Human Health and Performance Academy Lecture

Visual Impairment and Intracranial Pressure (VIIP):

What is it and what does it tell us about Spaceflight Physiology?

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Contributors

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- Dave Francisco
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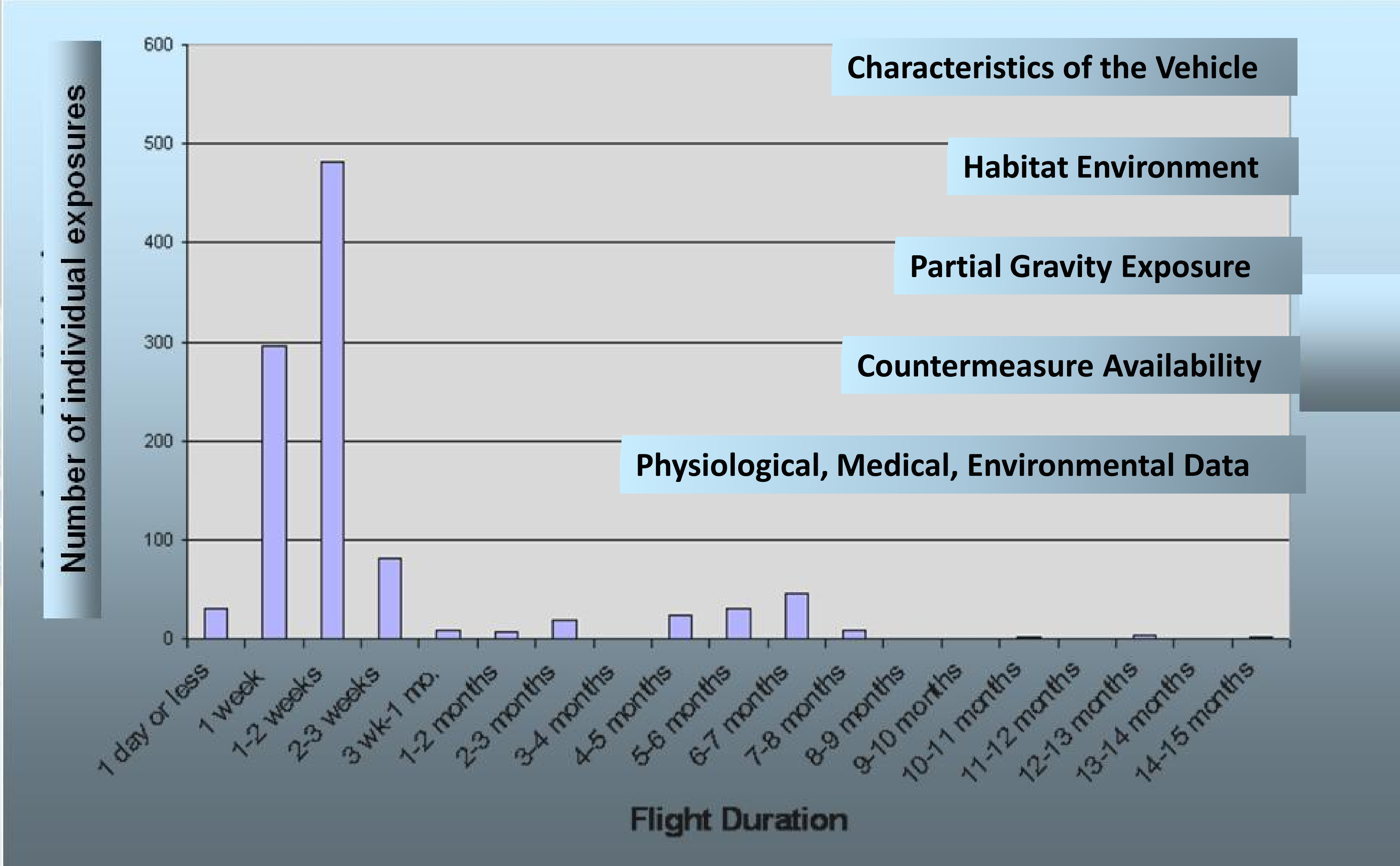
- LSAH - epidemiology
- BDRA – increment roll up
- HRP HHC Element
- VIIP RCAP
- VIIP IWG

Agenda

- Duration of Spaceflight
- Historical Context
- Spaceflight Physiology
- Data Collected
- Countermeasures
- Transition to Operations

- Visual Impairment and Intracranial Pressure
  - Incidence
  - Vascular, Central Nervous, Ocular components
  - Cardiovascular Physiology Refresher
  - Fluid shift
  - Imaging of the Eye and Evidence
  - Theory - ICP
  - Clinical Practice Guideline

Human Spaceflight Experience: The Long and the Short of it…



Historical Perspective

- Gemini 5 (8 day mission)
  - Visual Tester in-flight
  - Visual acuity measurement program
  - Large rectangles at ground sites in Texas and Australia.
  - No changes noted in astronaut visual acuity postflight.
  - Duntley et al, 1966

- Apollo
  - Retinal vascular photography reveals retinal vessels “decreased in size” at 3.5 hours into flight.
  - 100% oxygen atmosphere
  - No visual acuity changes
  - Hawkins and Zieglschmid, 1975

Shuttle

- 10-14 day missions
- Anecdotal reports of vision changes, but return to baseline.
- 1 astronaut with bilateral lens implants
- No optic disc edema cases, but an occasional choroidal fold.

- 122 crewmembers between 1995 and 1998, 15% indicated decrements in near vision on orbit. Returns to baseline.
- Paloski et al 2008

Differences Between Historical and Present

- Missions were 5 to 17 days generally (Skylab a notable exception)
- Astronaut age was mean of 38
- MRI and OCT not available
- Spacecraft ranged from 5.0 psi to 10.7 psi to 14.7 psi with varying oxygen concentrations

- Missions average 6 months on ISS
- Astronaut mean age 46.7
- MRI, OCT, Telemedicine fundoscopy
- 14.7 psi, 21% oxygen
- Robust exercise suite

Human Response to Spaceflight

Astronauts experience a spectrum of adaptations in flight and post flight

Exposures:

Launch & Landing Loads

Microgravity

Closed Environment (air and water)

