively. Consistent with improvements in total time were increments in power output equivalent to 5% in the  $F_{I}O_2$  0.26 trial and 9% in the  $F_{I}O_2$  0.60 trial ( $P < 0.05$ ). Whole-body  $VO_2$  ( $L \cdot \text{min}^{-1}$ ) was higher by 7% and 14% ( $P < 0.05$ ) in the  $F_{I}O_2$  0.26 and  $F_{I}O_2$  0.60 trials, respectively, and was highly correlated with the improvement in power output ( $r = 0.85$ ;  $P < 0.05$ ). Arterial oxyhemoglobin saturation ( $S_pO_2$ ) was significantly higher by 5% ( $F_{I}O_2$  0.26) and 8% ( $F_{I}O_2$  0.60) in the supplemental oxygen trials.

In a subsequent study, Wilber et al. (75) utilized near-infrared spectroscopy (NIRS) and reported that hemoglobin/myoglobin (Hb/Mb)-deoxygenation of m. vastus lateralis was 8% and 12% less at blood lactate threshold and  $VO_{2\text{max}}$ , respectively, during an  $F_{I}O_2$  0.60 trial versus a control trial ( $F_{I}O_2$  0.21), suggesting that supplemental oxygen enhances the availability of oxygen at the level of the capillary bed of the working skeletal muscle. Finally, Wilber et al. (74) reported that there was no significant difference in cellular oxidative stress during exercise when comparing supplemental oxygen trials ( $F_{I}O_2$  0.26,  $F_{I}O_2$  0.60) with a control trial ( $F_{I}O_2$  0.21), as determined by serum measurements of lipid hydroperoxides (LOOH) and reduced glutathione (GSH), as well as urinary measurements of malondialdehyde (MDA) and 8-hydroxydeoxygenase (9-OHdG). Based on these results (73-75), it was concluded that LH + TLO<sub>2</sub> results in significant increases in arterial oxyhemoglobin saturation and greater unloading of oxygen at the level of the capillary bed of the working muscle, contributing to significant increases in power output and exercise performance, without inducing additional cellular oxidative stress. In terms of practical application, these results provided support for elite athletes to use LH + TLO<sub>2</sub> as an altitude training strategy that allows them to effectively live/sleep high and train low with minimal travel or inconvenience.

The long-term training effects of LH + TLO<sub>2</sub> were evaluated by Morris et al. (42). U.S. national team junior cyclists completed a 21-day training period during which they lived and performed their moderate-intensity workouts at 1860 m (Colorado Springs), and performed their high-intensity interval training at simulated sea level using supplemental oxygen ( $F_{I}O_2$  0.26;  $P_{I}O_2$  159 Torr). Interval workouts were done 3 days per week, and each interval workout required the athletes to complete 5 x 5-minute cycling efforts at 105% to 110% of maximal steady-state heart rate. A control group of fitness-matched teammates completed the same training program at 1860 m using normoxic gas ( $F_{I}O_2$  0.21;  $P_{I}O_2$  128 Torr). Athletes using supplemental oxygen were able to train at a significantly higher percentage of their altitude-determined lactate threshold (126%) versus their counterparts who trained in normoxic conditions (109%). Following the 21-day training period, the athletes performed a 120-kJ cycling performance time trial in simulated sea level conditions ( $F_{I}O_2$  0.26;  $P_{I}O_2$  159 Torr). Results of the cycling performance test showed improvements of 2 seconds ( $P > 0.05$  vs. pre-training) and 15 seconds ( $P < 0.05$  vs. pre-training) for the normoxic-trained and LH + TLO<sub>2</sub>-trained cyclists, respectively (42). In agreement with Wilber et al. (73), the results of Morris et al. (42) demonstrated that high-intensity workouts at moderate altitude (1860 m) are enhanced through the use of supplemental oxygen. Further, Morris et al. (42) was the first to show that sea level endurance performance in elite athletes can be improved as a result of LH + TLO<sub>2</sub>.

