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Acute Mountain Sickness: Pathophysiology, Prevention, and Treatment

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Abstract Barometric pressure falls with increasing altitude and consequently there is a reduction in the partial pressure of oxygen resulting in a hypoxic challenge to any individual ascending to altitude. A spectrum of high altitude illnesses can occur when the hypoxic stress outstrips the subject's ability to acclimatize. Acute altitude-related problems consist of the common syndrome of acute mountain sickness, which is relatively benign and usually self-limiting, and the rarer, more serious syndromes of high-altitude cerebral edema and high-altitude pulmonary edema. A common feature of acute altitude illness is rapid ascent by otherwise fit individuals to altitudes above 3000 m without sufficient time to acclimatize. The susceptibility of an individual to high-altitude syndromes is variable but generally reproducible. Prevention of altitude-related illness by slow ascent is the best approach, but this is not always practical. The immediate management of serious illness requires oxygen (if available) and descent of more than 300 m as soon as possible. In this article, we describe the setting and clinical features of acute mountain sickness and high-altitude cerebral edema, including an overview of the known pathophysiology, and explain contemporary practices for both prevention and treatment exploring the comprehensive evidence base for the various interventions. (Prog Cardiovasc Dis 2010;52:467-484)

Keywords: Review; High, altitude; Hypoxia; Pathophysiology

Acute mountain sickness (AMS) and high-altitude cerebral edema (HACE) strike people who travel too fast to high altitudes that lie beyond their current level of acclimatization. In this paper, we describe the setting and clinical features of AMS and HACE, including an overview of the known pathophysiology, and then explain contemporary practices for prevention and treatment. Understanding AMS and HACE is important because AMS can sharply limit recreation and work at high altitude, especially in the first few days following arrival at a new, higher altitude, and if AMS worsens and HACE develops, the risk of fatality is significant.[1] Fortunately, most cases of AMS and HACE can be prevented or managed effectively with appropriate planning. The syndromes can be identified early and reliably without sophisticated instruments, and when AMS and HACE are recognized early, most cases respond rapidly with complete recovery in a few hours (AMS) to days (HACE).[2,3]

Symptoms and signs

High-altitude headache (HAH) is the primary symptom of AMS.[4] High-altitude headache in AMS usually occurs with some combination of other symptoms

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Abbreviations and Acronyms

AMS = Acute mountain sickness

CA = Carbonic anhydrase

CBF = Cerebral blood flow

HACE = High-altitude cerebral edema

GI = Gastrointestinal

HAH = High-altitude headache

HAPE = High-altitude pulmonary edema

ICP = Intracranial pressure

MRI = Magnetic resonance imaging

NO = Nitric oxide

PDE = Phospodiesterase inhibitors

SR = Systematic review

TCD = Transcranial Doppler

RCT = Randomized controlled trial

VEGF = Vascular endothelial growth factor

including insomnia, fatigue (beyond that expected from the day's activities), dizziness, anorexia, and nausea. The headache often worsens during the night and with exertion.[4,5] Insomnia is the next most frequent complaint. Poor sleep can occur secondary to periodic breathing, severe headache, dizziness, and shortness of breath, among other causes. Anorexia and nausea are common, with vomiting reported less frequently in trekkers to 4243 m.[6] Many sea-level residents are surprised on their first encounter with AMS by the debilitating lassitude that strikes. Decreased urinary output, independent of fluid intake, is common. Diagnostic physical findings in AMS only become apparent when the syndrome progresses to HACE. Prior to such progression, AMS is distinguished only by symptoms. The progression of AMS to HACE is marked by altered mental status, including impaired mental capacity, drowsiness, stupor, and ataxia. Coma may develop as soon as 24 hours after the onset of ataxia or change in mental status. The severity of AMS can be scored using the Lake Louise Questionnaire,[7] or the more detailed Environmental Symptoms Questionnaire (see Table 1),[8] or by the use of a simple analogue scale.[9] Today, more than 100 years after the first clear clinical descriptions of AMS and HACE,[2,3] we have advanced our understanding of the physiology of acclimatization to high altitude, and the pathophysiology of AMS and HACE, yet many important questions remain.

The setting

As altitude increases, barometric pressure falls (see Fig 1). This fall in barometric pressure causes a corresponding drop in the partial pressure of oxygen (21% of barometric pressure) resulting in hypobaric hypoxia. Hypoxia is the major challenge humans face at high altitude, and the primary cause of AMS and HACE. It follows that oxygen partial pressure is more important than geographic altitude, as exemplified near the poles where the atmosphere is thinner and, thus, barometric pressure is lower. Lower barometric pressure at the poles can result in oxygen partial pressures that are physiologically equivalent to altitudes 100 to 200 m higher at more moderate latitudes.[10] We define altitude regions as high altitude (1500-3500 m), very high altitude (3500-5500 m), and extreme altitude (>5500 m).[11]

Table 1
An individual has AMS as assessed by the Lake Louise self-assessment scoring system[7] when they fulfill the following criteria (a) recent ascent in altitude, (b) have a headache, and (c) have a total symptom score above 3

Symptoms:	
1. Headache:	
No headache	0
Mild headache	1
Moderate headache	2
Severe, incapacitating	3
2. GI symptoms:	
No GI symptoms	0
Poor appetite or nausea	1
Moderate nausea or vomiting	2
Severe nausea and vomiting incapacitating	3
3. Fatigue/weak:	
Not tired or weak	0
Mild fatigue/weakness	1
Moderate fatigue/weakness	2
Severe fatigue/weakness, incapacitating	3
4. Dizzy/lightheadedness:	
Not dizzy	0
Mild dizziness	1
Moderate dizziness	2
Severe, incapacitating	3
5. Difficulty sleeping:	
Slept well as usual	0
Did not sleep as well as usual	1
Woke many times, poor night's sleep	2
Could not sleep at all	3
Total symptom score:	
Clinical assessment:	
6. Change in mental status:	
No change	0
Lethargy/lassitude	1
Disoriented/confused	2
Stupor/semiconsciousness	3
7. Ataxia(heel to toe walking):	
No ataxia	0
Maneuvers to maintain balance	1
Steps off line	2
Falls down	3
Can't stand	4
8. Peripheral edema:	
No edema	0
One location	1
Two or more locations	2
Clinical assessment score:	
Total score:	

An additional clinical assessment scoring is sometimes used.
GI indicates gastrointestinal.