Chapter 24
Hemoglobin Mass and Aerobic Performance at Moderate Altitude in Elite Athletes

Jon Peter Wehrlin, Bernard Marti, and Jostein Hallén

Abstract Fore more than a decade, the live high–train low (LHTL) approach, developed by Levine and Stray-Gundersen, has been widely used by elite endurance athletes. Originally, it was pointed out, that by living at moderate altitude, athletes should benefit from an increased red cell volume (RCV) and hemoglobin mass (Hb_{mass}), while the training at low altitudes should prevent the disadvantage of reduced training intensity at moderate altitude. VO_{2max} is reduced linearly by about 6–8 % per 1000 m increasing altitude in elite athletes from sea level to 3000 m, with corresponding higher relative training intensities for the same absolute work load. With 2 weeks of acclimatization, this initial deficit can be reduced by about one half. It has been debated during the last years whether sea-level training or exposure to moderate altitude increases RCV and Hb_{mass} in elite endurance athletes. Studies which directly measured Hb_{mass} with the optimized CO-rebreathing technique demonstrated that Hb_{mass} in endurance athletes is not influenced by sea-level training. We documented that Hb_{mass} is not increased after 3 years of training in national team cross-country skiers. When athletes are exposed to moderate altitude, new studies support the argument that it is possible to increase Hb_{mass} temporarily by 5–6 %, provided that athletes spend >400 h at altitudes above 2300–2500 m. However, this effect size is smaller than the reported 10–14 % higher Hb_{mass} values of endurance athletes living permanently at 2600 m. It remains to be investigated whether endurance athletes reach these values with a series of LHTL camps.

Keywords Altitude training • Hypoxia • Red cell volume • VO_{2max}

J.P. Wehrlin (✉)
Swiss Federal Institute of Sport, Magglingen, Switzerland

Norwegian School of Sport Sciences, Oslo, Norway
e-mail: jon.wehrlin@baspo.admin.ch

B. Marti
Swiss Federal Institute of Sport, Magglingen, Switzerland

J. Hallén
Norwegian School of Sport Sciences, Oslo, Norway

R.C. Roach et al. (eds.), *Hypoxia*, Advances in Experimental Medicine and Biology 903, DOI 10.1007/978-1-4899-7678-9_24

24.1 Introduction

For several decades, altitude training has been used by endurance athletes and coaches to enhance sea-level performance. This "classical" altitude training has been performed by living and training at moderate altitude (live high–train high; LHTH). However, the scientific literature about performance effects of LHTH is equivocal since there are studies with improved [10, 14, 16, 27, 52], but also studies with unchanged [1, 5, 11, 18, 42, 43, 81] performance after LHTH. This encouraged the search for alternative strategies to use hypoxia as an additional stimulus for endurance athletes. In 1992, Levine and Stray-Gundersen [51] introduced the altitude training method "live high–train low" (LHTL). With living at moderate altitude, athletes theoretically should acquire the beneficial effects of altitude acclimatization, particularly an increase in hemoglobin mass (Hb_{mass}) and red cell volume (RCV) for maximizing the oxygen transport capacity. At the same time the low altitude or sea-level training would decrease the negative effects of reduced absolute training intensity caused by reduced VO_{2max} at altitude [48].

In 1997, Levine and Stray Gundersen showed in a complex study that the effect of LHTL on sea-level performance is superior to normal sea-level training or classical LHTH altitude training [49]. In elite sport, the LHTL paradigm has been widely used by endurance athletes during the last years. Altitude houses and tents have been developed in order that the LHTL can be conducted even at the home of the elite endurance trained athletes (ETA) [90]. Various studies using the LHTL paradigm have been conducted and the scientific debate has rather been why there are improvements in endurance athletes after LTHL than if there are improvements after LTHL [30, 50]. However, performance after LHTL altitude training is influenced by a wealth of confounding factors like the individual training plans, sickness, timing of performance after LHTL camp, and individual responses. In the last years there has also been a debate if there is an increase in Hb_{mass} and RCV with LHTL altitude training because several studies did not find this expected increase in elite athletes. The aim of this paper is therefore twofold: on one hand to review the expected negative effect of reduced VO_{2max} and associated reduced absolute training intensity when living and training at moderate altitude in elite endurance athletes (Part I) and on the other hand to review the expected beneficial effect of living at moderate altitude on hemoglobin mass and red cell volume (Part II).

24.2 Part I: Performance at Altitude in Elite Endurance Athletes

Optimal endurance performance relies upon frequency, duration, and intensity of training [38]. Especially with endurance performance, maintenance of training intensity appears to be the principle variable in optimizing subsequent endurance performance [39, 40]. Although VO_{2max} is not performance in a strictly physical

way (power per time), it clearly is one of the major characteristics that determine performance in endurance sport. VO_{2max} is generally accepted as the single best measure of the functional limit of the combined respiratory and circulatory systems to deliver oxygen to active muscles and the ability of the muscles to use oxygen [4] and is reproducible [41, 44]. Moreover, VO_{2max} is the most often studied and well-described effect of altitude exposure on exercise performance and is more or less independent of exercise protocol. At altitude, VO_{2max} is mainly physiologically affected by the reduction of air pressure that leads to reduced partial pressure of oxygen and consequently reduced oxygen flux at every step along the oxygen cascade. Consequently, VO_{2max} is reduced at altitude and this reduction is directly related to increased relative training intensity for the same absolute work load. The effect of decreased air density reducing air resistance is primarily relevant for endurance disciplines with high speeds like cycling etc. and will therefore not be discussed. In the performance at altitude part of this review, we first evaluate the "maximal" size effect of reduced VO_{2max} and absolute training intensity at altitude.

Fulco et al. [26] concluded in their review about aerobic performance at altitude one decade ago, that the reduction in VO_{2max} is larger in trained than in untrained subjects, in acute than after chronic hypoxic exposure and in unacclimatized versus acclimatized subjects. We therefore focused on studies which measured VO_{2max} for elite sport at altitudes up to 3000 m in acute hypoxia under laboratory settings (to avoid different acclimatization states) in trained sea level resident athletes ($VO_{2max} > 60$ ml kg^{-1} min^{-1}). Thereafter, we investigated in LHTH and LHTL studies if and how this reduction in VO_{2max} changes with increasing acclimatization of the elite endurance athletes.

24.2.1 Reduction of VO_{2max} in Acute Hypoxia

It was long believed that the sigmoid shape of the O_2–hemoglobin dissociation curve and the increased ventilation (VE) defend a reduction in arterial O_2 saturation (SaO_2) and VO_{2max} at altitudes below 1500 m. Buskirk et al. [11] concluded in 1967 that up to an altitude of 1524 m VO_{2max} is reduced only minimally, but thereafter is about 10.5 % per additional 1000 m. However, several more recent studies have shown that VO_{2max} can be reduced at altitudes even below 1000 m [29, 32, 83] and that there is a substantial individual difference in the reduction of VO_{2max} with increasing altitude [45, 47]. Although the reasons for this individual response are not clear, it seems that fitness level may be an important factor, as endurance-trained athletes (ETA; $VO_{2max} > 60$ ml kg^{-1} min^{-1}) have demonstrated a larger decline in VO_{2max} with increasing altitude compared with untrained individuals [45, 47]. It has been suggested that this is due to the fact that ETA have developed exercise-induced desaturation already at sea-level [12, 29, 83] and operate at the steeper part of the oxygen equilibrium curve at low altitudes [20].