## LIVE LOW + TRAIN HIGH

The live low + train high (LL + TH) model of altitude training is one in which athletes live in a natural, normobaric normoxic environment, and are exposed to discrete and relatively short intervals (5-180 min) of simulated normobaric hypoxia or hypobaric hypoxia. Normobaric hypoxia can be simulated via nitrogen dilution (e.g., Altitrainer 200® hypoxicator), oxygen filtration (e.g., Go2Altitude® hypoxicator), or inspiration of hypoxic gas. LL + TH can be utilized by athletes in the resting state (intermittent hypoxic exposure; IHE)

or during formal training sessions (intermittent hypoxic training; IHT). It is purported that IHE/IHT can enhance athletic performance by stimulating an increase in serum erythropoietin (sEPO) and erythrocyte volume (32,47,59), and can augment skeletal muscle mitochondrial density, capillary-to-fiber ratio, and fiber cross-sectional area (15,67) via up-regulation of hypoxia-inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ) (67). Because of its convenience, LL + TH via IHE/IHT is utilized by elite athletes in several countries.

This review of literature is limited to studies that evaluated IHE/IHT in athletes only (recreational to elite), and included a fitness/training-matched control group in the research design. Collectively, the empirical evidence regarding the efficacy of IHE/IHT on erythropoietic response and athletic performance is not extremely compelling. Only a minimal number of well-designed, well-controlled studies on trained or elite athletes have reported increments in hemoglobin concentration (9,22), and to this author's knowledge none have evaluated or reported any increases in robust erythropoietic markers such as soluble transferrin receptor (sTfR), erythrocyte volume and/or hemoglobin mass. Furthermore, no IHT study has demonstrated improvements in  $VO_{2max}$ , and only 31% have reported that athletic performance was enhanced following IHT (9,23,27,28,62), possibly due to improvements in efficiency/economy (27,28). In contrast, several studies have failed to demonstrate significant alterations in erythropoietic acceleration,  $VO_{2max}$  or post-IHT performance (1,18,20,21,26,29,52,53,65,66). One possible explanation for the preponderance of negative results in IHE/IHT studies may be related to the relatively short duration hypoxic "doses" administered in the various protocols used. It has been argued that in order for altitude/hypoxic acclimatization to be effective in accelerating erythropoiesis and ultimately enhancing performance, the hypoxic "dose" must be equivalent to an altitude of 2000 m to 2500 m for  $\geq 4$  weeks at a daily hypoxic exposure of  $\geq 22$  hours a day (34,38), as described by Drs. Levine and Stray-Gundersen. That argument has been countered by those who contend that the mechanism by which IHE/IHT enhances performance is non-hematological, and may be due to beneficial changes in skeletal muscle mitochondrial density, capillary-to-fiber ratio, and fiber cross-sectional area (15,67), which have been demonstrated in untrained individuals. It is apparent that further research is needed in the area of LL + TH via IHE/IHT, particularly as it relates to elite athletes. Future investigations should focus on potential IHE/IHT-induced changes in these skeletal muscle parameters, along with continued evaluation of the more conventional measures of sEPO, erythrocyte mass,  $VO_{2max}$ , and performance.

A final note regarding LL + TH via IHE/IHT relative to elite athletes. A number of studies have found IHE/IHT to be an effective method of pre-acclimatization prior to ascending to high altitude (> 4000 m) (8,48,57,58). Although those studies were conducted on mountaineers and soldiers, the findings certainly have implications for elite athletes. It appears that IHE/IHT may be utilized effectively by elite athletes either prior to competition at altitude (e.g., Mexico City, 2300 m) or prior to undergoing an extended altitude training block.

