

Altitude Illness

Medical Summary

Introduction

The most serious disorder resulting from travel to high elevations is altitude illness. Minor disorders include periodic breathing, peripheral edema, and high-altitude retinopathy. Additionally, high altitude/elevation may have adverse effects on travelers with certain preexisting medical conditions, notably cardiovascular, pulmonary, neurological, hematological, and endocrine conditions. Pregnant women, infants, and young children may require special consideration.

Altitude illness occurs when a traveler ascends to a higher elevation at a rate that precludes the body's ability to adjust. Adjustment to the reduced atmospheric pressure and the decreased oxygen delivery to the body's cells at the higher elevation is known as acclimatization, and factors affecting acclimatization include the elevation attained, the rate of ascent, the duration of exposure, genetic predisposition, and certain preexisting conditions. See Acclimatization, Risk of Altitude Illness, and Effects of High Elevations (> 2,500 to 3,000 m) on Preexisting Medical Conditions.

Altitude illness is generally divided into 3 syndromes: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE). Symptoms can range from mild to life threatening. Serious syndromes are rarely seen below 2,500 to 3,000 m (8,200-9,800 ft). Death can occur from the more severe forms of altitude illness. However, most symptoms can be prevented or minimized by proper acclimatization and/or preventive medications. AMS occurs in about 25% of travelers sleeping above 2,500 m in Colorado, whereas HACE rarely occurs. HAPE occurs in about 1 of 10,000 skiers in Colorado and 1 of 100 climbers above 4,270 m (14,000 ft). See Clinical Presentation.

Risk and prevention strategies vary depending on the type of travel planned, for example, travel to typical tourist destinations at relatively moderate elevations versus trekking in extremely high elevation situations. See Risk of Altitude Illness and Prevention.

Risk of Altitude Illness

The following categories, generated by expert opinion and not systematic studies, are intended to assess the risk of altitude illness of a planned ascent profile and the need for chemoprophylaxis.

Low risk:

- No history of altitude illness and ascending to less than 2,800 m (9,200 ft)
- Allowing ≥ 2 days to arrive at 2,500 to 3,000 m (8,200-9,800 ft) with subsequent increases in sleeping elevation (< 500 m [1,600 ft] per day)

Moderate risk:

- History of AMS and ascending from 2,500 to 3,000 m (8,200-9,800 ft) in 1 day
- No history of AMS and ascending to more than 2,800 m in 1 day
- Ascending more than 500 m per day (increase in sleeping elevation) at elevations of more than 3,000 m

High risk:

- History of AMS and ascending to $\geq 2,800$ m in 1 day
- History of HAPE or HACE
- Ascending to more than 3,500 m (11,500 ft) in 1 day
- Ascending more than 500 m per day (increase in sleeping elevation) above 3,500 m
- Very rapid ascents (e.g., < 7-day ascent of Mount Kilimanjaro)

Typical Tourist Destinations

Most travelers seen in travel medicine clinics are preparing for travel to typical tourist destinations at $\leq 3,000$ m. This group of travelers rarely experiences the more severe forms of altitude illness, such as HACE or HAPE, unless they are genetically predisposed. Mountain resorts are usually located, by design, at elevations ranging from 1,200 to 3,000 m (3,900-9,800 ft). Mild symptoms of altitude illness have been documented at these elevations, and HAPE occurs not infrequently at 2,500 to 3,000 m (8,200-9,800 ft). Daytime activities (e.g., skiing, hiking, sightseeing) may take travelers to higher elevations, but risk is reduced by descending to the lower resort elevation overnight.

Risk increases for those who rapidly ascend to destinations higher than 3,000 m and for those who fly (or who are otherwise transported) directly to these relatively higher destinations because these modes preclude gradual acclimatization. However, if the elevation gain in a day is the same for the person who flew directly and the person who hiked vigorously to that elevation, the

hiker may be more likely to be ill than the person who flew in. Examples of destinations that allow access to relatively high elevations without hiking (3,400-4,200 m [11,200-13,800 ft]) include Cuzco, Peru; La Paz, Bolivia; and Lhasa, Tibet.

High-Elevation Trekking Routes

Trekkers are at higher risk of HACE and HAPE at higher elevations, although the risk is lower compared to that of AMS.

Altitude illness affects 50% or more trekkers on popular high-elevation routes. For example, the death rate from complications of altitude sickness in Nepal is about 1 in 30,000 trekkers, or 2 to 3 deaths per year. Although trekking in the Himalayas affords the opportunity to acclimatize gradually, it brings trekkers to high elevations for longer periods of time than in most other situations. Consequently, the risk of dying from altitude illness is higher in this region.

Furthermore, most trekking itineraries take a "one-size fits all" approach toward the pace of the trek and thus cannot guarantee that altitude illness will not occur. Trekking agencies also feel pressure to offer *shorter* expeditions for busy people who cannot take long holidays. For example, Mount Kilimanjaro treks that summit in 5 days are offered, even when a 7-day ascent offers elevation gains more rapid than typical Himalaya treks.

Acclimatization

Acclimatization is a built-in adjustment mechanism that can optimize performance at higher elevations. If a person ascends more rapidly than the body can adjust, symptoms occur that are referred to as altitude illness.

Acclimatization seems to be determined by factors that are not known but may possibly be genetic. Some people adjust very easily to high elevation, whereas others cannot go above relatively moderate elevations of 3,000 m (9,800 ft) without experiencing symptoms.

No reliable screening methods exist to determine whether a traveler will be a good acclimatizer. However, history of response to elevation is generally a good indicator of acclimatization if the exposures are comparable.

