Title: Defining the “Dose” of Altitude Training: How High to Live for Optimal Sea Level Performance Enhancement

Running head: Optimal living altitude for sea level performance enhancement

Authors: Robert F. Chapman¹, Trine Karlsen², Gier K. Resaland², R-L Ge³, Matthew P. Harber⁴, Sarah Witkowski⁴, James Stray-Gundersen², Benjamin D. Levine⁴

¹Department of Kinesiology, Indiana University, Bloomington, IN; ²Norweigan University of Sport and Physical Education, Oslo, Norway; ³Research Center for High Altitude Medicine, Qinghai University, China; ⁴Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, The University of Texas Southwestern Medical Center, Dallas, TX.

Corresponding author: Benjamin D. Levine, M.D.

Institute for Exercise and Environmental Medicine

7232 Greenville Ave.

Dallas, TX 75231   PH: 214-345-4619   Fax: 214-345-4618

BenjaminLevine@texashealth.org
ABSTRACT

Chronic living at altitudes ~2500m causes consistent hematological acclimatization in most, but not all, groups of athletes; however, responses of erythropoietin (EPO) and red cell mass to a given altitude show substantial individual variability. We hypothesized that athletes living at higher altitudes would experience greater improvements in sea level performance, secondary to greater hematological acclimatization, compared to athletes living at lower altitudes. After 4 weeks of group sea level training and testing, 48 collegiate distance runners (32M, 16W) were randomly assigned to one of four living altitudes (1780m, 2085m, 2454m, or 2800m). All athletes trained together daily at a common altitude from 1250m - 3000m following a modified Live High – Train Low model. Subjects completed hematological, metabolic, and performance measures at sea level, before and after altitude training; EPO was assessed at various time points while at altitude. Upon return from altitude, 3000m time trial performance was significantly improved in groups living at the middle two altitudes (2085m and 2454m) but not in groups living at 1780m and 2800m. EPO was significantly higher in all groups at 24h and 48h, but returned to sea level baseline after 72h in the 1780m group. Erythrocyte volume was significantly higher within all groups after return from altitude, and was not different between groups. These data suggest that when completing a 4 week altitude camp following the Live High – Train Low model, there is a target altitude between 2000m and 2500m that produces an optimal acclimatization response for sea level performance.

Keywords: erythropoietin, maximal oxygen uptake, athletes
INTRODUCTION

The altitude training strategy of “Live High – Train Low” has been shown repeatedly to improve sea level endurance exercise performance and maximal oxygen uptake (VO2max) in cohorts of elite (37, 40, 43, 45) and sub-elite (27) endurance athletes. These improvements in performance have been linked, in large part, to the hematological acclimatization response to altitude (i.e. an increase in the oxygen carrying capacity of the blood) (7, 15, 26). Outcomes from our previous work show an average acute erythropoietin (EPO) increase at moderate altitude to ~150% of sea level baseline and average red cell mass (measured from the erythrocyte volume, defined as blood volume – plasma volume) increases of ~1.5 – 2.0 ml·kg⁻¹ after four weeks of altitude residence (12, 24, 27, 43). In these investigations, we have utilized a common altitude training site (Deer Valley / Salt Lake City, Utah, USA) with a fixed moderate living altitude of 2500m. While chronic living at 2500m has provided a robust enough hypoxic stimulus to cause significant hematological acclimatization in the majority of athletes, the responses of EPO and red cell mass to a given altitude show substantial individual variability (12, 17, 18, 21, 42). In fact, many athletes have shown a relatively mild acute and chronic EPO response to altitude, leading to no changes in red cell volume, VO2max, or sea level track performance, despite four weeks of chronic exposure to > 2500m (12, 18). Indeed, when this erythropoietic response is absent, there is little evidence that altitude works to improve endurance performance (42). These data would suggest that there may be a minimum threshold living altitude or hypoxic “dose” for adequate hematological acclimatization, and thus performance enhancement, in athletes completing altitude training regimens (25, 31, 34, 44, 47, 48).
To examine the threshold altitude concept for hematological responses, we previously studied 48 athletes using separate 24 hour hypobaric chamber exposures to four simulated altitudes of 1780m, 2085m, 2454m, and 2800m (17). While these athletes also showed large inter-individual variability of 24 hour EPO responses to altitude, the data suggested that the altitude induced increase in EPO is largely dependent on the hypoxic dose. Although EPO was significantly elevated over sea level baseline after 6 and 24 hours at all four simulated altitudes, the EPO response to the two highest simulated altitudes (2454m and 2800m) was significantly higher (~ 3 times as large at 24 hours) as the EPO response to 1780m and 2085m. This response would suggest that a threshold altitude of ~ 2100m – 2500m may exist to attain a sustained increase in group EPO response over 24 hours (17, 31, 47). If so, the outcomes of many altitude training studies could be largely influenced by the living altitude utilized, particularly if the living altitude is below this suggested 2100m – 2500m threshold. Ultimately, it remains unknown if chronic residence at differing strata of terrestrial altitudes will show the same hematological responses as short term exposure to simulated altitudes. For the athlete engaged in altitude training, the identification of an optimal living altitude holds tremendous practical application.

