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Defining the “dose” of altitude training: how high to live for optimal sea level performance enhancement

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

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Chapman RF, Karlsen T, Resaland GK, Ge RL, Harber MP, Witkowski S, Stray-Gundersen J, Levine BD. Defining the “dose” of altitude training: how high to live for optimal sea level performance enhancement. *J Appl Physiol* 116: 595–603, 2014. First published October 24, 2013; doi:10.1152/jappphysiol.00634.2013.—Chronic living at altitudes of ~2,500 m 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 with athletes living at lower altitudes. After 4 wk of group sea level training and testing, 48 collegiate distance runners (32 men, 16 women) were randomly assigned to one of four living altitudes (1,780, 2,085, 2,454, or 2,800 m). All athletes trained together daily at a common altitude from 1,250–3,000 m 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. On return from altitude, 3,000-m time trial performance was significantly improved in groups living at the middle two altitudes (2,085 and 2,454 m), but not in groups living at 1,780 and 2,800 m. EPO was significantly higher in all groups at 24 and 48 h, but returned to sea level baseline after 72 h in the 1,780-m 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-wk altitude camp following the live high-train low model, there is a target altitude between 2,000 and 2,500 m that produces an optimal acclimatization response for sea level performance.

erythropoietin; maximal oxygen uptake; athletes

THE ALTITUDE TRAINING STRATEGY of “live high-train low” (HiLo) has been shown repeatedly to improve sea level endurance exercise performance and maximal oxygen uptake ($\dot{V}O_{2\max}$) in cohorts of elite (37, 40, 43, 45) and subelite (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 laboratory’s 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 after 4 wk of altitude residence (12, 24, 27, 43). In these investigations, we have utilized a common altitude training site (Deer Valley, Salt Lake City, UT) with a fixed moderate living altitude of 2,500 m. While chronic living at 2,500 m 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, $\dot{V}O_{2\max}$, or sea level track performance, despite 4 wk of chronic exposure to >2,500 m (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, our laboratory previously studied 48 athletes using separate 24-h hypobaric chamber exposures to four simulated altitudes of 1,780, 2,085, 2,454, and 2,800 m (17). While these athletes also showed large interindividual variability of 24-h 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 h at all four simulated altitudes, the EPO response to the two highest simulated altitudes (2,454 and 2,800 m) was significantly higher (~3 times as large at 24 h) as the EPO response to 1,780 and 2,085 m. This response would suggest that a threshold altitude of ~2,100–2,500 m may exist to attain a sustained increase in group EPO response over 24 h (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 2,100- to 2,500-m 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 4 wk HiLo altitude training camp, with athletes assigned to one of four different locations of living altitude between 1,780 and 2,800 m. Based on current knowledge, we hypoth-

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esized 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 yr, 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 ($>1,500$ m) longer than 7 days in the previous 10 mo, permanent altitude residence of >3 mo during their lifetimes, or injury or illness that impaired normal training and racing before 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, 4 wk of supervised sea level training in Dallas, Texas were performed, during which exercise testing, simulated altitude exposure, blood testing, and iron maintenance or replacement therapy were 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 3 wk of sea level follow-up testing. The study protocol is displayed in Fig. 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.

