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"Living high-training low" altitude training improves sea level performance in male and female elite runners

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Stray-Gundersen, James, Robert F. Chapman, and Benjamin D. Levine. "Living high-training low" altitude training improves sea level performance in male and female elite runners. *J Appl Physiol* 91: 1113–1120, 2001.—Acclimatization to moderate high altitude accompanied by training at low altitude (living high-training low) has been shown to improve sea level endurance performance in accomplished, but not elite, runners. Whether elite athletes, who may be closer to the maximal structural and functional adaptive capacity of the respiratory (i.e., oxygen transport from environment to mitochondria) system, may achieve similar performance gains is unclear. To answer this question, we studied 14 elite men and 8 elite women before and after 27 days of living at 2,500 m while performing high-intensity training at 1,250 m. The altitude sojourn began 1 wk after the USA Track and Field National Championships, when the athletes were close to their season's fitness peak. Sea level 3,000-m time trial performance was significantly improved by 1.1% (95% confidence limits 0.3–1.9%). One-third of the athletes achieved personal best times for the distance after the altitude training camp. The improvement in running performance was accompanied by a 3% improvement in maximal oxygen uptake (72.1 ± 1.5 to 74.4 ± 1.5 ml·kg^{-1}·min^{-1}). Circulating erythropoietin levels were near double initial sea level values 20 h after ascent (8.5 ± 0.5 to 16.2 ± 1.0 IU/ml). Soluble transferrin receptor levels were significantly elevated on the 19th day at altitude, confirming a stimulation of erythropoiesis (2.1 ± 0.7 to 2.5 ± 0.6 μg/ml). Hb concentration measured at sea level increased 1 g/dl over the course of the camp (13.3 ± 0.2 to 14.3 ± 0.2 g/dl). We conclude that 4 wk of acclimatization to moderate altitude, accompanied by high-intensity training at low altitude, improves sea level endurance performance even in elite runners. Both the mechanism and magnitude of the effect appear similar to that observed in less accomplished runners, even for athletes who may have achieved near maximal oxygen transport capacity for humans.

endurance performance; hypoxia; erythropoietin; symmorphosis; maximal oxygen uptake; running; athletics

WE HAVE PREVIOUSLY SHOWN that 4 wk of acclimatization to moderate altitude (2,500 m) combined with training at low altitude (1,250 m) (HiLo) is superior to an equivalent training camp at sea level (24). This form of altitude training produced a 1.4% improvement in group sea level endurance performance in collegiate and recent postcollegiate runners (age 20 ± 2 yr). The mechanism for the improvement in performance with this approach appears to be twofold: an increase in red cell mass as a function of the hematological adaptation to moderate altitude, which produces an increase in maximal oxygen uptake ($\dot{V}O_{2\,max}$), plus the maintenance of sea level oxygen flux during low-altitude training, which preserves skeletal muscle structure and function and facilitates an improvement in sea level running performance.

However, despite numerous anecdotal reports of the success of altitude training for world class athletes, some recent reports have suggested that HiLo, or any form of altitude training, may not be advantageous for elite compared with collegiate level athletes (1, 2, 14). The concept of symmorphosis, as elaborated by Hoppeler and Weibel (17), argues that, for any system, such as the respiratory chain for oxygen transport, the maximal capacity of each parameter is adjusted quantitatively to match the structural and functional limits of the demands placed on the system as a whole. Thus, for the "elite athletes" of the animal kingdom, each step of the pathway of oxygen from the atmosphere to the mitochondria has evolved toward optimal function and maximal aerobic power, allowing little room for further adaptive improvement. Therefore, for elite human athletes, small, short-term improvements in one step of the oxygen cascade may be met by functional limits in other steps, minimizing the potential performance benefit of altitude training. However, elite human athletes living and training at sea level are unable to develop similar levels of circulating hemoglobin/red cell mass as "high-endurance" animal species who have the ability to autotransfuse by splenic contraction (23, 25). Thus raising circulating hemoglobin levels conceivably has the greatest potential for improving elite endurance performance in humans. In addition, the interaction between convective and diffusive components of

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oxygen transport, as described by Wagner (35), would predict an increase in $\dot{V}O_{2\,max}$ with increasing circulating hemoglobin and red cell mass. In support of these concepts, transfusion studies (5, 10, 37) and those administering recombinant erythropoietin (3, 4) suggest that an increase in red cell mass by itself will increase the $\dot{V}O_{2\,max}$ for all endurance athletes, regardless of performance level.

