Medical Summary

ALTITUDE ILLNESS

INTRODUCTION

Altitude illness occurs when one ascends more rapidly than the body can adjust ("acclimatize") to the reduced atmospheric pressure and decreased oxygen delivery to the body's cells at the higher altitude. Factors affecting acclimatization include the altitude attained, the rate of ascent, the duration of exposure, genetic predisposition, and certain preexisting conditions. (See "Acclimatization," "Risk," and "Effect of High Altitude on Preexisting Medical Conditions.")

Altitude illness is generally divided into 3 syndromes: acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), and high altitude cerebral edema (HACE). See "Syndromes and Symptoms."

Symptoms can range from mild to life-threatening. Although mild symptoms have been documented at relatively low altitudes of 1,200-1,800 m (3,900-5,900 ft), serious syndromes are rarely seen below 2,500-3,000 m (8,200-9,800 ft). While death can occur from the more severe forms of altitude illness, most symptoms can be prevented or minimized by proper acclimatization and/or preventive medications.

Risk and prevention strategies vary depending on the type of travel planned: travel to typical tourist destinations at relatively moderate heights or trekking in extreme 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, while 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 one will or will not be a good acclimatizer. However, past 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 6-48 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 (9,800 ft), 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 (9,800 ft) 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.
- It is useful to have a high altitude exposure at > 3,000 m (9,800 ft) for ≥ 2 nights within 30 days before a trek.

SYNDROMES AND SYMPTOMS

Altitude illness is generally divided into 3 syndromes: acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), and high altitude cerebral edema (HACE). These syndromes 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 begins as AMS but the symptoms become more severe. 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 from other causes that it is rarely a useful clinical sign of HAPE. Descent is mandatory as soon as HAPE is suspected, because the symptoms can progress rapidly and death can occur within hours of recognizing clinical HAPE. Unfortunately, exertion considerably worsens HAPE. Exertion by the sick person should be minimized during descent, but this is not always possible. 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 pre-terminal event.

Other Conditions

Virtually all people who sleep above 3,000 m (9,800 ft) have an alteration in their breathing during sleep. The result is a form of **periodic breathing** in which increasingly deep breaths are followed by a brief (5-30 seconds) 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 that can lead to other symptoms of altitude illness. As people with peripheral edema acclimatize, they often experience a profound diuresis and relief of symptoms. One can ascend with peripheral edema but must not ascend if other symptoms develop.

High altitude retinopathy refers to the rare development of retinal hemorrhages while staying at high altitude. Usually only discovered by trained doctors, the hemorrhages occur near the macula and typically present with a visual field deficit.

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 pre-terminal event)
	• Can present with or without cerebral symptoms[4]

1. Not all symptoms are necessary for each diagnosis. Bear in mind that "If one feels unwell at altitude, it is altitude illness until proven otherwise." (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, by measuring extremely low oxygen saturation, can help to distinguish between HAPE with severe hypoxia and HACE.

RISK OF ALTITUDE ILLNESS

Low risk:

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

Moderate risk:

- Prior history of AMS and ascending to 2,500-3,000 m (8,000-9,800 ft) in 1 day
- No prior history of AMS and ascending to > 2,800 m (9,200 ft) in 1 day
- Ascending > 500 m (1,600 ft) per day (increase in sleeping elevation) at altitudes > 3,000 m (9,800 ft)

High risk:

- History of AMS and ascending to ≥ 2,800 m (9,200 ft) in 1 day
- Prior history of HAPE or HACE
- Ascending to > 3,500 m (11,400 ft) in 1 day
- Ascending > 500 m (1,600 ft) per day (increase in sleeping elevation) above 3,500 m (11,500 ft)
- 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 (9,800 ft); it is rare for this group of travelers to experience the more severe forms of altitude illness, such as HAPE or HACE, 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). While mild symptoms of altitude illness have been documented at these altitudes, serious syndromes are rarely seen below 2,500-3,000 m (8,200-9,800 ft).
- Daytime activities (e.g., skiing, hiking, sightseeing) may take travelers to higher altitudes, but risk is lessened by descending to sleep at the resort altitude.