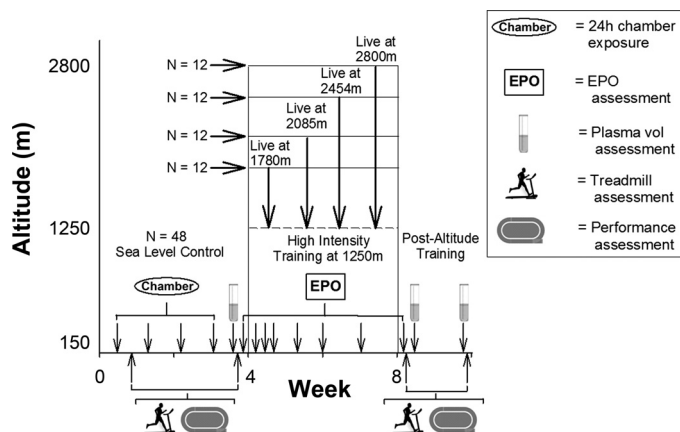


Fig. 1. Study timeline. Subjects completed 4 wk of sea level (SL) training, followed by 4 wk of HiHiLo altitude training (i.e., moderate altitude living, moderate altitude low-intensity base training, and high-intensity training at low altitude) (with groups assigned to different living altitudes), and 2 wk of postaltitude training at SL. Testing was completed at various time points throughout the experiment (see MATERIALS AND METHODS). EPO, erythropoietin.

Altitude Training Camp

Subjects were matched by sex, training history, $\dot{V}O_{2\max}$, and 3-km time in groups of four 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 before departure for altitude so that the mean 24-h EPO response to a simulated altitude of 2,454 m was similar between groups (see below under *Assessments: Decompression chamber exposure*). Subjects lived at Heber City (1,780 m), Park City (2,085 m), Deer Valley (2,454 m), or Guardsman's Pass (2,800 m). 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 1,250 and 3,000 m), 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 HiLo 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 (1,780–3,000 m), while higher intensity runs and aerobic interval training sessions were performed at the lowest possible altitude in Salt Lake City (1,250 m). All subjects received daily liquid iron supplementation (Feo-Sol, 9 mg elemental iron/ml) during both the 4-wk sea level and 4-wk altitude training camps, in doses based on prealtitude plasma ferritin concentration (5–45 ml/day). In testing the week before altitude exposure, all men had serum ferritin levels >30 ng/ml, and all women were >20 ng/ml.

Assessments

Treadmill assessment. Submaximal oxygen uptake ($\dot{V}O_2$) and $\dot{V}O_{2\max}$ were tested at sea level (Dallas, Texas) at four time points throughout the study, with the submaximal data published previously (28). *Test 1* was performed on initial athlete arrival for the study, *test 2* after 4 wk of sea level training in Dallas, *test 3* within the first 48 h after returning from altitude to Dallas, and *test 4* occurring 2 wk after returning to sea level. In the submaximal protocol, after a 15-min warm-up on the treadmill, subjects ran at a constant velocity of 14.4 km/h (9 mph). Metabolic variables [minute ventilation ($\dot{V}E$), $\dot{V}O_2$, heart rate] were recorded from the 4th min 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/h (9 mph) for men and 12.8 km/h (8 mph) for women at a 0% grade for 2 min, with the grade increasing 2% every 2 min until exhaustion. $\dot{V}O_2$ 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 3,000-m time trial races on a 400-m track in Dallas, Texas. Two time trial races were performed before, and two time trial races were performed after, the altitude training camp, each within 1–2 days of the $\dot{V}O_{2\max}$ 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 1,600 m of the 3,000-m 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 s.

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 min 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 min 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 rebreathing 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 4 wk before departure to altitude, subjects spent 24 h in a decompression chamber at simulated altitudes of 1,780, 2,085, 2,454, and 2,800 m in a pseudo-random order (the last simulated altitude for all subjects was fixed a priori at 1,780 m 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-h exposure. The temperature ($25 \pm 0.5^\circ\text{C}$), humidity ($28 \pm 1\%$), and CO_2 concentration ($0.07 \pm 0.02\%$) 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 h at each simulated altitude in the decompression chamber. During the altitude camp, EPO concentration was measured at 24, 48, and 72 h, and 1, 2, and 3 wk of altitude exposure, as well as the day following return to sea level in Dallas, Texas. For logistical reasons, in one-half of the subjects, EPO was measured in plasma by radioimmunoassay (Ramco, Houston, TX), and in the other one-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). Before the study, each athlete and his or her coach was given a global training template, previously used by the researchers in altitude training studies (27, 43), to design his or her individual training plan. This template has previously been successful in matching training impulse across multiple groups living and/or training at different altitudes. Athletes were asked to complete common work-

