

## [ Primary Care ]

# Athletes at High Altitude

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**Context:** Athletes at different skill levels perform strenuous physical activity at high altitude for a variety of reasons. Multiple team and endurance events are held at high altitude and may place athletes at increased risk for developing acute high altitude illness (AHAI). Training at high altitude has been a routine part of preparation for some of the high level athletes for a long time. There is a general belief that altitude training improves athletic performance for competitive and recreational athletes.

**Evidence Acquisition:** A review of relevant publications between 1980 and 2015 was completed using PubMed and Google Scholar.

**Study Design:** Clinical review.

**Level of Evidence:** Level 3.

**Results:** AHAI is a relatively uncommon and potentially serious condition among travelers to altitudes above 2500 m. The broad term AHAI includes several syndromes such as acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), and high altitude cerebral edema (HACE). Athletes may be at higher risk for developing AHAI due to faster ascent and more vigorous exertion compared with nonathletes. Evidence regarding the effects of altitude training on athletic performance is weak. The natural live high, train low altitude training strategy may provide the best protocol for enhancing endurance performance in elite and subelite athletes. High altitude sports are generally safe for recreational athletes, but they should be aware of their individual risks.

**Conclusion:** Individualized and appropriate acclimatization is an essential component of injury and illness prevention.

**Keywords:** high altitude pulmonary edema; high altitude cerebral edema; acute mountain sickness; altitude training

Exercise at altitude has been gaining popularity in recent decades. High altitude exercise ranges from casual hiking to highly competitive ultra-endurance races (eg, foot race, mountain biking, cross-country skiing) and even includes team sports. Travel to high altitude has potential significant health consequences. Not only are altitude and environmental factors a concern for the athletes' safety, but access is often a barrier to appropriate medical care. For safety reasons, proper acclimatization is important for those traveling to high altitudes. Altitude training is also thought to be beneficial for athletic performance, though the evidence for this is not clear. The purpose of this article is to review physiologic changes at high altitude, altitude illness, and medical considerations for both recreational and competitive athletes. We will discuss high altitude training for competitive athletes and unique considerations for traveling with teams to high altitude, as well as special groups of athletes such as young athletes, older athletes, and pregnant women.

## PHYSIOLOGIC RESPONSE TO ALTITUDE AND MEDICAL CONSIDERATIONS

Regarding human physiology, the most important environmental factors at high altitude are low atmospheric oxygen concentration and low barometric pressure. Other factors to consider are extreme temperature (cold and hot) and increased ultraviolet radiation. The human body responds in different ways to adapt to these changes.

### Acute Exposure

The body's first response to high altitude low oxygen concentration (hypoxia) is an increase in ventilatory response triggered by carotid body receptors.<sup>27,64</sup> Acute exposure to high altitude causes multiple compensatory changes, including increase in sympathetic activity with increased heart rate, cardiac output, and blood pressure. These responses eventually play a significant role in acclimatization. Hypoxic ventilatory

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Table 1. Pathophysiologic responses to high altitude<sup>10,21,23,24,27,49,64,73</sup>

System	Acute Exposure	Chronic Exposure
Pulmonary	Hypoxemia, ↑ventilation, ↓arterial oxygen saturation	Hypoventilation, pulmonary hypertension, ↑lung capillary blood volume, ↑lung diffusion capacity, exacerbation of chronic lung disease, HAPE on reascent of altitude residents
Cardiovascular	Transient ↑blood pressure, ↑heart rate, ↑venous tone, ↑cardiac output, peripheral edema	↓Systolic/diastolic blood pressure, right ventricular hypertrophy, right heart failure, arterial oxygen desaturation, ↑plasma triglyceride level, exacerbation of congenital heart disease
Hematologic	↑Hemoglobin concentration, ↓plasma volume, ↑erythropoietin, ↑D-dimer	Polycythemia, ↑O <sub>2</sub> carrying capacity of blood
Renal	↑Bicarbonate excretion, ↓plasma calcium and phosphate, hypocapnic respiratory alkalosis, ↑diuresis	Hyperuricemia, microalbuminuria, ↓renal plasma flow, ↑filtration fraction (preserved or mildly ↓glomerular filtration rate), glomerular hypertrophy
Neuropsychologic	↓Synthesis of neurotransmitters, cerebral vasodilation, mood changes, ↓cognitive function, ↓motor/sensory function	Cerebral hypoxia, biochemical dysfunction, ↓sleep quality, ↑mood disorders, ↓cognitive function
Exercise	↓Maximal oxygen consumption, ↓VO <sub>2</sub> max	↓Aerobic exercise capacity
Other	Retinopathy, anorexia	

