



# High-altitude exposure and its effects on special populations

Robert N. Suter, DO, Monica G. Kalra, DO

From the Methodist Charlton Medical Center, Family Practice and Sports Medicine Center, Dallas, TX.

## KEYWORDS:

High-altitude illness;  
High-altitude cerebral edema;  
Mountain sickness;  
Hypobaric hypoxia;  
Monge disease

Altitude illness is a spectrum of conditions that affect the majority of travelers to high elevations (>8200 ft [2500 m]). The rapid decrease in arterial oxygen saturation with increasing altitude is the physiologic basis for this group of disorders. Many travelers to high altitudes will experience symptoms of acute mountain sickness including headache, fatigue, dyspnea, and dizziness. Prolonged exposure can result in more serious pulmonary, central nervous system, and circulatory disorders. Core treatments for most altitude-related illnesses include descent, rest, medications, and supportive care. Children and travelers with chronic diseases are more susceptible to altitude illness compared with the general population. Pregnant women residing at high altitudes are at increased risk for pregnancy-induced hypertension, preeclampsia, and low-birth-weight infants. Early recognition and treatment of altitude illness can prevent life-threatening situations. Primary care physicians should counsel patients traveling to high altitudes about altitude illness and discuss medications available for mountain sickness prophylaxis.

© 2011 Elsevier Inc. All rights reserved.

High-altitude syndromes are a variety of conditions that affect as many as 90% of travelers to high altitudes. The severity of acute altitude illnesses range from self-limited to life-threatening and encompass a wide range of clinical and physiologic conditions. The key to treatment and prognosis of altitude illness is prompt identification of symptoms and modification of activity. Family physicians should counsel patients traveling to high elevations about the risks of altitude illness and discuss safe practices and available medications for prevention of symptoms (Table 1).

## Physiology: the effects of increasing altitude

The percentage of oxygen in the atmosphere remains constant (about 21%) at all elevations. As altitude in-

creases and barometric pressure decreases, there is a proportional decrease in the partial pressure of oxygen.<sup>1</sup> The decrease in average barometric pressure from 760 mm Hg at sea level to 523 mm Hg at 10,000 ft (3048 m) translates into a decrease in arterial oxygen saturation in non-acclimated healthy individuals from 97% to 90%. At 20,000 ft (6096 m), non-acclimated healthy individuals will average an oxygen saturation of 73%.<sup>2</sup> This hypobaric hypoxia is the basis for most altitude-related illnesses.

Immediate compensation mechanisms after ascent include modest increases in cardiac output and increased pulmonary ventilation. Over time, the human body adapts to hypoxemia and individuals are able to function with less hypoxic effects. This multifactorial process involves physiologic changes over days, weeks, and months and is referred to as acclimatization. Factors contributing to acclimatization include increased red blood cell mass, increased vascularity of tissues, and increased diffusion capacity in the lungs.<sup>2</sup>

Corresponding author: Robert N. Suter, DO, Methodist Charlton Medical Center, Family Practice and Sports Medicine Center, 3500 W. Wheatland Rd., Dallas, TX 75237.

E-mail address: [robertsuter@mhd.com](mailto:robertsuter@mhd.com).

**Table 1** Sample locations with elevations

Location	Elevation
Los Angeles, California, USA	233 ft (71 m)
Dallas, Texas, USA	430 ft (131 m)
Ayers Rock, Australia	2831 ft (863 m)
Lake Louise, Alberta, Canada	5449 ft (1661 m)
Mexico City, Mexico	7349 ft (2260 m)
Vail, Colorado, USA	8022 ft (2445 m)
Machu Picchu, Peru	8200 ft (2500 m)
Mauna Kea Observatory, Hawaii, USA	13 800 ft (4205 m)
South Mount Everest Base Camp, Nepal	17 590 ft (5360 m)

For the non-acclimated traveler, exposure to modest altitude may result in headache, tachypnea, and dizziness. These symptoms can develop within hours and are usually self-limited. Symptoms generally resolve in a few days without intervention. Exposure to higher altitudes for healthy individuals without proper acclimatization can result in mental status change, cerebral edema, pulmonary edema, coma, or death. For patients with certain cardiac and pulmonary conditions, exposure to modest altitudes may increase risks of complications from these diseases.