outs (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 (SaO_2) during sleep was determined by pulse oximetry (Ohmeda 3700, Louisville, CO). Measures were taken between 0400 and 0600 on the mornings, corresponding to 24-, 48-, and 72-h, and 1-, 2-, and 3-wk 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 means \pm SD, 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 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 α -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 before 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 men; two from the 1,780-m group and one from the 2,085-m group). Subject characteristics are displayed in Table 1. No differences in physical characteristics, $\dot{V}\text{O}_{2\text{max}}$, ferritin stores, or change in EPO concentration after 24 h of chamber exposure to a simulated altitude of 2,454 m were detected between the different living altitude groups at inclusion in the study.

Training

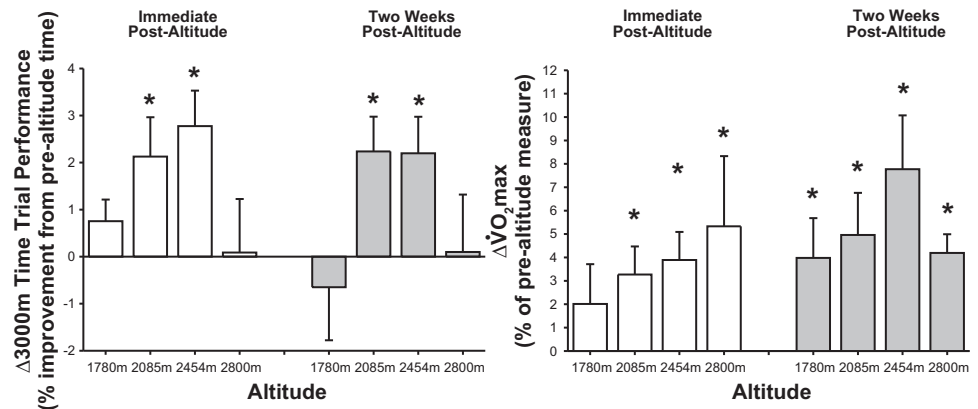
Training volume during the altitude training camp was not different between the four altitude living groups, and neither was the number of self-classified high-intensity workouts. The total volume of miles (1.609 km) run per person was 227 ± 48 , 219 ± 57 , 215 ± 54 , and 221 ± 56 mi. in the athletes living at 1,780, 2,085, 2,454, and 2,800 m, respectively. The number

Table 1. Subject characteristics

	Living Altitude			
	1,780 m	2,085 m	2,545 m	2,800 m
Men/women, no. of subjects	6/4	7/4	8/4	8/4
Age, yr	21.4 ± 3.1	20.1 ± 1.5	20.7 ± 1.6	21.2 ± 2.2
Height, cm	175.5 ± 10.1	174.7 ± 7.9	171.8 ± 8.6	175.3 ± 10.2
Mass, kg	64.7 ± 9.3	64.2 ± 8.4	62.6 ± 8.0	64.3 ± 9.2
$\dot{V}\text{O}_{2\text{max}}$, $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	63.9 ± 4.8	61.9 ± 6.7	61.3 ± 7.2	62.0 ± 7.1
Serum ferritin, ng/ml	33 ± 15	27 ± 7	34 ± 15	39 ± 17
ΔEPO after 24-h chamber exposure at 2,454 m, %	110 ± 73	116 ± 74	106 ± 88	103 ± 91

Values are means \pm SD. $\dot{V}\text{O}_{2\text{max}}$, maximal oxygen uptake; EPO, serum erythropoietin concentration; Δ , change.

Fig. 2. *Left*: percent change (Δ) in 3,000-m time trial performance at SL from prealtitude to immediate postaltitude (open bars) and 2-wk postaltitude (shaded bars). Note that a positive change indicates an improvement in performance. Values are means \pm SE. *Significant improvement from prealtitude. *Right*: percent change in maximal oxygen uptake ($\dot{V}O_{2\max}$; l/min) at SL from prealtitude to immediate postaltitude (open bars) and 2-wk postaltitude (shaded bars). Values are mean \pm SE. *Significant increase from prealtitude.



