Blood volume and hemoglobin mass in endurance athletes from moderate altitude

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ABSTRACT

SCHMIDT, W., K. HEINICKE, J. ROJAS, J. M. GOMEZ, M. SERRATO, M. MORA, B. WOLFARTH, A. SCHMID, and J. KEUL. Blood volume and hemoglobin mass in endurance athletes from moderate altitude. *Med. Sci. Sports Exerc.*, Vol. 34, No. 12, pp. 1934–1940, 2002. **Purpose:** To determine whether total hemoglobin (tHb) mass and total blood volume (BV) are influenced by training, by chronic altitude exposure, and possibly by the combination of both conditions. **Methods:** Four groups ($N = 12$, each) either from locations at sea level or at moderate altitude (2600 m) were investigated: 1) sea-level control group (UT-0 m), 2) altitude control group (UT-2600 m), 3) professional cyclists from sea level (C-0 m), and 4) professional cyclists from altitude (C-2600 m). All subjects from altitude were born at about 2600 m and lived all their lives (except during competitions at lower levels) at this altitude. tHb and BV were determined by the CO-rebreathing method. **Results:** $\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) was significantly higher in UT-0 m (45.3 ± 3.2) than in UT-2600 m (39.6 ± 4.0) but did not differ between C-0 m (68.2 ± 2.7) and C-2600 m (69.9 ± 4.4). tHb ($g \cdot kg^{-1}$) was affected by training (UT-0 m: 11.0 ± 1.1, C-0 m: 15.4 ± 1.3) and by altitude (UT-2600 m: 13.4 ± 0.9) and showed both effects in C-2600 m (17.1 ± 1.4). Because red cell volume showed a behavior similar to tHb and because plasma volume was not affected by altitude but by training, BV ($mL \cdot kg^{-1}$) was increased in C-0 m (UT-0 m: 78.3 ± 7.9; C-0 m: 107.0 ± 6.2) and in UT-2600 m (88.2 ± 4.8), showing highest values in the C-2600 m group (116.5 ± 11.4). **Conclusion:** In endurance athletes who are native to moderate altitude, tHb and BV were synergistically influenced by training and by altitude exposure, which is probably one important reason for their high performance. **Key Words:** MAXIMUM OXYGEN UPTAKE, ERYTHROPOIETIN, TRANSFERRIN RECEPTOR, ALTITUDE TRAINING, ALTITUDE RESIDENTS

It is a well-known fact that athletes born and living at moderate altitude, as e.g. Kenyan runners, Colombian cyclists, or Mexican walkers, are very successful in endurance competitions. As yet, only few structural and functional differences have been found between athletes living at altitude and those at sea level. In the muscle tissue of Kenyan runners, Saltin et al. (25) detected higher 3-hydroxyacyl-CoA-dehydrogenase (HAD) activity than in European athletes. They furthermore characterized the Kenyan athletes by individually very high $\dot{V}O_{2max}$ values and by generally higher running efficiency, a lower blood lactate concentration, and by extremely low ammonia accumulation during exercise (26). All these differences do not, however, satisfactorily account for the physiological mechanisms responsible for the extraordinary endurance performance of these athletes.

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Endurance performance, normally characterized as $\dot{V}O_{2max}$, is affected by several anatomic and physiological factors. According to Fick's law, $\dot{V}O_{2max}$ depends on cardiac output and the arteriovenous oxygen difference ($avDO_2$). This implicates that all factors influencing these physiological quantities may exert endurance limiting effects. The most important related to blood supply seem to be total blood volume (BV), which may limit venous return and thus stroke volume, and hemoglobin concentration, which determines the O_2-transport capacity and therefore the $avDO_2$. In a recently published paper, we recorded total hemoglobin mass and blood volumes approximately 35% higher in endurance athletes of different disciplines than in untrained subjects, whereas the hemoglobin concentration of both groups did not differ (19).

