Is Your Traveler Going to High Altitude?
Dr. Peter Hackett

• First came to Nepal in 1974
• Worked 3 seasons at Himalayan Rescue Association aid post
• Did an altitude illness survey that was published in *The Lancet*
• Appointed me to work in Nepal the first time

• We’ve been close friends for 35 years

Pheriche circa 1980
• In 1980 he attempted his first Himalayan peak
• In 1981 he climbed Mt. Everest (111th ascent)
• Now there have been over 6000 ascents
• Has published more than 100 original papers on altitude illness
• Has edited 6 books on altitude-related topics

High Altitude Pulmonary Edema
• Spent 8 seasons on Denali in Alaska doing pioneering research in HAPE and HACE

Peter and my future wife Jane on Denali in 1988
The most knowledgeable person in the world about altitude illness
Tour doctor for The Rolling Stones
What is Altitude Illness?
High Altitude Illness (HAI)

- 3 syndromes that occur in the first few days of exposure to high altitude hypoxia in persons unacclimatized to that altitude
  - Acute mountain sickness (AMS)
  - High altitude cerebral edema (HACE)
  - High altitude pulmonary edema (HAPE)
Other Altitude-related Problems

- Retinopathy, retinal hemorrhages
- Sleep periodic breathing (Cheyne-Stokes)
- Dry eye
- High altitude cough
- Aggravation of pre-existing conditions
What Causes Altitude Illness?
Hypoxia is the Cause of HAI

As air pressure decreases with altitude, number of molecules decreases (thin air)

\[ PO_2 = 0.21 \times \text{barometric pressure} \]

\[ PO_2 = \text{2/3rds at 10,000 ft (3050 m)} \]
\[ \text{1/2 at 18,000 ft (5500 m)} \]
\[ \text{1/3rd 29,000 ft (8848 m)} \]
Factors for Altitude Illness

- Inadequate acclimatization
  - Too high, too fast for an individual
- Altitude reached (degree of hypoxic stress)
- Rate of ascent (rapidity of hypoxic stress)
Factors for Altitude Illness

- Genetic factors – individual physiology
- Certain medical conditions (uncommon)
- Age, gender, and fitness not much effect
- Anyone/everyone can get HAI
It’s All About Acclimatization!

- **Time-dependent** process
- Individual variation
  - Genes interacting with environment
  - Acquired differences due to illness, surgery, pregnancy
- **Ventilatory response** is the key
Ventilation:

- **Breathing** increases on ascent to altitude (ventilatory acclimatization)

- PCO2 drops, pH increases, SaO2 improves a bit with time
Variability of Ventilation in Hypoxia

Acute response

$V_E$ (l/min)

$\Delta = 50$ l/min

$\Delta = 2$ l/min

$O_2$-saturation (%)
How Do Altitude and Rate of Ascent Influence AMS?
AMS and Severity Greater with Higher Altitude

20 hr exposure

Beidleman et al 2013
Slower Rate of Ascent $\equiv$ Less AMS

Prevalence of AMS

Days of Ascent to 15,000 ft

N = 827

Schneider, MSSE 34: 1886-91, 2002
How Do You Diagnose Altitude Illness?
Diagnosis of altitude illness

• Setting: unacclimatized person > 8200 ft (2500 m)
• Timing: 1-2 d for AMS, 3-4 d for HAPE
• Symptoms
• Physical findings
• Differential diagnosis
AMS – Time & Severity

Beidleman et al 2013
AMS: Clinical Picture

- Headache
- Loss of appetite, nausea, vomiting
- Dizziness
- Sleep disturbance
- Peripheral edema

Reviews: Hackett, NEJM 2001; Basnyat, Lancet 2003; Bärtsch, HAMB 2004
AMS: Clinical Picture

- Delayed onset: 4-8 hours
- Definition of AMS: Headache + 1 additional symptom

Hangover? Migraine?

