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ALTITUDE AND HYPOXIA TRAINING – EFFECTS ON PERFORMANCE CAPACITY AND PHYSIOLOGICAL FUNCTIONS AT SEA LEVEL*

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ABSTRACT

Athletes sometimes use hypoxic training to prepare for competitions at sea level because of the importance of oxygen transport and consumption for endurance performance. But, clear evidence for its effectiveness is lacking. Maximal oxygen uptake ($\dot{V}O_2$max) decreases in hypoxia, so training at altitude is harder. Hypoxic training may stimulate adaptation processes faster because relative work is greater in hypoxia than in normoxia.

A specific altitude training effect can only be proven if a relative equal exercise load (in % of $\dot{V}O_2$max) is more effective than during sea level training. Four of eleven studies have shown that training at high altitude improved sea level endurance performance or $\dot{V}O_2$max more than sea level training did. Only two of eight studies showed improved performance when training in hypoxia combined with living in normoxia. The results for living in hypoxia while training in normoxia (i.e., "live high, train low") are not convincing. There seems to exist a small specific altitude effect on performance capacity, which may be counteracted by negative influences, such as reduced stimulation of muscular metabolism. Training in hypoxic environments might have positive or negative effects on training success. Considerations include training the respiratory muscles, increased hypoxic ventilatory stimulation, different training stimulus of the left and right heart, increased red cell and plasma volume (the latter after descent), rightward shift of the oxygen dissociation curve, changes in muscle mass, enzymes and capillaries, shift from fat and muscle glycogen use to blood glucose combustion, reduced lactic acid and ammonia production, and changes in bicarbonate and non-bicarbonate buffer capacities.

Key words: acclimatization, blood volume, endurance, performance capacity

Introduction

Physical training at altitude is essential for success in competitions at altitude. However, the effects of training at altitude or in hypoxic conditions on sea level performance are controversial (39). This problem is the focus of this literature review.

Athletes, coaches, and many sport scientists believe that altitude training is an effective means for improving performance capacity at sea level by increasing blood hemoglobin concentration, which results from an increased erythropoietin production. Astonishingly, these opinions are based more on theoretical considerations than on actual measurements. We have to determine if this concept is truth or myth.

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Performance capacity and training intensity at altitude

The theoretical justification for hypoxic training to enhance sea level exercise performance is that limiting subsystems for oxygen transport and oxygen utilization might be specifically adapted and enhanced by training with reduced O_2 availability. Barometric pressure decreases and ambient and alveolar gases expand during ascent to altitude. While the fractional concentrations of gases in the air remain the same (i.e., 21% O_2), one liter of air contains fewer oxygen molecules than at sea level. For a given O_2 demand the ventilation volume must be increased correspondingly, even if alveolar PO_2 remains at the lowered value. To increase alveolar oxygen partial pressure (PAO_2) again the ventilation must rise further which becomes increasingly difficult as altitude increases. For example, at 3000 m the inspiratory PO_2 is as low as PAO_2 at sea level (100 mm Hg); PAO_2 is further decreased at altitude because of the pressure difference to ambient air imposed by oxygen extraction, CO_2 excretion and water vapour saturation. Consequently, oxygen diffusion from the alveoli to the blood slows. Reduced mass transport and diffusion pressure decrease maximal oxygen uptake ($\dot{V}O_2max$) by approximately 1 %/100 m - beginning at 1500 m of altitude - which can never be adequately compensated.

According to most investigators (e.g. 26), $\dot{V}O_2$ for submaximal work loads remains unchanged. But, an equal load imposes a greater strain on the organism at altitude than at sea level because it corresponds to a higher percentage of $\dot{V}O_2max$; therefore, it is an increased stimulus for many physiological functions, such as the endocrine response (24). Improved training results under these conditions are not altitude specific but are a consequence of increased training intensity, which may also be reached by other methods. Only enhanced performance after relatively equal training intensity (i.e., at equal percentage of altitude-adjusted $\dot{V}O_2max$) demonstrates specific benefits of altitude training.

The main drawback of altitude training is that various functions (*e.g.*, ATP synthesis per second in the working muscle) are less stimulated than at sea level (1). Thus, altitude training may cause improvements and deteriorations of different physiological and performance functions at the same time. Because of the dangers of physical deterioration, altitudes higher than 3000 m usually are not considered for athletic training.

