# Training in hypoxia vs. training in normoxia in high-altitude natives

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**R. Favier, H. Spielvogel, D. Desplanches, G. Ferretti, B. Kayser, A. Grünenfelder, M. Leuenberger, L. Tüscher, E. Caceres, and H. Hoppeler.** Training in hypoxia vs. training in normoxia in high-altitude natives. *J. Appl. Physiol.* 78(6): 2286–2293, 1995.—To determine the interactions between endurance training and hypoxia on maximal exercise performance, we performed a study on sedentary high-altitude natives who were trained in normoxia at the same relative ($n$ = 10) or at the same absolute ($n$ = 10) intensity of work as hypoxia-trained subjects ($n$ = 10). The training-induced improvement of maximal oxygen uptake ($\dot{V}O_{2\,max}$) in hypoxia-trained subjects was similar to that obtained in normoxia-trained sea-level natives submitted to the same training protocol (H. Hoppeler, H. Howald, K. Conley, S. L. Lindstedt, H. Claassen, P. Vock, and E. W. Weibel. *J. Appl. Physiol.* 59: 320–327, 1985). Training at the same absolute work intensity in the presence of increased oxygen delivery failed to provide a further increase in $\dot{V}O_{2\,max}$. $\dot{V}O_{2\,max}$ was not improved to a greater extent by simultaneously increasing absolute work intensity and $O_2$ delivery during the training sessions. In addition, training in normoxia is accompanied by an increased blood lactate accumulation during maximal exercise, leading to greater drops in arterial pH, bicarbonate concentration, and base excess. We conclude that, in high-altitude natives, *1*) training at altitude does not provide any advantage over training at sea level for maximal aerobic capacity, whether assessed in chronic hypoxia or in acute normoxia; *2*) $\dot{V}O_{2\,max}$ improvement with training cannot be further enhanced by increasing $O_2$ availability alone or in combination with an increased work intensity during the exercising sessions; and *3*) training in normoxia in these subjects results in a reduced buffer capacity.

maximal oxygen uptake; arterial hemoglobin saturation; buffer capacity; lactate

IN THEIR CONSTANT SEARCH for ways to improve performance, many athletes spend considerable resources to train at altitude. Even though there can be little doubt that training at altitude is fundamental to prepare an athlete for competition at altitude, the value of training at altitude for competition at sea level is still controversial. Thus several authors have reported an improved performance and an increase in maximal oxygen uptake ($\dot{V}O_{2\,max}$) after altitude training (2, 7, 8, 16, 22, 25), whereas others have observed no changes (1, 4, 14, 17). This lack of consensus between studies may be attributed to several factors. First, the level and duration of altitude exposure can vary considerably among studies, and none of the training studies has been carried out after altitude acclimatization, which requires several weeks or months to reach full expression (3, 30). Second, anorexia is reported as an almost inevitable consequence of sojourns at high altitude and leads to a substantial reduction in body and muscle masses (21). Third, by using subjects of widely different degrees of fitness, the impact of altitude exposure on adaptations to training may have been masked because endurance athletes appeared to be affected to a greater extent by hypoxia than were sedentary subjects (15, 26). Fourth, the training program used in previous studies was so variable that the effect of hypoxia on training-induced effects is difficult to appreciate.

Therefore, we designed a study in which most of the aforementioned confounding factors have been alleviated. For this purpose, we recruited high-altitude subjects who *1*) were born and lived at altitude (i.e., fully altitude acclimatized); *2*) did not present any sign of inadequate nutrition (i.e., not anorexic); *3*) displayed a similar level of aerobic capacity (i.e., displaying a $\dot{V}O_{2\,max}$ within the range reported for sedentary subjects; this condition is particularly important because that way one could expect greater changes in $\dot{V}O_{2\,max}$ with training); and *4*) were submitted to a training program previously used in sea-level natives (12).

In addition, it must be kept in mind that, if chronic exposure to altitude is accompanied by beneficial hematologic changes (increased $O_2$ transport capacity), the subject is still exposed to a reduced inspired $P_{O_2}$ ($P_{I_{O_2}}$). We reasoned that, if the subjects are trained while inhaling a gas mixture recreating a $P_{I_{O_2}}$ similar to that encountered at sea level, they should be able to sustain a higher absolute workload. Indeed, altitude-induced polycythemia has been shown to be a major contributor to maximal systemic oxygen transport and, as such, could be of considerable value for increasing work capacity while training at altitude in presence of an increased $P_{I_{O_2}}$ (13, 23). In support of this assumption, Levine et al. (16) have suggested that "the most efficient technique may well be to live at altitude and train at sea level."

The purposes of the present study were therefore intended to *1*) analyze the effects of endurance training in high-altitude natives and compare the results with those obtained in sea-level natives submitted to the same training protocol (12); *2*) test the hypothesis of better training-induced improvements by increasing $O_2$ availability during exercising sessions (16); and *3*) delineate which is the main factor with regard to increasing aerobic capacity during training: power output ($W_{max}$) or $O_2$ availability.

## METHODS

*Subjects.* Thirty male high-altitude residents from La Paz, Bolivia (~3,600 m altitude), were selected from 60 applicants. Genetically, the subjects ranged from Amerindian to European, with most being mestizos. The subjects were informed about the possible risks involved in this study before they gave their written consent to participate. Potential subjects were excluded from participation if they had resided for >1 mo at low altitude within 3 yr before the study or had participated in a physical-training program within 3 mo before the study. Before participating, each volunteer was examined by a physician and had to be free of any cardiovascular, pulmonary, or hematologic history.

*$\dot{V}O_{2\,max}$ measurements and procedures.* $\dot{V}O_{2\,max}$ was determined during an incremental exercise test on a cycle ergometer. Starting at 60 W, $W_{max}$ was increased by 30 W every 4 min until voluntary exhaustion. The subjects were verbally encouraged to continue exercise as long as possible, and the tests were considered indicative of $\dot{V}O_{2\,max}$ if two of the three following criteria were met: *1*) identification of a plateau in $O_2$ uptake ($\dot{V}O_2$) with an increase in $W_{max}$ (<150 ml $\dot{V}O_2$ increase), *2*) a respiratory exchange ratio > 1.1, and *3*) a peak heart rate (HR) within 5% of the age-predicted maximum HR.