HAPE, high altitude pulmonary edema.

response causes decreased alveolar CO<sub>2</sub>, hypocapnia, and respiratory alkalosis, which has an inhibitory effect on the central respiratory center. This limits further increase in ventilation (Table 1). The renal system responds to these changes by excreting bicarbonate and conserving hydrogen ions.<sup>23</sup> During acclimatization, parathyroid hormone level increases, which causes an increase in plasma calcium and phosphate levels. Altitude-induced diuresis occurs as an early stage of acclimatization.<sup>23,27</sup> There has been some suggestion that short-term high altitude exposure is a risk factor for hypercoagulation.<sup>25,62</sup> There are only a handful of published studies in this area and the majority of them were conducted during long air travel rather than ascent to high altitude. It seems this phenomenon is multifactorial (eg, hypoxia, hemoconcentration, hypohydration, cold temperature, use of constrictive clothing, and relative hypomobility due to extreme weather).<sup>25,62</sup> Athletes with sickle cell trait are also at high risk for sickling during exertion at high altitude.<sup>17</sup>

### Chronic Exposure

Increased hemoglobin concentration as a hematologic adaptation to high altitude among highlanders (typically residents at altitude >4000 m) has been reported for over a century (Table 1). This phenomenon is a result of erythropoietin

production by the kidneys.<sup>27,64</sup> Effects of chronic exposure to high altitude on other systems are summarized in Table 1.

### High Altitude Illness

During certain athletic events such as mountain races, athletes may experience very rapid ascent, which places them at high risk for developing altitude illness (Table 2). Risk factors for developing high altitude illness include previous episodes of high altitude illness, a faster rate of ascent, higher elevation, poor hydration, increased intensity of physical activity, and individual variability.<sup>4,20,26,36</sup>

Slow ascent to altitude is the hallmark of prevention for all acute high altitude illnesses (AHAIs). Guidelines recommend that once above 2500 m, altitude should be increased at a rate of 600 to 1200 m per 24-hour period.<sup>36</sup> Duration of an effective acclimatization also depends on the athlete's residing altitude and the altitude to which the athlete plans to ascend. Methods using hypobaric hypoxic chambers or true high altitude may be more effective for acclimatization than those using normobaric hypoxic conditions.<sup>20</sup> Pharmacologic prevention (Table 2) should be considered as an adjunct to slow ascent and proper acclimatization, or when this is not feasible (eg, during mountain bike and foot races). There are limited data on the effectiveness of agents other than acetazolamide for prevention

Table 2. Acute high altitude illness summary<sup>a</sup>

Condition	Symptoms and Signs	Treatment	Prophylaxis
Acute mountain sickness	Headache, anorexia, nausea, vomiting, dizziness, fatigue, weakness, insomnia	Descent, acetazolamide, dexamethasone, supplemental oxygen	Slow ascent, acetazolamide, dexamethasone
High altitude pulmonary edema	Dyspnea at rest, cough, decreased exercise performance, chest pain/tightness, low pulse oximetry, central cyanosis, tachypnea, tachycardia, rales, wheezing	Descent, supplemental oxygen, nifedipine, phosphodiesterase-5 inhibitors, salmeterol, portable hyperbaric chambers	Slow ascent, nifedipine, phosphodiesterase-5 inhibitors, salmeterol
High altitude cerebral edema	Change in mental status or ataxia in a person with AMS or HAPE	Descent, dexamethasone, acetazolamide, supplemental oxygen, portable hyperbaric chambers	Slow ascent, dexamethasone, acetazolamide

AMS, acute mountain sickness; HAPE, high altitude pulmonary edema.