There are only few studies that have tested the reduction of VO_{2max} for ETA in acute hypoxia at altitudes relevant (0–3000 m) for endurance disciplines in the

laboratory [12, 21, 29, 32, 47, 56–58, 80]. Three studies showed that VO_{2max} declines even at altitudes as low as 750–900 m [29, 32, 83] suggesting that the decrease is linear from sea-level to 3000 m.

However, none of these studies tested VO_{2max} from sea-level (0–300 m) to very low (300–1000 m), low (1000–2000 m) and moderate (2000–3000 m) altitude in the same athletes. In addition, the VO_{2max}-tests used in these studies were either incremental step tests to exhaustion or all out tests for a given distance. Under hypoxia, these protocols result in reduced absolute exercise intensity. It has therefore been hypothesized that one reason for the decreased VO_{2max} in hypoxia is the result of reduced maximal absolute intensity [55].

In order to test the hypothesis that there is no threshold altitude for decrement in VO_{2max}, we therefore measured VO_{2max} (Douglas bag system) at simulated altitude (hypobaric chamber) 300, 800, 1300, 1800, 2300, and 2800 m in a randomized and double blind order in endurance athletes with a $VO_{2max} > 60$ ml kg^{-1} min^{-1} [88]. To ensure that the results of reduced VO_{2max} would not be influenced by reduced muscle recruitment associated with reduced exercise intensity, our athletes absolved a preliminary VO_{2max} test from which we calculated individual constant speed to reach VO_{2max} by running at sea level between 2 and 6 min to exhaustion. Athletes thereafter ran at all different altitudes with these same speeds in order to reach VO_{2max}. Before each maximal running test to exhaustion, athletes additionally ran at an individual constant speed of 55 % of sea-level VO_{2max} in order to compare the altitude related effects between submaximal and maximal performance. As expected, we found a quite uniform and highly linear decrease in VO_{2max}, beginning already between 300 and 800 m and extending through 2800 m with a rate of decline of 6.3 % per 1000 m altitude (Fig. 24.1). Individual decreases in VO_{2max} ranged between 4.7 and 7.5 % per 1000 m, a small variation compared with that found in ETA earlier by Gore et al. [32] (+1 to −12 % change from 168 to 748 m above sea-level) or Billat et al. [6] (−8 to −24 % from sea-level to 2400 m). However, none of these studies or the other before mentioned studies included reported test-retest reproducibility. It is therefore not clear how much of the reported variability is methodological variation and how much is biological variation between the subjects. In our study the test-retest reproducibility (coefficient of variation) at 300 m was 1.4 %. The magnitude of the decrease in VO_{2max} was with 6.3 %/1000 m very close to the 7.2 %/1000 m calculated from the other studies which tested athletes with a $VO_{2max} > 60$ ml kg^{-1} min^{-1} in acute hypoxia in a laboratory (Fig. 24.2). The magnitude of this reduction is moreover very similar to the studies measuring the VO_{2max} at real altitudes after 1–2 days of exposure (mean reduction 7 %/1000 m; see next section). SpO_2 reduced also linearly (5.5 %/1000 m) and was strongly associated with the decrease in VO_{2max} with altitude. According to Ferretti et al. [20], the decrease in SpO_2 accounts for about 86 % of the decrease in VO_{2max}, which fits with the present study where approximately 70 % of the decrease in VO_{2max} could be explained by the decrease in SpO_2 at VO_{2max}. These results support the conclusion of Powers et al. [61] that a reduction of 1 % in SpO_2 below 92–93 % causes a decrease of ~1 % of VO_{2max}. Hence, the main mechanism for the hypoxia-induced decrease in VO_{2max} at low and moderate altitude is the decrease in SpO_{2max}. Maximal

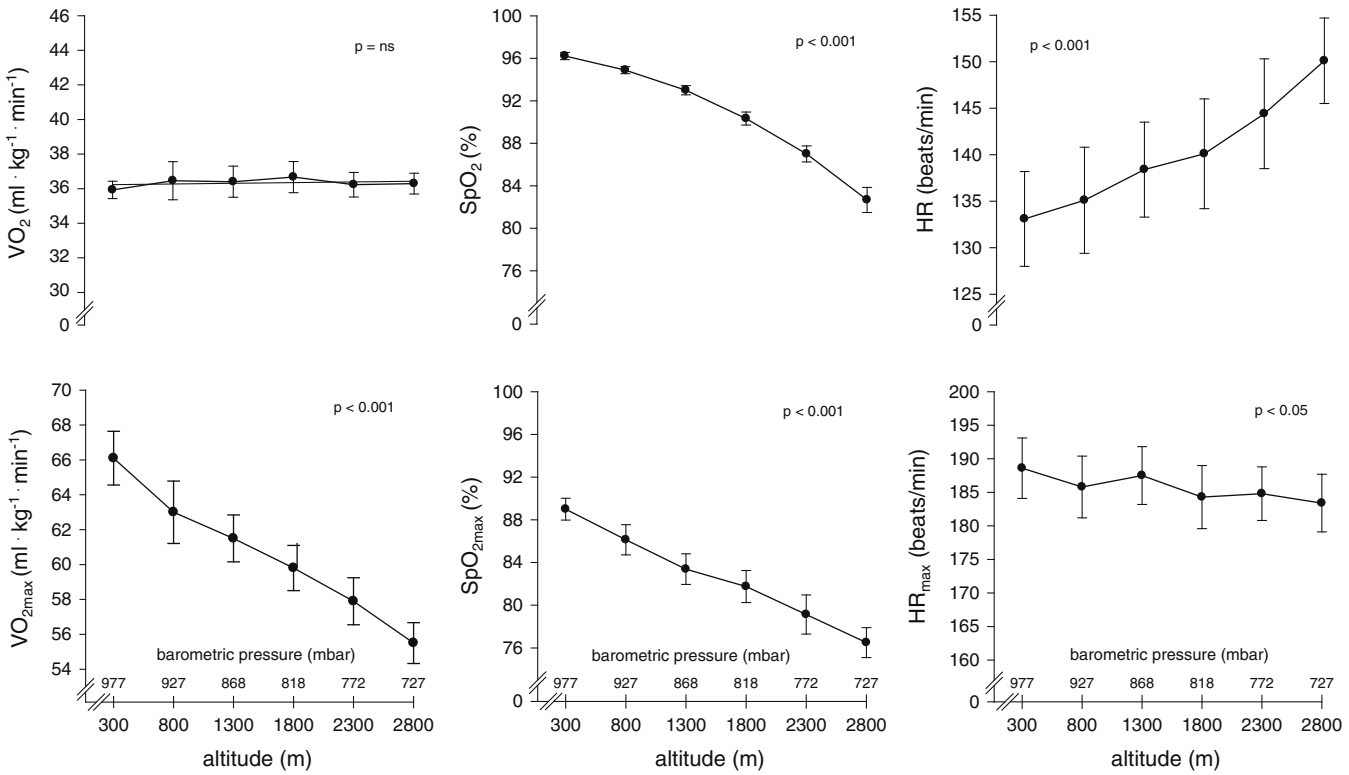

Fig. 24.1 Effect of acute simulated altitude exposure between 300 and 2800 m above sea level during submaximal exercise (*upper line*; 55 % of sea-level VO_{2max} identical absolute intensity at all altitudes) and maximal exercise (*lower line*; 107 % of sea-level VO_{2max}; identical absolute intensity at all altitudes) on oxygen uptake (VO_2 and VO_{2max}), arterial oxygen saturation (SpO_2 and SpO_{2max}), and heart rate (HR and HR_{max}). Modified after Wehrlin and Hallén [88]