Thus the present study was designed to investigate the effect of the HiLo paradigm on elite runners who were likely to be much closer to their ultimate performance potential than the athletes previously studied with this approach. The study was timed such that the athletes would be in the best shape of the year [i.e., after they had just completed the spring track season culminating with the National Collegiate Athletic Association (NCAA) championships and the USA Track and Field National Championships]. We hypothesized that the combination of acclimatization to 2,500 m and high-intensity training at 1,250 m would improve sea level performance in elite middle- and long-distance runners.

METHODS

Subjects

Twenty-six distance runners (17 men and 9 women) were recruited. Athletes were required to be competitive at a national level in an event from the 1,500 m to the marathon. Twenty-four of the 26 athletes were ranked in the US top 50 for their event in 1997. The athletes included two 1996 Olympians, and 50% of the athletes had competed in the 1996 US Olympic Trials. All but four athletes competed in the 1997 NCAA Championships or the 1997 USA Track and Field Championships or both. Three of those four athletes were attempting to run qualifying times up to the day of the meet. Exclusion criteria included altitude residence (>1,000 m) or recent illness or injuries preventing normal training and racing. The subjects gave their written consent to the study, which had received approval from the Institutional Review Board of the University of Texas Southwestern Medical Center.

Protocol

The study protocol was a modification of one previously developed by the authors for collegiate runners (24). Briefly, the athletes were assessed at sea level in the week before and the week after 27 days of living at 2,500 m (see Fig. 1). The NCAA Championships were held at sea level 3 wk before the altitude sojourn, and the USA Track and Field Championships ended 1 wk before the altitude sojourn. Individualized training plans were developed by the athlete and his or her coach. Plans were discussed with the investigators and conformed to a training template presented by the investigators (24). Athletes were required to perform high-intensity, high-velocity training at 1,250 m. All other training took place between 1,250 and 3,000 m with most of the training occurring between 2,000 and 2,800 m. This modification of the HiLo model, termed "HiHiLo," (living at moderate altitude, low-intensity base training at moderate altitude, high-intensity interval training at low altitude), has been demonstrated in pilot work to provide identical improvement in $\dot{V}O_{2\,max}$ and 5,000-m time as the original HiLo model (34). All athletes received oral liquid iron supplementation (Feo-Sol, 9 mg elemental iron/ml) with dose adjusted on the basis of plasma ferritin concentration (range: 5–45 ml/day).

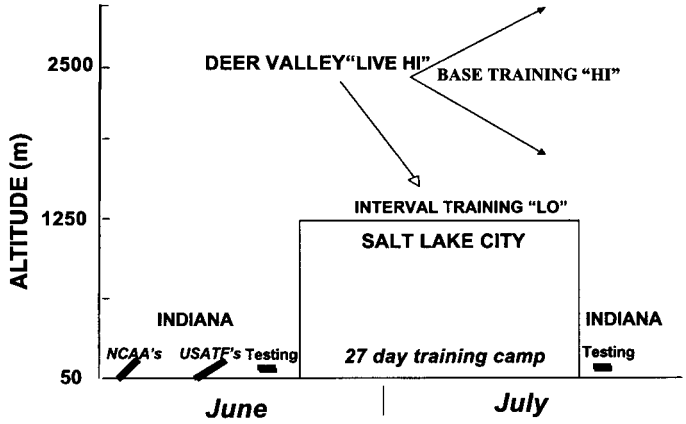

Fig. 1. Timetable for the experiment. NCAA, National Collegiate Athletic Association; USATF, USA Track and Field; Hi, high altitude; Lo, low altitude.

Assessments

Performance. Sea level performance was assessed by 3,000-m time trial races on a 400-m all-weather track (Indiana University, Bloomington, IN) the day before and 3 days after the altitude sojourn. The time trials were run in men's and women's heats in the early evening (1900 to 2000). Athletes were instructed to achieve the best time possible on each time trial. Experienced pace setters (athletes not otherwise involved in the project) 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 both the prealtitude and postaltitude time trials. Temperatures ranged from 25 to 27°C, relative humidity ranged between 50 and 75%, and there was no wind. Time was recorded for each subject to the nearest 0.1 s.