### High-altitude sleep disturbance (HASD) and periodic breathing

Most travelers to high altitude report altered patterns of sleep. Frequent or recurrent waking is the most common complaint. This is probably caused by alternating hyperventilation as a result of hypoxia and hypoventilation as a result of hypocapnia, a condition termed *periodic breathing*.<sup>3</sup>

Prophylactic acetazolamide (Diamox, Sigma Pharmaceuticals, Monticello, IA) may help maintain night-time oxygenation and improve sleep quality by decreasing periodic breathing.<sup>3</sup>

### Acute mountain sickness

Acute mountain sickness (AMS) is a condition that affects individuals who rapidly ascend to altitudes above 6500 ft (2000 m). Hypobaric hypoxia leads to a cascade of physiologic changes that alter capillary permeability, leading to mild dependent edema and most likely a minimal degree of cerebral edema. Diagnosis of AMS involves the development of headache in a person who has recently arrived at the higher altitude plus one of the following symptoms: fatigue, dizziness, anorexia, nausea, vomiting, or dyspnea on exertion.<sup>4</sup> For those ascending from sea level to 6500 ft (2000 m), the risk of symptoms is 25% for

adults.<sup>4</sup> Above 14800 ft (4500 m), risks of AMS symptoms increase to more than 50%.<sup>5</sup>

In general, risk factors for AMS include rapid ascent, final altitude attained, and age younger than 60. Gender, physical fitness, and recent respiratory infections do not appear to contribute significantly to AMS.

A slow rate of ascent and time for acclimation are the best ways to prevent AMS.<sup>5</sup> Travelers should be advised to stop ascent and rest at the onset of symptoms and to descend if symptoms do not improve or they worsen. Acetazolamide, a carbonic anhydrase inhibitor, promotes the excretion of bicarbonate from the kidneys, decreases PaCO<sub>2</sub>, and increases PaO<sub>2</sub>.<sup>6</sup> It has been shown to decrease AMS symptoms. The usual recommended dose is 125 to 250 mg twice daily, starting at least 24 hours before ascent and continued until descent has begun.<sup>7</sup>

### High-altitude pulmonary edema

High-altitude pulmonary edema (HAPE) is the most lethal acute syndrome encountered at high altitudes. It occurs in about 4% of travelers above 8200 ft (2500 m), depending on individual adaptability and the ascent rate. Rapid ascent (more than 9800 ft [3000 m] in 3 days) is associated with a higher incidence of HAPE. Previous episodes of HAPE are associated with recurrence rates greater than 50%. Symptoms of HAPE usually appear between one and four days after reaching high altitude and include decreased exercise tolerance and dry cough progressing to productive cough with clear or blood tinged mucous.<sup>8</sup> HAPE can develop with or without preceding AMS symptoms.

Hypobaric hypoxia can cause heterogeneous areas of pulmonary vasoconstriction and vasodilatation.<sup>8</sup> Concurrently, worsening hypoxia leads to increased pulmonary artery pressure. Under these conditions, areas of pulmonary vasodilatation can develop capillary leakage and alveolar hemorrhage. The resulting pulmonary edema appears as patchy infiltrates on chest radiographs.<sup>9</sup>

Arrangements for descent should be made immediately once HAPE is suspected, and pressurized suits and supplemental oxygen can be used if descent is delayed. Medications that can be considered for prophylaxis and treatment of HAPE include calcium channel blockers like nifedipine (Procardia, Pfizer, New York, NY) to prevent or blunt the hypoxia-induced rise in pulmonary artery pressure, and phosphodiesterase-5 inhibitors like tadalafil (Adcirca, United Therapeutics, Silver Spring, MD) to induce pulmonary arterial vasodilatation.<sup>9</sup> There is some evidence that acetazolamide may prevent calcium ion influx into pulmonary artery smooth muscle cells, leading to reduced hypoxic vasoconstriction. There is conflicting evidence whether glucocorticoids should be a first-line treatment for HAPE.<sup>6</sup>

**Table 2** Physical and environmental effects of altitude change

Altitude (ft)	Atmospheric PO <sub>2</sub> (mm Hg)	PaO <sub>2</sub> (mm Hg)
0	159	98
2000	148	90
4000	137	80
5000	132	66
6000	127	64
8000	118	60
10000	109	53

PaO<sub>2</sub> = partial pressure of oxygen in arterial blood.  
 Adapted from Gong H: Exposure to moderate altitude and cardio-respiratory diseases. *Cardiologica* 40:477, 1995.

