Altitude Illness

Medical Summary

Introduction

Altitude illness occurs when a traveler ascends to a higher altitude 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 altitude is known as acclimatization, and factors affecting acclimatization include the altitude attained, the rate of ascent, the duration of exposure, genetic predisposition, and certain preexisting conditions. See Acclimatization, Risk of Altitude Illness, and Effect of High Altitudes 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. Although mild symptoms have been documented at the relatively low altitudes of 1,200 to 1,800 m (3,900-5,900 ft), 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 Syndromes and Symptoms.

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

Acclimatization

Acclimatization is a built-in adjustment mechanism that can optimize performance at higher altitudes. 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 altitude, whereas others cannot go above relatively moderate heights of 3,000 m (9,800 ft) without experiencing symptoms.

Currently, no reliable screening methods exist to determine whether a traveler will be a good acclimatizer. However, history of response to altitude 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. Thus, tolerating a few hours at high altitude does not necessarily predict the response after spending the night at that altitude.

Acclimatization Advice

- Ascend gradually.
  - Do not ascend directly to altitudes 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 altitudes higher than 3,000 m during the day, return to a lower altitude to sleep. Many mountain resorts are located, by design, at lower altitudes ranging from 1,200 to 3,000 m.
- Once at 3,000 m, ascend no higher the 500 m (1,600 ft) per day to sleep.
- High-altitude exposure (> 3,000 m for ≥ 2 nights) is useful within 30 days of a trek.

Syndromes and Symptoms

The 3 syndromes, AMS, HACE, and HAPE, are believed to be connected pathophysiologically, but it is not known why cerebral symptoms predominate in some people and pulmonary symptoms predominate in others.

AMS presents as headache, anorexia, and fatigue, which can progress to nausea, vomiting, and extreme lassitude.

HACE is a more severe progression of AMS. Changes in consciousness and/or the presence of truncal ataxia, as elicited by the tandem gait test, usually establish the diagnosis of HACE, which can progress rapidly to coma and death. HACE can present alone or in combination with HAPE.

HAPE presents with unusual breathlessness upon exertion and, eventually, at rest. Cough is usually present, but cough at high altitude is so common due to other causes that it is rarely a useful clinical sign of HAPE. Descent is critical when HAPE is suspected because the symptoms can progress rapidly, and death can occur within hours of recognizing clinical HAPE. Exertion by the affected person should be minimized during descent to prevent worsening of HAPE. HAPE can present with or without cerebral symptoms. If pulmonary symptoms occur alone, the progression is from decreased exercise tolerance to severe breathlessness with exertion, substernal chest fullness, and ultimately breathlessness at rest. Breathlessness at rest can lead to the rapid development of fulminant pulmonary edema. The production of pink, frothy sputum is a preterminal event.

Other Conditions

Almost everyone who sleeps above 3,000 m (9,800 ft) has an alteration of their breathing pattern during sleep. The result is a form of *periodic breathing* in which increasingly deep breaths 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. The immediate improvement upon awakening is usually proof that pulmonary edema is not present. Nocturnal awakening with dyspnea has triggered panic attacks. If periodic breathing at altitude is disturbing to the trekker, acetazolamide (125 mg) taken before bed can relieve the problem.

Some people at altitude develop *peripheral edema* affecting the face, hands, and feet. Although harmless by itself, edema indicates 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 altitudes. Usually only discovered by trained doctors, the hemorrhages occur near the macula and typically present with a visual field deficit. Acute refractory changes (with either hyperopia or less frequently, myopia) have been reported to occur at very high altitudes in people who have had radial keratotomy, whereas LASIK and newer procedures appear to be associated with only minor visual disturbances.

