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Endurance Training at Altitude

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Abstract

Saunders, Philo U., David B. Pyne, and Christopher Gore. Endurance training at altitude. *High Alt. Med. Biol.* 10: 135–148, 2009.—Since the 1968 Olympic Games when the effects of altitude on endurance performance became evident, moderate altitude training (~2000 to 3000 m) has become popular to improve competition performance both at altitude and sea level. When endurance athletes are exposed acutely to moderate altitude, a number of physiological responses occur that can comprise performance at altitude; these include increased ventilation, increased heart rate, decreased stroke volume, reduced plasma volume, and lower maximal aerobic power ($\dot{V}o_{2max}$) by ~15% to 20%. Over a period of several weeks, one primary acclimatization response is an increase in the volume of red blood cells and consequently of $\dot{V}o_{2max}$. Altitudes >~2000 m for >3 weeks and adequate iron stores are required to elicit these responses. However, the primacy of more red blood cells for superior sea-level performance is not clear-cut since the best endurance athletes in the world, from Ethiopia (~2000 to 3000 m), have only marginally elevated hemoglobin concentrations. The substantial reduction in $\dot{V}o_{2max}$ of athletes at moderate altitude implies that their training should include adequate short-duration (~1 to 2 min), high-intensity efforts with long recoveries to avoid a reduction in race-specific fitness. At the elite level, athlete performance is not dependent solely on $\dot{V}o_{2max}$, and the "smallest worthwhile change" in performance for improving race results is as little as 0.5%. Consequently, contemporary statistical approaches that utilize the concept of the smallest worthwhile change are likely to be more appropriate than conventional statistical methods when attempting to understand the potential benefits and mechanisms of altitude training.

Key Words: athletes at altitude; red blood cells; work capacity; acclimatization

Introduction

The effects of training at moderate altitude on subsequent performance at altitude became particularly salient during the lead-up to the 1968 Mexico City Olympic Games (2300 m). Given that international-standard sporting events are often limited to <3500-m altitude, this review focuses on the moderate- to high-altitude range of 2000 to 3500 m. The continuum of altitude is nominally classified as near sea level (0 to 500 m), low (>500 to 2000 m), moderate (>2000 to 3000 m), high (>3000 to 5500 m), and extreme altitude (>5500 m) (Bartsch and Saltin, 2008). Examples of events held within the 2000- to 3500-m range include stages of Le Tour de France, Vuelta Espana, and Giro d'Italia cycling races. Some exceptions are football matches in La Paz, Bolivia (3600 m), and the Cycling Tour of Qinghai Lake, China, which has multiple peaks over 3500 m. While performance in short-distance events (e.g., 400-m running) is relatively unaffected at moderate altitude, times for distance events (e.g., 1500-, 5000-, 10,000-m and marathon running) are ~10% to 20% slower than the equivalent sea-level records (Peronnet et al., 1991; Fulco et al., 1998). The benefits of reduced air density at altitude favor short-distance events (Peronnet et al., 1991), whereas the reduction of $\dot{V}o_{2max}$ in proportion to the severity of hypoxia (Clark et al., 2007) becomes relatively more limiting in events longer than 1 to 2 min (Gastin, 2001).

Endurance athletes have been using classical altitude training for nearly half a century in pursuit of improving sea-level performance, and there is widespread belief that altitude training can enhance sea-level endurance performance (Dick, 1992). Classical altitude training refers to the training process of athletes living and training at natural altitude ranging from

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1800 to 3000 m for a period of 2 to 4 weeks to prepare for competitions at altitude or to improve their sea-level performance subsequent to adaptations gained during altitude acclimatization and/or associated training in hypoxia. Given that the intensity of endurance training is reduced at moderate to high altitude (Friedmann-Bette, 2008), a modified approach has been for athletes to live and sleep at moderate altitude and train at lower altitudes: the live-high, train-low (LHTL) method (Levine and Stray-Gundersen, 1997). In the last 10 yr, LHTL has largely supplanted classical altitude training in the scientific literature. Because the geography of many countries does not readily permit LHTL, a further refinement involves athletes living at simulated altitude under normobaric conditions and training near sea level (Rusko, 1996). Intermittent hypoxic exposure is another method involving brief periods (minutes to a few hours) of high or extreme hypoxic exposure to stimulate erythropoietin (EPO) production, although data to support any performance benefits for athletes competing at sea level are inconclusive (Julian et al., 2004).

The potential benefits of classical altitude training over other modalities of altitude exposure are that altitude acclimatization provides the stimulus for both central and peripheral adaptations, as well as an additional training load compared with sea level (Bartsch and Saltin, 2008). However, the reduced absolute training intensity associated with classical moderate altitude training (Levine and Stray-Gundersen, 1997) can be detrimental to any potential performance improvements. On the other hand, a few researchers have reported that elite endurance athletes have produced world-class performances subsequent to classical altitude training (Daniels and Oldridge, 1970; Bartsch and Saltin, 2008), where changes as small as 0.5% to 1% are important for elite athletes (refer to the subsection on the smallest worthwhile change). Nevertheless, we cannot discount the potential placebo effects of altitude training; that is, a favorable outcome occurs because the athletes believe in the benefits of training at altitude. It may also be that altitude training merely provides a high-quality training camp because of the increased focus on training, more time spent recovering between sessions, consistently having people to train with for all sessions, novelty of the venue, additional sports science support (where available), and being away from the distractions of home. A limitation of all controlled studies has been that the control group was aware that they were not at altitude.

In our work with elite endurance athletes at the Australian Institute of Sport, classical altitude training is the most popular modality for preparation for major competitions. These athletes also use other hypoxic modalities such as simulated LHTL at home instead of dealing with the stress and cost of overseas travel, since Australia has no natural moderate altitude suitable for training. A recent meta-analysis that examined the effects of various modalities of altitude training on sea-level performance provided moderate support for classical altitude training. There was a clear $1.9 \pm 2.3\%$ (mean $\pm$ 90% confidence limits) improvement in sea-level performance for uncontrolled studies using elite athletes, although the effect was an unclear $1.6 \pm 2.7\%$ change for controlled studies (Bonetti and Hopkins, 2009). Similarly, our regression analysis indicates that the mean effect of a 3-week camp (504 h) of classical altitude and LHTL training would elicit performance improvements of 1.8% and 2.5% (Fig. 1) for the classical and LHTL modalities, respectively. Although both correlation coefficients are not statistically significant, the regression approach is effectively a random-effect meta-analysis with equal weighting to all the studies with a covariate (hours of hypoxia) to estimate the effect of exposure to altitude on performance, as indicated by the slope (Fig. 1). However, it is uncertain if the training camp and placebo effects account for some, or even all, of any increase in performance. Despite the widespread belief that altitude training improves performance in endurance events (Dick, 1992), the placebo effect has been quantified at $\sim$1% to 3% (Clark et al., 2000; Beedie et al., 2006) and could be responsible for some or all of the improvements (also 1% to 3%; Gore et al., 2007) from altitude training studies.