Both acclimatization and the onset of altitude illness generally take from 6 to 48 hours; however, HAPE can occur up to 5 days after reaching a given elevation. Thus, tolerating a few hours at high elevation does not necessarily predict the response after spending the night at that elevation.

For travelers, several strategies (both pharmacological and nonpharmacological) are available to improve or hasten acclimatization during ascent to a high elevation. See Prevention.

Clinical Presentation

AMS and HACE are believed to be connected pathophysiologically, whereas HAPE has a different pathophysiology. All are a result of poor acclimatization but why cerebral symptoms predominate in some people and pulmonary symptoms predominate in others is unknown.

Table 1: Symptoms of Altitude Illness¹

AMS	Headache ² , which can progress from mild to excruciating Anorexia, which can progress to nausea and vomiting Fatigue, which can progress to extreme lassitude
HACE	Begins as AMS, becomes HACE when AMS has progressed to include: <ul style="list-style-type: none"> decreased level of consciousness and/or truncal ataxia (elicited by tandem gait test) Can progress rapidly to coma and death Can occur alone or in combination with HAPE

- Not all symptoms are necessary for each diagnosis. For evaluating other symptoms, see Differential Diagnosis.
- The headache associated with AMS is not characteristic enough to be pathognomonic of altitude illness.
- HAPE is in the differential diagnosis if pulse oximetry shows a low SpO₂ for a given elevation. HAPE is unlikely with a normal SpO₂.
- Descent is critical when HAPE is suspected because the symptoms can progress rapidly, and death can occur within hours of recognizing clinical HAPE.
- Minimize exertion during descent to prevent worsening of HAPE.
- Cough is usually present with HAPE but is so common at high elevations due to many other causes that it is rarely a useful clinical sign of HAPE.
- Mental status changes that resolve with oxygen administration were likely due to hypoxic encephalopathy versus true HACE.

HAPE ^{3, 4}	<p>Presents as decreased exercise tolerance (increased difficulty walking uphill), which can progress to:</p> <ul style="list-style-type: none">• severe breathlessness with exertion⁵• breathlessness at rest (which can lead to rapid development of fulminant pulmonary edema)• substantial chest fullness• cough⁶ <p>Eventually progresses to production of pink, frothy sputum (a preterminal event)</p> <p>Can present with or without cerebral symptoms⁷</p>
<ol style="list-style-type: none">1. Not all symptoms are necessary for each diagnosis. For evaluating other symptoms, see Differential Diagnosis.2. The headache associated with AMS is not characteristic enough to be pathognomonic of altitude illness.3. HAPE is in the differential diagnosis if pulse oximetry shows a low SpO₂ for a given elevation. HAPE is unlikely with a normal SpO₂.4. Descent is critical when HAPE is suspected because the symptoms can progress rapidly, and death can occur within hours of recognizing clinical HAPE.5. Minimize exertion during descent to prevent worsening of HAPE.6. Cough is usually present with HAPE but is so common at high elevations due to many other causes that it is rarely a useful clinical sign of HAPE.7. Mental status changes that resolve with oxygen administration were likely due to hypoxic encephalopathy versus true HACE.	

Differential Diagnosis

A complete history of the present illness and the presenting symptoms is critical for differentiating between altitude illness and other illness that may have significantly different implications. The elevation at which the trip began and the elevation at which the patient slept for each point up to the present should be obtained. Any altitude-related symptoms at these prior elevations should be identified.

To attribute symptoms to altitude illness, the symptoms must have begun during ascent or within the first several hours to 5 days of arrival at a given elevation; none of the altitude illness syndromes occur abruptly upon arrival at an elevation. A traveler who was asymptomatic at the high point of a trek cannot develop AMS while descending.

Virtually all life-threatening altitude illness is due to ascent despite recognizable symptoms that were either ignored or attributed to something else by the patient.

Headache, anorexia, nausea, vomiting, and profound fatigue can all be symptoms of AMS. Diarrhea is not associated with altitude illness. Mild fever can occur with HACE or HAPE, which can be a confusing finding. If the history and symptoms are compatible with altitude illness, the fever can usually be attributed to the altitude illness. However, fever would present only after the onset of other AMS symptoms. A fever that predates the symptoms of altitude illness should be attributed to other causes.

The headache associated with AMS is not characteristic enough to be pathognomonic of altitude illness. The headache can be constant, start at the back of the head and radiate forward, or be frontal and throbbing. All headaches at an elevation higher than 2,500 (8,200 ft) must be treated as altitude headaches, and no further ascent should be attempted until resolution.

The symptoms of altitude illness almost always have a gradual onset and worsen slowly over several hours. The sudden onset of severe neurological symptoms should raise suspicion of an intracranial problem. Lateralizing neurological findings are almost never due to AMS or HACE alone, and a cerebral vascular accident should be ruled out when such symptoms are present. Additionally, cranial nerve palsies (except for sixth cranial nerve palsies) are not associated with altitude illness.

Pulmonary embolism could account for a presentation that mimics HAPE and fails to improve with a significant descent.

Resolution of Altitude Illness

Evaluating travelers with altitude illness who have already descended from a high elevation is essential.

- Assume that the descent has definitively treated the altitude-related problem, so be alert either for complications of altitude illness or for the possibility of a different diagnosis.
- Persistent neurological symptoms that do not show rapid signs of improvement at low elevation should be investigated with brain imaging.
- In comatose patients, patients usually regain consciousness rapidly, although the coma may persist for several days. Altered sensorium and headache clear up first. Gait ataxia can persist for 24 to 48 hours post descent and is usually the last symptom to resolve.
- HAPE is difficult to differentiate from a pulmonary infection without imaging; a low threshold should be used for prescribing appropriate antibiotics if productive cough or fever persists. Chest x-rays in HAPE usually show fluffy infiltrates that are often more prominent on the right side than on the left. A dense consolidation should raise the question of pneumonia or pulmonary infarct.

