

**Beth A. Beidleman, Stephen R. Muza, Charles S. Fulco, Allen Cymerman, Dan T. Ditzler, Dean Stulz, Janet E. Staab, Scott R. Robinson, Gary S. Skrinar, Steven F. Lewis and Michael N. Sawka**

*J Appl Physiol* 95:1824-1832, 2003. First published Jun 20, 2003; doi:10.1152/jappphysiol.01160.2002

**You might find this additional information useful...**

---

This article cites 24 articles, 16 of which you can access free at:

<http://jap.physiology.org/cgi/content/full/95/5/1824#BIBL>

Updated information and services including high-resolution figures, can be found at:

<http://jap.physiology.org/cgi/content/full/95/5/1824>

Additional material and information about *Journal of Applied Physiology* can be found at:

<http://www.the-aps.org/publications/jappl>

---

This information is current as of October 14, 2008 .

## Intermittent altitude exposures improve muscular performance at 4,300 m

Beth A. Beidleman,<sup>1</sup> Stephen R. Muza,<sup>2</sup> Charles S. Fulco,<sup>2</sup> Allen Cymerman,<sup>2</sup>  
Dan T. Ditzler,<sup>1</sup> Dean Stulz,<sup>2</sup> Janet E. Staab,<sup>2</sup> Scott R. Robinson,<sup>2</sup>  
Gary S. Skrinar,<sup>3</sup> Steven F. Lewis,<sup>3</sup> and Michael N. Sawka<sup>2</sup>

<sup>1</sup>Biophysics and Biomedical Modeling Division and <sup>2</sup>Thermal and Mountain Medicine Division, United States Army Research Institute of Environmental Medicine, Natick 01760; and <sup>3</sup>Department of Health Sciences, Sargent College of Health and Rehabilitation Sciences, Boston University, Boston, Massachusetts 02215

Submitted 18 December 2002; accepted in final form 17 June 2003

**Beidleman, Beth A., Stephen R. Muza, Charles S. Fulco, Allen Cymerman, Dan T. Ditzler, Dean Stulz, Janet E. Staab, Scott R. Robinson, Gary S. Skrinar, Steven F. Lewis, and Michael N. Sawka.** Intermittent altitude exposures improve muscular performance at 4,300 m. *J Appl Physiol* 95: 1824–1832, 2003. First published June 20, 2003; 10.1152/jappphysiol.01160.2002.—Chronic altitude residence improves muscular performance at altitude, but the effect of intermittent altitude exposures (IAE) on muscular performance at altitude has not been defined. The purpose of this study was to determine the effects of 3 wk of IAE, in combination with rest and cycle training, on muscular performance at altitude. Six lowlanders ( $23 \pm 2$  yr,  $77 \pm 6$  kg; means  $\pm$  SE) completed a cycle time trial and adductor pollicis endurance test at sea level and during a 30-h acute exposure to 4,300 m altitude equivalent (barometric pressure = 446 mmHg) once before (pre-IAE) and once after (post-IAE) a 3-wk period of IAE (4 h/day, 5 days/wk, 4,300 m). During each IAE, three subjects cycled for 45–60 min/day at 60%–70% of maximal O<sub>2</sub> uptake and three subjects rested. Cycle training during each IAE did not appear to affect muscular performance at altitude. Thus data from all six subjects were combined. Three weeks of IAE resulted in 1) a  $21 \pm 6\%$  improvement ( $P < 0.05$ ) in cycle time-trial performance (min) from pre-IAE ( $32.8 \pm 3.7$ ) to post-IAE ( $24.8 \pm 1.2$ ), 2) a  $63 \pm 26\%$  improvement ( $P < 0.05$ ) in adductor pollicis endurance (min) from pre-IAE ( $9.2 \pm 2.8$ ) to post-IAE ( $14.8 \pm 4.2$ ), and 3) a  $10 \pm 4\%$  increase ( $P < 0.05$ ) in resting arterial O<sub>2</sub> saturation (%) from pre-IAE ( $82 \pm 2$ ) to post-IAE ( $90 \pm 1$ ). These improvements in muscular performance after IAE correlated strongly with increases in resting arterial O<sub>2</sub> saturation and were comparable to those reported previously after chronic altitude residence. IAE may therefore be used as an alternative to chronic altitude residence to facilitate improvements in muscular performance in athletes, soldiers, mountaineers, shift workers, and others that are deployed to altitude.

hypobaric hypoxia; ventilation; maximal O<sub>2</sub> uptake; submaximal work

ATHLETES, SOLDIERS, MOUNTAINEERS, shift workers, and others who perform strenuous effort at altitude im-

prove muscular performance after 2–3 wk of continuous altitude residence (8, 10, 11, 19). However, the drawbacks of continuous altitude residence such as isolation, tight living quarters, immunosuppression (17), increased oxidative stress (26), sleep disturbances (12), and general malaise (29) may outweigh the benefits. In contrast, daily intermittent altitude exposures (IAE) avoid or minimize such drawbacks and thus may provide a more acceptable alternative for improving muscular performance at altitude. The effect of IAE on muscular performance at altitude is, however, poorly defined.

The purpose of the present study was to determine the effects of 3 wk of IAE (4 h/day, 5 days/wk, 4,300 m), in combination with rest and exercise training, on cycle time-trial performance and adductor pollicis endurance at 4,300 m. We hypothesized that 3 wk of IAE would improve cycle time-trial performance and adductor pollicis endurance at 4,300 m. We also hypothesized that cycle training during IAE would further improve cycle time-trial performance related to the exacerbation of arterial hypoxemia during cycle-training sessions

### METHODS

**Volunteer test subjects.** Eight nonsmoking volunteers (6 men, 2 women) enrolled in this study. Two volunteers dropped out during the study, and six nonsmoking volunteers (5 men, 1 woman) with mean  $\pm$  SE age, body weight, and height of  $23 \pm 2$  yr,  $77 \pm 6$  kg,  $177 \pm 3$  cm, respectively, participated. One volunteer could not complete the adductor pollicis endurance test at post-IAE due to a thumb injury. Each was a lifelong, low-altitude resident and had no exposure to altitudes  $>1,000$  m for at least 6 mo immediately preceding the study. All volunteers received medical examinations, and none had any condition warranting exclusion from the study. All tested within normal ranges for pulmonary function. All had normal hemoglobin concentration ([Hb]) and serum ferritin levels. The woman had a normal menstrual cycle length ( $28 \pm 1$  days) over the 2-mo testing period, had not taken oral contraceptives or hormone therapy for the previous 6 mo and had never been pregnant. Testing

Address for reprint requests and other correspondence: B. A. Beidleman, Biophysics and Biomedical Modeling Division, United States Army Research Institute of Environmental Medicine, Natick, MA 01760 (E-mail: beth.beidleman@na.amedd.army.mil).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

was not controlled for menstrual cycle phase because of the reported lack of menstrual cycle effect on physical performance at altitude (1). All volunteers performed regular sea-level aerobic training (1–2 h/wk) before and during the study and were of average physical fitness. Each gave written and verbal acknowledgment of their informed consent and was made aware of their right to withdraw without prejudice at any time. Investigators adhered to the policies for protection of human subjects as prescribed in Army Regulation 70-25, and the research was conducted in adherence with the provisions of 45 CFR Part 46.