Risk increases for those who hike vigorously 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): La Paz, Bolivia; Lhasa, Tibet; and Cuzco, Peru.

High Altitude Trekking Routes

Trekkers are at higher risk of HAPE and HACE.

- Altitude illness affects 50% or more trekkers on popular high-altitude routes.
- The death rate from complications of altitude sickness in Nepal is about 1 in 30,000 trekkers, or 2-3 deaths per year.
- Although trekking in the Himalaya affords the opportunity to acclimatize gradually, it brings one to high altitude for *longer* periods of time than in most other situations, and consequently the risk of dying from altitude sickness is higher in this region.
- Most trekking itineraries take a "one-size fits all" approach towards the pace of the trek, and thus cannot guarantee that altitude illness will not occur.
- Trekking agencies feel pressure to offer *shorter* expeditions for busy people who cannot take long holidays. Mount Kilimanjaro treks that summit in 5 days are offered—when even 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 go to 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).
  - For example, travelers flying from Lima to Cusco
- See also "Acclimatization."

Preventive Strategies for Popular Tourist Destinations		
Destination	**Peak altitude**	**Comments**

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 land transportation to Cusco.
Mammoth Mountain, California, U.S.	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 go to higher altitudes during the day.
Quito, Ecuador	2,800 m (9,200 ft)	Some travelers fly into Quito and may benefit from acetazolamide prophylaxis while others may carry the medication to be used in response to altitude symptoms.
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.

Trekking

Trekkers should be taught that sensible itineraries, including gradual ascents, are only the first step in avoiding severe altitude illness. The main goal of altitude illness advice is to react appropriately if altitude symptoms occur. (See table below.)

Trekkers should be taught these safety rules:

- Learn 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 are getting worse while resting at the same altitude.

Lessen risk:

- Gradual ascent allows time to acclimatize.
- "Climb high, sleep low." Mountain climbers who reach higher altitudes during the day can lessen risk of symptoms by returning to the valleys to sleep.
- Recognize and acknowledge symptoms.
    - Cases of fatal altitude illness almost invariably result from ascent with symptoms that could have been recognized as due to altitude illness.
    - In organized trekking groups, there is a great deal of pressure to keep up with the group schedule, so as not to be left behind. Leaving a client behind is problematic logistically for a trekking group, thus contributing to the denial of altitude symptoms.
- See also "Acclimatization."

If symptoms appear:

- Do not ascend further; AMS symptoms will invariably worsen with ascent.
    - However, if the symptomatic person appears to have the ability to make it over a higher pass to sleep at a lower altitude that night, this is a risk that can be taken.
    - 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.
- Descent remains the treatment of choice, especially if symptoms worsen or fail to improve after resting at the same altitude for a period of time. Oxygen, medications, and/or the use of pressurized bags may be indicated.
- See "Treatment."

Preventive Strategies for Popular Trekking Destinations		
Destination	**Peak altitude**	**Comments**

Annapurna Circuit, Nepal	4,500 m (14,800 ft)	Most trekkers arrive to 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	5,364 m (17,600 ft)	Routes to the peak vary in their rates of ascent. Generally start acetazolamide prophylaxis as the climber ascends; continue until descent to the starting point. Prescribe dexamethasone and nifedipine for emergency treatment.
Kilimanjaro, Tanzania	5,895 m (19,300 ft)	Routes to the peak vary in rate of ascent; descent typically takes only 1-2 days. Generally, start acetazolamide prophylaxis as the climber ascends; continue until descent to the starting point. Prescribe dexamethasone and nifedipine for emergency treatment.

Preventive Strategies—Drugs

Acetazolamide (Diamox)

Acetazolamide has the longest history of use for preventing and treating AMS and works by improving one's acclimatization—not by masking symptoms.