In residents of different altitudes, the threshold for increasing hemoglobin mass, also resulting in higher hemoglobin concentration, was described as at an inspiratory PO_2 of about 70 mm Hg, i.e., between altitudes of 1600 and 3100 m (33). At higher altitude, the erythropoietic rate is considerably increased, leading to 80% higher red cell mass above 4300 m (27).

The success of the above-mentioned altitude athletes suggests that hypoxia specific effects may be responsible for their high endurance performance. The question arises as to whether the moderate altitude of these athletes' homes may suffice to increase hemoglobin mass. If this is

TABLE 1. Anthropometric data of the test subjects and performance characteristics obtained from the vita-maxima test.

Group	N	Age (yr)	Height (cm)	Mass (kg)	BMI	P_aO_2 (mm Hg)	SO_2 (%)	$\dot{V}O_{2,max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	Lac_{max} ($mmol \cdot L^{-1}$)	HR_{max} ($beat \cdot min^{-1}$)
UT-0 m	12	28.0 ± 5.1	183 ± 5.2	82.6 ± 8.3	24.6 ± 2.6			45.3 ± 3.2	11.2 ± 2.0	188 ± 8
UT-2600 m	12	24.6 ± 6.2	170 ± 4	66.9 ± 6.8	23.1 ± 2.3	61.9 ± 2.3	92.0 ± 0.9	39.6 ± 4.0	8.4 ± 2.4	183+ ± 4
C-0 m	12	27.3 ± 3.5	181 ± 5	71.8 ± 4.5	22.0 ± 1.4			68.2 ± 2.7	9.0 ± 2.1	194 ± 8
C-2600 m	12	28.8 ± 3.5	170 ± 6	61.0 ± 6.7	21.1 ± 1.5	63.3 ± 3.5	92.4 ± 1.2	69.9 ± 4.4	9.8 ± 2.0	183 ± 10

Presented are means and standard deviations; UT, untrained subjects; C, cyclists; Lac_{max}, maximum lactic acid concentration after exercise; HR_{max}, maximum heart rate during exercise; P_aO_2, arterial partial pressure of oxygen; SO_2, hemoglobin oxygen saturation in arterial blood.
+ indicates altitude affects ($P < 0.05$).

also evident in normal untrained subjects, the already acknowledged endurance-specific adaptation in red cell mass and blood volume may lead to synergistic effects in altitude athletes, thus improving their oxygen transport facilities and resulting in marked advantages in all endurance disciplines.

The aim of the present study was, therefore, to determine the total hemoglobin mass and blood volume in sedentary subjects and in elite endurance athletes native to sea level and to moderate altitude (2600 m). We expected to find elevated values in altitude residents and in sea-level athletes. We furthermore hypothesized that the combination of the effects of altitude and of training would influence hemoglobin synthesis and perhaps also blood volume expansion in altitude athletes.

MATERIALS AND METHODS

Test subjects. In total, 48 male subjects were included in the study after written informed consent. All experiments were performed with the permission of local ethical committees, and the subjects were allowed to withdraw at any point without any restrictions. The participants were highly trained cyclists and untrained control subjects either from altitude (2600 m) or from sea level. For the anthropometric and performance data see Table 1.

All altitude subjects were born at 2600 m (at the Altiplano around Bogota, Colombia) and had spent all their lives at this altitude with only minor interruptions of less than 6 months. Within the past 3 months, five of the cyclists spent 13 d at different lower altitudes (participation in a competition in Chile); one was in Europe for 10 wk, and another spent 6 d at sea level in Colombia. No differences in blood volume or other hematological data were found between the subgroups remaining at altitude continuously or intermittently. The cyclists (C-2600 m, $N = 12$) all had international competing experience, and most of them were members of the Colombian national team. Twelve untrained students from the National University of Bogota, who did not regularly practice sports, served as a control group (UT-2600 m). The cyclists from sea level (C-0 m, $N = 12$) were all members of an internationally competing German professional team and their corresponding control subjects (UT-0 m, $N = 12$) were recruited from the University of Bayreuth, Germany. At the time the tests were carried out, all cyclists had finished their yearly preparation period, which was similar for the athletes of both groups regarding training volume and intensity. Before the measurements were carried out, all subjects had to abstain from exhausting physical activity for at least 2 d.