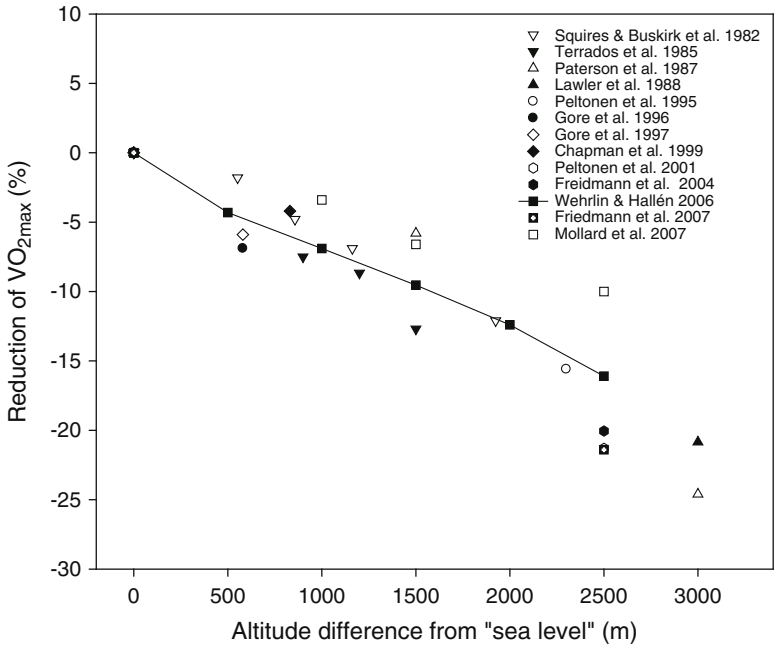

Fig. 24.2 Decline in VO_{2max} with altitude from sea-level values. "Sea-level" in these studies [12, 21, 22, 29, 32, 47, 53, 56, 57, 59, 80, 83, 88] is set at 0 m but varies originally from 0 to 362 m. Only studies which tested male unacclimatized ETA with a mean $VO_{2max} > 60$ ml kg^{-1} min^{-1} under laboratory conditions at acute hypoxia are included. Wehrlin and Hallén [88]

heart rate tended to decrease by about 2 beats per 1000 m increasing altitude (Fig. 24.1). Submaximal values showed as expected, that VO_2 for the same absolute speed is the same independent of altitude. SpO_2 reduced curvilinearly as did heart rate increase to compensate for the reduced oxygen content of the arterial blood.

24.2.2 VO_{2max} at Altitude with Increasing Acclimatization to Moderate Altitude

Surprisingly few studies have investigated the effect of moderate altitude exposure on VO_{2max} with increasing acclimatization in elite endurance athletes (Fig. 24.2). Most of these studies [1, 19, 62, 70] evaluated the effect of a LHTH altitude training camp on VO_{2max} in the run-up to the Olympic Games 1968 carried out in Mexico City at an altitude of 2240 m above sea level. Mean reduction of VO_{2max} in these athletes measured at sea level after 1–2 days at altitudes between 1822 and 2344 m was 7 % per 1000 m increasing altitude (range between 5.4 and 8.3 %). This reduction is, as mentioned, likewise very similar to the results of our laboratory study where the mean reduction of VO_{2max} was 6.3 % per 1000 m increasing altitude, or

the mean of our overview of the laboratory studies with endurance athletes, where VO_{2max} was reduced by 7.2 % per 1000 m increasing altitude. With increasing acclimatization, the reduction of VO_{2max} could be compensated by about 1/3 during 2–3 weeks in these LHTH studies. Only in one group of the legendary LHTH crossover study [1], VO_{2max} was compensated only by 10 %. In all other LHTH studies in Fig. 24.2, the compensation varied between 29 % [71] and 36 % [70]. When athletes do a 3 week LHTH altitude training camp at for instance 2500 m, VO_{2max} will therefore be reduced by about 15–20 % at the beginning and around 10 % at the end of the LHTH camp. In endurance athletes, this reduction in VO_{2max} will be associated with a reduction of absolute training intensity. It is important to note that these estimated values reference to training intensities near VO_{2max}. At lower training intensities, the athlete can profit from the sigmoidal reduction of SaO_2 that results in smaller altitude related effects (Fig. 24.1). However, combined with the recommended reduction of training volume [90] (20 % during the first week, 10 % during the third week) the absolute training stimulus is reduced considerably. To our knowledge, there is only one LHTL study which measured VO_{2max} several times during the altitude training camp. In the interesting study of Schuler et al. [78], elite cyclists lived for 21 days at an altitude of 2340 m above sea level (Sierra Nevada, Spain) and performed all training at altitude below 1100 m (30 min transport time). Mean decrease in VO_{2max} on day 1 at altitude was −12.6 % similar (−5.4 % per 1000 m increasing altitude) to the other LHTH studies (Fig. 24.3). The main point, however, is that the initial decrease in VO_{2max} was compensated by about 50 % after 14 days and by 70 % after 21 days.

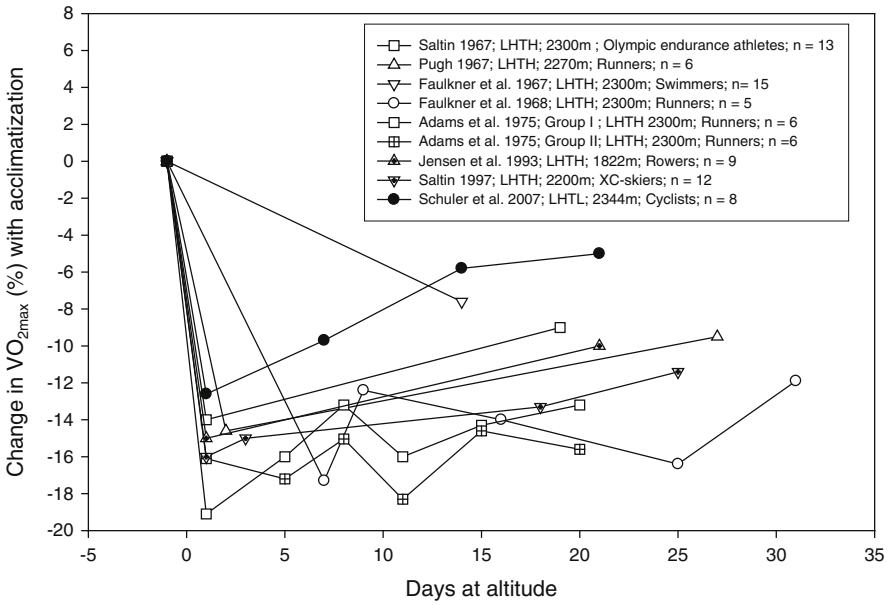

Fig. 24.3 Changes in maximal oxygen uptake (VO_{2max}) in relation to time spent at real moderate altitude in studies with a live high–train high (LHTH) [1, 18, 19, 43, 62, 70, 71] or a live high–train low (LHTL) [78] design in elite endurance-trained athletes

This result is more than the compensated 30 % in the LHTH studies at similar altitudes and raises the question if the LHTL concept should also be used to prepare for competition at altitude? This interesting question remains to be investigated. In summary, the results showed that VO_{2max} in elite endurance athletes in acute altitude exposure is linearly reduced by about 6–8 % per 1000 m increasing altitude from sea level to about 3000 m. This reduction was highly correlated with the decrease in SpO_2 and of course, with the increase in relative training intensity for the same absolute running speed. With living for 2–3 weeks LHTH acclimatization, the initial deficit in VO_{2max} can be reduced by about 1/3, whereas this deficit has been shown to be reduced by about 50–70 % with the LHTL approach.