Therefore, the purpose of this study was to examine the physiological and performance responses of athletes completing a four week “Live High – Train Low” altitude training camp, with athletes assigned to one of four different locations of living altitude between 1780m and 2800m. Based on current knowledge, we hypothesized that groups living at relatively higher altitude would demonstrate greater improvements in sea level performance measures, secondary to greater hematological acclimatization.
MATERIALS AND METHODS

Subjects. Forty-eight collegiate track and cross country runners (32 men and 16 women, 21 ± 2 yrs, 64.0 ± 8.4 kg, 174 ± 9 cm) volunteered to participate in the study and gave their informed consent after receiving information of the study protocol. Data from this cohort on responses to acute hypobaric hypoxia (16, 17) and submaximal exercise (28) have been published elsewhere. Exclusion criteria included altitude residence (>1500m) longer than seven days in the previous 10 months, permanent altitude residence of > three months during their lifetimes, or injury or illness that impaired normal training and racing prior to the study. All subjects gave written informed consent to a protocol approved by the Institutional Review Board of the University of Texas Southwestern Medical Center at Dallas and Presbyterian Hospital of Dallas.

Study protocol. The study protocol was a modified version of previous protocols developed by the authors (27, 43). In the first phase of the study, four weeks of supervised sea level training in Dallas, Texas was performed, during which exercise testing, simulated altitude exposure, blood testing, and iron maintenance or replacement therapy was initiated. In the second phase of the study, subjects were transported by airplane to Salt Lake City, Utah. Subjects were randomly assigned to one of four groups, and each group of subjects was transported by car to different locations at different altitudes in the Wasatch mountain area for a 28 day altitude training camp. In the third phase of the study, subjects returned by airplane to Dallas for three weeks of sea level follow-up testing. The study protocol is displayed in Figure 1. While in Dallas, all subjects were housed in the same corporate apartment housing complex. In Utah, subjects in each altitude group were housed in comparable vacation condominiums, typical of a ski resort area. Subjects slept one or two to a bedroom. Although food intake was not controlled, weekly
grocery shopping trips were supervised by research staffers to ensure healthy food choices were purchased.

Altitude training camp. Subjects were matched by sex, training history, VO\text{2}max, and 3K time in groups of 4, and then assigned in a balanced randomization to housing at four different altitudes in the Wasatch Mountain region near Salt Lake City. Four women and eight men were randomly assigned to each of the four altitudes, with slight adjustments in group assignments made prior to departure for altitude so that the mean 24 hour EPO response to a simulated altitude of 2454 m was similar between groups (see below under Assessments: Decompression chamber exposure). Subjects lived at Heber City (1780m), Park City (2085m), Deer Valley (2454m), or Guardsman’s Pass (2800m). During the training camp, subjects were requested to spend the majority of time at their living altitude, and were supervised by a staff member to ensure compliance. With some exceptions, subjects gathered daily for supervised training at the same altitude and location (between 1250m and 3000m), regardless of the subjects’ assigned living altitude. This effectively standardized the training altitude across all subjects for each day of the altitude exposure. Training followed the “HiHiLo” model of live high – train low altitude training (i.e. moderate altitude living, moderate altitude low intensity base training and high intensity training at low altitude) (43). Low intensity and moderate “base” training took place at moderate altitudes (1780-3000m), while higher intensity runs and aerobic interval training sessions were performed at the lowest possible altitude in Salt Lake City (1250m). All subjects received daily liquid iron supplementation (Feo-Sol, 9 mg elemental iron · ml\textsuperscript{-1}) during both the four week sea level and four week altitude training camps, in doses based on pre-altitude plasma ferritin
concentration (5-45 m\cdot\text{day}^{-1}). In testing the week prior to altitude exposure, all men had serum ferritin levels $> 30\ \text{ng}\cdot\text{mL}^{-1}$, and all women were $> 20\ \text{ng}\cdot\text{mL}^{-1}$.

Assessments

Treadmill assessment. Submaximal and maximal oxygen uptake ($\text{VO}_2\text{max}$) were tested at sea level (Dallas, Texas) at four time points throughout the study, with the submaximal data published previously (28). Test one was performed upon initial athlete arrival for the study, test two after four weeks of sea level training in Dallas, test three within the first 48 hours after returning from altitude to Dallas, and test four occurring two weeks after returning to sea level. In the submaximal protocol, after a 15 minute warm up on the treadmill, subjects ran at a constant velocity of 14.4 km\cdot h^{-1} (9 miles\cdot h^{-1}). Metabolic variables (minute ventilation, $\text{VO}_2$, heart rate) were recorded from the 4th minute of this exercise bout. For the maximal exercise protocol, subjects ran to volitional exhaustion following a modified Astrand / Saltin protocol (4). Subjects ran at a constant velocity of 14.4 km\cdot h^{-1} (9 miles\cdot h^{-1}) for men and 12.8 km\cdot h^{-1} (8 miles\cdot h^{-1}) for women at a 0% grade for 2 minutes, with the grade increasing 2% every 2 minutes until exhaustion. $\text{VO}_2$ was measured via the Douglas bag method, with fractional gas concentrations determined by mass spectroscopy (Marquette MGA 1100, Milwaukee, WI) and ventilatory volumes by a dry gas meter (Collins, Boston, MA). Maximal heart rate was measured from telemetry (Polar, Finland).

