

General introduction to altitude adaptation and mountain sickness

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The key elements in acclimatization aim at securing the oxygen supply to tissues and organs of the body with an optimal oxygen tension of the arterial blood. In acute exposure, ventilation and heart rate are elevated with a minimum reduction in stroke volume. In addition, plasma volume is reduced over 24–48 h to improve the oxygen-carrying capacity of the blood, and is further improved during a prolonged sojourn at altitude through an enhanced erythropoiesis and larger Hb mass, allowing for a partial or full restoration of the blood volume and arterial oxygen content. Most of these adaptations are observed from quite low altitudes [~ 1000 m above sea level (m a.s.l.)] and become prominent from 2000 m a.s.l. At these higher altitudes additional adaptations occur, one being a reduction in the maximal heart rate response and consequently a lower peak cardiac output. Thus, in spite of a normalization of the arterial oxygen content after 4 or more weeks at altitude, the peak oxygen uptake reached after a long acclimatization period is essentially unaltered compared with acute expo-

sure. What is gained is a more complete oxygenation of the blood in the lungs, i.e. SaO₂ is increased. The alteration at the muscle level at altitude is minor and so is the effect on the metabolism, although it is debated whether a possible reduction in blood lactate accumulation occurs during exercise at altitude. Transient acute mountain sickness (headache, anorexia, and nausea) is present in 10–30% of subjects at altitudes between 2500 and 3000 m a.s.l. Pulmonary edema is rarely seen below 3000 m a.s.l. and brain edema is not seen below 4000 m a.s.l. It is possible to travel to altitudes of 2500–3000 m a.s.l., wait for 2 days, and then gradually start to train. At higher altitudes, one should consider a staged ascent (average ascent rate 300 m/day above 2000 m a.s.l.), primarily in order to sleep and feel well, and minimize the risk of mountain sickness. A new classification of altitude levels based on the effects on performance and well-being is proposed and an overview given over the various modalities using hypoxia and altitude for improvement of performance.

Acute adjustments and acclimatization to various altitudes

Immediate adjustments and acclimatization to altitude involve the respiratory and the cardiovascular system, the oxygen-carrying capacity of the blood and, more gradually, some possible morphologic and functional adaptations in the skeletal muscle. The threshold altitude and the magnitude of the responses vary considerably between the different systems and also show a large inter-individual variability. The effects of various altitudes and of acclimatization on the different links in the oxygen transport chain of the human body are summarized in Fig. 1 and briefly discussed in order to establish the basis for proposing a classification of altitude levels with relevance to health and performance. The effects on mountain sickness in its various forms are shown in Fig. 2.

Ventilation and gas exchange

After an initial rise, ventilation continues to increase over 10–14 days due to increasing sensitivity of the

peripheral chemoreceptors to hypoxia. This results in a substantial increase in arterial oxygen saturation during the first 2 weeks at a given altitude. Increased ventilation at altitude causes respiratory alkalosis that is fully counter-regulated within 1 day at 2200 m above sea level (m a.s.l.) (Dempsey et al., 1972) while remaining incomplete at an altitude of 4100 m a.s.l. (Lundby et al., 2004a) or higher (Wagner et al., 2002). Full and partial-to-full compensation of respiratory alkalosis is accomplished by increased renal bicarbonate excretion, resulting in a reduced buffer capacity of plasma (Böning et al., 2008). Although acid–base balance is restored rapidly in blood at moderate altitudes, it may take longer at the cellular level, which contributes to the observation that intense exercise is difficult to perform within the first 2–3 days at altitudes of 2000 m a.s.l. or higher.

PaO₂ and consequently SaO₂ decrease during exercise at altitude because of a diffusion limitation predominantly due to lower alveolar PO₂ and increased pulmonary blood flow with exercise. This drop will be larger in endurance-trained athletes