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 1,780, 2,085, 2,454, and 2,800 m, respectively.

Primary Outcome Variable: 3,000-m Time Trial Performance

Sea level 3,000-m time trial performance significantly improved after altitude training in athletes living at 2,085 and 2,454 m at both the immediate and 2 wk postaltitude time points (Fig. 2, left). There was no significant change in sea level 3,000-m performance at either postaltitude time point in groups living at the highest and lowest altitudes.

Metabolic Variables

Metabolic data during maximal exercise are displayed in Table 2. $\dot{V}O_{2\max}$, when expressed as liters per minute, improved significantly from before to after altitude training in groups living at 2,085, 2,454, and 2,800 m, with no change in the group living at 1,780 m (Fig. 2, right). At the 2-wk time point after return from altitude, absolute $\dot{V}O_{2\max}$ was significantly higher than prealtitude in all groups. Relative $\dot{V}O_{2\max}$ responses (expressed as $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) differed slightly, due to variations in mass changes between groups (Table 2). While

there was no significant change in mass from pre- to postaltitude in the 1,780-, 2,086, and 2,454-m groups, mass did increase by 0.8 kg ($P = 0.045$) in the 2,800-m group. Maximal ventilation and maximal heart rate were not different before and after altitude training at any time point in all groups. Individual pre- and postaltitude $\dot{V}O_{2\max}$ values and 3,000-m race times for each altitude group are displayed in Fig. 3.

During submaximal exercise, steady-state $\dot{V}O_2$ was not different before and after altitude training at any time point in all groups. However, $\dot{V}E$ during submaximal exercise was lower or trended lower immediately postaltitude in the 1,780-m ($P < 0.05$) and 2,085-m groups ($P = 0.077$) and higher postexercise in the 2,454-m group (Fig. 4). Heart rate during submaximal exercise was significantly lower immediately postexercise in the 1,780- and 2,085-m groups. However, at the 2-wk postaltitude time point, heart rate during submaximal exercise was significantly lower in the 1,780-, 2,085-, and 2,454-m groups, but remained unchanged in the 2,800-m group.

Oxygenation During Sleep

SaO_2 values obtained during sleep over the course of the altitude camp are displayed in Fig. 5. Subjects displayed a consistent difference in SaO_2 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 Fig. 6. EPO significantly increased from sea level baseline to 24 h after arriving at altitude in all four altitude groups and remained significantly elevated over baseline after 48 h. At the 72-h time point at altitude, EPO was still significantly elevated in the three highest altitude groups; the 1,780-m cohort had an EPO concentration that had returned to sea level baseline ($99.8 \pm 15.8\%$ of sea level baseline). After 72 h of altitude exposure, EPO was significantly higher in the group living at 2,800 m compared with the group living at 1,780 m. Beginning with the 1-wk through the 3-wk at altitude time points, no differences were found between altitude and baseline EPO levels in any group. However, on return to sea level (postaltitude), EPO levels were significantly lower than prealtitude baseline values in all four altitude groups. Between groups on return to sea level, EPO was significantly lower in the 2,085- and 2,800-m cohorts than both the 1,780- and 2,464-m groups.

Figure 7 displays the EPO responses after 24 h in the hypobaric chamber vs. the same altitude in the field. While