Treadmill assessment. After a 15-min warm-up, the athlete ran to volitional exhaustion performing a protocol with constant velocity and increase in grade of 2% every 2 min. Inspired ventilation was measured by a dual-thermistor flow probe (Torrent 1200, Hector Engineering), and expired gas concentrations were measured in a 5-liter mixing chamber by mass spectrometer (Marquette RMS M-100, Milwaukee, WI). Heart rate was recorded at the end of each minute by telemetry (Polar). Percent arterial oxyhemoglobin saturation was measured by ear oximetry (Hewlett-Packard 47201A). Data were collected and displayed with the use of a data acquisition control system (Workbench for Windows 2.0, Strawberry Tree) sampling at 40 Hz. Values for arterial oxygen saturation, oxygen uptake, and minute ventilation were averaged over each minute of exercise.

Hematology assessment. Venous blood was drawn into tubes containing EDTA, with the subject in the supine position, between 0600 and 0700 on four occasions: 3 days before the altitude sojourn, after the first night at altitude (20 h), after 19 days at altitude, and 20 h after return to sea level. Whole blood was assayed in duplicate for hemoglobin concentration (Radiometer OSM-3) and hematocrit (spun capillary tubes). Plasma was then obtained by centrifugation and stored frozen (−80°C) until assayed. Plasma was assayed by RIA with commercial kits and a gamma counter (ISODATA 20–20) for ferritin (DSL, Webster, TX), erythropoietin (DSL), and soluble transferrin receptor concentrations (Orion).

Table 1. *Sea level performance*

	Pre-HiLo	Post-HiLo
3,000 m time, min:s		
Group (n = 22)	8:45.4 ± 0:39	8:39.6 ± 0:39*
Women (n = 8)	9:32.4 ± 0:11.1	9:26.9 ± 0:11.3*
Men (n = 14)	8:18.4 ± 0:14.0	8:12.6 ± 0:10.8†

Values are means ± SD. HiLo, living high-training low. *$P \leq 0.05$; †$P < 0.10$ pre vs. post.

Statistics

Data are presented in the tables as means ± SD. SPSS 6.1 was utilized for statistical calculations. Performance and $\dot{V}O_{2\,max}$ were compared by paired t-test. The hematologic data were compared by one-way ANOVA. Gender differences were tested by using a two-way ANOVA (altitude × gender). Significance was set at $P \leq 0.05$. When a significant effect was obtained, post hoc analysis was performed with the Student-Newman-Keuls test to identify differences.

RESULTS

Subjects

Fourteen men (25 ± 3 yr, 179 ± 5 cm, 63.6 ± 5.2 kg) and eight women (24 ± 3 yr, 168 ± 5 cm, 53.3 ± 4.9 kg) successfully completed the protocol for a total of 22 complete subjects. Four subjects (three men and one woman) suffered injury (n = 2) or illness (n = 2) during the sojourn that prevented normal training or racing and were not included in the analysis. There were no gender differences with respect to the response to the altitude sojourn; therefore, data for men and women are considered together.

Performance

Group 3,000-m performance at sea level was significantly improved after the HiLo treatment (Table 1 and Fig. 2). Men and women improved to similar extents, reducing time trial time by 5.8 s (95% confidence limits 1.8–9.8 s) or 1.1% (95% confidence limits 0.3–1.9%). Three athletes improved their sea level 3,000-m time by as much as 23 s, whereas one athlete ran 18 s slower.

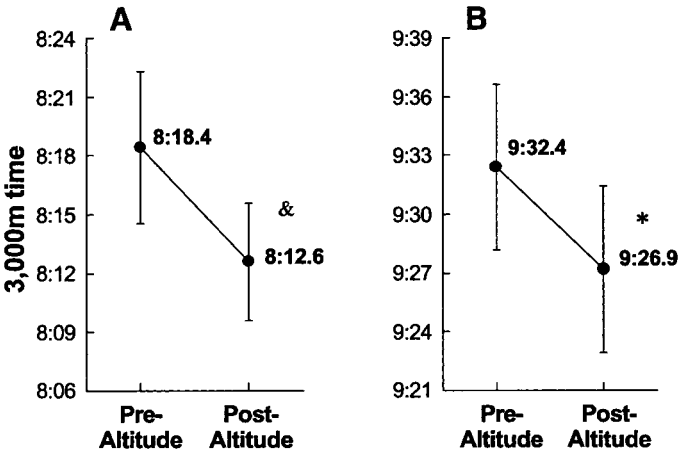

Fig. 2. Change in 3,000-m performance in elite male (*A*) and female (*B*) runners to a 4-wk living high-training low-altitude sojourn. *$P < 0.05$; &$P < 0.10$ compared with prealtitude.