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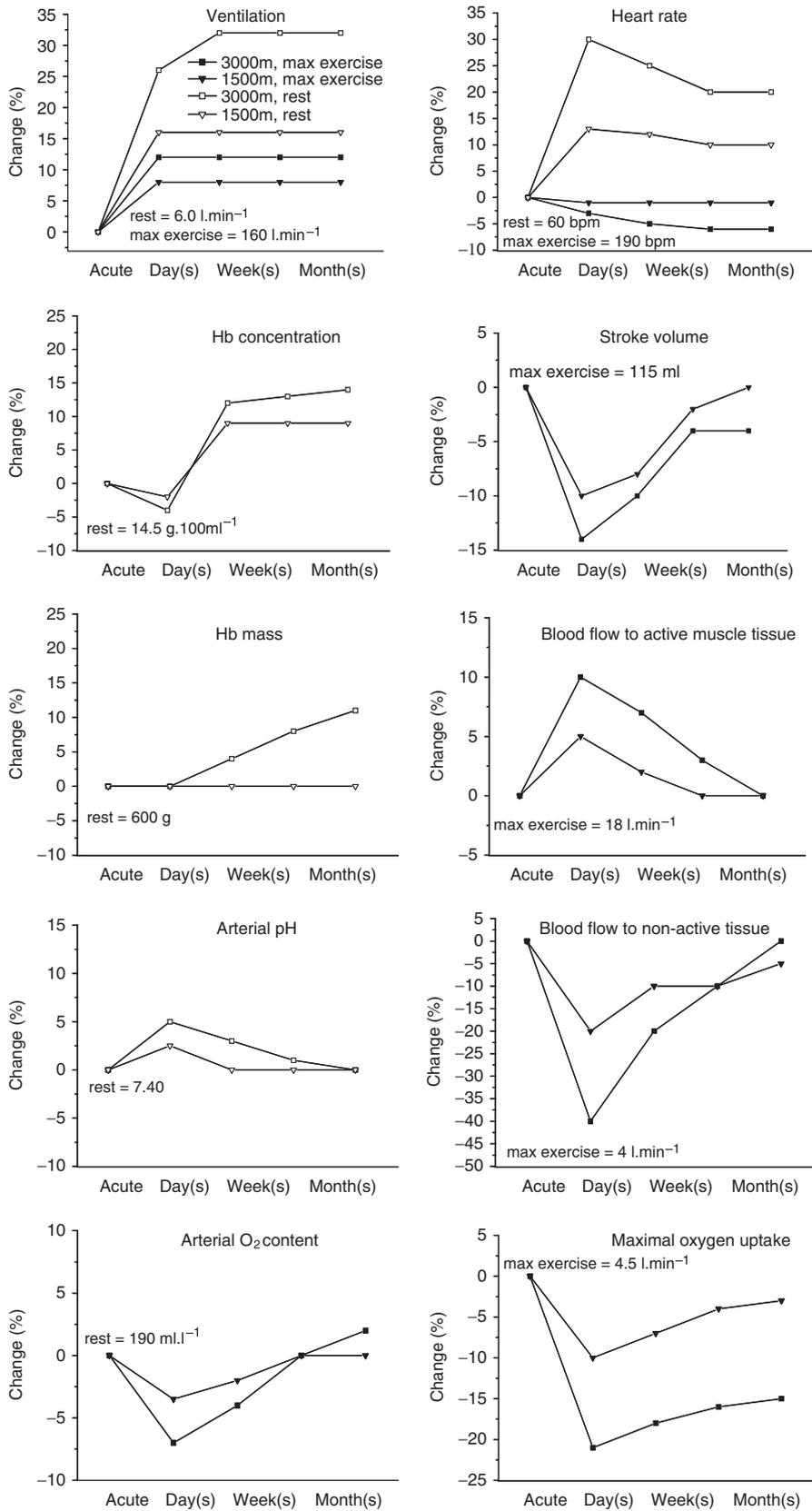


Fig. 1. In this composite graph a schematic summary is given for how key variables are altered as an effect of two altitudes (1500–2000 and 3000–3500 m a.s.l.). The x-axis denotes the time scale and the y-axis denotes relative changes, using sea level as baseline.

because of their higher maximal cardiac output, which is already apparent at an altitude of 580 m a.s.l. (Gore et al., 1996). In athletes (Wehrin & Hallén, 2005) with a sea-level VO_{2max} of 66 mL/kg/

min, SaO_2 (at maximum exercise measured by pulse oximetry) was 86% and 76% at altitudes of 800 and 2800 m a.s.l., respectively. In comparison, SaO_2 was 83% at 3050 m in untrained individuals (Wagner

