

Authors: Tamir Zitelny, MD, Blake Briggs, MD

Hypoxia at high altitudes can wreak havoc on the body, leading to a wide spectrum of illnesses. Recognizing the early signs, descending promptly, and treating aggressively when needed can be lifesaving. This review covers the high-yield, testable aspects of high-altitude sickness.



Board Bombs

Quick Pathophysiology

At high altitudes, atmospheric pressure decreases, leading to a decrease in the partial pressure of oxygen (PaO_2). In response, the body attempts to compensate through various mechanisms; one of which is hyperventilation, effectively inducing a state of respiratory alkalosis [2]. Additionally, the body increases heart rate and cardiac output to maintain adequate oxygen delivery, along with a more subacute rise in erythropoietin (EPO) production over the course of several days to weeks to enhance red blood cell production [4, 10]. However, despite all these compensatory mechanisms, altitude illnesses can arise due to inadequate oxygenation, fluid shifts, and in severe cases, cerebral or pulmonary edema. Sometimes these forms of compensation just are not enough! [8,17]

Spectrum of High-Altitude Illnesses

Acute Mountain Sickness (AMS) - "The high-altitude hangover"

AMS is the most common altitude illness. It occurs in individuals who ascend rapidly to elevations above 2,500 meters (8,200 feet) [2]. The hallmark symptom of AMS is headache, and it is often accompanied by nausea, dizziness, fatigue, and insomnia as well [4, 6]. The key to preventing AMS is ensuring a gradual ascent, allowing for more proper acclimatization. Symptoms can begin after only a few hours and will typically present during the first day at altitude. However, symptoms tend to resolve after one to three days - even without treatment - as the body adjusts physiologically to the lower oxygen levels. Acetazolamide, a carbonic anhydrase inhibitor, can help facilitate acclimatization by stimulating ventilation and counteracting our body's compensatory respiratory alkalosis [5, 19]. Treatment of AMS includes symptomatic relief with NSAIDs for headache, rarely supplemental oxygen, and even descent if symptoms continue to worsen [2].

High-Altitude Cerebral Edema (HACE) - "AMS on steroids"

HACE represents a progression of severe AMS and is a life-threatening condition that occurs due to cerebral edema from hypoxia-induced vascular permeability [3, 14]. It is commonly seen in individuals who ascend rapidly and *continue* to climb despite worsening symptoms. Clinically, HACE manifests with altered mental status (ranging from confusion to coma), ataxia, and severe headache [8]. Without intervention, patients can progress to death [8, 18]. **Immediate descent is crucial and is the only definitive treatment.** This is always the correct answer on the test. Further, the administration of dexamethasone is a great temporizing measure as it works to reduce cerebral swelling. Alongside dexamethasone, supplemental oxygen and hyperbaric therapy can also be valuable adjuncts, particularly when descent is not immediately feasible [3, 17].

High-Altitude Pulmonary Edema (HAPE) - "Non-cardiogenic edema at altitude"

HAPE is the most lethal of the altitude illnesses and results from increased pulmonary artery pressures leading to capillary leak and pulmonary edema [1, 12]. It typically affects individuals who ascend rapidly above 2,500 meters while engaging in strenuous exertion, particularly in cold environments. Those with a prior history of HAPE are at increased risk [1, 13]. Symptoms include dyspnea, cough (which may progress to pink frothy sputum in severe cases), cyanosis, tachypnea, and diffuse rales on auscultation [7, 15]. The mainstay of prevention is slow ascent; for those at high risk, prophylactic use of nifedipine can help reduce pulmonary hypertension [1]. Treatment involves immediate descent, supplemental oxygen, and hyperbaric therapy when available [6, 7]. CPAP or BiPAP may also be beneficial in severe cases [6].

Focused Management

Supplemental oxygen is the cornerstone of treatment and should be administered as soon as possible when altitude illness is suspected [5]. However, the only truly definitive treatment for these illnesses is descent, as it rapidly reverses the hypoxia driving the pathology [4]. Again, acetazolamide is particularly useful for AMS prevention, as it enhances acclimatization by promoting metabolic acidosis and stimulating ventilation [2]. In fact, acetazolamide is recommended for both treatment *and prophylaxis* for AMS in cases of more aggressive planned ascents. In cases of HACE, dexamethasone is effective in reducing cerebral swelling, while nifedipine can be

beneficial in HAPE by lowering pulmonary artery pressures and preventing further capillary leak [1, 16]. In remote environments, hyperbaric therapy can simulate descent and provide temporary relief until evacuation is possible [7].