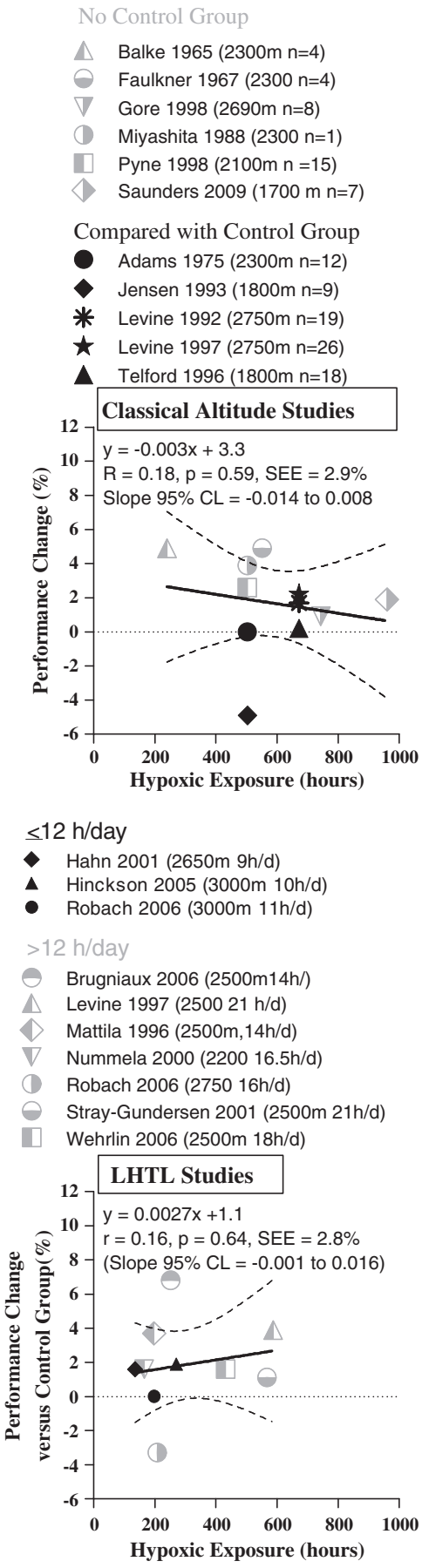
This review will focus primarily on classical altitude training by endurance athletes. The main subsections will contrast the physiological effects of acute and chronic hypoxia, compare the responses of high and low altitude residents, define a worthwhile change in performance resulting from altitude training, and provide guidelines for training while at altitude. The last two subsections will use distance running to describe training responses and guidelines at altitude.

Acute and Chronic Physiological Responses to Training at Altitude

Table 1 summarizes the acute and chronic responses to moderate altitude that are most strongly linked to performance.

Hypoxia inducible factor

When acutely exposed to a hypoxic environment, all functional systems of the body are affected, including the central nervous system, respiratory system, cardiovascular system, and muscles, a process that is mediated at the tissue level by rapid oxygen sensing (Rusko et al., 2004). The transcription factor, hypoxia inducible factor-1 (HIF-1), present in every tissue of the body, is the global regulator of oxygen homeostasis and plays a critical role in acute cardiovascular and respiratory responses to hypoxia (Semenza, 2004). HIF-1 expression is tightly regulated by oxygen tension and is virtually undetectable under normoxia due to rapid degradation of the HIF-1 subunits through the ubiquitin–proteasome pathway (Kallio et al., 1999). In normoxic conditions the half-life of HIF-1 is $\sim$5 min, but when exposed to hypoxia its half-life is increased by $\sim$30 min, allowing it to stabilize and accumulate in the cells and leading to the transcription of specific genes. HIF-1 expression and protein levels decay rapidly when cells are returned to normoxia (Huang et al., 1998). HIF-1 was identified for its role in regulating the transcription of the EPO gene (Wang et al., 1995); however, it is also induced by hypoxia in many cell lines and activates multiple genes, which in turn encode proteins that mediate adaptive responses, other than those of hematological origin (Sasaki et al., 2000). Parameters activated by HIF-1 include EPO and transferrin for iron metabolism and red cell production; vascular endothelial growth factor (VEGF) and others for angiogenesis and cell survival; glycolytic enzymes, including phosphofructokinase (PFK), hexokinase, and lactate dehydrogenase, all important for energy metabolism; glucose transporters 1 and 3 and monocarboxylate transporters 1 and 4, which are critical for glucose uptake and lactate metabolism by the muscles; carbonic anhydrase for pH regulation; nitric oxide synthase and heme oxygenase, which produce the vasodilators nitric oxide (NO) and carbon monoxide; and tyrosine hydroxylase that codes for a pivotal enzyme for dopamine synthesis, which accelerates ventilation (Sasaki et al., 2000).



Red cell volume and hemoglobin mass

The HIF-mediated responses to hypoxia associated with red blood cells and oxygen transport have garnered the greatest interest because maximal aerobic power ($\dot{V}o_{2max}$) is a major determinant of performance (di Prampero, 1986). The primary aim of several weeks of altitude training is to increase the total volume of red blood cells and oxygen delivery by increasing the oxygen-carrying capacity of the arterial blood (Rusko et al., 2004). At moderate altitude, the lower partial pressure of oxygen induces EPO production in the kidneys, which in turn stimulates the production of red blood cells in the bone marrow and yields downstream increases in $\dot{V}o_{2max}$ and thus performance (Levine and Stray-Gundersen, 1997; Stray-Gundersen et al., 2001; Levine et al., 2005). If the level of ~2200 m (Weil et al., 1968) and the duration (~several weeks) of moderate altitude are sufficient, there is almost universal support for an increase in blood EPO and red blood cells (Levine and Stray-Gundersen 1997; Rusko et al., 2003; Clark et al., 2009). During continuous exposure to classical altitude, serum EPO reaches a peak within 24 to 48 h and thereafter declines to near baseline levels (~10 IU/L) after about 1 week (Hahn and Gore, 2001). Our regression analysis for the pooled data of both classical and LHTL studies indicates that the mean increase in hemoglobin mass (Hb_{mass}) is ~7% after a 3-week exposure (=504 h). Given a standard error of estimate of 5.9%, the extent to which an individual might increase Hb_{mass} varies substantially (Fig. 2).