Hypoxic training and performance capacity

There are different forms of hypoxia training, such as living high-training high and living high-training low. Studies comparing classical altitude training ("living high - training high") with relatively equal sea level training are compiled in Table 1A. The number of studies using experimental and control groups is small. This review includes investigations in which the subjects had reached a steady performance level with relatively equal training intensity at low altitude before ascent. Only 5 of 11 studies - and 4 of 7 with control groups - showed that altitude training improved sea level performance. The investigation with the best design (i.e., cross-over design that used two parallel groups training at low and high altitude; 1) produced no clear difference in performance or $\dot{V}O_2max$. Few studies examined the effects of altitude training on sea level endurance times, but 2 of 3 papers demonstrated an effect.

Studies where subjects trained in hypoxia while remaining in normoxia for the rest of the day, revealed significant performance capacity increases in 2 of 8 studies. There was a non-significant tendency for

Table 1A. *Performance capacity after altitude or hypoxia training with equal relative intensity as in normoxia (in chronological order)*

Author	Altitude (m)	Duration (days)	Subjects	Controls	Max. performance	$\dot{V}O_2max$	Endurance
A. Altitude training							
Buskirk et al. (20)	4000	55-68	6 MR+LR	pre	0	0	
Faulkner et al. (25)	2300	14	15 S	pre	0	0	
Mellerowicz et al. (53)	1800-2500	28	11 LR	11 LR	↑	↑	
Liesen, Hollmann (48)	1950-2800	14	3 canoepaddlers	pre		(↑)	
Adams et al. (1)	2300	21	12 MR	12 id	↑↓	0↓	
Meller et al. (52)	2050	28	4 ut twins	4 id	(↑)	(↑)	
Mizuno et al. (54)	2100-2700	14	10 Ski	pre	0	0	↑
Ingjer, Myhre (38)	1900	21	7 Ski	7 id		0	
Svedenhag et al. (65)	2000	14	7 MR	6 LR		0	↑
Levine, Stray-Gundersen (45)	2500-3000	28	9 LR	10 LR	0	↑	0
Levine, Stray-Gundersen (47)	2500-3000	28	13 LR	13 LR	0	↑	

Table 1B. *Performance capacity after altitude or hypoxia training with equal relative intensity as in normoxia (in chronological order)*

Author	Altitude (m)	Duration (days)	Subjects	Controls	Max. performance	$\dot{V}O_2max$	Endurance
B. Artificial hypoxia only during training							
Roskamm et al. (57)	2250-3450	28	12 ut	6 ut	↑	↑	
Hollmann, Liesen (34)	4500	56-70	30 t	Pre		↑	↑
Terrados et al. (66)	2300	21-28	4 C	4 C	(↑)	0	(↑)
Levine et al. (42)	2500	35	7 ut	7 ut		0	0
Benoit et al. (9)	4500-5800	21	9 ut	9 ut		0	
Engfred et al. (24)	2500	35	7 ut	7 ut		0	↓
Emonson et al. (23)	2500	35	9 ut	9 ut		0	0
Vogt et al. (71)	3850	42	7 ut	8 ut	(↑)	(↑)	

Conditions for comparison: control group or very well trained initial status. Endurance: increased endurance time or decreased submaximal heart rate or lactic acid concentration. Maximal performance: laboratory test or (test) competition. LR long distance runner, MR middle distance runner, C cyclist, S swimmer, Ski long distance skiers, ut untrained, t trained, pre prealtitude performance, id control training with same subjects, ↑ increase, ↓ decrease, 0 no increase or not larger than in the controls, (...) not significant tendency, blank not measured.

an improvement in 2 additional investigations (Table 1B).

The reverse pattern — sleeping in hypoxic conditions and training in normoxia — produced a positive effect on aerobic and anaerobic performance. However, these data have only been published in abstracts (43, 46, 55). Levine and Stray-Gundersen(47), however, compared three groups of athletes that lived and trained at sea level, lived and trained at altitude (2500 m), or lived at altitude and trained at 1250 m. All subjects performed a preparatory 6 weeks of training at sea level and used relatively equal exercise intensity. The authors concluded that the live high-train low model is best. This is not convincing for various reasons. $\dot{V}O_2$max increased in both altitude groups similarly. The racing time for 5000m and the velocity at $\dot{V}O_2$max increased significantly only in the high-low group. But the comparison was made to baseline, not to the values at the end of the preparatory sea level training. Most of the improvement in performance and oxygen transport capacity occurred already at sea level.

The same researchers later developed the concept of responders and nonresponders (21). They compared the subjects with clear improvement in the 5000 m race to those whose performance deteriorated. They only found an increase in $\dot{V}O_2$max and blood volume in the former group. But this statistical approach is dubious — it is relatively easy to find significant effects, if you select the best results post hoc. The authors also mentioned differences in training intensity between responders and nonresponders, which may be the real cause for the variable response of the athletes.