Reviews: Hackett, NEJM 2001; Basnyat, Lancet 2003; Bärtsch, HAMB 2004
High Altitude Cerebral Edema

- Progression of CNS symptoms and signs in someone with AMS or HAPE
- Unusual below 10,000 ft; 3050m
- Hallmarks: ataxia and changed consciousness (acting drunk)
HAPE

Symptoms and signs

• Early symptoms: fatigue, weakness, dyspnea on exertion, dry cough

• Progress to: tachycardia, tachypnea, orthopnea and dyspnea at rest

• Pink or blood-tinged sputum is a very late finding

• Crackles usually start in right axilla
SportStat™ Pulse Oximeter
What Are The Two Key Observations That Distinguish Life-Threatening Altitude Illness?
Two Key Findings = Emergency

1) acting drunk (HACE)
   • Ataxia and change in consciousness

2) respiratory distress (HAPE)
   • Dyspnea at rest and weakness
What Are The X-Ray Findings in HAPE?
X-ray Findings in HAPE

- Non-cardiogenic edema
- Normal heart size
- Interstitial or alveolar infiltrates
- One or both lungs; R>L
- Easily confused with pneumonia
What Are The Brain Scan Findings in HACE?
Characteristic HACE MR Findings

Acute

“Footprint” post recovery

Hemosiderin deposits
How Should We Understand the Use of the Lake Louise Score?
The Lake Louise Score

• A research tool, not for clinical diagnosis

• Best questions for AMS:
  • Do you feel sick?
  • Do you have a headache?
  • Do you feel hung-over?
What is the Differential Diagnosis of Altitude Illness?
Differential Diagnosis of Altitude Illness

- AMS/HACE
  - Dehydration, exhaustion, hypothermia, hangover, carbon monoxide
  - Diabetic ketoacidosis, hyponatremia, hypoglycemia, drugs, infection, stroke, TIA
  - Infections, seizure disorder, psychiatric disorders, migraine, brain tumor
Differential Diagnosis of Altitude Illness

HAPE

- Asthma, infection, AMI, heart failure, PE,
- Mucus plugging, HVS, periodic breathing
How Can You Prevent Altitude Illness?
Preventive strategy depends on risk assessment.
Prevention Goals

• Goal is to prevent mod/severe HAI
  • Mild AMS may be unavoidable
  • Mild AMS is manageable
  • Maintain functional capacity (to descend)
  • Want to avoid death, evacuations, ruined trips
• Want our patient to **enjoy** the mountains!
Prevention Goals

• We know all we need to know to prevent ALL altitude illness deaths
Why Do People Still Die of Altitude Illness?
1. Lack of awareness
2. Denial
3. Misdiagnosis
4. Lack of treatment options
(Rate of Ascent) x (Altitude) = Risk

- Colorado ski resort – low/moderate risk
- Trekking in Nepal – low/moderate risk
- Flying to Quito, Cuzco, La Paz, Leh, Lhasa (all greater than 11,300 ft; 3450 m)
  - Moderate/high risk, but easily manageable
- Kilimanjaro – high risk, outrageous!
Risk Assessment for HAI

- **Sleeping** altitude
- Rate of ascent: time to acclimatize?
- Resident altitude
- Pre-acclimatization
Risk Assessment for HAI

- Physical exertion/ fitness
- Individual susceptibility/ past history
  - Predisposing factors?
    - Lung disease, absent CB, NMD
- Age < 50 years
How to Mitigate HAI

• Make an elevation profile for the trip
  • Illustrates risk nicely, shows trouble spots
  • Easy for patients to understand
• Advise on acclimatization strategy
• Consult WMS guidelines
Wilderness Medical Society Consensus Guidelines for the Prevention and Treatment of Acute Altitude Illness

Andrew M. Luks, MD; Scott E. McIntosh, MD, MPH; Colin K. Grissom, MD; Paul S. Auerbach, MD, MS; George W. Rodway, PhD, APRN; Robert B. Schoene, MD; Ken Zafren, MD; Peter H. Hackett, MD
WMS Recommendations: Rate of Ascent (Sleeping Altitude)

• Avoid ascent to ≥ 9,000 ft (2800 m) in one day

• After arrival at 8-10,000 ft (2500-3000m), increase sleeping elevation < 1500 ft (500m)/day, and add an extra day for acclimatization every 3300 ft (1000m)
Cuzco, Peru 11,150 ft (3400 m)

Urubamba 9400 ft (2870 m)
La Paz (El Alto) 13,615 ft (4150 m)
La Paz – A Vertical City
Hackett and Rennie, Lancet, 1976
Typical Kilimanjaro Ascent Profile