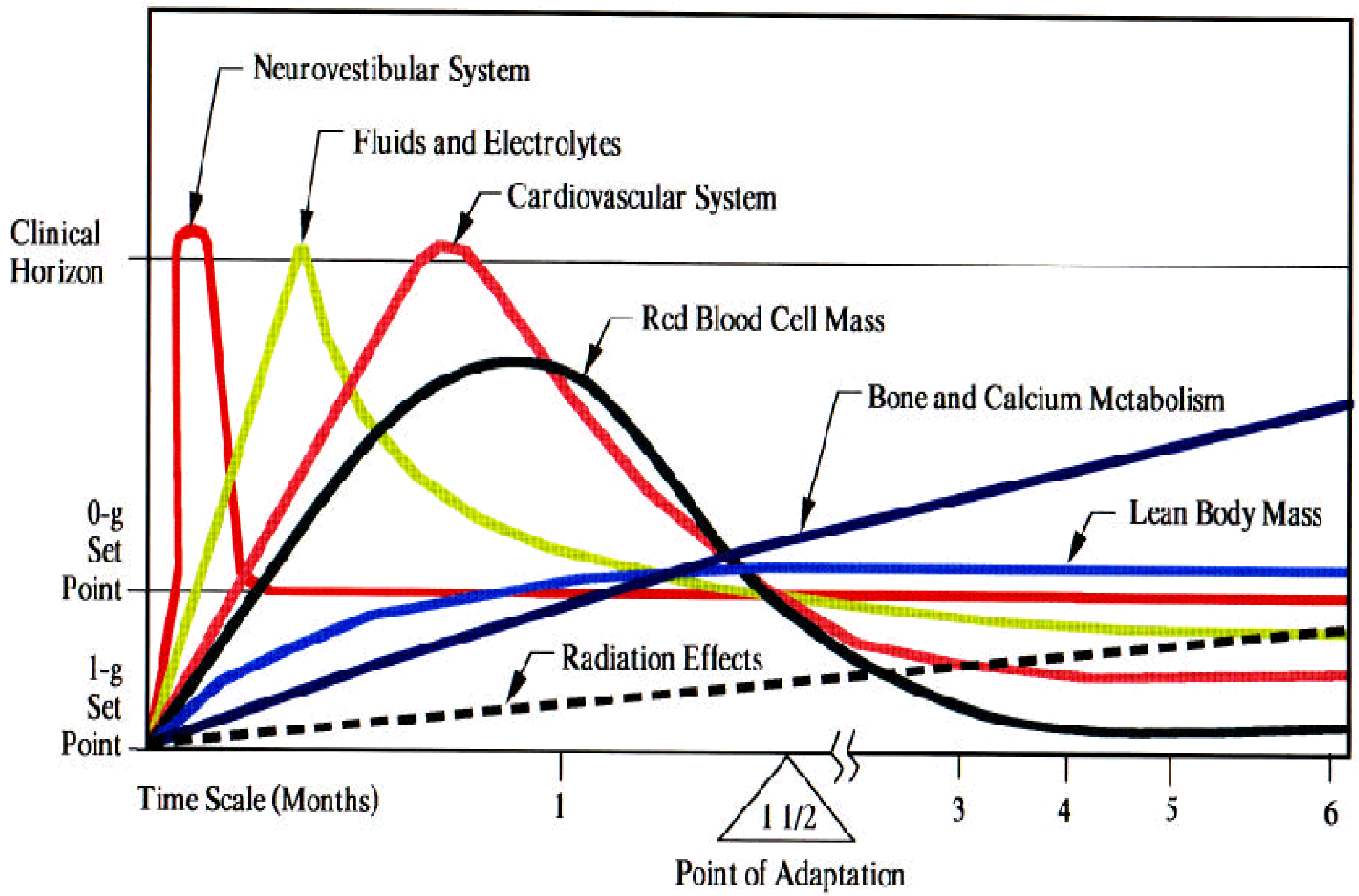
Confined Habitat

Radiation Exposure

Balance disorders
Cardiovascular deconditioning
Decreased immune function
Muscle atrophy
Bone loss

- Neurovestibular
- Cardiovascular
- Skeletal
- Muscular
- Immunological
- Nutritional
- Behavioral

Time Course of Physiological Changes During Weightlessness



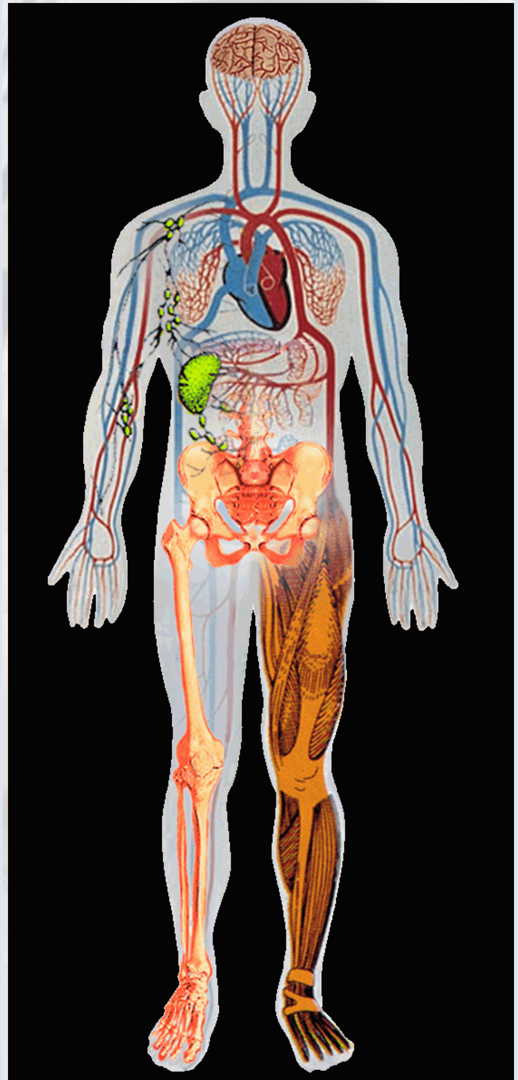
Physiological & Psychosocial Manifestations Associated with Space Flight

Bone
- ↓ Bone mineral content
- ↓ Bone mineral density
- ↑ Urinary calcium
- ↑ Renal stone risk

Skeletal Muscle
- ↓ Skeletal muscle mass
- ↓ Skeletal muscle strength
- ↓ Skeletal muscle endurance
- ↓ Skeletal muscle capillary density

Neurosensory
- ↑ Vestibular disturbances
- ↑ Space motion sickness
- ↓ Sensorimotor function
- ↓ Postural & locomotor stability

GI/Pharmacokinetics
- ↓ GI motility and PK



Cardiovascular
- ↓ Fluid volume
- ↓ Orthostatic tolerance
- ↓ Aerobic capacity
- ↑ Arrhythmias

Psychosocial
- ↑ Team issues
- ↑ Confinement issues
- ↑ Fatigue
- ↑ Stress
- ↑ Errors
- ↓ Cognitive Function

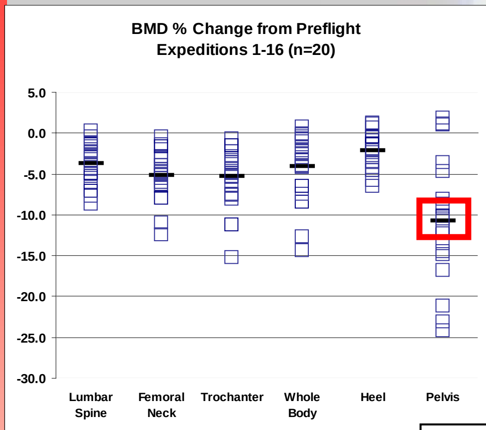
Environmental
- ↑ CO_2 (2-5 mmHg)*
- ↑ Hearing loss due to acoustics
- ↑ Radiation exposure
- ↑ Risk of cataracts/cancers
- ↑ Skin irritations due to microbial growths

Biomedical Data

- Data Collected via Medical Requirements
- Assessments of:
  - Bone
  - Cardiovascular
  - Aerobic Fitness
  - Sensory Motor
  - Functional Fitness
  - Nutritional Status