<sup>a</sup>Adapted from Hoffman et al.<sup>28</sup>

and treatment of acute mountain illness.<sup>36</sup> The adverse effects of acetazolamide are uncommon and include paraesthesia, urinary frequency, and dysgeusia.<sup>54</sup>

Athletes with acute mountain sickness (AMS) should not continue ascent until symptoms resolve and should consider descent if medical management does not resolve symptoms. Medical providers should advise athletes with high altitude cerebral edema (HACE) or high altitude pulmonary edema (HAPE) to immediately descend to a lower altitude and be followed for medical management. The preferred rate of deacclimatization has not been well studied.

Chronic mountain sickness (CMS) is an uncommon condition among highlanders. Its prevalence has direct correlation with altitude of residence. CMS is characterized by extreme polycythemia, pulmonary hypertension, severe right ventricular hypertrophy, low systemic blood pressure, hypoventilation, and chronic arterial oxygen desaturation.<sup>27,64</sup>

### Ultraviolet Radiation

High altitude athletes are at risk from the deleterious effects of ultraviolet (UV) radiation. With every gain of 1000 m in altitude, there is an increase in UV-A and UV-B exposure by approximately 10% to 20%.<sup>36</sup> Increasing UV exposure is correlated with a greater incidence of skin cancer, seborrheic dermatitis, and cataract formation.<sup>15,36,53,55</sup> Athletes should understand these risks and providers should ensure proper education, including wrap-around sunglasses with UV protection, adequate clothing, and sunscreen with a sun protection factor of at least 30.<sup>36</sup> Snow increases UV exposure risk by providing a reflective surface, and radiation is at its highest between 10 AM and 2 PM during the summer months.<sup>36,53</sup> This may cause snow blindness (UV keratitis).<sup>55</sup>

### Sleep Hygiene

At high altitude, athletes often complain of insomnia, frequent awakening, and restless sleep.<sup>8,61,63</sup> Unacclimated athletes may be more prone to poor sleep quality.<sup>8,61</sup> Subjectively, this is characterized by the sensation of suffocation or apnea and relieved by waking and several deep breaths, resulting in restless sleep.<sup>8,63</sup> Physiologically, athletes have a cycle of hyperventilation secondary to high altitude-associated hypoxia, subsequent hypocapnia, and decreased respiratory drive, which is followed by apnea and resumption of the cycle.<sup>61,63</sup> Appropriate sleep hygiene and pretravel management of jetlag are recommended.<sup>36</sup> In athletes requiring treatment of sleep disturbance, both acetazolamide and sleep medications (eg, low-dose benzodiazepines) have been effective.<sup>36,63</sup> Risks of taking medications such as benzodiazepine include ataxia, cognitive impairment, and fatigue, and should be weighed against the potential benefits.

### Nutrition

There are a few nutritional concerns for athletes at high altitude. First, there is an association between chronic high altitude exposure and significant weight loss.<sup>69</sup> This seems to be primarily due to loss of fat-free mass, which may have significant negative effects on physical performance.<sup>69</sup> Factors possibly contributing to this weight loss are decreased physical activity, hypoxia, irregular sleep pattern, cold exposure, and nutritional imbalance related to protein metabolism.<sup>1,19,34,50,69</sup> Based on a few small studies, it seems that increasing caloric intake is not the best way to retain fat-free mass at altitude.<sup>69</sup> Increasing protein intake, particularly leucine, may be a more practical strategy.<sup>69</sup> Significant weight loss occurs at altitude

above 5000 m. However, mild to moderate weight loss may occur with a shorter duration stay at lower altitude (3000-5000 m) due to increased basal metabolic rate, increased exertion, hypoxia-related appetite suppression, and restricted food availability.<sup>19,34</sup> There is also a tendency for hypohydration at high altitude.<sup>36</sup> This is likely multifactorial (eg, diuresis, decreased fluid intake). Adequate fluid intake is essential to avoid underperformance due to hypohydration particularly in warm climates. Because of strong demand for erythropoiesis, athletes should increase dietary and supplemental iron before traveling to high altitude.<sup>36</sup>

Overall, at high altitude, an athlete's nutritional strategy should include adequate caloric intake, which is usually difficult to achieve mainly because of difficult access to food and decreased appetite.<sup>34</sup> Inadequate caloric intake may cause significant weight loss for athletes staying at high altitude for more than 3 weeks.<sup>34</sup> To prevent glycogen storage deficit, a diet should consist of about 60% carbohydrates, 25% fat, and 15% protein.<sup>34</sup> This is particularly important for athletes staying at high altitude for more than a couple of weeks.<sup>34</sup>

## MEDICAL CONSIDERATIONS FOR SPECIAL POPULATIONS

The majority of research on risks of and patient care at high altitude is focused on healthy adults. However, it is also important to consider the particular risks faced by young athletes, pregnant women, and older athletes.