Other Conditions

Commonly, individuals who sleep above 3,000 m (9,800 ft) will have an alteration of their breathing pattern during sleep. The result is a form of *periodic breathing* in which increasingly deeper then shallower breaths (i.e., a crescendo-decrescendo pattern) are followed by a brief (5-30 s) period of apnea. The cycle then repeats itself. If the apneic episode is prolonged, the person may awaken suddenly with a profound sense of dyspnea. Nocturnal awakening with dyspnea has triggered panic attacks. If periodic breathing at a high elevation is disturbing to the trekker, acetazolamide (125 mg) taken before bed can relieve the problem.

Some people at higher elevations develop *peripheral edema* affecting the face, hands, and feet. Although harmless by itself, edema may indicate poor acclimatization, which can lead to other symptoms of altitude illness. As people with peripheral edema acclimatize, they often experience a profound diuresis and relief of symptoms. Trekkers can ascend with peripheral edema but must not ascend if other symptoms develop.

High-altitude retinopathy refers to the rare development of retinal hemorrhages at high elevations. Most of these hemorrhages are asymptomatic and are only discovered on systematic retinal exams. Large and/or specifically positioned hemorrhages near the macular, however, cause painless vision loss in the affected eye. Acute refractory changes (with either hyperopia or less frequently, myopia) have been reported to occur at very high elevations (> 6,000 m; 19,700 ft) in people who have had radial keratotomy resulting in functional blindness. This condition reverses readily with descent but could lead to a fatal outcome for a high-altitude mountaineer stranded with blindness. LASIK and newer procedures appear to be associated with only minor visual disturbances. Rarely, loss of vision has been associated with rapid ascent to high elevations and has been attributed to migraine-like spasm.

Prevention

Nondrug Prevention

Physical fitness at sea level does not influence the risk of altitude illness. The main goal of altitude illness advice is for travelers to react appropriately if altitude-related symptoms occur. Travelers should know the early symptoms of altitude illness and be willing to acknowledge them if they occur. General acclimatization recommendations:

- Ascend gradually.
 - Do not ascend directly to and sleep at elevations higher than 3,000 m, if possible.
 - If abrupt ascent is unavoidable (e.g., flying directly to the destination), consider the use of acetazolamide.
- Avoid alcohol and participate only in mild exercise for the first 48 hours.
- If participating in activities at elevations higher than 3,000 m during the day, return to a lower elevation to sleep. Many mountain resorts are located, by design, at lower elevations ranging from 1,200 to 3,000 m. Once at 3,000 m, increase the sleeping elevation by no more than 300 to 500 m (1000-1,600 ft) per day.

Trekkers should:

- Adhere to the adage, "climb high, sleep low." Mountain climbers who reach higher elevations during the day can lessen the risk of illness by returning to the valleys to sleep.
- Know the early symptoms of altitude illness and be willing to acknowledge them if they occur (see Symptoms chart).
 - Cases of fatal altitude illness generally result from ascent with symptoms that could have been recognized as due to altitude illness.
 - In organized trekking groups, a great deal of pressure exists to keep up with the group schedule so as not to be left behind. Leaving a client behind is logistically problematic for a trekking group, which contributes to the denial of altitude-illness symptoms.

If symptoms appear, trekkers:

- Should not continue to ascend; AMS symptoms will invariably worsen with ascent. A risk that can be taken, however, is if the symptomatic person appears to be able to make it over a higher pass to sleep at a lower elevation that night, for example, continued ascent of a few hundred feet to make it over a pass that descends thousands of feet on the other side is okay. A remaining ascent of several thousand feet to make it over the pass should not be done. In general, symptoms that begin in the morning, after spending the night at a new elevation, are more likely to clear up with rest at the same elevation than symptoms that began the day before while ascending to the camp.
- With AMS should descend if symptoms worsen or fail to improve after resting at the same elevation for a period of time. All persons with HAPE or HACE should descend to a lower elevation if feasible. Oxygen, medications, and/or the use of portable hyperbaric chambers may also be indicated if descent is not feasible.
- See Treatment and Self-Treatment.

