Visual Impairment Intracranial Pressure (VIIP) [aka Microgravity Ocular Syndrome (MOS)]

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Why We Do What We Do…
Recent VIIP/MOS Headlines:

- Too much space travel is hazardous for your eyeballs
- The mysterious syndrome impairing astronauts' sight
- Astronauts' eyes are at risk after too much time in space
- Space travel is causing visual impairment for some astronauts. Will this prevent travel to Mars?
VIIP/MOS: Clinical Findings

To date, 24 USOS ISS long-duration spaceflight astronauts have developed some or all of the following findings:

- **Ocular**
  - Hyperopic shift
  - Globe flattening
  - Choroidal folds
  - Cotton wool spots
  - Optic disc edema
  - Optic Nerve Sheath Distention

  **ALL are potential signs of elevated intracranial pressure (ICP)**

- **Mildly elevated post-flight intracranial pressure**
  - 21 - 29 cm H$_2$O range
    - Upper limit of normal: ~20 cm H$_2$O
    - Gray zone: 20.1 – 24.9 cm H$_2$O
Disc Edema = Modified Frisen Scale Grade ≥ 1 at first post-flight eye exam (via fundoscopy)
Globe Flattening = A change compared to preflight (via MRI or ultrasound)
Choroidal Folds = New or worsened compared to pre-flight (via OCT)
Cotton Wool Spot = Presence in-flight or post-flight (via fundoscopy)
Refractive Error = Change in cycloplegic (spherical) refraction ≥0.75D from preflight to first post-flight eye exam

24 crewmembers presented with one or more of these findings

- Disc Edema: 64
- Globe Flattening: 47
- Choroidal Folds: 47
- Cotton Wool Spot: 64
- Refractive Error: 47

Tested:
- Disc Edema: 10
- Globe Flattening: 12
- Choroidal Folds: 11
- Cotton Wool Spot: 7
- Refractive Error: 9

Occurred:
- Disc Edema: 54
- Globe Flattening: 35
- Choroidal Folds: 36
- Cotton Wool Spot: 57
- Refractive Error: 38
Clinical Findings: Hyperopic Shift

- Of the active astronaut population...
  - 80% wear vision correction (32% contact lenses)
  - Mean age = 47 yrs
  - Majority are presbyopic (i.e., a normal, age-related, progressively worsening inability to focus clearly on near objects)
- From postflight questionnaires (1989 - 2011): 25% of short-duration (Shuttle) & 50% of long-duration (ISS) mission astronauts report a subjective degradation in vision, especially at near
  - Provided “Space Anticipation Glasses”
Subjective Degradation in Vision (cont):

- Associated w/ **Hyperopic Shifts** in refractive error due to **Globe Flattening**
  - A 1 mm decrease in axial length will produce a ~3 diopter hyperopic shift
  - Largest shift to date is +1.75 diopters
  - In presbyopes: Typically decreases near visual acuity (VA), but leaves distant VA intact
Case Example:
- Male, mid 40s at time of flight
- No significant PMH/PSH/PFH
- No meds
- Normal BP (118/64)
- Normal lipids
- ECG Stress test normal w/ VO₂ max of 51ml/kg

Terrestrially: Globe flattening associated w/ papilledema (i.e., disc edema 2° to increased intracranial pressure); typically bilateral
Clinical Findings: *Choroidal Folds*

- Choroidal thickening due to vessel engorgement
- Induces choroidal and retinal folds
- Can resolve post-flight or can persist for 5+ yrs
- So far, no clinically-significant impact on BCVA

*Terrestrially:* Assoc. w/ choroidal tumors, scleritis, retrobulbar mass, papilledema/IH
Clinical Findings: *Cotton Wool Spots*

**Posterior pole fundoscopic images**
OD & OS for two ISS crewmembers
- Top arrows: Choroidal folds
- Bottom arrows: Cotton wool spots

**Example 1**

- **Cotton woods spots**
  - Abnormal retinal finding
  - Accumulations of axoplasmic material w/in retinal nerve fiber layer
  - Caused by ischemia → reduced axonal transport → swelling of axon → damaged nerve fibers
  - *Terrestrially*: Associated w/ diabetes, HTN, central retinal vein occlusion
Clinical Findings: Optic Disc Edema

Pre-flight fundoscopic images of the right (OD) & left (OS) optic discs

Post-flight images of optic discs, showing Grade 3 edema OD & Grade 1 edema OS
Clinical Findings: *Optic Disc Edema*

- **Terrestrially:** Optic disc edema is associated with:
  - **Unilateral:** Optic neuritis, optic neuropathy, retinal artery/vein occlusion
  - **Bilateral:** Increase in ICP…
    - IIH (→ “papilledema”)
    - Intracranial mass
    - Cerebral edema
    - Increased CSF production
    - Decreased CSF absorption
    - Obstructive hydrocephalus
    - Venous outflow obstruction
  - Typically reduces VA, enlarges blind spot, causes relative afferent pupillary defect & color impairment

Fundoscopic image of optic disc OD, 10 days after return to Earth
- Arrows: “C” shaped halo of edema
Clinical Findings: *Optic Nerve Sheath Δs*