Performance. Sea level performance was assessed by 3000 meter time trial races on a 400 meter track in Dallas, Texas. Two time trial races were performed before and two time trial races after
the altitude training camp, each within 1-2 days of the VO\textsubscript{2max} test. The time trial races were held between 0700 and 0800 in the morning and were run in separate women’s and men’s heats. Subjects were instructed to achieve the best time possible in each race. Experienced pace setters (athletes not involved in the study) were utilized to set a fast, competitive pace for the first 1600 meters of the 3000 meter race to ensure physiological rather than tactical performance. The pace setter or “rabbit” ran the same preselected race pace in all time trials. Time was recorded for each athlete to the nearest 0.1 second.

Hematology assessment. Plasma volume, blood volume, and erythrocyte volume (blood volume – plasma volume) were measured once at sea level before the altitude training camp and twice after the altitude training camp. Plasma volume was measured by using the Evans blue dye indicator-dilution technique (32). Subjects rested quietly for at least 30 minutes in the supine position, a known quantity of Evans blue dye was injected through a catheter placed in a peripheral vein, and venous blood was drawn at 10, 20 and 30 minutes after injection for the measurements of absorbance at 620 and 740 nm via spectrophotometry (model DU 600 Beckman, Brea, CA). Hematocrit was measured via microcentrifuge and blood volume was estimated by dividing plasma volume by 1 minus hematocrit, using appropriate corrections for trapped plasma and peripheral sampling (14). Total red cell volume was defined as blood volume minus plasma volume. This method has been compared recently in a different group of athletes against the carbon monoxide re-breathing technique with excellent agreement for the assessment of blood compartment volumes ($r^2 = 0.85$; 3% difference between methods) (20).
Decompression chamber exposure. The protocol and the outcomes from the same subject sample utilized in this study have been published previously (17). Briefly, each week for a total of four weeks prior to departure to altitude, subjects spent 24 hours in a decompression chamber at simulated altitudes of 1780m, 2085m, 2454m, and 2800m in a pseudo random order (the last simulated altitude for all subjects was fixed a priori at 1780m to minimize the effect of the chamber exposures on subsequent experiments conducted in the field). The simulated altitudes were chosen to match the terrestrial altitudes utilized in the study. Subjects were blinded to all simulated altitudes, and when decompression was started, the chamber operator would briefly “bounce” the simulated altitude over a wide range before settling at the treatment altitude. For comfort, only 12 athletes were in the chamber during any 24 hour exposure. The temperature (25 ± 0.5 °C), humidity (28 ± 1%), and CO2 concentration (0.07 ± 0.02%) in the chamber was carefully controlled.

EPO concentration. During the chamber exposure, EPO concentration was measured at sea level (before decompression) and after 6 and 24 hours at each simulated altitude in the decompression chamber. During the altitude camp, EPO concentration was measured at 24 hours, 48 hours, 72 hours, 1 week, 2 weeks, and 3 weeks of altitude exposure, as well as the day following return to sea level in Dallas, Texas. For logistical reasons, in half of the subjects, EPO was measured in plasma by radioimmunoassay (Ramco, Houston, TX), and in the other half, it was determined in serum with an enzyme-linked immunosorbent assay kit (Human EPO Quantikine IVD, catalog no. DEP00, R & D Systems). Comparison of the two methods and adjustments made are reported elsewhere (17).
**Training quantification and standardization.** Subjects kept daily training logs, which included training volume (recorded in units of miles run per day) and the number of “high-intensity” workout sessions (e.g. interval training or tempo runs performed at a pace, subjectively determined by the athlete, as being faster than lactate threshold pace). Prior to the study, each athlete and their coach were given a global training template, previously used by the researchers in altitude training studies (27, 43), in order to design their individual training plan. This template has previously been successful in matching training impulse (TRIMPS) across multiple groups living and/or training at different altitudes. Athletes were asked to complete common workouts (e.g. interval sessions, long runs, tempo efforts) together on the same day of the week, so that an overall group training milieu could be established.

**Oxygenation during sleep.** Arterial oxyhemoglobin saturation (SaO₂) during sleep was determined by pulse oximetry (Ohmeda 3700, Louisville, CO). Measures were taken between 0400 and 0600 on the mornings corresponding to 24h, 48h, 72h, 1 week, 2 week, and 3 week time points after arrival at altitude. These measures were utilized to document the desaturation differences between groups in relation to EPO production, as well as a potential marker affecting the quality of sleep and recovery.