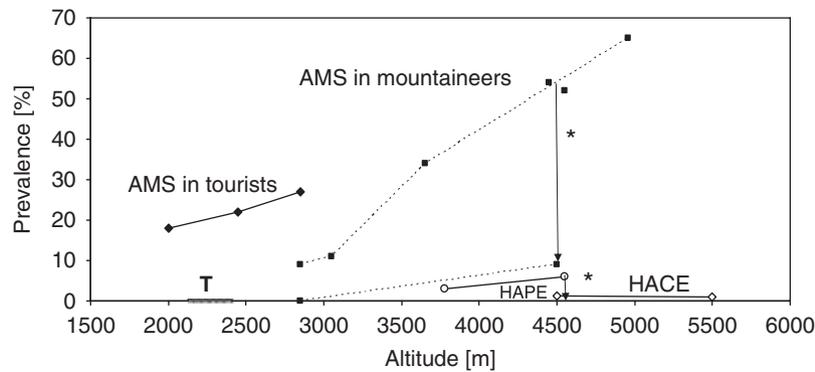


Fig. 2. Prevalence of acute high-altitude illnesses at various altitudes. *T* indicates the threshold altitude range for symptoms induced by hypoxia at rest (Muhm et al., 2007) and asterisk indicates effects of acclimatization and slow ascent. Data from Honigman et al. (1993), Maggiorini et al. (1990), Schneider et al. (2002), Dumont et al. (2000) (AMS), Bärtsch and Roach (2001), Bärtsch et al. (2002), and Schoene et al. (2001) (HACE and HAPE). AMS, acute mountain sickness; HACE, high-altitude cerebral edema; HAPE, high-altitude pulmonary edema.

et al., 1986) and as low as 73% at 4100 m in subjects with a sea-level $\text{VO}_{2\text{max}}$ of 56 mL/kg/min (Lundby et al., 2004a). In this latter group, SaO_2 increased to 76% and 79% after 2 and 8 weeks of acclimatization.

Independent of symptoms of acute mountain sickness (AMS; Fig. 2), sleep is disturbed in 50% of the subjects at 4559 m because of periodic breathing, which may occur during 60% of sleep time (Eichenberger et al., 1996) and may persist after acclimatization (Anholm et al., 1992). Even in athletes sleeping in moderate normobaric hypoxia, minor but persistent disturbances of sleep occur, expressed as a minor change of sleep architecture in EEG recordings at 2000 m a.s.l. (Koehle et al., 2007) or as an increase of arousals from 15 to 21 events per night at 2650 m a.s.l. (Kinsman et al., 2005) and an increase of apnoeas and hypopnoeas from 4 to 37 events per hour at 2500 m (Pedlar et al., 2005). In these studies, subjective assessment of sleep quality was not significantly affected, which is in agreement with findings in a study that progressively increased sleep altitude from 2500 to 3500 m a.s.l. in 500 m increments every five to six nights (Brugniaux et al., 2006). Sleep quality is, however, reduced by 26% and 44% at 3050 and 3500 m a.s.l. in non-acclimatized mountaineers (Maggiorini et al., 1990).

Blood

Hemoglobin concentration increases because of a rapid reduction of plasma volume and a delayed effect of increased erythropoiesis (Grover et al., 1986; Svedenhag et al., 1997; Lundby et al., 2007b). The combination of ventilatory acclimatization and increased oxygen-carrying capacity may lead to an oxygen content of arterial blood after acclimatization that is higher than at sea level, which is also the case at higher altitudes (Calbet et al., 2003b). A significant increase in red blood cell mass may already occur after 3 weeks at a minimum altitude

of 2100 m a.s.l. (Schmidt & Prommer, 2008), getting more pronounced as altitude increases (Lundby et al., 2006; see also Schmidt & Prommer, 2008). Repeated measurements of plasma volume during the early phase of an altitude stay are not available. However, with the very slow rate of increasing the Hb mass, the measure of Hb concentration is a good indicator of plasma volume changes. During the first 24–48 h, at even a low altitude (1500–2000 m a.s.l.), Hb concentration is elevated by 0.5–1.0 g/100 mL blood, which may correspond to a loss of plasma water of 0.2–0.3 L. At 3000 and 4000 m a.s.l., the rise in Hb concentration may amount to another 0.5–0.8 g/100 mL per 1000 m, indicating a decrease in plasma volume of 0.6–0.9 L (Saltin, 1966; Svedenhag et al., 1997; Calbet et al., 2004).

