**Chapter 50
High-altitude illnesses**

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**Introduction**

Altitude illness can be life-threatening if not recognized and adequately treated in a timely manner. Altitudes as low as 1,500 meters (m) cause physiological changes as the body adapts to the unique environment [1]. Rapid physiological adjustments can become pathological and perhaps fatal. More than 40 million tourists annually visit locations in the United States with elevations greater than 2,400 m [1]. Consequently, an increasing number of health professionals encounter high altitude pathologies. Despite research in altitude medicine, significant morbidity and mortality related to high altitude environments persist. This continual and growing public health risk emphasizes the need for education about altitude medicine not only for the lay person, but for all health professionals. In particular, the EMS physician must understand the pathophysiology and treatment for high altitude illness both as a potential responder and as a medical director for responders.

**Physiology**

High altitude is considered to be heights between 1,500 and 3,500 m (4,921 to 11,483 feet (ft)), very high altitude is between 3,500 and 5,500 m (11,483 to 18,045 ft) and extreme altitude is greater than 5,500 m (18,045 ft) [1]. No matter how high you climb, the percentage of oxygen in the air remains roughly 21%. What changes as you climb is the density of the air molecules. At sea level, the air molecules are densely packed together from the weight of the air above them. As you climb, there is less pressure on the air molecules and so they are more dispersed. This air pressure is called barometric pressure or atmospheric pressure.

Air molecules that are more dispersed translate into fewer molecules taken in with each breath. Thus, a breath at 3,500 m contains about 60% as much oxygen as at sea level. The concentration of the oxygen is still 21%, but there are fewer oxygen molecules available. At 5,000 m (the altitude of Everest Base Camp), each breath has about half the oxygen available at sea level and at 8,848 m (Mount Everest summit), each breath takes in about one-third as much as at sea level. As the level of inhaled oxygen decreases, the body responds with altitude acclimatization.

Many physiological changes occur as the human body is subjected to the stress of high altitude. Erythropoietin is released from the kidneys once hypoxic conditions are sensed. This hormone stimulates bone marrow to increase red blood cell production. Within 2 hours of ascent, erythropoietin can be measured [2]. Within 4–5 days, new red blood cells are in circulation. Over a period of weeks to months, red blood cell mass increases in proportion to the degree of hypoxia, allowing for an improved oxygen uptake and delivery.

The lungs respond by utilizing normally unused portions. As the human body ascends to altitude, breathing is deeper and faster. Sensing a fall in pO2, the carotid bodies located within the carotid artery signal the central respiratory center in the medulla to increase the rate of pulmonary ventilation. Increased ventilation decreases alveolar and blood concentrations of carbon dioxide, while trying to maintain a normal oxygen concentration. As carbon dioxide continues to fall, pH becomes alkalotic. This alkalosis will reach a maximum threshold in which the central respiratory center limits further increase in ventilation so as to prevent severe alkalosis.

Within 24–48 hours of persistent alkalosis, the kidneys begin to excrete bicarbonate in the urine. Bicarbonate diuresis reverses alkalosis and returns the body’s pH to a normal physiological level. This adjusted pH stimulates the cycle to begin again as the ventilatory response again increases, resulting in alkalosis, which prompts the kidneys to excrete bicarbonate. Ventilatory compensation reaches a maximum after 4–7 days at the same altitude [3]. For each increase in altitude, the cycle of pulmonary-renal events recurs.

Other physiological changes at altitude include dehydration, edema, and periodic breathing. The lower humidity and air pressure cause the skin and lungs to lose water through evaporation at a faster rate, resulting in dehydration if meticulous attention is not paid to fluid intake. As water is lost, the body tries to maintain fluid balances by minimizing the excretion of water and sodium. Fluid leaks from capillaries into tissues, causing edema. Most noticeable in the face, hands, and feet, high altitude edema seems to affect women more commonly than men. The edema usually worsens with ascent and resolves with descent. Periodic breathing is common at high altitude. As the body attempts to regulate oxygen and carbon dioxide, breathing may fall into a cycle of decreased breathing, followed by complete apnea for 3–15 seconds. Once the paCO2 has built up again, breathing resumes.

