CO$_2$ Effects in Space

Relationship to Intracranial Hypertension
CO₂ Effects Terrestrially

- Terrestrial atmospheric CO₂ level is 0.039% (0.30 mmHg)
- Above 2% (15.2 mmHg, 20,000 ppm), carbon dioxide may cause a feeling of heaviness in the chest and/or more frequent and deeper respirations.
  - If exposure continues at that level for several hours, minimal "acidosis" (an acid condition of the blood) may occur but more frequently is absent.
  - The concentration of carbon dioxide usually must be over about 2% (20,000 ppm) before most people are aware of its presence unless the odor of an associated material (auto exhaust or fermenting yeast, for instance) is present at lower concentrations.
- **Breathing rate** doubles at 3% (22.8 mmHg, 30,000 ppm) CO₂ and is four times the normal rate at 5% (38 mmHg, 50,000 ppm) CO₂. **At levels above 5%, concentration CO₂ is directly toxic.** [At lower levels we may be seeing effects of a reduction in the relative amount of oxygen rather than direct toxicity of CO₂.]
Terrestrial Effects

- Symptoms of high or prolonged exposure to carbon dioxide include rapid breathing, diminished mental alertness, impaired muscular coordination, faulty judgment, depression of all sensations, emotional instability, and fatigue.
- As intoxication progresses, nausea, vomiting, prostration, and loss of consciousness may result.
- Eventually this leads to convulsions, coma, and death.
Main symptoms of Carbon dioxide toxicity

**Visual**
- Dimmed sight

**Auditory**
- Reduced hearing

**Respiratory**
- Shortness of breath

**Muscular**
- Tremor

**Central**
- Drowsiness
- Mild narcosis
- Dizziness
- Confusion
- Headache
- Unconsciousness

**Skin**
- Sweating

**Heart**
- Increased heart rate and blood pressure

**Volume % in air**
- 1%
- 3%
- 5%
- 8%
Research Terrestrially - Navy Data

- **Animal Models**
  - Animal model- 1.5% (11.19 mmHg) CO$_2$ increased incidence of focal and tubular kidney calcification
  - Animal model 2 –at 1.5% (11.19 mmHg) showed significant bone loss of calcium and phosphorus with the commensurate increase in bone bicarbonate to compensate for acidosis.

- **Human Data**
  - Subject Exposure to 1.5% (11.19 mmHg) CO$_2$ – 42 days increased red cell calcium and renal excretion of Phosphorus. Calcium effect on cell membrane similar to narcosis.

- Schaefer
Research Terrestrially – Navy Data

- **Submarine Patrol Data**
  - Ten year comparison with Surface Vessels – Increase rate
  - Respiratory, GI, Urologic, and EENT illnesses. $\text{CO}_2 \geq 1\%$ (7.6 mmHg) \cite{TanseySchaefer}
  - Royal Navy – Patrols with $\text{CO}_2 \geq 1\%$ (7.6 mmHg) showed mild uncompensated respiratory acidosis with the respiratory parameters returning to normal. \cite{Pingre}
Terrestrial Research

- Animal Models
  - Chronic exposure showed elevated CBF in sheep even after termination of the hypercapnia.

- Human
  - Visuomotor decreases in performance with concentrations of as small as 1.2% (9.12 mmHg)
Terrestrial Research

- Chronic Exposure model - 0.7% (5.32 mmHg) and 1.2% (9.12 mmHg)
  - Showed increased cerebral blood flow, lactic acid build up with exercise, and mild performance impairment
  - Initial response is increased ventilation volume, alveolar dead space, and respiratory rate. Respiratory rate and minute volume return to normal in 2 weeks, but PaCO₂ and pH do not.
  - The CBF decreased after the initial exposure to a higher stabilized baseline. It was also noted that during the CO₂ exposure visual stimulation increased the CBF 30%.
  - Headaches were more frequent at the beginning of the 1.2% CO₂ trial.
Terrestrial Research

- Chronic Exposure model - 0.7% (5.32 mmHg) and 1.2% (9.12 mmHg)
  - Cerebral autoregulatory mechanisms were preserved during sustained mild and intense exposure levels of hypercapnia (Tested reaction to 5% [38.0 mmHg] during the chronic adaptation phases).
  - The superimposition of Head Down Tilt (HDT) with its increased CBF did not alter CBF responses.
  - Cerebral blood flow responses were similar in amplitude and pattern at both 0.7% (5.32 mmHg) and 1.2% (9.12 mmHg) CO₂.
Changes in Space
Physiological Changes with Microgravity

- Fluid shift to thorax and head – This results in intracranial pressure increases and congested cerebral circulation – increased CBF and Intravenous dilatation
- Plasma volume – decreased 17% in first 24 hours stabilizes to 15.9%
- Red cell mass – decreased by 10-11%
- Cardiac output – decreased by 17-20%
CO₂ Symptoms in space

- Primarily noted to be headache and visual changes.
- Noted onset at levels far lower than terrestrially
- Mission Control personnel noticed behavioral changes had occurred at lower levels in crewmembers. Procedural errors, unwarranted comments from crewmembers, and increased “agrivatioin”
- EVA crewmembers “felt better” post initiation of Oxygen pre-breath and donning the suit (100% O₂ and 4.3 psi environment).
CO₂ Symptoms in space

- CO₂ potent vasodilator
- Causes increased blood flow – problem in that the cerebral blood vessels are already congested
- Thought to be contributory to the symptoms occurring at lower levels.
Mechanisms
CO$_2$ Effects on Cerebral Blood Flow
CSF Production
Blood-CSF Interface in the Choroid Plexus

CEREBROSPINAL FLUID
(apical membrane)

CHOROID CELL CYTOPLASM

INTERSTITIAL FLUID or PLASMA ULTRAFILTRATE

INTERSTITIAL FLUID or PLASMA ULTRAFILTRATE

INTERSTITIAL FLUID or PLASMA ULTRAFILTRATE
Neuroendocrine targets of interest

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<td>Interleukin-1</td>
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<td>Neurotrophin-3</td>
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<td>Proctolin</td>
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<td>Vascular endothelial growth factor</td>
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<td>Vasopressin</td>
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*AR = autoradiography; IHC = immunohistochemistry; ISH = in situ hybridization; NB = Northern blotting; RBA = receptor binding assay; RGE = reporter gene expression; RPA = RNase protection assay; RT-PCR = reverse transcriptase-polymerase chain reaction.

*Repressed only during development.
What should we be looking for

- Arginine Vasopressin
- Atrial Naturiutetic Peptide
ANP Upregulated in Rat Choroid Plexus After 9 days Spaceflight (STS-40, 1994)
ANP Expression Returns to Normal Values After Mission Length (ML) Recovery (9 days)
STS-56 - 1995

Normal

Spaceflight, or Hind-Limb Unloading

Mission-Length Recovery Period