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."
- "Possible Mars Mission 'Showstopper': Vision Risks for Astronauts."
- "Astronauts Returning to Earth With Vision Problems."
- "Space travel is causing visual impairment for some astronauts. Will this prevent travel to Mars?"
To date, 24 USOS ISS long-duration spaceflight astronauts have developed some or all of the following findings:

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

**Ocular**

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
VIIP/MOS Clinical Findings
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”
Clinical Findings: *Hyperopic Shift*

- Subjective Degradation in Vision (cont):
  - Associated with *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
Clinical Findings: *Globe Flattening*

- **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

[Image of MRI scan]
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/IIH
Clinical Findings: **Cotton Wool Spots**

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

- **Cotton wools 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

*Example 1*

Post-flight
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 $\Delta$s

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

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

Post-Flight OD

ON Sheath: 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 mvmts (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 CO₂
    - ~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

- **Mercury**: $n = 6$
- **Gemini**: $n = 20$
- **Apollo**: $n = 33$
- **Apollo-Soyuz**: $n = 3$
- **Skylab**: $n = 9$
- **Mir**: $n = 7$
- **Space Shuttle**: $n = 710$
- **International Space Station**: $n = 55$ as of 6/14/16

*Person-flights; may include multiple-time flyers w/in program.
Why is this Happening?
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Microgravity $\rightarrow$ Cephalad fluid shift $\rightarrow$ Cerebral venous congestion

Adapted from Hargens & Richardson, Respiratory Physiology & Neurobiology. 2009

Adapted from Rowell, 1988
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 CO$_2$
~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
On-orbit Ultrasound Imaging

Elevated optic disc

ON sheath distention

ON tortuosity

(Post-flight)
Surveillance & Medical Data Collection

Fundoscope
Surveillance & Medical Data Collection

Optical Coherence Tomography (OCT)
Surveillance & Medical Data Collection

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 & Research Update
**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\textsubscript{2} and VIIP/MOS (EnviHab)
Questions?
Back-Up
The Lamina Cribosa & the Translaminar Pressure Gradient: A Mechanism for Papilledema

Area of Interest:

Area of Magnification

Translaminar Pressure Gradients:

1G

0G

CSFp

IOP

Translaminar Pressure Gradient

vitreous cavity

dural sheath of optic nerve

retinal pigmented epithelium (RPE)

optic disc (or optic papilla)

optic nerve

lamina cribrosa

sclera

choroid

sensory retina

retina vessels

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