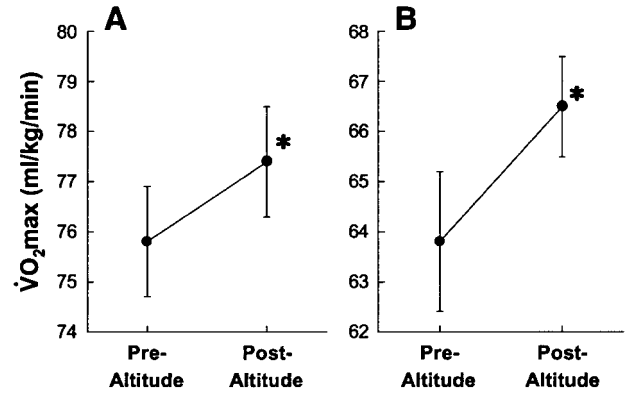

Fig. 3. Change in maximal oxygen uptake ($\dot{V}O_{2\,max}$) in elite male (*A*) runners and elite female (*B*) runners to a 4-wk living high-training low- altitude sojourn. *$P < 0.05$ compared with prealtitude.

Maximal Exercise

$\dot{V}O_{2\,max}$ was significantly increased by 3% after the altitude camp (see Fig. 3). Maximal ventilation was also significantly increased after the altitude camp (Table 2). There was a significant relationship between the change in $\dot{V}O_{2\,max}$ and the change in maximal minute ventilation (r = 0.67, P = 0.0006). Moreover, there was a less robust but still statistically significant relationship between the change in $\dot{V}O_{2\,max}$ and the change in 3,000-m running time (r = −0.48, P = 0.02). Maximal heart rate was unchanged. Arterial oxygen saturation was reduced to 89 ± 4% during maximal exercise but was unaffected by the altitude camp. Time to exhaustion on the treadmill was not significantly different.

Hematology Assessments

Hemoglobin concentration increased on acute ascent to altitude, remained elevated during the camp, and was significantly elevated on return to sea level (see Table 3). Hematocrit was significantly elevated when measured on the 19th day at altitude and remained significantly elevated on return to sea level. Plasma ferritin concentrations were not significantly altered from the initial value. However, despite oral iron supplementation, there was a trend (P = 0.07) for subsequent values to be lower than the initial value. Plasma erythropoietin concentration doubled after one night at

Table 2. $\dot{V}O_{2}max$

	Pre-HiLo	Post-HiLo
Time to exhaustion, min	8.8 ± 1.1	9.0 ± 1.0
$\dot{V}E$, l/min	152 ± 31	163 ± 34*
HR, beats/min	192 ± 7	191 ± 8
%Arterial saturation	89 ± 4	89 ± 4
$\dot{V}O_{2max}$, ml·kg^{-1}·min^{-1}	72.1 ± 6.9	74.4 ± 6.8*

Values are means ± SD; n = 22 (18 men, 8 women). $\dot{V}O_{2max}$, maximal oxygen uptake; $\dot{V}E$, minute ventilation; HR, heart rate. *$P \leq 0.05$ pre- vs. post-HiLo.

Table 3. *Hematologic assessments*

	Sea Level Pre-HiLo	Acute HiLo	Chronic HiLo	Sea Level Post-HiLo	*F*
Hemoglobin, g/dl	13.3 ± 1.1	14.3 ± 1.2*	15.1 ± 1.2*	14.3 ± 1.1*	†
Hematocrit, %	41.0 ± 2.5	40.6 ± 2.5	42.5 ± 2.6*	42.8 ± 2.8*	†
Ferritin, μg/ml	69 ± 79	39 ± 41	37 ± 33	34 ± 22	0.07
Erythropoietin, ng/ml	8.5 ± 2.5	16.2 ± 4.6*	9.7 ± 2.0	7.4 ± 2.1*	†
Soluble transferrin receptor, μg/ml	2.1 ± 0.7	2.0 ± 0.6	2.5 ± 0.6*	2.0 ± 0.5	†

Values are means ± SD. *$P < 0.05$ different from initial sea level value (Student-Newman-Keuls post hoc tests); †significant *F* statistic ($P \leq 0.05$) (1-way ANOVA).