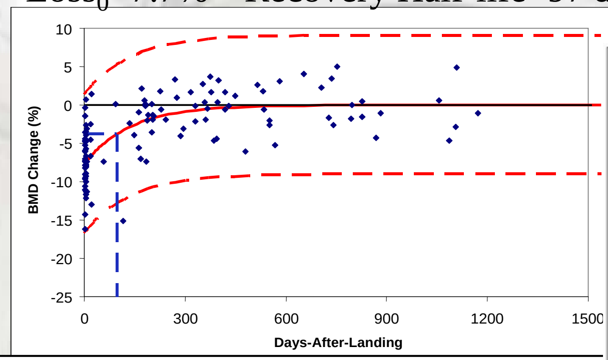
International Space Station

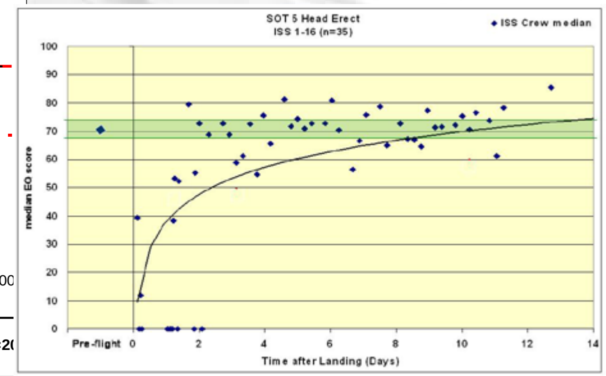
Medical Requirements collect physiological, medical and environmental data

