ALTITUDE AND THE ATHLETE

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Objectives

- Epidemiology
- Pathophysiology
- Clinical syndromes
- Treatment and Prophylaxis
- Training effects
- Tell a cautionary tale......
Altitude Related Disorders

“benign conditions?”
Altitude Related Disorders

History

- 1590 – Acosta
- 1894 HAPE - Musso
- 1913 – Ravenhill
  - Chilean Mining Co.
- “Ladrak”
  - (poison of the pass)
Altitude Related Disorders

Geography

- >2500m
- rate ascent exceeds acclimatization
Altitude Related Disorders

Epidemiology

- Himalayas
  - 30% @ 10K
  - 60% @ 20K

- Aconcagua 2000-1
  - 4200 climbers
  - 130/839 experts
  - 14 HAPE, 3 HACE
Altitude Related Disorders

**Epidemiology**

- **Colorado**
  - 25% skiers
    - Ski area data
  - 42% travelers to Summit Co, CO
    - Hackett, NEJM, 2001
- 12,000 + 60%
  - Imray, ProgCVDis 2010
Altitude Related Disorders

- Epidemiology
  - Montana
    - 45% skiers
      - NO idea about AMS
    - 30%....
      - LLC
      - Knew how high

Hatzenbeuhler, et al
Wild&EnvMed 20(3):257-60, 2009
Spectrum of Disease

Various Theories - all related

HYPO’S

baria

oxia

capnea

sense

BOTTOM LINE - Up too fast, variable
Pathophysiology probably all related

- **hypobaric hypoxia** key insult (<60mmHg)
- remember o2 sat depends on P
- **fluid shifts**: links all syndromes
  - Lung: ↑ PAP, cap permeability → leak/V-Q mismatch
    - VEGF release ↑ permeability
  - Intravascular depletion → 3rd spacing
- Cardiac: ↓ SV, CO

Korven, HighAltMedBio, 2004
Pathophysiology probably all related

- **Renal**
  retain fluid (no diuresis = AMS)
  paradoxical ↑ aldosterone/ADH

- **Neurogenic**
  fluid shifts - ↑ cerebral flow ↑ ICP → edema + ischemia - auto regulatory dysfunction
  - ↑ sympathetic, ↑ lung/renal effects

- **Cold potentiates all effects**
Pathophysiology probably all related

- **acid base** disturbance
  
  \( p\text{CO}_2 \) (ventilation)

  respiratory alkalosis

  slows breathing (night)

- **systemic inflammatory** process?

  - HAPE, see \( \uparrow \) CRP, IL 1+6

  - Free radicals probable role, NO mediated

Physiology

Acclimatization

- Recent findings: process may be initiated by molecular up-regulation of hypoxia inducible factor-1.12
- Increase respirations – increase Ao2
- Mild diuresis – less volume, more O2 per unit
- A lot of individual variation
  - Imray, et al ProgCVDs, 2010

* SEE SUMMARY TABLE
Clinical Syndromes
Clinical Syndromes

Most of the cases of high altitude diseases are preventable if on-site personnel identify the condition and implement appropriate care.

2005 ISMM Consensus
Lake Louise Consensus (ISMM)

- AMS
  - Headache AND
  - One other sx
- HACE (end stage AMS)
  - Δ MS or ataxia with AMS OR
  - Δ MS AND ataxia
- HAPE
  - 2Sgs AND 2Sxs

AMS Scoring System
1. Headache
2. GI symptoms
3. Fatigue/weakness
4. Dizzy/lightheaded
5. Difficulty sleeping
6. AMS
7. Ataxia
8. Peripheral edema

NB: some controversy, LLSS vs. ESQ-III, language barrier 20% discrepancy
Acute Mountain Sickness

- Symptoms
  - Headache
  - Sleep Disturbance
  - Dyspnea
  - GI
  - Performance drops
  - Assoc w/ ↑ body temp
  - NO Neuro Sx
  - “debilitating lassitude”
Acute Mountain Sickness

- **Symptoms**
  - **Headache**
    - ?r/t edema
    - Trigeminal complex – meninges
  - **Sleep**
    - Less slow wave, REM
    - r/t hypoxemia not hypoventilation

*Erba EurRespJrnl 2004*
Acute Mountain Sickness

- Self limited
  - several hours – days
- Can recur as go higher
- NB: barometric pressure
  - increases with decreased latitude
Acute Mountain Sickness

Risk
- male = female
  - Women 1.5 risk (?)
  - Pollock, HighAltMedBio 2005
- unable to hold breath, gag
- prior episode ??
- genetics ??
- Fitness - no effect
High Altitude Bronchitis