Table 1: Symptoms of Altitude Illness

Symptoms of Altitude Illness[1]	
AMS	• Headache[2]—can progress from mild to excruciating • Anorexia—can progress to nausea and vomiting • Fatigue—can progress to extreme lassitude

HACE	• Begins as AMS, becomes HACE when AMS has progressed to include:
	  ◦ Decreased level of consciousness and/or
	  ◦ Truncal ataxia (elicited by tandem gait test)
	• Can progress to coma and death
	• Can occur alone or in combination with HAPE

HAPE	• Presents as decreased exercise tolerance (increased difficulty walking uphill), which can progress to:
	  ◦ Severe breathlessness with exertion
	  ◦ Breathlessness at rest
	  ◦ Substantial chest fullness
	  ◦ Cough[3]
	• Eventually progresses to production of pink, frothy sputum (a preterminal event)
	• Can present with or without cerebral symptoms[4]

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. Cough is usually present with HAPE but has many other causes at altitude.
4. A pulse oximeter, which measures extremely low oxygen saturation, can help to distinguish HAPE from severe hypoxia and HACE.

Risk of Altitude Illness

Low risk:

- No history of altitude illness and ascending to < 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 > 2,800 m in 1 day
- Ascending > 500 m per day (increase in sleeping elevation) at altitudes > 3,000 m

High risk:

- History of AMS and ascending to ≥ 2,800 m in 1 day
- History of HAPE or HACE
- Ascending to > 3,500 m (11,500 ft) in 1 day
- Ascending > 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 ≤ 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 altitudes ranging from 1,200 to 3,000 m (3,900-9,800 ft). Although mild symptoms of altitude illness have been documented at these altitudes, serious syndromes are rarely seen below 2,500 to 3,000 m (8,200-9,800 ft). Daytime activities (e.g., skiing, hiking, sightseeing) may take travelers to higher altitudes, but risk is reduced by descending to the lower resort altitude overnight.

Risk increases for those who rapidly ascend to destinations > 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 altitude gain in a day is the same for the person who flew directly and the person who hiked vigorously to that altitude, the hiker may be more likely to be ill than the person who flew in. Examples of destinations that allow access to relatively high altitudes without hiking (3,400-4,200 m; 11,200-13,800 ft) include La Paz, Bolivia; Lhasa, Tibet; and Cuzco, Peru.

High-Altitude Trekking Routes

Trekkers are at higher risk of HACE and HAPE.

Altitude illness affects 50% or more trekkers on popular high-altitude 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 altitudes for *longer* periods of time than in most other situations. Consequently, the risk of dying from altitude sickness 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 altitude gains more rapid than typical Himalaya treks.

Prevention

Preventive Strategies—Traveler Education

Typical Tourist Destinations

- Descend to sleep at a lower altitude and ascend to a higher altitude during the day. For example, travelers typically stay in Mammoth Lakes, California (2,400 m; 7,900 ft) or nearby areas and ski at the higher altitudes of the mountain.
- Use acetazolamide prophylaxis, if indicated (e.g., if flying directly to the destination, such as travelers flying from Lima to Cusco).
- See also Acclimatization.

Table 2: Preventive Strategies for Popular Tourist Destinations

Preventive Strategies for Popular Tourist Destinations

Destination	Peak altitude	Comments
Mammoth Mountain, California	3,400 m (11,200 ft)	Travelers typically stay in Mammoth Lakes (2,400 m; 7,900 ft) or nearby areas and ski at the higher altitudes of the mountain.
Mont Blanc, France and Italy	4,810 m (15,800 ft)	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 altitudes during the day.
Bogota, Colombia	2,640 m (8,700 ft)	Travelers typically manage the altitude with hydration and rest.
Quito, Ecuador	2,800 m (9,200 ft)	Some travelers fly into Quito and may benefit from acetazolamide prophylaxis, whereas others may carry the medication to be used in response to altitude symptoms.
Cusco, Peru	3,400 m (11,200 ft)	For travelers flying from Lima to Cusco, acetazolamide prophylaxis 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.
La Paz, Bolivia	3,800 m (12,500 ft)	For travelers flying into La Paz, acetazolamide prophylaxis is recommended.
Lhasa, Tibet	3,700 m (12,100 ft)	For travelers flying into Lhasa, acetazolamide prophylaxis is recommended.
Addis Ababa, Ethiopia	2,400 m (7,900 ft)	Travelers typically manage the altitude with hydration and rest.