2,500 m and was not different from baseline after 19 days at the camp. Then plasma erythropoietin levels decreased significantly on return to sea level. Soluble transferrin receptor concentrations were significantly elevated (25%) after 19 days at altitude, consistent with active erythropoiesis (3, 5), and returned to baseline on return to sea level.

DISCUSSION

The major finding of this study is that, in this group of elite runners, sea level 3,000-m running performance improved significantly in response to a 27-day camp utilizing the HiLo paradigm. In fact, nine athletes recorded personal records at the distance after the HiLo camp, despite having prepared for and competed in national championship events just before the sojourn. The mechanism of the improvement appears to be similar to that previously described in carefully controlled studies of collegiate-level athletes (24) with a stimulation of erythropoiesis leading to an apparent increase in oxygen delivery to peripheral tissues as evidenced by *1*) a near doubling of plasma erythropoietin concentration and a 43% reduction in serum ferritin concentration despite oral iron supplementation on acute exposure to altitude, *2*) a rise in soluble transferrin receptor concentration with chronic exposure to altitude, and *3*) an increase in hemoglobin concentration and hematocrit on return to sea level with a decrease in plasma erythropoietin concentration below original sea level baseline.

Limitations

We must acknowledge that our study suffers from a major limitation shared by most research conducted in elite athletes: namely, the absence of a concurrent control group performing a similar training camp at sea level. Such a control group would be optimal to ensure that the athletes did not improve merely from the result of a training camp per se, rather than living high-training low. A number of lines of evidence, however, suggest that the study design employed in this experiment was sufficient to account for most of this effect. First, in our previous studies (24), which included many years of piloting work, we determined that for collegiate athletes at least 2 wk of controlled training were necessary to overcome the "training camp effect." For example, in one preliminary study of a sea level training camp, six male runners increased their $\dot{V}O_{2\,max}$ from 68 ± 1.5 to 70 ± 1.4 ml·kg^{-1}·min^{-1} after 2 wk of supervised training, but did not increase further after an additional 2 wk of training (70 ± 1.8 ml·kg^{-1}·min^{-1}) (Levine and Stray-Gundersen, unpublished observations). Thus, for all the 52 male and female athletes studied in our previously published reports (24, 34), after a 2-wk "lead-in" phase of supervised training there was no significant increase in $\dot{V}O_{2\,max}$ with an additional 4 wk of structured training at sea level (64 ± 0.8 to 64 ± 0.8 ml·kg^{-1}·min^{-1}). Moreover, after these 6 wk of sea level training by collegiate athletes in these studies, there was no further improvement obtained even by an outstanding training camp environment at sea level for an additional 4 wk (24). In the present study, we considered that the months of preparation by these elite athletes for their national championships were at least equivalent to the 2 wk of training applied to collegiate athletes a number of weeks after their competitive season for the purpose of minimizing the training camp effect. Additionally, on review of each athlete's training program leading up to the championships, all had peaked appropriately for this event. As far as could be determined from inspection of training logs and individual meetings with each athlete over the course of the study, no one had a change in training that could explain an improved performance.

We suspect, but cannot prove, that the athletes were equally motivated to give their best performance in precamp as well as postcamp time performance tests. We can say, however, that these athletes were all extremely competitive, and it was our clinical impression that motivation was high during all study races. Moreover, all the time trials were paced by an experienced pace setter who maintained the same running speed for 4 of 7.5 laps in both the pre- and postcamp trials. Finally, athletes were pushed to exhaustion in all treadmill tests, and there was no evidence from respiratory exchange ratio or heart rate that the athletes gave a better effort on the second test than the first (for example, maximal heart rate was 192 on the first test and 191 on the second test).

We also cannot exclude the possibility that the use of iron supplements to ensure adequate iron availability for erythropoiesis with altitude exposure (24) could have resulted in an increase in hemoglobin concentration independent of an altitude effect. We suspect this possibility is unlikely, however, for the following reasons. *1*) None of the athletes in this study was anemic or had small red blood cells typical of iron deficiency

anemia. All had normal hemoglobin concentration and hematocrit, and all had normal red cell size and distribution. *2*) Despite oral iron supplementation, the iron requirements of altitude exposure were such that bone marrow iron stores as measured by serum ferritin did not increase over the course of the training camp. In fact, ferritin decreased with each longitudinal measurement (Table 3), suggesting that bone marrow iron stores were more rather than less depleted at the end of the altitude camp. *3*) The baseline erythropoietin concentrations were normal and low, arguing against a physiologically significant anemia; anemia is the most potent stimulus to synthesis of erythropoietin (20). Thus the available evidence would argue against simple treatment of iron deficiency as the mechanism of the increase in hemoglobin and hematocrit in this study.