Our group did not detect performance improvements in triathletes after 14 days living high and training low (22). Also, an extended investigation in altitude natives in La Paz (3600 m of altitude) who trained either under their environmental conditions or in normoxia yielded no differences (26).

Summarizing the results the published studies do not clearly prove a specific altitude training effect but also do not allow to exclude it. Probably a small effect does exist which cannot be always statistically confirmed. There is no convincing evidence for a superiority of the living high and training low.

Altitude effects on specific physiological functions

In spite of the equivocal effect of altitude training on performance, the functions of various organs might be influenced positively and lead to:

1) improvements in oxygen transport
2) reduction of oxygen requirements (saving of O_2, anaerobic energy sources)
3) adaptation of enzymes and biochemical regulation to lowered oxygen pressures.

The key substance for many reactions seems to be the hypoxia-inducible factor 1 (HIF 1), a dimeric protein; its production and binding to DNA are increased in hypoxia (62). It stimulates the production of messenger RNA for erythropoietin (EPO), vascular endothelial growth factor (VEGF), glucose transporters and glycolytic enzymes. The system is also activated in skeletal muscle cells during hypoxia training (i.e., living low – training high, 71). The following is a systematic description of altitude acclimatization effects in various organs.

Respiration

The respiratory muscles are more effectively trained at altitude than at sea level because of the marked hyperventilation during exercise. The hypoxic ventilatory response increases and remains high during several weeks after descent (44, 63). After 8 days living in hypoxia and training in normoxia a 37% increase in ventilation

during cycling at a fixed velocity in normoxia has been observed (50). Alveolar PO_2 might rise because of both mechanisms and reduce the decrease of arterial O_2-saturation during exhausting exercise. The diffusion capacity of lungs and tissues is proportional to the area occupied by the red cells in the capillaries, which increases with the hematocrit value at altitude. However, after descent this effect plays a role only during few days because the hematocrit value is rapidly normalized (see below).

Heart

Maximal and submaximal exercise cardiac output is reduced at altitude (clearly above 3000 m), probably because of decreased vegetative stimulation (75), following down-regulation of β-adrenoceptors (2). This should result in a negative altitude training effect on the heart. For the right heart, however, this might be compensated for by an increased afterload stress caused by increased resistance resulting from hypoxic vasoconstriction in lung vessels. Another positive effect might also be a stimulation of myocardial capillary growth, which has been observed, with lowering of heart rate in animals (36).

After an initial increase, atrial natriuretic peptide secretion is reduced during altitude acclimatization. Also, atrial stretch receptors may become less sensitive due to chronic distension related to the high pulmonary vascular pressure (3). This might have relevance for blood pressure regulation because atrial natriuretic peptides causes vasodilation and stretch receptors in the atria help trigger increases in blood volume.

Blood

Red cell volume, hemoglobin concentration, and hematocrit increase in male high altitude residents above 2500 m of altitude (16, 72), but the threshold seems to be higher in females (unpublished results). At 2600 m above sea level we have

Table 2. *Change (%) in red cell (RCV) or blood volume (BV) after hypoxia (altitude or low pressure chamber)*

Author	N	RCV	BV	Training
Liesen, Hollmann (48)	3		+ 5	altitude training 1950-2800 m
Böning et al. (11)	11	+ 5	+ 5	ski course 2300 m
Stray-Gundersen (64)	10	+ 8		altitude training 2500 m
Levine, Stray-Gundersen (47)	13	+ 10		altitude training 2500 m.
Harper et al. (32)	134	+ 12		living at sea level, training at 2700 m
Levine et al. (43)	6	+ 12		sea level training, living at 2500 m
Laitinen et al. (41)	7	+ 8		sea level training, living at 2500 m
Levine, Stray-Gundersen (47)	13	+ 5		sea level training. living at 2500 m
Hütler et al. (37)	11	No change		training at 800 m, living at 2000 m
Ashenden et al. (5, 6)	25	No change		training at 600m, living at 2650–3000 m
Böning et al. (2001)	29	+ 16	+ 21	trained vs untrained altitude residents, 2600 m

found an additional 16 percent increase in red cell volume but a return to near normal hemoglobin concentration and hematocrit in medium level male native athletes (16). Short-term altitude training (Table 2) increases red cell volume by 10%, which is only slightly more than the 8% increase observed after sea level training in non-athletes (60). In sojourners as well as in residents, there is only a modest rise in serum erythropoietin concentration (10**,** 13, 16, 61), which suggests an increased sensitivity of erythrocyte precursor cells or additional unknown factors are responsible for the increase in red cell mass. In competitive runners the "live high - train low" method also increased red cell mass (6-11%, 46) - or prevented a decrease - compared to a "live low – train low" group (37). The mean rise in erythropoietin was again small (37, 41).