Maximal oxygen uptake

When an elite endurance athlete trains at altitude, the muscles' capacity to receive and consume oxygen exceeds the ability of the cardiovascular system to transport oxygen (Wagner, 2000). A consequence of acute exposure to altitude is a decrease in $\dot{V}o_{2max}$ and exercise performance. Highly trained athletes appear to be even more susceptible to this decrease upon acute exposure to altitude because of the large reduction in arterial oxygen saturation (Clark et al., 2007). The mechanism for this greater decline in $\dot{V}o_{2max}$ at altitude in endurance athletes is largely due to their very high cardiac output and high pulmonary blood flow. With lower diffusion gradients for oxygen transfer at the pulmonary capillaries at high altitude, the high pulmonary flow outstrips the diffusing capacity of the lungs (Levine et al., 2008). About 6% to 10% of sea level $\dot{V}o_{2max}$ and performance is lost for every 1000 m of acute exposure to altitude (Fulco et al., 1998; Wehrlin and Hallen, 2006; Clark et al., 2007). Decrements in aerobic per-

FIG. 1. The association between the duration of hypoxic exposure and the sea-level performance changes (from before to after altitude) for both classical altitude training (top panel) and LHTL training (bottom panel) derived by regression analysis. A positive slope indicates progressively greater improvement in sea-level performance with longer LHTL altitude exposure, whereas a negative slope indicates attenuation of performance improvements with longer duration of classical altitude training. Studies selected for inclusion are those that measured time trial performance for endurance-based events or power output for a given duration, such as an all-out 5-min effort on an ergometer. The regressions are the line of best fit and the associated 95% confidence limits (CL), where SEE is standard error of estimate.

Table 1. Physiologic Effects of Moderate–High Altitude (Hypobaric Hypoxia) or Equivalent Normobaric Hypoxia

Factor	*Minutes to hours to days*	*Days to weeks to months*
HIF-1	Half-life from 5 to 30 min leading to stabilization and accumulation in cells (Huang et al., 1998)	Transcription of genes that activate proteins responsible for RBC production, angiogenesis/cell survival, energy metabolism and accelerated ventilation (Sasaki et al., 2000)
Erythropoiesis	↑Serum EPO within 1 to 2 days, returns to near sea-level values after 1 to 2 wk (Hahn and Gore, 2001; Levine and Stray-Gundersen, 2006) ↑Soluble transferrin receptor (Koistinen et al., 2000; Hahn and Gore, 2001; Wehrlin et al., 2006) ↑% Reticulocytes (Mairbaurl et al., 1986; Grover et al., 1998; Friedmann et al., 1999; Wehrlin et al., 2006)	↔EPO (Heinicke et al., 2005) ↑Red cell volume and Hb_{mass} (Levine and Stray-Gundersen 2006; Sawka et al., 2000; Wehrlin et al., 2006)
Blood	↓Plasma volume proportional to altitude (e.g., ∼15% ↓at 3000 m) (Sawka et al., 2000), which results in a hemoconcentration (↑ Hct, ↑[Hb] and ↑ red cell count) (Hoyt and Honig, 1996), but not true accelerated erythropoiesis ↑Resting pH (Lenfant et al., 1971) and ↓arterial Pco_2 (Schneider, 1921) secondary to the ↑ventilation	↔Blood volume despite ↑ in red cell volume and Hb_{mass} (Levine and Stray-Gundersen, 1997; Wehrlin et al., 2006)
Vo_{2max}	↓ ∼7%/1000 m for well-trained athletes (Fulco et al., 1998; Clark et al., 2007)	Improves but remains depressed, e.g., ↓13% initially at 2340 m, but only ↓6% after 14 days at this altitude (Schuler et al., 2007)
Heart	↑Resting Q from ↑HR rather than SV (Vogel and Harris, 1967); after several days ↓Q during submaximal exercise associated with ↓ SV (Saltin et al., 1968; Ferretti et al., 1990; Wolfel et al., 1994), but ↑HR; $\downarrow HR_{max}$ common >3500 m (Saltin et al., 1968); acute, ↓1.9 beats/min^{-1}/1000 m of altitude between 300 and 2800 m (Wehrlin and Hallen, 2006).	↓Q_{submax} (Calbet et al., 2003) ↓Q_{max} (Sutton et al., 1988)
Ventilation	↑At rest (Huang et al., 1984; Schoene, 1997; Burtscher et al., 2006), during submaximal (Klausen et al., 1970; Burtscher et al., 2006; Clark et al., 2007) and maximal exercise (Saltin 1967; Forte et al., 1997; Lundby et al., 2004)	↑During submaximal exercise (Calbet et al., 2003) ↑↑During maximal exercise (Calbet et al., 2003)
Lactate	↑Blood lactate (La^-) during submaximal exercise (Dill et al., 1931) ↔maximal blood La^- (Dill et al., 1931)	↓Blood La^- during submaximal exercise and ↓maximal blood La^- (Wagner and Lundby, 2007); somewhat controversial, possibly the same lactate response to acute and chronic hypoxia if maintain muscle mass and high levels of training (Wagner and Lundby, 2007)
Muscle	↑La^- accumulation in muscle as well as La^- release from contracting muscle during standardized submaximal exercise (Brooks et al., 1998)	↓ Production or ↑clearance of La^- (Clark et al., 2004); ↑utilization carbohydrates (Brooks et al., 1992; Brooks et al., 1998) and ↓utilization free fatty acids (Roberts et al., 1996a; Roberts et al., 1996b); ↓diffusion distance from capillaries to muscle fibers (Hoppeler et al., 1990) secondary to ↓muscle mass, which may be beneficial for O_2 transfer, albeit that chronic exposure of humans to extreme altitude results in loss of mitochondria (Hoppeler et al., 1990); ↑mitochondrial capacity; ↔oxidative enzyme activities (Terrados et al., 1988; Mizuno et al., 1990; Saltin et al., 1995); ↔glycolytic enzyme activities if maintain high intensity training (Stray-Gundersen et al., 1999); ↑(Mizuno et al., 1990; Saltin et al., 1995) or ↓(Stray-Gundersen et al., 1999) muscle buffering capacity; ↑(Gelfi et al., 2004) or ↔myoglobin content (Reynafarje 1962; Tappan and Reynafarje, 1957; Terrados et al., 1986)
Immune function	↑Likelihood of illness (Bailey et al., 1998)	↑Likelihood of illness (Mazzeo, 2005), possibly modulated by training load (Pyne et al., 2000)
Oxygen cost of submaximal exercise	↔Clark et al., 2007; Ostler et al., 2008	Controversial ↓(Green et al., 2000) or ↔ (Lundby et al., 2007)