Respiratory gas exchange parameters were measured with an open-circuit system described in detail elsewhere (9). Before and after training, each participant completed two incremental cycle ergometric tests while breathing one of two treatment gases: hypoxic [chronic hypoxia: barometric pressure ~500 mmHg, inspired $O_2$ fraction ($FI_{O_2}$) 0.209] or normoxic (acute normoxia: barometric pressure ~500 mmHg, $FI_{O_2}$ 0.314). The testing sequence was randomized, and at least 24 h separated the tests. The normoxic gas was calculated to give a $PI_{O_2}$ equivalent to sea level. The normoxic gas mixture was obtained by a vacuum cleaner providing air in which the $O_2$ concentration was increased by adding $O_2$ from a tank through a flowmeter. The gas mixture was then introduced into a 200-liter plastic container that acted as mixing chamber. The concentration of $O_2$ in the mixture was monitored at the outlet of the plastic tank, i.e., close to the mouth of the subject.

HR was continuously monitored by bipolar electrocardiographic telemetry (Sport tester). Arterial oxygen saturation ($Sa_{O_2}$) measurements were made with an ear oximeter (Biox 3000, Ohmeda). The ear lobe was cleansed and massaged vigorously to increase perfusion before ear clip attachment. Blood samples from the fingertip were taken at rest and during the last minute of each exercise level for measurements of lactate (Yellow Springs lactate analyzer). Blood arterialization of the finger was achieved by inducing hyperemia with friction with an ointment (Trafuril, Ciba Geigy). Blood samples were taken at rest and during the last minute of the maximal exercise level for measurements of $P_{O_2}$, $P_{CO_2}$, and pH (model 280 blood gas analyzer, Ciba Corning). The instrument was calibrated with standards of known concentrations.

*Physical training.* Training was performed 5 times/wk for 30 min/day at a constant workload on an ergometer the same as that used in the performance test. Training was continued for 6 wk.

The 30 subjects were randomly assigned to one of three groups. One group trained at high altitude at 70% of $\dot{V}O_{2\,max}$ determined in hypoxia (H; $n$ = 10). The two other groups trained at high altitude while inhaling the normoxic gas mixture at the same relative workload (70% of the normoxic $\dot{V}O_{2\,max}$; $N_{rel}$; $n$ = 10) or at the same absolute workload (70% of hypoxic $\dot{V}O_{2\,max}$; $N_{abs}$; $n$ = 10) as the H control group.

The initial workload was determined for each individual from manually fitted plots of HR and blood lactate vs. $W_{max}$ obtained during the first (pretraining) performance test. During each workout, the HR was recorded after 10 and 30 min. Lactate was determined weekly at rest and after 10 and 30 min of exercise. The workload of the next training session was increased in steps of 5 W as soon as the HR and/or the lactate after 30 min had dropped enough to indicate that the subject could perform at the next higher workload, i.e., subjects were training at constant relative intensities judged by HR and plasma lactate levels.

TABLE 1. *Anthropometric and hematologic characteristics of subjects before training*

| | H | $N_{rel}$ | $N_{abs}$ |
|---|---|---|---|
| Age, yr | 24.2±0.7 | 24.9±1.2 | 23.5±0.7 |
| Height, cm | 167±1 | 168±2 | 170±1 |
| Weight, kg | 62.0±2.6 | 60.3±2.9 | 62.4±1.9 |
| BMI, kg/m$^2$ | 22.3±0.7 | 21.4±0.9 | 21.5±0.5 |
| BSA, m$^2$ | 1.69±0.04 | 1.68±0.05 | 1.72±0.03 |
| %Fat | 16.2±0.8 | 16.8±1.3 | 14.1±1.3 |
| Body density | 0.996±0.020 | 1.002±0.005 | 0.998±0.003 |
| Hct, % | 50.4±0.8 | 51.8±1.1 | 52.3±0.7 |
| Hb, g/dl | 17.3±0.2 | 18.0±0.4 | 17.6±0.2 |

Values are means ± SE. H, hypoxia-trained group; $N_{rel}$, normoxia-trained group at same relative power output as H group; $N_{abs}$, normoxia-trained group at the same absolute power output as H group; BMI, body mass index; BSA, body surface area; Hct, hematocrit; Hb, hemoglobin.

*Test-retest $\dot{V}O_{2\,max}$ reliability.* To determine the test-retest reliability of $\dot{V}O_{2\,max}$ under our experimental conditions, some subjects performed either a hypoxic ($n$ = 12) or a normoxic ($n$ = 11) $\dot{V}O_{2\,max}$ determination 4 mo after training (detraining test). The intraclass correlation coefficient ($r$) for the pretraining and detraining reliability of $\dot{V}O_{2\,max}$ was 0.95, and the coefficient of (random) variation was 11%. The mean difference in $\dot{V}O_{2\,max}$ between the two tests was 3.8%, confirming the reproducibility of $\dot{V}O_{2\,max}$ by use of our testing protocol and instrumentation.

For statistical comparisons of group means (before and after training, hypoxia vs. normoxia, and training in hypoxia vs. training in normoxia), a two-way analysis of variance with repeated measures was used followed by a post hoc Fisher's protected least significant difference test. The level of significance was set at 5%.

## RESULTS

The anthropometric and resting hematologic characteristics of the subjects are shown in Table 1 and are similar in the three groups.

At rest, before training, in response to acute normoxia, all the subjects displayed a significant increase in arterial $P_{O_2}$ and $Sa_{O_2}$ with no changes in arterial $P_{CO_2}$ and pH (data not shown). During maximal exercise, both $W_{max}$ and $\dot{V}O_{2\,max}$ were significantly improved by acute normoxia in all groups (Tables 2 and 3). By contrast, neither maximal HR nor the ventilatory equivalent (maximal minute ventilation/$\dot{V}O_{2\,max}$) nor maximal blood lactate was different in chronic hypoxia and acute normoxia.