- Cough (dry)
- Mild DOE
- NO
  - SOB
  - Fever
  - Desat
High Altitude Bronchitis vs. HAPE

- Altitude gain
- 2 Sg, 2Sx
  - dyspnea at rest, cough, weakness, decreased exercise performance, chest tightness or congestion
  - crackles, wheezing
  - central cyanosis, tachypnea, tachycardia
High Altitude Pulmonary Edema (H A P E)

- Young cold males*
- Prior episode
- Fever, cough, frothy
- Respiratory c/o
- O2 Desat (85 at 4500)
- Exam/X-ray variable
- Grade 1-3
- Mortality 10%

* one small study, n=63, ?fem>male. Dallimore, WEM 2009
High Altitude Cerebral Edema (HACE)

Very high altitude
AMS, visual, ataxia, focal CNS
(tandem gait best test)
Coma - 60% fatal
May deteriorate quickly
Neuro symptoms: from Imray, eta al, Prog CVDis, 52(2010) 467-484
High Altitude Retinal Hemorrhage (HARE)

Self-limited

Frequent at very high altitude
Exercise potentiates
Beware refractory surgery
Decreased color discrimination
H.A.F.E.

Remember Boyle’s Law
Altitude and Other Illness

- Cardiac:
  - risk MI
  - angina
  - CHF

- Pulmonary: COPD, pulmonary hypertension
  - “Common sense guidelines” (no evidence)
  - Stage I (>50% FEV1) – no limitations
  - Stage III (<35% FEV1) – limit travel to altitude
Altitude and Other Illness

- Diabetes: risk ketosis, hypoglycemia, retinopathy
- SCA
- Infectious disease ??
- BUT--- no increased risk for AMS
Altitude and Pregnancy

Minimal risk

Avoid very high

? Preeclampsia risk for HAPE

Exposure

Dehydration

Sun

Cold

Dry air
Other conditions

- Thrombosis
  - Polycythemia
  - Hemoconcentration
- Post meal syncope
- ? Immune function decline
- Sub acute (chronic exposure)
  - Pulm Htn, CHF
  - Resolves if leave

Anand and Wu HighAltMedBio 2004
Other conditions

- Neurologic that are NOT r/t altitude illness
  - Often focal
  - TIA
  - Scotomata, optic disc swells
  - Venous thrombosis
  - Seizures
  - Syncope
  - Double vision

*Basnyat HighAltMedBio 2004*
Other conditions

- Facial Edema
Nutritional concerns

Increase BMR
Decrease appetite
(have a headache?
have seconds!)
Treatment

- RAPID DESCENT !!
- Adjuncts
  - Oxygen
    - 2-3 lpm
  - Hyperbaric chamber
    - simulates descent
    - works quickly
  - Hydration!!
    - Tea is OK
      (Scott et al, Eur J Appl Phys, 2004)
Treatment

- RAPID DESCENT !!
- Medications
  - Diamox *(mult studies)*
    - 3.5x risk if not on
    - increase bicarbonate excretion
    - metabolic acidosis
    - increase ventilation
    - 125 mg. QD - BID
    - don’t drink beer! (or soda)
    - *limit if abnl LFT’s*
Treatment

- RAPID DESCENT !!

- Medications
  - Dexamethsone
    - Stabilizes endothelium
  - Cerebral edema
  - Pulmonary edema
  - 4 mg q6 treat
  - 4 mg q12 prevent
  - Rebound
Treatment

- RAPID DESCENT !!

Medications
- Aspirin/NSAID’s/Aceto
  - Effective: HA
    (Harris, JEmergMed,2003)
- Gabapentin
  - Effective for HAH ??
  - 2 studies:
    - Iranian resort
    - PCRCT (?blinding)
Treatment

- RAPID DESCENT !!

- Medications
  - Diuretics
    - ↓ K+, pH
    - Cautious use
  - Nifedipine (HAPE)
    - Reduces PAP
    - 20-30 mg ER q12
      (Bartsch, et al, NEJM, 1991)
  - Ginkgo – 60 tid, conflicting data
Treatment

- RAPID DESCENT !!
- Medications
  - Anti emetics
  - Zolpidem
    - Does not impair respiration
  - Salmeterol
    - 125 mcg BID
    - may prevent HAPE
      (Sartori, et al, NEJM 2002)
Treatment

- RAPID DESCENT !!

