High Altitude Medicine

David A. Connett, DO, FACOFP, dist
High Altitude Syndromes

- Acute Mountain Sickness (AMS)
- High Altitude Cerebral Edema (HACE)
- High Altitude Pulmonary Edema (HAPE)
- High Altitude Deterioration
- High Altitude Pulmonary Hypertension
- Chronic Mountain Sickness
Moderate altitude
- 5,000–10,000 feet above sea level
- Highest U.S. ski resorts

High altitude
- 10,000 – 18,000 feet above sea level
- High peaks in the lower 48, Europe

Extreme altitude
- Greater than 18,000 feet above sea level
- Denali, Himalaya, Karakoram, Andes
High Altitude

- **High Altitude**—5,000 feet to 11,500 feet
  - Minor impairment of arterial oxygen transport
    - arterial SaO2 > 90%
  - AMS common with rapid ascent above 8000 feet

- **Very High Altitude**—11,500 feet to 18,000 feet
  - Maximum arterial SaO2 < 90%, PAO2 < 60 torr
  - Most common range for serious altitude sickness

- **Extreme Altitude**—over 18,000 feet
  - Marked hypoxemia and hypercapnia
# Incidents of Altitude Illness in Various Groups

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Number at Risk per Year</th>
<th>Sleeping Altitude (feet)</th>
<th>Maximum Altitude Reached (feet)</th>
<th>Average Rate of Assent (days low altitude)</th>
<th>Percent with AMS</th>
<th>Percent with HAPE and/or HACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western State Visitors</td>
<td>30 million</td>
<td>6500 ft. 8000 ft. &gt;9800 ft.</td>
<td>11,500 ft.</td>
<td>1–2</td>
<td>18–20 22 27–42</td>
<td>0.01</td>
</tr>
<tr>
<td>Mount Everest</td>
<td>6000</td>
<td>18,000 ft.</td>
<td>1–2 (fly in) 10–13(walk)</td>
<td>47 23</td>
<td>1.6 0.05</td>
<td></td>
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<tr>
<td>Mount Denali</td>
<td>800</td>
<td>20,321 feet</td>
<td>3–7</td>
<td>30</td>
<td>2–3</td>
<td></td>
</tr>
<tr>
<td>Mount Rainier</td>
<td>6000</td>
<td>14,409 ft.</td>
<td>1–2</td>
<td>67</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Indian soldiers</td>
<td>Unknown</td>
<td>18,000 ft.</td>
<td>1–2</td>
<td></td>
<td>2.3–15.5</td>
<td></td>
</tr>
</tbody>
</table>
Neurological consequences of increasing altitude

Gradual decompression (e.g., from walking to altitude):
- 32% of climbers have hallucinations above 7500 m
- MRI changes, including white matter hyperintensities and cortical atrophy above 7000 m
- Memory retrieval impaired

Acute decompression (e.g., from aircraft explosion):
- Loss of consciousness
- Dizziness or tingling
- Altered night vision

PO2 (mmHg) vs Altitude (m):
- Extreme altitude:
  - Everest (8848 m)
- Very high altitude:
  - Aconcagua (6962 m)
- High altitude:
  - Kilimanjaro (5895 m)
- Commercial aircraft are pressurized to an altitude equivalent of 1500-2500 m

Symptoms vary among individuals and rate of ascent:
- 40
- 50
- 100
- 150

Learning and spatial memory impaired
- Psychomotor impairment detectable with FTT/pegboard
- Complex reaction time slows
- AMS and HACE possible
Environment at High Altitude

- Barometric pressure falls with increasing altitude in logarithmic fashion
- Partial pressure of oxygen decreases resulting in hypoxia
- Altitude changes with distance from equator, hypoxia worse at the poles.
- Pressure is lower in winter than in summer.
- Temperature decreases with altitude 1000 feet for every 3.56°F
- Ultraviolet light increases by 4% every thousand feet
Change in Oxygen Concentration with Altitude

% O2 available at altitude compared to sea level

Altitude x 1000 m

x 1000 ft 5 10 15 20 25

Vail

Breckenridge
Oxygen Levels at Altitude

OXYGEN LEVELS
AT DIFFERENT LOCATIONS
AND ELEVATIONS

- Mount Everest, Nepal, 29,035 feet
  33% OXYGEN
- Mount Denali, Alaska, 20,320 feet
  48% OXYGEN
- La Rinconada, Peru, 16,700 feet
  55% OXYGEN
- Kilimanjaro, 19,710 Feet
- Pikes Peak, Colorado, 14,110 feet
  61% OXYGEN
- Mount Fuji, Japan, 12,388 feet
  65% OXYGEN
- Vail Ski Resort, Colorado, 11,570 feet
  66% OXYGEN
- Denver, Colorado, 5,280 feet
  84% OXYGEN
- Sea Level, 0 feet
  100% OXYGEN
How does the height affect?
No medical exam can determine a person’s aptitude to height. There is no difference in sex or age. The height and the cold are the two variables that are more dangerous in climbing to the summit of America.