From the data reported in Fig. 1, it can be seen that, with respect to exercise intensity, the H and $N_{rel}$ groups were similarly trained. Indeed, training workloads, blood lactate concentration, and HR at 30 min were

TABLE 2. *$W_{max}$, $\dot{V}O_2$, $\dot{V}E$, RER, HR, $Sa_{O_2}$, blood lactate, and absolute and relative $W_{4\,mM}$ during exercise in hypoxia before and after training*

| | Before Training | | | After Training | | |
|---|---|---|---|---|---|---|
| | H | $N_{rel}$ | $N_{abs}$ | H | $N_{rel}$ | $N_{abs}$ |
| $W_{max}$, W | 173±6 | 162±9 | 177±10 | 214±11* | 208±11* | 212±9* |
| $\dot{V}O_2$, l/min | 2.42±0.10 | 2.31±0.11 | 2.64±0.09 | 2.79±0.13* | 2.69±0.15* | 2.86±0.15* |
| $\dot{V}E$, l/min | 127.7±5.4 | 127.5±7.1 | 136.0±9.0 | 145.0±9.5 | 150.5±9.3* | 151.7±9.7* |
| RER | 1.21±0.02 | 1.15±0.02 | 1.17±0.02 | 1.15±0.02 | 1.12±0.01 | 1.17±0.02 |
| HR, beats/min | 192±3 | 186±4 | 189±3 | 189±3 | 181±4 | 187±3 |
| $Sa_{O_2}$, % | 87.6±1.3 | 91.9±0.7 | 89.6±0.7 | 87.4±1.2 | 89.9±0.8 | 88.8±0.8 |
| Lactate, mM | 8.5±0.5 | 8.4±0.3 | 8.1±0.5 | 8.3±0.6 | 9.1±0.4 | 8.3±0.6 |
| Absolute $W_{4\,mM}$, W | 124±7 | 111±9 | 123±9 | 163±12* | 149±9* | 163±11* |
| Relative $W_{4\,mM}$, $\%W_{max}$ | 71.5±2.6 | 68.0±3.1 | 69.9±3.3 | 74.0±5.0 | 71.7±2.0 | 76.4±2.2 |

Values are means ± SE. $W_{max}$, power output; $\dot{V}O_2$, $O_2$ uptake; $\dot{V}E$, ventilation; RER, respiratory exchange ratio; HR, heart rate; $Sa_{O_2}$, arterial $O_2$ saturation; absolute $W_{4\,mM}$, workload measured at 4 mM lactate; relative $W_{4\,mM}$, workload at which lactate reaches 4 mM. * Significantly different from before training.

similar in the two groups during the 6 wk of training. By contrast, the $N_{abs}$ group, who trained at the same absolute workload as the H group but inhaled the normoxic gas mixture during the training session, displayed a significantly reduced HR and lactate level at 30 min.

In response to training, $W_{max}$ and $\dot{V}O_{2\,max}$ were significantly improved, whether training was performed in hypoxia or normoxia (Tables 2 and 3). The improvement of $\dot{V}O_{2\,max}$ with training was similar in the H and normoxia-trained groups, whether tested in hypoxia or in normoxia (Fig. 2). Interestingly, the $N_{abs}$ group, who trained at a lower relative intensity, displayed a similar increase in $\dot{V}O_{2\,max}$ compared with that in the H or $N_{rel}$ groups (Fig. 2).

With respect to maximal HR and blood lactate at maximal exercise, it can be shown that they remained unaffected by changes in $O_2$ concentration in the inhaled gas or by training (Tables 2 and 3). By contrast, the $O_2$ saturation measured during maximal exercise was affected by the $O_2$ ambient concentration and by training. Thus, before training, $Sa_{O_2}$ decreased during maximal exercise whether cycling in hypoxia or normoxia (Fig. 3), and the decrease was more pronounced in hypoxia than in normoxia. After 6 wk of training, it appeared that the H subjects displayed a significantly greater desaturation whether cycling in hypoxia or in normoxia (Fig. 3), whereas the normoxia-trained groups maintained a similar desaturation in hypoxia and normoxia compared with pretraining.

Blood lactate kinetics during exercise was clearly affected by $O_2$ tension and by training, as indicated by the increase in workload measured at 4 mM lactate ($W_{4\,mM}$; Tables 2 and 3). However, by calculating the relative workload at which lactate reaches 4mM (calculated as $\%W_{max}$), we found that in H and $N_{rel}$ groups there was a significant increase in $W_{4\,mM}$ with training when exercising in normoxia but not in hypoxia (Tables 2 and 3).

With regard to the acid-base status in relation to ambient oxygenation and/or training, there were some interesting findings. First, before training, blood pH, lactate concentration, and base excess concentration ([BE]) measured at maximal exercise were identical whether the subjects exercised in hypoxia or normoxia (Figs. 4 and 5). After training, it appears that the $N_{rel}$ and $N_{abs}$ groups have a reduced buffer capacity, as shown by the greater drops in pH, bicarbonate concentration ($[HCO_3^-]$), and [BE] after than before training when exercising in normoxia and in the $N_{rel}$ group when tested in hypoxia. It had to be mentioned that the H group displayed, before and after training, a similar decrease in pH and [BE], a decrease in blood lactate, and a maintained $[HCO_3^-]$.