In spite of the high red cell volume, an increased hemoglobin concentration has been observed only intermittently after a return from altitude (11, 25**,** 30, 31, 38, 49, 64, 65), apparently because of a rapid rise of plasma volume above pre-altitude levels. The cause might be a reduced sensitivity of the atrial stretch receptors that occurs as the hypoxic vasoconstriction ceases. Also, athletes constantly living at altitude possess high plasma volumes (16), which leads to an average 21 % increase in total blood volume. The resulting improved filling of heart and vessels is a positive factor during athletic activity, whereas the expected increase of arterio-venous difference by a rise of the hemoglobin concentration does not occur. Such an increase could be caused by a rightward shift of the oxygen-hemoglobin dissociation curve caused by an increase in 2,3-diphosphoglycerate (DPG) concentration in the red cells at altitude (e.g., 12, 49). After short altitude stays the additional amount of DPG disappears rapidly with the end of the respiratory alkalosis, which had stimulated its formation. During prolonged altitude sojourns, the proportion of young red cells that contain especially high DPG concentrations increases. This change persists for some time after descent (11, 12, 49). The reduction of mean red cell age improves metabolic, buffering and rheologic properties of the red blood cell. But, these effects are also observed after sea level training (60).

Muscle

The commonly held perception that hypoxia increases mitochondrial volume and oxidative enzyme capacity in humans is not consistent with the results of recent studies. In fact, these values decrease at altitudes above 4300 m (35). Similar results were obtained after altitude training (2700 m) as well as training in a low pressure chamber with equal relative exercise intensity (54, 58, 66). Recently, however, Vogt, et al. (71) described an increase of mitochondrial density and mRNA for myoglobin following 6 weeks of hypoxic training (3850 m simulated altitude). Low pressure chamber training at equal absolute workload causes an increased oxidative capacity and myoglobin concentration compared to normoxia (35, 40, 68, 67). Anaerobic metabolic enzymes are unaffected by altitude, except perhaps during the early acclimatization phase and during very severe hypoxia (27); however, the hypoxia training at 3850 m of simulated altitude stimulated the production of mRNA for phosphofructokinase (71).

In older investigations of the capillary network (54, 58, 67, 66), only Mizuno, et al. (54) detected more capillaries after prolonged altitude exposure, but this occurred in subjects who were probably not fully trained during the preceding low level training. In animal experiments, altitude exposure caused an enlargement of the muscle cell surface by tortuosity (undula-

ting surface) but did not stimulate the growth of new capillaries (4). At very high altitude an increase of capillary density only resulted from a decrease in fiber diameter (35). After living low – training high, however, Vogt et al. (71) observed increased mRNA concentrations for the vascular endothelial growth factor and also a greater increase in capillary length density after hypoxia than normoxia training.

Metabolism

The widely-held opinion that fat oxidation increases with altitude acclimatization (73) has been abandoned. If substrate utilization was adapted for the increased metabolic need under hypoxic conditions (56), a decreased fat consumption by the working legs could be demonstrated at 4300 m. Muscle carbohydrate consumption is shifted from glycogen to a higher proportion of blood glucose as fuel and lactate production decreases (8, 17,18,19); this so called lactate paradox disappears approximately 2-3 weeks after descent (33), but the importance for performance and measurements of the anaerobic threshold after return to sea level is unknown. If these results from studies at very high altitude without systematic training may be extrapolated to usual altitude training, is not clear. Also the causes of the metabolic changes are not exactly known. Besides insufficient carbohydrate uptake a dissociation in catecholamine secretion (decrease of epinephrine, increase of norepinephrine), a tighter metabolic control and a better efficiency after acclimatization are discussed (17, 18, 19,20, 27, 28, 33, 51). A high efficiency has been described occasionally for natives (33, 59) and recently for a small group of sojourners after 21 days at 6,194 m (29); it is doubtful if similar changes may occur at moderate altitude after a short stay. A reduced oxygen need during running might be a general characteristic of African athletes, possibly because of biomechanical differences of the legs compared to other races.

The blood ammonia concentration increase during exercise is reduced within 13 days at 4300 m (74), a similar change was observed even 12 days after descent (65). This is an interesting phenomenon since NH_3 may be a cause of fatigue.

