ACUTE MOUNTAIN SICKNESS AND HEMOCENTRATION IN NEXT GENERATION SPACECRAFT

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ESA Workshop on Hypoxic Bed Rest Study
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topics

Is there a problem with the equivalent air altitude concept to assess hypobaric hypoxia?

Is there a medical concern about secondary polycythemia?

A bed rest hypoxia study can help.
equivalent air altitude concept

### 10.3 ALTITUDE-PRESSURE TABLE

<table>
<thead>
<tr>
<th>(1) Altitude m</th>
<th>(2) Altitude ft.</th>
<th>(3) (P_b) mm Hg</th>
<th>(4) ((P_b - 47)) mm Hg</th>
<th>(5) (.209 \times (P_b - 47)) mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>760</td>
<td>713</td>
<td>149</td>
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<td>609</td>
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<td>118</td>
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<td>17</td>
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<td>44000</td>
<td>116</td>
<td>69</td>
<td>14</td>
</tr>
<tr>
<td>14030</td>
<td>46000</td>
<td>106</td>
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</tr>
<tr>
<td>14640</td>
<td>48000</td>
<td>96</td>
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<td>10</td>
</tr>
<tr>
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<td>50000</td>
<td>87</td>
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<td>8</td>
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<td>8</td>
</tr>
<tr>
<td>16470</td>
<td>54000</td>
<td>67</td>
<td>22</td>
<td>8</td>
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<td>56000</td>
<td>57</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>17690</td>
<td>58000</td>
<td>47</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

\[
P_{\text{I}O_2} = (P_B - 47) \times F_{\text{I}O_2}
\]

Underlying Assumptions:

- Efficient and frequent EVAs will drive exploration program.
- Low pressure suit is always preferred to high pressure suit.
- There is operational value to a short in-suit prebreathe.
- Vehicle atmosphere may not prevent risk of DCS during EVA.
  - Shuttle and ISS atmospheres are examples.
- Dedicated hyperbaric treatment capability may not be present.

Atmosphere Design Considerations:

- No significant risk of fire – bad experience with 100% O₂.
- Limit hypoxia – you need O₂ with every breath.
- Prevent DCS and VGE.
  - Better to prevent than treat DCS, or to constantly embolize the lung.
- Optimize atmosphere to allow safe and efficient EVAs.
spacecraft atmospheres -- 2006

<table>
<thead>
<tr>
<th>Environment</th>
<th>$P_B$ psia</th>
<th>$F_{O_2}$ (%)</th>
<th>$P_{O_2}$ mmHg</th>
<th>$P_{A_2}O_2$ mmHg</th>
<th>Actual Altitude ft</th>
<th>Equivalent Air Altitude ft</th>
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</thead>
<tbody>
<tr>
<td>CEV</td>
<td>10.2</td>
<td>26.5</td>
<td>127</td>
<td>85</td>
<td>9,750</td>
<td>4,000</td>
</tr>
<tr>
<td>our model*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSAM</td>
<td>8.0</td>
<td>32.0</td>
<td>117</td>
<td>77</td>
<td>16,000</td>
<td>6,000</td>
</tr>
<tr>
<td>our model*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HABITAT</td>
<td>7.6</td>
<td>32.0</td>
<td>111</td>
<td>71</td>
<td>17,000</td>
<td>9,500</td>
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<tr>
<td>our model*</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$P_{O_2}$ is inspired O₂ partial pressure, computed as $(P_B \text{ mmHg} - 47) \cdot F_{O_2}$ (as decimal fraction).

$P_{A_2}O_2$ is computed acute alveolar oxygen partial pressure from alveolar oxygen equation.


equivalent air altitude model - ascent on enriched O₂

\[ F_{1O_2} = \frac{P_{1O_2}}{(P_B - 47)} \]
acute mountain sickness

Signs and symptoms include headache, nausea, dizziness, fatigue, vomiting and sleeplessness following a recent gain in altitude with at least several hours at the new altitude in a hypoxic environment; likened to a bad hangover.
The incidence of AMS is highly variable.