Test protocol. The altitude subjects were tested and monitored at the laboratories of the Centro Nacional de Servicios Biomedicos, which is situated at an altitude of 2600 m in the city of Bogota, Colombia. The experiments performed with the sea-level groups took place at two different medical centers in Germany. To avoid methodological errors when comparing the results from these three laboratories, identical medical equipment was used for the blood volume measurements, and all experiments were supervised by the same physician.

To determine $\dot{V}O_{2max}$, maximum blood lactate concentration, and maximum heart rate, all subjects performed a vita-maxima test by using a cycle ergometer (in Germany: Excalibur, Lode, Groningen, The Netherlands; in Colombia: Er 900, Jäger, Germany). Preceded by a 5-min warm-up period at 100 W, the workload was increased by steps of 50 W every 3 min until subjective exhaustion.

During the exercise tests at sea level, oxygen consumption was continuously determined by a portable spirometry-system (MetaMax, Cortex, Leipzig, Germany); at altitude a Quinton spirometer (Qmc, Bothell, WA) was used. Comparison of both spirometers on the same subject yielded identical oxygen consumption rates. Heart rate was continuously registered by a Polar monitoring system (Polar Vantage NV, Polar Electro Oy, Kempele, Finland). Lactic acid concentration was measured before and at 3-min intervals during and twice after the test in 20-μL blood obtained from a hyperemized ear lobe (ESAT 6661, Eppendorf, Hamburg, Germany). The acid base status was determined before and at the end of exercise in 80-μL arterialized blood by using the blood gas analyzing system ABL 520 (Radiometer, Copenhagen, Denmark).

Determination of hemoglobin mass and total blood volume. At least 1 h after the vita-maxima tests, when plasma volumes had returned to their preexercise values (28), total hemoglobin mass (tHb), total blood volume (BV), as well as plasma (PV) and erythrocyte (RCV) volumes were determined by the CO-rebreathing method according to Burge and Skinner (6) with minor modifications. At sea level, 50 mL of CO were added when body weight was lower than 75 kg, and 60 mL CO when body weight was higher than 75 kg. At altitude, the added CO volume was calculated by multiplying the body weight by the factor 1.3 (cyclists) or 1.2 (untrained subjects). For all tests at sea level and at altitude, identical equipment was used. For a detailed description and accuracy of the methods see (19).

TABLE 2. Hb-concentration, Hb-mass, and blood volumes.

Group	N	[Hb] (g·dL^{-1})	Hct (%)	tHb (g)	RCV (mL)	BV (mL)	PV (mL)
UT-0 m	12	15.3 ± 0.8	45.8 ± 2.0	913 ± 133	2690 ± 371	6448 ± 741	3758 ± 404
UT-2600 m	12	16.3^{+} ± 0.7	48.5^{++} ± 1.7	896 ± 109	2657 ± 290	5892 ± 585	3235 ± 324
C-0 m	12	15.8 ± 0.7	47.4 ± 1.9	1109 ± 133	3324 ± 390	7685 ± 661	4361 ± 309
C-2600 m	12	15.8 ± 0.7	47.8 ± 1.5	1038 ± 122	3141 ± 356	7076 ± 785	3934 ± 456

Presented are means and standard deviations; UT, untrained subjects; C, cyclists; [Hb], hemoglobin concentration; tHb, total hemoglobin mass; RCV, red cell volume; BV, total blood volume; PV, plasma volume. Because of different body size differences in blood volumes are not indicated.
In the case of [Hb] and Hct + indicates altitude affects.
+ , $P < 0.05$, ++ $P < 0.01$.