**Study design.** This study used an unblinded two-factor (test condition and group) experimental design. The test conditions were defined as sea level (SL), before IAE (pre-IAE), and after IAE (post-IAE). The groups were defined as rest and cycle training during IAE. Each volunteer completed a cycle time trial and adductor pollicis endurance test under SL conditions and during a 30-h acute exposure to 4,300 m altitude-equivalent (barometric pressure = 446 mmHg) once before and once after a 3-wk period of IAE (4 h/day; 5 days/wk, 4,300 m) (Fig. 1). To set submaximal cycle work intensity, maximal  $\dot{V}O_{2\max}$  was also measured at SL, pre-IAE, and post-IAE. To minimize the impact of potential learning effects, all volunteers performed two preliminary  $\dot{V}O_{2\max}$  and adductor pollicis endurance tests (one at 4,300 m, one at SL) and two preliminary cycle time-trial performance tests (both at SL) before definitive data collection. At SL, Pre-IAE, and Post-IAE, exercise was performed at approximately the same time of day and same number of hours after the last meal.

**IAE.** Volunteers were weighed in the morning before each IAE (wearing t-shirts, shorts, and socks) and were encouraged to maintain constant body weight throughout the study. During each IAE, the three volunteers randomly assigned to the resting group sat in their bunks, watched television, listened to music, read books, and wrote letters for the 4-h altitude exposure. In contrast, the three volunteers randomly

assigned to the exercise training group exercised for ~45–60 min, starting within 15 min of arriving at altitude, and then rested for the remainder of the 4-h altitude exposure. The exercise performed during each IAE consisted of continuous constant work rate and interval training on a cycle ergometer (model 818E, Monark) at an intensity corresponding to ~70–85% of pretraining altitude maximal heart rate (HR). As exercise training progressed, cycle work rates were adjusted, if necessary, to ensure achievement of appropriate training HR during each training session. Arterial  $O_2$  saturation ( $SaO_2$ ) using a finger pulse oximeter (model N-200, Nellcor, Pleasanton, CA), and HR using a wireless HR watch (model 8799, Computer Instruments, Hempstead, NY) were periodically measured on both groups of volunteers.

At the end of each altitude exposure, all volunteers remained resting in the hypobaric chamber so that their total exposure time to hypobaric hypoxia, including a 15-min decompression and 15-min recompression, was 4 h/day. Volunteers were encouraged to drink water to replace any fluid loss during exercise and/or altitude exposure. All volunteers were required to maintain (i.e., not increase or decrease) their 1–2 h/wk aerobic training at SL to maintain their prestudy level of physical fitness. Physical activity monitor logs were kept throughout the 5-wk study.

**Environmental conditions.** All testing and training were performed in a hypobaric chamber maintained at a temperature and relative humidity of  $21 \pm 2^\circ\text{C}$  and  $45 \pm 5\%$ , respectively. The SL testing was performed at ambient barometric pressure (~760 mmHg), and all altitude exposures were conducted at an altitude-equivalent of 4,300 m (~446 mmHg).

**Diet.** The quantity of food consumed was not limited. However, to limit the potential effects that diet may have on cycle time-trial performance, volunteers were given meals of identical nutrient and caloric content during each 30-h test condition at SL, pre-IAE, and post-IAE. Food intake was recorded and analyzed for energy content and percentage of

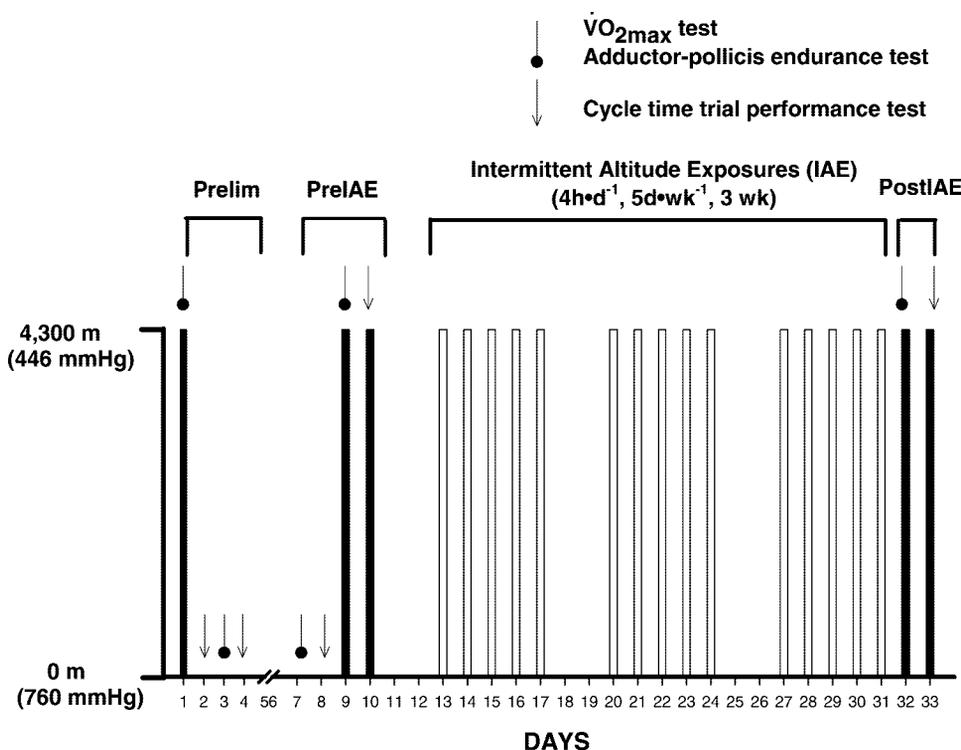


Fig. 1. This study used an unblinded 2-factor experimental design in which each test volunteer's (5 men, 1 woman) maximal  $O_2$  uptake ( $\dot{V}O_{2\max}$ ), cycle time-trial performance, and adductor pollicis endurance were evaluated during preliminary measurements (Prelim), at sea level (SL), and during  $\leq 30$ -h exposures to 4,300 m altitude-equivalent [barometric pressure (PB) = 446 mmHg] before (pre-IAE) and immediately after (post-IAE) a 3-wk period of intermittent altitude exposures (IAE) (4 h/day; 5 days/wk, 4,300 m).

contribution of macronutrients (Nutritionist III v.6.0, Houston, TX). At no time during the entire study were volunteers allowed to consume caffeine.

**Exercise performance testing.** Volunteers were required to abstain from alcohol for at least 24 h before all testing and not exercise on the testing day. Before each exercise test on an electromagnetically braked cycle ergometer (model 800s, Sensormedics, Yorba Linda, CA), the volunteer was weighed (wearing t-shirt, shorts, and socks) to the nearest 0.1 kg. During exercise, HR was determined from continuous ECG recordings (Cardiovit AT-6C; Schiller Canada, Nepean, ON, Canada),  $\text{SaO}_2$  was measured by finger pulse oximetry (model N-200, Nellcor), and systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by using an automated system (model 4240, Suntech, Raleigh, NC). Respiratory gas measurements [i.e., minute ventilation ( $\dot{V}_E$ ),  $\text{O}_2$  uptake ( $\dot{V}\text{O}_2$ ),  $\text{CO}_2$  production ( $\dot{V}\text{CO}_2$ )] were made in the mixing-chamber mode by using an open-circuit metabolic measurement system (Vmax 229, Sensormedics) calibrated with certified gases and volume standard. The respiratory exchange ratio (RER) was calculated from  $\dot{V}\text{O}_2$  and  $\dot{V}\text{CO}_2$  measurements. The ventilatory equivalent for  $\text{CO}_2$  ( $\dot{V}_E/\dot{V}\text{CO}_2$ ) was calculated from each subject's  $\dot{V}_E$  and  $\dot{V}\text{CO}_2$  data. Mean arterial pressure (MAP) was calculated as  $0.333(\text{SBP} - \text{DBP}) + \text{DBP}$ .