**Statistical analysis.** Data were analyzed using IBM SPSS version 20 statistical software. All data values are reported as mean ± standard deviation, except where noted. A Shapiro-Wilk test was utilized and all dependent variables were determined to be normally distributed. Therefore, parametric statistics was used in all further analyses. Two-way split plot repeated measures analysis of variance (ANOVA) with *a priori* tests of simple main effects (and Fisher’s least
significant difference post hoc analysis) were used to determine differences in dependent
measures at different time points within altitude groups. The same procedure was also used to
determine differences in dependent measures between altitude groups at the same time point.
One way ANOVAs were used to determine differences in baseline subject characteristics
between altitude groups. The alpha level for significance was set at $p < 0.05$.

RESULTS

Subjects. A total of 45 athletes (29 men and 16 women) successfully completed the full protocol.
One athlete dropped out prior to travel to altitude for personal reasons; one was in a car accident
in Utah and was unable to complete the altitude exposure; and one became ill and was unable to
complete the post-altitude testing (all males; two from the 1780m group and one from the 2085m
group). Subject characteristics are displayed in table 1. No differences in physical
characteristics, VO$_2$max, ferritin stores, or change in EPO concentration after 24 h of chamber
exposure to a simulated altitude of 2454m were detected between the different living altitude
groups at inclusion in the study.

Training. Training volume during the altitude training camp was not different between the four
altitude living groups, and neither was the number of self-classified high intensity workouts. The
total volume of miles (1.609 km) run per person was 227 ± 48, 219 ± 57, 215 ± 54, and 221 ± 56
in the athletes living at 1780m, 2085m, 2454m, and 2800m respectively. The number of athlete
reported high intensity workouts per week was 3.8 ± 1.5, 3.8 ± 0.8, 3.1 ± 1.1, and 3.9 ± 1.5
workouts in the athletes living at 1780m, 2085m, 2454m, and 2800m respectively.
Primary Outcome Variable: 3000 meter time trial performance. Sea level 3000 meter time trial performance significantly improved after altitude training in athletes living at 2085m and 2454m at both the immediate and two weeks post-altitude time points (figure 2, left). There was no significant change in sea level 3000m performance at either post-altitude time point in groups living at the highest and lowest altitudes.

Metabolic variables. Metabolic data during maximal exercise are displayed in Table 2. $\dot{V}O_2_{\text{max}}$, when expressed as L.min$^{-1}$, improved significantly from before to after altitude training in groups living at 2085m, 2454m, and 2800m with no change in the group living at 1780m (figure 2, right). At the two week time point after return from altitude, absolute $VO_2_{\text{max}}$ was significantly higher than pre-altitude in all groups. Relative $VO_2_{\text{max}}$ responses (expressed as mL·kg$^{-1}$·min$^{-1}$) differed slightly, due to variations in mass changes between groups (table 2). While there was no significant change in mass from pre- to post-altitude in the 1780m, 2086m, and 2454m groups, mass did increase by 0.8 kg ($p=0.045$) in the 2800m group. Maximal ventilation and maximal heart rate was not different before and after altitude training at any time point in all groups. Individual pre- and post-altitude $VO_2_{\text{max}}$ values and 3000m race times for each altitude group are displayed in figure 3.

During submaximal exercise, steady state $VO_2$ was not different before and after altitude training at any time point in all groups. However, minute ventilation during submaximal exercise was lower or trended lower immediately post-altitude in the 1780m ($p<0.05$) and 2085m groups ($p=0.077$) and higher post-exercise in the 2454m group (figure 4). Heart rate during submaximal exercise was significantly lower immediately post exercise in the 1780m and 2085m groups. However, at the two weeks post altitude time point, heart rate during submaximal
exercise was significantly lower in the 1780m, 2085m, and 2454m groups, but remained unchanged in the 2800m group.

**Oxygenation during sleep.** SaO2 values obtained during sleep over the course of the altitude camp are displayed in figure 5. Subjects displayed a consistent difference in SaO2 across most time points between the two lowest and two highest altitude groups.

**EPO response.** EPO concentrations at various altitude time points are displayed in figure 6. EPO significantly increased from sea level baseline to 24 hours after arriving at altitude in all four altitude groups, and remained significantly elevated over baseline after 48 hours. At the 72 hour time point at altitude, EPO was still significantly elevated in the 3 highest altitude groups; the 1780m cohort had an EPO concentration which had returned to sea level baseline (99.8 ± 15.8% of sea level baseline). After 72 hours of altitude exposure, EPO was significantly higher in the group living at 2800m compared with the group living at 1780m. Beginning with the one week through the three week at altitude time points, no differences were found between altitude and baseline EPO levels in any group. However, upon return to sea level (post-altitude), EPO levels were significantly lower than pre-altitude baseline values in all four altitude groups. Between groups upon return to sea level, EPO was significantly lower in the 2085m and 2800m cohorts than both the 1780m and 2464m groups.