24.3 Part II: Effect of Training and Altitude Exposure on Hb_{mass} and RCV

24.3.1 Methodological Aspects

By its nature, blood volume compartments can't be measured directly. All the known methods for blood volume compartment determinations are based on the dilution principle and are more or less directly. However, until 1990 only few data on Hb_{mass} and RCV for training and altitude conditions were available because the prevailing direct determination methods at that time were based on radioactive markers like the ^{51}Cr or ^{99}mTc method and were associated with considerable side effects. The T-1824 method (called Evans blue dye) was another method often used to determine plasma volume and then calculate RCV with the help of hematocrit values but this is also an invasive technique. The CO-rebreathing modified by Thomsen et al. [84], Burge and Skinner [9], and Schmidt and Prommer [77] provide the possibility to measure Hb_{mass} noninvasively directly without any side-effects. However, when comparing results of different training studies in normoxia and hypoxia, one has to take into account that not all techniques have the same precision and are suitable to answer training or hypoxic related questions. In their meta-analysis, Gore et al. [31] concluded that the CO-rebreathing method with a mean error of 2.2 % (90 % confidence interval 1.4–3.5 %) and the ^{51}Cr Method with a mean error of 2.8 % (90 % confidence interval 2.4–3.2 %) are the best measures for research on blood-related changes in oxygen transport and research. The T-1824 (Evans Blue) technique with a mean error of 6.7 % (90 % confidence interval 4.9–9.4 %) should only be used with care for clinical applications. Results from earlier studies with the Evans Blue technique should therefore be interpreted with care. In addition, the Evans blue technique has been questioned for estimating RCV after hypoxic exposure because of possible albumin leakage after exposure to altitude that would result in false high RCV values [2].

24.3.2 *Effects of Sea Level Training on RCV and Hb_{mass}*

Higher Hb_{mass} and BV in endurance athletes have been frequently assumed to be due to erythropoietic adaptation to the training process. Sawka et al. [74] concluded that exercise training, less than 11 days, leads to no change in RCV and that exercise training of more than 21 days leads to an increase in RCV of about 8 %. The conclusion that RCV did not change within 11 days seems to be clear. Several studies showed no increase after 10–12 days endurance training [13, 33, 34]. However, in our opinion, it is not clear that RCV increased after 21 days: with one exception, all other studies, which used radioactive isotope methodologies, showed no increase in RCV. In the study of Green (RCV measured with ^{51}Cr method), RCV did not increase after 4 weeks endurance training [34]. This is supported by the results of Ray et al. [63], where the subjects either trained for 8 weeks in a supine or an upright position and RCV did not increase (RCV measured with the ^{99}mTc method). Also Shoemaker failed to provoke changes in RCV with the ^{51}Cr method [79]; RCV was unchanged after 3, 6 and 11 weeks of endurance training. Only Remes et al. [64] (^{51}Cr method) reported that a group of 30 subjects increased RCV 4.1 % after 6 months of military training. Further evidence that 3–4 weeks endurance training does not increase RCV or Hb_{mass}, comes from a series of recent experiments where the Hb_{mass} has been measured with the "new" CO-rebreathing method. Gore et al. [28] reported, that neither endurance training for 4 weeks in a cold nor hot environment increased Hb_{mass} in male and female endurance athletes. Also 12 weeks of rowing in elite endurance athletes did not increase Hb_{mass} [28]. These findings are in line with our recent study, where national team cross-country skiers did not increase Hb_{mass} with 5 month of endurance training (Wehrlin et al. [86]), 1 year of endurance training in adolescents [17] and even 3 years of endurance training in national team cross-country skiers (see Fig. 24.4). Interestingly, the studies that measured RCV with the Evans blue-dye technique (T-1824) increased RCV after endurance training: Schmidt et al. [75] reported an 8 % increase in RCV after 3 weeks and Wartburton et al. [85] showed an increase of +12.5 % in an interval training group and +11.5 % in a continuous training group, but subjects increased RCV already in the first training week by about 8 %. This means in absolute values, that RCV in the interval group increased 24 ml/kg from the pretest, to 26 ml/kg in week 1 and 27 ml/kg in week 12, while the continuous training group started with 26 ml/kg and increased to 28 ml/kg after 1 week and 29 ml/kg after 12 weeks; this seems to be questionable. However, Schmidt and Prommer [76] reported recently an increased (6.4 %) Hb_{mass} in relatively untrained subjects after training 9 months for a marathon.

In summary, when measurement technique is taken into account, it seems it is very difficult to increase Hb_{mass} and RCV with normoxic endurance training, especially for already endurance trained athletes.

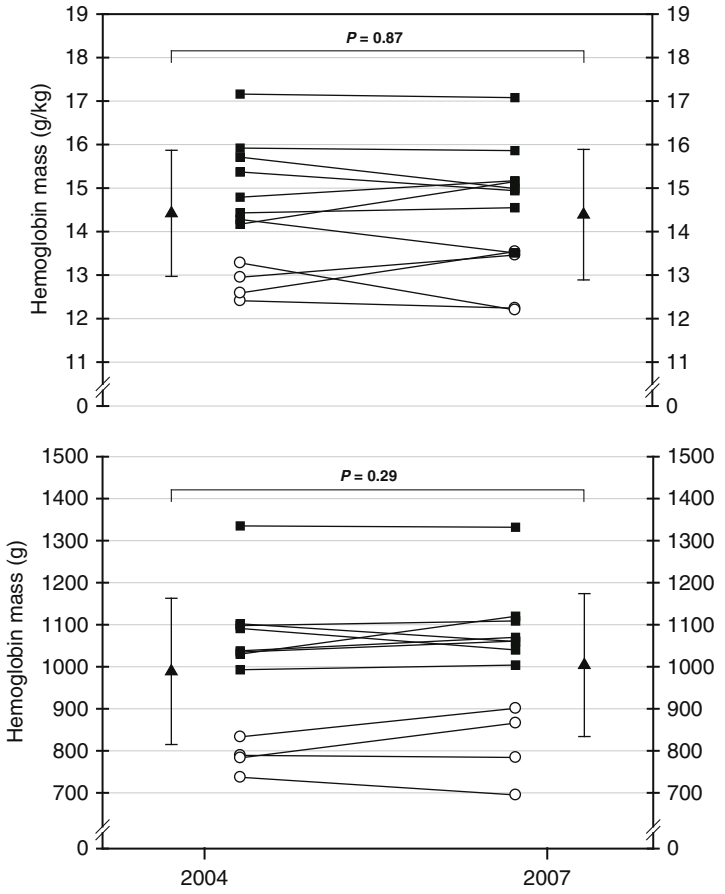

Fig. 24.4 Effect of 3 years endurance training between 2004 and 2007 on total (g) and relative (g/kg) hemoglobin mass in 12 Swiss national team cross-country skiers. ○ represent female, ■ male athletes and ▲ represent mean values ± SD. *P* indicates the *P*-value