### Chronic mountain polycythemia

Monge disease, also known as *chronic mountain polycythemia*, is characterized by the development of excessive red blood cell mass for a given altitude. Typically, patients become symptomatic with hemoglobin levels >20 mg/dL.<sup>7</sup>

Characteristic complaints include headache, impaired concentration, drowsiness, and chest congestion. Males are affected more than females and most patients have other chronic conditions that can cause hypoxemia such as chronic obstructive pulmonary disease (COPD) or sleep apnea. Therapies include phlebotomy, descent from altitude, and use of respiratory stimulants like acetazolamide.<sup>3</sup>

### Altitude and exercise

Exercise capacity is diminished with increased altitude largely because of decreased oxygen consumption at high elevations. Exercise capacity is linearly correlated to atmospheric oxygen (Table 2) up to an altitude of 13,000 ft (4000 m). At greater altitudes, the decrease in exercise ability is exponential. Acclimatization improves exercise competence, but it does not return to baseline.

A 2009 study found dexamethasone (Decadron, Merck & Co., Inc., Whitehouse Station, NJ) treatment on the day before exercise and on the days of activity improves oxygen uptake in high altitudes.<sup>10</sup> Investigators used echocardiography during low-intensity exercise to compare pulmonary artery pressures between participants who received dexamethasone and those who did not. The dexamethasone group was found to have significantly decreased pulmonary artery pressures. This is thought to be related to corticosteroid stimulation of nitric oxide (a vasodilator) in the pulmonary vasculature.

Along with prophylactic medications, lifestyle changes may also improve exercise capacity. Some studies support the idea of “Living high–training low”.<sup>11</sup> This theory is based on increased erythropoietin levels in hypoxic conditions. Elevated erythropoietin expands red blood cell mass

and allows a greater surface area for oxygen to bind. Once the athlete returns to sea level, he is able to perform with greater intensity. A 1997 study using 39 competitive runners validated this theory by showing increased velocity and oxygen consumption in those who underwent four weeks of training at 4100 ft (1250 m) while residing at 8200 ft (2500 m).

### Altitude and ultraviolet radiation

Ultraviolet radiation (UVR) increases by 6% to 8% for every 1000-meter increase in altitude. Acute reactions caused by UVR exposure include skin erythema and ocular keratitis.<sup>12</sup> Reactions with long latency consist of various forms of skin cancers, skin aging, and cataract formation.<sup>12</sup>

Snow and ice cause UVR reflection and increase eye damage by a factor of 16. Patients hiking in snow-covered terrain should be instructed to avert their eyes from the ground and wear sunglasses with UVR protection at all times.<sup>12</sup>

Fair-skinned people are at highest risk for altitude-related skin cancer. Preventive measures for skin cancer include wearing long sleeved shirts, avoiding the sun between 10 AM and 4 PM, and using sunscreen with SPF 30, which blocks both UVA and UVB radiation.

### Altitude exposure in patients with chronic diseases

Patients with chronic diseases that can cause hypoxemia are at highest risk for experiencing exacerbations traveling or relocating to high altitudes.<sup>3</sup> Patients with COPD and/or pulmonary hypertension may have increased dyspnea and

**Table 3** Children’s Lake Louise Acute Mountain Sickness Scoring System: Fussiness Score

Amount of unexplained fussiness						
0	1	2	3	4	5	6
No fussiness			Intermittent fussiness		Constant fussiness	
Intensity of fussiness						
0	1	2	3	4	5	6
No fussiness			Moderate fussiness		Hard crying and extreme fussiness	

Children were scored by combining the mean fussiness score (0–6) with the pediatric symptom score (0–9). Total score 7 (including a fussiness score 4 and pediatric symptom score 3) is considered to be diagnostic of acute mountain sickness.