Figure 7 displays the EPO responses after 24 hours in the hypobaric chamber versus the same altitude in the field. While there was no difference in the mean EPO response between the chamber and the field within each group, the responses to the same altitude (real or simulated) showed substantial individual variability within and across subjects.
Hematological response. Erythrocyte volume, whether expressed in absolute (L) or relative (mL·kg\(^{-1}\)) terms, was significantly increased pre- to immediately post-altitude in all four altitude groups (figure 8). However, by the two week post-altitude time point, erythrocyte volume was not significantly different from pre-altitude levels in any altitude group. There were no differences in erythrocyte volume between altitude groups at any time point. No differences were observed in blood volume or plasma volume (in either absolute or relative terms) between groups at any time point. Similarly, plasma volume was not different at any time point within any of the four altitude groups.

DISCUSSION

The primary finding of this investigation is that improvements in sea level endurance performance and maximal oxygen uptake after a 4 week Live High – Train Low altitude training camp are influenced by the living altitude utilized. Whether immediately upon return or two weeks after return to sea level, athlete groups who lived at the middle of our altitude range (2085m and 2454m) significantly improved mean sea level 3k time trial performance (~2-3%), while athlete groups living on the low and high ends of our altitude range (1780m and 2800m) demonstrated no changes in sea level 3k performance. These performance changes occurred despite equivalent increases in red cell mass within all four altitude groups, suggesting that altitude induced erythropoiesis may be necessary, but is not sufficient by itself to improve sea level performance. The data suggest that when completing an altitude camp utilizing a 4 week...
HiLo training model, there is a target living altitude between (and perhaps around) 2000m to 2500m that produces an optimal acclimatization response for sea level performance.

**Is There a Threshold Altitude for Optimal Performance Enhancement?**

The lowest living altitude of 1760m appears to be sub-optimal for improving sea level performance. The rate of EPO formation in response to acute hypoxic exposure has been demonstrated to be proportional to the level of hypoxic stress (13), which matches previously published hypobaric chamber exposure data utilizing our athlete cohort (17). In that study, the 24 hour EPO response to a simulated altitude of 1780m was approximately one–third the size of the response to simulated altitudes of 2454m and 2800m. Extending this finding to chronic altitude exposure in the field, we hypothesized that the higher an athlete lived during an altitude training camp, the greater the acute and chronic EPO response would be. Consistent with this hypothesis, SaO2 measured during sleep in the field was reliably lower in the two highest living groups compared to the two lowest altitude groups across the four week altitude camp (figure 5). Although all four altitude groups significantly increased EPO over sea level baseline at the 24 hour time point, EPO levels in the 1780m group had returned to sea level baseline in just 72 hours while it remained elevated in the higher altitude groups (figure 6). To quantify another way, over the first 72 hours at altitude, the area under the curve for EPO relative to sea level baseline (assuming linear changes in EPO between the 24, 48, and 72 hour time points) was 33%, 36%, and 44% less for the 1780m group relative to the 2085m, 2454m, and 2800m groups respectively. This outcome would suggest that the 1780m group had less erythropoietic stimulus to increase red cell mass than the higher altitude groups.
However, in contrast to our hypothesis, measures of changes in red cell mass after four weeks of HiLo altitude training were ~6% higher in all four altitude groups after return to sea level. We speculate (but cannot prove) that the amount of time spent training at moderate altitude in these athletes may have been enough of a supplemental hypoxic stimulus to augment the effect of the background altitude environment. Indeed, Robertson and colleagues (38) suggested that living high in conjunction with training both high and low was a particularly potent combination for increases in Hb mass, though their comparison group was only athletes living low and training high, not living high and training low. Thus the overall EPO profile within our cohort of athletes living > 2000m was essentially indistinguishable, at least as determined from a single measure taken early in the morning. It also may be that EPO has benefits on performance independent of its effects on erythropoiesis, such as improved cardiac and endothelial function (8), though such benefits have been difficult to isolate (28, 35). From a methodological standpoint, a lack of differences in red cell mass between altitude groups despite EPO differences may simply be a function of a lack of sensitivity of the Evans Blue dye method for determining plasma volume (see Limitations section below). Regardless of these speculations, these observations provide further evidence that the performance enhancement from an altitude training camp is not a linear function of the augmentation in red cell mass which appears to be necessary, but not sufficient for performance enhancement after HiLo altitude training.

Is There a Ceiling Altitude for Optimal Performance Enhancement?