EPO, erythropoietin; [Hb], hemoglobin concentration, Hb_{mass}, hemoglobin mass; Hct, hematocrit; HR, heart rate; La^-, lactate; SV, stroke volume; Q, cardiac output; Pco_2, partial pressure of carbon dioxide; o_2, arterial oxygen saturation; Vo_{2max} maximum aerobic power.; ↑, increase; ↓, decrease; ↔, no change; ↑↑, large increase.

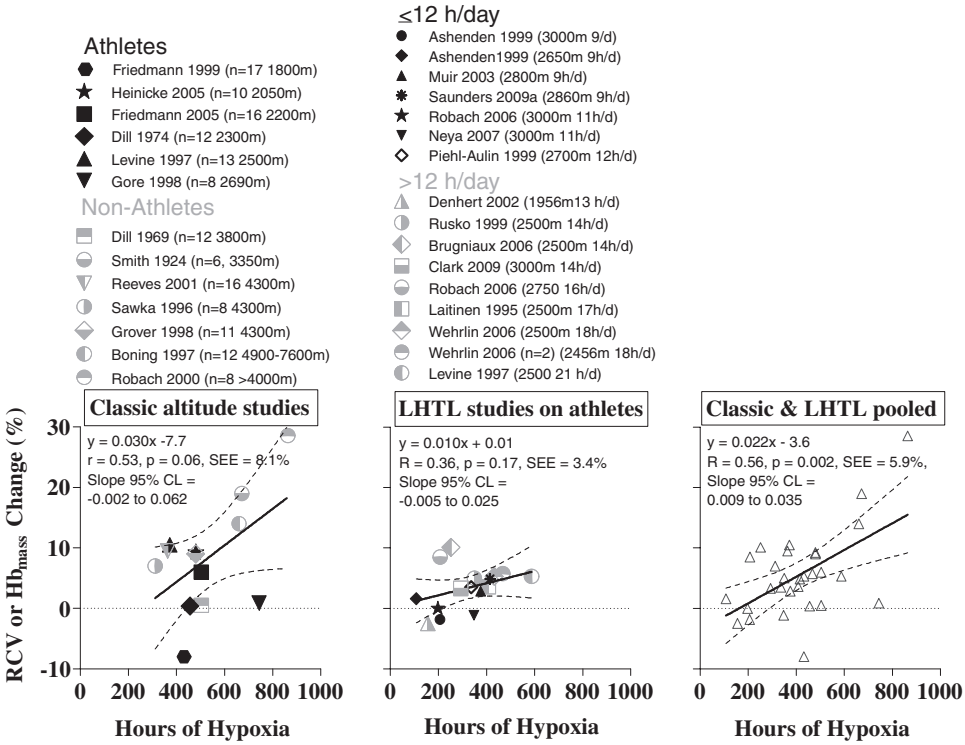


FIG. 2. The association between the duration of hypoxic exposure and the changes in red cell volume (RCV) or hemoglobin mass (Hb_{mass}) in response to both classical altitude training (left panel), LHTL training (middle panel), and for both classical and LHTL combined (right panel) derived by regression analysis. Studies selected for inclusion are those that measured RCV using Evans blue dye or Hb_{mass} using carbon monoxide rebreathing, when the longer-duration classical altitude studies have frequently been conducted on nonathletes. The regressions are the line of best fit and the associated 95% confidence limits (CL), where SEE is standard error of estimate.

formance are evident at modest altitudes as low as 600 m (Gore et al., 1996). In contrast, during submaximal exercise the $\dot{V}O_2$ for a given absolute work rate appears to be independent of the acute exposure to altitude (Pugh et al., 1964; Clark et al., 2007). Therefore, at any given absolute exercise work rate, a higher percentage of $\dot{V}O_{2max}$ is required than at sea level, leading to a higher relative exercise intensity when at altitude (Beidleman et al., 2008). This sequence leads to an association of acute exposure to exercise at altitude with a slower pace for fixed work rates in endurance activities. As an example, the time to complete 216- and 156-kJ time trials for men and women was 60% to 70% longer at 4300 m than at sea level (Beidleman et al., 2003). Similarly, the time taken to complete a 720- kJ time trial was >70% longer at day 3 at 4300 m in the placebo group (Fulco et al., 2005).

Exercise at moderate altitude is associated with an acute reduction in arterial oxygen content (Cao_2) that is usually restored within a week and increased beyond sea-level quantities with 2 to 3 weeks of altitude training (Schuler et al., 2007). This increase in Cao_2 at moderate altitude results in a concomitant increase in $\dot{V}O_{2max}$ at altitude higher than that attained with acute exposure to hypoxia (Saltin, 1967; Schuler et al., 2007). Acclimatization to high altitudes at or above 4100 m (over weeks or months) results in a similar response in Cao_2 (initial decrease followed by restoration and rise above sea-level value). However, there is no associated restoration in $\dot{V}O_{2max}$ at altitude (Schuler et al., 2007), raising the possibility of a threshold altitude over which increases in Cao_2 have no beneficial effect on $\dot{V}O_{2max}$. The likely mechanism of this response is a reduced peak muscle blood flow at these high altitudes. Despite the absence of an increase in $\dot{V}O_{2max}$ with chronic exposure to high altitude, submaximal exercise performance can improve by 20% to 60% after 2 to 3 weeks of high altitude exposure (Maher et al., 1974). This improvement should translate to improved competition performance through better fractional utilization of $\dot{V}O_{2max}$.