TABLE 3. *$W_{max}$, $\dot{V}O_2$, $\dot{V}E$, RER, HR, $Sa_{O_2}$, blood lactate, and absolute and relative $W_{4\,mM}$ during exercise in normoxia before and after training*

| | Before Training | | | After Training | | |
|---|---|---|---|---|---|---|
| | H | $N_{rel}$ | $N_{abs}$ | H | $N_{rel}$ | $N_{abs}$ |
| $W_{max}$, W | 194±7† | 180±10† | 200±10† | 231±10*† | 222±12*† | 231±11*† |
| $\dot{V}O_2$, l/min | 2.64±0.10† | 2.46±0.10† | 2.77±0.11† | 3.02±0.13*† | 2.94±0.15*† | 3.04±0.12*† |
| $\dot{V}E$, l/min | 135.6±4.9 | 136.1±6.5 | 137.1±8.8 | 141.3±8.6 | 151.1±9.7 | 155.8±6.3* |
| RER | 1.12±0.02 | 1.15±0.02 | 1.17±0.04 | 1.11±0.02 | 1.11±0.02 | 1.13±0.02 |
| HR, beats/min | 194±4 | 188±4 | 191±3 | 187±4 | 182±4 | 190±2 |
| $Sa_{O_2}$, % | 96.4±0.4† | 97.9±0.6† | 95.4±0.6† | 96.1±0.8† | 97.4±0.4† | 96.1±0.7† |
| Lactate, mM | 8.6±0.6 | 8.0±0.2 | 7.3±0.6 | 7.9±0.5 | 8.6±0.6 | 7.9±0.5 |
| Absolute $W_{4\,mM}$, W | 130±8 | 124±9† | 146±9† | 187±10*† | 171±12*† | 179±14*† |
| Relative $W_{4\,mM}$, $\%W_{max}$ | 66.8±3.1 | 68.9±2.6 | 73.4±3.2 | 81.0±2.9* | 76.7±1.8*† | 76.7±3.0 |

Values are means ± SE. * Significantly different from before training. † Significantly different from hypoxia.

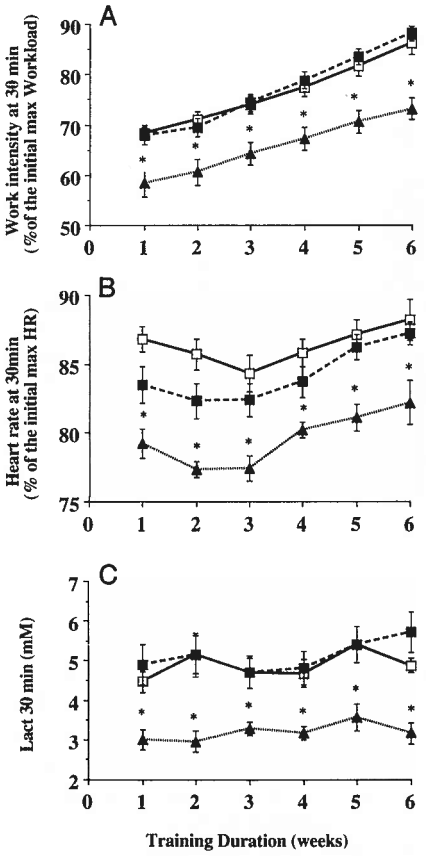


FIG. 1. Work intensity (*A*), heart rate (*B*; HR), and blood lactate (*C*; Lact) at 30 min during exercise bout throughout training. Work intensity and HR are expressed as percentage of initial maximal values obtained during 1st maximal test (pretraining). ■, Hypoxia-trained group (H); □, normoxia-trained group at same relative power output as H group ($N_{rel}$); ▲, normoxia-trained group at same absolute power output as H group ($N_{abs}$). Values are means ± SE. * Significantly different from $N_{rel}$ and H ($P < 0.05$).

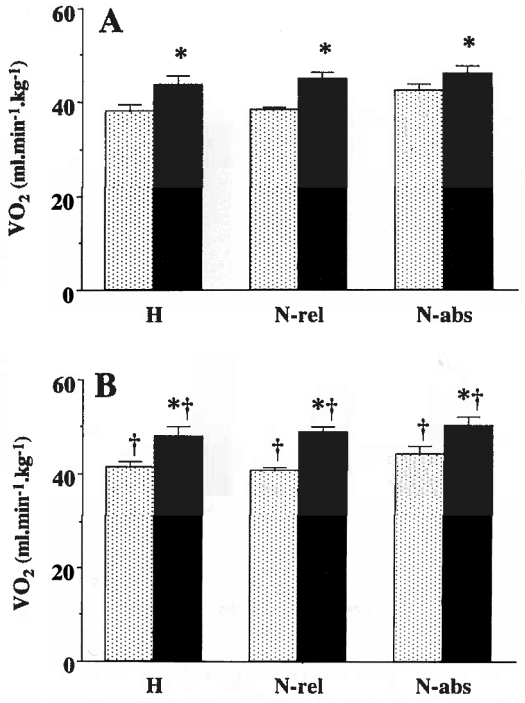


FIG. 2. Influence of training on maximal oxygen uptake ($\dot{V}O_2$) measured in hypoxia (*A*) and in normoxia (*B*) in the 3 groups of subjects trained with different protocols. Stippled bars, before training; solid bars, after training. Values are means ± SE. * Significantly different from pretraining ($P < 0.05$). † Significantly different from hypoxia ($P < 0.05$).

## DISCUSSION

Since the late 1960s, several investigations have been devoted to analyzing the beneficial effects of training at altitude, but there is no clear evidence as to whether training at a reduced $PI_{O_2}$ has an additional effect to training at sea level (1, 2, 4, 6, 8, 14, 16, 17, 22, 25). In some of these studies, it appears that the subjects were only exposed to altitude during the exercising sessions (2, 6, 16, 22, 25), whereas in others (1, 4, 8, 14, 17), the subjects were exposed continuously to hypoxia but for a relatively short period of time (from 2 to 4 wk), insufficient for altitude acclimatization (3, 30).