Table 2. Metabolic variables

	<i>n</i>	Prealtitude	Immediate Postaltitude	2 wk Postaltitude
$\dot{V}O_{2\max}$, $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$				
1,780 m	10	63.9 ± 4.8	64.0 ± 5.8	64.8 ± 6.2
2,085 m	11	61.9 ± 6.7	$63.0 \pm 5.6^*$	$63.9 \pm 5.7^*$
2,454 m	12	61.3 ± 7.2	$63.3 \pm 7.8^*$	$64.6 \pm 7.5^*$
2,800 m	12	62.0 ± 7.1	62.5 ± 7.2	$63.8 \pm 7.3^*$
$\dot{V}E_{\max}$, l/min BTPS				
1,780 m	10	137.1 ± 17.0	139.5 ± 20.2	140.7 ± 22.6
2,085 m	11	138.9 ± 22.1	141.6 ± 21.4	143.2 ± 21.5
2,454 m	12	139.3 ± 25.2	140.8 ± 27.7	144.4 ± 22.5
2,800 m	12	147.7 ± 28.4	151.0 ± 28.8	152.3 ± 27.9
HR_{\max} , beats/min				
1,780 m	10	196 ± 10	194 ± 11	196 ± 9
2,085 m	11	194 ± 9	192 ± 9	193 ± 9
2,454 m	12	197 ± 9	197 ± 9	195 ± 10
2,800 m	12	192 ± 10	191 ± 10	191 ± 10

Values are means \pm SD; *n*, no. of subjects. $\dot{V}E_{\max}$, minute ventilation at maximal exercise; HR_{\max} , maximal heart rate. *Significantly different from prealtitude.

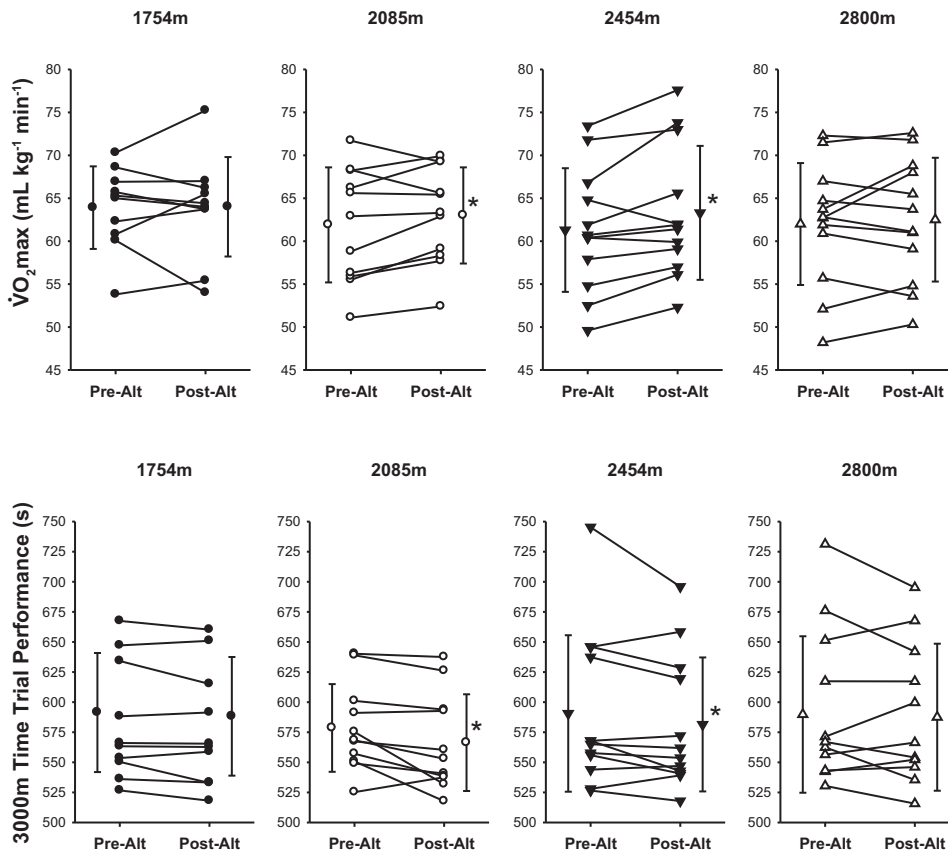


Fig. 3. $\dot{V}O_{2max}$ (top) and 3,000-m time trial performance (bottom). Values are from measures completed at SL and pre- and postaltitude training. Connected data points are paired individual values for each subject. Single data points with error bars represent mean \pm SD for each condition within each altitude group. *Significantly different from prealtitude.