Erythrocyte volume (RCV), blood volume (BV), and plasma volume (PV) were calculated as follows (formula 1–3):

1) RCV = tHb/MCHC·100
2) BV = RCV·100/Hct·F
3) PV = BV − RCV

where MCHC = mean corpuscular hemoglobin concentration, Hct = hematocrit, F = cell factor (0.91 at sea level (9); 0.93 at altitude calculated from (27)).

Other measurements. In cubital venous blood samples taken after 15 min in a sitting position before the CO-rebreathing period, we immediately determined the hemoglobin concentration ([Hb]) by the ABL 520 (Radiometer, Copenhagen, Denmark) and the hematocrit value (Hct) by microhematocrit centrifugation at 20,900 U·min^{-1}. The rest of the blood samples were centrifuged, and the plasma was frozen at −20°C. For the hormonal measurements and for the determination of the iron status, the samples were flown on dry ice to our laboratories in Germany.

The plasma erythropoietin (EPO) concentration was measured by a chemiluminescence immunoassay (Nichols Institute, San Juan Capistrano, CA) using a mouse monoclonal and a sheep polyclonal antibody. The intra-assay coefficient of variation (CV) at physiological concentrations was 3.4%, the interassay CV 6.5%. The sensitivity was 1.2 mU·mL^{-1}.

The determination of the plasma concentration of the soluble transferrin receptor (TFR) was based on a sandwich enzyme immunoassay using two different monoclonal antibodies (R&D Systems, Minneapolis, MN). The CV of this test kit was 5.7% and 5.9%, respectively. The sensitivity was 0.5 nmol·L^{-1}.

The parameters of the iron status were determined by routinely used test kits: serum-iron concentration (SI) photometrically (Roche Diagnostics, Mannheim, Germany); ferritin concentration by a chemiluminescence immunoassay (Chiron Diagnostics Cooperation, East Walpole, MA); and transferrin concentration (TF) by a nephelometric method (Behring, Marburg, Germany).

Statistics. All data are presented as mean value ± SD. Statistical comparisons were performed by a one-way analysis of variance (ANOVA), and the unpaired *t*-test, including Bonferroni correction, was used to evaluate the significance of differences between single groups. Linear regression analysis was performed to prove any relationship between two variables.

RESULTS

The anthropometric and performance data of all groups are presented in Table 1. [Hb] and Hct in the untrained groups were significantly influenced by altitude showing higher values in UT-2600 m than in UT-0 m (Table 2). There were, however, no differences between the groups of athletes. The absolute values for tHb and the blood volumes are presented in Table 2. Because of different body sizes, statistical comparisons were not undertaken. For better comparison of the single groups, all values were calculated for kg body weight, and the data are presented in Figures 1 and 2.

tHb (UT-0: 11.0 ± 1.1 g·kg^{-1}) was clearly affected by altitude (UT-2600: 13.4 ± 0.9 g·kg^{-1}) and even more ($P < 0.01$) by training (C-0 m: 15.4 ± 0.9 g·kg^{-1}). In C-2600 m, the effects of both altitude and training were evident (17.1 ± 1.4 g·kg^{-1}, Fig. 1). As expected, red cell volume (RCV) was influenced similarly to tHb (Fig. 2), also showing significant altitude and training effects, which were combined in C-2600 m. PV was clearly influenced by training but not by altitude effects. In the trained groups, PV was 33% higher at sea level (UT-0 m: 45.7 ± 5.3 mL·kg^{-1}, C-0 m: 60.8 ± 3.0 mL·kg^{-1}), and similarly elevated at altitude (UT-2600 m: 48.1 ± 3.1 mL·kg^{-1}, C-2600 m: 64.9 ± 7.3 mL·kg^{-1}) when compared with their corresponding controls. As the sum of RCV and PV, blood volume (UT-0 m: 78.3 ± 7.9 mL·kg^{-1}) was affected ($P < 0.001$) more by training (Tr-0: 107.0 ± 6.2 mL·kg^{-1}) than by altitude (UT-