$\dot{V}\text{O}_{2\text{ max}}$ .  $\dot{V}\text{O}_{2\text{ max}}$  was measured during incremental, progressive cycling exercise to exhaustion. After resting measurements were conducted during sitting on the cycle ergometer, volunteers warmed up for 3 min at 60 W. For the next 2 min, the work rate was increased to 80–100 W for women and 120–150 W for men. Thereafter, work rate for men and women was increased every 2 min by 30 W at SL and 25 W at pre-IAE and post-IAE until the volunteers were unable to maintain a constant pedaling rate of 60 rpm. A blood sample was obtained from an arm vein at rest and 3-min postexhaustive for analysis of lactate concentration ([Lac]), [Hb], and hematocrit (Hct).

**Cycle time trial.** The time to complete a fixed amount of work on a cycle ergometer, consisting of 216 kJ of total work for men and 156 kJ of total work for women, was used as a measure of cycle time-trial performance. A shorter time from one testing condition to the next was considered an improvement in performance and vice versa. During the time trial, volunteers were free to manually increase or decrease the work rate on the cycle ergometer by 5-W increments. There were no restrictions on the number of 5-W changes or their direction. This type of time-trial performance test has been shown to have a high repeatability and low coefficient of variation (13). Respiratory gas measurements were not made during the cycle time trial.

Immediately before completion of the cycle time trial, resting measurements were made on the cycle ergometer and volunteers completed two consecutive 15-min work bouts at 40 and 70% of their individual altitude-specific, pre-IAE  $\dot{V}\text{O}_{2\text{ max}}$ . Breath-by-breath measurement of end-tidal  $\text{CO}_2$  production ( $\text{PET}_{\text{CO}_2}$ ) was made twice at rest and during the last 2 min of both 15 min work bouts. Volunteers consumed 5 ml water/kg body wt 1 h before beginning cycle testing. An indwelling catheter was placed in an arm vein at least 40 min before the first resting blood sample. After a 40-min sitting equilibration period, blood samples were drawn at rest, 10 min into the first 15-min work bout, 10 min into the second 15-min work bout, and immediately after the cycle time trial for measurement of [Lac], osmolarity, [Hb], and Hct.

**Adductor pollicis endurance.** Adductor pollicis endurance was measured during intermittent 5-s static muscle contractions at a target force of 50% of individual rested preexercise

altitude-specific maximal voluntary contraction (MVC) force followed by 5 s of rest (i.e., duty cycle 0.5) until exhaustion. At the end of every minute (i.e., every 6th contraction), an MVC was performed for the full 5 s instead of the 50% MVC force contraction. When the MVC force fell to or below the target force or the target force could not be maintained for 5 s, subjects were considered exhausted and were instructed to stop the submaximal contractions. Time to exhaustion was calculated as the time from the start of the MVC of rested muscle immediately preceding the first submaximal contraction to the end of the MVC performed at the point of exhaustion. The methods and device used have been described earlier (8). Resting  $\text{SaO}_2$  was measured before the adductor pollicis endurance test.

**Blood analyses.** Heparinized blood was used to measure blood [Lac] in duplicate (model 2300 YSI analyzer; Yellow Springs Instruments, Yellow Springs, OH). Serum was used to measure osmolarity by freezing-point depression (model 2430 Multi-osmometer, Precision Systems, Natick, MA). Whole blood [Hb] was measured in duplicate by absorbance wavelength spectrophotometry (Cell Dyn 3500, Abbott Diagnostic, Abbott Park, IL), and Hct was measured by using aliquots of heparinized blood and the microcapillary method. [Hb] and Hct determinations were used to calculate changes in plasma volume (6). Arterial  $\text{O}_2$  content ( $\text{CaO}_2$ ; ml/l) was calculated as the product of  $\text{SaO}_2 \times [\text{Hb}] \times 1.34 \text{ ml O}_2/\text{g} [\text{Hb}]$ .

**Statistical analyses.** A two-way repeated-measures ANOVA was used to analyze differences between the independent group factor (rest and cycle training) and repeated-measures test condition factor (SL, pre-IAE, and post-IAE) for all muscular performance and  $\dot{V}\text{O}_{2\text{ max}}$  measurements. Three-way ANOVAs, with repeated measures on the additional factor of exercise duration, were used for blood and physiological measurements made during the muscular performance and  $\dot{V}\text{O}_{2\text{ max}}$  tests. Significant main effects and interactions were analyzed by using Tukey's least significant difference test. Pearson's product-moment correlation coefficients were calculated for the relationships between changes in resting  $\text{SaO}_2$  and changes in 1) cycle time-trial performance and 2) adductor pollicis endurance. Statistical significance was set at  $P < 0.05$ . All data are presented as means  $\pm$  SE.

## RESULTS

Although arterial  $\text{O}_2$  desaturation was 5–10% greater during cycle training compared with rest during each IAE, cycle training did not appear to further improve cycle time-trial performance at altitude. Thus, for statistical analyses, data from all six subjects were combined. For performance measurements, individual responses are also provided.

**Volunteer test subjects.** Mean body weights, heights, energy intakes, and percentages of contributions of carbohydrate, fat, and protein to the diet were not different between testing conditions. Mean body weight also did not change from baseline during the 5-wk course of the study. Time spent in physical activity at SL per week was not different between groups and did not change from baseline in any of the test subjects during the 5-wk course of the study.

**$\dot{V}\text{O}_{2\text{ max}}$  data.** Individual and group  $\dot{V}\text{O}_{2\text{ max}}$  data ( $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) are presented in Fig. 2. All individuals exhibited a decrease in  $\dot{V}\text{O}_{2\text{ max}}$  from SL to pre-IAE. Five of the six subjects exhibited an increase in  $\dot{V}\text{O}_{2\text{ max}}$  from pre-IAE to post-IAE.  $\dot{V}\text{O}_{2\text{ max}}$  decreased  $23 \pm 3\%$

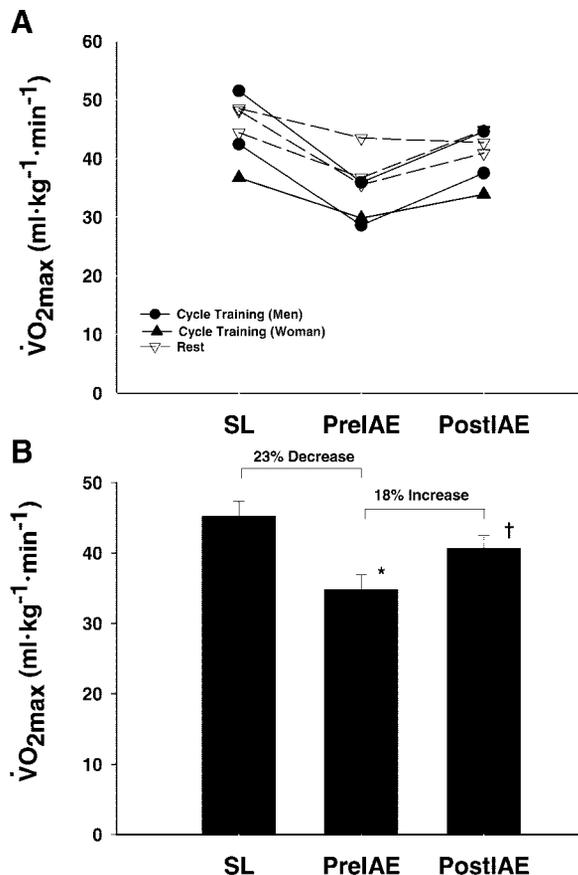


Fig. 2.  $\dot{V}O_{2\max}$  was measured in 6 volunteers at SL, and during  $\leq 30$ -h exposures to 4,300 m altitude-equivalent ( $P_B = 446$  mmHg) before (pre-IAE) and immediately after (post-IAE) a 3-wk period of IAE (4 h/day; 5 days/wk, 4,300 m). A: individual data. B: group data. \* $P < 0.05$  from SL; † $P < 0.05$  from Pre-IAE.

