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
Research Terrestrially - Navy Data

- **Animal Models**
  - Animal model - 1.5% (11.19 mmHg) CO₂ 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) CO₂ – 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) 
    - Tansey and Schaefer
  - Royal Navy – Patrols with $\text{CO}_2 \geq 1\%$ (7.6 mmHg) showed mild uncompensated respiratory acidosis with the respiratory parameters returning to normal. 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% \((9.12 \text{ mmHg})\)
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 PaCO$_2$ and pH do not.
  - The CBF decreased after the initial exposure to a higher stabilized baseline. It was also noted that during the CO$_2$ exposure visual stimulation increased the CBF 30%.
  - Headaches were more frequent at the beginning of the 1.2% CO$_2$ trial.
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).
CO$_2$ Symptoms in space

- CO$_2$ 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
Neuroendocrine targets of interest

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<td>Vascular endothelial growth factor</td>
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<td>Vasopressin</td>
<td>VIP&lt;sub&gt;1&lt;/sub&gt;, VIP&lt;sub&gt;2&lt;/sub&gt;</td>
<td>AR</td>
<td>verteins et al. (1997)</td>
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1AR = 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 Naturiutetetic 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