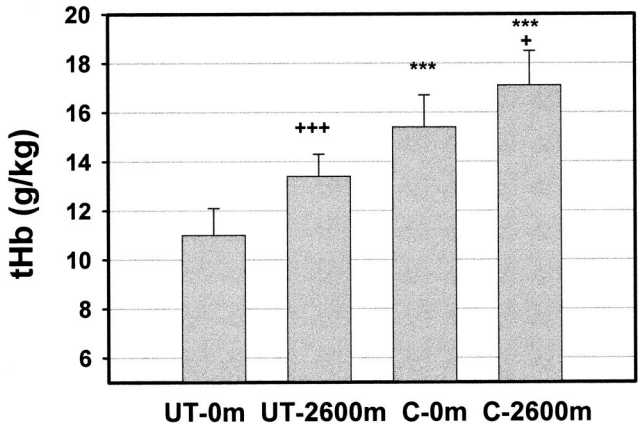

FIGURE 1—Total hemoglobin mass (tHb) calculated for kg body mass in highly trained cyclists from 2600 m and from sea level (0 m) and in their corresponding control groups. UT, untrained subjects; C, cyclists; + indicates altitude affects; * indicates training effects; +,* = $P < 0.05$, ++, = $P < 0.01$, +++,*** = $P < 0.001$.**

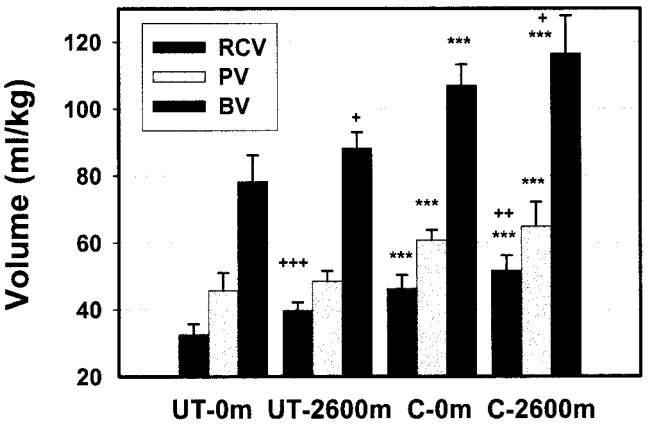

FIGURE 2—Red cell volume (RCV), plasma volume (PV) and total blood volume (BV) in trained and untrained subjects from different altitudes. For further information see Figure 1.

2600 m: 88.2 ± 4.8). In C-2600 m, again, altitude and training effects were apparent, leading to extraordinarily high blood volumes (116.5 ± 11.4 $mL \cdot kg^{-1}$, Fig. 2).

Erythropoietic activity did not seem to be systematically influenced by altitude nor by training: plasma EPO concentration was similar in all investigated groups and the TFR concentrations were only slightly increased in UT-2600 m compared with UT-0 m (Table 3). When TFR was, however, related to body mass ($[TFR] \cdot PV \cdot kg^{-1}$), there was a close correlation with tHb ($g \cdot kg^{-1}$) ($r = 0.701$, $P < 0.001$), and significant altitude and training effects became evident, which were also both present in C-2600 m (Table 3). Plasma iron and transferrin values were all within the normal range and were not influenced by effects of training nor of altitude. Solely in C-2600 m was the plasma ferritin concentration significantly different from the other groups due to very high values in some athletes.

To check whether the results related to body mass (kg) are influenced by the anthropometric differences between the Colombian and German groups we determined the body fat content and lean body mass in athletes and sedentary subjects from both countries (Table 4). As we found very similar relationships between body fat and BMI in the respective groups, any influence of body size on our results can be excluded.