Table 2: Preventive Strategies for Popular Trekking and Tourist Destinations

Destination	Approximate Peak Elevation Attained	Mode of Arrival to Peak Elevation	Comments
Mount Aconcagua, Argentina	6,960 m (22,800 ft)	Trek	Routes to the peak vary in rate of ascent (14-20 days). Descent typically takes 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Ojos del Salado, Chile	6,890 m (22,600 ft)	Trek	Routes to the peak vary in rate of ascent (9-15 days). Descent typically takes 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Mount Denali, United States	6,190 m (20,300 ft)	Trek	Routes to the peak vary in rate of ascent (12-15 days). Descent typically takes 2-3 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Kilimanjaro, Tanzania	5,900 m (19,300 ft)	Trek	Routes to the peak vary in rate of ascent (5-9 days). Descent typically takes 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Mount Elbrus, Russia	5,640 m (18,500 ft)	Trek	Routes to the peak vary in rate of ascent (4-5 days). Descent typically takes 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Annapurna Circuit, Nepal	5,420 m (17,800 ft)	Trek	Most trekkers arrive at Pokhara (up to 1,740 m [5,700 ft]) and can acclimatize gradually during the trek (16-20 days). Because some routes reach significantly higher elevations, acetazolamide chemoprophylaxis is beneficial.
Everest Base Camp, Nepal	5,380 m (17,700 ft)	Trek	Routes to the peak vary in their rates of ascent (10-12 days). Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the starting point is initiated.
Mount Kenya, Kenya	5,200 m (17,100 ft)	Trek	Routes to the peak vary in rate of ascent (4-7 days). Descent typically takes only 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Mont Blanc, France and Italy	4,810 m (15,800 ft)	Trek	Travelers typically stay in Chamonix (1,035 m [3,400 ft]) or other villages in the valley (up to 1,462 m [4,800 ft]) and ascend to higher elevations during the day.
Mount Matterhorn, Switzerland	4,480 m (14,700 ft)	Trek	Routes to the peak vary in rate of ascent (2-3 days). Descent typically takes only 1-2 days. Generally, climbers should start acetazolamide chemoprophylaxis 1 day before they ascend and continue until descent to the final camp is initiated.
Inca Trail, Peru	4,220 m (13,800 ft)	Trek	Most trekkers fly from Lima to Cuzco, a rapid ascent. An alternative is to travel via Arequipa (see below for description for Cusco) or descend from Cusco to the Sacred Valley for acclimatization before beginning the trek.
Mount Kinabalu, Malaysia	4,100 m (13,400 ft)	Trek	Travelers typically stay in the coastal town of Kota Kinabalu and travel by bus to the park entrance to begin the climb to an overnight stop at 3,300 m (10,827 ft) before summiting and then descending the next day. Acetazolamide chemoprophylaxis is recommended.
Mount Fuji, Japan	3,780 m (12,400 ft)	Trek	Many mountain lodges at 2,300 to 3,700 m (7,500-12,400 ft) are available for overnight stays for climbers during their ascent.
Lhasa, Tibet	3,650 m (12,000 ft)	Trek	For travelers flying into Lhasa, acetazolamide chemoprophylaxis is recommended.
La Paz, Bolivia	3,640 m (11,900 ft)	Flight	For travelers flying into La Paz, acetazolamide chemoprophylaxis is recommended.

Trek: Denoted elevation reached gradually or in stages by foot or motor vehicle

Flight: Denoted elevation reached immediately upon disembarkation from an aircraft usually originating from a much lower elevation.

Destination	Approximate Peak Elevation Attained	Mode of Arrival to Peak Elevation	Comments
Cusco, Peru	3,400 m (11,200 ft)	Flight	For travelers flying from Lima to Cusco, acetazolamide chemoprophylaxis is recommended. Alternatives to sleeping in Cusco after arriving on a flight are 1) descend to Ollantaytambo (2,800 m [9,200 ft]) for the first 2 nights or 2) go to Arequipa (2,300 m [7,500 ft]) for a few days before using land transportation to Cusco.
Mammoth Mountain, California	3,370 m (11,100 ft)	Trek	Travelers typically stay in Mammoth Lakes (2,400 m [7,900 ft]) or nearby areas and ski at the higher elevations of the mountain.
Quito, Ecuador	2,850 m (9,400 ft)	Flight	Some travelers fly into Quito and may benefit from acetazolamide chemoprophylaxis, whereas others may carry the medication to be used in response to altitude-related symptoms.
Bogota, Colombia	2,640 m (8,700 ft)	Flight	Travelers typically manage the elevation with hydration and rest.
Machu Picchu, Peru	2,430 m (8,000 ft)	Flight	Travelers typically manage the elevation with hydration and rest.
Addis Ababa, Ethiopia	2,360 m (7,700 ft)	Flight	Travelers typically manage the elevation with hydration and rest.
Kathmandu, Nepal	1,400 m (4,600 ft)	Flight	Travelers typically manage the elevation with hydration and rest.

Trek: Denoted elevation reached gradually or in stages by foot or motor vehicle
Flight: Denoted elevation reached immediately upon disembarkation from an aircraft usually originating from a much lower elevation.

Drug Prevention

See Table 3: Medications for Chemoprophylaxis and Treatment of High-Altitude Illness for dosing.

Acetazolamide (Diamox)

Acetazolamide has the longest history of preventing and treating AMS and works by hastening or improving acclimatization, not by masking symptoms.

- Indications for AMS and HACE prophylaxis: Consider chemoprophylaxis for travelers anticipating rapid ascent to sleeping elevations above 2,800 m (9,200 ft).
- For dosage, see Literature Watch Review: *Acetazolamide Dosage*.
- Side effects:
 - Acetazolamide is a carbonic anhydrase inhibitor that causes a mild bicarbonate diuresis and acidifies blood, which then causes an increase in respiration centrally. This imperceptible hyperventilation may result in paresthesia in the fingers and toes, and, occasionally, perioral paresthesia. Mention these side effects when prescribing acetazolamide, otherwise the person may suspect an allergic reaction and needlessly stop the medication.
 - Acetazolamide gives carbonated beverages a metallic taste.
 - Nausea may occur.
 - Photosensitivity reactions may occur.
- Allergic reactions to acetazolamide are extremely rare.
 - Acetazolamide is a nonantibiotic sulfonamide drug. Due to different chemical structures, no cross-reactivity occurs between sulfonamide antibiotics and nonantibiotics.
 - Persons with an isolated allergy to sulfonamide antibiotics have no increased risk of an allergic reaction when taking acetazolamide.
 - Risk of an allergic reaction to acetazolamide may be increased in people with multiple drug allergies or with allergies to multiple antibiotics.
 - Individuals with a history of life-threatening reactions to sulfa drugs or multiple drug allergies should have a test dose of acetazolamide administered in a controlled environment at home before their trip. Those with a history of mild sulfa reactions or rashes can safely take acetazolamide.