### Young Athletes

Children are not at greater risk of altitude illness than adults and may actually be at lower risk.<sup>37,38,71</sup> In addition, children do not experience altitude illness of greater severity than adults.<sup>38</sup> Male children and children with a greater body mass index may be at greater risk for altitude illness compared with other children, though there is no correlation between altitude illness and physical fitness.<sup>70</sup>

Certain underlying medical conditions including a history of prematurity with respiratory distress syndrome, pulmonary hypertension, congenital cardiovascular or pulmonary abnormalities, current respiratory infection, trisomy 21, and obstructive sleep apnea increase a child's risk of AMS.<sup>32,47</sup> Children who develop severe altitude illness including HAPE should be evaluated for underlying cardiopulmonary abnormality.<sup>32,47</sup>

Diagnosis of AMS can be more difficult in children than in adults. Fussiness is a common symptom of AMS in preverbal children, as well as symptoms of decreased appetite, gastrointestinal symptoms, and lack of playfulness.<sup>71,72</sup> The Lake Louise Age-Adjusted Symptom Score is available for use in verbal children and uses more age-appropriate language for assessment of symptoms.<sup>60</sup>

As for adults, treatment of altitude-related illness in children consists primarily of descent to lower altitude. Medications for treatment and prevention of altitude-related illnesses in children

are the same as used for adults. It is important to remember that use of these medications is based on clinical experience not on primary studies in children.<sup>32</sup>

### Pregnant Women

Pregnant women who live at high altitude are known to have increased rates of intrauterine growth restriction (IUGR) and preeclampsia.<sup>12,33,48</sup> Women who are at high risk for IUGR or preeclampsia are advised to avoid travel to high altitude.<sup>30</sup>

However, less data are available about the risks of pregnant women traveling from sea level to high altitude. Pregnant women are not believed to be at increased risk of altitude illness.<sup>46</sup> Acetazolamide is contraindicated in the first trimester and after 36 weeks gestation.<sup>30,31</sup> A higher rate of spontaneous abortion has been suspected but not consistently supported by evidence.<sup>32</sup> However, women at increased risk of spontaneous abortion are advised to avoid travel to high altitude.<sup>30</sup>

Increased risk of IUGR and preeclampsia at high altitude are thought to be related to relative hypoxia. Exercise also has the potential to cause fetal hypoxia in the case of compromised uteroplacental circulation.<sup>30,31</sup> Pregnant women should allow 2 to 3 days for acclimatization before exercising at all over 2500 m and 2 full weeks before strenuous exercise.<sup>30</sup>

Because of the lack of data on exercise in pregnancy at high altitude, formal recommendations vary. The American College of Obstetricians and Gynecologists endorses exercise at altitudes up to 1830 m.<sup>16,18,32</sup> The Society of Obstetricians and Gynaecologists of Canada cited no adverse effects with moderate exercise at 1800 to 2500 m and recommends acclimatization prior to exercise above 2500 m.<sup>18,32</sup> These recommendations are for healthy women with healthy pregnancies; women with high-risk pregnancy conditions such as hypertension, preeclampsia, IUGR, anemia, diabetes, and maternal smoking should avoid exercise at high altitude.<sup>31</sup>

Given the lack of data in this area, pregnant women should be cautious regarding exercise and should be sure to make any decisions in consultation with their obstetric provider.<sup>32</sup>

### Older Athletes

Aging is not a risk factor for altitude illness, and in fact, may be protective against severe altitude illness.<sup>51,52</sup> The reason for this is not well understood, but it may be due to the known decrease in brain size with aging, which results in an increase in cranial compliance.<sup>51,52</sup>

