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REVIEW

# Prevention of high altitude illness

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**Summary** High altitude illness — Acute Mountain Sickness (AMS), High Altitude Cerebral Edema (HACE) and High Altitude Pulmonary Edema (HAPE) — can be prevented or limited in severity by gradual ascent and by pharmacologic methods. The decision whether to use pharmacologic prophylaxis depends on the ascent rate and an individual's previous history of altitude illness. This review discusses risk stratification to determine whether to use pharmacologic prophylaxis and recommends specific drugs, especially acetazolamide, dexamethasone and nifedipine. This review also evaluates non-recommended drugs. In addition, this review suggests non-pharmacologic methods of decreasing the risk of severe altitude illness. There are also brief sections on how to decrease sleep disturbance at high altitude, travel to high altitude for patients with pre-existing illness and advice for travelers ascending to high altitude.


## Introduction

Death from high altitude illness is a terrible waste and almost always avoidable. Suffering from high altitude illness is always unpleasant and usually preventable. For residents of altitudes below 2500 m, especially those who live at altitudes less than 1200 m, travel to altitudes above 2500 m carries a risk of high altitude illness, especially acute mountain sickness (AMS), high altitude cerebral edema (HACE) and high attitude pulmonary edema (HAPE). Sleep disturbance at altitude is normal, even in the absence of altitude illness.

Altitude illness is caused by decreased oxygen availability due to low atmospheric pressure (hypobaric hypoxia). Although the percentage of oxygen in ambient air is constant at about 21%, atmospheric pressure decreases as altitude increases. At higher altitudes less oxygen is available, leading to hypoxia. Acclimatization is the process by which people who travel to high altitude adapt physiologically to hypoxia over a period of days to weeks. A rate of ascent that is

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faster than the rate of acclimatization results in altitude illness. Individuals differ greatly in the rate at which they can ascend without developing altitude illness. Most healthy people can acclimatize to a wide range of altitudes. The fact that acclimatization is adaptive rather than maladaptive is likely related to human adaptations that allow the fetus to tolerate a hypoxic existence.

### Acute high altitude illnesses

AMS is a complex of symptoms affecting individuals who travel to high altitude. The diagnosis is based on the presence of headache and at least one other cerebrally-mediated symptom including anorexia, nausea, vomiting, dizziness, fatigue or poor sleep [1]. Onset is typically 6–12 h after arrival at altitude [2], but can be seen in as little as 2 h and as long as 4 days [3]. HACE is the severe form of AMS. HACE is differentiated from AMS by encephalopathic signs of confusion and ataxia.

HAPE, a type of noncardiogenic pulmonary edema, is the pulmonary form of acute altitude illness. It is the most common serious altitude illness and the most common cause of death from altitude illness [4]. Onset is most frequently after the second night at altitude. Early symptoms are fatigue, weakness, dyspnea on exertion and dry cough [5]. These progress to shortness of breath at rest with tachycardia, tachypnea, low-grade fever and orthopnea. A cough with frothy pink sputum is a late sign. HAPE may be associated with AMS or HACE, but can occur without AMS. The pathophysiology of HAPE is not completely understood, but pulmonary hypertension is an important etiologic factor. Cold exposure and exertion are risk factors for the development of HAPE [6–8].

Children living at high altitude are at risk for re-ascent or re-entry HAPE after spending 2 weeks or more at sea level [9,10]. The fact that re-entry HAPE requires spending at least 2 weeks at sea level suggests that loss of acclimatization is an important factor. Children living at high altitude likely develop increased pulmonary hypertension in response to rapid ascent.

Poor sleep with disordered sleep stages and periodic breathing is normal at high altitude and not necessarily pathological [11]. Periodic breathing of altitude, which occurs almost exclusively during sleep and is not associated with heart failure, is not the same as Cheyne–Stokes breathing, which is occurs in patients with congestive heart failure. Periodic breathing of altitude and Cheyne–Stokes breathing are both characterized by cycles of crescendo-decrescendo respiration with apneic pauses. The cycles of Cheyne–-Stokes breathing (40–90 s) are longer than the cycles of altitude periodic breathing (12–34 s) [12]. Apneic pauses, related to changes in respiratory control at altitude, can lead to severe hypoxemia, which may cause morning headaches and may worsen AMS. Periodic breathing decreases with acclimatization, but does not completely resolve [13].

## Prevention of acute mountain sickness

### Gradual ascent

The most effective method to prevent AMS is gradual ascent. Observational data are overwhelmingly clear, although there are few prospective studies [14,15]. Individuals who have previous experience can adjust their rate of ascent based on whether they have acclimatized rapidly or slowly in the past.

AMS takes several hours to develop. The critical altitude determining whether AMS develops is the altitude at which the traveler sleeps each night, referred to as "sleeping altitude." This is probably due to relative hypoxemia during sleep compared to the awake state.

For unacclimatized individuals going from sea level or from altitudes below 1200 m directly to altitudes above 2500 m, spending one or more nights at an intermediate elevation, typically 1500–2200 m decreases the risk of AMS [16].

Ideally, travelers ascending above 3000 m should spend 2 or 3 nights at 2800–3000 m before ascending further. There is no standard guideline regarding the nightly gain in sleeping altitude but there are some published recommendations. (Please see Table 1: Recommendations For Gradual Ascent.) The Himalayan Rescue Association (HRA) has traditionally recommended ascending no more than 300 m/day with a rest day (no ascent in sleeping altitude) for every additional 600–900 m and no single day gain greater than 800 m [17]. The Wilderness Medical Society (WMS) guidelines recommend limiting ascent to 500 m/day with a rest day every 3–4 days [18]. Because there is so much individual variation in the rate of acclimatization, neither of these general recommendations offers complete protection against AMS. Individuals are less likely to develop AMS by following the more conservative HRA guidelines. The goal of guidelines for gradual ascent is not complete prevention of AMS. Some individuals will develop AMS in spite of adherence to the guidelines, but it is more likely to be mild and less likely to be life-threatening (HACE).

Following the "mountaineers rule: climb high, sleep low," is commonly thought to aid acclimatization. The only evidence in favor of this practice is anecdotal. Travelers who do not have symptoms can safely ascend as far as they like during the day, especially on rest days. This takes advantage of the fact that altitude illness takes hours to develop. Moderate exercise, avoiding strenuous exercise, maintaining adequate hydration, eating a high carbohydrate diet [19] and avoiding the use of sedative/hypnotic drugs, including alcohol, are all thought to help prevent AMS.

Aerobic exercise training confers no advantage for acclimatization, although it is definitely helpful to prepare for activities such as trekking and climbing at low or high

**Table 1 Recommendations for gradual ascent.** Intended for individuals going from altitude <1200 m directly to altitudes >2500 m. Optional: Spend 1 or more nights at an intermediate altitude (1500–2200 m). Optional: Spend 2–3 nights at 2800–3000 m before further ascent.

| Recommendation | HRA [17] | WMS [18] |
|---|---|---|
| Daily ascent (sleeping altitude) | 300 m | 500 m |
| Rest day | Every 600–900 m | Every 3–4 days |
| Maximum single day gain | 800 m | No recommendation |