While our initial hypothesis presumed changes in performance and maximal oxygen uptake after 4 weeks of HiLo training would be primarily dependent on the increasing magnitude of hematological acclimatization as living altitude increased, we failed to see an improvement in
relative VO₂max (with initial return to sea level) or performance in the 2800m group. The increases in acute and chronic EPO, as well as RCM, were of the same or greater magnitude in the highest altitude group as in the middle altitude groups (2085m and 2454m) who displayed improved performance, suggesting hematological factors are not the cause. The most likely explanation for the lack of performance improvement immediately upon return to sea level in the 2800m group is an accumulated influence of negative acclimatization factors related to living at this highest altitude. Some potential factors include (but are not limited to) increased incidence of sleep apnea and other disturbances in sleep quality / quantity or an increased incidence of mild acute mountain sickness (AMS), both of which begin to display at threshold altitudes below 2800m (5, 46). If so, the overall training response (i.e. both the training stimulus and recovery from training) could have been substantially poorer in the 2800m group versus the lower altitude groups. We do not have direct data on the incidence of either impaired sleep or AMS in our subjects, which if present likely did not carry across all four weeks of altitude residence. However, SaO₂ during sleep was consistently lower in the 2800m group at all time points throughout the study (figure 5).

Additionally, our data do suggest that negative effects associated with increased ventilatory acclimatization at the highest living altitude may be a contributing factor to the lack of performance improvement in the 2800m group. With chronic residence at altitude, ventilatory acclimatization causes a progressive, time-dependent increase in ventilation both at rest and at all exercise workloads (6). Generally, this increase in ventilation is viewed as a positive adaptive benefit for altitude residence, one that helps to defend alveolar oxygen partial pressure (PO₂) and creates a higher pressure head for diffusion of O₂ into the arterial blood (41). However, when the athlete ultimately returns to sea level, the gain in the ventilatory response to exercise that
developed with acclimatization to altitude often persists as an elevated exercise minute ventilation ($V_E$), both at submaximal and maximal workloads (19, 27, 43, 49). Interestingly, during submaximal steady state running in our subjects at 14.5 km $\cdot$ h$^{-1}$ (9 miles $\cdot$ hr$^{-1}$), $V_E$ was (or trended) 3-4% lower in the two lowest altitude groups immediately upon return to sea level, while $V_E$ was (or trended) 4-5% higher in the two highest altitude groups (figure 4).

Submaximal steady state HR followed a similar pattern, with significant declines (~2%) at the lowest two altitudes immediately upon return to sea level, and no change in the two highest altitude groups. We believe these longitudinal differences in the response to constant pace submaximal exercise is indicative of the balance between ventilatory and HR responses to an increase in aerobic fitness after a 4 week HiLo training camp and the progressive ventilatory acclimatization that comes from higher living altitudes. Specifically at the lowest two altitudes, the data suggest that the increase in overall aerobic fitness was greater than the amount of ventilatory acclimatization; while at the higher two altitudes, the opposite was the case.

Augmented ventilatory acclimatization, as measured by greater ventilation during submaximal exercise in the 2800m group, may have negatively affected both training during the altitude camp and race performance upon return to sea level. As ventilation increases with progressive exercise, the muscular work necessary to ventilate the lungs increases in an exponential manner, even at altitude where air density is slightly reduced. At very high ventilatory volumes, a small increase in $V_E$ causes a disproportionate increase in both the work and oxygen cost of breathing (1, 22). Additionally, in many elite endurance athletes, exercise at high work rates results in the achievement of expiratory flow limitation (10, 22). Even impending expiratory flow limitation during exercise causes the athlete to hyperinflate the lung, increasing end-inspiratory and end-expiratory lung volumes (30), a response which causes a
substantial increase in the work and cost of breathing (1) and dyspnea (2). As ventilatory feedback cues are the most potent indicator of effort and work output during exercise (33, 39), a heightened ventilatory response to racing at sea level or training while at altitude in the 2800m group may have provided a strong enough stimuli for the athletes in that cohort to modulate work output, slowing their racing or training pace. Ultimately, our data would suggest that endurance athletes who live at 2800m (or higher) do not demonstrate a group improvement in sea level performance after an altitude camp, which we speculate to be due in part to negative factors associated with acclimatization to this altitude.

Limitations

Despite the use of a number of control procedures to minimize the group training and training camp effects on performance, several methodological and logistical limitations must be considered when evaluating this data. Approximately 300m separated each living altitude group, and while we felt this stratification would be adequate in separating out acclimatization and subsequent performance responses between groups, it is possible this amount of living altitude difference was not enough to discern clear differences in dependent measures. For example, factors such as alterations in the barometric pressure with weather changes, (which in the mountains may be quite local could have altered the actual living environment), may have changed the effective altitude for different groups. Additionally, while part of the living altitude assignments for each subject was based on the 24 hour chamber response to 2454m (in an attempt to control for the individual EPO response to altitude), it is possible that the EPO response to the various assigned living altitudes in the field are not a linear and equal deviation from the chamber response to 2454m across all subjects. Within each altitude cohort, we saw
significant individual variability in the 24 hour EPO response to the same altitude in the chamber versus in the field (figure 7), which suggests the inherent difficulty (as suggested elsewhere (12)) in trying to predict the EPO response at altitude using a short term chamber exposure.