Machame Route Contour

Altitude

- 6000m
- 5000m
- 4000m
- 3000m
- 2000m
- 1000m

Machame gate  Machame Camp  Shira Camp  Barranco Camp  Barafu Camp

Stella Point  Uhuru Peak

Lava Tower  Barranco Wall

Altitude

- 20,000 ft
- 17,500 ft
- 15,000 ft
- 12,500 ft
- 10,000 ft
- 7,500 ft
- 5,000 ft
- 2,500 ft

Day 1  Day 2  Day 3  Day 4  Day 5  Day 6

Mweka Village
Pre-Acclimatization

Prevalence of AMS at 15K ft

Nights ≥ 10,000 ft in prior 2 months (Pre-Acclimatization)

Schneider, MSSE 34: 1886-91, 2002
Major Predictors of AMS at 14,950 ft (4559 m)

n = 827

Slow ascent: > 3 days above 2000 m

- Ascent
  - Slow
    - Yes: 8%
    - No: 21%
  - Fast
    - Yes: 23%
    - No: 45%

Pre-exposure
- Yes
- No
Pre-acclimatization
Recommendations for a safe ascent

• The individual safe ascent rate depends on degree of susceptibility and pre-acclimatization
• Physical fitness is not protective
• Trial and error situation
• Error signal: symptoms of AMS or beginning HAPE
Recommendations for a safe ascent

• Rest at same altitude with initial onset of AMS
• Immediate descent when signs of beginning HACE or HAPE
• Never leave a sick person alone
Does Having Altitude Illness Once Make You More Susceptible in the Future?
• No, it demonstrates you are susceptible at that altitude and rate of ascent
What Drugs Are Used to Prevent Altitude Illness?
Agents for Prevention of AMS

- Acetazolamide
- Dexamethasone
- Ibuprofen
- Ginkgo biloba
- Aminophylline
- Gabapentin
- sumatriptan
Agents That Don’t Work

- Anti-oxidants
- Aldactone
- PDE-5 inhibitors
- Nifedipine
- Ginkgo?
- Leukotriene blockers
- Magnesium
Acetazolamide

- $\text{CO}_2 + \text{H}_2\text{O} = \text{H}_2\text{CO}_3 = \text{H}^+ + \text{HC}0_3^-$
- Blocks carbonic anhydrase, especially kidney
- Produces bicarbonate diuresis, metabolic acidosis
- Stimulates ventilation, raises PO2, “drops” altitude
- Promotes ion exchange across BBB
Acetazolamide Prophylaxis

• 125 to 250 mg BID (5 mg/kg/day) starting day before travel until day 2 or 3 at altitude
• Test dose may be useful
• Allergic to sulfonamides? May be OK
• Some side effects are dose-related
  • Paresthesiae, metallic taste, taste of CO2 from carbonation, malaise, nausea, myopia
Dexamethasone for Prevention

- Indicated for high-risk situation
- Or alternative to acetazolamide
- 4 mg bid to 4 mg qid, start on ascent
  - Higher dose for intense exercise (soldiers, rescuers)
- Use less than one week
- Gaining popularity for summit day
Ibuprofen for AMS Prevention

• 2 studies
• 600 mg tid during ascent to 3750 m
• N = 86; 43% AMS with ibu, 69% placebo
• N = 232
  • ITT, small improvement in AMS
  • Completed protocol, no difference
  • Severe AMS the same
• Requires more investigation
Inhaled steroids to prevent AMS?

The American Journal of Medicine
29 April 2014

- Inhaled budesonide and oral dexamethasone prevent acute mountain sickness: a double-blind randomized controlled trial
- Cheng-Rong Zheng et al
For Travelers Making an Abrupt Ascent to Altitude, When Do You Offer Acetazolamide?
Table 3. Risk Categories for Acute Mountain Sickness

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| Low 10-15%    | • Individuals with no prior history of altitude illness and ascending to ≤ 2800 m;  
                • Individuals taking ≥ 2 days to arrive at 2500-3000 m with subsequent increases in sleeping elevation < 500 m/day and an extra day for acclimatization every 1000 m |
| Moderate 15-30%| • Individuals with prior history of AMS and ascending to 2500-2800 m in 1 day  
                • No history of AMS and ascending to ≥ 2800 m in 1 day  
                • Individuals with prior history of HAPE or HACE and ascending to 2500-2800 m in 1 day  
                • Consider Acetazolamide |
| High >40%     | • History of AMS and ascending to ≥ 2800 m in 1 day  
                • All individuals with a prior history of HAPE or HACE and ascending to ≥ 2800 m in 1 day  
                • Very rapid ascents (e.g., < 7 day ascents of Mt. Kilimanjaro)  
                • Recommend Acetazolamide, Consider dexamethasone |