Finally, because of time constraints associated with performing the study in elite athletes during peak competition periods, the subjects were not as completely characterized, nor were the details of the training program as rigorously controlled to the same extent as in previous work (24). However, the same basic training template was used for the protocol, and key parameters were measured in both populations, including erythropoietin and hemoglobin concentrations, $\dot{V}O_{2\,max}$, and time trial performance, that allowed comparison to our previous studies.

When the results from carefully controlled, comprehensively assessed studies on collegiate runners are compared with the results of the present study (see Table 4), the results are remarkably similar in both direction and magnitude of the effect. In addition, when similar parameters were measured, the results suggest that the same mechanism produced the effect, i.e., an increase in erythropoietin leading to an increase in hemoglobin concentration, increased $\dot{V}O_{2\,max}$, and increased performance. Therefore, we believe that the compromises made in this study to evaluate elite athletes during a time of peak fitness did not compromise the validity of the results.

The Unique Model of Elite Athletes

Elite athletes of the animal kingdom provide a unique model of the concept of symmorphosis, whereby the structural design of all components comprising a system is matched quantitatively to functional demand (17). For example, foxes, dogs, and horses have ~2.5 times the mass-specific rate of oxygen consumption compared with sedentary species of the same body size, such as the agouti, goat, or steer. For such animals, the mechanism of this large adaptive range of oxygen consumption appears due to a large mitochondrial volume, matched by a large muscle capillary volume and vascular conductance in skeletal muscle; a higher hemoglobin concentration; and a large maximal stroke volume. The redundancy in the pulmonary system of nonathletic species, manifested by excess ventilatory and diffusing capacity, is nearly eliminated in the athletic species, confirming the principle of symmorphosis. In other words, comparative studies suggest that such "athletes" are operating at or close to the upper limit of their structural capacity for convective transport of oxygen at $\dot{V}O_{2\,max}$.

If this analysis is also relevant for humans, it could be argued that elite human athletes would have a smaller adaptive capacity for increasing oxygen transport than less accomplished athletes, such as those originally reported using the HiLo approach. Although the amount of published data examining truly elite athletes undergoing altitude training is limited, at least one small study of world-class Australian cyclists, before and after a 31-day altitude camp (2,690 m), recently reported no changes in hemoglobin mass nor sea level $\dot{V}O_{2\,max}$ despite an improvement in performance (14). The authors suggested that the outcome was, at least in part, due to limited adaptive reserve in such athletes (14), particularly in the lung, which is essentially static to training. For example, elite endurance athletes display pulmonary gas-exchange limitations at sea level of a greater magnitude and prevalence than lesser trained individuals, part of which is accounted for by limitations in ventilation (8). However, in the present study, we observed an increase in maximal ventilation that was commensurate with the increase in $\dot{V}O_{2\,max}$. We cannot determine from the data in this experiment whether the increase in maximal ventilation was simply a consequence of the increased $\dot{V}O_{2\,max}$ or rather the cause of the increased $\dot{V}O_{2\,max}$ as a function of increased ventilatory work. An increase in ventilation during exercise that persists for a period of time after return to sea level would be an expected result of ventilatory acclimatization to high altitude and suggests that, at least in these athletes, flow limitation did not restrict maximal ventilation to a major degree. We speculate that if the initial increase in $\dot{V}O_{2\,max}$ was, at least in part, required to support an increase in ventilatory work from altitude acclimatization, then the restoration of normal respiratory control over time after return to sea level would allow the increased oxygen transport capacity to be directed to working skeletal muscle, thus providing an explanation for the oft-cited observation (9) that many athletes achieve their best performances after a period of reac-

Table 4. *Comparison of elite and collegiate athletes for changes in selected hematologic and performance variables*

	ΔEpo, %	ΔHb, g/dl	$\Delta\dot{V}O_{2\,max}$, ml·kg^{-1}·min^{-1}	ΔPerformance, %
Elite runners (n = 22; 14 M, 8 F)	103 ± 74%	1.0 ± 1.1	2.3 ± 2.6	1.1
College runners (n = 26; 18 M, 8 F)	59 ± 40%	1.1 ± 0.7	2.5 ± 2.4	1.4

Values are means ± SD. Δ, change in; Epo, erythropoietin; M, men; F, women. Performance refers to 3,000-m racing time (elite runners) or 5,000-m racing time (college runners).

climatization to sea level. Further study will be necessary to confirm or exclude this hypothesis.