Adapted from Yaron M, Waldman N, Niermeyer S, et al: The diagnosis of acute mountain sickness in preverbal children. *Arch Pediatr Adolesc Med* 152:683, 1998.

**Table 4** Children's Lake Louise Acute Mountain Sickness Scoring System: Pediatric Symptom Score

Eating	0: Normal
	1: Slightly less than normal
	2: Much less than normal
	3: Vomiting or not eating
Playfulness	0: Normal
	1: Playing slightly less
	2: Playing much less than normal
	3: Not playing
Sleeping	0: Normal
	1: Slightly less or more than normal
	2: Much less or more than normal
	3: Not able to sleep

Children were scored by combining the mean fussiness score (0–6) with the pediatric symptom score (0–9). Total score  $\geq 7$  (including a fussiness score  $\geq 4$  and pediatric symptom score  $\geq 3$ ) is considered to be diagnostic of acute mountain sickness.

Adapted from Yaron M, Waldman N, Niermeyer S, et al: The diagnosis of acute mountain sickness in preverbal children. *Arch Pediatr Adolesc Med* 152:683, 1998

should consider additional or increased supplemental oxygen. Patients with sleep apnea can experience hypoxemia during sleep. Appropriate use of continuous positive airway pressure equipment should be encouraged.<sup>3</sup>

The physiologic response to high-altitude exposure can result in a modest rise in blood pressure, mainly because of increased sympathetic tone. Hypertensive patients should be counseled about continuing their medications during travel to high altitudes.<sup>3</sup>

Patients with sickle cell trait should avoid extreme exertion without acclimatization to high altitudes. Sickle cell disease poses special risks, and travel to even modest altitudes can result in vaso-occlusive crises.<sup>3</sup>

## Altitude illness in children

In addition to adult patients with chronic diseases, infants and children are also highly susceptible to altitude sick-

ness. Factors that predispose children to altitude illness include reduced surfactant (preterm infants), reduced airway diameters, and increased airway reactivity in response to hypoxia.<sup>13</sup>

According to a 2008 study, children are 20% more likely to develop AMS when compared with adults.<sup>14</sup> They are also more likely to have increased tachycardia and decreased oxygen saturation after rapid ascent.

AMS in young children presents differently than in adults. Signs and symptoms are less specific and include fussiness, poor sleep, vomiting, and decreased appetite.<sup>14</sup> The Children's Lake Louise AMS Score was developed in 1998 to assess AMS in preverbal children.<sup>13</sup> It uses fussiness and a pediatric symptom score (symptoms include appetite, playfulness, and sleep) as diagnostic measures of AMS (Tables 3 and 4). A score greater than seven indicates altitude disease.

Pharmacological treatment for altitude illness has not been studied in children. In life-threatening situations, a pediatric dose of acetazolamide should be used.<sup>15</sup> When cerebral edema or severe AMS is suspected, oxygen and dexamethasone should be given in combination with immediate descent<sup>15</sup> (Table 5).

## Altitude and pregnancy

Pregnant patients residing in high altitudes are at increased risk for diminished fetal growth and low-birth-weight infants. Chronic hypoxemia causes systemic vasodilatation, which leads to decreased preload and, inevitably, lower maternal cardiac output.<sup>16</sup> In altitudes above 4900 ft (1500 m), this may cause intrauterine growth restriction. There is an associated 65-g decrease in birth weight for every 1600 ft (500 meter) increase in altitude over 6600 feet (2000 m).<sup>17</sup>

Altitude related fetal growth is also affected by impaired maternal development during pregnancy. Studies in guinea pigs link chronic hypoxia to decreased vascular DNA synthesis.<sup>18</sup> This causes incomplete remodeling of uteroplacental vessels and leads to decreased uterine blood flow at term.<sup>19</sup>

**Table 5** SORT: Key Recommendations For Practice

Clinical recommendation	Evidence rating	References
A slow rate of ascent and appropriate time for acclimation are recommended to prevent AMS.	B	5
Acetazolamide 125–250 mg twice daily, starting at least 24 hours before ascent and continued until descent begins has shown to decrease AMS symptoms.	B	7
In life-threatening situations of altitude illness in children, a pediatric dose of acetazolamide is recommended.	C	15
When cerebral edema or severe AMS is suspected in children, oxygen and dexamethasone should be given in combination with immediate descent.	C	15

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series.