- Roach (1998) reports that 25% of people are affected by a quick ascent to 2,000 m (6,600 ft).
- Montgomery (1989) shows 25% incidence of three or more symptoms at 2,000 m and that half with these symptoms took medication for relief of symptoms.
- Houston (1982) starts his list of AMS symptoms at altitudes above 2,100 m (7,000 ft).
- Muhm (2007) reports 11% AMS in large sample during 20 hrs at 2,438 m (8,000 ft).

So about 15% expected at 7,000 ft.

How do results from these actual altitudes translate to our equivalent air altitudes?
Rahn and Fenn (1956) disproved the simple notion of equivalent air altitude, and conclude, “It is evidently not enough to equate the inspired $O_2$ tensions …”

Since 1980s researchers have questioned the conventional wisdom that the symptoms of AMS are solely due to low $O_2$ partial pressure.

- Accumulated anecdotal evidence shows descent is more effective for relief of AMS than enriched $O_2$ alone.

Savourey (2003) speaks of the “specific response to hypobaric hypoxia”.

So the door is open to investigate an independent $P_B$ effect on AMS.
normobaric hypoxia, hypobaric hypoxia, and hypobaric normoxia

Tucker Loeppky

Roach

Levine

Hirai
The pressure effect is real, so to understand the total hypoxic stress means you have to understand the interaction between hypoxic \( P_{1O_2} \) and \( P_B \).

Any bed rest hypoxia study should use the actual atmospheric conditions and not the equivalent air altitude, even if it makes the study more complicated.
NASA atmosphere experience

ambient oxygen fraction vs. ambient pressure (mmHg)

- Apollo-211
- Skylab-148
- habitat-111
- LSAM-117
- Shuttle / CEV-127
- research data

Ambient oxygen fraction vs. ambient pressure diagram with marked data points for different missions.
So…..

- Are astronauts at potential risk for AMS? About 25% worst case probability (guesstimate) with 0% once acclimatization occurs.

- This is baseline estimate given direct ascent to 8.0 psia with 32% O₂ and no consideration of μG-AMS interaction.

- Greater potential risk of AMS than the current EAAs suggest.

  - Finalize a plan to mitigate the risk even if risk is unclear.

  - Take the opportunity to quantify the risk with focused research.
secondary polycythemia
<table>
<thead>
<tr>
<th>Reference</th>
<th>Pre – Post HCT</th>
<th>Upper Range</th>
<th>Time Hrs</th>
<th>Supine</th>
<th>6-HD</th>
<th>PIO2 mmHg</th>
<th>Plasma Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stevens (1966) and Lynch (1967)</td>
<td>44 51</td>
<td>54</td>
<td>624</td>
<td>✓</td>
<td>___</td>
<td>95</td>
<td>2928 to 2318 ml PV (-21%) 2265 to 2398 ml RBC (+6%) 5193 to 4716 ml TBV (-9%)</td>
</tr>
<tr>
<td>Waligora (1982)</td>
<td>43 46*</td>
<td>47</td>
<td>28</td>
<td>___</td>
<td>✓</td>
<td>108</td>
<td>no data</td>
</tr>
<tr>
<td>Fulco (1985)</td>
<td>42 48</td>
<td>52</td>
<td>114</td>
<td>✓</td>
<td>___</td>
<td>84</td>
<td>19% ↓ PV, 10% ↓ TBV, 15.1 to 16.8 g/dl HB</td>
</tr>
<tr>
<td>Martin (1986)</td>
<td>42 46**</td>
<td>50</td>
<td>144</td>
<td>___</td>
<td>✓</td>
<td>150</td>
<td>3704 to 3271 ml PV (-12%)</td>
</tr>
<tr>
<td>Loeppky (1993a,b)</td>
<td>47+ 49</td>
<td>53</td>
<td>168</td>
<td>___</td>
<td>___</td>
<td>98</td>
<td>5% ↓ PV, 16.5 to 17.5 g/dl HB 20% ↓ PV, 16.5 to 19.0 g/dl HB</td>
</tr>
<tr>
<td></td>
<td>47+ 52</td>
<td>54</td>
<td>168</td>
<td>___</td>
<td>✓</td>
<td>98</td>
<td></td>
</tr>
</tbody>
</table>

* only 8 hrs were at 8,000 ft (PIO2 was 108 mmHg)
** normoxic 6-HD
+ hypoxic exposure only
# subjects lived at 5,400 ft (PIO2 was 120 mmHg)
other considerations

- Does μG modify the likelihood or character of AMS?
  - Redistribution of lung fluid – 25% increase in CapBV
  - Increased interstitial edema – puffy face response
  - Increased incidence of HAPE?