Post-flight ultrasound image of globe, optic nerve (ON; purple), and optic nerve sheath (green). Showing:
- ON Sheath distention
- ON tortuosity

**ON Sheath terrestrially:**
- Normal diameter (ONSD) < 5.9 mm
- Enlargement typically associated w/ increased ICP

Post-Flight OD

12 mm
Common Characteristics of the Cases
Common Characteristics of the Cases

- ~6 month duration ISS mission
  - [No clinically-significant signs during short-duration flights]
  - Dose response??
- All had normal pre-flight eye exams
- Past medical history:
  - Negative for systemic disease
  - None had used medications before/during their mission that could increase ICP (e.g., vitamin A, tetracycline, corticosteroids, or nalidixic acid)
Common Characteristics of the Cases

- *None* complained of headaches, transient vision loss, double vision, pulsatile tinnitus, or vision changes during eye movements (i.e., the classic symptoms of idiopathic intracranial hypertension)

- *None* experienced loss in best-corrected visual acuity, color vision, or stereopsis

- Right eye affected more than left in all cases

- ISS cabin
  - Normal pressure & oxygen
  - Elevated CO$_2$
    - ~0.33-0.5% avg, w/ avg peak ~0.7%
    - 10x terrestrially: ~0.03-0.04%
We are just entering, relatively speaking, the long-duration phase of space exposure…

**Next Generation Missions**

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<th>Mission</th>
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<td>Mir</td>
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<tr>
<td>International Space Station</td>
<td>n = 55 as of 6/14/16</td>
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* Person-flights; may include multiple-time flyers w/in program
Why is this Happening?
Why is this Happening?

Microgravity → Cephalad fluid shift → Cerebral venous congestion
Why is this Happening?

- **Current Risk Statement:**
  
  “Visual Impairment Intracranial Pressure” (VIIP)

  "Given that the microgravity environment causes cephalad fluid shift in astronauts, there is a probability that astronauts will have intracranial hypertension (IHT) to some degree, which if left untreated, could lead to deleterious health effects.”
Why is this Happening?

- **Hypothesis #1**: Increased intracranial pressure
  - The original theory, hence the name “Visual Impairment Intracranial Pressure”

- **Hypothesis #2**: This is a local ocular eye problem

- **Hypothesis #3**: Slight IOP reduction + slight ICP increase

- **Hypothesis #4**: Folate-dependent 1-carbon metabolic pathway altered

- **Hypothesis #5**: Vessel congestion placing pressure locally around optic nerve (“Circle of Zinn-Haller” theory)
  - In µGravity, head venous pressure ≈ 15-20 mmHg
    - Standing terrestrially ≈ −20 mmHg
In-flight Exacerbating Factors??

**Resistive Exercise**

**High Oral Sodium Intake**
- Prepackaged Foods...
- Up to 5000+ mg/day

**High CO₂**
- ~10x terrestrial levels

**In-flight Pharmaceuticals**
Medical Surveillance
Surveillance & Medical Data Collection

- 49 ISS expedition missions have been completed (since 2000)
- Sentinel case occurred in 2005
  - Optic disc edema and cotton wool spot
- Surveillance/medical data collection is ongoing and has evolved
  - Began some “VIIP” related testing in 2008 (w/ Exp 18)
  - Inconsistent testing until Feb 2010 (Exp 23) when Eye MED B came into effect
Surveillance & Medical Data Collection

Terrestrially
- 3T MRI – Special “NASA Astronaut” protocol 12-18 months prior to launch

Terrestrially & On-Orbit
- Vision Exam
  - Visual Acuity (near & far)
  - Amsler grid
- Ocular Ultrasound
- Fundoscopy
- Optical Coherence Tomography (OCT)
- Tonometry (when clinically indicated)
Surveillance & Medical Data Collection

Visual Acuity & Amsler Grid
Surveillance & Medical Data Collection

On-orbit Ultrasound Imaging

ON sheath distention
ON tortuosity

12 mm

(Post-flight)
Surveillance & Medical Data Collection

Fundoscope
Optical Coherence Tomography (OCT)
Note: Representative OCT report; Not actual astronaut data
Surveillance & Medical Data Collection

Optical Coherence Tomography (OCT)

Pre-flight OD

Post-flight OD
Clinical Update: Feb17

**Ongoing clinical work**

- Correlation between ocular structural changes (OCT) and chronic effect on visual function (visual fields testing)
- Correlation of subcortical white matter hyperintensities (WMH) found on MRI and VIIP/MOS signs – 2017
- Refinement of cardiovascular parameters and their correlation with VIIP/MOS signs – 2017
- We are evaluating the next generation OCT, “OCT2” to determine if it will enhance on orbit imaging/data acquisition
What We Are Watching Coming From Our Research Colleagues

- Ocular Health Study and the Fluid Shifts Study – both finish data collection this summer
- Clinical relevance of MRI-based findings
- Implementation of direct ICP measures study pre and post mission
- Correlation between HDT with CO$_2$ and VIIP/MOS (EnviHab)
Questions?
Back-Up
The Lamina Cribosa & the Translaminar Pressure Gradient: A Mechanism for Papilledema

Area of Interest:

Translaminar Pressure Gradients:

1G  0G