A more detailed analysis of human vs. nonhuman athletes suggests, in fact, that the most likely avenue for elite human athletes to improve oxygen transport would be to raise their red cell mass and circulating hemoglobin concentration. In human athletes, red cell mass is the one component of the oxygen cascade that does not increase to the level observed in "elite athletes" of the animal kingdom. Humans do not clearly autotransfuse by splenic contraction at the onset of exercise like horses (25) and dogs (23). This effect raises exercise hematocrit well into the 50s in those species. Thus, when the oxygen-carrying capacity of the blood is increased in elite athletes, either by acute red blood cell infusion (5, 10, 37) or by chronic administration of recombinant human erythropoietin (3, 4), $\dot{V}o_{2\,max}$ increases. The results shown in the present study are in the same direction as and half the magnitude of the results obtained by either an acute (transfusion) or chronic increase in red cell mass (exogenous rhEPO administration). At least one uncontrolled study has suggested altitude-induced improvements in $\dot{V}o_{2\,max}$ in undeniably elite athletes (7). One of these subjects (JR) went on to set a world record after living at altitude and training intermittently at sea level.

Some investigators, failing to observe an increase in hemoglobin/myoglobin mass after brief periods of time in normobaric hypoxic environments (8–10 h/night for 10 days to 3 wk), have questioned the erythropoietic effect of moderate altitude exposure (1, 2). However, the evidence in favor of such an altitude-mediated erythropoiesis is quite compelling. Cross-sectional studies in the Peruvian Andes (19, 28, 32) as well as in the Colorado Rockies (36) have demonstrated clearly that there is an elevated red cell mass in natives of high altitude that is proportional to the oxyhemoglobin saturation (19, 36).

Moreover, when sea level natives ascend acutely to altitude, there is an increase in iron turnover by more than twofold that begins within the first few hours of exposure and peaks by ~2–3 wk (12, 18, 28). Direct examination of the bone marrow during acute high-altitude exposure has documented a dramatic increase in nucleated red blood cells, virtually doubling by 7 days, indicative of accelerated erythropoiesis (18, 28). Although most of these data are from altitudes higher than the 2,500 m studied in the present experiment, our elite endurance athletes spent significant time exercising at low-moderate altitudes, which causes further arterial desaturation (8), suggesting that athletes may have a greater stimulation of erythropoiesis for the same altitude than a more sedentary population.

As in the present study with elite athletes, previous studies have also shown that both iron turnover (18, 28) as well as erythropoietin concentrations (6, 15, 20, 24, 30) return to sea level values relatively rapidly during chronic altitude exposure. Nevertheless, the red cell mass continues to increase for up to 8 mo of chronic altitude exposure, at least at altitudes above 4,000 m (28), suggesting that this level of stimulated erythropoiesis is elevated for the absolute level of the arterial oxygen content. Thus when altitude natives or altitude sojourners return to sea level, there is a suppression of erythropoietin (6, 12, 15, 20, 24, 30), a reduction in iron turnover and bone marrow production of erythroid cell lines (18, 28), and a decrease in red cell survival time (28, 29). The change in the ratio of hemoglobin concentration to erythropoietin concentration over the time course of the present study (decrease with acute exposure, increase during chronic exposure, and further increase on return to sea level) is further evidence for the stimulation of erythropoiesis on ascent and deceleration of the erythropoiesis on return to sea level in these athletes following the living high-training low model of altitude training.

Many other factors exist, however, that may compromise the ability of small studies to document clearly an increase in red cell mass with moderate altitude exposure, and that may have led to divergent results with different groups of elite athletes. Duration of altitude exposure, in terms of both time/day at altitude and number of weeks, may play an important effect: studies employing 8–10 h hypoxia/day have not been effective (1, 2), whereas those employing 16 h hypoxia/day have shown an increased in hemoglobin/myoglobin mass using the same methods (31). Inflammatory cytokines (e.g., IL-1) also may limit the increase in erythropoietin in response to hypoxia (11, 13, 21), suggesting that the presence of injury or infection could impair the erythropoietic response to altitude.