( $P < 0.05$ ) from SL ( $45.2 \pm 2.1$ ) to pre-IAE ( $34.8 \pm 2.1$ ) and increased  $18 \pm 4\%$  ( $P < 0.05$ ) from pre-IAE to post-IAE ( $40.7 \pm 1.7$ ).

Maximal ventilatory and cardiovascular responses are presented in Table 1.  $\dot{V}O_{2\max}$  decreased ( $P < 0.05$ ) from SL to pre-IAE and then increased ( $P < 0.05$ ) from pre-IAE to post-IAE. Maximal  $\dot{V}_E/\dot{V}_{CO_2}$  increased ( $P < 0.05$ ) from SL to pre-IAE and further increased ( $P < 0.05$ ) from pre-IAE to post-IAE.  $Sa_{O_2}$ , measured at maximal exercise, also decreased ( $P < 0.05$ ) from SL to pre-IAE and then increased ( $P < 0.05$ ) from pre-IAE to post-IAE. The [Hb], measured at maximal exercise, was decreased at pre-IAE compared with SL but did not change from pre-IAE to post-IAE.  $Ca_{O_2}$ , measured

at maximal exercise, decreased ( $P < 0.05$ ) from SL to pre-IAE and then increased ( $P < 0.05$ ) from pre-IAE to post-IAE. Maximal HR was decreased at both pre-IAE and post-IAE compared with SL. Maximal MAP and RER were similar at SL, pre-IAE and post-IAE. There were no differences in maximal Hct or [Lac] in any of the testing conditions. There were no differences in the percentages of change in calculated plasma volume from rest to maximal exercise at SL, pre-IAE, or post-IAE.

**Cycle time-trial data.** Individual and group cycle time-trial data are presented in Fig. 3. All individuals exhibited a decrement in cycle time-trial performance (i.e., increase in time) from SL to pre-IAE. Five of the six subjects exhibited an improvement in cycle time-trial performance (i.e., decrease in time) from pre-IAE to post-IAE. There was a  $61 \pm 14\%$  decrement ( $P < 0.05$ ) in cycle time-trial performance (min) from SL ( $20.2 \pm 1.4$ ) to pre-IAE ( $32.8 \pm 3.7$ ) and  $21 \pm 6\%$  improvement ( $P < 0.05$ ) from pre-IAE to post-IAE ( $24.8 \pm 1.2$ ).

Ventilatory and cardiovascular responses, measured at rest, at 40 and 70% of altitude-specific pre-IAE  $\dot{V}O_{2\max}$ , and after the cycle time trial are presented in Table 2. From SL to pre-IAE, resting and exercise  $\dot{V}_E/\dot{V}_{CO_2}$  increased ( $P < 0.05$ ) while resting and exercise  $PET_{CO_2}$  and  $Sa_{O_2}$  decreased ( $P < 0.05$ ). From pre-IAE to post-IAE, resting  $\dot{V}_E/\dot{V}_{CO_2}$  and resting and exercise  $Sa_{O_2}$  increased ( $P < 0.05$ ). The  $PET_{CO_2}$ , measured at 70% of altitude-specific pre-IAE  $\dot{V}O_{2\max}$ , increased ( $P < 0.05$ ) from pre-IAE to post-IAE. Resting and exercise [Hb] were similar at SL, pre-IAE, and post-IAE. From SL to pre-IAE, resting and exercise  $Ca_{O_2}$  decreased ( $P < 0.05$ ) and then increased ( $P < 0.05$ ) from pre-IAE to post-IAE. Resting and exercise HR increased ( $P < 0.05$ ) from SL to pre-IAE and decreased ( $P < 0.05$ ) from pre-IAE to post-IAE. There were no differences in resting or exercise MAP, RER, Hct, or osmolality at SL, pre-IAE, or post-IAE. There were no differences in the percentages of change in calculated resting plasma volume from SL to pre-IAE and from pre-IAE to post-IAE. There were no differences in the percentages of change in calculated plasma volume from rest through exhaustive exercise at SL, pre-IAE, and post-IAE. There were strong correlations between the percent decrement in cycle time-trial performance and percent decrease in resting  $Sa_{O_2}$  from SL to pre-IAE ( $r = 0.79$ ,  $P = 0.06$ ) and also between the percent improvement in cycle time-trial performance and per-

Table 1. Combined group ventilatory and cardiovascular responses measured at maximal exercise

Condition	Time	$\dot{V}O_2$ , l/min	$\dot{V}_E/\dot{V}_{CO_2}$	$Sa_{O_2}$ , %	[Hb], g/dl	$Ca_{O_2}$ , mlO <sub>2</sub> /l	HR, beats/min	MAP, mmHg	RER
SL	Max	$3.42 \pm 0.33$	$36.5 \pm 1.1$	$98 \pm 1$	$15.9 \pm 0.4$	$212 \pm 5$	$190 \pm 6$	$103 \pm 5$	$1.10 \pm 0.03$
Pre-IAE	Max	$2.73 \pm 0.31^*$	$46.6 \pm 2.3^*$	$70 \pm 3^*$	$15.4 \pm 0.3^*$	$137 \pm 6^*$	$180 \pm 5^*$	$100 \pm 2$	$1.14 \pm 0.03$
Post-IAE	Max	$3.16 \pm 0.29^\dagger$	$55.7 \pm 1.7^{\dagger*}$	$78 \pm 3^{\dagger*}$	$15.7 \pm 0.4$	$167 \pm 5^{\dagger*}$	$176 \pm 4^*$	$110 \pm 6$	$1.04 \pm 0.02$

Values are means  $\pm$  SE;  $n = 6$  subjects. SL, sea level; pre-IAE, before intermittent altitude exposure (IAE); post-IAE, after IAE;  $\dot{V}O_2$ , oxygen uptake;  $\dot{V}_E/\dot{V}_{CO_2}$ , ventilatory equivalent for carbon dioxide;  $Sa_{O_2}$ , arterial oxygen saturation; [Hb], hemoglobin concentration;  $Ca_{O_2}$ , arterial oxygen content; HR, heart rate; MAP, mean arterial pressure; RER, respiratory exchange ratio. \* $P < 0.05$  from SL; † $P < 0.05$  from pre-IAE.

