RESPIRATION AND SLEEP AT HIGH ALTITUDE

2nd Advanced Course in “Mountain Medicine”

MAY 25-27
OLYMPUS MOUNTAIN

MANOS VAGIAKIS
Pulmonologist-Intensivist
Director of ICU and Sleep Disorder Center
“Evangelismos” Hospital
Athens, Greece
Respiration

Breathing in

Active Phase
INHALATION

- air inflates the lungs

Passive Phase
EXHALATION

diaphragm descends

Breathing out

- air is forced out

diaphragm relax
Respiratory System

• *Respiration* is the exchange of gases between the body and its tissues and the outside ambient air.

• The main objective of respiration is to add oxygen and remove carbon dioxide.
Air enters through the nose, mouth, trachea to the bronchial tree.
The problem area in hypoxic hypoxia is circled.
\[ \text{PACO}_2 = \text{PIO}_2 - \frac{\text{PACO}_2}{R} + F \]

\[ \text{PCO}_2 = \frac{\dot{V}\text{CO}_2}{\dot{V}_A} \times K \]
$O_2 = 150 \text{ mm Hg}$

$CO_2 = 0$

$O_2 = 100$
$CO_2 = 40$

$O_2 = 40$
$CO_2 = 45$

Γυσιολογική
The Lung

• Within the red blood cell, there is Hemoglobin, which function as specialized oxygen transport system that allows far more oxygen to be carried by blood.

• At high altitude, we need to increase rate and depth of breathing in order to get enough oxygen into our lung.
Figure 6.1 Electron micrograph showing a pulmonary capillary (C) in the alveolar wall. Note that in many places, the thickness of the blood-gas barrier is less than 0.3 μm. The large arrow shows the diffusion path from the alveolar gas to the interior of the red blood cell (EC), and includes the alveolar epithelium (EP), interstitium (IN), and the capillary endothelium (EN). These are grouped as (2) in the figure: plasma (P), and red blood cell (R). Other labeled structures include fibroblasts (FB), and the basement membrane (BM). From Weibel, 1970.
Σχήμα 6.1. Καμπύλη διάκλαδωσης του $O_2$ (συνεχής γραμμή) στους 37°C με pH 7.4 και $P_{CO_2}$ 40 mm Hg. Στο σχήμα απεικονίζεται και η ολική μυγκένωση του $O_2$ στο αίμα για αιμοσφαιρίζη 15 g/dl/100 ml.
Hypoxia

• State of blood when it has an **not enough supply of oxygen** for the requirements of the tissues and body cells

• **This can** cause impairment of body function especially brain.

• Death will follow if oxygen lack continues.
Hypoxic Hypoxia

A deficiency in Alveolar oxygen exchange

Reduced $pO_2$ in the lungs (high altitude)

Body tissue

Red blood cells
Symptoms of hypoxia

- **Sensory loss** - vision, especially for color, is affected early, and then touch, orientation, and hearing are impairment.

- **Impairment of consciousness** - as hypoxia progresses the individual’s level of consciousness drops until he becomes confused, then semiconscious, and unconscious. Unless he is rescued he will die and at high altitude death can occur within a few minutes.
\[ P_t = P_1 + P_2 + P_3 \ldots + P_n \]

Where \( P_t \) = total pressure

\[ P_1 + P_2 + P_3 \ldots + P_n \] = partial pressures of the constituent gases

**Box 1: Dalton’s Law of partial pressures**

**Respiratory Physiology at Altitude**

C Sandberg¹, J Naylor²
FIG. 2. Solid line shows the barometric pressure–altitude relationship on Mt. Everest from AMREE. The three data points are the Base Camp, Camp 5, and Everest summit. The broken line indicates the ICAO Standard Atmosphere. Note that the actual pressures are consistently higher than predicted from the Standard Atmosphere. On the summit the difference is 17 mmHg (West et al., 1983c).
As barometric pressure decreases with ascent inspired oxygen tension drops significantly.
The Brain

- Parietal lobe
- Frontal lobe
- Occipital lobe
- Temporal lobe
Effect of lack oxygen to Brain

Lack of oxygen to the brain, lead to the failure of the brain function such as

• Inability to do normal physical activities,
• Distorted vision
• Difficulty with memorizing
• Difficulty in judgment and decision making
• Loss of thinking ability
• Fail to communicate and write well
Why important to recognize?