Key Distinctions Among Altitude Illnesses

How do you tell the difference on the test? AMS is the most common and most mild form of altitude illness, typically occurring above 2,500 meters [5]. In contrast, HACE and HAPE are life-threatening emergencies that require immediate intervention [5, 8]. HACE should be suspected in any patient presenting with ataxia and altered mental status at altitude [8, 14]. HAPE, the most fatal of the altitude illnesses, can rapidly progress but responds well to oxygen and descent [7]. Prevention remains the best strategy, with gradual ascent and pre-exposure to moderate altitudes serving as the most effective methods [4, 18]. Certain populations, including those with a history of HAPE, sickle cell disease, and congestive heart failure, are at particularly high risk [6, 13].

Take Home Points:

- Altitude illnesses are a product of inadequate compensation by the body to the decreased partial pressure of oxygen in the environment; or rather overly aggressive ascent that does not properly allow the body to acclimate
- For a traveler, rate of ascent is the most notable factor for precipitation of altitude illness
- Unlike AMS, HACE and HAPE are true medical emergencies and can lead to death if not addressed in a timely manner
- In all instances, descend, administer oxygen, and initiate appropriate pharmacologic therapy [5]. For HACE, that's dexamethasone. For HAPE, that's oxygen and nifedipine.

References

1. Bärtsch, P., Maggiorini, M., Ritter, M., et al. (1991). Prevention of high-altitude pulmonary edema by nifedipine. *New England Journal of Medicine*, 325(18), 1284-1289.
2. Hackett, P. H., Roach, R. C. (2001). High altitude illness. *New England Journal of Medicine*, 345(2), 107-114.
3. Hackett, P. H., Yarnell, P. R., Hill, R., et al. (1998). High-altitude cerebral edema evaluated with magnetic resonance imaging. *JAMA*, 280(22), 1920-1925.
4. Imray, C., Booth, A., Wright, A., Bradwell, A. (2011). Acute altitude illnesses. *BMJ*, 343, d4943.
5. Luks, A. M., Hackett, P. H. (2022). Medical conditions and high-altitude travel. *New England Journal of Medicine*, 386(4), 364-373.
6. Maggiorini, M., Bärtsch, P., Oelz, O. (1997). Association between raised body temperature and acute mountain sickness: cross sectional study. *BMJ*, 315(7105), 403-404.
7. Schoene, R. B. (2008). Unraveling the mechanisms of high-altitude pulmonary edema. *Annals of Internal Medicine*, 149(2), 137-138.
8. Wilson, M. H., Newman, S., Imray, C. H. (2009). The cerebral effects of ascent to high altitudes. *Lancet Neurology*, 8(2), 175-191.
9. Basnyat, B., Murdoch, D. R. (2003). High-altitude illness. *Lancet*, 361(9373), 1967-1974.
10. West, J. B. (2004). The physiologic basis of high-altitude diseases. *Annals of Internal Medicine*, 141(10), 789-800.
11. Richalet, J. P. (2010). High altitude and hypoxia: physiology and pathophysiology. *Springer Science & Business Media*.
12. Pollard, A. J., Murdoch, D. R. (2003). The high-altitude medicine handbook. *Routledge*.
13. Bailey, D. M., Bartsch, P., Knauth, M., & Baumgartner, R. W. (2009). Emerging concepts in acute mountain sickness and high-altitude cerebral edema: from the molecular to the morphological. *Cellular and Molecular Life Sciences*, 66(22), 3583-3594.
14. Peacock, A. J. (1998). Oxygen at high altitude. *British Medical Journal*, 317(7165), 1063-1066.
15. Moore, L. G. (2001). Human genetic adaptation to high altitude. *High Altitude Medicine & Biology*, 2(2), 257-279.
16. Houston, C. S. (2005). Going higher: oxygen, man, and mountains. *The Mountaineers Books*.
17. Hackett, P. H., & Roach, R. C. (2004). High-altitude medicine. *Travel Medicine*, 8(4), 226-233.
18. Bartsch, P., & Swenson, E. R. (2013). Acute high-altitude illnesses. *New England Journal of Medicine*, 368(24), 2294-2302.
19. Gallagher, S. A., & Hackett, P. H. (2004). High-altitude illness. *Emergency Medicine Clinics of North America*, 22(2), 329-355.
20. Kayser, B., & Verges, S. (2013). Hypoxia, energy balance, and obesity: from pathophysiological mechanisms to new treatment strategies. *Obesity Reviews*, 14(7), 579-592.