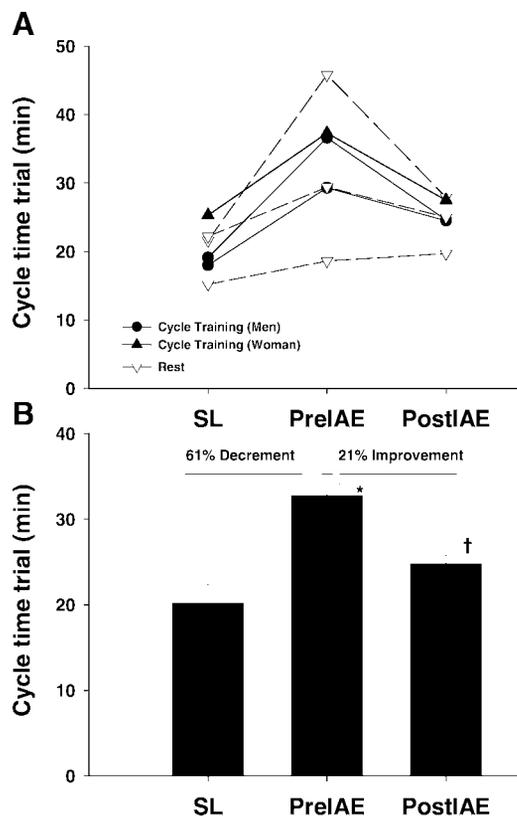


Fig. 3. Cycle time-trial performance was measured in 6 volunteers at SL and during  $\leq 30$  h exposures to 4,300 m altitude-equivalent (PB = 446 mmHg) before (pre-IAE) and immediately after (post-IAE) a 3-wk period of IAE (4 h/day; 5 days/wk, 4,300 m). A: individual data. B: group data. \* $P < 0.05$  from SL; † $P < 0.05$  from Pre-IAE.

cent increase in resting  $\text{SaO}_2$  from pre-IAE to post-IAE ( $r = 0.87$ ;  $P = 0.02$ ) (Fig. 4).

**Adductor pollicis endurance data.** Individual and group adductor pollicis endurance data are presented in Fig. 5. All individuals exhibited a decrement in adductor pollicis endurance from SL to pre-IAE. Four of the five individuals improved adductor pollicis en-

durance from pre-IAE to post-IAE. Adductor pollicis endurance time (min) decreased  $31 \pm 9\%$  ( $P < 0.05$ ) from SL ( $13.4 \pm 2.8$ ) to pre-IAE ( $9.2 \pm 2.8$ ) and increased  $63 \pm 26\%$  ( $P < 0.05$ ) from pre-IAE to post-IAE ( $14.8 \pm 4.2$ ). The MVC force (N) was similar at SL ( $141 \pm 19$ ), pre-IAE ( $130 \pm 18$ ) and post-IAE ( $128 \pm 15$ ). Resting  $\text{SaO}_2$  (%) measured immediately before the adductor pollicis endurance test decreased ( $P < 0.05$ ) from SL ( $98 \pm 1$ ) to pre-IAE ( $82 \pm 2$ ) and then increased ( $P < 0.05$ ) from pre-IAE to post-IAE ( $87 \pm 1$ ). There were strong correlations between the percent decrement in adductor pollicis endurance and percent decrease in resting  $\text{SaO}_2$  from SL to pre-IAE ( $r = 0.87$ ;  $P = 0.05$ ) and also between the percent improvement in adductor pollicis endurance and percent increase in resting  $\text{SaO}_2$  from pre-IAE to post-IAE ( $r = 0.92$ ;  $P = 0.02$ ) (Fig. 4).

## DISCUSSION

This study tested the hypothesis that 3 wk of IAE, in combination with rest and cycle training, would improve muscular performance at 4,300. Our major findings were that 3 wk of IAE induced a  $21 \pm 6\%$  improvement in cycle time-trial performance, a  $63 \pm 26\%$  improvement in adductor pollicis endurance, and a  $10 \pm 4\%$  increase in resting  $\text{SaO}_2$ . These improvements in muscular performance after IAE were comparable to those reported previously after chronic altitude residence (8, 10, 11, 19). IAE may therefore be used as an alternative to chronic altitude residence to facilitate improvements in muscular performance in athletes, soldiers, mountaineers, shift workers, and others that are deployed to altitude.

The most likely explanation for the improved muscular performance after 3 wk of IAE was the increase in ventilation and corresponding increase in resting  $\text{SaO}_2$ , measured immediately before both the cycle time-trial performance and adductor pollicis endurance tests. Because [Hb] and Hct were not increased from pre-IAE to post-IAE, improved arterial  $\text{O}_2$  carry-

Table 2. Combined group ventilatory and cardiovascular responses measured at rest and during submaximal exercise

Condition Time	$\dot{V}\text{O}_2$ l/min	$\dot{V}\text{E}/\dot{V}\text{CO}_2$	$\text{PETCO}_2$ , Torr	$\text{SaO}_2$ , %	$\text{CaO}_2$ , mlO <sub>2</sub> /l	HR, beats/min	MAP, mmHg	RER
SL								
Rest	$0.36 \pm 0.03$	$36.1 \pm 1.1$	$38.8 \pm 1.4$	$99 \pm 1$	$191 \pm 4$	$72 \pm 6$	$82 \pm 3$	$0.90 \pm 0.02$
40%	$1.44 \pm 0.11$	$28.1 \pm 0.6$	$41.8 \pm 0.9$	$99 \pm 1$	$200 \pm 5$	$116 \pm 5$	$88 \pm 1$	$0.97 \pm 0.02$
70%	$2.42 \pm 0.26$	$31.2 \pm 1.5$	$36.3 \pm 2.0$	$98 \pm 1$	$206 \pm 4$	$163 \pm 3$	$96 \pm 4$	$1.02 \pm 0.02$
EX				$98 \pm 1$	$207 \pm 5$	$184 \pm 3$	$95 \pm 3$	
Pre-IAE								
Rest	$0.37 \pm 0.02$	$48.3 \pm 1.0^*$	$30.8 \pm 0.6^*$	$82 \pm 2^*$	$168 \pm 7^*$	$93 \pm 7^*$	$87 \pm 2$	$0.85 \pm 0.03$
40%	$1.16 \pm 0.09^*$	$43.1 \pm 1.0^*$	$30.9 \pm 0.9^*$	$76 \pm 3^*$	$163 \pm 8^*$	$131 \pm 8^*$	$92 \pm 1$	$0.88 \pm 0.01^*$
70%	$1.82 \pm 0.21^*$	$44.7 \pm 1.9^*$	$27.8 \pm 1.3^*$	$74 \pm 2^*$	$161 \pm 7^*$	$158 \pm 7$	$94 \pm 2$	$1.00 \pm 0.03$
EX				$76 \pm 2^*$	$161 \pm 4^*$	$160 \pm 6^*$	$93 \pm 2$	
Post-IAE								
Rest	$0.37 \pm 0.04$	$54.4 \pm 1.8^{*\dagger}$	$28.3 \pm 1.0^*$	$90 \pm 1^{*\dagger}$	$182 \pm 8^\dagger$	$78 \pm 6^\dagger$	$92 \pm 3$	$0.87 \pm 0.03$
40%	$1.09 \pm 0.09^*$	$46.0 \pm 1.2^*$	$28.4 \pm 0.9^*$	$84 \pm 2^{*\dagger}$	$175 \pm 8^{*\dagger}$	$114 \pm 6^\dagger$	$95 \pm 4$	$0.88 \pm 0.02^*$
70%	$1.83 \pm 0.22^*$	$46.8 \pm 1.6^*$	$24.4 \pm 1.3^{*\dagger}$	$78 \pm 2^*$	$168 \pm 7^*$	$145 \pm 7^{*\dagger}$	$99 \pm 4$	$0.95 \pm 0.02^*$
EX				$79 \pm 1^*$	$174 \pm 4^{*\dagger}$	$162 \pm 5^*$	$95 \pm 1$	

Values are means  $\pm$  SE;  $n = 6$  subjects.  $\text{PETCO}_2$ , end-tidal carbon dioxide production. \* $P < 0.05$  from SL; † $P < 0.05$  from Pre-IAE.