Cardiac and metabolic responses and ventilation

Other physiological responses to moderate altitude include an acute increase in heart rate during submaximal exercise that in turn increases cardiac output. This hemodynamic response compensates for the reduced oxygen content of the blood to ensure that adequate amounts of oxygen are transported to the tissues, including exercising muscles (Mazzeo, 2008). The other factor determining cardiac output is stroke volume, which initially is only marginally affected during exercise at altitude; but more prolonged exposure leads to a decrease in stroke volume secondary to a decrease in plasma volume (Mazzeo, 2008). Altitude acclimatization at 4300 m for 21 days decreased the reliance on fat as a fuel at both rest and during low-intensity (50% $\dot{V}O_{2max}$) cycling (Roberts et al., 1996a). A shift toward increased dependence on glucose metabolism and away from reliance on fatty acid consumption under conditions of acute and chronic hypoxia is advantageous, because glucose is an $\sim$10% more efficient fuel in terms of generating adenosine triphosphate (ATP) per mole of O_2 (Brooks et al., 1991; Green et al., 2000; Gore et al., 2001). Acute

exposure to hypoxia causes an immediate increase in minute ventilation (V_E), mediated primarily by hypoxic stimulation of the peripheral chemoreceptors. Resting ventilatory acclimatization to chronic hypoxic exposure, however, is characterized by an initial rapid increase in V_E, followed by ventilatory depression after 20 to 30 min of hypoxia; then, over a period of hours to days, there is a gradual and progressive time-dependent increase in V_E (Townsend et al., 2002). During submaximal exercise, V_E is significantly elevated with acute moderate hypoxia (Clark et al., 2007) and during submaximal and maximal exercise after both LHTL (Gore et al., 2001) and classical altitude training (Faulkner et al., 1967).

Muscles

At the level of the muscles, acute hypoxia decreases the myoglobin oxygen saturation and, therefore, the intramyocellular oxygen partial pressure is substantially lower at hypoxia under resting conditions and during all submaximal workloads up to $\dot{V}O_{2max}$ (Hoppeler et al., 2008). HIF-1- mediated signaling affects many genes with a functional significance in skeletal muscle tissue (Hoppeler and Vogt, 2001). During exercise, the deprivation of oxygen alters muscular responses and endurance training can increase muscle oxidative capacity and muscle capillary supply (Hoppeler et al., 2008). Moreover, responses should be more pronounced when exercising at altitude because the deprivation of oxygen to the muscles is greater (Hochachka et al., 1983). A few weeks spent at moderate to high altitude may slightly compromise muscle function. However, prolonged exposure to extremely high altitude can lead to a significant loss of muscle fiber cross-sectional area and a decrease of mitochondrial volume density that, combined, reduce mitochondrial volume by up to 30% (Hoppeler et al., 2003). This loss results in an increased capillary density due to the same number of capillaries supplying a smaller tissue space. Nevertheless, any loss of muscle mass by an athlete is likely to be detrimental in terms of performance. In particular, short-duration activities requiring a large strength–power component will be particularly affected; but those activities requiring body movement for a longer period of time may actually benefit from reduced body mass as long as $\dot{V}O_{2max}$ and the power to mass ratio are maintained. Although controversial (West and van Hall, 2007), several months spent at extreme to high altitude may reduce anaerobic metabolism, as evidenced by reduced lactate concentrations during exercise compared with levels attained upon recent ascent to altitude. However, at altitudes and durations more typical of those used by athletes (LHTL at 3000 m for $\sim$3 weeks), the evidence from both muscle and blood data did not indicate that lactate accumulation during intense exercise was depressed, nor was the calculated anaerobic ATP production (Gore et al., 2001). High altitude suppresses muscle Na^+/K^+-ATPase content and activity, and this enzyme is critical to maintaining membrane excitability and hence is linked to fatigue (Aughey et al., 2005). However, exposure to moderate altitude (3000 m LHTL for 23 nights) led to a small 3% decrease in Na^+/K^+-ATPase activity, but no change in plasma K^+ regulation or work output during high-intensity cycling (Aughey et al., 2005). These responses suggest that this duration of LHTL was insufficient to adversely affect muscle function, but does not preclude more deleterious effects with higher altitudes or longer-duration exposures.

Collectively, the physiological acclimatization responses to training at moderate altitude for several weeks are beneficial for competition at altitude (Gore et al., 2008) and probably for improved sea-level performance (Bonetti and Hopkins, 2009), although the placebo effect of well-conducted altitude camps cannot be discounted. In addition to the increase in red blood cells and subsequent increase in sea level $\dot{V}O_{2max}$, chronic training at moderate altitude (for a period of several weeks) can enhance muscle efficiency, probably at a mitochondrial level, and improve both muscle buffering and the ability to tolerate lactic acid production. A detailed review of nonhematological adaptations to hypoxia that can improve sea-level endurance performance has been published recently (Gore et al., 2007).

Responses in High Altitude Natives Compared with Low Altitude Residents

Numerous studies have investigated performance at altitude and adaptation to high altitude in high altitude natives compared with their counterparts from sea level. High altitude natives are defined as individuals born, raised, and living above 2500 m (Brutsaert, 2008). Extensive research has focused on blood because of its role in oxygen transport and the inference that the universal human adaptive response is a proliferation of red blood cells, because it has been exhibited by Europeans with brief exposure to altitude and by Andean high altitude natives with millennia of exposure (Beall et al., 1998). With regard to physical performance at altitude, only 3 people have reached the top of Mt. Everest 10 or more times, all of these being high altitude native Sherpas (Brutsaert, 2008). Natives to the Andean highlands have a high hemoglobin concentration [Hb] relative to their sea-level counterparts (Arnaud et al., 1979). In contrast, Sherpa and Tibetan males residing at 3600 to 4000 m have mean [Hb] 1 to 2 g/dL lower than predicted on the basis of Andean data (Beall and Reichsman, 1984). Beall and colleagues (1998) compared the mean [Hb] in Tibetan natives of the Himalayas (3800 to 4065 m) with life-long Bolivian highlanders of the Andes (3900 to 4000 m); and both groups of altitude natives were compared with sea-level residents from the third National Health and Nutrition Examination Survey (NHANES III) conducted in the United States. The Tibetans had a significantly lower [Hb] than the Bolivians and, additionally, the Tibetans had [Hb] closely resembling that of the sea-level residents from NHANES III. The contrasting [Hb] in these two populations, which both have millennia of exposure to the same high altitude stress, indicates that the human body is capable of more than one pattern of physiological adaptation to hypoxia (Beall et al., 1998).