Similarly, other individual responses to altitude living or training could have influenced the amount of change in performance after the altitude camp. For example, elite athletes who show mild arterial oxyhemoglobin desaturation during heavy exercise at sea level show a disproportionate decline in VO$_2$max (9, 23) and race performance (11) at a fixed altitude, which may have affected training while at altitude. However, while training volume and the number of quality workout sessions was not different between groups, the training impulse was not measured and may have in fact differed between altitude cohorts. We speculate that the significant differences between groups in pre- to post-altitude 3000m performance may be partially the result of differences in training between groups, secondary to differing altitude acclimatization responses to the various altitudes (and not to divergent hematological responses as we originally hypothesized). This would need to be tested directly. Finally, for determining red cell mass, we utilized the Evans Blue dye method, which has both support (20) and concerns (3, 35) regarding its precision compared to other methods of red cell or hemoglobin mass determination, such as carbon monoxide rebreathing. While there is likely enough noise and individual variability in the multiple systems and dependent variables measured to preclude elucidation of direct linear mechanistic relationships, from an integrative standpoint, the data do suggest an optimal living altitude for sea level performance.

In conclusion, four weeks of Live High – Train Low altitude training, living at 2085m and 2454m, resulted in significantly improved sea level race performance and maximal oxygen uptake in a cohort of trained distance runners. Athletes living at elevations lower (1780m) and
higher (2800m) than those altitudes demonstrated no changes in sea level performance after the altitude camp. This data suggest that when completing an altitude training camp, there is an optimal living altitude for producing improvements in sea level performance.

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Figure Legends

Figure 1. Study timeline. Subjects completed four weeks of sea level training, followed by four weeks of HiHiLo altitude training (with groups assigned to different living altitudes), and two weeks of post-altitude training at sea level. Testing was completed at various time points throughout the experiment (see Methods).

Figure 2. (Left) Percent change in 3000m time trial performance at sea level from pre-altitude to immediate post-altitude (open bars) and two-weeks post altitude (closed bars). Note that a positive change indicates an improvement in performance. Values are mean ± SE. * Significant increase from pre-altitude. (Right) Percent change in VO2max (L·min⁻¹) at sea level from pre-altitude to immediate post-altitude (open bars) and two-weeks post altitude (closed bars). Values are mean ± SE. * Significant increase from pre-altitude.

Figure 3. (Top) Maximal oxygen uptake (VO2max) and (Bottom) 3000m time trial performance. Values are from measures completed at sea level, pre- and post-altitude training. Connected data points are paired individual values for each subject. Single data points with error bars represent mean ± SD for each condition within each altitude group. * Significantly different from pre-altitude.

Figure 4. (Left) Percent change in minute ventilation (VE) and (Right) percent change in heart rate (HR) during submaximal steady state exercise at 14.4 km · h⁻¹ (9 miles · h⁻¹) at sea level from pre-altitude to immediate post-altitude (open bars) and two-weeks post altitude (closed bars). Note that a positive change indicates an improvement in performance. Values are mean ± SE. * Significant increase from pre-altitude.

Figure 5. Arterial oxyhemoglobin saturation (SaO₂) measured during sleep. Values are mean ± SE. Letters indicate significant differences at the same time point at the p < 0.05 level: a = 1780m different from 2454m; b = 1780m different from 2800m; c = 2085m different from 2454m; d = 2085m different from 2800m.

Figure 6. Erythropoietin (EPO) concentration, expressed as a percent of sea level, pre-altitude baseline, at various time points. Values are mean ± SE. * Significantly different from pre-altitude baseline in all four altitude groups. # Significantly different from pre-altitude baseline in the 2085m, 2454m, and 2800m groups only. + Significantly different from pre-altitude baseline in the 2085m and 2800m groups only.

Figure 7. Erythropoietin (EPO) concentration, expressed as a percent of sea level, pre-altitude baseline, after 24 hours in a hypobaric chamber versus the same altitude in the field. Connected data points are paired individual values for each subject. Single data points with error bars represent mean ± SD for each condition within each altitude group.
Figure 8. Percent change in erythrocyte volume at sea level from pre-altitude to immediate post-altitude (open bars) and two-weeks post altitude (closed bars). Values are mean ± SE.

* Significant increase from pre-altitude.
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Living Altitude</th>
<th>1780m</th>
<th>2085m</th>
<th>2545m</th>
<th>2800m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/women, number of subjects</td>
<td>6/4</td>
<td>7/4</td>
<td>8/4</td>
<td>8/4</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>21.4 ± 3.1</td>
<td>20.1 ± 1.5</td>
<td>20.7 ± 1.6</td>
<td>21.2 ± 2.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175.5 ± 10.1</td>
<td>174.7 ± 7.9</td>
<td>171.8 ± 8.6</td>
<td>175.3 ± 10.2</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>64.7 ± 9.3</td>
<td>64.2 ± 8.4</td>
<td>62.6 ± 8.0</td>
<td>64.3 ± 9.2</td>
</tr>
<tr>
<td>VO_{2}max (mL · kg{\textsuperscript{-1}} · min{\textsuperscript{-1}})</td>
<td>63.9 ± 4.8</td>
<td>61.9 ± 6.7</td>
<td>61.3 ± 7.2</td>
<td>62.0 ± 7.1</td>
</tr>
<tr>
<td>Serum ferritin (ng · mL{\textsuperscript{-1}})</td>
<td>33 ± 15</td>
<td>27 ± 7</td>
<td>34 ± 15</td>
<td>39 ± 17</td>
</tr>
<tr>
<td>ΔEPO after 24 hr chamber exposure at 2454 m (%)</td>
<td>110 ± 73</td>
<td>116 ± 74</td>
<td>106 ± 88</td>
<td>103 ± 91</td>
</tr>
</tbody>
</table>