The Altitude
- 6,962 m: 37% lung capacity
- 5,000 m: 50% lung capacity
- 3,000 m: 75% lung capacity
- Nivel mar: 100% lung capacity

As we ascend, the air pressure and partial of oxygen decreases progressively and this may be the cause of many height inconveniences.

About 50% of the Aconcagua climbers had suffered one or more AMS’s symptoms.

Temperature
Should be 37 °, hypothermia is less than 35 °.

Symptoms of AMS
- Digestion is impaired by the lack of oxygen
- Gastrointestinal symptoms
- Pulmonary symptoms
- Lassitude: Profesiva fatigue in 24 to 48 hours
- Ataxia: Lack of equilibrio
- Insomnia
- Headache
- Peripheral edema: Swelling around the eyes and face, hand or foot
- Urine retention
- Severe AMS: It is characterized by the presence of pulmonary edema and/or brain, require immediate descent and medical assistance

How to prevent Acute mountain sickness
1. Ascent graduate. Start the rise below 3000 mt.
2. A night of acclimatization every 1000 meters.
3. Abundant hydration (5 liters per day).
4. You can achieve higher blood oxygen levels with a diet with 70 to 80% carbohydrate.

Source: Aconcagua, la cima de America.
Acute Mountain Sickness

- Rapid ascent to 8200 feet from altitudes below 5000 feet for unacclimatized
- Headache
  - Throbbing, by temporal or occipital worse at night
- Fatigue
- Dizziness/lightheadedness
- Anorexia and nausea
- Difficulty sleeping
Acute Mountain Sickness Differential Diagnosis

- Viral illness
- Hangover
- Exhaustion
- Dehydration
- Hypothermia
- Sedatives/hypnotic medications
- Carbon monoxide
Acute Mountain Sickness

- Usually self-limited
- If untreated may persist for weeks
- May precede HACE or HAPE
- Responds well to treatment
## Distribution of Symptoms and signs in 154 Trekkers Nepal with AMS

<table>
<thead>
<tr>
<th>Severity</th>
<th>Percent</th>
<th>Symptoms</th>
</tr>
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<tbody>
<tr>
<td>Mild</td>
<td>65</td>
<td>Headache, anorexia, nausea and malaise</td>
</tr>
<tr>
<td>Moderate</td>
<td>30</td>
<td>Unrelieved headache, vomiting, reduced urine output</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>Altered consciousness, ataxia, rales, cyanosis, dyspepsia at rest, possible papilledema</td>
</tr>
</tbody>
</table>
Pathophysiology AMS

↓ $P_iO_2$ at altitude → Hypoxia → Apnea during sleep → Hypocapnia → Hyperventilation
Pathophysiology AMS

- Alveolar hypoxia
  - Hyperresponsive pulmonary vasculature
  - Exercise
  - Hypoxic pulmonary vasoconstriction (uneven)
  - Increased capillary pressure (some capillaries)
  - Damage to capillary wall (stress failure)
  - High permeability edema (patchy distribution)
  - Exposed basement membranes
    - Neutrophil activation
      - Release of inflammatory markers
    - Platelet activation
      - Fibrin thrombi
  - Descent, oxygen, nifedipine
  - Restricted vascular bed (unilateral PA)
Pathophysiology AMS

HEADACHE + other symptoms of AMS

increased permeability of cerebral vessels

Systemic production of: IL-1, TNF alfa, PAF, endothelin

Mitochondrion

ATP
  ↓
  ADP
  ↓
  AMP

adenosine

inosine

hypoxanthine

HYPOXIA

neutrophils

NOS activation

Input: Ca++, H2O, Na+

activation of calcium-dependent protease

xanthine oxidase

hypoxanthine + xanthine oxidase + low% O2

Hypoxantine + xanthine oxidase + low% O2

1

Urate + H2O2 + O2

2

Fe3+

3

O2 + OH− + OH−

4

alterations in cell membranes
DNA mutations
alterations in protein

Peroxynitrite ONOO−

NO + ROS

NO production

1 – SOD, GPX;
2 – CATALASE;
3 – VIT. C
4 – VIT. E

H2O + O2

1

2

3

4
Acute Mountain Sickness Management
The Golden Rules

# 1 AMS symptoms at altitude are AMS until proven otherwise
# 2 Don’t ascend further if you have symptoms
# 3 Descend if very ill or not improving. Descend immediately for ataxia or decreased consciousness
# 4 Don’t let anyone with AMS descend alone
Treatment Mild AMS