High altitude natives have higher limits of work performance at altitude compared with their sea-level counterparts as is demonstrated by a higher mean $\dot{V}O_{2max}$ at altitude, a smaller decrement in $\dot{V}O_{2max}$ between sea level and altitude, and an enhanced pulmonary gas exchange (Brutsaert, 2008). The superior performance capacity at altitude of the Tibetan Sherpas is not necessarily an exceptional $\dot{V}O_{2max}$, but rather improved exercise economy, lung function, maximal cardiac output, and levels of blood oxygen saturation (Wu and Kayser, 2006). Compared with fully acclimatized lowlanders, high altitude natives of Ethiopia demonstrate a similar [Hb], serum EPO concentration, and oxygen saturation within the normal sea-level range (Beall et al., 2002). Ethiopian

highlanders, like Tibetans, have exceptional adaptations of oxygen uptake and/or delivery that are not associated with an increased red blood cell production in the presence of a hypoxemic stimulus (Beall et al., 2002). The success of Ethiopian distance runners, who predominantly live in the highlands of Ethiopia (2000 to 3000 m), demonstrates the performance benefits of altitude natives competing at sea level and at altitude.

In contrast, a recent review analyzed the likelihood of football teams winning when playing at different altitudes based on their altitude of residence (Gore et al., 2008). The analysis revealed that teams from moderate to high altitude are much less likely to win away at lower altitudes than at home. This outcome may be a consequence of high altitude natives being relatively unable to increase their $\dot{V}O_{2max}$ at sea level (Hochachka et al., 1991; Favier et al., 1995). For instance, a sea-level resident who has spent a few days at 3500 m would increase $\dot{V}O_{2max}$ by ~25% upon return to sea level, whereas an altitude resident from 3500 m taken to sea level would only increase $\dot{V}O_{2max}$ by about two-thirds of this amount (Gore et al., 2008). This discrepancy highlights the fact that there can be detrimental effects on sea-level performance if athletes stay too long at high altitudes and why there are not many great endurance athletes (competing at sea level) from the Himalayas or Andes despite lifelong residence at high altitude. In contrast, East Africans from moderate altitude are the dominant force in distance running. Living at high altitude may not be the only factor associated with the small number of top-class endurance athletes coming from lifelong residence at high altitude. Other factors, such as reduced training and competitive opportunities and limited access to facilities, might also explain the lack of success of individual athletes residing at high altitudes.

Smallest Worthwhile Change for an Athlete at Altitude

Coaches and athletes are critically interested in the magnitude of benefit from altitude training, as are researchers evaluating the various forms of classical altitude training, LHTL, and intermittent hypoxic exposure. However, individual variation affects all physiological responses to altitude, including performance (Chapman et al., 1998). Because altitude training studies with elite athletes have often used small sample sizes (~6 to 12 subjects) and thus have low statistical power, interpretation of the results after an intervention may benefit from consideration of practical and clinical effects on performance and not only conventional statistical significance (Hopkins et al., 2009). The smallest worthwhile change (SWC) in performance is about half the typical variation in an athlete's performance from competition to competition or ~0.5% to 1% (Hopkins and Hewson, 2001). However, we also have to take into account the typical error of measurement (or uncertainty) to detect changes in performance <www.sportsci.org/resource/stats/ssdetermine.html>. With $p = 0.05$ and power = 80%, 64 athletes would be required for a fully controlled study to detect a 1% improvement in performance if the typical error (or uncertainty) for performance is also 1% (Fig. 3). No altitude studies have used sample sizes of this magnitude; therefore, an alternative approach involving magnitude-based inferences and precision of estimation is emerging (Bonetti and Hopkins, 2008). Most altitude studies with elite athletes have been underpowered: the SWC is small (~0.5% to 1%), whereas the race-to-race variation of an elite athlete is similar (~1%), and the typical error of a good field or laboratory test is relatively larger (~1.5%). We advocate contemporary statistical analyses and interpretations to detect worthwhile changes in athlete performance resulting from altitude training where the signal (performance benefit) may be of smaller magnitude than the noise (or uncertainty) of the performance test (Hopkins et al., 2009). Additionally, Cohen's effect sizes (Cohen, 1988) to represent the magnitude of the difference between two groups in terms of the fraction or multiple of the between-subject standard deviation can also be calculated. Effect sizes are relatively robust to small sample sizes, as is common when working with truly elite athletes, and when combined with the SWC they offer a method to avoid false negative conclusions about the efficacy of interventions such as classical altitude training.

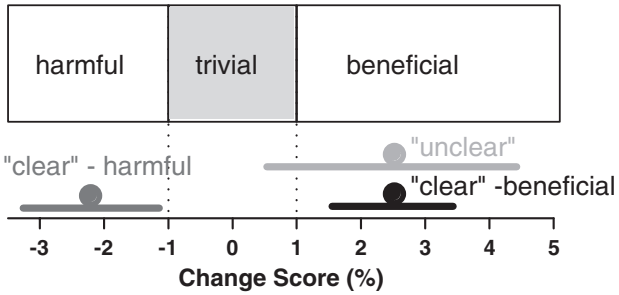


FIG. 3. Representation of smallest worthwhile change of 1% and its interpretation based on the appropriate typical error of a test and the magnitude of change (Hopkins et al., 2009). Top line (gray): if an athlete changes performance by 2.5% from pre- to postaltitude and the typical error is ±2.0%, the true change (0.5% to 4.5%) is unclear, since it possibly lies within the trivial band (±1.0%) of the smallest worthwhile change. Bottom line (black): if an athlete changes performance by 2.5% from pre- to postaltitude and the typical error is ±1.0%, the true change (1.5% to 2.5%) is clear. In this case, it is also clear that the performance change is beneficial, since the typical error lies outside the trivial band of the smallest worthwhile change. Left line (dark gray): if an athlete changes performance by −2.2% from pre- to postaltitude and the typical error is ±1.1%, the true change is clear (−1.1% to −3.3%) and likely harmful to performance.