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 (liters) or relative (ml/kg) terms, was significantly increased pre- to immediately postaltitude in all four altitude groups (Fig. 8). However, by the 2-wk postaltitude time point, erythrocyte volume was not significantly different from prealtitude 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 $\dot{V}O_{2max}$ after a 4-wk HiLo altitude training camp are influenced by the living altitude utilized. Whether immediately upon return or 2 wk after return to sea level, athlete groups who lived at the middle of our altitude range (2,085 and 2,454 m) significantly improved mean sea level 3-km time trial performance (~2–3%), while athlete groups living on the low and high ends of our altitude range (1,780 and 2,800 m) demonstrated no changes in sea level 3-km performance. These performance changes occurred despite equivalent increases in red cell mass within all

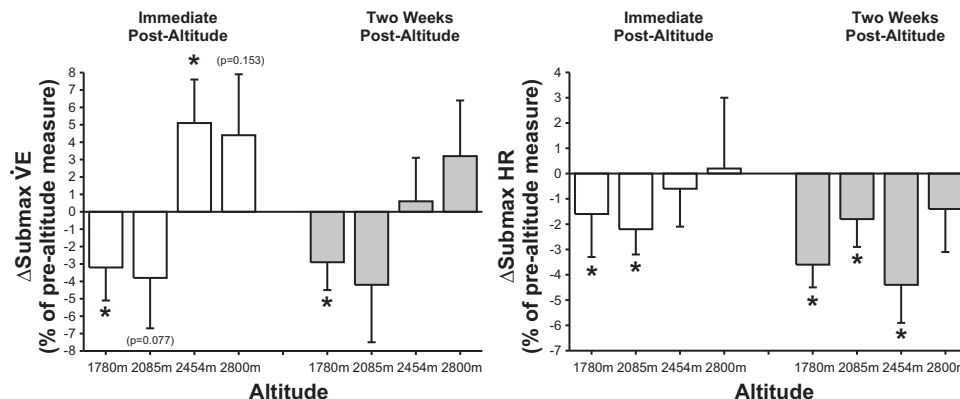


Fig. 4. Percent change in minute ventilation ($\dot{V}E$; left) and percent change in heart rate (HR; right) during submaximal steady-state exercise at 14.4 km/h (9 mph) at SL from prealtitude to immediate postaltitude (open bars) and 2-wk postaltitude (shaded bars). Note that a positive change indicates an improvement in performance. Values are means \pm SE. *Significant increase from prealtitude.

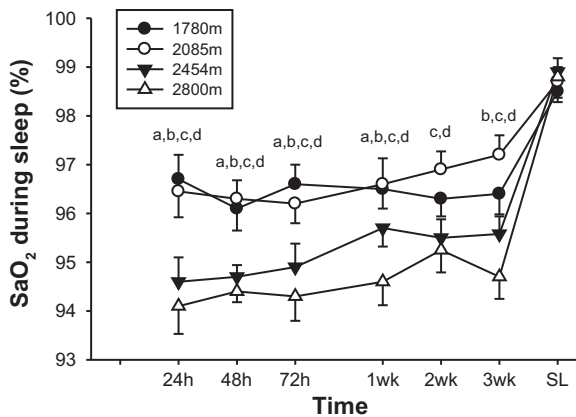


Fig. 5. Arterial oxyhemoglobin saturation (SaO_2) measured during sleep. Values are means \pm SE. Letters indicate significant differences at the same time point at the $P < 0.05$ level: ^a 1,780 m different from 2,454 m; ^b 1,780 m different from 2,800 m; ^c 2,085 m different from 2,454 m; ^d 2,085 m different from 2,800 m.

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-wk HiLo training model, there is a target living altitude between (and perhaps around) 2,000 to 2,500 m that produces an optimal acclimatization response for sea level performance.

Is There a Threshold Altitude for Optimal Performance Enhancement?