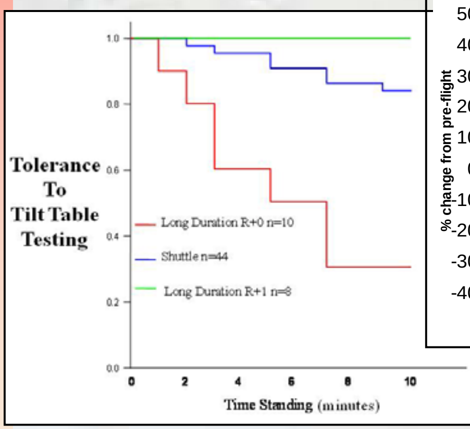


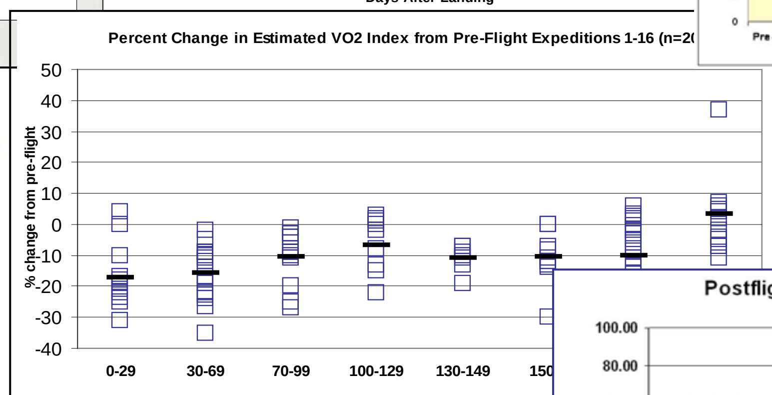
Pelvis

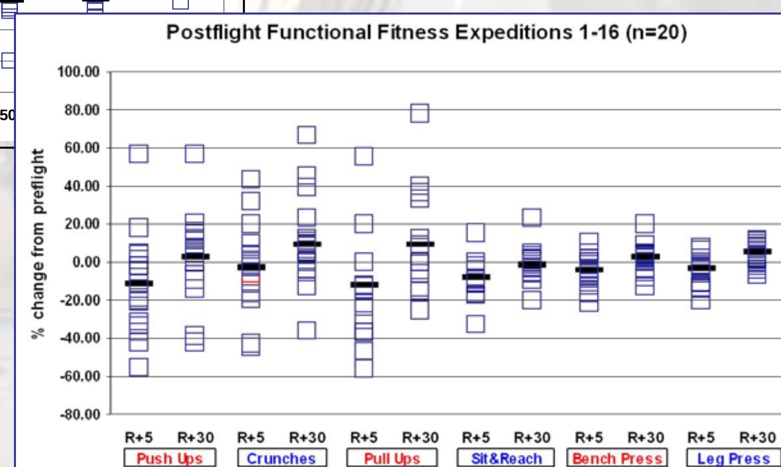
$Loss_0$=7.7% Recovery Half-life=97 d











Data can be used to assess the individual or the population

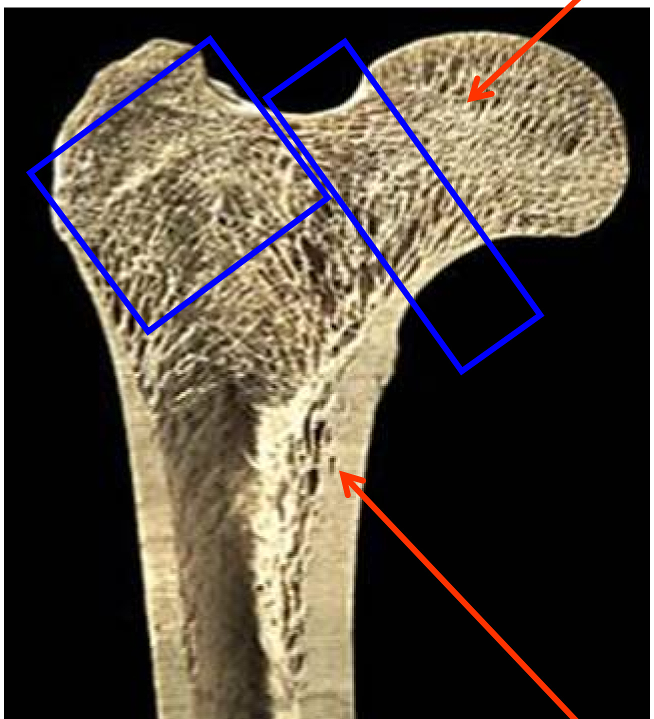
Bone compartments or bone types

Cancellous “Spongy” Bone/Trabecular Bone

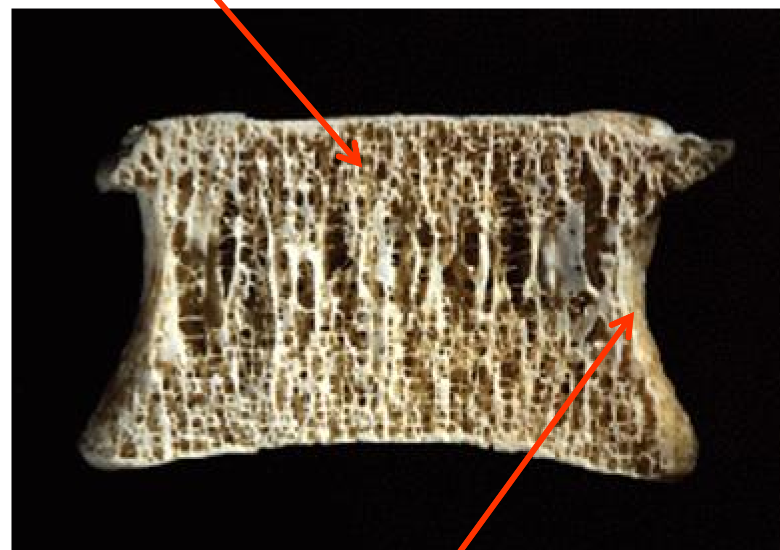
PROXIMAL FEMUR

Trochanter

Femoral Neck



VERTEBRAL BODY

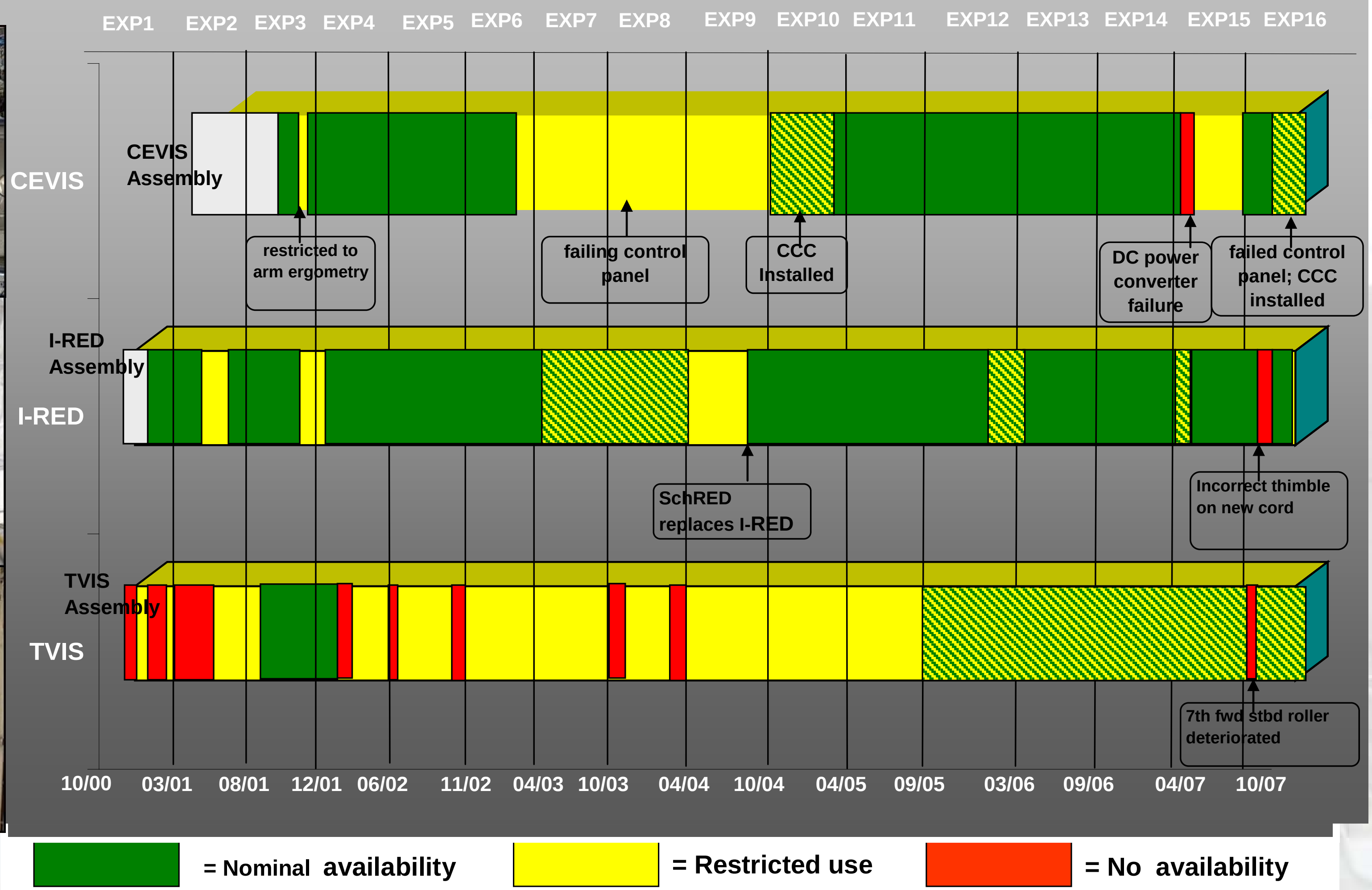


Cortical Bone/ “Compact Bone”

An example of a spaceflight adaptation that is well described but still lacks understanding of time course, recovery, and long term risk

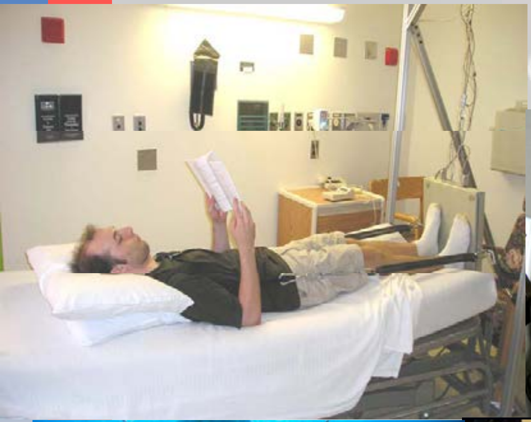
Sources: L. Mosekilde; SL Bonnick; P Crompton

ISS Exercise Hardware Availability Timeline



Countermeasures

Research





Operational



A consequence of human spaceflight

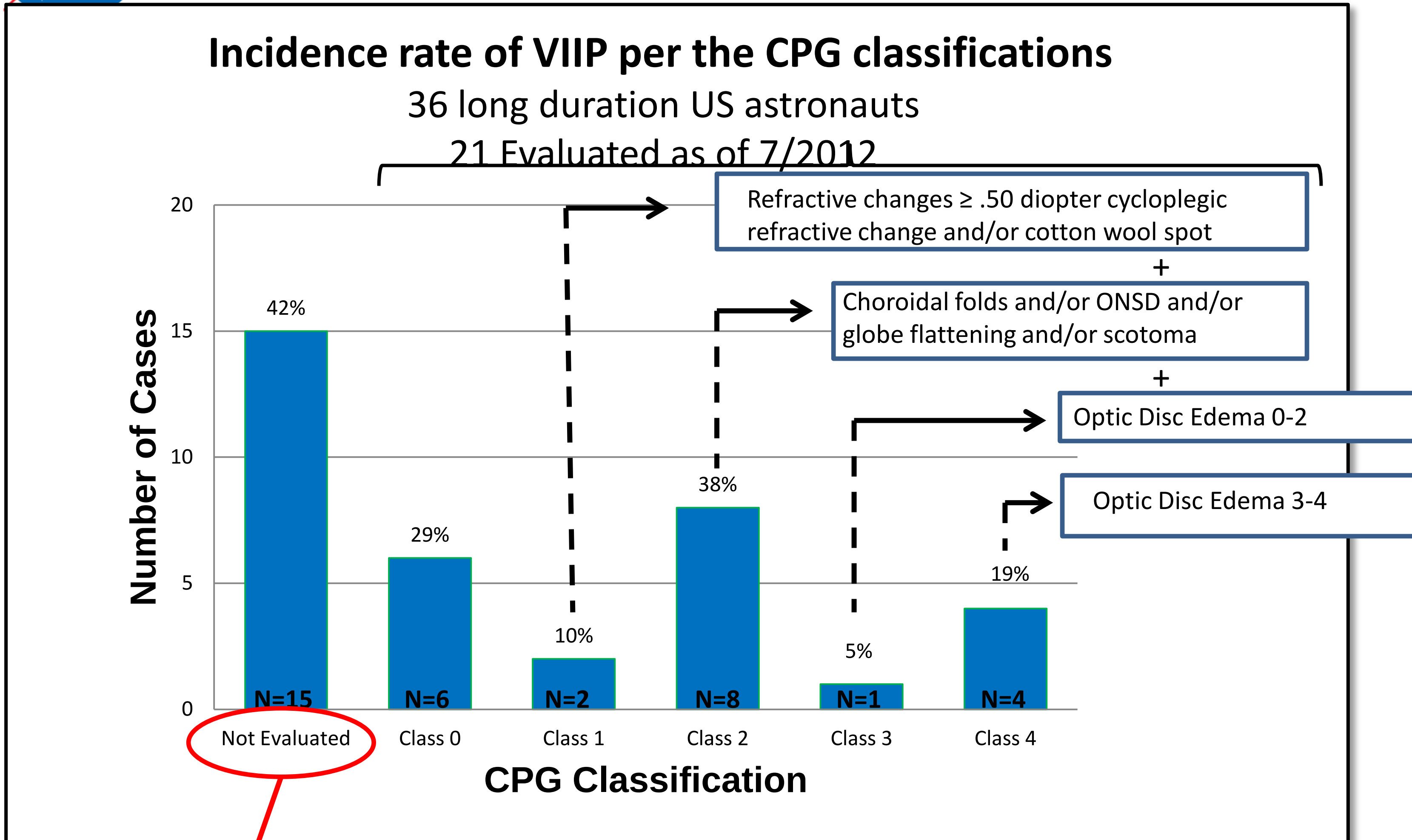
- Visual Impairment and Intracranial Pressure (VIIP)
- **What is the problem?**
  - Optic Disc Edema, Globe Flattening, Choroidal Folds, Hyperopic Shifts and Raised Intracranial Pressure has occurred in Astronauts During and After Long Duration Space Flight
- **What is the risk?**
  - Given that all astronauts experience a microgravity-induced cephalad fluid shift and that both symptomatic and asymptomatic individuals have exhibited optic nerve sheath edema on MRI, there is a high probability that all astronauts have some degree of idiopathic intracranial hypertension. Those that are susceptible (due to eye architecture, anatomy, narrow disc, etc.) have a high likelihood of developing either choroidal folds or papilledema, and the degree of edema will determine impairment and long-term or permanent vision loss.