The circulatory system responds to altitude with an increase in sympathetic activity, which causes a mild increase in blood pressure. After 24 hours, bicarbonate diuresis begins to decrease pH as well as stroke volume. Fortunately, this decrease in blood volume rarely causes myocardial strain as echocardiographic studies demonstrate a lack of myocardial stress with a decreased stroke volume [4]. Additionally, with acclimatization, resting heart rate returns to normal, except at extreme altitudes. Paradoxical pulmonary hypoxic vasoconstriction shunts blood away from poorly aerated, injured, or diseased lung alveoli to healthy alveoli so as to maintain adequate oxygenation. When exposed to a high altitude environment, this phenomenon occurs throughout the lungs, leading to complete pulmonary vasoconstriction and mild pulmonary hypertension which is usually managed well by the body. Cerebral blood flow depends on the overall balance of hypoxic vasodilation and hypocapnia-induced vasoconstriction. This balance is rigorously tested in high altitude hypoxic environments. One study demonstrated a cerebral blood flow increase of 24% on abrupt ascent to 3,810 m and subsequent return to normal over 3–5 days [5]. With severe hypoxia at high altitude, this delicate autoregulation of vasodilation and vasoconstriction becomes impaired, leading to several pathophysiological states discussed below.

**Acute mountain sickness**

**Pathophysiology**

Acute mountain sickness (AMS) is the most common of the attitude illnesses. AMS has been described in altitudes as low as 2,500–2 700 m [1]. We do not fully understand the exact pathophysiology of AMS but it is thought that genetics may play a role. The pathophysiology of AMS includes minor hypoventilation, interstitial edema, and increased sympathetic drive [6,7].

Several theories regarding the cause of AMS are circulating. One theory suggests that AMS results from mild brain swelling. A study using brain imaging of patients with moderate-to-severe AMS showing white matter edema with an elevated intracranial pressure (ICP) supports this concept [8]. However, those with mild AMS do not have cerebral edema [9–14]. Hence, this hypothesis only partially explains AMS. Other investigators have postulated that an increase in ICP causes AMS. Although some studies demonstrate an increase of ICP in AMS using optic nerve sheath diameter and lumbar puncture pressure, other studies demonstrate no change in pressure [14–17]. Thus, evidence that ICP is elevated in mild AMS remains limited. A third hypothesis, known as the tight fit hypothesis, theorizes that persons with smaller intracranial and intraspinal cerebral spinal fluid capacity are predisposed to develop AMS, because they cannot tolerate brain swelling compared to those who have more room to accommodate [18].

**Symptoms**

Most unacclimatized persons traveling to high altitude experience a mild form of AMS. The most common complaint is headache followed by fatigue, anorexia, and dizziness [14,19]. Headache is described as throbbing, bitemporal, and worse at night. Additionally, Valsalva maneuvers or bending over exacerbate the headache. Anorexia and nausea are common. Frequent waking from sleep, periodic breathing, and a feeling of suffocation are exaggerated in patients with AMS. Symptoms are often described as similar to an alcohol hangover [1]. Additionally, persons with AMS may complain of a deep inner chill, vomiting, dyspnea on exertion (although pulmonary symptoms vary widely), and lassitude. Symptoms typically begin within 24–48 hours of reaching altitude and resolve in 3–5 days at the same altitude.

There are no pathognomonic physical exam findings associated with AMS. Pulse may range from bradycardia to tachycardia [7,14,20]. Blood pressure may range from normal to postural hypotension. Rales may be present and oxygen saturation changes correlate poorly in the diagnosis of AMS [21]. Fundoscopic examination may reveal venous dilation as well as retinal hemorrhages, but are not diagnostic. Finally, a decrease in urine output demonstrating poor alkalotic diuresis may also be an early finding of AMS. It is always key to remember that there are *no* neurological deficits associated with AMS [14,22–25].

**Treatment**

Management depends on the severity of AMS. Mild AMS can be treated by halting further ascent to allow for acclimatization. This may take 3–4 days. Additionally, acetazolamide accelerates acclimatization by increasing bicarbonate diuresis. This may prevent AMS or accelerate treatment if given early enough [26,27]. Acetazolamide is typically given as 250 mg by mouth (PO) twice a day or as a single dose. Symptomatic treatment with analgesics such as ibuprofen (or other non-steroidal antiinflammatories), acetaminophen (650–1,000 mg PO), or aspirin (500–650 mg PO) should be considered [28]. Antiemetics such as ondasetron can be provided. Dexamethasone (4–8 mg PO, intramuscularly (IM) or intravenously (IV)) appears to treat symptoms of AMS by an unknown mechanism. However, it has been shown that symptoms increased when dexamethasone was removed in 24 hours [1]. AMS patients should avoid alcohol and other respiratory depressants to avoid further hypoxemia.