Hormones are important for metabolic regulation but they have been rarely investigated after return to sea level. Total and globulin-bound testosterone (69) increased temporarily 3 days after altitude training. Elevated resting concentrations of cortisol after descent might indicate a subclinical overtraining state (70). It is also conceivable that the above mentioned changes of plasma catecholamine levels and in addition a reduced β-adrenoceptor density (2) persist some time after descent. Low pressure chamber training during 5 weeks influenced many endocrine reactions during exercise, but these were not substantially different than absolutely or relatively equivalent intensities of normoxic training (24).

Buffering

At altitude blood buffering becomes less effective because of bicarbonate loss via the kidneys, but the bicarbonate stores are rapidly replenished after descent (12, 13). An increase of the hemoglobin mass as well as a high proportion of young red cells increases the amount of non-bicarbonate buffers in blood and interstitial fluid above prealtitude values. We have observed unexpectedly high extracellular non-bicarbonate buffer capacities during exercise in mountaineers after return to the lowland (15) and in residents at moderate altitude (unpublished results); but this might partly result from differences in lactate and proton transport across muscle cell membranes. Mizuno, et al. (54) and Saltin, et

al. (58) observed a small increase in non-bicarbonate muscle buffer capacity after altitude training which correlated with an improvement of endurance (running for 2-4 min, 54). After expeditions to extreme altitudes loss of muscle mass probably counteracts this improvement: whole body non-bicarbonate buffering (per liter fluid) was reduced in mountaineers after descent (14).

Conclusions

Various physiological changes from acclimatization to hypoxia that persist after descent (e.g., trained respiratory muscles, increased alveolar PO_2, increased blood volume, reduced erythrocyte age, increased mitochondrial volume and capillary length density in muscles, decreased lactate and ammonia concentration, increased buffer capacity) should contribute to improved endurance capacity. The inconsistent effect on performance might result from concomitant deteriorating changes or from unequal disappearance rates of functional adaptations. Also maximal oxygen uptake - which has been measured in most studies - is relatively insensitive to moderate performance capacity changes. Possibly endurance time measurements are better apt to demonstrate an effect.

Other factors affect the advantages and disadvantages of altitude training. Changes in physical and psychic stimuli in the mountains might positively influence the training process. Also an acceleration of training adaptations without increasing levels of maximal performance is conceivable. Banister and Woo (7) observed such accelerations during alternating normoxic and hypoxic training; the intensity was, however, absolutely equal. Sprinters for whom aerobic metabolism is not especially important use the increased speed at altitude following from the low air resistance to train under competition - like conditions.

Negative effects might result from reduced caloric intake and sleep disturbances. To avoid these drawbacks as well as to maintain the exercise intensity at a sufficient level, training altitudes at about 2000 m are preferred. The opinions on other conditions and considerations (e.g., only training or sleeping in hypoxia, best day for competitions after descent, optimal altitude exposure) remain controversial.

Comparisons of sea level natives after altitude training to athletes born and raised at altitude can only be made with caution; the organisms of the latter are influenced by hypoxia lasting for decades and often by genetic adaptations. There are few exceptional findings in these subjects, including improved efficiency, a high activity of the fat-metabolizing enzyme 3-hydroxyacyl-CoA-dehydrogenase, and a low blood concentration of ammonia during exercise at altitude and sea level (58, 59). NH_3 concentration is reduced during short-term acclimatization to hypoxia (74), which may attenuate fatigue and account for the commonly described feeling of an improved sense of well being after altitude training.