24.3.3 Hemoglobin Mass: Effects of Moderate Altitude Exposure in Elite Endurance Athletes

When we started our experiments in 2002, it was quite unclear if a normal LHTL camp increases RCV and Hb_{mass} because the different studies showed controversial results: in the classic, carefully controlled, LHTL study conducted by Levine and Stray-Gundersen [49], RCV increased by ~5 % in the LHTL group after living for 4 weeks at 2500 m and training at 1250 m. These results were questioned [2] however, because they measured RCV indirectly with the Evans blue dye method and there have been doubts about the adequacy of this method for estimating RCV after hypoxic exposure [2, 35], and they reported similar increases in RCV in the 4-week

sea-level training phase and even a decrease in RCV in the control group [49]. However, at first glance, the effect of LHTL on RCV and Hb_{mass} was confusing. In some studies, Hb_{mass} and/or RCV was increased after real [49] and artificial LHTL altitude training camps [46, 67] while other studies reported no change after LHTL with real [15], artificial [2, 3] as well as LHTH at real altitude [24, 27, 28, 81, 82]. Ashenden pointed out, that with one exception [27] all studies using the Evans blue dye method showed an increase in RCV whereas all studies using the CO-rebreathing method to directly determine Hb_{mass} showed no increase in Hb_{mass}. However, when looking at the "hypoxic dose" (living altitude combined with the duration of altitude exposure) it was obvious, that most studies that showed no increase in Hb_{mass} and RCV used a lower hypoxic dose than the studies that reported increases in Hb_{mass} and RCV. We therefore started a controlled study with elite endurance athletes (national team orienteers and cross-country skiers) to measure the changes in Hb_{mass} and RCV with the CO-rebreathing method and an estimated adequate hypoxic dose similar to that used by Levine and Stray-Gundersen [49]. The orienteers (altitude group) completed a 24-day LHTL phase living 18 h per day at 2456 m and training at 1800 and 1000 m above sea level in the Swiss Alps. The cross-country skiers (control group) completed a normal training phase, which consisted of living and training between 500 and 1600 m for 24 days. Indeed, Hb_{mass} and RCV were increased by 5.3 and 5 % ($p < 0.01$) in the orienteers whereas there was no change in Hb_{mass} and RCV of the cross-country skiers. The changes in Hb_{mass} and RCV were different between the groups ($p < 0.01$) [89]. Because another theory [27] to explain the failure to increase Hb_{mass} with LHTL was that the athletes in the studies with increased Hb_{mass} were not "world class," our two best world class runners (we did not have more) also performed a LHTL training camp. They lived for 26 days at the same place (Muottas Muragl, Engading valley, Switzerland) at 2456 m and trained at 1800 m. Hb_{mass} (+3.9 and +7.6 %) and RCV (+5.8 and +6.3 %) were increased [87] indicating that it is possible to increase Hb_{mass} and RCV in world class athletes.

In Fig. 24.5, we include the results of all studies in which endurance-trained athletes participated in either a LHTH or LHTL altitude training camp and measured Hb_{mass} and/or RCV [2, 3, 8, 15, 23, 27, 36, 46, 49, 54, 60, 65–67, 72, 73, 81, 86, 87, 89]. At first glance, the effect of LHTL and LHTH on Hb_{mass} and RCV is confusing reaching from no effect to increases in Hb_{mass} and RCV of about 10 %.

We grouped the studies according to the hypoxic doses they used (hours spent at altitude) (Fig. 24.5). Group A [2, 3, 15, 54, 65, 72] includes the studies where the athletes spent about 100–300 h at altitude and reported no change in Hb_{mass} or RCV. The studies in group B [23, 37, 46, 49, 67, 73, 86, 87, 89] include athletes who spent between 350 and 550 h at altitude and whose Hb_{mass} or RCV increased about 4–7 %. Group C is the LHTH group from the classic Levine and Stray-Gundersen study [49] in which athletes spent about 700 h at altitude and RCV increased by 10 %. In group D, athletes spent between about 500 and 750 h at altitude, but Hb_{mass} remained unchanged [27, 60, 81]. In group E, the athletes spent only about 200–250 h at altitude, but Hb_{mass} was increased by 8–10 % [8, 66]. Based on the fact that Hb_{mass} in lifelong residents [37] of moderate altitude

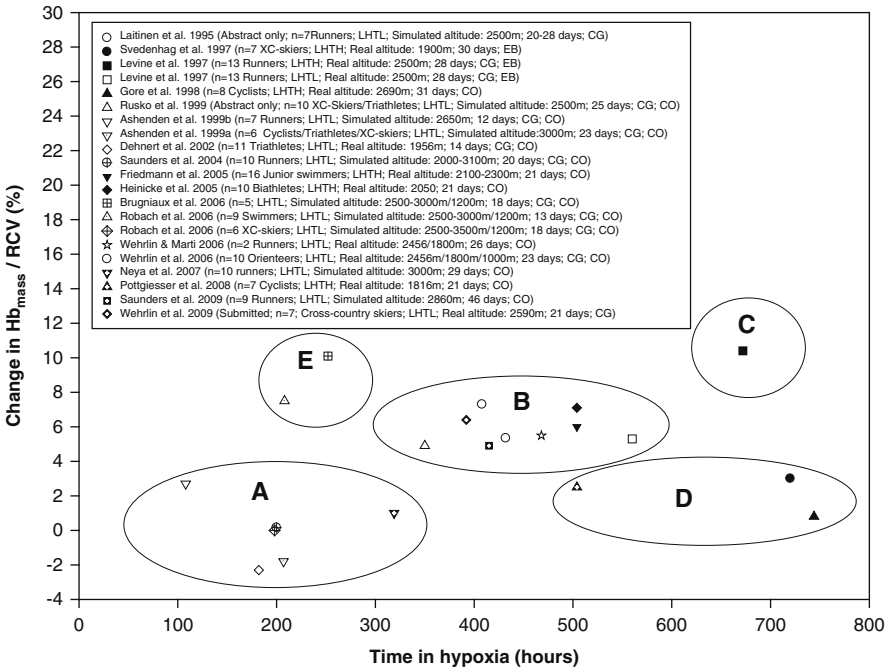

Fig. 24.5 Change in hemoglobin mass (Hb_{mass}) or red cell volume (RCV) in relation to time spent at altitude in studies with endurance-trained athletes RCV [2, 3, 8, 15, 23, 27, 36, 46, 49, 54, 60, 65–67, 72, 73, 81, 86, 87, 89]. Reported are: number of subjects (*n*), the sport, the type of altitude training (LHTH = live high–train high; LHTL = live high–train low), the nature of the altitude (real or simulated), the living altitude, days spent at altitude, use of a control group (CG) and technique used for measurement of Hb_{mass} or RCV (EB = Evans blue dye; CO = carbon monoxide rebreathing). A, B, C, D and E refer to the text

(2600–3550 m), including athletes [7, 76], is elevated, it has been suggested [48, 68, 69] that moderate altitude increases Hb_{mass} and RCV and that the "hypoxic dose" (living altitude combined with the time spent at altitude) used in altitude training plays a major role in whether or not Hb_{mass} and RCV are increased. Rusko et al. [68] concluded, that the minimum dose necessary to attain a hematological acclimatization is >12 h per day for at least 3 weeks (about 250 h) at an altitude of 2100–2500 m. Wilber, Stray-Gundersen, and Levine recommend to live for 4 weeks, >22 h per day at an altitude between 2000 and 2500 m [91]. As expected, there is a clear dose-response relationship between the groups A, B, and C in Fig. 24.5. In group A, the hypoxic dose was probably too low, whereas the hypoxic dose (350–550 h at 2100–2600 m) in group B was high enough to increase Hb_{mass} or RCV by about 5 %. The results of Group C results indicate that Hb_{mass} and RCV can be increased further with a higher hypoxic exposure, as shown by Heinicke et al. [37], where Hb_{mass} was increased by 11 % after a 6-month exposure to 3550 m in soldiers.