For moderate-to-severe AMS, descent is the treatment. One may descend as far as necessary, but a drop of 500–1,000 m is usually effective. Also, lightweight portable hyperbaric chambers mirror descent and can also effectively treat AMS. These hyperbaric chambers are manually inflated fabric pressure bags. Typically an inflation of 2 psi is roughly equivalent to a drop in altitude of 1,600 m, though the exact equivalent of psi to altitude drop depends on the initial altitude [29,30]. Additionally, oxygen given at 0.5–1 L/min by mask or nasal cannula (NC) is an effective treatment for moderate-to-severe AMS.

**High altitude cerebral edema**

**Pathophysiology**

High altitude cerebral edema (HACE) is life threatening. With increasing altitude and decreasing atmospheric pressure, capillaries begin to leak, causing edema. When fluid leaks into the closed space of the brain, HACE occurs. Studies demonstrate cerebrospinal fluid pressures of more than 300 millimeters of water and severe edema on cerebral imaging, and autopsies demonstrate petechial hemorrhages along with severe edema [10,31]. Much like AMS, there is a spectrum of HACE ranging from reversible HACE to severe, end-stage HACE. Reversible HACE demonstrates vasogenic edema whereas end-stage HACE produces gray matter (cytotoxic) edema [32]. As cytotoxic edema progresses, cerebral cells are separated from capillaries, resulting in failure to transport oxygen and nutrients to the cells, leading to brain cell death. Intracranial pressure increases as edema continues on a systemic level [33]. As compression of the brain develops, third and sixth nerve palsies may present, as well as other neurological symptoms [34].

**Symptoms**

Unlike AMS, HACE has a more dramatic presentation. The classic symptoms are ataxic gait, severe lassitude, and altered consciousness. Altered consciousness can range from confusion to drowsiness to coma. Additionally headache, nausea, and vomiting may occur. Other neurological presentations such as hallucinations, cranial nerve palsies, seizures, and paralysis have been described, but may not be as common [10,14,35–37]. The progression from AMS to HACE can be as quick as 12 hours, but typically develops in 1–3 days.

**Treatment**

Recognition and treatment of HACE must be swift. At first presentation of ataxia or altered mentation, descent should begin immediately. Treatment with dexamethasone (4–8 mg IV, IM, or PO) followed by 4 mg every 4–6 hours should also be started. Additionally, oxygen therapy via mask or NC at 4 L/min should be initiated and titrated to an oxygen saturation of greater than 90%. If the patient is comatose, rescuers should proceed to advanced airway management. Hyperventilation should be used with caution as hyperventilation in an already alkalotic patient can be catastrophic. Furosemide has been successfully used to reduce fluid overload in the cranial vault [14,38]. It is also reasonable to postulate that hypertonic saline and mannitol can reduce ICP, even without the appropriate studies. Coma for severe HACE can last from an average of 5.6 days to up to 3 weeks, with full recovery in about 2.4 weeks [9]. However, if not recognized and treated appropriately, death will occur.

**High altitude pulmonary edema**

**Pathophysiology**

Three physiological factors drive high altitude pulmonary edema (HAPE): excessive pulmonary hypertension, high-protein permeability leak, and persistent hypoxic exposure. Excessive pulmonary hypertension is a direct result of the paradoxic pulmonary hypoxic vasoconstriction. In the case of high altitude environments, the entire lung is hypoxic, resulting in diffuse vasoconstriction of the pulmonary capillaries. The degree of constriction varies among individuals. While pulmonary hypertension is one of the three necessary factors of HAPE, it is not necessarily the cause, as all persons exposed to high altitude environment have some form of pulmonary hypertension. It is hypothesized that uneven hypoxic pulmonary vasoconstriction results in overshunting of blood to relatively non-constricted vessels. This leads to high pressures and eventual capillary leakage, causing lung edema [39–42].