The lowest living altitude of 1,760 m appears to be suboptimal 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-h EPO response to a simulated altitude of 1,780 m was approximately one-third the size of the response to simulated altitudes of 2,454 and 2,800 m. 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, SaO_2 measured during sleep in the field was reliably lower in the two highest living groups compared with the two lowest altitude groups across the 4 wk altitude camp (Fig. 5). Although all four altitude groups significantly increased EPO over sea level baseline at the 24-h time point, EPO levels in the 1,780-m group had returned to sea level baseline in just 72 h, while it remained elevated in the higher altitude groups (Fig. 6). To quantify another way, over the first 72 h 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-h time points) was 33, 36, and 44% less for the 1,780-m group relative to the 2,085-, 2,454-, and 2,800-m groups, respectively. This outcome would suggest that the 1,780-m 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 4 wk of HiLo altitude training were \sim 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, although 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 $>2,000$ m 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), although 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* 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 $\dot{V}O_{2max}$ after 4 wk 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 $\dot{V}O_{2max}$ (with initial return to sea level) or performance in the 2,800-m group. The increases in acute and chronic EPO, as well as red cell mass, were of the same or greater magnitude in the highest altitude group as in the middle-altitude groups (2,085 and 2,454 m), who displayed improved performance, suggesting hematological factors are not the cause. The most likely explanation for the lack of

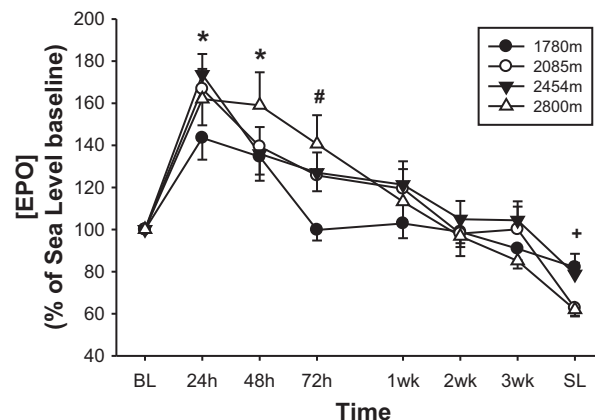


Fig. 6. EPO concentration ([EPO]), expressed as a percentage of SL, prealtitude baseline, at various time points. Values are means \pm SE. *Significantly different from prealtitude baseline in all four altitude groups. #Significantly different from prealtitude baseline in the 2,085-m, 2,454-m, and 2,800-m groups only. +Significantly different from prealtitude baseline in the 2,085-m and 2,800-m groups only.

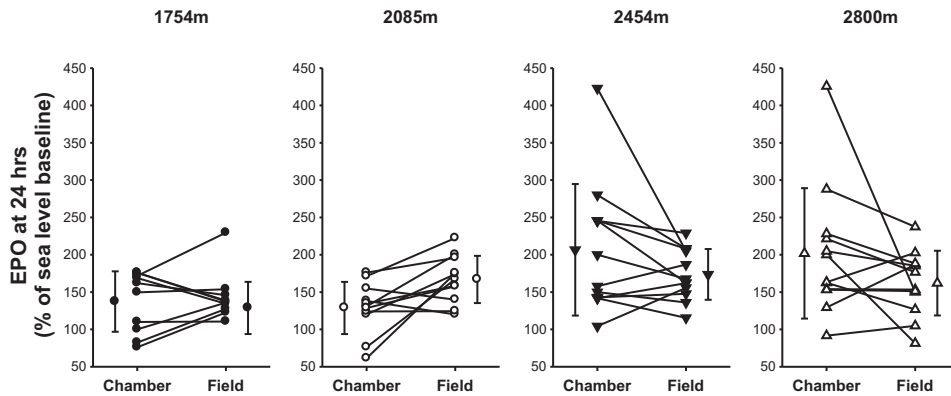


Fig. 7. [EPO], expressed as a percentage of SL, prealtitude baseline, after 24 h in a hypobaric chamber vs. the same altitude in the field. Connected data points are paired individual values for each subject. Single data points with error bars represent mean \pm SD for each condition within each altitude group.