Trekking

Sensible itineraries, including gradual ascents, are only the first step to avoiding severe altitude illness. The main goal of altitude-illness advice is for travelers to react appropriately if altitude symptoms occur (see table below).

Trekkers should be taught these safety rules:

- Know the early symptoms of altitude illness and be willing to acknowledge them if they occur (see Symptoms chart).
- Never ascend to sleep at a higher altitude with any symptoms of altitude illness.
- Descend if symptoms become worse while resting at the same altitude.

Trekkers can lessen risk by:

- gradually ascending, which allows time to acclimatize (see Acclimatization).
- adhering to the adage, "climb high, sleep low." Mountain climbers who reach higher altitudes during the day can lessen the risk of illness by returning to the valleys to sleep.
- recognizing and acknowledging symptoms.
  - 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 altitude that night. In general, symptoms that begin in the morning, after spending the night at a new altitude, are more likely to clear up with rest at the same altitude than symptoms that began the day before while ascending to the camp.

- should descend, especially if symptoms worsen or fail to improve after resting at the same altitude for a period. Descent is the treatment of choice, but oxygen, medications, and/or the use of portable hyperbaric chambers may also be indicated.
- See Treatment.

Table 3: Preventive Strategies for Popular Trekking Destinations

Preventive Strategies for Popular Trekking Destinations		
Destination	**Peak altitude**	**Comments**
Mount Fuji, Japan	3,780 m (12,400 ft)	Many mountain lodges at 2300 to 3780 m (7,500-12,400 ft) are available for overnight stays for climbers during their ascent.
Inca Trail, Peru	4,200 m (13,800 ft)	Most trekkers fly from Lima to Cuzco, a rapid ascent. An alternative is to travel via Arequipa (see previous table description for Cusco).
Annapurna Circuit, Nepal	5,416 m (17,800 ft)	Most trekkers arrive at Pokhara (up to 1,740 m; 5,700 ft) and can acclimatize gradually during the trek. Because some routes reach significantly higher elevations, acetazolamide prophylaxis is beneficial.
Everest Base Camp, Nepal	5,360 m (17,600 ft)	Routes to the peak vary in their rates of ascent. Generally, climbers should start acetazolamide prophylaxis as they ascend and continue until they descend to the starting point. Prescribe dexamethasone and nifedipine for emergency treatment.
Kilimanjaro, Tanzania	5,890 m (19,300 ft)	Routes to the peak vary in rate of ascent. Descent typically takes only 1 to 2 days. Generally, climbers should start acetazolamide prophylaxis as they ascend and continue until descent to the final camp at 4,270 m (14,000 ft) is initiated. Prescribe dexamethasone and nifedipine for emergency treatment.

Preventive Strategies—Drugs

See Table 4: Medications for Prophylaxis and Treatment of High Altitude Illness for dosing.

Acetazolamide (Diamox)

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

- Indications for AMS and HACE prophylaxis: Consider chemoprophylaxis for travelers anticipating rapid ascent to sleeping altitudes 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 allergy to sulfonamides have no increased risk of an allergic reaction when taking acetazolamide.
  - Risk of an allergic reaction may be increased in people with multiple drug allergies.
  - 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 prophylaxis 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 altitudes beyond tourist-destination altitudes.
  - Dexamethasone can be considered for persons for whom acetazolamide is unequivocally contraindicated for AMS prevention.
  - 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

Nifedipine (Procardia; Adalat)

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

- Indications for prophylaxis: reserved for the small subgroup of people who are highly 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 prophylaxis: 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.

Differential Diagnosis

A complete history of the present illness is critical for diagnosing altitude illness. The altitude at which the trip began and the altitude at which the patient slept for each point up to the present should be obtained. Any altitude-related symptoms at these prior heights should be identified.

To attribute symptoms to altitude illness, the symptoms must have begun during ascent. A traveler who was asymptomatic at the high point of a trek cannot develop AMS while descending. In almost all instances of severe altitude illness, the history will identify symptoms of AMS at a lower height that were ignored or attributed to something else by the patient.