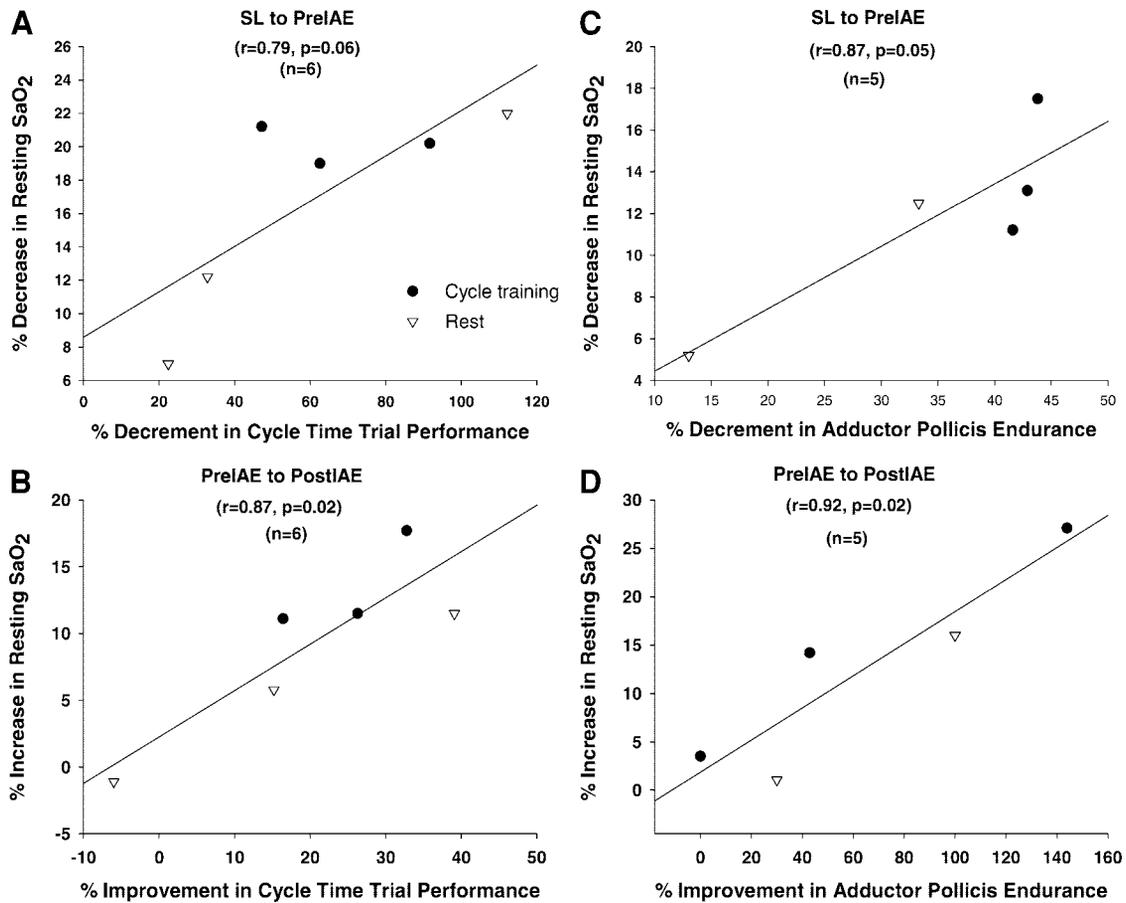


Fig. 4. Correlation between the %decrement in cycle time-trial performance and %decrease in resting arterial  $O_2$  saturation ( $SaO_2$ ) from SL to pre-IAE (A), the %improvement in cycle time-trial performance and %increase in resting  $SaO_2$  from pre-IAE to post-IAE (B), the %decrement in adductor pollicis endurance and %decrease in resting  $SaO_2$  from SL to pre-IAE (C), and the %improvement in adductor pollicis endurance and %increase in resting  $SaO_2$  from pre-IAE to post-IAE (D).

ing capacity related to hematological changes, per se, cannot explain the large improvements in muscular performance. A recent report of unchanged maximal exercise performance after acclimatization to 5,260 m altitude after dramatically altering [Hb] via hemodilution (3) seems consistent with our observations. Given the lack of change in HR and MAP during the cycle time trial and unchanged plasma volume from pre-IAE to post-IAE, it is unlikely that changes in cardiac output and therefore pulmonary capillary red cell transit time can explain the improvement in cycle exercise performance.

From pre-IAE to post-IAE, the strong correlation between the percent improvement in cycle time-trial performance and percent improvement in resting  $SaO_2$  ( $r = 0.87$ ) as well as the very strong correlation between the percent improvement in adductor pollicis endurance and percent improvement in resting  $SaO_2$  ( $r = 0.92$ ) support the hypothesis that improved muscular performance resulting from IAE is closely linked with increased  $SaO_2$ . The increase in  $SaO_2$  and commensurately augmented  $P_{O_2}$  gradient at post-IAE compared with pre-IAE may have improved  $O_2$  delivery from the muscle capillary to the mitochondria. An

improved muscle capillary-to-mitochondria  $O_2$  delivery is likely to have resulted in less perturbation of the phosphorylation potential (i.e.,  $[ATP]/[ADP][P_i]$ ) in active muscle and improved muscular performance because increases in  $P_i$  and ADP have been associated with increased muscular fatigue (20, 30).

Because of the  $18 \pm 4\%$  increase in  $\dot{V}O_{2\max}$  from pre-IAE to post-IAE, we cannot dismiss the possibility that a portion of the  $21 \pm 16\%$  improvement in cycle time-trial performance may be attributable to cycle training during IAE. Although low subject numbers limit between-group conclusions from our findings, the very strong correlations between the percent changes in arterial oxygenation and percent changes in cycle and adductor pollicis performance both from SL to pre-IAE and from pre-IAE to post-IAE (Figs. 4 and 6) imply that arterial oxygenation was the major determinant of changes in muscular performance with acute and then repeated intermittent exposures to hypobaric hypoxia. In contrast, training during IAE is likely to have had a much more limited effect on performance. This conclusion is supported by established evidence that SL endurance training does not improve  $SaO_2$  (24) and those of others (14, 22), indicating that training at