A consequence of human spaceflight

- Visual Impairment and Intracranial Pressure (VIIP)
  - Operational processes (medical requirement) put in place to diagnose and manage 2008 (fundoscope and eye ultrasound)
  - Sentinel case found retrospectively (2005; Exp 11)
  - Integrated approach kicked off to address the issue: 2010
  - Research and Clinical Advisory Panel formulated in 2011
  - Occupational Health Research Protocol developed 2012
  - 9 Studies funded in 2012

Vision Impairment & Intracranial Pressure Risk Update

Incidence Rate



These crewmembers did not have MRIs, OCTs or cycloplegic refraction – NASA is in the process of obtaining this information/evaluation

21 crew members have been evaluated
15 have symptoms – 15/21 = 71%
Class 3 and 4 – 5/21 = 24%

VIIP: A Three-Part Story

1. The Vascular System

Demographic
- Gender
- Age
- Race

Body Composition
- Height
- Weight
- % Lean Body Mass
- %Fat Body Mass

Cardiac
- Resting Blood pressure
- Resting Cardiac output

Biochemistry
- Homocysteine
- Lipids (LDL, HDL, TGs)
- Serum Insulin
- HbA1c
- Fasting serum glucose

Fitness
- MVO2 (max oxygen uptake)

+

2. The Brain

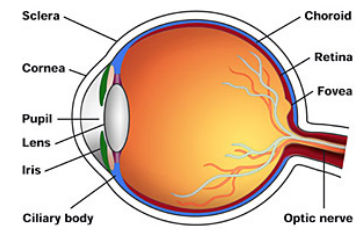
MRI Intracranial (Pre/Post)
- Peak CSF flow
- CSF Production
- Glove Flattening
- Globe Axial Length
- Optic Nerve Tortuosity

Ultrasound (Pre/In/Post)
- ONSD
- Nerve/Sheath Ratio

Environmental
- CO2 Levels

+

3. The Eye



Intraocular pressure

Corneal Thickness

Visual acuity (Pre/In/Post)

Refractive error (Pre/Post)

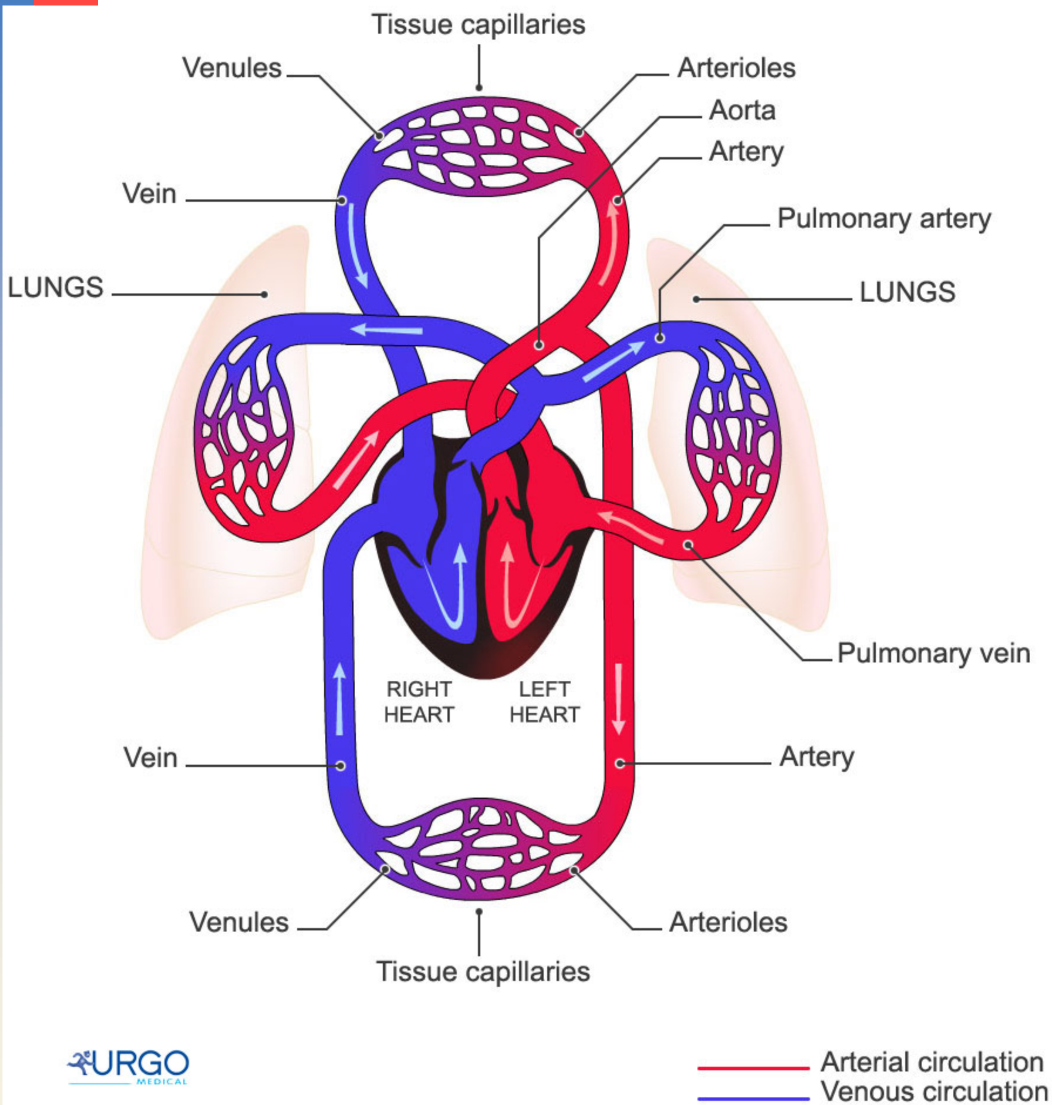
Optic Disc:Cup ratio (Pre/Post)