In group D, Hb_{mass} was unchanged despite the fact that the athletes in the two studies [27, 81] spent more than 700 h at altitude. In the first study [81], the athletes spent 30 days LHTH at an altitude of 1900 m, an altitude which might be too low to cause an increase Hb_{mass} and RCV. In the second study, Gore et al. [27] reported no increase in absolute Hb_{mass} after 31 days LHTH at 2690 m, though the authors pointed out that all athletes succumbed to illness during the period, which can have depressive effects on erythropoiesis [25]. Finally, group E showed a Hb_{mass} increase of 8–10 % with a relatively low hypoxic dose. The nine AG athletes in the study by Robach et al. [66] lived at simulated altitudes between 2500 and 3000 m for only 13 nights (16 h per day). However, the reproducibility of the method used to determine Hb_{mass} was not investigated and one athlete increased Hb_{mass} by 31 %, which seems to be an unnaturally high increase in after only 13 days at altitude. The mean increase would have been reduced to about 4.7 % when excluding the result of this athlete. In the study by Brugniaux et al. [8] five athletes from the AG lived for 18 days at simulated altitudes between 2500 and 3000 m. Hb_{mass} increased by 10.1 % and RCV was elevated by 9.2 % though the latter result was not statistically significant. Visual analysis of the individual RCV data showed that two of five athletes increased RCV by 20–30 %, which also seems to be unnaturally high. In both studies, a low amount of CO (44 and 49 ml) was used. In endurance athletes with high absolute Hb_{mass} and RCV this will lead to a very low ΔCOHb and low reproducibility of measurement [9].

In summary, we conclude that one altitude training period (LHTL) with a hypoxic dose of living more than 400 h at an altitude of about 2300–2500 m can increase Hb_{mass} and RCV. A lower hypoxic dose may have little or no effect on erythropoiesis. Hb_{mass} and RCV can even be increased in world class athletes with already high Hb_{mass} and RCV levels.

24.3.4 Hemoglobin Mass: Effects of Long-Term Living at Moderate Altitude in Elite Athletes

There is no doubt that moderate altitude residents posses higher Hb_{mass} than comparable habitants from lowland. Schmidt and Prommer [76] recently performed a Meta-Analysis (with their own data) where they with a cross-sectional design compared Hb_{mass} in sea-level and altitude (2600 m) resident subjects, subdivided in four groups characterized by different VO_{2max}. In all male groups, Hb_{mass} was between 9 and 14 % higher in the altitude than in the sea level groups, and a similar picture was found for the females with slight differences [76]. The higher RCV was compensated by a lower plasma volume that resulted in similar blood volumes in altitude and sea level resident subjects. It remains to be investigated whether endurance athletes reach these values with a series of LHTL camps.

24.4 Conclusions

In acute hypoxia, VO_{2max} is reduced linearly by about 6–8 % per 1000 m increasing altitude in elite athletes from sea level to 3000 m, with corresponding higher relative training intensities for the same absolute work load. With 2 weeks of acclimatization, this initial deficit can be reduced by about one half. In elite endurance athletes, Hb_{mass} is not increased with years of normal sea-level endurance training. However, when exposed for more than 400 h to altitudes between 2300 and 2500 m, Hb_{mass} increases temporarily by 5–6 %. This effect size is smaller than the reported 10–14 % higher Hb_{mass} values of endurance athletes living permanently at 2600 m.

References

1. Adams WC, Bernauer EM, Dill DB, Momar JB. Effects of equivalent sea-level and altitude training on VO_2max and running performance. J Appl Physiol. 1975;39(2):262–6.
2. Ashenden MJ, Gore CJ, Dobson GP, Hahn AG. "Live high, train low" does not change the total haemoglobin mass of male endurance athletes sleeping at a simulated altitude of 3000 m for 23 nights. Eur J Appl Physiol Occup Physiol. 1999;80:479–84.
3. Ashenden MJ, Gore CJ, Martin DT, Dobson GP, Hahn AG. Effects of a 12-day "live high, train low" camp on reticulocyte production and haemoglobin mass in elite female road cyclists. Eur J Appl Physiol Occup Physiol. 1999;80:472–8.
4. Åstrand PO, Rodahl K. Textbook of work physiology. New York, NY: McGraw-Hill; 1986.
5. Bailey DM, Davies B, Romer L, Castell L, Newsholme E, Gandy G. Implications of moderate altitude training for sea-level endurance in elite distance runners. Eur J Appl Physiol Occup Physiol. 1998;78:360–8.
6. Billat VL, Lepretre PM, Heubert RP, Koralsztein JP, Gazeau FP. Influence of acute moderate hypoxia on time to exhaustion at vVO2max in unacclimatized runners. Int J Sports Med. 2003;24:9–14.
7. Boning D, Rojas J, Serrato M, Ulloa C, Coy L, Mora M, Gomez J, Hutler M. Hemoglobin mass and peak oxygen uptake in untrained and trained residents of moderate altitude. Int J Sports Med. 2001;22:572–8.
8. Brugniaux JV, Schmitt L, Robach P, Nicolet G, Fouillot JP, Mouterau S, Lasne F, Pialoux V, Saas P, Chorvot MC, Cornolo J, Olson NV, Richalet J-P. Eighteen days of "living high, training low" stimulated erythropoiesis and enhance aerobic performance in elite middle-distance runners. J Appl Physiol. 2006;100:203–11.
9. Burge CM, Skinner SL. Determination of hemoglobin mass and blood volume with CO: evaluation and application of a method. J Appl Physiol. 1995;79:623–31.
10. Burtscher M, Nachbauer W, Baumgartl P, Philadelphy M. Benefits of training at moderate altitude versus sea level training in amateur runners. Eur J Appl Physiol Occup Physiol. 1996;74:558–63.
11. Buskirk ER, Kollias J, Akers F, Prokop EK, Reategui EP. Maximal performance at altitude and on return from altitude in conditioned runners. J Appl Physiol. 1967;23(2):259–66.
12. Chapman RF, Emery M, Stager JM. Degree of arterial desaturation in normoxia influences VO2max decline in mild hypoxia. Med Sci Sports Exerc. 1999;31(5):658–63.
13. Convertino VA, Mack GW, Nadel ER. Elevated central venous pressure: a consequence of exercise training-induced hypervolemia? Am J Physiol. 1980;48:657–64.
14. Daniels J, Oldridge N. The effect of alternate exposure to altitude and sea level on world-class middle-distance runners. Med Sci Sports Exerc. 1970;2:107–12.