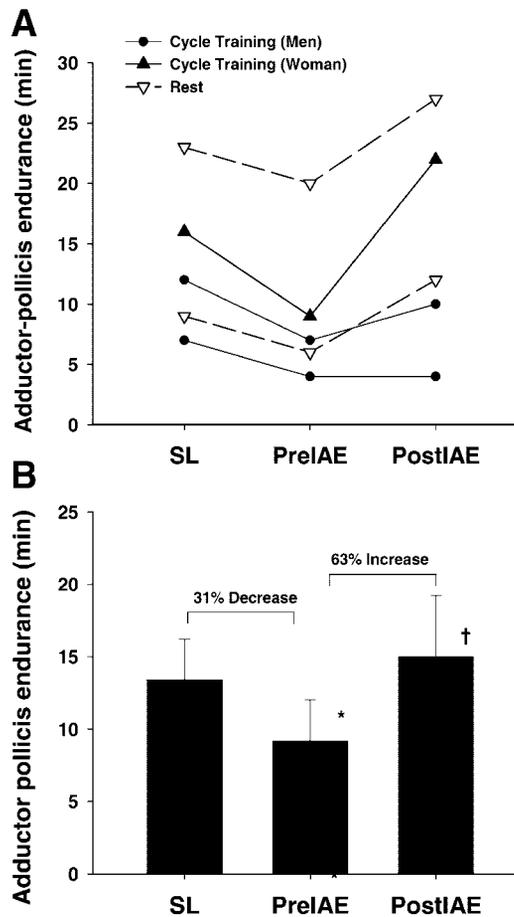


Fig. 5. Adductor pollicis endurance was measured in 5 volunteers at SL and during  $\leq 30$ -h exposures to 4,300 m altitude-equivalent ( $P_B = 446$  mmHg) before and immediately after a 3-wk period of IAE (4 h/day; 5 days/wk, 4,300 m). A: individual data. B: group data. \* $P < 0.05$  from SL; † $P < 0.05$  from pre-IAE.

altitude, per se, does not exert a prominent independent effect on  $Sa_{O_2}$ . Further support for the conclusion that arterial oxygenation was more important than training on muscular performance in hypobaric hypoxia is the fact that the adductor pollicis muscle was not trained during 3 wk of IAE yet exhibited a marked improvement in endurance performance. This improvement appears primarily attributable to the observed increase in ventilation and corresponding increase in  $Sa_{O_2}$  and  $O_2$  delivery.

Increases in  $\dot{V}O_{2\max}$  at altitude after a period of IAE combined with exercise training have been observed previously (2, 5, 23, 27), but these studies did not employ resting control groups. Typically,  $\dot{V}O_{2\max}$ , measured at altitude, does not increase with chronic altitude residence because the increase in  $Ca_{O_2}$  is typically offset by a decrease in cardiac output due to a decrease in stroke volume (11, 21, 25, 28). In our IAE study, the increase in  $Ca_{O_2}$  was not likely offset by a decrease in cardiac output because HR and MAP during maximal exercise and plasma volume remained unchanged from pre-IAE to post-IAE. Thus the potential for improvement in  $\dot{V}O_{2\max}$  after IAE may be greater than with chronic altitude residence. A recent chronic altitude

residence study, conducted at 5,260 m, did not find any relationship between an increase in  $O_2$  delivery with altitude acclimatization and improved maximal exercise performance (4). They attributed the lack of change in  $\dot{V}O_{2\max}$  from acute to chronic altitude residence, despite an increase in  $Ca_{O_2}$  and unchanged cardiac output, to a redistribution of the extra systemic  $O_2$  transported after altitude acclimatization to other tissues other than working muscles. Because we did not measure cardiac output distribution in this study, we cannot speculate whether IAE would induce these same changes in cardiac output distribution.

Although we did not measure the mechanisms responsible for the increase in ventilation after IAE, we can speculate that either an increased hypoxic and/or hypercapnic ventilatory drive may be responsible. Previous studies have reported an increase in both of these parameters after chronic altitude residence (7, 31). Others (14, 16, 18) have reported an increase in the hypoxic ventilatory response, measured at sea level, after resting intermittent exposures to altitude as well as a correlation between the change in hypoxic ventilatory response at rest and ventilation during submaximal exercise (15). Thus it is entirely reasonable to assume that an increased hypoxic ventilatory drive may be the mechanism driving the increase in both the resting and exercise ventilation after IAE.

Although others have related improved muscular performance after chronic altitude residence to changes in substrate utilization (23) and less cardiac work (32), these factors do not appear to explain our improved cycle time-trial performance after 3 wk of IAE. The RER results, measured at rest or any time point during the two 15-min work bouts preceding the cycle time trial, were not affected by 3 wk of IAE, nor was [Lac] reduced at exhaustion. Lessening of cardiac work is unlikely because HR at any time point during the cycle time-trial performance test was unchanged from pre-IAE to post-IAE. The improvement in cycle time-trial performance from pre-IAE to post-IAE also cannot be attributed to differences in diet or fluid hydration status because these were controlled before each trial.

The present study is the first to examine the effects of IAE on cycle time-trial performance and adductor pollicis endurance at 4,300 m. Thus we cannot compare our results to previous studies examining the effects of IAE on muscular performance, but we can compare the magnitude of our results to the results from previous chronic altitude residence studies. After 2–3 wk of chronic altitude residence, previous studies have reported  $\sim 45$ – $60\%$  improvements in large-muscle endurance at 4,300 m (11, 19). Our finding of an  $\sim 21\%$  improvement in cycle time-trial performance after 3 wk of IAE was less than improvements reported after chronic altitude residence, but we employed a closed-ended cycle time-trial test and others employed an open-ended endurance test to exhaustion. Thus the room for improvement when using the type of test we employed was much less. In a recent chronic altitude residence study, a cycle time-trial test similar to the one we used was employed to evaluate large-muscle

endurance and the results were similar to ours (C. Fulco, unpublished observation, September, 2002).

Our finding of an ~63% improvement in adductor pollicis endurance from pre-IAE to post-IAE was almost double the ~20–30% improvements reported after chronic altitude residence studies (8–10). Reasons for the differences between studies may be related to the timing of the measurement. In the chronic altitude residence studies (8–10), adductor pollicis endurance was evaluated 24–48 h after initial introduction to altitude whereas we measured adductor pollicis endurance ~1–4 h after initial introduction to altitude. Adductor pollicis endurance may show the greatest deterioration within the first few hours of altitude exposure because this is the period of greatest hypoxemia. Thus our greater initial decrement in adductor pollicis endurance may have left a greater reserve for improvement after 3 wk of IAE.

In conclusion, this study found that 3 wk of IAE improved cycle time-trial performance and adductor pollicis endurance  $21 \pm 6$  and  $63 \pm 26\%$ , respectively. These improvements in muscular performance after IAE were comparable to those reported previously after chronic altitude residence. IAE may therefore be used as an alternative to continuous altitude exposure to facilitate improvements in muscular performance in athletes, soldier, mountaineers, and shift workers that are deployed to altitude.

We thank the test volunteers for their participation and cooperation in this study. We gratefully acknowledge the technical and logistical support provided by Sgt. Dave DeGroot, Sgt. James Moulton, Vinnie Forte, Jr., Doreen Hafeman, Michelle Mayo, and Lauren Cavanaugh. The efforts of all chamber crew operators, medical support staff, and central blood laboratory personnel are also gratefully acknowledged.