OCT (Pre/Post)
- RNFL
- RPE angle
- Optic nerve head
- Choroidal Folds

High Res Retinal Photography
- Retinal hemorrhages
- Cotton wool spots

Optical Biometry (Pre/Post)
- Globe axial length

Cardiovascular Physiology Background



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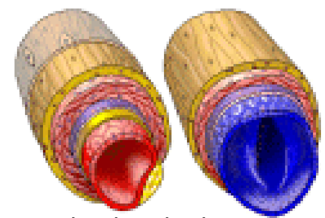
Blood Vessel Compliance $C = \frac{\Delta V}{\Delta P}$



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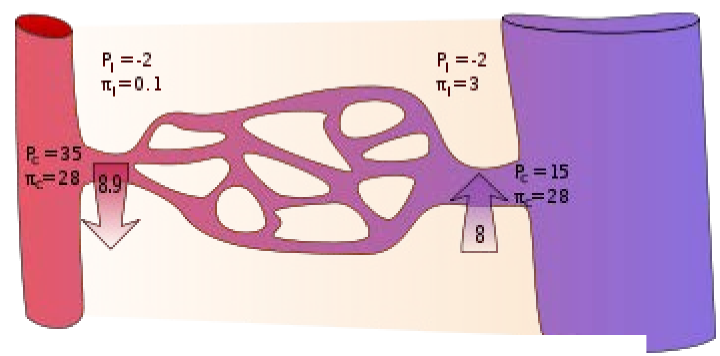
Venous compliance is approximately 30 times larger than arterial compliance

Starling Equation:
hydrostatic and oncotic forces (the so-called **Starling forces**) in the movement of fluid across capillary membranes



The Starling equation reads as follows:

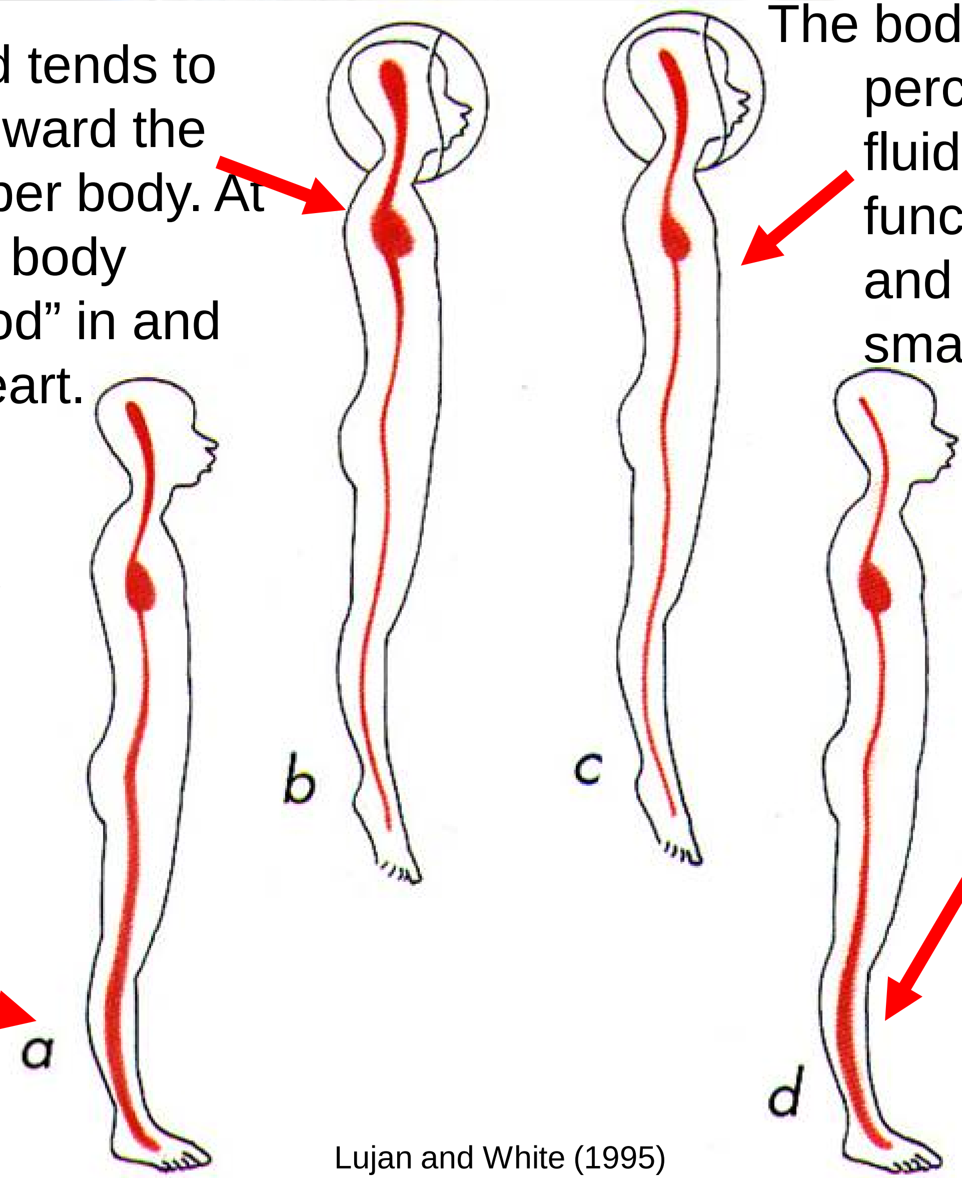
$$J_v = K_f([P_c - P_i] - \sigma[\pi_c - \pi_i])$$

http://en.wikipedia.org/wiki/Starling_equation#cite_note-1

Fluid Shifts during Space Flight

In space, the fluid tends to redistribute toward the chest and upper body. At this point, the body detects a "flood" in and around the heart.

On Earth, gravity exerts a downward force to keep fluids flowing to the lower body.



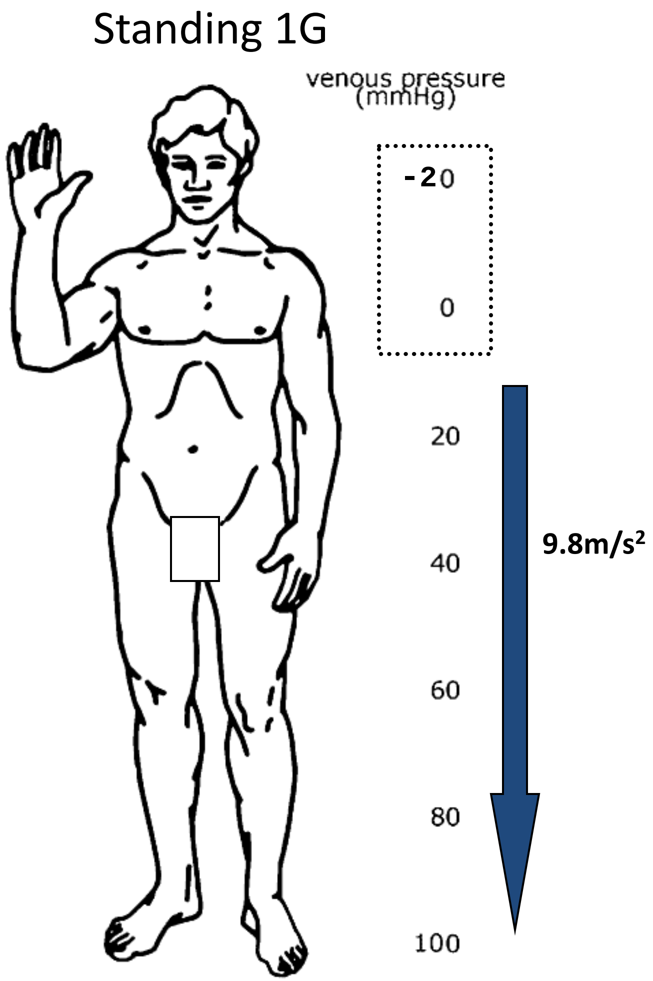
Lujan and White (1995)