To our knowledge, the present study is the first that examined the influence of training on altitude natives, i.e., in fully altitude-acclimatized subjects. By using such subjects, we suspected that the anorexia encountered during chronic exposure to hypoxia even in comfortable conditions (21) must be alleviated. Even though we did not check the energy intake in our altitude natives, it has been shown that the body mass index [weight (kg)/height ($m^2$)] can be considered as a relatively good measure of nutritional status (10). From the data reported in Table 1, it appears that our subjects are within the normal range of anthropometric

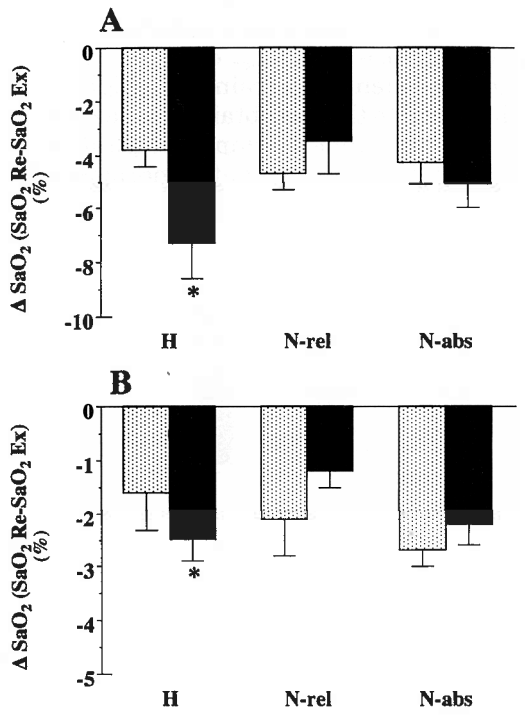


FIG. 3. Training-induced effects on arterial saturation changes ($\Delta Sa_{O_2}$) from rest ($Sa_{O_2}$ Re) to maximal exercise ($Sa_{O_2}$ Ex) in hypoxia (*A*) and normoxia (*B*) in the 3 groups. Stippled bars, before training; solid bars, after training. Values are means ± SE. * Significantly different from other groups in same $O_2$ environment ($P < 0.05$).

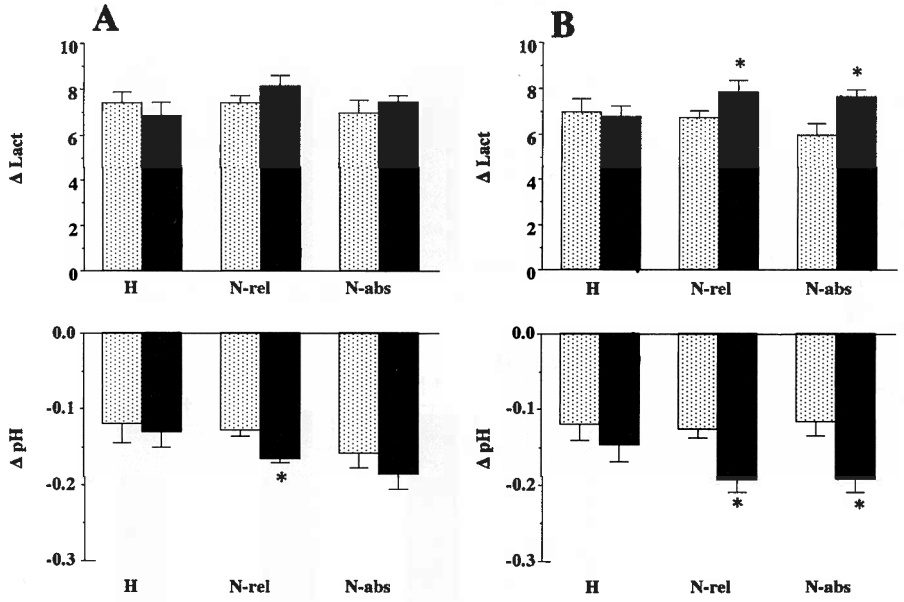


FIG. 4. Exercise-induced changes in blood lactate (ΔLact) and pH (ΔpH) before (stippled bars) and after training (solid bars) while exercising in hypoxia (*A*) and normoxia (*B*). * Significantly different from before training in same $O_2$ environment ($P < 0.05$).

standards (10), and their hematologic status [hematocrit (Hct) and hemoglobin (Hb)] is within the standard range of values reported for natives residing at 3,500–3,700 m (3, 28).

In chronic hypoxia before training, $\dot{V}O_{2\,max}$ averaged 39.7 ± 0.8 ml·min$^{-1}$·kg$^{-1}$ (range 31.9–49.7 ml·min$^{-1}$·kg$^{-1}$), i.e., a value previously reported for sedentary young Andean natives (18). The training protocol used in this study, in which subjects worked at a HR >80% of his own maximum for two-thirds of the training session (H group; Fig. 1), proved to be very effective. Indeed, a total of 15 h of exercise during 6 wk resulted in a mean increase in $\dot{V}O_{2\,max}$ of ~15% (Table 2). The $\dot{V}O_{2\,max}$ improvement with training in high-altitude natives is identical to the one obtained in sea-level natives (~14%) with the same training program in terms of intensity and duration (12) but in normoxia. It has to be mentioned, however, that in this previous study (12) the initial (pretraining) aerobic capacity ($\dot{V}O_{2\,max}$) of the subjects was significantly higher than the values measured in our sedentary subjects. One could thus expect that training in sedentary highland natives would result in a greater improvement in $\dot{V}O_{2\,max}$, which is obviously not the case. The fact that our altitude natives, when trained with the same protocol as sea-level natives (12), improved their $\dot{V}O_{2\,max}$ to the same extent suggests that training during chronic exposure to hypoxia does not provide an additional effect over training in normoxia. This conclusion is supported by some but not all the investigations obtained in sea-level natives acclimatized to altitude simultaneously to the training program (1, 2, 4, 6, 8, 14, 16, 17, 22, 25). Among this abundant but not exhaustive literature, it must be recognized that in five (2, 6, 16, 22, 25) of the six studies