15. Dehnert C, Hutler M, Liu Y, Menold E, Netzer C, Schick R, Kubanek B, Lehmann M, Boning D, Steinacker JM. Erythropoiesis and performance after two weeks of living high and training low in well trained triathletes. Int J Sports Med. 2002;23:561–6.
16. Dill DB, Adams WC. Maximal oxygen uptake at sea level and at 3090m altitude in high school champion runners. J Appl Physiol. 1971;30(6):854–9.
17. Eastwood A, Bourdon PC, Withers RT, Gore CJ. Longitudinal changes in haemoglobin mass and VO2max in adolescents. Eur J Appl Physiol. 2009;105:715. doi:10.1007/s00421-00008-00953-x.
18. Faulkner JA, Daniels JT, Balke B. Effects of training at moderate altitude on physical performance capacity. J Appl Physiol. 1967;23(1):85–9.
19. Faulkner JA, Kollias J, Favour CB, Buskirk ER, Balke B. Maximum aerobic capacity and running performance at altitude. J Appl Physiol. 1968;24(5):685–91.
20. Ferretti G, Moia C, Thomet JM, Kayser B. The decrease of maximal oxygen consumption during hypoxia in man: a mirror image of the oxygen equilibrium curve. J Physiol. 1997;498:231–7.
21. Friedmann B, Bauer T, Menold E, Bartsch P. Exercise with the intensity of the individual anaerobic threshold in acute hypoxia. Med Sci Sports Exerc. 2004;36:1737–42.
22. Friedmann B, Frese F, Menold E, Bartsch P. Effects of acute moderate hypoxia on anaerobic capacity in endurance-trained runners. Eur J Appl Physiol. 2007;101:67–73.
23. Friedmann B, Frese F, Menold E, Kauper F, Jost J, Bartsch P. Individual variation in the erythropoietic response to altitude training in elite junior swimmers. Br J Sports Med. 2005;39:148–53.
24. Friedmann B, Jost J, Rating T, Weller E, Werle E, Eckardt KU, Bartsch P, Mairbaurl H. Effects of iron supplementation on total body hemoglobin during endurance training at moderate altitude. Int J Sports Med. 1999;20:78–85.
25. Fry RW, Morton AR, Keast D. Overtraining in athletes. An update. Sports Med. 1991;12:32–65.
26. Fulco CS, Rock PB, Cymerman A. Maximal and submaximal exercise performance at altitude. Aviat Space Environ Med. 1998;69:793–801.
27. Gore CJ, Hahn A, Rice A, Bourdon P, Lawrence S, Walsh C, Stanef T, Barnes P, Parisotto R, Martin D, Pyne D, Gore C. Altitude training at 2690m does not increase total haemoglobin mass or sea level VO2max in world champion track cyclists. J Sci Med Sport. 1998;1:156–70.
28. Gore CJ, Hahn AG, Burge CM, Telford RD. VO2max and haemoglobin mass of trained athletes during high intensity training. Int J Sports Med. 1997;18:477–82.
29. Gore CJ, Hahn AG, Scroop GC, Watson DB, Norton KI, Wood RJ, Campbell DP, Emonson DL. Increased arterial desaturation in trained cyclists during maximal exercise at 580m altitude. J Appl Physiol. 1996;80(6):2204–10.
30. Gore CJ, Hopkins WG. Counterpoint: positive effects of intermittent hypoxia (live high:train low) on exercise performance are not mediated primarily by augmented red cell volume. J Appl Physiol. 2005;99:2055.
31. Gore CJ, Hopkins WG, Burge CM. Errors of measurement for blood volume parameters: a meta-analysis. J Appl Physiol. 2005;99:1745–58.
32. Gore CJ, Little SC, Hahn AG, Scroop GC, Norton KI, Bourdon PC, Woolford SM, Buckley JD, Stanef T, Campbell DP, Watson DB, Emonson DL. Reduced performance of male and female athletes at 580 m altitude. Eur J Appl Physiol Occup Physiol. 1997;75:136–43.
33. Green HJ, Hughson RL, Thomsen JA, Sharratt MT. Supramaximal exercise after training-induced hypervolemia. J Appl Physiol. 1987;62:1944–53.
34. Green HJ, Sutton JR, Coates G, Ali M, Jones S. Response of red cell and plasma volume to prolonged training in humans. J Appl Physiol. 1991;70:1810–5.
35. Hahn AG, Gore CJ, Martin DT, Ashenden MJ, Roberts AD, Logan PA. An evaluation of the concept of living at moderate altitude and training at sea level. Comp Biochem Physiol A Mol Integr Physiol. 2001;128:777–89.
36. Heinicke K, Heinicke I, Schmidt W, Wolfarth B. A three-week traditional altitude training increases hemoglobin mass and red cell volume in elite biathlon athletes. Int J Sports Med. 2005;26:350–5.

37. Heinicke K, Prommer N, Cajiagal J, Viola T, Behn C, Schmidt W. Long-term exposure to intermittent hypoxia results in increased hemoglobin mass, reduced plasma volume and elevated erythropoietin plasma levels in man. Eur J Appl Physiol. 2003;88:535–43.
38. Hickson RC, Bomze HA, Holloszy JO. Linear increase in aerobic power induced by a strenuous program of endurance exercise. J Appl Physiol. 1977;42:372–6.
39. Hickson RC, Kanakis RC, Davis J. Reduced training duration and effects on aerobic power, endurance, and cardiac growth. J Appl Physiol. 1982;58:225–9.
40. Hickson RC, Rosenkoetter MA. Reduced training frequency and maintenance of increased aerobic power. Med Sci Sports Exerc. 1981;13:13–6.
41. Howley ET. Criteria for maximal oxygen uptake. Review. Med Sci Sports Exerc. 1995;27:1292–301.
42. Ingjer F, Myhre K. Physiological effects of altitude training on elite male cross country skiers. J Sports Sci. 1992;10:37–47.
43. Jensen K, Nielsen TS, Fiskestrand JO, Lund JO, Christensen NJ, Secher NH. High-altitude training does not increase maximal oxygen uptake or work capacity at sea level in rowers. Scand J Med Sci Sports. 1993;3:256–62.
44. Katch VL, Sady SS, Freedson P. Biological variability in maximum aerobic power. Med Sci Sports Exerc. 1982;14:21–4.
45. Koistinen P, Takala T, Martikkala V, Leppaluoto J. Aerobic fitness influences the response of maximal oxygen uptake and lactate threshold in acute hypobaric hypoxia. Int J Sports Med. 1995;16:78–81.
46. Laitinen H, Alopaeus K, Heikkinen R, Hietanen H, Mikkelson L, Tikkanen HO, Rusko H. Acclimatization to living in normobaric hypoxia and training in normoxia at sea level in runners. Med Sci Sports Exerc. 1995;27:S109.
47. Lawler J, Powers SK, Thompson D. Linear relationship between VO2max and VO2max decrement during exposure to acute hypoxia. J Appl Physiol. 1988;64:1486–92.
48. Levine BD. Intermittent hypoxic training: fact and fancy. High Alt Med Biol. 2002;3:177–93.
49. Levine BD, Stray-Gundersen J. "Living high-training low": effect of moderate-altitude acclimatization with low-altitude training on performance. J Appl Physiol. 1997;83:102–12.
50. Levine BD, Stray-Gundersen J. Point: positive effects of intermittent hypoxia (live high:train low) on exercise performance are mediated primarily by augmented red cell volume. J Appl Physiol. 2005;99:2053–5.
51. Levine BD, Stray-Gundersen J. A practical approach to altitude training: where to live and train for optimal performance enhancement. Int J Sports Med. 1992;13 Suppl 1:S209–12.
52. Mizuno M, Juel C, Bro-Rasmussen T, Mygind E, Schibye B, Rasmussen B, Saltin B. Limb skeletal muscle adaptation in athletes after training at altitude. J Appl Physiol. 1990; 68:496–502.
53. Mollard P, Woorons X, Letournel M, Cornolo J, Lamberto C, Beaudry M, Richalet J-P. Role of maximal heart rate and arterial O2 saturation on the decrement of VO2max in moderate acute hypoxia in trained and untrained men. Int J Sports Med. 2007;28:186–92.
54. Neya M, Enoki T, Kumai Y, Sugoh T, Kawahara T. The effects of nightly normobaric hypoxia and high intensity training under intermittent normobaric hypoxia on running economy and hemoglobin mass. J Appl Physiol. 2007;103:828–34.
55. Noakes TD, Peltonen JE, Rusko HK. Evidence that a central governor regulates exercise performance during acute hypoxia and hyperoxia. J Exp Biol. 2001;204:3225–34.
56. Paterson DJ, Pinnington H, Pearce AR, Morton AR. Maximal exercise cardiorespiratory responses of men and women during acute exposure to hypoxia. Aviat Space Environ Med. 1987;58:243–7.
57. Peltonen JE, Rantamaki J, Niittymaki SP, Sweins K, Viitasalo JT, Rusko HK. Effects of oxygen fraction in inspired air on rowing performance. Med Sci Sports Exerc. 1995;27:573–9.
58. Peltonen JE, Tikkanen HO, Ritola JJ, Ahotupa M, Rusko HK. Oxygen uptake response during maximal cycling in hyperoxia, normoxia and hypoxia. Aviat Space Environ Med. 2001;72:904–11.
59. Peltonen JE, Tikkanen HO, Rusko HK. Cardiorespiratory responses to exercise in acute hypoxia, hyperoxia and normoxia. Eur J Appl Physiol. 2001;85:82–8.