Dexamethasone (Decadron)

Dexamethasone works by improving symptoms rather than by improving acclimatization. Thus, travelers may rapidly become ill if they stop or deplete their supply of dexamethasone.

- Indications for chemoprophylaxis of AMS and HACE (uncommon situations):
 - Dexamethasone can be used for the prevention of altitude illness in extreme circumstances, such as the sudden need to perform a rescue at extreme elevations beyond tourist-destination elevations.
 - Dexamethasone can be considered for persons for whom acetazolamide is unequivocally contraindicated for AMS prevention or people who are intolerant of the medication and its side effects.
 - Dexamethasone should not be used for prevention of altitude illness in pregnant women or children.
- Side effects:
 - Euphoria
 - Increased need for insulin or oral agents in diabetics

Ibuprofen (Motrin, Advil)

Ibuprofen is a nonsteroidal anti-inflammatory drug that was found to be noninferior to acetazolamide in one study for the prevention of AMS and high-altitude headache but is not recommended over acetazolamide or dexamethasone. See *Literature Watch Review: Ibuprofen—Suitable for Prophylaxis of Acute Mountain Sickness?*

Indications for chemoprophylaxis: short-term (1-2 days) prevention of headache at high elevations.

Nifedipine (Procardia, Adalat)

Nifedipine is a calcium channel blocker that effectively lowers pressure in the pulmonary artery.

- Indications for chemoprophylaxis: reserved for the small subgroup of people who are susceptible to HAPE.
- Indications for treatment: almost always used only for treatment of HAPE and only in adults. It should not be used in children.

Sildenafil (Viagra) and Tadalafil (Cialis)

Sildenafil and Tadalafil are phosphodiesterase-5 inhibitors that cause pulmonary vasodilatation and lower pulmonary artery pressure.

- Indications for chemoprophylaxis: Tadalafil is recommended in persons who are susceptible to HAPE, based on a single, small, controlled trial. Tadalafil appeared effective in reducing the incidence of HAPE in some reports, but systematic studies are lacking.

Salmeterol (Serevent), previously recommended as an adjunctive medication for chemoprophylaxis of HAPE, is no longer recommended due to limited clinical experience with it at high elevations.

Other Prevention

Ginkgo biloba has been evaluated, but results vary widely. Therefore, this herbal supplement is not recommended for prevention or treatment of altitude illness.

Treatment and Self-Treatment

Descent remains the critical treatment of all altitude syndromes, but the availability of bottled oxygen and portable hyperbaric chambers (for trekkers) and the recognition of the value of 3 medications (acetazolamide, dexamethasone, and nifedipine) have expanded treatment choices when confronted with altitude illness. Descent is not necessary in most cases of AMS but is an urgent priority in persons with HAPE or HACE.

Nondrug Treatment

- Descent is the treatment of choice for both tourists and trekkers.
 - Descent usually improves altitude illness.
 - In severe cases, however, descent must continue until clear signs of improvement are recognized or until the person is below the elevation at which symptoms started.
 - Descent until all symptoms are gone is not necessary because symptoms can take from 48 to 72 hours to clear.
 - Any sign of improvement usually indicates the crossing of a tolerable elevation, and further improvement can be expected.
- Oxygen is the second treatment choice for both tourists and trekkers and is a valuable adjunct to the treatment of altitude illness, particularly HAPE and HACE.
 - Oxygen is available at many tourist locations, often from the front desk of the hotel.

- Bottled oxygen is carried on many trekking expeditions. However, bottled oxygen is expensive and heavy to carry, thus an insufficient oxygen supply may exist. For example, a highly compressed expedition oxygen bottle will last for 6 hours at a flow of 2 liters/minute but will only last for 3 hours at a therapeutic rate for altitude illness, which is 4 liters/minute.
- Portable oxygen concentrators may be more feasible if electrical power is assuredly available.
- Portable hyperbaric chamber (for trekkers)
 - Groups on long treks or climbs to very high elevations (where rapid descent might be precluded) should consider carrying a portable hyperbaric chamber (e.g., Gamow Bag, Hyperlite, etc.), which can effectively mimic descent. The amount of "descent" achieved within the chamber depends on the elevation at which it is used and the pressure to which the bag is inflated. For example, the chamber can physiologically lower the traveler with symptoms at 4,200 m (13,800 ft) to the equivalent of an elevation of 2,800 m (9,200 ft).
 - A 1-hour treatment in a portable hyperbaric chamber is usually enough to dramatically improve mild to moderate AMS. In more severe cases, several hours in the chamber may be necessary. Occasionally, relapse may occur and repeat treatments may then be necessary. Persons generally tolerate being placed supine in the chamber, but those with severe HAPE may have difficulty lying flat.
 - The effects of bottled oxygen versus pressurization appear to be equal. However, the hyperbaric chamber has the advantage of having an indefinite period of use provided people are available to continue working the foot pump, with the capability of treating multiple patients or repeating treatments for the same person.

Drug Treatment

See Table 3: Medications for Chemoprophylaxis and Treatment of High-Altitude Illness for dosing.

Acetazolamide (Diamox)

Treatment should begin when the onset of symptoms is noted and continued for at least 1 day after all symptoms have cleared. If AMS symptoms reoccur with further ascent, the drug can be restarted.

Acetazolamide is also very effective for treating the periodic breathing and sleep apnea that occur at higher elevations. If a person sleeping at a higher elevation is troubled by awakening with a profound sense of breathlessness, acetazolamide (125 mg) at bedtime will eliminate this problem. However, many reasons exist for poor sleep at high elevations, so obtaining a detailed history is essential.