Virtually all life-threatening altitude illness is due to ascent despite recognizable symptoms. The key to preventing severe altitude illness is to never ascend when symptoms are present.

Other illnesses that mimic altitude sickness can occur at altitude, and these illnesses may have significantly different implications. The key to differentiating between altitude illness and other medical conditions at altitude is the history of the present illness and the presenting symptoms.

Headache, anorexia, nausea, vomiting, and profound fatigue can all be symptoms of AMS. Diarrhea is not associated with altitude illness. 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 can be a throbbing frontal headache. All headaches at altitude must be treated as altitude headaches, and no further ascent should be attempted until resolution of any headache.

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 6th cranial nerve palsies) are not associated with altitude illness.

Rarely, loss of vision has been associated with rapid ascent to high altitude and has been attributed to migraine-like spasm. As noted earlier, people who have undergone radial keratotomy to correct vision have developed severe hyperopia or myopia at altitude and have become functionally blind. This condition reverses readily with descent, but it could lead to a fatal outcome for a high-altitude mountaineer stranded with blindness.

Multiple pulmonary emboli 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 altitude is essential.

- Assume that the descent has definitively treated the altitude 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 altitude 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 postdescent and is usually the last symptom to resolve.
- HAPE is a high risk for a subsequent pulmonary infection, and 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.

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.

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 altitude at which symptoms started.
  - It is not necessary to descend until all symptoms are gone because symptoms can take from 48 to 72 hours to clear.
  - Any sign of improvement usually indicates the crossing of a tolerable altitude, 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.
  - 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 hyperbaric chamber (for trekkers)
  - Groups on long treks or climbs to very high altitudes (where rapid descent might be precluded) should consider carrying a hyperbaric chamber (e.g., the Gamow Bag), which can effectively mimic descent. The amount of "descent" achieved within the chamber depends on the elevation at which the descent began, but it is usually about one-third of the current altitude. For example, the chamber can physiologically lower the traveler with symptoms at 4,200 m (13,800 ft) to the equivalent of an altitude 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 prone 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, with the capability of treating multiple patients or repeating treatments for the same person.

Drug Treatment

See Table 4: Medications for Prophylaxis 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 altitude. If a person sleeping at altitude 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 altitude, 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 altitude. These drugs can also prevent headaches when started a few hours before ascent to altitudes of 3,400 to 4,900 m (11,200-16,100 ft).

Gingko biloba has been evaluated, but results vary widely. Therefore, this herbal supplement is not recommended as an effective therapy for altitude illness.

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

Positive end expiratory pressure (PEEP), which is used for treatment of HAPE at altitude, 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 4: Medications for Prophylaxis and Treatment of High Altitude Illness

Medications for Prophylaxis and Treatment of High Altitude Illness

Medication	Dosage	Indications	Precautions	Side effects
Acetazolamide (Diamox)	<u>Adult</u> Prophylaxis: 125 mg every 12 hours; 250 mg every 12 hours if > 100 kg (220 lb) Treatment: 250 mg every 12 hours <u>Pediatric</u> Prophylaxis and treatment: 2.5 mg/kg/dose every 12 hours	For prophylaxis of AMS and HACE and treatment of AMS. For prophylaxis, medication should be taken the day before ascending, each day during ascent, and for 24 to 48 hours after arrival (arriving and staying) at	Severe allergic reactions to acetazolamide are extremely rare. Persons with multiple drug allergies or a history of a life-threatening reaction to sulfa drugs should have acetazolamide administered in a controlled environment	Almost always causes paresthesias of fingers and toes, and occasionally causes perioral paresthesias Occasionally causes nausea Increased photosensitivity