• Because the nervous system tissues have a heavy requirement for oxygen, especially the brain (and eyes), most hypoxic symptoms are directly or indirectly related to the nervous system (brain).

• If hypoxia is prolonged, serious problems develop with ultimate death. In extreme cases (prior to death), some brain cells are actually killed, and they cannot be regenerated.
FIG. 6. Cognitive performance during Operation Everest III. Variations of performance during a simple task (Pegboard test) and a complex task (adding another stimulus) compared to a control group staying in normoxia as reference. Note that performance is significantly altered at 8000 m and above and much more altered in complex than simple tasks (Bouquet et al., 1999).
Ventilatory responses to acute hypoxia may be divided into three stages:

a. Ascent to high altitude produces a fall in arterial oxygen tension.

b. This stimulates peripheral chemoreceptors to increase tidal volume and respiratory rate.

PAO2 increase but CO2 falls alkalosis.
\[ P_{ACO_2} = P_{IO_2} - \frac{P_{ACO_2}}{R} + F \]

\[ PCO_2 = \frac{\dot{V}CO_2}{\dot{V}_A} \times K \]
Figure 5.1 Hypoxic ventilatory response to $PA_{CO_2}$ and arterial oxygen saturation ($SA_{O_2}$).
VENTILATORY RESPONSES TO ACUTE HYPOXIA

Over several days the kidneys excrete bicarbonates, decreases PH and allows further increase in ventilation. (ACCLIMATIZATION).
VENTILATORY RESPONSES TO ACUTE HYPOXIA

Ventilatory responses to acute hypoxia may be divided into three stages:

c. Residents at high altitude: fall in minute ventilation and a loss of the normal ventilatory drive to hypoxia.
FIG. 3. Diagram relating resting PaO\textsubscript{2} and Paco\textsubscript{2} at various altitudes during of Operation Everest III (filled diamonds, arterialized blood gases) and Operation Everest II (open squares, arterial blood gases). SL: sea level; RSL: 2 days after return to normoxia. Note that at RSL, PaO\textsubscript{2} is equivalent to PaO\textsubscript{2} at SL, but Paco\textsubscript{2} is lower due to a persistent hyperventilation. Data from Operation Everest II were obtained from Sutton et al. (1988) and Malconian et al. (1993).
FIG. 4. Variations in pH during Operation Everest III. Note a progressive increase in pH with altitude (respiratory alkalosis) and, for a given altitude, a progressive decrease of pH with time (partial renal compensation of alkalosis): see, for example, at 7000 and 8000 m.
### Table 2. Comparison of Arterial $P_{aO_2}$, $P_{aCO_2}$, and pH Estimates and Measurements at 8400 m and above from AMREE, OE II, OE III, and CXE

<table>
<thead>
<tr>
<th></th>
<th>$P_B$ (mmHg)</th>
<th>$P_{IO_2}$ (mmHg)</th>
<th>$P_{aO_2}$ (mmHg)</th>
<th>$P_{aCO_2}$ (mmHg)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMREE, Camp 6, 8400 m</td>
<td>267</td>
<td>46</td>
<td>No estimate</td>
<td>12.9</td>
<td>7.58</td>
</tr>
<tr>
<td>AMREE, summit, 8848 m</td>
<td>253</td>
<td>43</td>
<td>28</td>
<td>7.5</td>
<td>7.75</td>
</tr>
<tr>
<td>OE II, “summit”</td>
<td>253</td>
<td>43</td>
<td>30</td>
<td>12</td>
<td>7.56</td>
</tr>
<tr>
<td>OE III (Comex), “summit”</td>
<td>253</td>
<td>43</td>
<td>30.6</td>
<td>11.9</td>
<td>7.58</td>
</tr>
<tr>
<td>CXE, Balcony, 8400 m</td>
<td>272</td>
<td>47</td>
<td>24.6</td>
<td>13.3</td>
<td>7.53</td>
</tr>
</tbody>
</table>

$P_B$, barometric pressure; $P_I$, moist inspired air. Figures in italics are estimates (not direct measurements) of arterial values. The level of precision for quoted estimates and measurements is taken from the original reports.
**Table 1. Individual Values for Arterial \( P_{Ao_2} \), \( P_{aco_2} \), and pH in 4 CXE Subjects at 8400 m on Everest**