## **SIMULATED ALTITUDE: LEGAL AND ETHICAL ISSUES**

Recently, the use of simulated altitude by elite athletes has come under review by the WADA. The rationale behind the WADA review is related to the fact that WADA officials are concerned that some athletes who are exploiting illegal erythropoietic agents are making use of "utilization of simulated altitude" as a false explanation for their abnormally elevated hemoglobin and hematocrit levels, thereby circumventing WADA's Prohibited Substance/Method List. WADA considers "artificially-induced hypoxic conditions" to include hypobaric hypoxia (barometric pressure chamber), normobaric hypoxia via nitrogen dilution (nitrogen apartment; Altitrainer 200<sup>®</sup> hypoxicator), or normobaric hypoxia via oxygen filtration (hypoxic apartment/tent; Go2Altitude<sup>®</sup> hypoxicator).

In order for a substance/method to be placed on WADA's Prohibited List, it must meet two of the following three criteria (35):

1. Scientific evidence or experience demonstrates that the method or substance has the potential to enhance, or enhances sport performance.
2. Medical evidence or experience suggests that the use of the substance or method represents an actual or potential health risk to the athlete.
3. The use of the substance or method violates the spirit of sport.

The WADA scientific, medical and ethics committees have thoroughly evaluated the evidence regarding "artificially-induced hypoxic conditions" and reached the following conclusions in May 2006 (35):

1. Artificially-induced hypoxic conditions can significantly enhance performance when properly applied, by increasing the endogenous production of EPO with a subsequent elevation of red blood cell production and a better oxygen transfer to the muscles.
2. Under proper medical supervision, when reliable equipment was used, and when moderate altitude simulation was reproduced, no significant signs of health risk were reported.
3. Following consultations with the WADA Ethics Review Panel it was concluded unanimously that artificially-induced hypoxic conditions should be considered as violating the WADA spirit of sport criterion.

Collectively, these conclusions made by the WADA scientific, medical and ethics committees indicated that criteria 1 and 3 had been satisfied, and therefore "artificially-induced hypoxic conditions" were to be considered for inclusion on the WADA Prohibited List for 2007. In response to these initial conclusions, WADA conducted additional consultations throughout the summer of 2006 with its stakeholders, as well as scientific experts in the area of altitude/hypoxic training. The debate was amplified when several members of the international scientific community responded collectively in opposition to WADA's consideration of banning simulated altitude devices (<http://altitudeforall.info/index.html>).

The final decision regarding "artificially-induced hypoxic conditions" was made in September 2006 by the WADA Executive Committee and announced by WADA Chairman Richard Pound as follows:

"In response to our stakeholders who requested that there be full consideration of hypoxic conditions in the context of the Prohibited List, WADA performed a scientific and ethical review of the matter, and engaged in a thorough consultation with experts and stakeholders. While we do not deem this method appropriate for inclusion on the List at this time, we still wish to express the concern that, in addition to the results varying individually from case to case, use of this method may pose health risks if not properly implemented and under medical supervision." (<http://altitudeforall.info/index.html>)

This statement indicated that WADA does not prohibit the use of “artificially-induced hypoxic conditions” by elite athletes, at least through 2010. However, it should be noted that all “hypobaric/hypoxic practices are [currently] prohibited” in Italy, as mandated by the Italian Health Ministry in June 2005 (Decree of the Italian Ministry of Health 13.04.2005. Section 5, Subsection M.1, June 3, 2005) in response to an incident involving professional cyclists competing in the 2005 Giro d'Italia (Stage 10; 18 May 2005). The Italian law regarding simulated altitude is totally independent of any current and future WADA rulings, and presently has judicial precedence over any WADA rulings in areas of Italian jurisdiction. Finally, the International Olympic Committee has prohibited the use of simulated altitude devices within the boundaries of the Olympic Village since the 2000 Sydney Olympics, and this mandate is expected to apply to all future summer and winter Olympic Games.