Values are mean ± SD. VO_{2}max, maximal oxygen uptake; EPO, serum erythropoietin concentration.
Table 2. Metabolic Variables.

<table>
<thead>
<tr>
<th>Altitude</th>
<th>Pre-Altitude</th>
<th>Immediate Post-Altitude</th>
<th>Two Weeks Post-Altitude</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VO₂max mL·kg⁻¹·min⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1780m (n=10)</td>
<td>63.9 ± 4.8</td>
<td>64.0 ± 5.8</td>
<td>64.8 ± 6.2</td>
</tr>
<tr>
<td>2085m (n=11)</td>
<td>61.9 ± 6.7</td>
<td>63.0 ± 5.6*</td>
<td>63.9 ± 5.7*</td>
</tr>
<tr>
<td>2454m (n=12)</td>
<td>61.3 ± 7.2</td>
<td>63.3 ± 7.8*</td>
<td>64.6 ± 7.5*</td>
</tr>
<tr>
<td>2800m (n=12)</td>
<td>62.0 ± 7.1</td>
<td>62.5 ± 7.2</td>
<td>63.8 ± 7.3*</td>
</tr>
<tr>
<td></td>
<td>VEmax L·min⁻¹ BTPS</td>
<td></td>
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</tr>
<tr>
<td>1780m (n=10)</td>
<td>137.1 ± 17.0</td>
<td>139.5 ± 20.2</td>
<td>140.7 ± 22.6</td>
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<tr>
<td>2085m (n=11)</td>
<td>138.9 ± 22.1</td>
<td>141.6 ± 21.4</td>
<td>143.2 ± 21.5</td>
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<tr>
<td>2454m (n=12)</td>
<td>139.3 ± 25.2</td>
<td>140.8 ± 27.7</td>
<td>144.4 ± 22.5</td>
</tr>
<tr>
<td>2800m (n=12)</td>
<td>147.7 ± 28.4</td>
<td>151.0 ± 28.8</td>
<td>152.3 ± 27.9</td>
</tr>
<tr>
<td></td>
<td>HRmax beats·min⁻¹</td>
<td></td>
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</tr>
<tr>
<td>1780m (n=10)</td>
<td>196 ± 10</td>
<td>194 ± 11</td>
<td>196 ± 9</td>
</tr>
<tr>
<td>2085m (n=11)</td>
<td>194 ± 9</td>
<td>192 ± 9</td>
<td>193 ± 9</td>
</tr>
<tr>
<td>2454m (n=12)</td>
<td>197 ± 9</td>
<td>197 ± 9</td>
<td>195 ± 10</td>
</tr>
<tr>
<td>2800m (n=12)</td>
<td>192 ± 10</td>
<td>191 ± 10</td>
<td>191 ± 10</td>
</tr>
</tbody>
</table>

Values are mean ± SD. VO₂max, maximal oxygen uptake; VEmax, minute ventilation at maximal exercise; HRmax, maximal heart rate. * Significantly different from pre-altitude.
Time Trial Performance (% improvement from pre-altitude time)

VO2max (% of pre-altitude measure)

* Immediate Post-Altitude
* Two Weeks Post-Altitude

Altitude
1780m 2085m 2454m 2800m 1780m 2085m 2454m 2800m
<table>
<thead>
<tr>
<th>Altitude (m)</th>
<th>Pre-Alt</th>
<th>Post-Alt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1754</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2085</td>
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<tr>
<td>2454</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2800</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**VO₂max (mL kg⁻¹ min⁻¹)**

- 1754m:...
- 2085m:...
- 2454m:...
- 2800m:...

**3000m Time Trial Performance (s)**

- 1754m:...
- 2085m:...
- 2454m:...
- 2800m:...
Altitude

Submax VE (% of pre-altitude measure)

Immediate Post-Altitude

Two Weeks Post-Altitude

*p=0.077*

*p=0.153*

Submax HR (% of pre-altitude measure)

Immediate Post-Altitude

Two Weeks Post-Altitude

*p=0.037*

*p=0.33*

*p=0.033*

*p=0.033*

*p=0.033*
Altitude

1780m 2085m 2454m 2800m 1780m 2085m 2454m 2800m

Red Cell Mass Volume (% of pre-altitude measure)

Immediate Post-Altitude

Two Weeks Post-Altitude

* * *

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