- Stop ascent, rest, acclimatize at same altitude
- Acetazolamide, 125 to 150 mg twice a day, to speed acclimatization
- Symptomatic treatment as necessary with analgesics and anti-medicines or
- Descend 1500 feet or more
Low-flow oxygen, if available
Acetazolamide, 125 two 250 mg twice a day with or without Dexamethasone, 4 mg PO, IM, IV q 6hr
Hyperbaric therapy or Immediate descent
Instant Descent Inside a Bag

- 0.14 atmosphere (102 torr) above ambient pressure
- 14,000 feet simulates 8000 feet
- CO2 buildup minimal if used properly (and maybe helpful)
High Altitude Pulmonary Edema

- The most common cause of death from high-altitude illness.
- Most often after second night at new altitude
- Apparent abrupt onset
- May occur in the absence of Acute Mountain Sickness
HAPE Symptoms and Signs

- Early symptoms: fatigue, weakness, dyspnea on exertion, dry cough
- Progression two: tachycardia, tachypnea, and orthopnea and dyspnea at rest
- Pink or blood-tinged sputum is a very late finding
- Crackles usually start in right axilla
Pathophysiology of HAPE

- Pulmonary arterial vasoconstriction
  - HPV
  - Mediator imbalance

- Pulmonary vascular remodeling (LATE)

- Muscular vessels close at low lung volumes

- Extrinsic compression of pulmonary capillaries, veins, lymphatics:
  - High PEEP, P plat
  - Edema

- Pulmonary vein constriction
  -Raised PVR
  - Raised LAP
  - Co-existing LV dysfunction

- Intravascular occlusion
  - Inflammation
  - EC activation
  - Microthrombosis
**Intact blood gas barrier**

$P_c < 18 \text{ mmHg}$

**Interstitial edema**
Opening of endothelial gaps

$P_c = 18-20 \text{ mmHg}$

**Alveolar edema**
Opening if the endothelial and epithelial gaps

$P_c > 20 \text{ mmHg}$

*Water without albumin*

*Water + albumin + red blood cells*
Pathophysiology of HAPE

Obliteration of the pulmonary microcirculation. Silicone casts from postmortem specimens illustrating obliteration of the pulmonary microcirculation in a patient 3 wk following onset of acute lung injury (A), compared with that from a patient without pulmonary disease (B). With thanks to Professor Warren Zapol.
Treatment HAPE

- Minimize exertion and keep warm
- Oxygen, 4 to 6 L/min until improving it, then 2 to 4 L/min
- Dexamethasone, 4 mg PO, IM, IV q 6hr
HAPE Prevention

- Graded ascent
- Nifedipine for HAPE susceptibles
  - 20 mg orally every eight hours or 30 mg every 12 hours—starting 24 hours before arrival and continuing for three days
HAPE Prevention

- Dexamethasone 8 mg every 12 hours (also helps to prevent Acute Mountain Sickness)
- Tadalafil 10 mg every 12 hours (no benefit for Acute Mountain Sickness)
- Salmeterol 125 µg every 12 hours (some benefit for Acute Mountain Sickness)
- All regimes start 24 hours prior to assent and continue at altitude
HACE - High Altitude Cerebral Edema

A life threatening form of Acute Mountain Sickness. Several factors are involved in causing a build-up of fluid in the brain that leads to severe headache, vomiting, lethargy, confusion, drowsiness and ultimately coma.