- Medications
  - Theophylline 300mg
    - DBRCT/PC
    - Significant reduced:
      - Periodic breathing events in sleep
      - Desats
      - AMS symptoms

Kupper, JTravMed, 2008
Treatment

- RAPID DESCENT !!
- Phosphodiesterase -5 inhibitors (pulm vasodil)
  - Sildenafil - ? Prevent HAPE
  - Tadalafil vs. dexamethasone
    - Dexa better MV02, lower PAP, higher 02 saturation

Fischler, AmJResp&CritCareMed, 2009
## Evidence-based recommendations for the treatment of acute mountain sickness and HACE

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Descent</strong></td>
<td>&gt;300 m</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td><strong>Oxygen supp</strong></td>
<td>35% at 4300 m</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td><strong>Hyperbaric chamber</strong></td>
<td>193 mBar 1h</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td><strong>Acetazolamide</strong></td>
<td>125-500 mg BD</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td><strong>Dexamethasone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMS</td>
<td>8 mg stat</td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>HACE</td>
<td>8 mg/d</td>
<td>1</td>
<td>A</td>
</tr>
</tbody>
</table>

Adapted from Imray et al, ProgCVDis, 2010.
Training Effects

- Mexico City Olympics
- Adaptations (2-3wk)
  - Increase EPO
    - r/t HIF-1
  - Increase DPG
  - Increase ventilation
  - ? Improve muscle biochemistry
  - Increase RBC, RCV

Heinicke, IJSM, June 2005: 26 (5). p350-355
Training Effects

- Positive Effects
  - 2-3 weeks to accrue
  - retain 2-3 weeks
- Live high - Train low
  - Effects of altitude are from acclimatization NOT from training in hypoxia (e.g., EPO, RBC)
Training Effects

- Negative Effects
  - BMR increase
  - CO decrease
  - Blood flow to skeletal muscle declines
PREVENT*

- Acclimatize !!
  - Recent exposure protective (50%)
- Sleep low, Ski high
- ?Identify at risk
  - Sea level response to HA not predictive
    - Grant, et al. BJSM, Apr 2002: 36 (2). p.141-146

* SEE SYLLABUS FOR EBM TABLE
PREVENT*

- Water, not beer
  - Euhydrate  (study in normobaric hypoxia)  
    *Richardson 2009*
  - Red wine ??  
    *Schafer, 2002*
- Diamox
- Ibuprofen
- ?? Cobalt reduce oxidative stress

*Shrivastava, NeurochemInt’l, 2008*
Thank you

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Physiology

- Ventilatory Threshold
  - Decreases
  - Antioxidants may blunt

- “Secondary inflammation reported in HAPE is most likely a nonspecific response to stress-induced failure of capillaries”
High Altitude Pulmonary Edema (H A P E)

1 - Mild

- Dyspnea on exertion
- dry cough
- fatigue while moving uphill
- HR (rest) < 90-100
- RR (rest) <20
- dusky nail beds or
- exertional desaturation
- localized crackles, if any
- Minor exudate involving less than 25% of one lung field
High Altitude Pulmonary Edema (H A P E)

2 - Moderate

- Dyspnea at rest
- Weakness
- Fatigue on level walking
- Raspy cough
- HR 90-110
- RR 16-30
- Cyanotic nail beds
- Crackles present
- Infiltrate in 50% of one lung or areas of both lungs
High Altitude Pulmonary Edema (H A P E)

3 - Severe

- Dyspnea at rest
- extreme weakness
- Orthopnea
- productive cough
- HR > 110, RR > 30
- facial & nailed cyanosis
- Bilateral crackles
- blood-tinged sputum
- Stupor -- coma
- Bilateral infiltrates > 50% of each lung
Intermittent hypoxic training (IHT)
- discontinuous use of normobaric or hypobaric hypoxia to
  - reproduce features of altitude acclimatization
  - ultimate goal: improve sea-level athletic performance


(1) provide hypoxia at rest
  ▶ stimulate altitude acclimatization

(2) provide hypoxia during exercise
  ▶ enhance the training stimulus

OR

(1) Living high (>2500m) - training low
  ▶ shown to improve sea-level endurance performance.