performance improvement immediately on return to sea level in the 2,800-m 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, both of which begin to display at threshold altitudes below 2,800 m (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 2,800-m group vs. the lower altitude groups. We do not have direct data on the incidence of either impaired sleep or acute mountain sickness in our subjects, which, if present, likely did not carry across all 4 wk of altitude residence. However, SaO_2 during sleep was consistently lowest in the 2,800-m group at all time points throughout the study (Fig. 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 2,800-m 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 and creates a higher pressure head for diffusion of O_2 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 \dot{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/h (9 mph), \dot{V}_E was (or trended) 3–4% lower in the two lowest altitude groups immediately upon return to sea level, whereas \dot{V}_E was (or trended) 4–5% higher in the two highest altitude groups (Fig. 4). Submaximal steady-state HR followed a similar pattern, with significant declines (\sim 2%) at the lowest two altitudes immediately after 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-wk 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 ventila-

tory acclimatization, whereas, at the higher two altitudes, the opposite was the case.

Augmented ventilatory acclimatization, as measured by greater ventilation during submaximal exercise in the 2,800-m group, may have negatively affected both training during the altitude camp and race performance on 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 \dot{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 that 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 2,800-m 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 2,800 m (or higher) do not demonstrate a group improvement in sea level performance after an altitude camp,

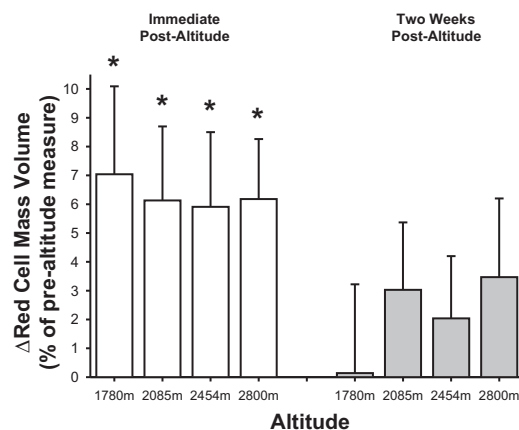


Fig. 8. Percent change in erythrocyte volume at SL from prealtitude to immediate postaltitude (open bars) and 2-wk postaltitude (shaded bars). Values are means \pm SE. *Significant increase from prealtitude.

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 300 m 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-h chamber response to 2,454 m (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 2,454 m across all subjects. Within each altitude cohort, we saw significant individual variability in the 24-h EPO response to the same altitude in the chamber vs. in the field (Fig. 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 $\dot{V}O_{2\max}$ (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 postaltitude 3,000-m 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 with 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, 4 wk of HiLo altitude training, living at 2,085 and 2,454 m, resulted in significantly improved sea level race performance and $\dot{V}O_{2\max}$ in a cohort of trained distance runners. Athletes living at elevations lower (1,780 m) and higher (2,800 m) than those altitudes demonstrated no changes in sea level performance after the altitude camp. These 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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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: R.F.C., J.S.-G., and B.D.L. conception and design of research; R.F.C., T.K., G.K.R., R.-L.G., M.P.H., S.W., J.S.-G., and B.D.L. analyzed data; R.F.C., T.K., G.K.R., R.-L.G., M.P.H., S.W., J.S.-G., and B.D.L. interpreted results of experiments; R.F.C., J.S.-G., and B.D.L. prepared figures; R.F.C., J.S.-G., and B.D.L. drafted manuscript; R.F.C., T.K., G.K.R., R.-L.G., M.P.H., S.W., J.S.-G., and B.D.L. edited and revised manuscript; R.F.C., T.K., G.K.R., R.-L.G., M.P.H., S.W., J.S.-G., and B.D.L. approved final version of manuscript; T.K., G.K.R., R.-L.G., M.P.H., S.W., J.S.-G., and B.D.L. performed experiments.

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