Cardiovascular system

Despite a continuing increase in sympathetic activity over time at high altitude (Hansen & Sander, 2003), maximum heart rate decreases with increasing altitude because of an increased vagal tone (Boushel et al., 2001) and also possibly because of the down-regulation of β -receptors (Richalet et al., 1988b; see also Favret & Richalet, 2007). There is an ongoing discussion about the altitude at which a drop in maximal heart rate occurs and the time frame in which, after the transition to the hypoxic condition, a lowered maximal heart rate occurs. In a study of the acute response to 4000 m a.s.l., no reduction in either cardiac output or maximal heart rate were found, resulting in a maintained stroke volume (Stenberg et al., 1966). However, it may be a question of hours before hypoxia elicits its effect. It appears that already after 4 h an effect can be observed, and after 8 h it is quite manifest, and the maximal heart rate continues to decrease in the days thereafter (Saltin, 1996; Lundby et al., 2001). While Lundby et al. (2001) did not find this reducing effect on the heart

rate at 3300 m a.s.l. in a small group of five subjects, other investigators reported a reduced maximal heart rate at 520 mmHg (about 3000 m a.s.l.) (Koistinen et al., 1995), at 15% O₂ (corresponding to about 2500 m a.s.l.) (Friedmann et al., 2005) and as low as 580 mmHg (about 2100 m a.s.l.) (Saltin, 1996). There appears to be considerable inter-individual variation in the heart rate response at moderate altitude (Friedmann et al., 2005). The practical importance is that the athletes easily train at a higher altitude at an intensity that is too high if they are guided by their heart rate that is not adjusted for the possible change in maximal heart rate. This is reinforced by the fact that the submaximal exercise heart rate response is elevated at low to high altitude (Fig. 1).

The reduction in maximal heart rate at more severe hypoxia has been explained by a lowering of the work of the heart and the demand for a high myocardial oxygen consumption, as the rate–pressure product will be lower. A limitation to this explanation is the finding that the heart rate is not fully reaching sea-level peak values when the oxygen content of the arterial blood is acutely elevated during the acclimatization period (Åstrand & Åstrand, 1958; Boushel et al., 2001; Lundby et al., 2007a). It can be argued that what triggers the regulation is O₂ tension rather than O₂ content, although it is the latter variable that really counts with regard to oxygen supply. An alternative explanation is that the lowering of the maximal heart rate means a lower pulmonary blood flow and an increased mean transit time for the red cells passing through the lungs, especially at peak exercise. This allows for an optimal oxygenation of the blood while passing the lungs and thereby secures an optimal saturation of the arterial blood (see Boushel et al., 2001).

It is of note that the low O₂ tension does not appear to impair a good performance of the heart even at extremely high altitudes (Saltin et al., 1968). It is true that stroke volume is lower at altitude and contributes somewhat to the lowered cardiac output at maximal effort (Saltin et al., 1968). This is primarily due to less optimal filling conditions for the heart, as plasma volume and central blood volume are affected by the acclimatization period (Calbet et al., 2002, 2003a). Direct support for this view was, however, not obtained in studies where plasma volume was restored without affecting the peak cardiac output (Calbet et al., 2004). Filling pressures were not measured and direct evaluation of the heart dynamics was not performed in any of these studies, which means that at present a well-founded explanation cannot be provided.

Pulmonary artery pressure starts to rise because of hypoxic vasoconstriction at an altitude of approximately 3000 m a.s.l. in healthy individuals. Pulmonary artery pressure rises by about 60% (Bärtsch et al., 1991) and systemic blood pressure increases during 20

days at 4300 m a.s.l. because of increasing sympathetic activity (Reeves et al., 1992). At moderate altitude, however, significant changes in blood pressure are unlikely to occur because it does not change or decrease in exercising patients with metabolic syndrome at an altitude of 2000 m a.s.l. (Mair, 2007).

Skeletal muscle

Muscle function and morphology

Hypoxia has been proposed as a key inducer of adaptation in skeletal muscle not only at altitude but also with physical training (for reference, see Saltin & Gollnick, 1983; Baar, 2006). This discussion was further supported by studies on guinea-pigs in the Andes and in Lima, which found that animals in the Andes had more capillaries and mitochondrial enzymes than animals living in Lima (Reynafarje, 1962). These results have not been confirmed either in humans or in rats (Saltin & Gollnick, 1983; Lundby et al., 2004b). An explanation of the early findings was probably that the animals living at altitude were free to run around in a fairly well-sized yard, whereas the animals in Lima were kept in cages. It is likely, thus, that the activity rather than the hypoxia caused the observed adaptations. These data demonstrate that the muscle can adapt at altitude, but to what extent hypoxia is a major player is more uncertain.