#### DISCLOSURES

The views, opinions and/or findings in this report are those of the authors and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

#### REFERENCES

1. Beidleman BA, Rock PB, Muza SR, Fulco CS, Forte VA Jr, and Cymerman A. Exercise  $\dot{V}_E$  and physical performance are not affected by menstrual cycle phase at altitude. *J Appl Physiol* 86: 1519–1526, 1999.
2. Benoit H, Germain M, Barthelemy JC, Denis C, Castells J, Dormois D, Lacour JR, and Geysant A. Pre-acclimatization to high altitude using exercise with normobaric hypoxic gas mixtures. *Int J Sports Med* 13: S213–S216, 1992.
3. Calbet JAL, Radegran G, Boushel R, Sondergaard H, Saltin B, and Wagner PD. Effect of blood haemoglobin concentration on  $\dot{V}O_{2\max}$  and cardiovascular function in lowlanders acclimated to 5260 m. *J Physiol* 545: 715–728, 2002.
4. Calbet JAL, Boushel R, Radegran G, Sondergaard H, Wagner PD, and Saltin B. Why is  $\dot{V}O_{2\max}$  after altitude acclimatization still reduced despite normalization of arterial  $O_2$  content? *Am J Physiol Regul Integr Comp Physiol* 284: R304–R316, 2003.
5. Desplanches D, Hoppeler H, Linossier MT, Denis C, Claassen H, Dormois D, Lacour JR, and Geysant A. Effects of training in normoxia and normobaric hypoxia on human muscle ultrastructure. *Pflügers Arch* 425: 263–267, 1993.
6. Dill DB and Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol* 37: 247–248, 1974.
7. Forster HV, Dempsey JA, Birnbaum ML, Reddan WG, Thoden JS, Grover RF, and Rankin J. Comparison of ventilatory responses to hypoxic and hypercapnic stimuli in altitude-sojourning lowlanders, lowlanders residing at altitude and native altitude residents. *Fed Proc* 28: 1274–1279, 1969.
8. Fulco CS, Cymerman A, Muza SR, Rock PB, Pandolf KB, and Lewis SF. Adductor pollicis muscle fatigue during acute and chronic altitude exposure and return to sea level. *J Appl Physiol* 77: 179–183, 1994.
9. Fulco CS, Friedlander AL, Muza SR, Rock PB, Robinson S, Lammi E, Baker-Fulco CJ, Lewis SF, and Cymerman A. Energy intake deficit and physical performance at altitude. *Aviat Space Environ Med* 73: 758–765, 2002.
10. Fulco CS, Rock PB, Muza SR, Lammi E, Cymerman A, Kambis KW, Lewis SF, Butterfield G, Braun B, Reeves JT, Beidleman BA, Zamudio S, and Moore L. Effect of Menstrual Cycle Phase on Muscle Fatigue and Physical Performance During High Altitude Acclimatization. Natick, MA: US Army Res. Inst. of Environ. Med., 1998. (Technical Report T98-8)
11. Horstman D, Weiskopf R, and Jackson RE. Work capacity during 3-wk sojourn at 4,300 m: effects of relative polycythemia. *J Appl Physiol* 49: 311–318, 1980.
12. Hultgren HN. Sleep. In: *High Altitude Medicine*, edited by Hultgren HN. Stanford, CA: Hultgren Publications, 1997, p. 368–379.
13. Jeukendrup A, Saris WHM, Brouns F, and Kester ADM. A new validated endurance performance test. *Med Sci Sports Exerc* 28: 266–270, 1996.
14. Katayama K, Sato Y, Ishida K, Mori S, and Miyamura M. The effects of intermittent exposure to hypoxia during endurance exercise training on the ventilatory responses to hypoxia and hypercapnia in humans. *Eur J Appl Physiol* 78: 189–194, 1998.
15. Katayama K, Sato Y, Morotome Y, Shima N, Ishida K, Mori S, and Miyamura M. Intermittent hypoxia increases ventilation and  $Sa_{O_2}$  during hypoxic exercise and hypoxic chemosensitivity. *J Appl Physiol* 90: 1431–1440, 2001.
16. Katayama K, Sato Y, Shima N, Qiu JC, Ishida K, Mori S, and Miyamura M. Enhanced chemosensitivity after intermittent hypoxic exposure does not affect exercise ventilation at sea level. *Eur J Appl Physiol* 87: 187–191, 2002.
17. Klokker M, Kharazmi A, Galbo H, Byghjerg I, and Pedersen BK. Influence of in vivo hypobaric hypoxia on function of lymphocytes, neutrocytes, natural killer cells, and cytokines. *J Appl Physiol* 74: 1100–1106, 1993.
18. Levine BD, Friedman DB, Engfred K, Hanel B, Kjaer M, Clifford PS, and Secher NH. The effect of normoxic or hypobaric hypoxic endurance training on the hypoxic ventilatory response. *Med Sci Sports Exerc* 24: 769–775, 1992.
19. Maher JT, Jones LG, and Hartley LH. Effects of high altitude exposure on submaximal endurance capacity of man. *J Appl Physiol* 37: 895–898, 1974.
20. Matheson GO, Allen PS, Ellinger DC, Hanstock CC, Gheorghiu D, McKenzie DC, Stanley C, Parkhouse WS, and Hochachka PW. Skeletal muscle metabolism and work capacity: a  $^{31}P$ -NMR study of Andean natives and lowlanders. *J Appl Physiol* 70: 1963–1976, 1991.
21. Pugh LGCE, Gill MB, Lahiri S, Milledge JS, Ward MP, and West JB. Muscular exercise at great altitudes. *J Appl Physiol* 19: 431–440, 1964.
22. Rodriguez FA, Casas H, Casas M, Pages T, Rama R, Ricart A, Ventura JL, Ibanez J, and Viscor G. Intermittent hypobaric hypoxia stimulates erythropoiesis and improves aerobic capacity. *Med Sci Sports Exerc* 31: 264–268, 1999.
23. Roskamm H, Landry F, Samek L, Schlager M, Weidemann H, and Reindell H. Effects of a standardized ergometer training program at three different altitudes. *J Appl Physiol* 27: 840–847, 1969.

24. **Saltin B, Blomqvist B, Mitchell JH, Johnson RL Jr, Wil-denthal K, and Chapman CB.** Response to submaximal and maximal exercise after bed rest and training. *Circulation* 38, *Suppl* 7: 1–78, 1968.
25. **Saltin B, Grover RF, Blomqvist CG, Hartley LH, and John-son RL.** Maximal oxygen uptake and cardiac output after 2 weeks at 4,300 m. *J Appl Physiol* 25: 400–409, 1968.
26. **Simon-Schnass IM.** Risk of oxidative stress during exercise at high altitude. In: *Exercise and Oxygen Toxicity*, edited by Sen CK, Packer L, and Hanninen O. New York: Elsevier, 1994, p. 191–210.
27. **Vogt M, Puntchart A, Geiser J, Zuleger C, Billeter R, and Hoppeler H.** Molecular adaptations in human skeletal muscle to endurance training under simulated hypoxic conditions. *J Appl Physiol* 91: 173–182, 2001.
28. **Wagner PD, Gale GE, Moon RE, Torre-Bueno JR, Stolp BW, and Saltzman HA.** Pulmonary gas exchange in humans exercising at sea level and simulated altitude. *J Appl Physiol* 61: 260–270, 1986.
29. **Ward JP, Milledge JS, and West JB.** Acute mountain sick-ness. In: *High Altitude Medicine and Physiology*. London: Ar-nold, 2000, p. 215–231.
30. **Westerblad H, Allen DG, and Lannergren J.** Muscle fatigue: lactic acid or inorganic phosphate the major cause? *News Physiol Sci* 17: 17–21, 2002.
31. **White DP, Gleeson K, Pickett CK, Rannels AM, Cymerman A, and Weil JV.** Altitude acclimatization: influence on periodic breathing and chemoresponsiveness during sleep. *J Appl Physiol* 401–412, 1987.
32. **Young AJ and Young PM.** Human acclimatization to high terrestrial altitude. In: *Human Performance Physiology and En-vironmental Medicine at Terrestrial Extremes*, edited by Pandolf KB, Sawka MN, and Gonzalez RR. Indianapolis, IN: Benchmark, 1988, p. 497–543.