## SUMMARY

Many contemporary elite endurance athletes in summer and winter sport incorporate some form of altitude/hypoxic training within their year-round training plan, believing that it will provide the “competitive edge” to succeed at the Olympic level. This paper has presented both anecdotal and scientific evidence relative to the efficacy of several contemporary altitude/hypoxic training models and devices currently used by Olympic-level athletes for the purpose of legally enhancing performance. “Live high + train low” altitude training is employed by elite athletes using: 1) natural/terrestrial altitude, 2) normobaric hypoxia via nitrogen dilution (e.g., nitrogen apartment) or oxygen filtration (e.g., hypoxic tent), and 3) normobaric normoxia via supplemental oxygen. Research regarding several of these LH + TL strategies is either limited or equivocal, particularly regarding optimal LH + TL hypoxic “dose”, as well as the physiological mechanisms that potentially impact post-altitude performance. Regarding the safety and health aspects of LH + TL, recent evidence suggests that living at a simulated altitude > 3500 m may have an impact on immunocompetence, but this effect may not have physiologically significant consequences.

A somewhat opposite approach to LH + TL is the altitude/hypoxic training strategy of “live low + train high”, in which athletes live in a natural, normobaric normoxic environment, and train for brief intervals using simulated normobaric hypoxia via nitrogen dilution (e.g., Altitrainer 200® hypoxicator), oxygen filtration (e.g., Go2Altitude® hypoxicator) or hypobaric hypoxia (barometric pressure chamber). LL + TH is utilized by athletes in the resting state (IHE) or during formal training sessions (IHT). Collectively, the empirical evidence regarding the efficacy of LL + TH via IHE/IHT on erythropoietic response and endurance performance is not overly persuasive, and additional research is needed in this area, especially among elite athletes. The current literature does suggest, however, that IHE/IHT may be an effective pre-acclimatization strategy for elite athletes prior to training or competing at altitude.

Recently, several of these altitude/hypoxic training strategies and devices underwent critical review by WADA for the purpose of potentially banning them as an illegal performance-enhancing substance/method. Ultimately, WADA decided to refrain from including “artificially-induced hypoxic conditions” on the 2007 Prohibited List. However, it should be noted that use of all “hypobaric/hypoxic practices” was outlawed in Italy in June 2005, and this Italian law has judicial precedence within the boundaries of Italy over any WADA rulings regarding simulated altitude. In addition, the International Olympic Committee has prohibited the use of simulated altitude devices within the boundaries of the Olympic Village since the 2000 Sydney Olympics, and this mandate is expected to apply to all future summer and winter Olympic Games.