**Symptoms**

The most common cause of death related to high altitude illness is HAPE. Victims are typically young athletic males with a rapid ascent from sea level who may not have had HAPE on previous high altitude adventures. Typically, HAPE occurs within the first 2–4 days of ascent higher than 2,500 m, and most commonly on the second night [15]. The earliest signs may be decreased exercise performance and increased recovery time. Additionally, fatigue, weakness, and dyspnea on exertion become more obvious. Persistent dry cough develops with other signs of increasing hypoxia, including cyanotic nail beds and lips. AMS occurs in 50% of individuals with HAPE [39]. Symptoms are worse at night and eventually tachycardia and tachypnea develop at rest. More severe forms of HAPE result from increasing respiratory distress.

**Treatment**

Treatment for HAPE depends on the severity of the illness. The earlier HAPE is recognized, the better the outcome. The best treatment is *early* descent of only 500–1,000 m. After 2–3 days at this altitude, the patient may re-ascend. Supplemental high-flow oxygen (4 L/min or more) for more than 24 hours is also essential. If descent is too slow or delayed, administration of high-flow oxygen is life saving. Climbers should not wait for rescue and should descend immediately. Oftentimes waiting for help has proven fatal.

Other treatments include resistance on expiration (expiratory positive airway pressure) or continuous positive airway pressure, which can act as a temporizing measure [43]. If unavailable, pursed lip breathing can be effective. Additionally, diuretics such as furosemide (80 mg every 12 hours) may be used [14]. Phosphodiesterase-5 inhibitors (e.g. sildenafil) demonstrate potential for prevention for HAPE, but have not been approved for treatment [44–46]. Calcium channel blockers such as nifedipine (30 mg slow release every 12–24 hours) reduce pulmonary vascular resistance while improving arterial oxygenation [47]. However, clinical improvement remains minimal with diuretics and calcium channel blockers when compared to descent and supplemental oxygen.

Once at a more appropriate elevation, recovery is the rule before any re-ascent can be attempted [48]. Typically, bed rest and oxygen sufficient to keep oxygen saturation greater than 90% are key, and medications are rarely necessary. If treated promptly and correctly, intubation is rarely required. Patients should be warned that recovery may take up to 2 weeks and return to normal activity should be gradual.

## Considerations for the medical director

Education for altitude illnesses is key for any EMS physician or medical director. Instruction to medics, first responders, rescuers, and potential patients should be emphasized. Education should be focused on recognition of altitude illness, especially early signs of HACE and HAPE. Differentiation of temporizing treatments, including acetazolamide, from definitive life-saving treatments, like descent, must also be stressed.

Climbers themselves should also be made aware. Although direct education for all potential patients is impossible, indirect education through pamphlets, websites, and frequently asked questions can be made readily available. Instruction should also focus on ensuring frequent contact with appropriate parties, such as a base camp or climbing partner, as well as dispelling treatment myths, such as that simple hydration can treat all climbing pathologies. Identification of climbers can be acquired through the National Park Service, which requires registration of individuals who want to climb to high altitudes.

Finally, interagency cooperation and training with multiple services must be considered by the medical director. Frequent communication and training with rescue teams, first responders, EMS agencies, and hospitals can further facilitate a smoother response should such illnesses present. Input from a variety of personnel may aid in the modification or creation of flexible protocols that allow responders to think critically while simultaneously providing definitive end goals. These exercises can also help the system anticipate unforeseen barriers such as weather, resources, and communications. Such interdepartmental options can facilitate the identification and acquisition of pertinent equipment, from supplemental oxygen to portable hyperbaric chambers, needed for response.

## Conclusion

Travel to high altitude locations can be fun and incredibly gratifying. However, there remains a real risk to health and potentially life when exposed to such extreme environments. Hypoxia is the main insult the body endures. The delicate balance of physiological compensation for hypoxia aids in the comprehension of pathology that may follow.

Of all pathologies described, AMS is the most benign. However, it must be remembered that mild AMS can evolve into severe life-threatening HACE. Like HACE, HAPE can kill very quickly. HAPE remains the most common cause of death of all high altitude illnesses. Definitive treatment for AMS, HACE, and HAPE is descent of about 500–1,000 m as well as supplemental oxygen. Other medical treatments are available, but only as temporizing measures.

There are many factors that a medical director has to be concerned with, but chiefly the EMS system's knowledge of altitude illnesses in conjunction with cooperation between rescue teams, first responders, and hospitals play an important role in the treatment of these patients. The risk of high altitude illness increases as more people participate in travel and recreational activities in these environments. The challenges of high altitude illness are many, but preparation through education and training can help save lives and keep such adventures fun, entertaining, and safe.

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