Adults with controlled, stable chronic lung disease can do well at high altitude but should be prepared for exacerbation. If on oxygen, an individual will likely have to increase the FiO<sub>2</sub> at altitude. A portable pulse oximeter can be a guide. Patients with chronic obstructive pulmonary disease should be prepared with medications and possibly oxygen in case of exacerbation.<sup>13,44</sup> Though the obstructive component of obstructive sleep apnea does not worsen at altitude, hypoxia can be worsened by concomitant relative central sleep apnea or increase in sleep-disordered breathing.<sup>13</sup> Acetazolamide improves the apnea-hypopnea index and oxygen saturation in obstructive sleep

apnea patients with or without continuous positive airway pressure use.<sup>39</sup>

Individuals with unstable cardiovascular disease should be cautious at altitude, while those with well-controlled disease usually do well. In patients with labile or resistant hypertension, nocturnal O<sub>2</sub> at altitude may help with blood pressure control.<sup>13</sup> However, patients with stable hypertension should not have to adjust their medications.<sup>43</sup> Individuals with a history of congestive heart failure should be cautious for development of AMS as this is associated with fluid retention.<sup>13</sup> An older adult's prognosis related to high altitude is based on his or her medical conditions and general physical fitness.

## CONCERNS FOR ATHLETIC TEAMS TRAVELING TO HIGH ALTITUDE

Physicians of athletic teams traveling to relatively high altitude locations (eg, Denver at 1610 m and Mexico City at 2250 m) should be familiar with prevention and management of AHAI as well as special considerations for specific conditions and populations. Athletes with sickle cell trait should be counseled about the potential risk of acute sickling with exertion. If possible, early arrival to the event is highly recommended, and the medical team should discuss the importance of adequate hydration and caloric intake for better performance. Athletic teams often question the need for and utility of supplemental oxygen for athletes at high altitude, but in reality, this should not be necessary for healthy children and adults. If an athlete is so hypoxic as to require supplemental oxygen, HAPE or another pulmonary problem should be considered.

## ALTITUDE TRAINING

Altitude training has emerged as a way to gain a tactical advantage over the competitor. It entails breathing in a reduced percentage of oxygen (hypoxia), either natural or simulated, with a goal of improved athletic performance. The optimal altitude for this type of training is unknown; however, most research studies have been conducted at moderate altitudes (2000-3000 m). At these elevations, a reliable erythropoietin response has been observed with minimal side effects.<sup>11,14,42,57,58</sup>

There are 3 basic models for altitude training: live high, train high (LHTH); live low, train high (LLTH); and live high, train low (LHTL). In locations where training at altitude is not always geographically possible, simulated altitudes are often employed. Altitude training can be simulated (normobaric hypoxia) through an altitude simulation room, tent, or hypobaric chamber.<sup>66</sup>

### Live High, Train High

Some team sports also have facilities at altitudes in the 1800- to 2500 m range. LHTH is often utilized because of a general consensus among athletes that it improves endurance performance.<sup>22</sup> There is a dose-response relationship with the degree of hypoxia resulting in increased red cell mass. However, there is concern that elevations higher than 3000 m can result in

loss of training intensity and subsequent muscle wasting,<sup>42</sup> excess ventilatory work, and increased likelihood of acute mountain sickness. These side effects may cause stress on the athletes and can outweigh any positive erythropoietic benefits.<sup>11,57</sup> While training at altitude does allow for acclimatization, endurance athletes often are not able to train at the same intensity as compared with sea level training.<sup>65</sup> Performance outcomes at LHTH are equivocal, and some positive results in uncontrolled studies can be explained by placebo effect.<sup>6</sup> Another drawback of living at persistently high altitudes and returning to sea level is the challenge of heat acclimatization back at sea level after being at a cooler high altitude temperature.