## REFERENCES

1. Abellan, R., A.F. Remacha, R. Ventura, M.P. Sarda, J. Segura, and F.A. Rodriguez. Hematologic response to four weeks of intermittent hypobaric hypoxia in highly trained athletes. *Haematologica* 90:126-127, 2005.
2. Ashenden, M.J., C.J. Gore, G.P. Dobson, and A.G. Hahn. "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.* 80:479-484, 1999.
3. Ashenden, M.J., C.J. Gore, D.T. Martin, G.P. Dobson, and A.G. Hahn. Effects of a 12-day "live high, train low" camp on reticulocyte production and haemoglobin mass in elite female road cyclists. *Eur. J. Appl. Physiol.* 80:472-478, 1999.
4. Ashenden, M.J., C.J. Gore, G.P. Dobson, et al. Simulated moderate altitude elevates serum erythropoietin but does not increase reticulocyte production in well-trained runners. *Eur. J. Appl. Physiol.* 81:428-435, 2000.
5. Aughey, R.J., C.J. Gore, A.G. Hahn, et al. Chronic intermittent hypoxia and incremental cycling exercise independently depress muscle in vitro maximal Na<sup>+</sup>-K<sup>+</sup>-ATPase activity in well-trained athletes. *J. Appl. Physiol.* 98:186-192, 2005.
6. Aughey, R.J., S.A. Clark, C.J. Gore, et al. Interspersed normoxia during live high, train low interventions reverses an early reduction in muscle Na<sup>+</sup>-K<sup>+</sup>-ATPase activity in well-trained athletes. *Eur. J. Appl. Physiol.* 98:299-309, 2006.
7. Bailey, D.M., and B. Davies. Physiological implications of altitude training for endurance performance at sea level: A review. *Br. J. Sports Med.* 31:183-190, 1997.
8. Beidleman, B.A., S.R. Muza, P.B. Rock, et al. Exercise responses after altitude acclimatization are retained during reintroduction to altitude. *Med. Sci. Sports Exerc.* 29:1588-1595, 1997.
9. Bonetti, D.L., W.G. Hopkins, and A.E. Kilding. High-intensity kayak performance after adaptation to intermittent hypoxia. *Int. J. Sports Physiol. Perform.* 1:246-260, 2006.
10. Brugniaux, J.V., L. Schmitt, P. Robach, et al. Eighteen days of "living high, training low" stimulate erythropoiesis and enhance aerobic performance in elite middle-distance runners. *J. Appl. Physiol.* 100:203-211, 2006.
11. Brugniaux, J.V., L. Schmitt, P. Robach, et al. Living high-training low: tolerance and acclimatization in elite endurance athletes. *Eur. J. Appl. Physiol.* 96:66-77, 2006.
12. Buskirk, E.R., J. Kollias, R.F. Akers, E.K. Prokop, and E.P. Reategui. Maximal performance at altitude and on return from altitude in conditioned runners. *J. Appl. Physiol.* 23:259-266, 1967.
13. Chick, T.W., D.M. Stark, and G.H. Murata. Hyperoxic training increases work capacity after maximal training at moderate altitude. *Chest* 104:1759-1762, 1993.
14. Clark, S.A., R.J. Aughey, C.J. Gore, et al. Effects of live high, train low hypoxic exposure on lactate metabolism in trained humans. *J. Appl. Physiol.* 96:517-525, 2004.
15. Desplanches, D., and H. Hoppeler. Effects of training in normoxia and normobaric hypoxia on human muscle ultrastructure. *Pflugers Arch.* 425:263-267, 1993.
16. Fulco, C.S., P.D. Rock, and A. Cymerman. Maximal and submaximal exercise performance at altitude. *Aviat. Space Environ. Med.* 69:793-801, 1998.
17. Fulco, C.S., P.D. Rock, and A. Cymerman. Improving athletic performance: Is altitude residence or altitude training helpful? *Aviat. Space Environ. Med.* 71:162-171, 2000.
18. Glyde-Julian, C.G., C.J. Gore, R.L. Wilber, et al. Intermittent normobaric hypoxia does not alter performance or erythropoietic markers in highly trained distance runners. *J. Appl. Physiol.* 96:1800-1807, 2004.