		highest altitude. Persons who become and remain symptomatic beyond 48 hours should continue to take acetazolamide each evening for several more days to help them sleep.	before the trip. Persons with a history of mild sulfa reactions or rashes can safely take acetazolamide.	
Dexamethasone (Decadron)	Adult Prophylaxis in uncommon situations: 2 mg every 6 hours or 4 mg every 12 hours Treatment: AMS: 4 mg every 6 hours HACE: initial dose of 8 mg followed by 4 mg every 6 hours Oral, IM, and IV dosages are interchangeable. Pediatric Prophylaxis: none Treatment for AMS and HACE only: 0.15mg/kg/dose every 6 hours up to 4 mg	For treatment of the cerebral symptoms of AMS. Although effective for prophylaxis of AMS and HACE, it should be recommended for that purpose only in extreme circumstances (*see text above*).	Does not treat or prevent high-altitude pulmonary edema.	Euphoria Can increase the need for insulin or oral agents in diabetics
Ibuprofen (Advil, Motrin)	Adult Prophylaxis or treatment: 600 mg every 8 hours Pediatric Not recommended	For prophylaxis and treatment of headache at high altitude. For prophylaxis, medication should be started a few hours before ascent.	Risk of gastrointestinal bleeding may be increased at high altitudes.	Gastrointestinal irritation and bleeding Increased photosensitivity
Nifedipine (Procardia; Adalat)	Adult Prophylaxis or treatment: 20 mg sustained release every 8 hours or 30 mg sustained release every 12 hours Pediatric Not recommended	For treatment of HAPE. Can be used for prophylaxis of HAPE in known susceptible individuals (*see text*).	Limited studies only	Hypotension Headache Rash Urticaria
Salmeterol (Serevent)	Adult Prophylaxis: 125 µg (5 puffs) inhaled every twice a day Treatment: none Pediatric Not recommended	Can be used as adjunctive medication for prophylaxis of HAPE in known susceptible individuals.	For use only in addition to oral medications, not as monotherapy for prevention of HAPE.	Musculoskeletal pain Headache Prolonged QT interval (rare)
Sildenafil (Viagra)	Adult Prophylaxis: 50 mg every 8 hours Treatment: none Pediatric Not recommended	Can be used for prophylaxis of HAPE in known susceptible individuals.	Avoid in patients with hypertension, hypotension, or coronary artery disease.	Flushing Indigestion Headache Insomnia Visual disturbance
Tadalafil (Cialis)	Adult Prophylaxis: 10 mg twice a day Treatment: none Pediatric Not recommended	Can be used for prophylaxis of HAPE in known susceptible individuals.	Avoid in patients with hypertension, hypotension, arrhythmias, or coronary artery disease.	Flushing Indigestion Nausea Myalgia Headache Respiratory tract infection

Effect of High Altitudes on Preexisting Medical Conditions

Very few studies have measured the direct effect of altitude on various medical conditions; therefore, most advice is anecdotal. In general, the more severely limited a patient's exercise is at sea level, the worse he or she will do at altitude. If traveling to altitude is important to the patient, he or she should initially go to high altitude areas with excellent medical care available. An intermediate altitude should be attempted first, to determine if exposure to altitude can be tolerated.

Some high-altitude areas add a significant factor of remoteness. Travelers who are anxious about preexisting conditions may be unfit to go because they may be more than 24 hours away from medical help if problems arise. The best way to resolve these issues is individual counseling, including a discussion of the potential risk, remoteness, and the traveler's motivation for going.

Cardiovascular System

The risk of new ischemic cardiac events at altitude appears to be extremely low, seemingly no higher than the background rate of ischemic events in similarly aged persons at low altitude. Furthermore, a stress ECG has low sensitivity for detecting an insignificant possible occurrence, so requiring an ECG prior to being approved for a high-altitude journey is not likely to be helpful.

If hiking and/or climbing are routine activities for the person involved, and if exercise is not limited by any symptoms, concern would be low regarding trekking to high altitude. If the traveler has a sedentary lifestyle, exertion or trekking at high altitude is ill advised, just as a sudden increase in activity at lower altitudes would be. A gradual training program should be prescribed to prepare the traveler for a trek. The ability to hike steadily for at least 4 hours over steep terrain should be a minimum requirement for trekking in high mountains.

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

Persons with a history of successful coronary revascularization who are currently exercising without symptoms have no contraindication to altitude.

Persons with congestive heart failure can experience difficulties at high altitude because even a little stress on the heart can produce 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 altitude until it is can be remedied.