References

1. Adams W.C., Bernauer E.M., Dill D.B., Bomar jr. J.B. 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. Antezana A.M., Richalet J.P., Antezana G., et al. Adrenergic system in high altitude residents. Int. J. Sports Med. 13: S96-S100, 1992.
3. Antezana A.M., Richalet J.P., Noriega I., et al. Hormonal changes in normal and polycythemic high-altitude natives J. Appl. Physiol. 79: 795-800, 1995.
4. Appell H.J. Morphological studies on skeletal muscle capillaries under conditions of high altitude training. Int. J. Sports Med. 1: 103-109, 1980.
5. Ashenden M.J., Gore C.J., Martin D.T., et al. 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. 80: 472-488, 1999.
6. Ashenden M.J., Gore C.J., Dobson G.P., Hahn A.G. "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.80: 479-484, 1999.
7. Banister E.W., Woo W. Effects of simulated altitude training on aerobic and anaerobic power. Eur. J. Appl. Physiol. 38: 55-69, 1978.
8. Bender P.R., Groves B.M., McCullough R.E., et al. Decreased exercise muscle lactate release after high altitude acclimatization. J. Appl. Physiol. 67: 1456-1462, 1989.
9. Benoit H., Germain M., Barthélémy J.C., et al. Pre-acclimatization to high altitude using exercise with normo-baric hypoxic gas mixtures. Int. J. Sports Med. 13: S213-S216, 1992.
10. Berglund B. High-altitude training. Aspects of haematological adaption. Sports Med. 14: 289-303, 1992.
11. Böning D. Wirkungen eines akuten Sauerstoffmangels auf die Blutelektrolytkonzentrationen bei höhenangepaßten und nicht höhenangepaßten Menschen. Pflügers Arch. 314: 217-230, 1970.
12. Böning D., Trost F., Braumann K.M., et al. Altitude acclimatization in skiing lowlanders. Int. J. Sports Med. 1: 191-198, 1980.
13. Böning D., Maassen N., Jochum F., et al. After-Effects of High Altitude on Blood. Int. J. Sports Med. 18: 179-185, 1997.
14. Böning D., Maassen N., Steinacker J., et al. Carbon dioxide storage and nonbicarbonate buffering in the human body before and after an Himalayan expedition. Eur. J. Appl. Physiol. 79: 457-466, 1999.
15. Böning D, Steinacker J., Maassen N., Thomas A. Extracellular pH defense against lactic acid in normoxia and hypoxia before and after a Himalayan expedition. Eur. J. Appl. Physiol. 84: 78-86, 2001.
16. Böning D., Rojas J., Serrato M., et al. Hemoglobin mass and peak oxygen uptake in untrained and trained residents of moderate altitude. Int. J. Sports Med. 22: 572-578, 2001.
17. Brooks G.A., Butterfield G.E., Wolfe R.R., et al. Increased dependence on blood glucose after acclimatization to 4,300 m. J. Appl. Physiol. 70: 919-927, 1991.
18. Brooks G.A., Butterfield,G.E., Wolfe R.R., et al. Decreased reliance on lactate during exercise after acclimatization to 4,300 m. J. Appl. Physiol. 71: 333-341, 1991.
19. Brooks G.A., Wolfel E.E., Groves B.M., et al. Muscle accounts for glucose disposal but not blood lactate appearance during exercise after acclimatization to 4,300 m. J. Appl. Physiol. 72: 2435-2445, 1992.
20. Buskirk E.R., Kollias J., Akers R.F., et al. Maximal performance at altitude and on return from altitude in conditioned runners. J. Appl. Physiol. 23: 259-266, 1967.
21. Chapman R.F., Stray-GundersenJ., Levine B.D. Individual variation in response to altitude training. J. Appl. Physiol. 85: 1448-1456, 1998.
22. Dehnert Ch., Peterle C., Lormes W., et al. Effect of sleep-high/training low on performance and wellbeing in well trained triathletes. Med. Sci. Sports Exerc. 29: S136, 1997.
23. Emonson D.L., Aminudin A.H.K., Wight R.L., et al. Training-induced increase in sea level $\dot{V}O_2$max and endurance are not enhanced by acute hypobaric exposure. Eur. J. Appl. Physiol. 76, 8-12, 1997.
24. Engfred K., Kjaer M., Secher N.H., et al. Hypoxia and training-induced adaptation of hormonal responses to exercise in humans. Eur. J. Appl. Physiol. 68: 303-309, 1994.
25. Faulkner J.A., Daniels J.T., Balke B. Effects of training at moderate altitude on physical performance capacity. J. Appl. Physiol. 23: 85-89, 1967.
26. Favier R., Spielvogel H., Desplanches D., et al. Training in hypoxia vs. training in normoxia in high-altitude natives. J. Appl. Physiol. 78: 2286-2293, 1995.
27. Green H. J. Adaptations at extreme altitude: metabolic implications during exercise. Int. J. Sports Med. 13, Suppl 1: S163-S165, 1992.
28. Green H.J., Sutton J.R., Wolfel E.E., et al. Altitude acclimatization and energy metabolic adaptations in skeletal muscle during exercise. J. Appl. Physiol. 73: 2701-2708, 1992.
29. Green H.J, Roy B, Grant S., et al. Increases in submaximal cycling efficiency mediated by altitude acclimatization. J. Appl. Physiol. 89: 1189-1197, 2000.
30. Hansen J.E., Vogel J.A., Stelter G.P., Consolazio C.F. Oxygen uptake in man during exhaustive work at sea level and high altitude. J. Appl. Physiol. 23: 511-522, 1967.
31. Haralambie G., Keul J., Theumert F. Protein-, Eisen- und Kupfer-Veränderungen im Serum bei Schwimmern vor und nach Höhentraining. Eur. J. Appl. Physiol. 35: 21-31, 1976.
32. Harper K.M., Stray-Gunderson J., Schecter M.B., Levine B.D. Training at moderate altitude causes profound hypoxemia during exercise in competitive runners. Med. Sci. Sports Exerc. 27: S110, 1995.
33. Hochachka P.W., Stanley C., Matheson G.O., et al. Metabolic and work efficiencies during