19. Gore, C.J., A.G. Hahn, R.J. Aughey, et al. Live high:train low increases muscle buffer capacity and submaximal cycling efficiency. *Acta Physiol. Scand.* 173:275-286, 2001.
20. Gore, C.J., F.A. Rodriguez, M.J. Truijens, N.E. Townsend, J. Stray-Gundersen, and B.D. Levine. Increased serum erythropoietin but not red cell production after 4 wk of intermittent hypobaric hypoxia (4,000-5,500 m). *J. Appl. Physiol.* 101:1386-1393, 2006.
21. Hahn, A.G., R.D. Telford, D.M. Tumilty, et al. Effect of supplemental hypoxic training on physiological characteristics and ergometer performance in elite rowers. *Excel* 8:127-138, 1992.
22. Hamlin, M.J., and J. Hellemans. Effects of intermittent normobaric hypoxia on blood parameters in multi-sport endurance athletes. *Med. Sci. Sports Exerc.* 36 (Suppl. 5):S337, 2004.
23. Hendriksen, I.J.M., and T. Meeuwssen. The effect of intermittent training in hypobaric hypoxia on sea-level exercise: A cross-over study in humans. *Eur. J. Appl. Physiol.* 88:396-403, 2003.
24. Hinckson, E.A., and W.G. Hopkins. Changes in running endurance performance following intermittent altitude exposure simulated with tents. *Eur. J. Sport Sci.* 5:15-24, 2005.
25. Hinckson, E.A., W.G. Hopkins, J.S. Fleming, T. Edwards, P. Pfitzinger, and J. Hellemans. Sea-level performance in runners using altitude tents: A field study. *J. Sci. Med. Sport* 8:451-457, 2005.
26. Karlsen, T., O. Madsen, S. Rolf, and J. Stray-Gundersen. Effects of 3 weeks hypoxic interval training on sea level cycling performance and hematological parameters. *Med. Sci. Sports Exerc.* 34 (Suppl. 5):S224, 2002.
27. Katayama, K., H. Matsuo, K. Ishida, S. Mori, and M. Miyamura. Intermittent hypoxia improves endurance performance and submaximal exercise efficiency. *High Alt. Med. Biol.* 4:291-304, 2003.
28. Katayama, K., K. Sato, H. Matsuo, K. Ishida, K. Iwasaki, and M. Miyamura. Effect of intermittent hypoxia on oxygen uptake during submaximal exercise in endurance athletes. *Eur. J. Appl. Physiol.* 92:75-83, 2004.
29. Katayama, K., Y. Sato, Y. Morotome, et al. Ventilatory chemosensitive adaptations to intermittent hypoxic exposure with endurance training and detraining. *J. Appl. Physiol.* 86:1805-1811, 1999.
30. Kinsman, T.A., C.J. Gore, A.G. Hahn, et al. Sleep in athletes undertaking protocols of exposure to nocturnal simulated altitude at 2650 m. *J. Sci. Med. Sport* 8:222-232, 2005.
31. Kinsman, T.A., N.E. Townsend, C.J. Gore, et al. Sleep disturbance at simulated altitude indicated by stratified respiratory disturbance index but not hypoxic ventilatory response. *Eur. J. Appl. Physiol.* 94:569-575, 2005.
32. Knaupp W., S. Khilnani, J. Sherwood, S. Scharf, and H. Steinberg. Erythropoietin response to acute normobaric hypoxia in humans. *J. Appl. Physiol.* 73: 837-840, 1992.
33. Laitinen, H., K. Alopaeus, R. Heikkinen, et al. Acclimatization to living in normobaric hypoxia and training at sea level in runners. *Med. Sci. Sports Exerc.* 27 (Suppl. 5):S109, 1995.
34. Levine, B.D. Intermittent hypoxic training: Fact and fancy. *High Alt. Med. Biol.* 3:177-193, 2002.
35. Levine, B.D. Should "artificial" high altitude environments be considered doping? *Scand. J. Med. Sci. Sports* 16:297-301, 2006.
36. Levine, B.D., and J. Stray-Gundersen. A practical approach to altitude training: Where to live and train for optimal performance enhancement. *Int. J. Sports Med.* 13 (Suppl.1):S209-S212, 1992.
37. Levine, B.D., and J. Stray-Gundersen. "Living high-training low": Effect of moderate-altitude acclimatization with low-altitude training on performance. *J. Appl. Physiol.* 83:102-112, 1997.
38. Levine, B.D., and J. Stray-Gundersen. Dose-response of altitude training: How much altitude is enough? In: *Hypoxia and Exercise*. New York, NY: Springer, 2006, pp. 233-247.
39. Martin, D.T., A.G. Hahn, H. Lee, A.D. Roberts, J. Victor, and C.J. Gore. Effects of a 12-day "live high, train low" cycling camp on 4-min and 30-min performance. *Med. Sci. Sports Exerc.* 34 (Suppl. 5):S274, 2002.