(2) Living low-training high
Altitude acclimatization effect in IHT demonstrated by:

(1) living high-training low improves performance in athletes of all abilities

(2) Mechanism of this improvement is primarily an
   - Increase in erythropoietin, increasing red cell mass,
   - Improved $V(O_2\text{max})$ - performance
BUT:
Training at altitude (or under hypoxia) leads to opposite effect –
- reduced speeds
- reduced power output
- reduced oxygen flux
Therefore: not likely to provide any advantage

Training Effects

- Positive Effects
  - Increase RBC, RCV
TABLE 1. Physiologic changes during acclimatization to maintain tissue oxygen (O2) delivery

Involuntary increase in ventilation
Increased hemoglobin concentration
Hemoconcentration because of decrease in plasma volume (within days)
Increased red blood cell mass (2–3 wk)
Increased affinity of hemoglobin for O2
Steep portion of O2 disassociation curve
Leftward shift of O2 disassociation curve from decreased PCO2 and increased pH
Increased tissue O2 extraction with lowering of mixed venous O2
Decreased cardiac output
Increased time for O2 diffusion from alveolus to capillary because of slower blood flow
Attenuates rise in pulmonary artery and capillary pressure

From, Palmer, AJMedSci, 2010
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dose</th>
<th>Level of Evidence</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>Slow ascent</td>
<td>300-3000</td>
<td>1-2</td>
<td>A</td>
</tr>
<tr>
<td>Avoid exercise</td>
<td>2</td>
<td></td>
<td>B</td>
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<tr>
<td>Hydrate</td>
<td>N/A</td>
<td>2-3</td>
<td>C</td>
</tr>
<tr>
<td>Oxygen supp.</td>
<td>2 L min⁻¹</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>PEEP</td>
<td>5 cm H2O</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Carbohydrate rich diet</td>
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<td>3</td>
<td>C</td>
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<tr>
<td>Acetazolamide</td>
<td>250 mg-1 g daily</td>
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<tr>
<td>Methazolamide</td>
<td>150 mg/d</td>
<td>2</td>
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<tr>
<td>Dexamethasone</td>
<td>8 mg/d</td>
<td>1</td>
<td>A</td>
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<tr>
<td>Medroxy-progesterone</td>
<td>60 mg/d</td>
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<tr>
<td>Theophylline</td>
<td>375 mg BID</td>
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<tr>
<td>Ginkgo biloba</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Effective 240 mg/d</td>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Not effective 240 mg/d</td>
<td>1</td>
<td>B</td>
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<tr>
<td>Sumatriptan</td>
<td>50 mg once</td>
<td>2</td>
<td>B</td>
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</table>

Adapted from Imray et al, ProgCVDIs, 2010. Compiled by Oxford Centre for EBM
<table>
<thead>
<tr>
<th>Condition</th>
<th>Drug/Intervention</th>
<th>Dose</th>
<th>Adapted from</th>
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</thead>
<tbody>
<tr>
<td>High altitude headache</td>
<td>Stop ascent/rest</td>
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<tr>
<td></td>
<td>Paracetamol</td>
<td>1g QDS</td>
<td>Imray et al, ProgCVDiss, 2010</td>
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<tr>
<td></td>
<td>Ibuprofen</td>
<td>400 mg TDS</td>
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<tr>
<td>AMS Mild</td>
<td>Stop ascent / rest</td>
<td>24 hours</td>
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<td>(Lake Louise Score &lt;4)</td>
<td>Paracetamol</td>
<td>1g QDS</td>
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<tr>
<td></td>
<td>Ibuprofen</td>
<td>400 mg TD</td>
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</tr>
<tr>
<td></td>
<td>Acetazolamide</td>
<td>125-500 mg BD</td>
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</tr>
<tr>
<td></td>
<td>Descend</td>
<td>300-500 m</td>
<td></td>
</tr>
<tr>
<td>AMS Moderate/severe</td>
<td>Descend</td>
<td>300-500 m</td>
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<td>(Lake Louise Score &gt;4)</td>
<td>Paracetamol</td>
<td>1g QDS</td>
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</tr>
<tr>
<td></td>
<td>Ibuprofen</td>
<td>400 mg TD</td>
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<td></td>
<td>Acetazolamide</td>
<td>125-500 mg BD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dexamethsone</td>
<td>4 mg QDS PO, IM, IV</td>
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</tr>
<tr>
<td></td>
<td>Oxygen</td>
<td>1-2 l min⁻¹</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 h hyperbaric chamber</td>
<td>193 mBar</td>
<td></td>
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<tr>
<td>HACE</td>
<td>Immediate descent</td>
<td>&gt;300-500 m</td>
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<tr>
<td></td>
<td>Oxygen</td>
<td>2-4 l min⁻¹</td>
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<tr>
<td></td>
<td>Dexamethsone</td>
<td>4 mg QDS PO, IM, IV</td>
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<tr>
<td></td>
<td>Hyperbaric chamber (if able to protect airway)</td>
<td>193 mBar</td>
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</table>