exercise in Andean natives. J. Appl. Physiol. 70: 1720-1730, 1991.
34. Hollmann W., Liesen H. The influence of hypoxia and hyperoxia training in a laboratory on the cardio-pulmonary capacity. In: Keul, J. (Ed) *Limiting factors of physical performance*. Thieme Stuttgart 1973.
35. Hoppeler H., Desplanches D. Muscle structural modifications in hypoxia. Int. J. Sports Med. 13: S166-S168, 1992.
36. Hudlicka O., Brown, M.D., Walter H., et al. Factors involved in capillary growth in the heart. Mol. Cell. Bioch. 147: 57-68, 1995.
37. Hütler M., Schick R., Dehnert C., et al. „Sleep high-train low", effects of the hypoxia component. Int. J. Sports Med. 19: S17, 1998.
38. Ingjer F., Myhre K. Physiological effects of altitude training on elite male cross-country skiers. J. Sports Sciences 10: 37-47, 1992.
39. Jackson C.G.R., Sharkey B.J. Altitude, training and human performance. Sports Med. 6: 279-284, 1988.
40. Jansson E., Terrados N., Norman B., Kaijser L. Effects of training at simulated high altitude on exercise at sea level. Scand. J. Med. Sci. Sports 2: 2-6, 1992.
41. Laitinen H., Alopaeus K., Heikkinen R., et al. Acclimatization to living in normobaric hypoxia and training in normoxia at sea level in runners. Med. Sci. Sports Exerc. 27, Suppl 5: S109, 1995.
42. Levine B.D., Engfred K., Friedman D.B., et al. High altitude endurance training: effect on aerobic capacity and work performance. Med. Sci. Sports Exerc. 22: S35, 1990.
43. Levine B.D., Stray-Gundersen J., Duhaime G., et al. „Living high - training low": The effect of altitude acclimatization/normoxic training in trained runners. Med. Sci. Sports Exerc. 23: S25, 1991.
44. Levine B.D., Friedman D.B., Engfred K., et al. The effect of normoxic or hypobaric endurance training on the hypoxic ventilatory response. Med. Sci. Sports Exerc. 24: 769-775, 1992.
45. Levine B.D., Stray-Gundersen J. A practical approach to altitude training: where to live and train for optimal performance enhancement. Int. J. Sports Med. 13: S209-S212, 1992.
46. Levine B.D., Friedmann B., Stray-Gundersen J. Confirmation of the „high-low" hypothesis: living at altitude-training near sea level improves sea level performance. Med. Sci. Sports Exerc. 28: S124, 1996.
47. Levine B.D., Stray-Gundersen J. „Living high-training low": effect of moderate-altitude acclimatization with low-altitude training on performance J. Appl. Physiol. 83: 102-112, 1997.
48. Liesen H., Hollmann W. Der Einfluß eines zweiwöchigen Höhentrainings auf die Leistungsfähigkeit im Flachland, gemessen an spiroergometrischen und metabolischen Parametern. Sportarzt Sportmed. 8: 157-161, 1972.
49. Mairbäurl H., Schobersberger W., Humpeler E., et al. Beneficial effects of exercising at moderate altitude on red cell oxygen transport and on exercise performance. Pflügers Arch. 406: 594-599, 1986.
50. Mattila V., Rusko H. Effect of living high and training low on the sea level performance in cyclists. Med. Sci. Sports Exerc. 28: S156, 1996.
51. Mazzeo R.S., Bender P.R., Brooks G.A., et al. Arterial catecholamine response with acute and chronic high-altitude exposure. Am. J. Physiol. 261: E419-E424, 1991.
52. Meller W., Mellerowicz H., Lübs E., Kieper C. Vergleichende Untersuchungen über Wirkungen von Kurz- und Langausdauertraining in der Höhe an eineiigen Zwillingen. Sportarzt Sportmed. 27: 232-238, 1976.
53. Mellerowicz H., Meller W., Woweries J., et al. Vergleichende Untersuchungen über Wirkungen von Höhentraining auf die Dauerleistung in Meereshöhe. Sportarzt Sportmed. 21: 207-240, 1970.
54. Mizuno M., Juel C., Bro-Rasmussen Th., et al. Limb skeletal muscle adaptation in athletes after training at altitude. J. Appl. Physiol. 68: 496-502, 1990.
55. Nummela A., Jouste P., Rusko H. Effect of living high and training low on sea level anaerobic performance in runners. Med. Sci. Sports Exerc. 28: S124, 1996.
56. Roberts A.C., Butterfield G.E., Cymerman A., et al. Brooks G.A. Acclimatization to 4,300-m altitude decreases reliance on fat as a substrate. J. Appl. Physiol. 81: 1762-1771, 1996.
57. Roskamm H., Landry F.,Samek L., et al. Effects of a standardized ergometer training program at three different altitudes. J. Appl. Physiol. 27: 840-847, 1969.
58. Saltin B., Kim C.K., Terrados N., et al. Morphology, enzyme activities and buffer capacity in leg muscles of Kenyan and Scandinavian runners. Scan. J. Med. Sci. Sports 5: 222-230, 1995.
59. Saltin B., Larsen H., Terrados N., et al. Aerobic exercise capacity at sea level and at altitude in Kenyan boys, junior and senior runners compared with Scandinavian runners. Scan. J. Med. Sci. Sports 5: 209-221, 1995.
60. Schmidt W., Maassen N., Trost F., Böning D. Training induced effects on blood volume, erythrocyte turnover and haemoglobin oxygen binding properties. Eur. J. Appl. Physiol. 57: 490-498, 1988.
61. Schmidt W., Eckardt K., Hilgendorf A., et al. Effects of maximal and submaximal exercise under normoxic and hypoxic conditions on serum erythropoietin level. Int. J. Sports Med. 12: 457-461, 1991.
62. Semenza G L.HIF-1: mediator of physiologi-