For information about the SORT evidence rating system, go to: <http://www.aafp.org/afpsort.xml>.

Elevated blood pressure is another problem associated with high-altitude pregnancy. Pregnancy-induced hypertension and preeclampsia are four times more common in women living in elevations above 8200 ft (2500 m). Inciting factors may include increased vascular reactivity, oxidative stress, and decreased prostaglandin production. Although much data has been collected, most reports are inconclusive in determining the etiology of hypertension in high-altitude pregnancy.<sup>19</sup>

## Acknowledgments

The authors wish to thank Sarah Holder, DO, and Brett Johnson, MD, for their help in preparation of this manuscript.

## References

1. Levitzky MG: The respiratory system under stress. In: *Pulmonary physiology*, 7th ed. McGraw-Hill, 2007, pp 228-247
2. Guyton AC: Aviation, high-altitude, and space physiology. In: Guyton AC, Hall JE, eds. *Textbook of medical physiology*. Philadelphia: Saunders, 2000
3. Hackett PH, Hargrove J: High-altitude medical problems. In: Tintinalli JE, Kelen GD, Stapczynski JS, et al, eds. *Tintinalli's emergency medicine: a comprehensive study guide*, 7th ed. McGraw-Hill, 2010, chapter 216.
4. Committee to Advise on Tropical Medicine and Travel: Statement on High Altitude Illnesses. In: Canada Communicable Disease Report, 1998. Available online at: <http://www.phac-aspc.gc.ca/publicat/ccdr-mtc/98vol24/24sup/acs4.html>. Accessed December 9, 2010
5. Milledge JS: Altitude medicine and physiology including heat and cold: A review. *Travel Medicine and Infectious Disease* 4:223-7, 2006
6. Wright AD, Breary SP, Imray CHE: High hopes at high altitudes: pharmacotherapy for acute mountain sickness and HACE and HAPE. *Expert Opin Pharmacother* 9:119-127, 2008
7. Luks AM, Swenson ER: Medication and dosage considerations in the prophylaxis and treatment of high altitude illness. *Chest* 133:744-55, 2008
8. Rupert J, Koehle MS: Evidence for a genetic basis for altitude related illness. *High Alt Med Biol* 7:150-68, 2006
9. Bärtsch P, Gibbs SR: Effect of altitude on the heart and the lungs. *Circulation* 116:2191-202, 2007
10. Fischler M, Maggionni M, et al: Dexamethasone but not tadalafil improves exercise capacity in adults prone to high-altitude pulmonary edema. *Am J Respir Crit Care Med* 180:346-52, 2009
11. Levine B, Stray-Gundersen J: "Living high-training low": effect of moderate-altitude acclimatization with low-altitude training on performance. *J Appl Physiol* 83:102-12, 1997
12. Ambach W, Blumthaler M, Schopf T: Increase of biologically effective UVR with altitude. *J Wilderness Med* 4:189-97, 1997
13. Samuels MP: The effects of flight and altitude. *Arch Dis Child* 89:448, 2004
14. Kohler M, Kriemler S, Wilhelm EM: Children at high altitude have less nocturnal periodic breathing than adults. *Eur Respir J* 32:189-97, 2008
15. Kohler M, Kriemler S, Wilhelm EM, et al: The diagnosis of acute mountain sickness in preverbal children. *Arch Pediatr Adolesc Med* 152:683, 1998
16. Kametas NA, McAuliffe F, Krampfl E, et al: Maternal cardiac function during pregnancy at high altitude. *Br J Obstet Gynecol* 111:1051, 2004
17. Mortola JP, Frappell PB, Aguero L, et al: Birth weight and altitude: a study in Peruvian communities. *J Pediatr* 136:324, 2000
18. Rockwell LC, Keyes LE, Moore LG: Chronic hypoxia diminishes pregnancy-associated DNA synthesis in guinea pig uteroplacental arteries. *Placenta* 21:313-9, 2000
19. Moore LG: Fetal growth restriction and maternal oxygen transport during high altitude pregnancy. *High Alt Med Biol* 4:141-56, 2003