- Potential negative synergy on combining mild hypoxia and adaptation to μG – increase in hematocrit leads to increased blood viscosity.
  - Six reports suggest this may not be a significant concern – keep hematocrit below 55%.
Baseline “worst case” potential risk of AMS is about 25% based on direct ascent to 8.0 psia with 32% O₂.
  - EAA model should be replaced with an iso-hypoxic model.

Staged depressurization scheme is a practical mitigation approach.

Current depressurization to 10.2 psia in CEV and 4-day transit to moon is not anticipated to induce signs or symptoms of AMS.

Eventual transition to LSAM at 8.0 psia and 32% O₂ after some acclimatization will reduce potential risk << 25%, but precise estimate is not yet available.

Due to uncertainty about potential AMS risk:
  - Flight Surgeons should prepare.
  - Focused research should proceed.
  - Current analytical efforts should continue.
Questions ?
Based on this 1991 committee’s recommendations:

- A diagnosis of AMS is based on a recent gain in altitude, at least several hours (>2) at the new altitude, and the presence of headache and at least one of the following symptoms: gastrointestinal upset, fatigue or weakness, dizziness or lightheadedness and difficulty sleeping.

- A score of three points or greater on the AMS Self-Report Questionnaire alone or in combination with the clinical assessment score is diagnostic of AMS.

Several signs and symptoms of AMS are shared with motion sickness – confounding a diagnosis of each!
### Self Report Questionnaire

Each question asked and the sum is calculated as the AMS self report score.

<table>
<thead>
<tr>
<th>Question</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Headache</td>
<td>No headache</td>
<td>Mild Headache</td>
<td>Moderate Headache</td>
<td>Severe Headache, incapacitating</td>
</tr>
<tr>
<td>Gastrointestinal Symptoms</td>
<td>No gastrointestinal symptoms</td>
<td>Poor appetite or nausea</td>
<td>Moderate nausea or vomiting</td>
<td>Severe nausea &amp; vomiting, incapacitating</td>
</tr>
<tr>
<td>Fatigue and/or Weakness</td>
<td>Not tired or weak</td>
<td>Mild fatigue/weakness</td>
<td>Moderate fatigue/weakness</td>
<td>Severe fatigue / weakness, incapacitating</td>
</tr>
<tr>
<td>Dizziness/ Lightheadedness</td>
<td>Not Dizzy</td>
<td>Mild dizziness</td>
<td>Moderate dizziness</td>
<td>Severe dizziness, incapacitating</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>Slept as well as usual</td>
<td>Did not sleep as well as usual</td>
<td>Woke many times, poor night's sleep</td>
<td>Could not sleep at all</td>
</tr>
</tbody>
</table>
Clinical Assessment

The interviewers ratings of three signs is added to the self-report score.

<table>
<thead>
<tr>
<th>Sign</th>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Change in Mental Status</td>
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<td>No Change in Mental Status</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Lethargy / lassitude</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Disoriented/confused</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Stupor / semiconsciousness</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Coma</td>
</tr>
<tr>
<td>7. Ataxia (heel to toe walking)</td>
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<td>No Ataxia</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Maneuvers to maintain balance</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Steps off line</td>
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<tr>
<td></td>
<td>3</td>
<td>Falls down</td>
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<tr>
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<td>4</td>
<td>Can't stand</td>
</tr>
<tr>
<td>8. Peripheral Edema</td>
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<td>No peripheral edema</td>
</tr>
<tr>
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<td>1</td>
<td>Peripheral edema at one location</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Edema at two or more locations</td>
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