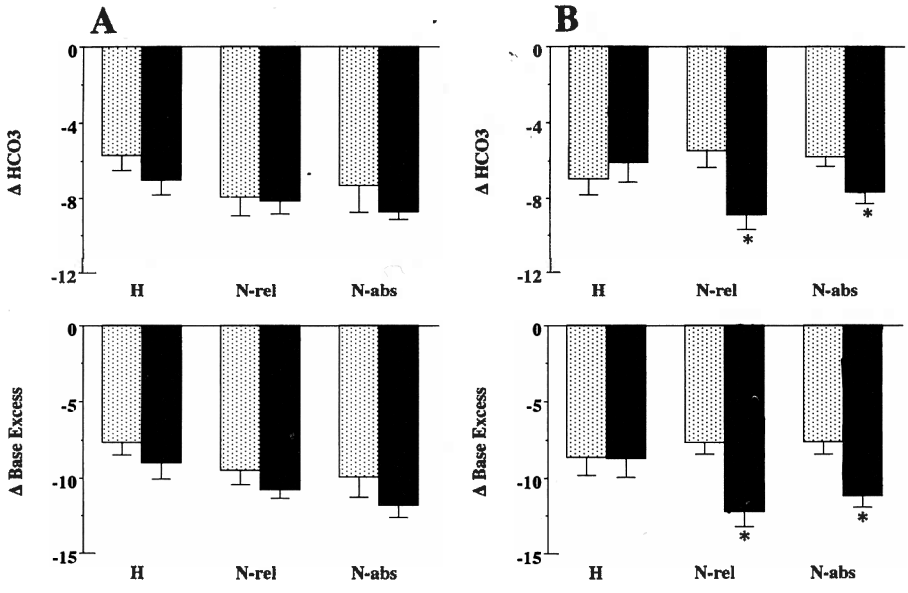


FIG. 5. Exercise-induced changes in bicarbonate ($\Delta HCO_3^-$) and base excess before (stippled bars) and after training (solid bars) while exercising in hypoxia (*A*) and normoxia (*B*). * Significantly different from before training in same $O_2$ environment ($P < 0.05$).

reporting an increased performance after training at altitude the subjects were living at low altitude but exercised at altitude or hypoxia. It seems, therefore, that hypoxia could have a cumulative effect with training only when hypoxia is restricted to the period of daily exercising sessions. Although it is not specifically reported in these previous studies, we can assume that no increase in Hb and/or Hct was observed in the subjects exposed intermittently to hypoxia, whereas our subjects displayed high Hb and Hct (Table 1). This would suggest that an increased Hb concentration provided by altitude acclimatization does not help for increasing $\dot{V}O_{2\,max}$ with training. In support of this assumption, Schaffartzik et al. (23) have recently shown that reducing Hb concentration after acclimatization to 3,800 m altitude does not reduce $\dot{V}O_{2\,max}$ when measured in hypoxia ($FI_{O_2} = 0.12$).

One of the reasons evoked to explain the inability of chronic hypoxia to act synergistically with training was that training intensity (i.e., in terms of absolute workload) is reduced at altitude compared with that at sea level in relation to the lower aerobic capacity in hypoxia. It can be thus hypothesized that, if subjects are chronically exposed to hypoxia but exercise in an $O_2$-enriched environment, they should be able to train at a similar workload than at sea level, and this strategy has been claimed to improve performance at sea level (16). Indeed, we found that acute exposure to normoxia increased $W_{max}$ by ~12% and $\dot{V}O_{2\,max}$ by ~6% (Tables 2 and 3).

Nevertheless, the present results show that, despite a mean increased workload of ~7% during the exercising sessions, the $N_{rel}$ group displayed a training-induced increase in $\dot{V}O_{2\,max}$ in hypoxia (~17%) and in normoxia (~20%) not significantly different from those obtained in the H group (15 and 16% for hypoxia and normoxia, respectively; Fig. 2). This inability of better improvement in $\dot{V}O_{2\,max}$ with training in normoxia is intriguing because it can be calculated that the $O_2$ flow to the exercising muscles is increased by normoxia. Indeed, arterial $O_2$ concentration ($Ca_{O_2}$; ml/l) can be deduced from Hb and $Sa_{O_2}$ as $Ca_{O_2} = 1.34 \times Hb \times Sa_{O_2}$, where 1.34 is the physiological $O_2$ binding coefficient of Hb. Therefore, in hypoxia, $Ca_{O_2}$ can be approximated to 21.7 ml $O_2$/l and in normoxia to 23.7 ml $O_2$/l. Considering that maximal cardiac output of high-altitude natives is not modified by acute exposure to normoxia (29), it can be inferred that $O_2$ flow is increased by ~9% by inhalation of the normoxic gas mixture but remained ineffective for improving $\dot{V}O_{2\,max}$ to a greater extent. It might be that the increase in absolute workload during the training sessions provided by normoxia was not sufficient to ensure a better improvement in aerobic capacity. That work intensity changes need to be of sufficient amplitude is supported by the data obtained in the $N_{abs}$-trained group for which work intensity was reduced compared with the $N_{rel}$ group during the training sessions but resulted in a similar increase in $\dot{V}O_{2\,max}$ that averaged ~9 and ~13% in hypoxia and normoxia, respectively (Tables 2 and 3, Fig. 2). Whether increasing the $O_2$ fraction of the inspired air during training into the hyperoxic range ($FI_{O_2}$ 0.5–1.0) would have permitted more of an increase in the sustainable work intensity during training and thus better improvement in $\dot{V}O_{2\,max}$ remains to be tested, but, if one assumes that the switch from normoxia to hyperoxia can increase $\dot{V}O_{2\,max}$ by 5–10% (31), it would have been possible, by inhaling a hyperoxic gas mixture, to increase further the workload during the training sessions and thus to increase $\dot{V}O_{2\,max}$ to a greater extent. Nevertheless, the present data suggest that changes in $W_{max}$ during training must be large (>10%) to result in significant training-induced changes in $\dot{V}O_{2\,max}$.