There is also a marked individual variability in the response to altitude training. We have previously reported that, even with the optimal method of HiLo or HiHiLo training, only slightly more than 50% of athletes will be robust responders (i.e., improvement by more than the group mean) to altitude, in part because

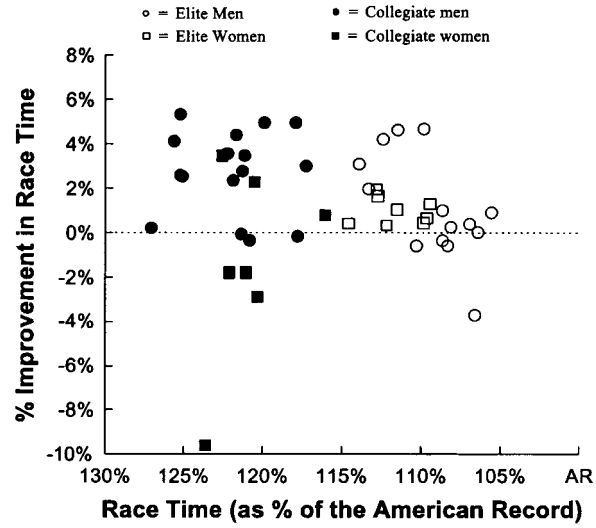

Fig. 4. Comparison of athletes of various performance levels and the change in performance from a 4-wk living high-training low altitude sojourn. Race time represents the initial time trial presented as a percent of the American record (AR) in the event at the time. The change in performance is the percent change from the precamp time trial to the postcamp time trial.

of a prominent and sustained increase in erythropoietin at altitude leading to an increase in red cell mass (6). Although the genetic mechanisms responsible for determining the erythropoietic response to hypoxia in humans have not been entirely worked out, animal models suggest that this response may be transcriptionally regulated (26). Moreover, at least some individuals have genetic polymorphisms in the erythropoietin gene (33) or the erythropoietin receptor (27) that may profoundly influence the erythropoietic response to hypoxia (22). It is possible, therefore, particularly in studies with relatively small sample sizes, that the presence of significant numbers of nonresponders could bias the study outcome in favor of no detectable response.

Practical Implications for Performance of Elite Athletes

In previous work examining collegiate athletes (6, 24), we identified a 1.4% improvement in 5,000-m performance, a 2.5 ± 2.4 $ml \cdot kg^{-1} \cdot min^{-1}$ improvement in $\dot{V}O_{2\,max}$, and a 1.1 ± 0.7 g/dl increase in hemoglobin concentration after 4 wk at 2,500 m. In this study, we obtained a 1.1% improvement in 3,000 m performance, a 2.3 ± 2.6 $ml \cdot kg^{-1} \cdot min^{-1}$ improvement in $\dot{V}O_{2\,max}$, and a 1.0 ± 1.1 g/dl in hemoglobin concentration in elite runners. When all the athletes who have completed a HiLo or HiHiLo camp in our studies are examined together, there is no influence of performance ability on the response to such altitude training (Fig. 4).

Figure 4 also demonstrates that, although substantial individual variability remains within all athletes, the variation is smaller for the elite subjects. Thus the coefficient of variation for the collegiate athletes was 3.3%, whereas that for the elite athletes was just over half as great, or 1.9%. Because of this reduced variability, the percent improvement, expressed as a fraction of the variation within the elite population, is 0.58, well within the criteria of 0.5–0.7 recently recommended for the identification of a "worthwhile" enhancement of performance for elite athletes (16). Although a 1.1% improvement in performance may not seem like a large effect, at an elite level in sports, races are won or lost by small fractions of a percent. Thus the benefit of a HiLo or HiHiLo altitude training camp has the potential to substantially improve race outcome for individual elite athletes.

In conclusion, despite having prepared for and competed in national championship events, elite runners improved sea level running performance by 1.1% (95% confidence limits 0.3–1.9%) after 27 days of living at moderate altitude (2,500 m) and performing high-intensity training at low altitude (1,250 m). Data collected indicate that the magnitude and mechanism of the effect are similar to those obtained in collegiate runners undergoing the same experimental paradigm. The mechanism involves expansion of the red cell mass and an increase in circulating hemoglobin levels, accompanied by maintenance of oxygen flux to working muscle. Thus the HiLo training approach is effective in improving sea level running performance ranging from 50 to 90% of the world record in events lasting from ~7 to 20 min. We believe that this paradigm can be used to enhance sea level performances that are dependent on high levels of oxygen transport.

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