<table>
<thead>
<tr>
<th></th>
<th>( P_{ao_2} ) (mmHg)</th>
<th>( P_{aco_2} ) (mmHg)</th>
<th>pH</th>
<th>( PAo_2 ) (mmHg)</th>
<th>Alveolar–arterial oxygen difference (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td>29.5</td>
<td>12.3</td>
<td>7.55</td>
<td>32.4</td>
<td>2.89</td>
</tr>
<tr>
<td>Subject 2</td>
<td>19.1</td>
<td>15.7</td>
<td>7.45</td>
<td>26.9</td>
<td>7.81</td>
</tr>
<tr>
<td>Subject 3</td>
<td>21.0</td>
<td>15.0</td>
<td>7.52</td>
<td>27.4</td>
<td>6.44</td>
</tr>
<tr>
<td>Subject 4</td>
<td>28.7</td>
<td>10.3</td>
<td>7.60</td>
<td>33.2</td>
<td>4.51</td>
</tr>
</tbody>
</table>
FIG. 3. The Balcony on the SE ridge of Everest, the location of arterial blood gas sampling at 8400 m. Note Sherpa with vacuum flask containing iced-water slurry for transport of blood samples to bench-top blood gas analyzer at Camp 2 (6400 m), May 2007.
Figure 6.3 Calculated time course for $P_{O_2}$ in the resting human pulmonary capillary at sea level. Note that there is ample time for equalization of the $P_{O_2}$ between alveolar gas and end-capillary blood. $V_i = 300$ mL min $^{-1}$, $D_{O_2} = 40$ mL min $^{-1}$ mm Hg $^{-1}$. (From West and Wagner 1989.)

Figure 6.4 Calculated time course of the $P_{O_2}$ along the pulmonary capillary for a climber at rest on the summit of Mount Everest. Note that there is considerable difference in equalization of alveolar uptake with a large alveolar end-capillary $P_{O_2}$ difference. $P_{O_2}$ $254$ mm Hg, $V_i = 350$ mL min $^{-1}$, from West et al. 1983b.
FIG. 4. Maximal O₂ uptake plotted against the inspired Po₂. The upper line shows the AMREE data, and the Vo₂max on the summit is just over 1 L · min⁻¹. The lower line shows the data from the Silver Hut Expedition (West et al., 1983a).
FIG. 5. Hypoxic ventilatory response (HVR) of 8 members of the expedition. Remarkably, CK reached the summit first, CP second, and PH third. A strong HVR is necessary to maintain the alveolar Po$_2$ at extreme altitude by greatly reducing the alveolar Pco$_2$, as shown by Fig. 3.
Sleep At high altitude

Sleep Stages:
- N1
- N2
- N3
- REM
ΣΤΑΔΙΟ  Ν1
ΣΤΑΔΙΟ Ν2
ΣΤΑΔΙΟ Ν3
ΣΤΑΔΙΟ REM
Sleep at high altitude is associated with increased fragmentation, by frequent awakenings and a reduction in stage 3/4 sleep.

All-night sleep plots for a single subject during a night at sea level (upper plot) and the first night at altitude (lower plot). A, awake; R, REM sleep; D, stage 1; 2, stage 2; 3/4, stages 3 and 4.
Breathing pattern and arterial oxygen saturation (Sao₂) in a normal subject during sleep at high altitude (4300 meters). Such a pattern is seen throughout much of sleep in most individuals after ascent. There is characteristic, monotonously repetitive, machinery-like periodic alternation of apnea and repetitive clusters of hyperpneic breaths.
Breathing pattern and arterial oxygenation in a subject with chronic mountain polycythemia during sleep at his native altitude of 3100 meters. The breathing pattern consists of an undulating depth of breathing with oscillation of arterial oxygen saturation ($\text{Sao}_2$).
Figure 1—The hypnogram obtained in a subject during a night at 490 m (top panel) shows a normal distribution of sleep stages and several NREM/REM sleep cycles. In contrast, the hypnogram recorded during the 1st night at 4559 m (middle panel) reveals predominantly superficial sleep stages with frequent awakenings, very rare deep sleep stages 3 and 4, and no REM sleep. The hypnogram from the 3rd night at 4559 m (bottom panel) reveals a partial restoration of normal sleep architecture.
Table 1—Sleep study results