DISCUSSION

Volumes in altitude residents. Chronic altitude has long been known to have an influence on red cell mass. Most previous studies were, however, carried out at relatively high altitudes in the South American Andes at 4390 and 4540 m, and reported red cell volumes elevated by more than 80% compared with those of subjects at sea level (27,20). The critical arterial oxygen tension at which red cell mass starts to increase is about 70 mm Hg (SO_2 approximately 95%), as can be calculated from data from Caucasian natives to 1600 and 3100 m (33). In our study, we first determined tHb in subjects between these altitudes. Because the arterial PO_2 (61.9 mm Hg in UT-2600 m) and SO_2 (92.0%) were lower than the threshold mentioned above, the increase in tHb by 22% in UT-2600 m compared with UT-0 m is easily explainable.

The augmented red cell mass in UT-2600 m could be due to increased erythropoietic activity. Despite higher Hct in UT-2600 m than in UT-0 m, [EPO] is not decreased as we have already previously reported for natives to 3600 m (31) but even tends to higher values. The TFR concentration, which in the case of no iron deficiency correlates with the EPO activity at the erythrocyte precursor cells (8), is also significantly elevated by about 35%, proving the EPO effect at moderate altitude.

At first glance, the unchanged plasma volume at altitude seems surprising, because acute hypoxia was described as lowering PV by fluid movements out of the vascular bed (16) and enhancing diuretic processes (23). In the few studies dealing with blood volumes under chronic hypoxia, however, PV did not differ in natives to 3100 m from those at sea level (33). And even at higher altitudes (4390 m), a moderate decrease in PV (−37%) did not completely compensate for an increase in RCV (+83% (27)), resulting in elevated BV. In the present study, PV was similar in both control groups, indicating that in completely adapted subjects a down-regulation in PV to improve the oxygen transport capacity does not occur. The present study further proves that living under chronic hypoxia is associated with increased total blood volume. The underlying changes in blood volume regulation might be in part due to lower central venous pressure, as was observed during altitude acclimatization (15).

Volumes in endurance trained subjects from sea level. In previous studies the levels of tHb and of blood volumes were mostly described as being considerably higher in trained athletes than in sedentary subjects. First, Kjellberg et al. (21) found a training dependent increase in tHb and in BV from 11.5 $g \cdot kg^{-1}$ and 75 $mL \cdot kg^{-1}$ in untrained subjects, to 13.6 $g \cdot kg^{-1}$ and 90.1 $mL \cdot kg^{-1}$ in athletes with low training intensity, and to 15.7 $g \cdot kg^{-1}$ and 103.4 $mL \cdot kg^{-1}$ in athletes with high training intensity. These high volumes were confirmed later by e.g. (10,12). In a recently published study (19), we found tHb values of about 15 $g \cdot kg^{-1}$ and BV values of 105 $mL \cdot kg^{-1}$ in athletes from different endurance disciplines, the range of which was similar to the results reported here for C-0 m. In contrast to UT-2600 m, the increase in BV by 37% is due to both a higher PV and a higher RCV, which proves the different effects of altitude and training adaptation: In endurance athletes, PV expansion related to training is followed by delayed elevated red cell production probably in order to normalize the lowered Hct value (see 7,30). Despite unchanged plasma EPO concentrations (29), the accelerated erythropoiesis after exercise has been proven by increased transferrin receptor expression on membranes of rat erythroblasts (24). We may confirm this higher erythropoietic activity by 47% higher values of TFR (referred to body mass) in C-0 m than in UT-0 m (Table 3).

Volumes in athletes from altitude. As mentioned above, the mechanisms leading to higher tHb and RCV

TABLE 3. Iron status and parameters of erythropoietic activity in plasma.