There is almost a consensus among scientists in the field that mitochondrial enzyme activities are unaltered or possibly lowered during a prolonged stay at altitude (Saltin & Gollnick, 1983; Saltin, 1996; Hoppeler et al., 2003; Howald & Hoppeler, 2003; Mizuno et al., 2008). In contrast, several muscle-related proteins involved in the transport of bicarbonate, hydrogen ions, and lactate are up-regulated in hypoxia, and the same is true for the red cell membrane proteins (Juel et al., 2003). These adaptations markedly augment the transport capacity of these ions, which in turn improve the dynamics of maintaining the acid–base balance at altitude. The sodium–potassium pump may be down-regulated in skeletal muscle (Green et al., 1999). Whether this change has a functional significance has not been tested; however, it might limit the propagation of the action potential in the muscle fiber (Juel, 1986). What is known, however, is that time to exhaustion during short-term exercise is improved after a stay at altitude (Mizuno et al., 1990). The explanation is probably either an improved muscle buffer capacity or other non-hematological adaptations in the muscle (Mizuno et al., 1990, 2008; Gore et al., 2007).

More of a controversy is the effect of hypoxia on the degree of capillarization. This is in part related to the fact that HIF-1 α is affected by hypoxia and believed to be an inducer of elevating VEGF (Rundq-

vist, 2008). However, when studying VEGF expression in human skeletal muscle, VEGF mRNA is not enhanced (Lundby et al., 2004b). This is in agreement with many studies in rats and humans, showing that muscle capillarization is not increased when expressed as number of capillaries per fiber (Sillau & Banchemo, 1978; Mizuno et al., 1990). It is true that the number of capillaries per unit of area can be higher, especially at higher altitudes. The experiments on rats have given indications of the fibers changing shape toward ellipsoid rather than circular, thereby reducing the distance to the center of the muscle fiber (Sillau & Banchemo, 1977). The explanation is that the muscle fiber size is often reduced at altitude. This reduction in cross-sectional area of the muscle fiber may amount to 20–30% above 4000 m a.s.l. (see Saltin & Gollnick, 1983; Mizuno et al., 2008; see also Hoppeler et al., 2008). The number of capillaries per unit area will be elevated correspondingly. Before addressing the question of muscle fiber hypotrophy at altitude, it should be stated that muscle fiber types are essentially unaffected by hypoxia based on the results of a large number of studies cited above.

The question to be answered is whether the reduction in muscle fiber size at altitude is a reflection of the loss in body weight when staying at high altitude. It is common to relate this reduction in body weight to a lack of appetite and proper food combined with a high-energy turnover. A study by Butterfield et al. (1992) on well-fed subjects at Pike Peak demonstrated that it was possible to maintain body weight at that altitude (just above 4000 m a.s.l.). Unfortunately they did not determine fat content and muscle mass, giving no insights to the raised question. In fact no study is available where body composition has been determined before and after a stay at high altitude. In two studies, body weight was maintained at altitude and muscle fiber size was measured. In one, sea-level residents lived for an average of 32 weeks at 3700 m a.s.l. and kept reasonably physically active. Muscle fiber size in the legs was reduced by 10–15% (Saltin & Gollnick, 1983). In the other study, subjects stayed at 4100 m a.s.l. for 8 weeks. Leg muscle fiber size tended to become reduced by 8% (Lundby et al., 2004b). Reviewing a large set of studies, it appears that muscle fiber size is not reduced below an altitude of 3500 m a.s.l., but the higher the altitude, the sooner and more pronounced the hypotrophy observed. Indirect investigations of the protein turnover in the whole body of man with a stable isotope technique show that both protein degradation and synthesis rates were unaffected by hypoxia at 4500 m a.s.l. (Lundby et al., 2008). This may imply that the primary reason for muscle fibers to be reduced in size is malnutrition and lowered activity level. It is worth noting, however, that in the Lundby study the subjects were both physically active and ate well.

Muscle metabolism

It is generally believed that, at altitude, carbohydrates are the preferred substrate by the muscle during exercise and that there is a lowered fat combustion compared with at sea level (Brooks et al., 1991, 1992). There are also studies at high altitude suggesting that glucose administration during prolonged physical activity is beneficial (Fulco et al., 2005). The hypoxia, in part through elevated adrenalin levels in the blood, stimulates glycolysis and increases the availability of pyruvate either for further oxidation in the mitochondria or for lactate production (Roberts et al., 1996). Moreover, as O₂ is limited, the muscle and the body will gain more energy from each gram of carbohydrate being metabolized in the mitochondria than from a gram of fatty acids. The problem is, however, that in these studies proper correction for the lowered maximal oxygen uptake was not made. In other words, the comparison has not been performed at the same relative work intensity. If that is done there is no real difference, at least not up to an altitude of 4100 m a.s.l. (Saltin, 1996; Lundby & van Hall, 2002).