Dexamethasone (Decadron)

Field studies have demonstrated that dexamethasone is effective in treating mild to moderate AMS and improving HACE prior to the onset of coma.

The use of dexamethasone can make a patient feel better while waiting to see if evacuation is necessary, or it can allow a person who is currently unable to walk to feel well enough to descend under his or her own power. Once dexamethasone is given, the person should not ascend to sleep at a higher elevation until dexamethasone has been discontinued for 24 hours or more.

Nifedipine (Procardia; Adalat)

Nifedipine is useful but not dramatically effective in the treatment of HAPE; it works mainly by reducing pulmonary artery pressure.

Other Treatments

Nonsteroidal anti-inflammatory drugs (such as ibuprofen and acetylsalicylic acid) are effective in treating headache associated with high elevation. These drugs can also prevent headaches when started a few hours before ascent to elevations of 3,400 to 4,900 m (11,200-16,100 ft).

Although sedatives are usually not recommended at high elevation, a short-acting benzodiazepine, temazepam (Restoril, 10 mg orally), has demonstrated effectiveness in improving sleep at high elevation. For people with known insomnia at baseline, this may be a reasonable choice when traveling to high elevations.

Positive end expiratory pressure (PEEP), which is used for treatment of HAPE at higher elevations, has been associated with a beneficial response. However, it requires a special mask (which must be carried), and no systematic study has been conducted to assess its efficacy or that of continuous positive airway pressure (CPAP).

Table 3: Medications for Chemoprophylaxis and Treatment of High-Altitude Illness

Medication	Does and Quantity ¹	Indications	Precautions	Side Effects

Medication	Does and Quantity ¹	Indications	Precautions	Side Effects
Acetazolamide (Diamox)	<p>Chemoprophylaxis <u>Adult:</u> 125 mg every 12 hrs; 250 mg every 12 hrs if > 100 kg (220 lb) <u>Pediatric:</u> 2.5 mg/kg/dose every 12 hrs</p> <p>Treatment <u>Adult:</u> 250 mg every 12 hrs Prescribe: 6 tablets <u>Pediatric:</u> 2.5 mg/kg/dose every 12 hrs Prescribe: Weight dependent</p>	<p>For chemoprophylaxis of AMS and HACE and treatment of AMS</p> <p>For chemoprophylaxis, medication should be taken the day before ascending, each day during ascent, and for 24 to 48 hrs after arrival (arriving and staying) at highest elevation.</p> <p>Persons who become and remain symptomatic beyond 48 hrs can continue to take acetazolamide each evening for several more days to help them sleep.</p>	Severe allergic reactions to acetazolamide are extremely rare. See Prevention for details.	<p>Almost always causes paresthesia of fingers and toes, and occasionally causes perioral paresthesia</p> <p>Occasionally causes nausea</p> <p>Increased photosensitivity</p> <p>Altered taste of carbonated beverages</p> <p>Frequent urination</p>
Dexamethasone (Decadron)	<p>Chemoprophylaxis in uncommon situations <u>Adult:</u> 2 mg every 6 hrs or 4 mg every 12 hrs <u>Pediatric:</u> Not recommended</p> <p>Treatment <u>Adult AMS:</u> 4 mg every 6 hrs <u>Adult HACE:</u> initial dose of 8 mg followed by 4 mg every 6 hrs Prescribe: 6 tablets <u>Pediatric AMS and HACE:</u> 0.15mg/kg/dose every 6 hrs up to 4 mg Prescribe: Weight dependent Oral, IM, and IV dosages are interchangeable.</p>	<p>For treatment of the cerebral symptoms of AMS</p> <p>Although effective for chemoprophylaxis of AMS and HACE, it should be recommended for that purpose only in extreme circumstances (see text above).</p>	Does not treat or prevent high-altitude pulmonary edema.	<p>Euphoria</p> <p>Can increase the need for insulin or oral agents in diabetics</p> <p>Use for > 7 days requires a tapering regimen to discontinuation due to suppression of the hypothalamic-pituitary-adrenocortical axis.</p>
Ibuprofen (Advil, Motrin) — noninferior to acetazolamide in limited studies	<p>Chemoprophylaxis <u>Adult:</u> 600 mg every 8 hrs <u>Pediatric:</u> Not recommended</p> <p>Treatment <u>Adult:</u> 600 mg every 8 hrs Prescribe: 9 tablets <u>Pediatric:</u> Not recommended</p>	<p>For short-term (1-2 days) chemoprophylaxis only and for treatment of headache at high elevations</p> <p>For chemoprophylaxis, medication should be started a few hours before ascent</p>	Risk of gastrointestinal bleeding may be increased at high elevations.	<p>Gastrointestinal irritation and bleeding</p> <p>Increased photosensitivity</p>

1. The quantity of medication to be prescribed for chemoprophylaxis is itinerary dependent.

Medication	Does and Quantity ¹	Indications	Precautions	Side Effects
Nifedipine (Procardia; Adalat)	Chemoprophylaxis <u>Adult</u> : 30 mg sustained release every 12 hrs <u>Pediatric</u> : Not recommended	For treatment of HAPE. Can be used for chemoprophylaxis of HAPE in known susceptible individuals (<i>see text</i>).	Limited studies only	Hypotension Headache Rash Urticaria
	Treatment <u>Adult</u> : 30 mg sustained release every 12 hrs Prescribe: 6 tablets <u>Pediatric</u> : Not recommended			
Sildenafil (Viagra)	Chemoprophylaxis <u>Adult</u> : 50 mg every 8 hrs <u>Pediatric</u> : Not recommended	Can be used for chemoprophylaxis of HAPE in known susceptible individuals.	Avoid in patients with hypertension, hypotension, or coronary artery disease. Do not use concomitantly with nifedipine.	Flushing Indigestion Headache Insomnia Visual disturbance
	Treatment None			
Tadalafil (Cialis)	Chemoprophylaxis <u>Adult</u> : 10 mg twice per day <u>Pediatric</u> : Not recommended	Can be used for chemoprophylaxis of HAPE in known susceptible individuals.	Avoid in patients with hypertension, hypotension, arrhythmias, or coronary artery disease. Do not use concomitantly with nifedipine.	Flushing Indigestion Nausea Myalgia Headache Respiratory tract infection
	Treatment None			