cal and pathophysiological responses to hypoxia J. Appl. Physiol., 88: 1474 1480, 2000.
63. Steinacker J.M., Halder A., Liu Y., et al. Hypoxic ventilatory response during rest and exercise after a Himalaya expedition. Eur. J. Appl. Physiol. 73: 202-209, 1996.
64. Stray-Gundersen J., Alexander C., Hochstein A., et al. Failure of red cell volume to increase to altitude exposure in iron deficient runners. Med. Sci. Sports Exerc. 24: S90, 1992.
65. Svedenhag J., Saltin B., Johansson C., Kaijser L. Aerobic and anaerobic exercise capacities of elite middle-distance runners after two weeks of training at moderate altitude. Scan. J. Med. Sci. Sports 1: 205-214, 1991.
66. Terrados N., Melichna J., Jansson E., Kaijser L. Effects of training at simulated altitude on performance and muscle metabolic capacity in competitive road cyclists. Eur. J. Appl. Physiol. 57: 203-209, 1988.
67. Terrados N., Jansson E., Sylven C., Kaijser L. Is hypoxia a stimulus for synthesis of oxidative enzymes and myoglobin? J. Appl. Physiol. 68: 2369-2372, 1990.
68. Terrados N. Altitude training and muscular metabolism. Int. J. Sports Med. 13, Suppl 1: S 206-S209, 1992.
69. Tsai L., Pousette Ĺ., Carlström K., et al. Anabolic and catabolic hormonal response of elite runners to training at high altitude. Scand. J. Med. Sci. Sports 2: 10-15, 1992.
70. Vasankari T.J., Rusko H., Kujala U.M., Huhtaniemi I.T. The effect of ski training at altitude and racing on pituitary, adrenal and testicular function in men. Eur. J. Appl. Physiol. 66: 221-225, 1993.
71. Vogt M., Puntschart A., Geiser J., et al. Molecular adaptions in human skeletal muscle to endurance training under simulated hypoxic conditions. J. Appl. Physiol. 91: 173-182, 2001
72. Weil J.V., Jamieson G., Brown D.W., Grover R.F. The red cell mass - arterial oxygen relationship in normal man. J. Clinical Invest. 47: 1627-1639, 1968.
73. Young A.J., Evans W.J., Cymerman A., et al. Sparing effect of chronic high-altitude exposure on muscle glycogen utilization. J. Appl. Physiol. 52: 857-862, 1982.
74. Young P.M., Rock P.B., Fulco Ch.S., et al. Altitude acclimatization attenuates plasma ammonia accumulation during submaximal exercise. J. Appl. Physiol. 63: 758-764, 1987.
75. Young A.J., Young P.M. Human acclimatization to high terrestrial altitude, In: Pandolf, K.B., Sawka, M.M., Gonzales, R.R. (Eds) *Human performance physiology and environmental medicine at terrestrial extremes.* Benchmark Press inc., Indianapolis, 1988, pp. 497-543.

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