60. Pottgiesser T, Ahlgrim C, Ruthardt S, Dickhuth H, Schumacher Y. Hemoglobin mass after 21 days of conventional altitude training at 1816m. J Sci Med Sport. 2009;12:673. doi:10.1016/j.jsams.2008.06.005.
61. Powers SK, Lawler J, Dempsey JA, Dodd S, Landry G. Effects of incomplete pulmonary gas exchange on VO2max. J Appl Physiol. 1989;66:2491–5.
62. Pugh LGCE. Athletes at altitude. J Physiol. 1967;192:619–46.
63. Ray CA, Cureton KJ, Ouzts HG. Postural specificity of cardiovascular adaptations to exercise training. J Appl Physiol. 1990;69:2202–8.
64. Remes K, Vuopio P, Harkonen M. Effect of long-term training and acute physical exercise on red cell 2,3-diphosphoglycerate. Eur J Appl Physiol Occup Physiol. 1979;42:199–207.
65. Robach P, Schmitt L, Brugniaux JV, Nicolet G, Duvallet A, Fouillot JP, Mouterau S, Lasne F, Pialoux V, Olson NV, Richalet J-P. Living high-training low: effect on erythropoiesis and maximal aerobic performance in Nordic skiers. Eur J Appl Physiol. 2006;97:695–705.
66. Robach P, Schmitt L, Brugniaux JV, Roels B, Millet G, Hellard P, Nicolet G, Duvallet A, Fouillot JP, Mouterau S, Lasne F, Pialoux V, Olson NV, Richalet J-P. Living high-training low: effect on erythropoiesis and aerobic performance in highly-trained swimmers. Eur J Appl Physiol. 2006;96:423–33.
67. Rusko H, Tikkanen HO, Pavolainen L, Hämälainen K, Kalliokoski A, Puranen A. Effect of living in hypoxia and training in normoxia on sea level VO2max and red cell mass. Med Sci Sports Exerc. 1999;31:S86.
68. Rusko HK, Tikkanen HO, Peltonen JE. Altitude and endurance training. J Sports Sci. 2004;22:928–45.
69. Rusko HK, Tikkanen HO, Peltonen JE. Oxygen manipulation as an ergogenic aid. Curr Sports Med Rep. 2003;2:233–8.
70. Saltin B. Aerobic and anaerobic work capacity at 2300m. Med Thorac. 1967;24:205–10.
71. Saltin B. The physiology of competitive c.c. skiing across a four decade perspective; with a note on training induced adaptations and role of training at medium altitude. In: Müller E, Schmwameder H, Kornexl E, Raschner C, editors. Science and skiing. Aachen: Meyer & Meyer Sport; 1997.
72. Saunders PU, Telford RD, Pyne DB, Cunningham RB, Gore CJ, Hahn A, Hawley JA. Improved running economy in elite runners after 20 days of simulated moderate-altitude exposure. J Appl Physiol. 2004;96:931–7.
73. Saunders PU, Telford RD, Pyne DB, Hahn A, Gore CJ. Improved running economy and increased hemoglobin mass in elite runners after extended moderate altitude exposure. J Sci Med Sport. 2009;12:67–72.
74. Sawka MN, Convertino VA, Eichner ER, Schnieder SM, Young AJ. Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. Med Sci Sports Exerc. 2000;32:332–48.
75. Schmidt W, Maassen N, Böning D. Training induced effects on blood volume, erythrocyte turnover and haemoglobin oxygen binding properties. Eur J Appl Physiol. 1988;57:490–8.
76. Schmidt W, Prommer N. Effects of various training modalities on blood volume. Scand J Med Sci Sports. 2008;18(Suppl1):57–69.
77. Schmidt W, Prommer N. The optimised CO-rebreathing method: a new tool to determine total haemoglobin mass routinely. Eur J Appl Physiol. 2005;95:486–95.
78. Schuler B, Thomsen JJ, Gassmann M, Lundby C. Timing the arrival at 2340m altitude for aerobic performance. Scand J Med Sci Sports. 2007;17:588–94.
79. Shoemaker JK, Green HJ, Coates G, Ali M, Grant S. Failure of prolonged exercise training to increase red cell mass in humans. Am J Physiol. 1996;270:121–6.
80. Squires RW, Buskirk ER. Aerobic capacity during acute exposure to simulated altitude, 914 to 2286 meters. Med Sci Sports Exerc. 1982;14:36–40.
81. Svedenhag J, Piehl-Aulin K, Skog C, Saltin B. Increased left ventricular muscle mass after long-term altitude training in athletes. Acta Physiol Scand. 1997;161:63–70.
82. Telford RD, Graham D, Sutton JR, Hahn A, Campbell DA. Medium altitude training and sea level performance. Med Sci Sports Exerc. 1996;28:S124.

83. Terrados N, Mizuno M, Andersen H. Reduction in maximal oxygen uptake at low altitudes; Role of training status and lung function. Clin Physiol. 1985;5(3):75–9.
84. Thomsen JK, Fogh-Andersen N, Bülow K, Devantier A. Blood and plasma volumes determined by carbon monoxide gas, ^{99m}TC-labeled erythrocytes, ^{125}I-albumin and the T 1824 technique. Scand J Clin Lab Invest. 1991;51:185–90.
85. Wartburton DE, Haykowski MJ, Quinney HA, Blackmore D, Teo KK, Mcgavock J, Humen D. Blood volume expansion and cardiorespiratory function: effects of training modality. Med Sci Sports Exerc. 2004;36:991–1000.
86. Jon Peter Wehrlin. Dissertation from the Norwegian School of Sport Sciences. 2008. Altitude and Endurance Athletes - Effects of Acute and Chronic Hypoxic Exposure. ISBN Nr. 978-82-502-0413-3.
87. Wehrlin J, Marti B. Live high-train low associated with increased haemoglobin mass as preparation for the 2003 World Championships in two native European world class runners. Br J Sports Med. 2006;40:e3.
88. Wehrlin JP. Linear decrease in VO2max and performance with increasing altitude in endurance athletes. Eur J Appl Physiol. 2006;96:404–12.
89. Wehrlin JP, Zuest P, Hallen J, Marti B. Live high-train low for 24 days increases hemoglobin mass and red cell volume in elite endurance athletes. J Appl Physiol. 2006;100:1938–45.
90. Wilber RL. Altitude training and athletic performance. Champaign, IL: Human Kinetics; 2004.
91. Wilber RL, Stray-Gundersen J, Levine BD. Effects of hypoxic “Dose” on physiological responses and sea-level performance. Med Sci Sports Exerc. 2007;39:1590–9.