<table>
<thead>
<tr>
<th></th>
<th>Zurich 490 m</th>
<th>Margherita hut 1st night 4559 m</th>
<th>Margherita hut 3rd night 4559 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in bed (min)</td>
<td>464 (456,484)</td>
<td>485 (462,497)</td>
<td>496*# (486,509)</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>417 (387,439)</td>
<td>320* (280,391)</td>
<td>360* (282,392)</td>
</tr>
<tr>
<td>NREM stages 1 and 2 (%)</td>
<td>73 (69,75)</td>
<td>91* (88,93)</td>
<td>78*# (70,90)</td>
</tr>
<tr>
<td>NREM stages 3 and 4 (%)</td>
<td>18 (16,23)</td>
<td>6* (4,7)</td>
<td>11# (6,20)</td>
</tr>
<tr>
<td>REM (%)</td>
<td>8 (6,12)</td>
<td>3* (0,5)</td>
<td>4# (1,12)</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>93 (90,94)</td>
<td>69* (64,80)</td>
<td>75* (55,84)</td>
</tr>
<tr>
<td>Arousal index (/h)</td>
<td>5.4 (3.5,7.3)</td>
<td>17.9* (5.9,28.5)</td>
<td>5.7# (2.7,15.1)</td>
</tr>
<tr>
<td>AHI TST (/h)</td>
<td>0.1 (0,0.1)</td>
<td>60.9* (21.4,79.2)</td>
<td>86.5* (19.1,95.4)</td>
</tr>
<tr>
<td>AHI NREM (/h)</td>
<td>3.1†† (1.2,5.8)</td>
<td>58.7* (20.1,81.4)</td>
<td>91.3‡‡ (20,102.2)</td>
</tr>
<tr>
<td>AHI REM (/h)</td>
<td>5.5 (2.3,11.1)</td>
<td>27.8 (0,103.9)</td>
<td>2.1 (0,19.8)</td>
</tr>
<tr>
<td>Oxygen desaturation index (&gt; 3% dips/h of time in bed)</td>
<td>0.1 (0.4,2)</td>
<td>31.8* (13.3,75.9)</td>
<td>28.8* (13.7,51)</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>96 (95,96)</td>
<td>67* (64,69)</td>
<td>71*# (69,78)</td>
</tr>
<tr>
<td>End-tidal PCO₂ (mmHg)</td>
<td>41 (40,44)</td>
<td>29* (23,31)</td>
<td>29* (27,30)</td>
</tr>
<tr>
<td>Minute ventilation (L/min)</td>
<td>4.4 (3.1,5.3)</td>
<td>6.3* (5.3,8.6)</td>
<td>5.1*# (4.6,6.7)</td>
</tr>
<tr>
<td>Tidal volume (mL)</td>
<td>293 (209,300)</td>
<td>335* (262,399)</td>
<td>258 (225,334)</td>
</tr>
<tr>
<td>Breath rate (/min)</td>
<td>16 (14,17)</td>
<td>20* (19,22)</td>
<td>20* (19,22)</td>
</tr>
<tr>
<td>Heart rate (/min)</td>
<td>56 (50,61)</td>
<td>81* (74,92)</td>
<td>84* (75,89)</td>
</tr>
</tbody>
</table>

N = 16. AHI TST, AHI NREM, AHI REM = apnea-hypopnea index during total sleep time, NREM, and REM sleep, respectively. SpO₂ = mean oxygen saturation during sleep. *P < 0.05 vs. 490 m. #P < 0.05 vs. 4559 m 1st night. ††P < 0.05 NREM vs. REM.
Figure 2—Medians and quartile ranges (bars, vertical lines) of the apnea/hypopnea index (AHI) and the apnea/hypopnea related arousal index at 490 m and the 1st and the 3rd night at 4559 m. Only 11% and 4% of the apneas/hypopneas were followed by an arousal during the 1st and the 3rd nights, respectively. *P < 0.05 vs. 490 m, #P < 0.05 vs. the 1st night at 4559 m.
Impedance plethysmograms show irregular, nonperiodic, breathing during sleep at 2850 meters in four subjects susceptible to high-altitude pulmonary edema.
Schematic representation of potential mechanisms by which carbonic anhydrase inhibitors (e.g., acetazolamide) decrease periodic breathing during sleep at high altitude. These agents promote a bicarbonate diuresis, which lessens alkalosis and reduces apnea but augments hyperventilation and hypocapnia. This suggests that alkalosis may be more important than hypocapnia in the genesis of periodic breathing.
Average arterial oxygen saturation (Sao₂) in a sleeping subject at altitude (5360 m) without *(blue area)* and with *(yellow area)* acetazolamide. Treatment raised and stabilized arterial oxygen saturation.