Group	N	EPO ($mU \cdot mL^{-1}$)	TFR ($nmol \cdot L^{-1}$)	TFR ($nmol \cdot kg^{-1}$)	Iron ($\mu g \cdot dL^{-1}$)	Ferritin ($ng \cdot mL^{-1}$)	Transferrin ($mg \cdot dL^{-1}$)
UT-0 m	12	9.9 ± 2.3	17.3 ± 3.4	0.77 ± 0.16	118 ± 44	115 ± 56	213 ± 44
UT-2600 m	12	11.1 ± 4.5	23.2 ± 3.6	1.12^{++} ± 0.15	97 ± 27	143 ± 85	225 ± 31
C-0 m	12	11.3 ± 3.2	18.5 ± 3.1	1.13^{***} ± 0.22	124 ± 43	132 ± 74	197 ± 20
C-2600 m	12	10.1 ± 4.2	21.4 ± 4.5	$1.38^{+,*}$ ± 0.29	105 ± 28	630 ± 510	219 ± 44

Presented are means and standard deviations; UT, untrained subjects; C, cyclists; EPO, erythropoietin; TFR, soluble transferrin receptor.
+ indicates altitude affects, *indicates training effects; +,* = $P < 0.05$; ++,** = $P < 0.01$; +++,*** = $P < 0.001$.

differ considerably in UT-2600 m and C-0 m. In altitude athletes (C-2600 m), both stimuli [1) direct hypoxia due to their stay at altitude and 2) compensation of the training induced increase in PV] exist and do not counterbalance each other, i.e., altitude and training exert additive effects leading to extremely high values for tHb and RCV, which are 55% higher than in UT-0 m. At first glance, the erythropoietic activity in this group is not mirrored by plasma EPO and TFR concentrations. Because plasma TFR, however, is not regulated by a feedback system but depends solely on erythropoietic activity and PV is not a constant quantity in the groups investigated here, the plasma TFR related to body weight ($mmol \cdot kg^{-1}$) is a more reliable variable than its corresponding plasma concentration ($mmol \cdot L^{-1}$). This value is significantly higher compared with C-0 m and UT-2600 m, thus also indicating special altitude and training effects on erythropoietic activity.

The effects of altitude training on the hematological system have so far only been determined in lowlanders exposed to altitude for a short period of time. Some of these studies described no increases (12), others showed moderate (about 1% increases per week (3)) or higher effects on tHb (22). In our study, the hemoglobin mass and blood volumes were first determined in elite endurance athletes born and living at moderate altitude (2600 m). The most important results are the synergistic effects of altitude and training on the total hemoglobin mass, which have produced the highest values ever observed for endurance athletes. In various studies, Ashenden et al. (1,2) reported no effects of simulated intermittent altitude on tHb in trained male and female athletes. As Böning et al. (5) found no differences in tHb in native female sea level and altitude (2600 m) residents, the lacking hypoxic stimulus in female athletes at this altitude (2) can be explained. Furthermore, according to (1) only changes in tHb exceeding about 7% may be detectable, i.e., the effects of relatively small increases after altitude training periods may not be obvious. Levine and Stray-Gundersen (22) found a 9% increase in red cell mass after 4 wk at 2500 m, a fact that fits well with the 11% higher tHb in C-2600 m compared with C-0 m of our study. However, because $\dot{V}O_{2max}$ and RCM were lower in their (22) subjects, we cannot judge whether the high values of our altitude athletes can be also reached in sea-level athletes after altitude training camps.

All of our subjects were born at altitude. Because the population around Bogota stems from aborigines, who possibly first started to live at that altitude 10,000 yr ago, and from lowlanders, who have been immigrating from Europe and Africa for 500 yr, effects on the red cell system due to genetic adaptation must be taken into consideration (4). It is, however, still not clear whether the high tHb values found in the athletic altitude group can be seen to represent the maximum effect of adaptation that sea-level athletes could also attain during very long periods of altitude training or whether a genetic predisposition is necessary for effective erythropoiesis.

As already discussed for UT-2600 m, in C-2600 m, PV is also not negatively affected by altitude, which thus leads to high BV (49% more than in UT-0 m). This volume expansion requires substantial changes in central venous volume regulation regarding central venous pressure and/or volume receptor sensitivity.