1. The quantity of medication to be prescribed for chemoprophylaxis is itinerary dependent.

Effects of High Elevations (> 2,500 to 3,000 m) on Preexisting Medical Conditions

Breathing air at sea level (21% oxygen) has a total barometric pressure of 760 mmHg and a partial pressure of oxygen of 160 mmHg. Breathing air and oxygen pressures at an altitude/elevation of 3,000 m (still 21% oxygen) fall to 532 mmHg and 112 mmHg, respectively. Acclimatization compensates for this difference over a few days. Most mountain resorts are situated at elevations below 2,500 to 3,000 m above sea level, the elevation at which physiological acclimatization mechanisms take effect. These mechanisms impose an increased demand on the cardiovascular system, on pulmonary ventilation, on red blood cell production, and on blood oxygen-carrying capacity leading to an increase in blood pressure and a decrease in energy reserve. No evidence exists that these mechanisms are harmful in the healthy individual.

Until recently, few studies have measured the direct effect of high elevations on various medical conditions; therefore, most advice was anecdotal. Even now, despite recent research, the base for validated advice is scant. In general, the more severely limited a patient's exercise tolerance is at sea level, the worse it will be at high elevations. Some high-elevation areas add a significant factor of remoteness from medical care if problems arise; travelers who are anxious about preexisting conditions may be unfit to travel. Travelers with heart disease should seek individual advice before ascending to high elevations.

Cardiovascular System

Travelers with Chronic, Stable Cardiac Conditions

The risk of new ischemic cardiac events at high elevations appears to be extremely low, seemingly no higher than the background rate of ischemic events in similarly aged persons at low elevations. Therefore, a stress ECG is not helpful in predicting such an event. However, sudden cardiac death (SCD) is the most frequent cause of nontraumatic death in males aged

> 34 years during leisure time activities (e.g., downhill skiing and hiking) at elevations of 3,000 m. Although prior myocardial infarction is the most important risk factor for SCD, other triggers that may unmask latent ischemic heart disease at higher elevations include unusual physical activity during the first days upon arrival and prolonged abstinence from food and fluid intake during exercise.

Travelers with silent *ischemic heart disease* appear to be safe up to at least 4,500 m (14,800 ft), but above 8,000 m (26,200 ft), undetected coronary plaques could pose a risk for infarction despite a normal baseline ECG. Patients with low-risk ischemic heart disease stabilized by percutaneous stenting or surgical coronary bypass surgery appear to be safe exercising (absence of signs of ischemia or arrhythmias) at approximately 3,450 m (11,300 ft), but data are limited. Following stenting, intense physical activity may be as great a hazard as high elevation. Therefore, persons with a history of successful coronary revascularization 6 to 12 months after the procedure, and who are currently exercising without symptoms, have no known contraindication for going to high elevations. Individuals who do not engage in physical activity at low elevations should not do so at high elevations. A training program should be prescribed to prepare an unfit traveler for a long trek at high elevations. The ability to hike steadily for at least 4 hours over steep terrain should be a minimum requirement for trekking in high mountains.

Heart failure is often associated with comorbidities. Although travelers should expect to have a reduction in maximum physical activity at high elevations in proportion to their exercise capacity at sea level, no evidence exists that an elevation of 3,450 m aggravates stable heart failure.

Certain drugs used to treat heart failure (beta blockers and angiotensin-converting enzyme [ACE] inhibitors) and the diuretic acetazolamide may interfere with adaptation mechanisms, but no evidence of harm exists.

Blood pressure increases (systolic increase is > diastolic) modestly and steadily during ascent to high elevations (e.g., + 30-40 mmHg at Everest Base Camp), although the response varies between individuals and by method of measurement. Travelers with systemic arterial hypertension who are well controlled on antihypertensive medications and who are going for a short tourist trip to moderate elevations do not need to adjust dosage. The blood pressure of hypertensive trekkers traveling to elevations higher than 4,000 m needs monitoring, and treatment may need to be adjusted, although there is no evidence that high elevations pose a risk of intracranial bleeding.

Travelers with Unstable Cardiac Conditions

In general, travelers with unstable cardiac conditions should not fly without special precautions and are therefore unfit for travel to high elevations. See *Cardiovascular Disease and Air Travel*.

Differentiating between angina, breathlessness at high elevation, and HAPE can be extremely difficult. Theoretically, a person with stable angina controlled by medication could visit high elevations, but if the person subsequently had prolonged chest pain, help could be days away on a trek. Thus, persons with angina, even if controlled at sea level, should be discouraged from high-elevation trekking.

Persons with congestive heart failure can experience difficulties at high elevations because even a little stress on the heart can induce failure. If these individuals wish to visit the mountains, they should limit themselves to moderate activity and stay in areas that have medical care readily available. Uncompensated congestive heart failure is a contraindication to going to high elevations.