AMS: Acute mountain sickness; HACE: High altitude cerebral edema; HAPE: High altitude pulmonary edema

Notes:
• Altitudes listed in the table refer to the altitude at which the person sleeps
• Ascent is assumed to start from elevations < 1200 m
• The risk categories described above pertain to unacclimatized individuals
AMS VS Sea-sickness

• AMS
  • New environment
  • Adjustment w/ time
  • Self-limited (usually)
  • Rarely life-threatening
  • Easy prophylaxis
    • Side effects minor
    • Resistance to use

• Sea-sickness
  • New environment
  • Adjustment w/ time
  • Self-limited
  • Might want to die
  • Easy prophylaxis
    • Side effects moderate
    • Commonly used
Are There Pre-Existing Conditions that Pre-Dispose to Altitude Illness?
Conditions Increasing HAI Risk

• Inability to increase ventilation
  • Carotid body damage from surgery, radiation
  • Lung disease, especially restrictive
  • Neuromuscular disease affecting thorax

• Increased intracranial pressure or space occupying lesions

• Pulmonary circulation abnormalities
  • Congenital, pulmonary hypertension of any cause
Are There Pre-Existing Conditions that Can Get Worse at Altitude?
Conditions Possibly Aggravated by Altitude

- Lung disease (not asthma)
- Heart problems
  - Coronary artery disease, arrhythmia, failure
- Hypertension
- Post radial keratotomy
- Seizure disorders
- Migraine
- Sickle cell disease or trait
What Do You Advise Patients About the Cardiac Risk of Going to Altitude?
Cardiac Recommendations for Altitude

- Usual risk stratification and evaluation
- For those with known CAD:
  - Normal exercise test and good exercise capacity = OK to go
- Arrhythmia
  - Need good control, and a plan for exacerbations
- Heart failure, low EF
  - Good control, plan for decompensation
How Do You Treat Altitude Illness Once it Occurs?
AMS Treatment

• A 30 year old female hiker at 10,000 ft in Colorado with severe headache, insomnia, anorexia, and nausea. $\text{SpO}_2$ is 89% (normal), lungs are clear to auscultation, and neuro exam is normal. You diagnose acute mountain sickness.

• What do you recommend for treatment?
AMS Rx: considerations

- Logistics
  - Terrain, weather, time of day, available help
- Severity
  - Severe more urgent
- Expertise
- Rx availability
  - Medical kit, oxygen. etc
Treatment options for AMS

- Descent (>1000 ft (300 m) or until you see improvement
- Oxygen (low flow to conserve)
- Hyperbaric bag (Min 2 hrs, 4-6 ideal)
- Halt ascent; acclimatize further
Treatment options for AMS

- Symptomatic meds: ibuprofen, ondansetron
- Acetazolamide: 250 mg BID
- Dexamethasone: 4 mg q6h (incredibly effective)
- Combinations of above
HAPE Treatment

• Oxygenation the highest priority
• Descent, minimize exertion
• Mild/mod cases: bed rest and oxygen
• Severe illness: high flow O2 and descent
• Hyperbaric bag, EPAP, PEEP, pulmonary toilet
• Beta-agonists?
Oxygen Breathing Resolves HAPE Over 36 Hours
Pulmonary Vasodilators

• Oxygen (descent, hyperbaric treatment)
• Oral agents:
  • CA++ channel blockers - nifedipine
  • PDE inhibitors to increase c-GMP - tadalafil
  • Dexamethasone
Prevention of HAPE

- Slow, graded ascent
- Avoid overexertion
- Meds:
  - Nifedipine
  - Sildenafil
  - Salmeterol
  - Acetazolamide
  - Dexamethasone
Medical Kit for AMS

• Diamox for prevention, or to speed acclimatization
• Dexamethasone for treatment, (4 mg q 6 hrs)
• Ondansetron (4 mg ODT q 2-4 hrs)
• Ibuprofen (600 mg every 8 hrs)
• Nifedipine, Viagra; lay vs medical persons
• Albuterol or salmeterol inhaler
The End