- Indications for prophylaxis: Consider for chemoprophylaxis in travelers anticipating rapid ascent to sleeping altitudes above 2,800 m (9,200 ft).
- Dose: The recommended prophylactic dose of acetazolamide is 125 mg twice daily (250 mg/day total). See table below. (See Literature Watch Review "Acetazolamide Dosage.")
  - The advantage of this dose over previously used doses of 500 mg/day is that there is a lower rate of side effects with the lower dose.
  - Acetazolamide is available in 125 mg and 250 mg tablets and 500 mg sustained-release capsules.
  - When indicated, acetazolamide can be used in children for the prevention (and treatment) of AMS at 2.5mg/kg/dose every 12 hours.
  - Schedule: Start taking acetazolamide the day before ascent, take the drug each day of ascent, and continue taking it for 24-48 hours after arrival at 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. (See table, below.)
- 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 paresthesias in the fingers and toes, and, occasionally, peri-orally. It is important to mention these side effects when prescribing acetazolamide; otherwise the person may suspect an allergic reaction and needlessly stop the medication.
  - Taking acetazolamide gives carbonated beverages a metallic taste.
  - Nausea may occur.
- Allergic reactions to acetazolamide are extremely rare.
  - Acetazolamide is a non-antibiotic sulfone drug (not a sulfa drug); 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 persons 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 the trip. Those with a history of mild sulfa reactions or rashes can take acetazolamide safely.
- See table below for treatment dosing.

Dexamethasone (Decadron)

Dexamethasone works by improving symptoms rather than improving acclimatization. Thus, there is the potential to get sick rapidly if one stopped taking or ran out of dexamethasone.

- Indications for prophylaxis of AMS (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.
    - Because neither pregnant women nor children should be found in this situation, dexamethasone would not be used for prevention in these populations.
  - Dexamethasone can be considered for persons for whom acetazolamide is unequivocally contraindicated for AMS prevention.
- Dosing for prophylaxis: 2-4 mg every 8-12 hours
- Side effects:
  - Euphoria
  - Can increase the need for insulin or oral agents in diabetics.
- See table below for treatment dosing.

Medications[1] for Prophylaxis and Treatment of High Altitude Illness

Medication	Adult dosage	Indications	Precautions	Side effects
Acetazolamide (Diamox)	Prophylaxis: 125 mg every 12 hours Treatment: 250 mg every 12 hours	For prophylaxis and treatment of acute mountain sickness. For prophylaxis, medication should be taken the day before ascending, each day during ascent, and for 24-48 hours after arrival at 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.	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 before the trip. Persons with a history of mild sulfa reactions or rashes can take acetazolamide safely.	Almost always causes paresthesias of fingers and toes, and occasionally peri-orally. Occasionally causes nausea.
Dexamethasone (Decadron)	Treatment: initial dose of 8 mg followed by 4 mg every 6 hours; oral, IM, and IV dosages are interchangeable. Prophylaxis in uncommon situations: 2-4 mg every 8-12 hours	For treatment of the cerebral symptoms of acute mountain sickness. Although effective for prophylaxis of AMS, it should be recommended for that purpose (*see text above*) only in extreme circumstances.	Does not treat or prevent high altitude pulmonary edema.	Euphoria. Can increase the need for insulin or oral agents in diabetics.
Ibuprofen (Advil, Motrin)	600 mg every 8 hours	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.
Nifedipine (Procardia; Adalat)	20 mg sustained release every 8 hours or 30 mg sustained release every 12 hours	For treatment of high altitude pulmonary edema. Can be used for prophylaxis of HAPE in known susceptible individuals (*see text*).	Limited studies only	Hypotension Headache Rash Urticaria
Salmeterol (Serevent)	125 µg (5 puffs) inhaled every 12 hours	Can be used as adjunctive medication for prophylaxis of HAPE in known susceptible	For use only in addition to oral medications, not as monotherapy for prevention of HAPE.	Musculoskeletal pain Headache

		individuals.		Prolonged QT interval (rare)
Sildenafil (Viagra)	50 mg every 8 hours	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)	10 mg every 12 hours	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
1. Doses given are for adults. The pediatric dose for acetazolamide is 2.5 mg/kg/dose every 12 hours (prophylaxis or treatment). Nifedipine should not be used in children; dexamethasone may be used only for treatment of AMS and HACE in children at a dose of 0.15 mg/kg/dose every 6 hours (see "Infants and Children").				