Another controversy is the blood lactate response to exercise at altitude. There is a consensus that at acute exposure to altitude there is an exaggerated lactate response for a given workload. During prolonged exposure to altitude the so-called lactate paradox states that during an acclimatization period, maximal lactate concentration is reduced and the submaximal lactate levels tend to or are also reduced when compared at the same relative workload. The phenomenon is observed at higher altitudes and barely or not at all below 2–2500 m a.s.l. (Dill et al., 1931; West, 1986; Saltin, 1996).

The lactate paradox concept has been challenged and has been the subject of intense debates in two journals in 2007 (van Hall, 2007; Wagner & Lundby, 2007; West, 2007). No agreement between those engaged in the debate has been reached. This is unfortunate, but the fact that the difference in findings cannot be explained is even more of a challenge. To measure blood lactate concentration at rest and during exercise even in a field setting is not too difficult. One suggestion is that the exercise paradigm, exercise time, and blood sampling site or time after the exercise may lead to an erroneous conclusion regarding the lactate response (van Hall, 2007). Practically, the question is of minor importance at low and medium altitude.

VO_{2max}

Aerobic performance decreases with altitude. VO_{2max} is significantly decreased in highly trained athletes already at 600 m a.s.l. (Gore et al., 1997). One study in endurance athletes finds a linear decrease between

300 and 2800 m a.s.l. of about 6% per 1000 m (Wehrlin & Hallén, 2005), whereas aerobic performance decreases at a rate of 1% per 100 m gain in altitudes above 1500 m in non-trained or only slightly trained individuals (Fulco & Cymerman, 1998). In trained and untrained individuals there is considerable inter-individual variability of the altitude-induced reduction of aerobic performance (Friedmann et al., 2005). It has been shown that acclimatization improves sub-maximum performance substantially at altitudes <4300 m a.s.l. (Fulco et al., 2005). Relevant improvement of $\text{VO}_{2\text{max}}$ with acclimatization may occur up to 2340 m a.s.l. (Saltin, 1996; Schuler et al., 2007); however, it is usually not observed in studies at higher altitudes (Maher et al., 1974; Calbet et al., 2003b; Lundby et al., 2004a; Fulco et al., 2005). The reduction in $\text{VO}_{2\text{max}}$ of about 45% with acute exposure to 5300 m a.s.l. may be explained by almost equal contributions of reduced inspiratory PO_2 , impaired gas exchange, and a reduction in cardiac output and peak leg blood flow (Calbet et al., 2003a). The persistent reduction of $\text{VO}_{2\text{max}}$ at this altitude after acclimatization, despite normalization of oxygen content, is explained by a failure of cardiac output to normalize and by the fact that more of the blood flow is directed to non-exercising tissues (see Fig. 1 and Calbet et al., 2003b). As a consequence of the reduced aerobic capacity, endurance training with an identical absolute workload at different altitudes always translates to a more intense training at the higher altitude expressed in percentage of $\text{VO}_{2\text{max}}$.

Modalities of training

Classic high-altitude training involves living and training at altitudes between 2000 and 2800 m a.s.l. for a period of 2–4 weeks. *Living high and training low*, introduced by Levine & Stray-Gundersen (1997), consists of living about 20 h/day at an altitude of 2800 m a.s.l. and training at an altitude of 1200 m a.s.l., which already impairs maximum aerobic performance in well-trained subjects. The original high–low concept has been modified by the same group to performing only interval training at low altitude, while all other training and living takes place at moderate altitude (Stray-Gundersen et al., 2001; Wehrlin et al., 2006; see also Friedmann et al., 2008).

The concept of high–low was taken to near sea level by building houses in which ambient PO_2 can be decreased either by adding nitrogen to the ambient air or by hypobaria. When a whole house (or a room) is available with such an environment it is possible for athletes to spend more than half a day in hypoxia, which is usually equivalent to an altitude of about 2500 m. A further modification of the high–low concept is to reduce exposure time to hours spent sleeping at night under a tent (*sleep high, train low*).

The daily exposure to hypoxia with sleeping high and training low is therefore reduced to only about 8 h, which is considerably less compared with the original concept of high–low, while the level of hypoxia is still comparable (Wilber, 2001; see also Stray-Gundersen et al., 2008).