### Live Low, Train High

LLTH is a model of altitude training where athletes live in a natural environment (normobaric normoxic) and are exposed to short intervals (5-180 minutes) of simulated normobaric hypoxia or hypobaric hypoxia.<sup>65</sup> The hypoxic exposures can be done at rest or during exercise training. Intermittent hypoxic exposures are effective in preacclimatization in athletes before ascending to high altitude. However, the effect seen on performance has been mixed, and this strategy does not seem to improve endurance capacity any more than training in the natural environment.<sup>65</sup>

### Live High, Train Low

With LHTL, athletes either live/recover at moderate altitude (2000 to 3000 m; hypobaric hypoxia) or use simulated altitude (normobaric hypoxia) and train at lower altitude or sea level. In addition to acclimatization, LHTL methods enhance exercise performance at altitude and sea level as athletes gain physiological benefits at altitude while maintaining workout volume and intensity training at a lower altitude.<sup>65</sup> To sustain a hypoxic erythropoietic effect with altitude training, the athlete must accumulate approximately 300 to 400 hours by living at a minimum altitude of 2000 m for more than 14 to 16 hours per day for at least 19 to 20 days.<sup>22,41,66,67</sup> The response to altitude training is individualized, and not everyone benefits the same.<sup>14</sup> Furthermore, the potential physiological response seems to be reduced in athletes with high red cell volume, such as elite endurance athletes.<sup>45</sup> However, the degree of physiologic response does not necessarily predict performance, as larger physiological responses are expected during preseason and in less fit individuals.

In a meta-analysis, hypobaric hypoxia LHTL offers the best chance for enhancing endurance performance in elite and subelite athletes.<sup>9</sup> In a second study, there were significant differences in the responses to LHTL training camp in hypobaric hypoxia groups compared with normobaric hypoxia groups.<sup>56</sup> There was greater performance enhancement in the hypobaric hypoxia group 3 weeks after LHTL and increased hematological changes, although some of the differences were thought to be secondary to increased exposure time in the hypobaric hypoxia group.<sup>56</sup> In a double-blind, placebo-controlled study of 16

endurance cyclists, there was no difference in time trials or changes in measured physiologic variables after 4-week exposure to normobaric hypoxia at 2500 m versus placebo.<sup>59</sup> Alternatively, a second study comparing hypobaric hypoxia to normobaric hypoxia with acute exposure at 4300 m in cyclists concluded that exposure to normobaric hypoxia may not induce the same hypoxic stimulus and training benefit as exposure to hypobaric hypoxia.<sup>3</sup>

The development of hypoxic facilities (eg, hypoxic dormitories or tents, hypobaric chambers) increases the opportunity for hypoxic altitude training, especially when geographically challenged. Altitudes of around 2500 m can be simulated by reducing the oxygen content from the normal 21% down to about 15% by diluting the oxygen with nitrogen. These are often called hypoxic/nitrogen houses. Hypoxic tents are easy to use and very portable. Tents can simulate altitudes up to 4000 m. Large and small barometric steel chambers are available, but these are high in cost and are limited in availability. Respiratory masks increase respiratory muscle strength rather than resulting in physiologic changes. Respiratory muscle training has resulted in benefit to exercise performance in less fit individuals.<sup>29</sup> Although studies have shown mixed results, there is some evidence that suggests nitrogen dilution may enhance sea level performance in elite athletes, provided a sufficient dose of simulated altitude is applied (12-16 hours for 4 weeks at an elevation of 2500-3000 m).<sup>40,68</sup>

The optimal altitude for an athlete depends on the athlete's sport, current residing altitude, and altitude of the event.<sup>22</sup> Athletes that may derive the most benefit from altitude training are those that cover long distances with repeated high-intensity effort.<sup>2,22</sup> There are divergent data on whether physiologic responses of hypobaric hypoxia and normobaric hypoxia are similar or different. Hypobaric hypoxia LHTL currently provides the best protocol for enhancing endurance performance in elite and subelite athletes, while some normobaric hypoxia protocols are effective in subelite athletes.<sup>9</sup> When geographically challenged, hypoxic/nitrogen houses or tents are an alternative and can help with acclimatization.

## CONCLUSION

Appropriate acclimatization duration varies among athletes. General consensus is that athletes should arrive at moderate altitude at least 2 weeks before a given event.<sup>4,35,36</sup> Physiologic changes of altitude typically improve with acclimatization and resolve with descent to lower altitude.<sup>32</sup> Because of the potentially dangerous nature of high altitude illnesses, conservative management, including prompt descent to lower altitude, is essential to prevent life-threatening conditions. Altitude training is a popular training method particularly among elite athletes. Effects of altitude training on athletic performance seem to be at best minimum and temporary. Most studies were conducted on individual endurance athletes; hence, the effects on team-sport athletic performance is unknown.<sup>5,7</sup>

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