Immediate descent from altitude is essential for treatment if HACE is suspected.
High Altitude Cerebral Edema

- Progression of cerebral signs and symptoms of Acute Mountain Sickness
- Truncal ataxia (other focal neurologic deficits may also occur)
- Severe lassitude
- Altered consciousness or coma
- Especially common with High Altitude Pulmonary Edema
Brain MR images of two mountaineers. Left: A mountaineer who climbed to altitudes above 7,000 meters. Right: A mountaineer who survived a high altitude cerebral edema (HACE). The arrows point to the corpus callosum. This part of the corpus callosum is normal in the left image, whereas in the HACE survivor it shows black spots representing multiple microhemorrhages. Images courtesy of Dr. Michael Knauth, PhD.
High Altitude Cerebral Edema

- Early Symptoms
  - Headache
  - Anorexia
  - Nausea
  - Emesis
  - Photophobia
  - Fatigue
  - Irritability
  - Decrease socialization

- Late Symptoms
  - Ataxia (appendicular to truncal)
  - Irrationality
  - Hallucinations
  - Visual disturbances
  - Focal neurological deficits
  - Abnormal reflexes
Treatment HACE

- Immediate descent or evacuation
- Oxygen, 2 to 4 L/min
- Dexamethasone, 4 mg PO, IM, IV q 6hr
- Hyperbaric therapy
Acclimatization

- Hematologic Effects:
  - Increase red cell production/Hb

Stimulus: Hypoxia due to decreased RBC count, decreased availability of O₂ to blood, or increased tissue demands for O₂
Factors Increased by Acclimatization

- Acute
  - Ventilation
  - Heart rate
  - Cerebral blood flow
  - Diuresis increased hematocrit
- Ventilation
- Red blood cell mass
- Metabolism (tissue changes)
Acclimatization to High Altitude

- Rapid ascent and exposure to the altitude at the summit of Mount Everest 29,028 feet results in loss of consciousness in a few minutes and death shortly thereafter.
- Acclimatization occurs over time
- Ability to Acclimatize varies from individuals
- Just a few days at sea level may make one susceptible to AMS or HAPE
Other Aids to Acclimatization

- “Climb high. Sleep low.”
- High carbohydrate diet
- Mild exercise—avoid exertion
- Avoid alcohol and sleeping medications
High Altitude Medical
Contraindications/Cautions

- **Contraindications**
  - Uncompensated left heart failure
  - Pulmonary hypertension
  - Sickle cell anemia
  - Moderate–severe COPD
  - Seizure disorders

- **Cautions**
  - History of left heart failure
  - Cardiac arrhythmias
  - Cerebral vascular disease
  - Sleep apnea
  - Sickle Trait
Authorized Pre-existing Medical conditions for a High Altitude

- Age
- Fitness
- Obesity
- Diabetes
- Hypertension
- CABG; stable angina; compensated left heart failure
- Asthma
- Mild COPD
- Pregnancy
Pre-existing Chronic Lung Disease

- Hypoxemia and pulmonary hypertension worsen
- Consider supplemental oxygen
- Maximize pulmonary function prior to assent
- Patients with mild to moderate COPD may do well
Pre-existing Coronary Artery Disease

- Little evidence-based data
- There is no evidence for increased coronary events. There may be a protective event.
- Increased catecholamines might increase arrhythmias.
- Angina threshold may be decreased
Pre-existing Hypertension

- Blood pressure increases mildly in healthy persons
- Patient should continue usual medications
- Hypertension in visitors is transient and should not be treated
Pre-existing Pregnancy

- Commercial air travel is safe
- Complicated pregnancy avoid:
  - Altitude exposure
- Pregnant low land women avoid:
  - Staying above 13,000 feet
  - Going above 20,000 feet
Sleep at High Altitude

- Fragmented sleep stages with frequent awakenings
- Periodic breathing normal above 10,000 feet
Treating AMS

- The mainstay of treatment of AMS is rest, fluids, and mild analgesics: acetaminophen (Tylenol), aspirin, or ibuprofen. These medications will not cover up worsening symptoms. The natural progression for AMS is to get better, and often simply resting at the altitude at which you became ill is adequate treatment. Improvement usually occurs in one or two days, but may take as long as three or four days. Descent is also an option, and recovery will be quite rapid.
Acute Mountain Sickness Management The Golden Rules

- #1 AMS symptoms at altitude are AMS until proven otherwise
- #2 Don’t ascend further if you have symptoms
- #3 Descend if very ill or not improving. Descend immediately for ataxia or decreased consciousness
- #4 Don’t let anyone with AMS descend alone
Treating AMS

- A frequent question is how to tell if a headache is due to altitude. See Golden Rule I.
- Altitude headaches are usually nasty, persistent, and frequently there are other symptoms of AMS; they tend to be frontal (but may be anywhere), and may worsen with bending over.
- However, there are other causes of headaches, and you can try a simple diagnostic/therapeutic test.
Treating AMS

- Dehydration is a common cause of headache at altitude. Drink one liter of fluid, and take some acetaminophen or one of the other analgesics listed above.
- If the headache resolves quickly and totally (and you have no other symptoms of AMS) it is very unlikely to have been due to AMS.
Hypoxic Ventilatory Response (HVR)
Indications for Acetazolamide