Blood pressure increases modestly as one ascends to high altitude. Systolic pressure is increased more than diastolic. Travelers who are well controlled on antihypertensive medications and who are going for a short tourist trip to moderate altitude do not need to adjust dosage. Expatriates and long-stay travelers at altitudes over 2,500 m (8,200 ft) may require dose adjustment after arrival. Persons with unstable blood pressure need close monitoring during their stay at altitude and access to a medical setting where drugs can be quickly adjusted or blood pressure rapidly stabilized.

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) and, theoretically, are at increased risk for developing HAPE. Persons with any significant degree of COPD will do poorly at high altitude.

Because HAPE is associated with hypertension, people with primary pulmonary hypertension may not do well at altitude.

Despite the theoretical concern that persons with asthma may be at increased risk at altitude from the effects of cold and exercise, most asthmatics have generally done well at altitude, possibly due to the greatly decreased presence of allergens at high altitude. Nevertheless, persons with asthma should be instructed to carry their medications with them at all times.

Neurological System

Anecdotally, altitude may lower the threshold for having a seizure. Those with uncontrolled or poorly controlled seizures should avoid altitude, 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 at altitude and strongly associated with migrainous headache at altitude.

Hematological System

Even moderate altitudes, such as those encountered in airplane travel, can trigger a sickle cell trait (SCT) crisis in a person with SCT or disease. Typical tourist altitudes (such as in Cusco, La Paz, Quito, and Llasa) will often cause crises and splenic infarcts in those with SCT, even without physical exertion.

Dark-skinned patients born outside the U.S., especially in developing countries, may never have been tested for SCT as children. High altitude is clearly contraindicated in this population.

In both SCT and disease, significant physical exertion increases risk of sickle cell crisis at low altitudes, and less exertion is required to precipitate a crisis at higher altitudes, even in altitudes tolerated at rest.

Patients with low red cell counts could have trouble adjusting to high altitude because their oxygen-carrying capacity is already low. These individuals should proceed with caution. Patients 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 altitude if they are comfortable with self-monitoring and willing to pay closer-than-usual attention to their glucose balance.

Glucose meters may lose calibration at high altitude.

High altitude can be associated with severe ketoacidosis (for reasons that are unclear), which can lead to death. Risk factors for developing ketoacidosis at altitude include intercurrent illness (gastroenteritis, respiratory infection, and altitude illness) and the possible adverse interplay of respiratory alkalosis, which could mask a deepening metabolic acidosis. Acetazolamide may further block the body's attempt to correct the acidosis.

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

Shoreland does not recommend high-altitude trekking for pregnant women because of the isolation from readily available medical care that would be required in the event of early labor or complications of pregnancy.

No data are available concerning the risks of altitude on the fetus. No cases have been reported of high altitude exerting a negative outcome on pregnancy in a trekker or climber. However, due to the remote location of many high-altitude destinations, Shoreland advises pregnant women to avoid high altitude in the first or last trimester and to obtain an ultrasound to confirm an intrauterine pregnancy. Short stays at intermediate altitudes 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 altitude of 3,000 to 3,600 m (9,800-11,800 ft), thus Shoreland recommends that pregnant women avoid exposures above that elevation.

The main drugs used for altitude illness prevention or treatment (acetazolamide, dexamethasone, and nifedipine) are Class C drugs, which are given during pregnancy only when the benefit outweighs the potential risk. Acetazolamide is specifically not recommended for pregnant women. Oxygen, which is readily available to pregnant women in typical high-altitude 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 altitudes.

Infants and Children

Travel to altitude combined with remote location should be discussed with parents, although travel to altitudes 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 altitudes commonly faced on tourist trips better than adults.

Although there is limited published information, acetazolamide has been used safely in children for other indications; experts suggest a prophylaxis 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 altitude, 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 prophylaxis in children, and 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 altitude. However, concern exists that the increased risk of thromboembolism in women taking oral contraceptives at sea level might be compounded by high altitude, 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 altitude (above 6,000 m; 19,700 ft) should consider discontinuing the medication.