40. Mattila, V., and H. Rusko. Effect of living high and training low on sea level performance in cyclists. *Med. Sci. Sports Exerc.* 28 (Suppl. 5):S157, 1996.
41. McLean, S.R., J.C. Kolb, S.R. Norris, and D.J. Smith. Diurnal normobaric moderate hypoxia raises serum erythropoietin concentration but does not stimulate accelerated erythrocyte production. *Eur. J. Appl. Physiol.* 96:651-658, 2006.
42. Morris, D.M., J.T. Kearney, and E.R. Burke. The effects of breathing supplemental oxygen during altitude training on cycling performance. *J. Sci. Med. Sport.* 3:165-175, 2000.
43. Niess, A.M., E. Fehrenbach, G. Strobel, et al. Evaluation of stress response to interval training at low and moderate altitudes. *Med. Sci. Sports Exerc.* 35:263-269, 2003.
44. Nummela, A., and H. Rusko. Acclimatization to altitude and normoxic training improve 400-m running performance at sea level. *J. Sports Sci.* 18:411-419, 2000.
45. Pedlar, C., G. Whyte, S. Emegbo, N. Stanley, I. Hindmarch, and R. Godfrey. Acute sleep responses in a normobaric hypoxic tent. *Med. Sci. Sports Exerc.* 37:1075-1079, 2005.
46. Piehl-Aulin, K., J. Svedenham, L. Wide, B. Berglund, and B. Saltin. Short-term intermittent normobaric hypoxia - haematological, physiological and mental effects. *Scand. J. Med. Sci. Sports* 8: 132-137, 1998.
47. Powell, F.L., and N. Garcia. Physiological effects of intermittent hypoxia. *High Alt. Med. Biol.* 1:125-136, 2000.
48. Richalet, J.P., J. Bittel, J.P. Herry, et al. Use of a hypobaric chamber for pre-acclimatization before climbing Mount Everest. *Int. J. Sports Med.* 13 (Suppl. 1):S216-S220, 1992.
49. Robach, P., L. Schmitt, J.V. Brugniaux, et al. Living high-training low: effect on erythropoiesis and aerobic performance in highly-trained swimmers. *Eur. J. Appl. Physiol.* 96:423-433, 2006.
50. Robach, P., L. Schmitt, J.V. Brugniaux, et al. Living high-training low: effect on erythropoiesis and maximal aerobic performance in elite Nordic skiers. *Eur. J. Appl. Physiol.* 97:695-705, 2006.
51. Roberts, A.D., S.A. Clark, N.E. Townsend, M.E. Anderson, C.J. Gore, and A.G. Hahn. Changes in performance, maximal oxygen uptake and maximal accumulated oxygen deficit after 5, 10 and 15 days of live high:train low altitude exposure. *Eur. J. Appl. Physiol.* 88:390-395, 2003.
52. Rodriguez, F.A., M.J. Truijens, N.E. Townsend, et al. Effects of four weeks of intermittent hypobaric hypoxia on sea level running and swimming performance. *Med. Sci. Sports Exerc.* 36 (Suppl. 5):S338, 2004.
53. Roels, B., G.P. Millet, C.J.L. Marcoux, O. Coste, D.J. Bentley, and R.B. Candau. Effects of hypoxic interval training on cycling performance. *Med. Sci. Sports Exerc.* 37:138-146, 2005.
54. Rusko, H.K., A. Leppavuori, P. Makela, and J. Leppaluoto. Living high, training low: a new approach to altitude training at sea level in athletes. *Med. Sci. Sports Exerc.* 27 (Suppl. 5):S6, 1995.
55. Rusko, H.K., H. Tikkanen, L. Paavolainen, I. Hamalainen, K. Kalliokoski, and A. Puranen. Effect of living in hypoxia and training in normoxia on sea level  $VO_{2max}$  and red cell mass. *Med. Sci. Sports Exerc.* 31 (Suppl. 5):S86, 1999.
56. Saunders, P.U., R.D. Telford, D.B. Pyne, et al. Improved running economy in elite runners after 20 days of simulated moderate-altitude exposure. *J. Appl. Physiol.* 96:931-937, 2004.
57. Savourey, G., N. Garcia, Y. Besnard, A.-M. Hanniquet, M.-O. Fine, and J. Bittel. Physiological changes induced by pre-adaptation to high altitude. *Eur. J. Appl. Physiol.* 69:221-227, 1994.
58. Savourey, G., N. Garcia, J.-P. Caravel, et al. Pre-adaptation, adaptation and de-adaptation to high altitude in humans: hormonal and biochemical changes at sea level. *Eur. J. Appl. Physiol.* 77:37-43, 1998.
59. Schmidt, W. Effects of intermittent exposure to high altitude on blood volume and erythropoietic activity. *High Alt. Med. Biol.* 3:167-176, 2002.