There are reports demonstrating a drop in $Sa_{O_2}$ and arterial $P_{O_2}$ during maximal exercise at sea level (5, 15, 19, 26, 27). So far, this has been observed only in highly trained subjects (5, 15, 19, 26) or at least for a $\dot{V}O_2 > 3.0$ l/min (27). This arterial desaturation during intense exercise has been attributed to inadequate hyperventilation (15, 19, 25) and/or to diffusion limitation (25, 27). One wonders if endurance training could result in greater arterial desaturation whether exercising in hypoxia or normoxia. In the present study, we found that, after training in normoxia, $Sa_{O_2}$ is maintained compared with pretraining whether the subjects exercised in hypoxia or normoxia (Fig. 3). In contrast, in the H group, we found a greater $Sa_{O_2}$ drop during maximal exercise whether normoxic or hypoxic. The reasons for such a difference between training in hypoxia and training in normoxia are not readily apparent but could be related to a relatively reduced ventilatory response in the H group after training (Tables 2 and 3).

It is well known that lactate metabolism is affected both by hypoxia (20) and by training (7), but little is known about the influence of training in hypoxia compared with training in normoxia (1). The present results show that before training blood lactate concentration at maximal exercise in high-altitude natives is in a similar range (7–9 mM; Tables 2 and 3) than that observed in lowlanders exposed to prolonged (24) hypoxia. In response to training, blood lactate measured at exhaustion was similar in all groups whether trained in hypoxia or in normoxia (Tables 2 and 3). During the last 20 yr, the concept of an anaerobic threshold has been developed and is thought to be a sensitive indicator of training efficacy and performance, regardless of the method for anaerobic threshold detection (for a review see Ref. 11). In the present study, we found that the absolute $W_{4\,mM}$ was significantly increased both by training and by normoxia (Tables 2 and 3). Nevertheless, on a relative basis, the $W_{4\,mM}$ (%$W_{max}$) measured in hypoxia was unchanged whatever the training program (hypoxia vs. normoxia or low work intensity vs. high work intensity). These data suggest that $W_{4\,mM}$ cannot be used as a reliable index of training efficacy in subjects chronically exposed to and tested in hypoxia.

Recently, it has been suggested that training at altitude could affect the acid-base status and buffer capacity (17). Before training, inhalation of a normoxic gas mixture was found to have a minimal effect on acid-base status during maximal exercise (Figs. 4 and 5). After training, we found that arterial pH measured at exhaustion was lower in the $N_{rel}$ and $N_{abs}$ groups when tested in normoxia and in the $N_{rel}$ group when tested

in hypoxia (Fig. 4). This greater drop in pH could be linked to the cumulative effect of a significant increase in lactate accumulation and a reduced buffer capacity (lower $[HCO_3^-]$; Fig. 5). This altered buffer capacity of normoxia-trained individuals is further evidenced by a greater drop in [BE] (Fig. 5). It is noteworthy to mention that, in contrast to the results obtained in normoxia-trained subjects, the H group was better able to maintain plasma pH (Fig. 4), suggesting a maintained buffer capacity. Indeed, this group displayed a lower reduction in [BE] and a well-maintained $[HCO_3^-]$ (Fig. 5). All of these adaptations remain to be explored in future studies, but they suggest that training in hypoxia in high-altitude natives, although not providing any advantage in aerobic capacity (similar changes in $\dot{V}O_{2\,max}$), could be beneficial for anaerobic metabolism (maintained buffer capacity) compared with those in normoxia-trained individuals.

From the present study, it can be concluded that endurance training in high-altitude natives results in an improvement of maximal aerobic capacity similar to that observed in sea-level natives, suggesting that, for aerobic metabolism, training in hypoxia does not confer any advantage over training in normoxia even when altitude acclimatization is well established. Nevertheless, it seems that training in hypoxia could be beneficial for anaerobic metabolism by maintaining buffer capacity. Increasing $O_2$ availability during training sessions in high-altitude natives does not provide a better training-induced improvement in $\dot{V}O_{2\,max}$. In addition, small, although significant, changes in absolute work intensity during the exercising sessions do not significantly modify the training-induced increase in $\dot{V}O_{2\,max}$. Last, endurance training during chronic exposure to hypoxia results in an enhanced arterial $O_2$ desaturation not only during exercise in hypoxia but also in normoxia, a condition that could be unfavorable for performance at sea level.