No evidence exists that high elevations induce cardiac arrhythmias in healthy, trained individuals. However, individuals with uncontrolled ventricular arrhythmia should neither fly nor travel to high elevations.

Pulmonary System

Persons who have chronic obstructive pulmonary disease (COPD) will have increased difficulties in a hypoxic environment (although they may be partially acclimatized to hypoxia). Persons with severe COPD will do poorly at high elevations; persons with mild to moderate COPD usually do well.

Because HAPE is associated with exaggerated pulmonary vascular responses to hypoxia following ascent, people with primary pulmonary arterial hypertension (PAH) may not do well at high elevation. Individuals with mild PAH (WHO Group 1) controlled by vasodilator treatment appear to tolerate elevations up to 2,500 m; but should not trek. Those with more severe disease should not travel to high elevations.

Despite the theoretical concern that persons with asthma may be at increased risk at high elevations from the effects of cold and exercise, most asthmatics with mild, well-controlled disease have generally done well, possibly due to the greatly decreased presence of allergens at high elevations. Nevertheless, persons with asthma should be instructed to carry their medications with them at all times and carry a supply of medications to treat an exacerbation. Travel should be avoided in the setting of worsening

control or a recent exacerbation. No data exist regarding persons with moderate to severe persistent disease; extreme caution should be applied if these persons express interest in going to high elevations.

Neurological System

Anecdotally, higher elevations may lower the threshold for having a seizure. Those with uncontrolled or poorly controlled seizures should avoid higher elevations, but those who are well controlled on medication have no real contraindication to such travel, especially if medical help will be nearby. A history of migraine has been shown to be associated with increased risk of headache and strongly associated with migrainous headaches at higher elevations.

Hematological System

Even moderate altitudes, such as those encountered in airplane travel, can trigger a sickle cell crisis in a person with sickle cell trait (SCT) or disease. Typical tourist elevations (such as in Cusco, La Paz, Quito, and Lhasa) will often cause crises and splenic infarcts in those with SCT, even without physical exertion. In both SCT and disease, significant physical exertion increases risk of sickle cell crisis at low elevations, and less exertion is required to precipitate a crisis at higher elevations, even at elevations tolerated at rest.

Dark-skinned persons born outside the US, especially in developing countries, may never have been tested for SCT as children and may be at risk of a sickle cell crisis.

Persons with low red cell counts from other causes could have trouble adjusting to high elevations because their oxygen-carrying capacity may already be low. These individuals should proceed with caution. Persons with polycythemia could experience problems with sludging and a risk of blood clots and embolism.

Endocrine System

Persons with stable diabetes can safely travel to high elevations if they are comfortable with self-monitoring and willing to pay closer-than-usual attention to their glucose balance.

Glucometers may provide inaccurate glucose readings and insulin pumps may administer incorrect doses at high elevations.

A further practical problem for diabetics is the need to keep insulin supplies close at hand and unfrozen during a long, cold, backcountry journey.

Other Considerations

Pregnancy

No data are available concerning the risks of high elevations on the fetus. No cases have been reported of high elevation exerting a negative outcome on pregnancy in a trekker or climber. However, due to the remote location of many high-elevation destinations, pregnant women should avoid high-elevation trekking because of the isolation from readily available medical care that would be required in the event of early labor or complications of pregnancy.

Short stays at intermediate elevations up to 2,500 m appear to have low risk for women after 20 weeks gestation with uncomplicated pregnancies. Oxygen saturation may not be well maintained above an elevation of 3,000 to 3,600 m (9,800-11,800 ft), thus pregnant women should not sleep at these elevations or higher.

The main drugs used for altitude-illness prevention or treatment (acetazolamide, dexamethasone, and nifedipine) have been shown to be teratogenic in animals but no adequate studies have been done in humans; only use during pregnancy when the benefit outweighs the potential risk. Oxygen, which is readily available to pregnant women in typical high-elevation tourist destinations such as La Paz, Cusco, or Lhasa, is the primary treatment for altitude illness, should it occur. HACE and HAPE are uncommon at tourist-destination elevations.

Infants and Children

Travel to high elevations combined with remote location should be discussed with parents, although travel to elevations up to 2,500 m is low risk for healthy children.

Children have a risk similar to adults for AMS, but AMS may be more difficult to assess in preverbal children. The signs of AMS (nausea, vomiting, and irritability) are very nonspecific in young children and could be mistaken for other conditions. Some data suggest that older children and teens may tolerate the moderate elevations commonly faced on tourist trips better than adults.

Although limited published information exists, acetazolamide has been used safely in children for other indications; experts suggest a chemoprophylaxis dose of 2.5 mg/kg/dose (maximum 125 mg per dose) given orally every 12 hours.

HAPE and HACE are not well reported in traveling children due to the infrequency of children traveling to high elevations, but HAPE may be more likely to occur with concurrent viral illnesses. Dexamethasone may be used only for treatment of AMS and HACE in children at a dose of 0.15 mg/kg every 6 hours.

Nifedipine is not recommended for chemoprophylaxis in children; use of nifedipine for the treatment of altitude illness has not been studied in children.

Oral Contraceptives

No data exist regarding the safety of oral contraceptives at high elevations. However, concern exists that the increased risk of thromboembolism in women taking oral contraceptives at sea level might be compounded by high elevations, thus the practice of prescribing oral contraceptives to prevent menstruation during a trek is discouraged.

Women taking oral contraceptives who will not spend much time higher than 4,200 m (13,800 ft) can probably safely continue to take oral contraceptives. Women climbing to extremely high elevations (above 6,000 m [19,700 ft]) should consider discontinuing the medication to avoid the potential increased risk of thromboembolism.

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