60. Schmitt, L., G. Millet, P. Robach, et al. Influence of "living high-training low" on aerobic performance and economy of work in elite athletes. *Eur. J. Appl. Physiol.* 97:627-636, 2006.
61. Stray-Gundersen, J., R.F. Chapman, and B.D. Levine. "Living high-training low" altitude training improves sea level performance in male and female elite runners. *J. Appl. Physiol.* 91:1113-1120, 2001.
62. Terrados, N., J. Melichna, C. Sylven, E. Jansson, and L. Kaijser. Effects of training at simulated altitude on performance and muscle metabolic capacity in competitive road cyclists. *Eur. J. Appl. Physiol.* 57:203-209, 1988.
63. Tiollier, E., L. Schmitt, P. Burnat, et al. Living high-training low altitude training: Effects on mucosal immunity. *Eur. J. Appl. Physiol.* 94: 298-304, 2005.
64. Townsend, N.A., C.J. Gore, A.G. Hahn, et al. Living high-training low increases hypoxic ventilatory response of well-trained endurance athletes. *J. Appl. Physiol.* 93:1498-1505, 2002.
65. Truijens, M.J., H.M. Toussaint, J. Dow, and B.D. Levine. Effect of high-intensity hypoxic training on sea-level swim performances. *J. Appl. Physiol.* 94:733-743, 2003.
66. Ventura, N., H. Hoppeler, R. Seiler, A. Binggeli, P. Mullis, and M. Vogt. The response of trained athletes to six weeks of endurance training in hypoxia or normoxia. *Int. J. Sports Med.* 24:166-172, 2003.
67. Vogt, M., A. Puntchart, J. Geiser, C. Zuleger, R. Billeter, and H. Hoppeler. Molecular adaptations in human skeletal muscle to endurance training under simulated hypoxic conditions. *J. Appl. Physiol.* 91:173-182, 2001.
68. Wallechinsky, D. *The Complete Book of the Winter Olympics* (Turin 2006 Edition). Toronto, Ontario: Sport Media Publishing, Inc. 2006, pp. 97-132.
69. Wehrin, J.P., P. Zuest, J. Hallen, and B. Marti. Live high-train low for 24 days increases hemoglobin mass and red cell volume in elite endurance athletes. *J. Appl. Physiol.* 100:1938-1945, 2006.
70. Wilber, R.L. Current trends in altitude training. *Sports Med.* 31:249-265, 2001.
71. Wilber, R.L. Performance at sea level following altitude training. In: *Altitude Training and Athletic Performance*. Champaign, IL: Human Kinetics, 2004, pp. 83-118.
72. Wilber, R.L. Current practices and trends in altitude training. In: *Altitude Training and Athletic Performance*. Champaign, IL: Human Kinetics, 2004, pp. 183-223.
73. Wilber, R.L., P.L. Holm, D.M. Morris, G.M. Dallam, and S.D. Callan. Effect of F<sub>I</sub>O<sub>2</sub> on physiological responses and cycling performance at moderate altitude. *Med. Sci. Sports Exerc.* 35:1153-1159, 2003.
74. Wilber, R.L., P.L. Holm, D.M. Morris, et al. Effect of F<sub>I</sub>O<sub>2</sub> on oxidative stress during interval training at moderate altitude. *Med. Sci. Sports Exerc.* 36:1888-1894, 2004.
75. Wilber, R.L., J. Im, P.L. Holm, et al. Effect of F<sub>I</sub>O<sub>2</sub> on hemoglobin/myoglobin-deoxygenation during high-intensity exercise at moderate altitude. *Med. Sci. Sports Exerc.* 37 (Suppl. 5):S297, 2005.