Determinants of Running Performance

The factors that affect running performance have been widely investigated and described by various equations derived from Wilkie's model (Wilkie, 1980). For any given distance and runner, the best performance time will be achieved when the metabolic power required to cover a given distance is equal to the runner's $\dot{V}O_{2max}$ (Wilkie, 1980; Capelli, 1999). Some 20 years ago di Prampero (1986) demonstrated that endurance running speed is a function of an athlete's $\dot{V}O_{2max}$, the maximal fraction of $\dot{V}O_{2max}$ that can be maintained for the duration of a run (fractional utilization), and the energy cost of running per unit distance (running economy). Equations utilizing the energy cost of running, $\dot{V}O_{2max}$, and the fractional utilization of anaerobic energy stores have been used to predict performances for different running distances (Lacour et al., 1990; di Prampero et al., 1993; Capelli, 1999). These equations can be used as a basis for endurance performance in other modalities such as cycling, rowing, and swimming. For altitude training to be effective, it needs to improve the

specific capacities described by this model. Clearly, there is good evidence that an adequate dose of altitude will increase the Hb_{mass} and the corresponding $\dot{V}o_{2max}$ and possibly economy subsequent to mitochondrial efficiency. However, the power that can be sustained for 30 min is different from 15 min compared with 3 min (Bull et al., 2000). Consequently, there is a need for altitude studies to consider the spectrum of endurance performance after an altitude sojourn, rather than just one performance task of a specific duration.The performance of an endurance athlete outside competition is problematic at the best of times, even with just a single performance effort, let alone multiple performances. Nevertheless, a limitation of virtually all altitude studies of which we are aware is that they have examined only one type of endurance performance, such as a 5000-m time trial (Levine and Stray-Gundersen, 1997; Gore et al., 2001; Saunders et al., 2009b).

Implications for Endurance Training at Altitude

Decades of research into the use of altitude to prepare for competitions at altitude (Pugh et al., 1964; Dill and Adams, 1971; Gore et al., 2008) and sea level (Bonetti and Hopkins, 2008) have demonstrated that altitude training can be a valuable tool in an elite athlete's preparation. However, effective altitude training requires a foundation of at least several years of training at a high level. We do not recommend this methodology of training for developmental athletes who usually lack fundamental experiences, such as adequate international competition experience, and who can readily gain a more than a 1% performance benefit from conventional training at sea level. The fact that elite athletes across virtually all endurance sports continue to use classical altitude training (Dick, 1992; Friedmann-Bette, 2008) over all other hypoxic modalities suggests that it is a key factor in optimizing competition performance. Therefore, designing and implementing effective altitude training programs could provide a competitive advantage. It has been proposed that due to the reduction in oxygen transport at moderate altitude some elite athletes are not able to maintain the training velocities required for competitive fitness (Chapman et al., 1998). This contention is not supported by several studies that demonstrate improved sea-level performance after a period of classical altitude training (Daniels and Oldridge, 1970; Dill and Adams, 1971; Burtscher et al., 1996; Bailey et al., 1998). The impaired $\dot{V}o_{2max}$ at altitude (Clark et al., 2007) will reduce absolute training intensity in endurance exercise measured by velocity for a given distance. However, the relative training intensity is higher at any given speed due to the hypoxia-induced reduction in $\dot{V}o_{2max}$ and, therefore, altitude training can be used as an added stimulus to train at higher intensities than possible at sea level (Friedmann-Bette, 2008). In running, this can be particularly beneficial, because the increased running intensity is not associated with the increased mechanical trauma associated with running at the high velocities required to match this intensity at sea level. Another explanation proposed to account for the lack of adaptation from altitude training are altitude-related illness and depleted iron stores prior to altitude exposure (Mazzeo, 2005). It is essential for athletes undertaking periods of altitude training to have adequate ferritin levels, ensured by oral iron supplements while at altitude, and to avoid illness. Exercise at altitude can lead to immune suppression through sympathoadrenal pathways that increase the release of epinephrine and impairment of T-cell activation and proliferation, which increases the risk of infection during initial exposure to altitude (Mazzeo 2005). Avoiding illness is not always possible, but the risks can be reduced by easing into training initially at altitude so that an athlete's immune system is not placed under excessive stress from both hypoxia and hard training. With acclimatization the immune suppression is lessened over time, with epinephrine release returning to sea-level values and T-cell function returning to near sea-level values (Mazzeo, 2005); hence training load can be incremented.

Performance in shorter events ($\sim$1 to 2 min) is relatively unaffected at moderate altitude (Peronnet et al., 1991), and this fact can be utilized when training elite athletes at altitude. To avoid a reduction in race-specific fitness, athletes should undertake a series of shorter race-pace efforts where velocity is not compromised (or possibly enhanced due to the reduced air density; Peronnet et al., 1991) and for which they have longer recoveries than at sea-level to maintain speed during the entire training session. For example, distance runners may undertake a session of ten 400-m efforts with 1-min recovery at sealevel. At moderate altitude, the session of ten 400-m efforts can still be completed at the same absolute pace as at sea level, but with the recovery lengthened to 2 to 3 min between each effort. With acclimatization and partial restoration of $\dot{V}o_{max}$ at altitude, the duration of the interval efforts can be increased and/or the recovery times decreased. This approach fits with the general model that we use when training athletes at altitude, that is, taking the first few days to a week to acclimatize to the altitude. Lower-intensity, higher-volume training is accompanied by shorter-interval work to maintain competition velocities. As acclimatization occurs, the intensity of longer training intervals can be increased.

There is considerable interindividual variability in the reduction of aerobic power during acute exposure to hypoxia (Gore et al., 1996; Clark et al., 2007) or during living and training at moderate altitude. Consequently, individual adjustment of training intensity and periodization of training at altitude are required to avoid overtraining or detraining (Friedmann-Bette, 2008). In the initial days at altitude, athletes should avoid maximal exercise to minimize any exercise-induced decrease in EPO production, increase in hemolysis, and acute inflammatory reactions (Berglund, 1992). The severity of altitude, time spent training at altitude, history of altitude training, timing of training leading into competition, and whether there is a lower- altitude training option are all important factors to consider when designing the training program at moderate altitude. A summary of recommendations for altitude training at varying altitude levels is given in Table 2. The severity of altitude is important because the amount of time taken to adapt to the hypoxic stress is proportionally longer. For elite endurance athletes, we consider altitudes from 1800 to 2500 m to be optimal for classical altitude training, although one study showed that 21 days classical altitude training at 1816 m may not be high enough to increase Hb_{mass} (Pottgiesser et al., 2008). Moreover, this altitude is below the 2200-m threshold likely to increase red cell volume (Weil et al., 1968). Altitudes lower than 1800 m do not appear to provide sufficient hypoxic stimulus for key physiological adaptation. Altitudes much higher than 2500 m have greater potential to cause overtraining and to compromise the ability of an athlete to absorb and respond to the hypoxic and training stimuli.