Nifedipine (Procardia; Adalat)

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

- Prophylaxis: Reserved for the small subgroup of people who are highly susceptible to HAPE.
- 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)

Phosphodiesterase-5 inhibitors cause pulmonary vasodilatation and lower pulmonary artery pressure.

- Tadalafil is recommended as prophylaxis 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

The history of the present illness is critical in diagnosing altitude illness. The history should elicit the altitude at which the trip began and the altitude at which the victim slept at each point up to the present time. Any altitude-related symptoms at these prior heights should be elicited.

In order to attribute symptoms to altitude illness, they must begin during ascent. A person who has been 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 ascending 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 they 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, and it 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 pre-dates 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 neurologic symptoms should raise suspicion of an intracranial problem.

Lateralizing neurologic findings are almost never due to AMS or HACE alone. One should be concerned about cerebral vascular accident when lateralizing symptoms are present. Additionally, cranial nerve palsies, with the possible exception of 6th cranial nerve palsies, are not associated with altitude illness.

Rarely, loss of vision has been associated with traveling rapidly to high altitude and has been attributed to migraine-like spasm. Reports have surfaced that people who have undergone radial keratotomy to correct vision have developed severe short-sightedness at altitude and become functionally blind. This condition reverses readily with descent, but it could lead to 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

It is essential to evaluate travelers with altitude illness who have already descended from altitude.

- One can assume that the descent has definitively treated the altitude problem, so one should now be alert either for complications of altitude illness or for the possibility of a different diagnosis.
- Persistent neurologic symptoms that do not show rapid signs of improvement at low altitude should be investigated with brain imaging.
- In severely comatose patients, the coma can, rarely, persist for several days, but patients usually regain consciousness fairly rapidly. Altered sensorium and headache clear up first. Gait ataxia can persist for 24-48 hours post descent 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 to prescribe appropriate antibiotics if productive cough or fever persists. Chest x-ray in HAPE usually shows fluffy infiltrates that are often more prominent on the right side than 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 pressurization bags (for trekkers), and the recognition of the value of 3 medications (acetazolamide, dexamethasone and nifedipine) have expanded treatment choices when confronted with altitude illness.

Non-Drug Treatment

- Descent is the treatment of choice for both tourists and trekkers.
  - Descent invariably 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 up to 48-72 hours to clear.
  - Any sign of improvement usually heralds 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.
  - Bottle oxygen is carried by many trekking expeditions. However, bottled oxygen is expensive and heavy to carry, and thus there is usually insufficient oxygen available. A highly compressed expedition oxygen bottle at a flow of 2 liters/minute will last for 6 hours. At 4 liters/minute, which is more likely to be therapeutic for altitude illness, one gets only 3 hours of therapy.
- Pressurization bags (for trekkers)
  - Groups on long treks or climbs to very high altitude where rapid descent might be precluded should consider carrying a pressurization bag which can effectively mimic descent. "Gamow" is one brand name. The amount of "descent" achieved within the bag depends on the elevation at which the descent began, but it is usually about 1/3 the current altitude. For example, the bag 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 pressurization bag is usually enough to dramatically improve mild to moderate AMS. In more severe cases, several hours in the bag may be necessary. Occasionally, relapse may occur and repeat treatments may then be necessary. Persons generally tolerate being placed prone in the bag, but those with severe HAPE may have

difficulty lying flat.
- The effects of bottled oxygen versus pressurization appear to be equal. However, the pressurization bag has the advantage of having an indefinite period of use, with the ability to treat multiple patients or repeated treatments for the same person.

Drug Treatment

Acetazolamide (Diamox)

Limited data support treatment of adults using a dose of 250 mg twice daily, although smaller doses may be effective. The usual pediatric dose is 2.5 mg/kg/dose twice daily.

Treatment should begin when the onset of symptoms are noted and continued for at least 1 day after all symptoms have cleared. If AMS symptoms recur with further ascent, the drug can be re-started.