Recently, shorter applications of hypoxia at rest during daytime have been suggested for improvement of sea-level performance. This modality allows the application of a stronger hypoxic stimulus, equivalent to an altitude between 5000 and 6000 m a.s.l., which is in general well tolerated by healthy individuals when applied for a few minutes only. The rationale for this procedure is most likely the hypothesis of inducing acclimatization to hypoxia in a shorter time with a stronger stimulus. Two modalities exist: *persistent exposure* at rest to altitudes (or normobaric hypoxia) of up to 5500 m a.s.l. for up to 3 h, and *intermittent hypoxic exposure*, which consists of six to nine consecutive cycles of breathing hypoxic air for 6 min followed by room air for 4 min. The level of hypoxia is usually 11% or 10%, which corresponds to 5000–6000 m a.s.l. at sea level. When applying normobaric hypoxia, one needs to consider that the altitude at which nitrogen-enriched air is applied has a large effect on the resulting partial pressure of oxygen, and thus on the “treatment altitude” for a given level of FIO_2 . This is particularly important for low levels of FIO_2 : 10% O_2 will result in a PO_2 equivalent to 5800 m a.s.l. at sea level, to 6725 m a.s.l. at 1000 m a.s.l., and to 7750 m a.s.l. at 2000 m a.s.l., as shown in Fig. 3.

A further modality of using hypoxia with the intention to achieve greater improvement of performance compared with living and training at low altitude is to *train in hypoxia and live in normoxia*. Various levels of hypoxia ranging from 2000 to 5500 m a.s.l. are used with this approach. When analyzing the results of these studies, one has to bear in mind that hypoxia decreases maximum aerobic performance and that training with equal workloads in hypoxia vs. normoxia therefore means training at a higher relative workload in hypoxia. In this case, it will not be possible to distinguish between effects by hypoxia and those by increased workload. If the question is whether training in hypoxia has greater effects than training in normoxia, it is important to train at the same relative workload.

High-altitude illnesses

AMS

AMS consists of non-specific symptoms, such as headache, loss of appetite or nausea, insomnia, dizziness, and peripheral edema, which usually occur with a latency of eight or more hours after exposure to high altitude or hypoxia. Usually AMS resolves spontaneously within 1–3 days if no further ascent

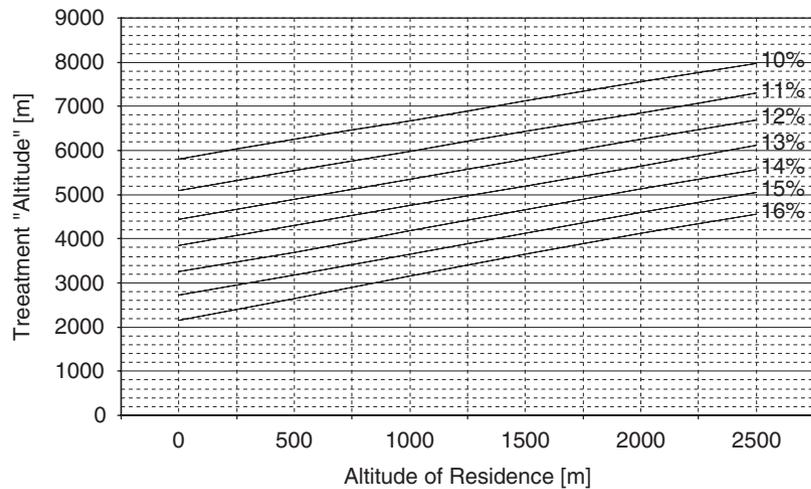


Fig. 3. Treatment “altitude” for a given FIO_2 increases with the altitude at which the treatment is performed. The barometric pressure (P_B) of the treatment altitude can be calculated according to the formula $P_{B(\text{treatment})} = P_{B(\text{residency})} \times FIO_{2(\text{chamber})} / 0.209$.

occurs and exertion is avoided (Hackett & Roach, 2001). Individual susceptibility, rate of ascent, and degree of previous acclimatization are the major predictors (Schneider et al., 2002). There appears to be a threshold altitude of about 2100 m a.s.l. for significant development of AMS with exposure to hypobaric hypoxia at rest (Muhm et al., 2007). At altitudes between 2500 and 3000 m, the prevalence of AMS is between 10% and 30%, depending on the population and the definition of AMS (Fig. 2). At these altitudes, AMS is usually mild, transient, and does not progress to more severe symptoms of altitude illnesses, such as cerebral or pulmonary edema. At altitudes of 4000–4500 m a.s.l., the prevalence of AMS is 40–60%, and in some susceptible individuals treatment with oxygen, dexamethasone, and descent are necessary for improvement and prevention of progression to cerebral edema (Bärtsch & Roach, 2001). When going to altitudes above 3000 m, staged ascent and/or prevention of AMS by acetazolamide (2×250 mg/day) may be necessary in order to avoid physical discomfort within the first few days of altitude exposure. A low hypoxic ventilatory response (HVR) may be associated with increased susceptibility to AMS (Moore et al., 1986; Richalet et al., 1988a), and HVR tends to be lower in endurance-trained athletes (Schoene, 1982).