- Rapid ascent to altitudes over 10,000 feet
- Past history of recurrent Acute Mountain Sickness
- Treatment of Acute Mountain Sickness
- Periodic breathing or poor sleep
Acetazolamide (Diamox®)

- Acetazolamide (Diamox®) is a medication that forces the kidneys to excrete bicarbonate, the base form of carbon dioxide; this re-acidifies the blood, balancing the effects of the hyperventilation that occurs at altitude in an attempt to get oxygen.
- This re-acidification acts as a respiratory stimulant, particularly at night, reducing or eliminating the periodic breathing pattern common at altitude.
- Its net effect is to accelerate acclimatization. Acetazolamide isn't a magic bullet, cure of AMS is not immediate. It makes a process that might normally take about 24–48 hours speed up to about 12–24 hours.
Acetazolamide is a sulfonamide medication, and persons allergic to sulfa medicines should not take it. Common side effects include numbness, tingling, or vibrating sensations in hands, feet, and lips. Also, taste alterations, and ringing in the ears. These go away when the medicine is stopped.

Since acetazolamide works by forcing a bicarbonate diuresis, you will urinate more on this medication. Uncommon side effects include nausea and headache. A few trekkers have had extreme visual blurring after taking only one or two doses of acetazolamide; fortunately they recovered their normal vision in several days once the medicine was discontinued.
Acetazolamide Use & Dosage:

- For treatment of AMS: We recommend a dosage of 250 mg every 12 hours. The medicine can be discontinued once symptoms resolve. Children may take 2.5 mg/kg body weight every 12 hours.

- For Periodic Breathing: 125 mg about an hour before bedtime. The medicine should be continued until you are below the altitude where symptoms became bothersome.
Dosage of Acetazolamide

- **Prevention**
  - 125 mg twice a day (or 500 mg slow release daily)
  - Start 12 hours before ascent
  - Continue first day at altitude

- **Treatment**
  - 125–250 mg twice a day until improved

- **Sleep**
  - 62.5–280 mg at dinner time
MYTH: acetazolamide hides symptoms

- Acetazolamide accelerates acclimatization. As acclimatization occurs, symptoms resolve, directly reflecting improving health.
- Acetazolamide does not cover up anything – if you are still sick, you will still have symptoms. If you feel well, you are well.
MYTH: acetazolamide will prevent AMS from worsening during ascent

- Acetazolamide DOES NOT PROTECT AGAINST WORSENING AMS WITH CONTINUED ASCENT. It does not change Golden Rule II. Plenty of people have developed HAPE and HACE who believed this myth.
MYTH: acetazolamide will prevent AMS during rapid ascent

- This is actually not a myth, but rather a misused partial truth.
- Acetazolamide does lessen the risk of AMS, that's why we recommend it for people on forced ascents.
- This protection is not absolute, however, and it is foolish to believe that a rapid ascent on acetazolamide is without serious risk.
- Even on acetazolamide, it is still possible to ascend so rapidly that when illness strikes, it may be sudden, severe, and possibly fatal.
MYTH: If acetazolamide is stopped, symptoms will worsen

- There is no rebound effect. If acetazolamide is stopped, acclimatization slows down to your own intrinsic rate.
- If AMS is still present, it will take somewhat longer to resolve; if not – well, you don't need to accelerate acclimatization if you ARE acclimatized. You won't become ill simply by stopping acetazolamide.
Adverse Effects of Acetazolamide

- Peripheral paresthesia, polyuria
- Less common: nausea, drowsiness
- Ruins taste of carbonated beverages, including beer
- A drug (hypersensitivity, marrow suppression, crystal urea)
- Sulfa drug – allergy
Other Drugs to Prevent Acute Mountain Sickness

- Dexamethasone
  - Indicated with contraindication to Acetazolamide
  - Also used in conjunction with acetazolamide for rapid ascent above 10,000 feet (rescue)
  - Dosage 4 mg every six hours
Acute Mountain Sickness (AMS)
- Anorexia
- Nausea
- Vomiting
- Insomnia
- Dizziness
- Lassitude
- Fatigue
- Lightheaded

High Altitude Cerebral Edema (HACE)
- Headache
- Disorientation
- Loss of coordination
- Memory loss
- Psychotic behavior
- Coma

High Altitude Pulmonary Edema (HAPE)
- Chest tightness
- Persistent cough
- Frothy sputum
- Feeling of imending suffocation during sleep