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 effectively eliminate this problem. However, there are many reasons for poor sleep at high altitude, so a careful history is of use.

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.

- For AMS, the usual adult dose is 4 mg every 6 hours, whether administered orally, intramuscularly or intravenously.
- For treatment of HACE, an initial dose of 8 mg is recommended.

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 move up to sleep at a higher elevation until dexamethasone has been discontinued for 24 hours or more.

Nifedipine (Procardia; Adalat)

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

- The usual adult treatment dose is 20 mg sustained release every 8 hours or 30 mg sustained release every 12 hours.
- Nifedipine has not been studied in treating children and is not recommended for this use.

Other Treatments

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

Gingko biloba has been evaluated but results vary widely; therefore it is not recommended as an effective therapy for altitude illness.

Morphine has been used cautiously at altitude as an adjunct to treatment for HAPE. Physicians should be aware of the potential for respiratory suppression and consequent worsening of the patient's condition. However, treatment of HAPE with morphine at altitude has been shown to be safe and allows the patients to feel better more rapidly than oxygen therapy alone.

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

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 person'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 see 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, since they may be 24-48 hours or more from medical help if problems arise. The best way to resolve these issues is individual counseling, including discussing 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 in detecting a one-in-a-million 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 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, as would be a sudden increase in activity at lower altitudes. A gradual training program should be prescribed in order to prepare 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. 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, since even a little stress on the heart can produce failure. If they 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 anti-hypertensive 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.

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

Persons with asthma were thought to be at increased risk at altitude, theoretically due to the possible adverse effects of cold and exercise. However, these persons have generally done well at altitude, possibly due to the greatly decreased presence of allergens at high altitude. Nevertheless, persons with asthma should be cautioned to carry their medications with them at all times.

Neurologic System

Anecdotally, altitude may lower the threshold for having a seizure. Those with uncontrolled or poorly controlled seizures should avoid altitude, but those well-controlled on medication have no real contra-indication to such travel, especially if medical help will be nearby.

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 or sickle cell disease. Typical tourist altitudes (such as in Cusco, La Paz, Quito, and Llasa) will often cause crises and splenic infarcts in those with sickle trait, even without physical exertion.

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

In both sickle trait 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.

People with low red cell counts could experience difficulty adjusting to high altitude, because their oxygen-carrying capacity would already be low. They 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 travel safely to high altitude if they are comfortable with self-monitoring and willing to pay closer attention than usual 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) and has led to deaths. 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 at close hand and unfrozen during a long, cold, backcountry journey.

OTHER CONSIDERATIONS

Pregnancy

Shoreland recommends against 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.

Travel in a developing country carries the risk of diarrhea and other infectious diseases, as well as the potential for trauma in conveyances.

There are no data available concerning the risks of altitude on the fetus. There are no reported cases of high altitude exerting a negative outcome on pregnancy in a trekker or climber. Oxygen saturation is fairly well maintained up to an altitude of 3,000-3,600 m (9,800-11,800 ft), so it is recommended that pregnant women avoid exposures above that elevation.

An adverse pregnancy outcome could be due to many causes. However, if an adverse outcome occurs during travel to high altitude, the mother may be concerned that high altitude exposure was the cause, thus causing self-recrimination in the decision to travel to high altitude while pregnant. Therefore, this issue should be addressed, carefully weighing the need to go on a particular high altitude trip while pregnant against the potential for regret should there be an adverse outcome of the pregnancy.

The 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. 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 always be cause for careful discussion with parents.

Children have a risk similar to adults for acute mountain sickness (AMS), but AMS may be more difficult to assess in the preschool and younger-aged children, especially pre-verbal children. The signs of AMS (nausea, vomiting, and irritability) are very non-specific 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 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.

Respiratory syncytial virus (RSV) has been shown to be more severe in children aged < 5 years who are at higher altitude; this has not yet been confirmed for other respiratory viruses.

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.

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 at extremely high altitude on expeditions (above 6,000 m; 19,700 ft) should consider discontinuing the medication. The practice of some clinicians of prescribing oral contraceptives to prevent menstruation during a trek should be discouraged.