Iron status and possible doping effects. In all groups investigated, the mean values of ferritin, iron, and transferrin were within the normal range, excluding any iron-deprived state. The very high ferritin values in some of the professional cyclists, and especially in altitude athletes, may be due to oral iron substitution and also partly to intravenous iron application, which may lead to hazardous iron overloading (14). Another influence on plasma ferritin concentration, which has not so far been explained, may be a specific hypoxic effect. In a recent study, we found very high ferritin values in altitude residents from 3500 m and also in subjects intermittently exposed to the same altitude for more than 20 yr (18).

Although all athletes denied using any doping practices by EPO application or blood infusions, such an abuse can never be completely ruled out. The high ferritin values in some athletes, which is known to be sometimes associated with EPO abuse, may also be a hint in this direction. We

TABLE 4. Body mass index and fat content of athletes and sedentary subjects from 2600 m and from sea level.

Group	N	Age (yr)	Height (cm)	Mass (kg)	BMI	Body Fat (%)	$\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)
Controls (0 m)	14	28.1 ± 6.1	185 ± 6	80.8 ± 8.2	23.5 ± 2.5	14.0 ± 3.4	53.6 ± 8.4
Controls (2600 m)	13	22.7 ± 1.2	173 ± 5	66.9 ± 6.8	22.0 ± 1.4	9.3 ± 1.6	41.7 ± 1.7
Athletes (0 m)	15	20.4 ± 1.1	181 ± 3	69.8 ± 5.3	21.3 ± 1.2	7.9 ± 2.2	65.0 ± 3.8
Athletes (2600 m)	12	24.5 ± 6.0	169 ± 5	57.8 ± 4.7	20.3 ± 2.0	7.0 ± 0.7	55.2 ± 1.2

Presented are means and standard deviations of data obtained by a follow-up study. Body fat was determined by measuring six skinfolds (triceps, biceps, subscapular, abdominal, midtight, and medial calf) as described by (17).

therefore divided the altitude athletes into two subgroups ($N = 6$, each), one with low ferritin (195.4 ± 91.1 $ng \cdot mL^{-1}$) and the other with high plasma ferritin concentrations (1064.1 ± 405.5 $ng \cdot mL^{-1}$). No significant differences in tHb and blood volumes were found, but a tendency to higher values in the low-ferritin group (tHb: 17.4 ± 1.6 vs 16.7 ± 1.3 $g \cdot kg^{-1}$; BV: 122.2 ± 14.0 vs 110.9 ± 6.2 $mL \cdot kg^{-1}$; $\dot{V}O_{2max}$: 71.4 ± 5.9 vs 68.4 ± 2.3 $mL \cdot kg^{-1} \cdot min^{-1}$) suggests that the high ferritin value is not related to EPO abuse. Furthermore, blood doping seems to be unlikely in the altitude athletes, because they were characterized by a tendency to lower Hct than their controls. Even if some athletes from sea level, who tended to relatively high Hct values, used artificial EPO application, the claim of our study that volumes are higher in altitude athletes than in sea-level athletes would not be affected.

Practical importance of high tHb and BV. As shown in Table 1, $\dot{V}O_{2max}$ does not differ between both endurance groups at their respective altitudes, which thus indicates a complete compensation of the reduced inspiratory PO_2 in C-2600 m. According to (11), $\dot{V}O_{2max}$ considerably decreases when untrained subjects from sea level are acutely exposed to altitude (by 1% every 100 m above 1500 m). In endurance athletes, a fall in $\dot{V}O_{2max}$ was already demonstrated at altitudes lower than 1000 m, i.e., at 900 m (32) and at 580 m (13). Whether these relationships are also valid for altitude athletes competing at lower altitudes seems to be questionable. However, we may assume that $\dot{V}O_{2max}$ of C-2600 m, which is already high at altitude, further improves at sea level and leads to advantages during competitions at altitude and at sea level. The extent of this advantage has to be investigated and may provide further insights not only into the effects of a life-long altitude training but also into those of doping and genetic influences on endurance sports.

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