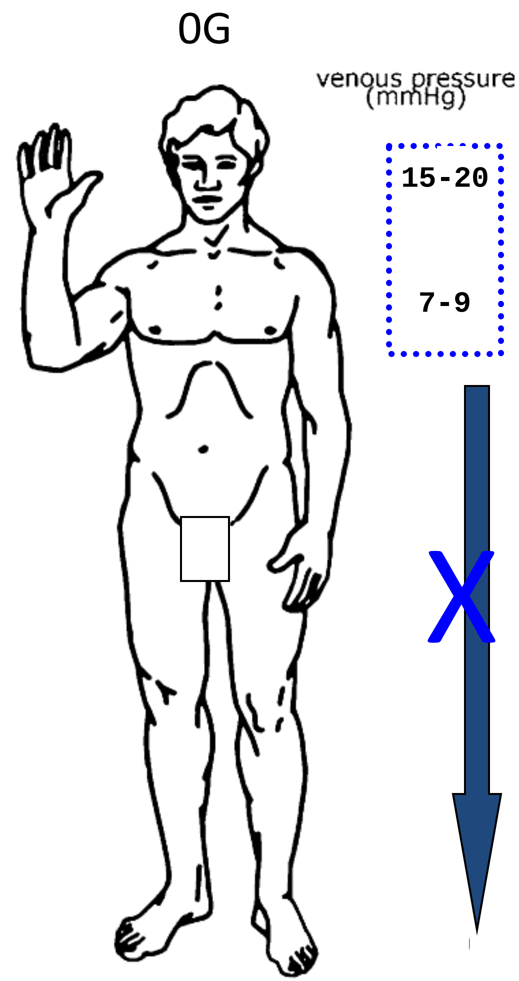
The body rids itself of this perceived "excess" fluid. The body functions with less fluid and the heart becomes smaller.

Upon return to Earth, gravity again pulls the fluid downward, but there is not enough fluid to function normally on Earth.

Lujan and White (1995)

Redistribution of Venous Pressures From 1G to 0G





- Cranium is rigid
- Venous congestion
- Obligate arterial flow
- Transcapillary leak
- ++ICP~30-40

1. Hirvonen et al. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laproscopic hysterectomy, Acta Anaesthesiologica Scandiavica. 1995
2. Hinghofer-Szalkay Gravity, the hydrostatic indifference concept and the cardiovascular system. European Journal of Applied Physiology, 2010
3. Chapman et al. The Relationship between Ventricular Fluid Pressure and Body Position in Normal Subjects with Shunts. *Neurosurgery* 1990
4. Gisolf et al. Human cerebral outflow pathway depends on posture and central venous pressure. Journal of Physiology, 2004.

Integrated Vision Impairment & Intracranial Pressure Project

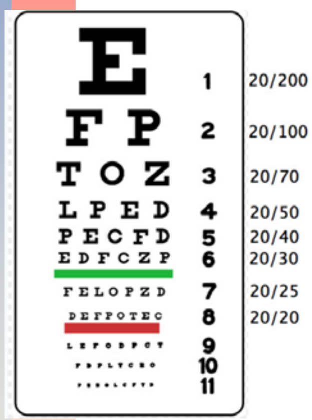
Risk Background - Symptoms

Background:

- 15 known “clinical cases” (of 36 long duration crew members)
  - Each with different degrees of symptoms
  - Does not currently include data from international partners
  - Current assessment of Russian participation underway

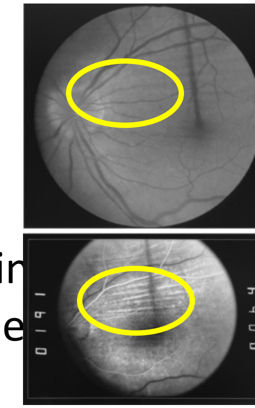
•Hyperopic Shifts

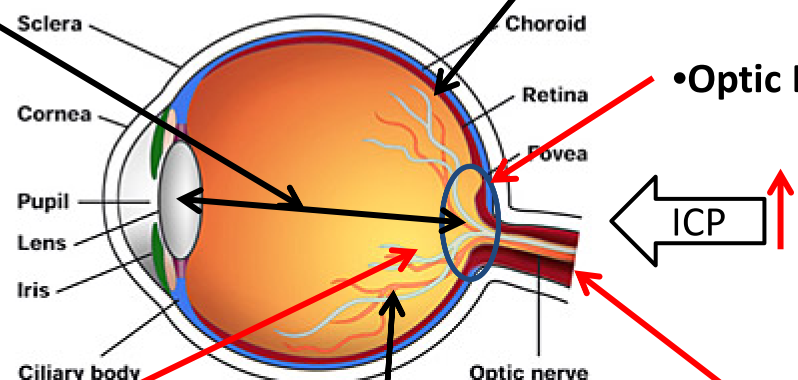
-Up to +1.75 diopters



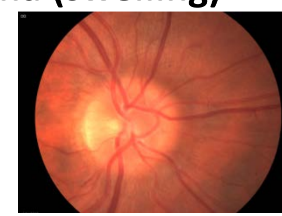
•Choroidal Folds

parallel grooves in the posterior pole

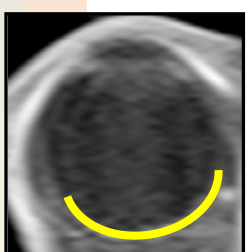




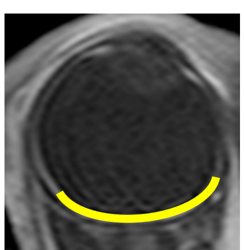
•Optic Disc Edema (swelling)