HACE

HACE is usually preceded by progressive symptoms of AMS. It is characterized by progressive truncal ataxia, clouded consciousness, and variable focal neurologic symptoms. Without treatment, coma usually develops within 1–2 days, and death occurs rapidly because of brain herniation. Vasogenic edema has been demonstrated by MRI (Hackett et al., 1998). Treatment consists of administration of supplemental oxygen, dexamethasone, and descent. HACE rarely occurs below 4000 m a.s.l. (Fig. 2), and the prevalence at 4000–5000 m a.s.l. is 0.5–1.5%.

HACE can be avoided by preventing AMS or by fast and adequate treatment of AMS.

High-altitude pulmonary edema (HAPE)

HAPE is a non-cardiogenic edema that is due to a non-inflammatory capillary leak caused by an abnormally high hypoxic pulmonary vasoconstriction (Bärtsch et al., 2005). Early symptoms are dyspnoea, decreased performance, and cough. In advanced cases, dyspnoea at rest, orthopnoea, and pink frothy sputum occur (Bärtsch, 1999). HAPE is rare below 3000 m a.s.l. and is usually associated with abnormalities in the pulmonary circulation. Prevalence of HAPE after rapid ascent to 4550 m a.s.l. within 24 h, including an overnight stay at 3600 m a.s.l., is 6% in a general mountaineering population (Fig. 2) and 60–70% in HAPE-susceptible individuals (Bärtsch et al., 2002). Susceptible individuals are characterized by an abnormal increase in pulmonary artery pressure with exposure to hypoxia and also during normobaric exercise (Grünig et al., 2000). This abnormal response pattern of the pulmonary circulation can be found in about 10% of the population in Germany (Grünig et al., 2005). The rate of ascent, the altitude of exposure, and exertion are the major risk factors for development of HAPE, in addition to individual susceptibility based on an abnormal pulmonary hypoxic vasoconstriction. HAPE can be avoided in susceptible individuals with slow ascent (300–400 m/day above 2000 m a.s.l.). If slow ascent is not possible, HAPE can also be prevented by drugs that lower pulmonary artery pressure, such as nifedipine (Bärtsch et al., 1991), sildenafil, or dexamethasone (Maggiorini et al., 2006). Treatment consists of administration of supplemental oxygen, application of pulmonary vasodilators (nifedipine or tadalafil), and descent. Mortality is estimated to be 50% if no treatment is possible (Lobenhoffer et al., 1982), while adequate treatment leads to a complete recovery without sequelae.

Definitions of altitude

Based on the effects of altitude and acclimatization on performance and well-being in healthy individuals, the expert panel proposes the following definition of altitudes:

Near sea level (between 0 and 500 m a.s.l.): No altitude-related effects on well-being or athletic performance.

Low altitude (between 500 and 2000 m a.s.l.): No altitude-related effects on well-being but relevant impairment of performance possible, particularly in highly trained athletes and above 1500 m. This can be overcome completely by acclimatization to this altitude.

Moderate altitude (between 2000 and 3000 m a.s.l.): Effects of altitude on well-being in non-acclimatized subjects with minor sleep disturbances or symptoms of AMS may occur after nine or more hours of exposure. Discomfort is transient during the first days. Maximum aerobic performance decreases significantly with a large inter-individual variability in well-trained athletes; however, it can be restored largely by acclimatization. Significant erythropoietic response occurs within 3–4 weeks.

High altitude (between 3000 and 5500 m a.s.l.): AMS occurs in a large number of non-acclimatized individuals during the first days of exposure. Susceptible individuals may develop HAPE above 3000 m a.s.l. and HACE above 4000 m a.s.l., which may necessitate descent. Staged ascent is recommended to avoid these illnesses. The altitude will significantly reduce athletic performance even after full acclimatization.

Extreme altitude (above 5500 m a.s.l.): 5500 m a.s.l. appears to be the ceiling for long-term adaptation in humans, as the highest permanent settlements are at this altitude (West, 2002).

Key words: training modalities, hypoxia, high altitude, acclimatization, aerobic performance, acute mountain sickness, high-altitude pulmonary edema, high-altitude cerebral edema (HACE).

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