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## REFERENCES

1. **Adams, W. C., E. M. Bernauer, D. B. Dill, and J. B. Bomar, Jr.** Effects of equivalent sea-level and altitude training on $\dot{V}O_{2\,max}$ and running performance. *J. Appl. Physiol.* 39: 262–266, 1975.
2. **Banister, E. W., and W. Woo.** Effects of simulated altitude training on aerobic and anaerobic power. *Eur. J. Appl. Physiol. Occup. Physiol.* 38: 55–69, 1978.
3. **Bouverot, P.** Circulatory adaptations. In: *Adaptation to Altitude Hypoxia in Vertebrates,* edited by D. S. Farner. Berlin: Springer-Verlag, 1985, chapt. 4, p. 61–93.
4. **Buskirk, E. R., J. Kollias, R. F. Ackers, E. K. Prokop, and E. P. Reategui.** Maximal performance at altitude and on return from altitude in conditioned runners. *J. Appl. Physiol.* 23: 259–266, 1967.
5. **Dempsey, J. A., P. G. Hanson, and K. S. Henderson.** Exercise-induced arterial hypoxaemia in healthy human subjects at sea level. *J. Physiol Lond.* 355: 161–175, 1984.
6. **Desplanches, D., H. Hoppeler, M. T. Linossier, C. Denis, H. Claassen, D. Dormois, J. R. Lacour, and A. Geyssant.** Effects of training in normoxia and normobaric hypoxia on human muscle ultrastructure. *Pfluegers Arch.* 425: 263–267, 1993.
7. **Donovan, C., and G. A. Brooks.** Endurance training affects lactate clearance, not lactate production. *Am. J. Physiol.* 244 (*Endocrinol. Metab.* 7): E83–E92, 1983.
8. **Faulkner, J. A., J. T. Daniels, and B. Balke.** Effects of training at moderate altitude on physical performance capacity. *J. Appl. Physiol.* 23: 85–89, 1967.
9. **Favier, R., H. Spielvogel, D. Desplanches, G. Ferretti, B. Kayser, and H. Hoppeler.** Maximal exercise performance in chronic hypoxia and acute normoxia in high-altitude natives. *J. Appl. Physiol.* 78: 1867–1874, 1995.
10. **Frisancho, A. R.** *Anthropometric Standards for the Assessment of Growth and Nutrition Status.* Ann Arbor: Univ. of Michigan Press, 1990.
11. **Heck, H., A. Mader, G. Hess, S. Mücke, R. Müller, and W. Hollmann.** Justification of the 4 mM lactate threshold. *Int. J. Sports Med.* 6: 117–130, 1985.
12. **Hoppeler, H., H. Howald, K. Conley, S. L. Lindstedt, H. Claassen, P. Vock, and E. W. Weibel.** Endurance training in humans: aerobic capacity and structure of skeletal muscle. *J. Appl. Physiol.* 59: 320–327, 1985.
13. **Horstman, D., D. Weiskopf, and R. E. Jackson.** Work capacity during 3-wk sojourn at 4,300 m: effects of relative polycythemia. *J. Appl. Physiol.* 49: 311–318, 1980.
14. **Kollias, J., E. R. Buskirk, R. F. Ackers, E. K. Prokop, P. T. Baker, and E. Picon-Reategui.** Work capacity of long-time residents and newcomers to altitude. *J. Appl. Physiol.* 24: 792–799, 1968.
15. **Lawler, J., S. K. Powers, and D. Thompson.** Linear relationship between $\dot{V}O_{2\,max}$ and $\dot{V}O_{2\,max}$ decrement during exposure to acute hypoxia. *J. Appl. Physiol.* 64: 1486–1492, 1988.
16. **Levine, B. D., R. C. Roach, and C. S. Houston.** Work and training at altitude In: *Hypoxia and Mountain Medicine,* edited by J. R. Sutton, G. Coates, and C. S. Houston. Burlington, VT: Queen City Printers, 1992, p. 192–201.
17. **Mizuno, M., C. Juel, T. Bro-Rasmussen, E. Mygind, B. Schibye, B. Rasmussen, and B. Saltin.** Limb skeletal muscle adaptation in athletes after training at altitude. *J. Appl. Physiol.* 68: 496–502, 1990.
18. **Paz-Zamora, M., J. Coudert, J. Ergueta, E. Vargas, and N. Gutierrez.** Respiratory and cardiocirculatory responses of acclimatization of high altitude natives (La Paz, 3500 m) to tropical lowland (Santa Cruz, 420 m). In: *Topics in Environmental Physiology and Medicine. High Altitude Physiology and Medicine,* edited by W. Brendel and R. A. Zink. New York: Springer-Verlag, 1982, chapt. 4, p. 21–27.
19. **Powers, S. K., D. Martin, M. Cicale, N. Collop, D. Huang, and D. Criswell.** Exercise-induced hypoxemia in athletes: role of inadequate hyperventilation. *Eur. J. Appl. Physiol. Occup. Physiol.* 65: 37–42, 1992.
20. **Reeves, J. T., E. E. Wolfel, H. J. Green, R. S. Mazzeo, A. J. Young, J. R. Sutton, and G. A. Brooks.** Oxygen transport during exercise at altitude and the lactate paradox: lessons from operations Everest II and Pikes Peak. *Exercise Sports Sci. Rev.* 20: 275–296, 1992.
21. **Rose, M. S., C. S. Houston, C. S. Fulco, G. Coates, J. R. Sutton, and A. Cymerman.** Operation Everest II: nutrition and body composition. *J. Appl. Physiol.* 65: 2545–2551, 1988.
22. **Roskamm, H., F. Landry, L. Samek, M. Schlager, H. Weideman, and H. Reindell.** Effects of a standardized ergometer training program at three different altitudes. *J. Appl. Physiol.* 27: 840–847, 1969.
23. **Schaffartzik, W., E. D. Barton, D. C. Poole, K. Tsukimoto,**

**M. C. Hogan, D. E. Bebout, and P. D. Wagner.** Effect of reduced hemoglobin concentration on leg oxygen uptake during maximal exercise in humans. *J. Appl. Physiol.* 75: 491–498, 1993.

24. **Sutton, J. R., J. T. Reeves, P. D. Wagner, B. M. Groves, A. Cymerman, M. K. Malcomian, P. B. Rock, P. M. Young, S. D. Walter, and C. S. Houston.** Operation Everest II: oxygen transport during exercise at extreme simulated altitude. *J. Appl. Physiol.* 64: 1309–1321, 1988.
25. **Terrados, N., J. Melichna, C. Sylven, E. Jansson, and L. Kaijser.** Effects of training at simulated altitude on performance and muscle metabolic capacity in competitive road cyclists. *Eur. J. Appl. Physiol. Occup. Physiol.* 57: 203–209, 1988.
26. **Terrados, N., M. Mizuno, and H. Andersen.** Reduction in maximal oxygen uptake at low altitude: role of training status and lung function. *Clin. Physiol. Oxf.* 5, *Suppl.* 3: 75–79, 1985.
27. **Torre-Bueno, J. R., P. D. Wagner, H. A. Saltzman, G. E. Gale, and R. E. Moon.** Diffusion limitation in normal humans during exercise at sea level and simulated altitude. *J. Appl. Physiol.* 58: 989–995, 1985.
28. **Tufts, D., J. D. Haas, J. L. Beard, and H. Spielvogel.** Distribution of hemoglobin and functional consequences of anemia in adult males at high altitude. *Am. J. Clin. Nutr.* 42: 1–11, 1985.
29. **Vogel, J. A., L. H. Hartley, and J. C. Cruz.** Cardiac output during exercise in altitude natives at sea level and high altitude. *J. Appl. Physiol.* 36: 173–176, 1974.
30. **Ward, M. P., J. S. Milledge, and J. B. West.** *High Altitude Medicine and Physiology.* Cambridge, UK: Cambridge Univ. Press, 1989.
31. **Welch, H. G.** Effects of hypoxia and hyperoxia on human performance. *Exercise Sports Sci. Rev.* 15: 191–221, 1987.