Table 2. Training Recommendations Based on Alitude Level

Altitude (m)	*<1800*	*1800 to 2200*	*2200 to 3000*	*3000 to 3500*	*>3500*
Duration (weeks)	4 to 8	3 to 6	2 to 4	2 weeks	Not recommended
Typical training loads	Near normal to sea level	Lower intensity early; longer recoveries required for intense interval sessions	Higher volume, lower intensity throughout; intervals more around 5- to 10-km race pace	Low to moderate intensity training with emphasis on volume	Very minimal intensity during training and long build-in period required
Positives	Minimal training intensity disruption and shorter build-in period required for intense training	High enough to increase red blood cell production, especially over ~2000 m	Relative intensity increased by 14% to 21%; means same metabolic load even though velocity is slower than at sea level	High training velocities during sprint training; almost certain increase in red blood cell production	Extremely high training velocities during sprint training
Negatives	Too low to induce increase in red blood cell production	Training intensity compromised (~3% to 6%) during 1500-m to 10-km race-pace interval sessions, especially early in camp	1500-m to 10-km race-pace training compromised (~6% to 12%) at 3000 m	Can cause overtraining and the inability to respond to hypoxia and training stimuli; 10,000 m race-speed training compromised by ~15% at 3500 m	Too high and can lead to significant muscle atrophy;1500-m to 10-km race-pace training severely compromised
Ancillary factors prior to altitude training	Ideally conducted after a period of altitude training at higher altitude earlier in the preparation year	Iron supplement in few days preceding camp; efficacy of altitude camp is moderated by preceding "form;" being fresh and illness free; beneficial to have prior altitude training in previous years	Iron supplement in few days preceding; ideally, athletes should be fresh and illness free	Iron supplement for week or two beforehand; ideally, athletes should be fresh and illness free; only attempt altitude training this high if athletes have had several beneficial experiences at lower altitudes	Iron supplement in weeks preceding; essential to be fresh and illness free
Ancillary factors while at altitude	Useful as a top-up prior to competitions so that high-quality training can be undertaken at this lower altitude; these recommendations are for distance runners, but general guidelines are applicable for other endurance athletes	Daily iron supplements; allow for adequate recovery between training; no intense longer- duration work in first few days; compared with sea level, 2 to 3 times longer recoveries advisable during interval sessions (1500-m to 5-km race pace)	Daily iron supplements; start off easy with no intense training, especially in first week to avoid overtraining; 5- 10-km race-pace intervals done with 1.5 to 2 times longer recoveries than at sea level	Daily iron supplements; concentrate on low intensity, higher volume training; short efforts (≤200 m) to retain neuromuscular patterning; longer recoveries (3 to 4 times sea-level equivalent) for interval sessions (focus on 10-km race pace).	Daily iron supplements; only low-intensity training possible; some short-duration (≤200 m) speed work to retain neuromuscular patterning; very long recoveries (4 to 5 times sea-level equivalent) in longer-interval sessions (focus on 10- to 21.1-km race pace)

These recommendations are for distance runners but general guidelines are applicable for other endurance athletes.

The time spent at altitude is another critical factor; there is no point in making the effort to travel and train at altitude if the length of exposure is insufficient to stimulate worthwhile adaptations. At least 2 weeks is recommended for altitude training designed to improve competition performance at altitude (Schuler et al., 2007) and 3 to 4 weeks when using altitude training to improve sea-level performance (Rusko et al., 2004). Anecdotally, many endurance athletes spend longer than 4 weeks training at altitude, which may achieve better responses; however, such claims require further systematic investigation. The additional benefits of extended altitude training, if any, need to be quantified and evaluated against the cost and time away from home. Figure 1 indicates that 2 to 4 weeks elicits the best results in performance across classical altitude studies that have measured competitive performance, and that longer duration at altitude does not elicit more substantial performance improvements and may even cause deterioration in performance gains from the initial 2 to 4 weeks. It is recommended that no more than 2 months be spent at altitude at any one time and that it is more beneficial for athletes to undertake short blocks (2 to 4 weeks) more frequently throughout the year.

Recent unpublished work with athletes at the Australian Institute of Sport indicates that longer than 8 weeks is required between altitude training stints to maximize the training afterward. A longer exposure also ensures that athletes are not excessively fatigued going into a subsequent altitude training camp, training phase, or competition. The periodization of the training year and the training phase prior to an altitude camp are other factors to consider carefully. It is advisable for endurance athletes to use altitude training several times throughout a competition year. The emphasis of training can be tailored to meet the demands of the training phase of the athletes. For example, in the early build-up period, when athletes are trying to increase the volume of training and high quality training is not as critical, a longer period of altitude training can be undertaken with the focus on accumulating a high volume of training utilizing the hypoxic stimulus, rather than on accumulating high intensity training. There should be adequate periods at sea level between these multiple altitude exposures (>8 weeks) to capitalize on increased capacities gained from altitude and to ensure that athletes are fresh and motivated for training at altitude for each camp.

On the other hand, we have used low- to moderate-altitude training during a competitive season in elite middle-distance runners (Saunders et al., 2009b). In this particular study, seven elite middle-distance runners lived at ~1800 m and did all their low- to moderate-intensity running at 1700 to 2200 m. However, because the athletes were in their competitive season, they completed all high quality sessions at a 900-m altitude to maintain the 800- to 1500-m race-pace interval training required to stay race fit. This protocol resulted in improved competitive performance by 1.9% (90% confidence limits, 1.3% to 2.5%).

Conclusions

In summary, altitude training has been used by elite athletes and coaches and researched extensively for the past five decades. The general consensus in the athletic community is that altitude training can improve endurance performance. Several modalities of altitude–hypoxic training have been developed to provide the best compromise between hypoxic acclimatization and maintaining high intensity training in the face of a reduced $\dot{V}o_{2max}$. Among these modalities, classical altitude training, during which athletes live and train at moderate altitude, appears to be the most popular, and can, according to a recent meta-analysis (Bonetti and Hopkins, 2008), provide benefits for sea-level performance in endurance events. When embarking on classical altitude training camps, it is important to allow sufficient time (at least 2 weeks), to ensure that the exposure is worthwhile (in terms of physiological acclimatization and particularly the increase of red blood cells), to use moderate-altitude venues from 1800 to 2500 m, to carefully design and monitor the training done at altitude to allow the body to adapt to hypoxia and avoid illness or overtraining (including sufficient short-duration, high-intensity training to minimize the reduction in race-specific fitness), and to ensure adequate iron levels by using oral supplementation as necessary. Multiple (two to four) classical altitude camps throughout a year may elicit the greatest benefit for sea-level performance of elite endurance athletes. Altitude training needs to fit within the competition schedule of an athlete and not compromise the quality of their basic training completed near sea level.

Disclosures

Authors Saunders, Pyne, and Gore have no conflicts of interest or financial ties to disclose.

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