•Globe Flattening



Normal Globe



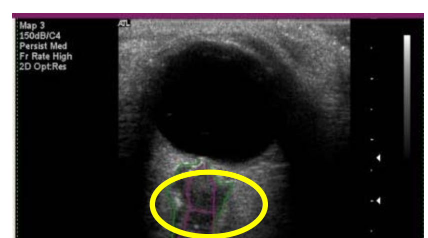
Flattened Globe

MRI Orbital Image showing globe flattening

•Altered Blood flow

“cotton wool” spots

•Increased Optic Nerve Sheath Diameter

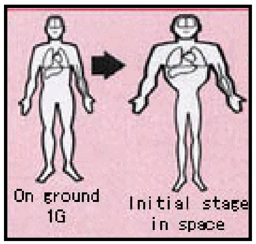


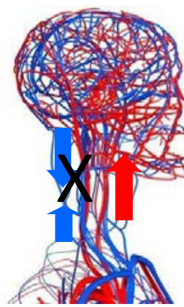
•Scotoma

Altered/Disrupted Visual Field

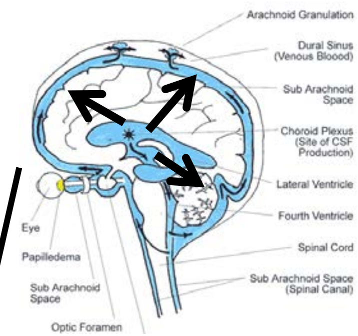
Current Hypothesis

1. Fluid Shift due to Microgravity

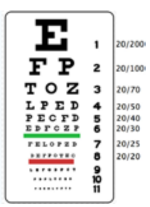




2. Fluid shift causes increased intracranial pressure (ICP) (?)

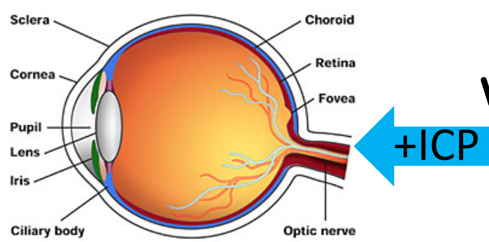


3. ICP transmitted to optic nerve and eye

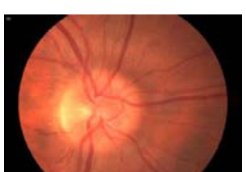


•**Hyperopic Shifts**

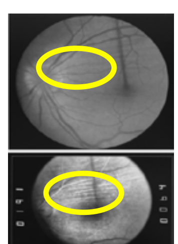
-Up to +1.75 diopters



•**Optic Disc Edema (swelling)**

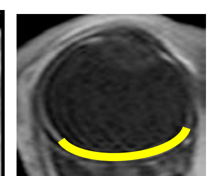


•**Choroidal Folds** parallel grooves in the posterior pole



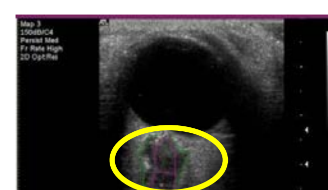
•**Globe Flattening**

Normal Globe



Flatten Globe

•**Increased Optic Nerve Sheath Diameter**



Potential for Serious Functional Impairment:

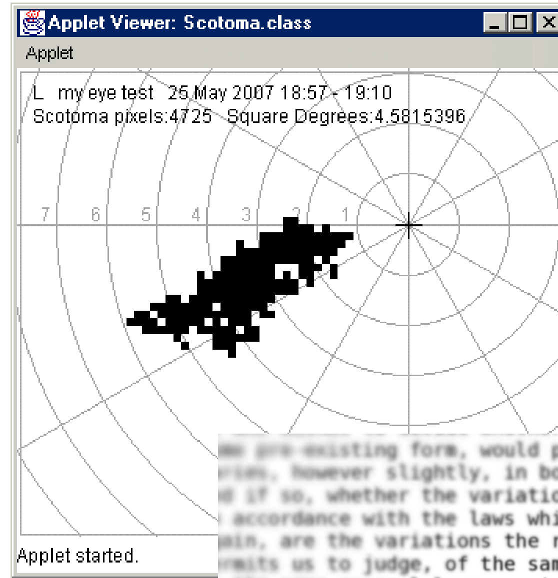
Hyperopia

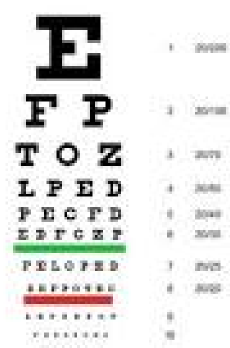
Hyperopia, or farsightedness, is a condition of the eye where incoming rays of light impinge on the retina before converging into a focused image, resulting in difficulty seeing nearby objects clearly.
(Illustration by Electronic Illustrators Group.)

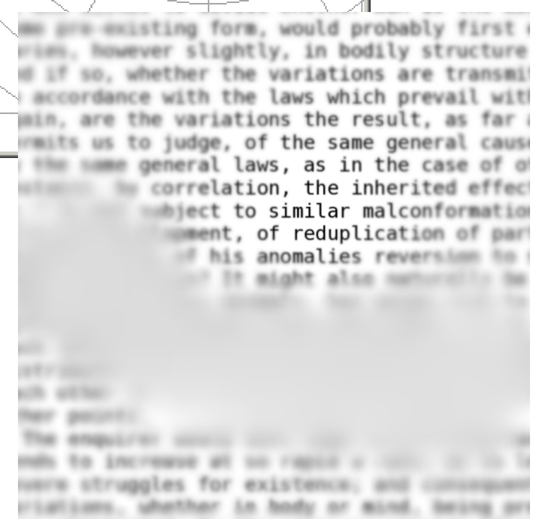
Image can be located at :
http://medical-dictionary.thefreedictionary.com/hyperopia

Changes in visual acuity are assessed with regular vision testing on orbit

Scotoma







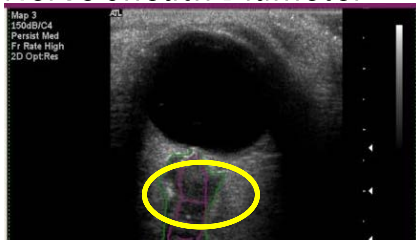
VIIP- Hardware
On –Orbit Ocular Measures

•Ultrasound is used to track optic nerve sheath diameter and globe flattening pre-, in-, and post flight

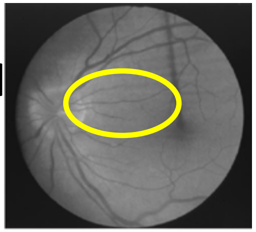
•Current fundoscope (PanOptic) can not detect choroidal folds

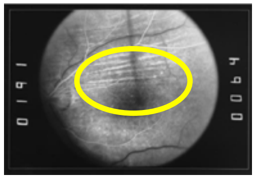
•New Hardware:
- •Fundoscope with better resolution (ISS CR Approved June 2012)
  - •Will give qualitative data
- •Optical Coherence Tomography (OCT)
  - •Will give quantitative data: progression of choroidal folds and nerve fiber layer changes

Increased Optic Nerve Sheath Diameter

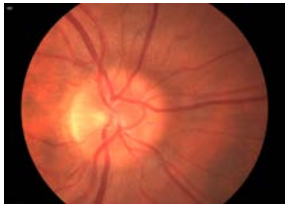


Choroidal Folds - parallel grooves in the back of the eye

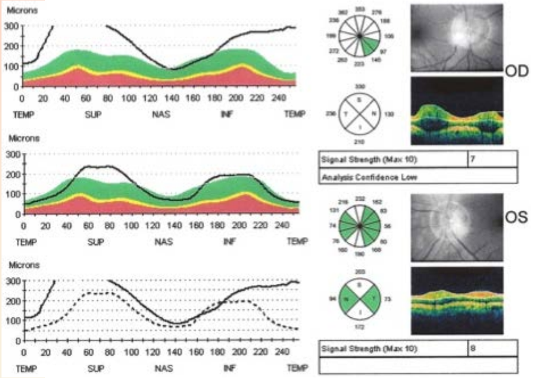


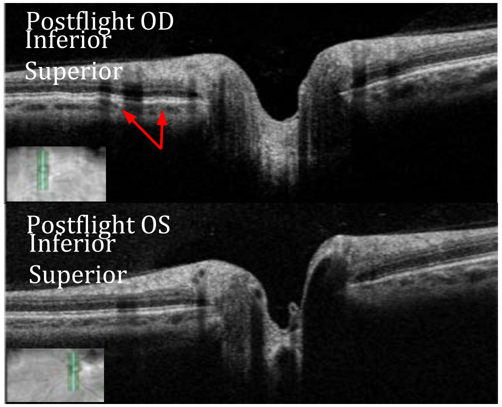


Optic Disc Edema



Altered Blood flow
"cotton wool" spots





Optical Coherence Tomography (OCT) measures

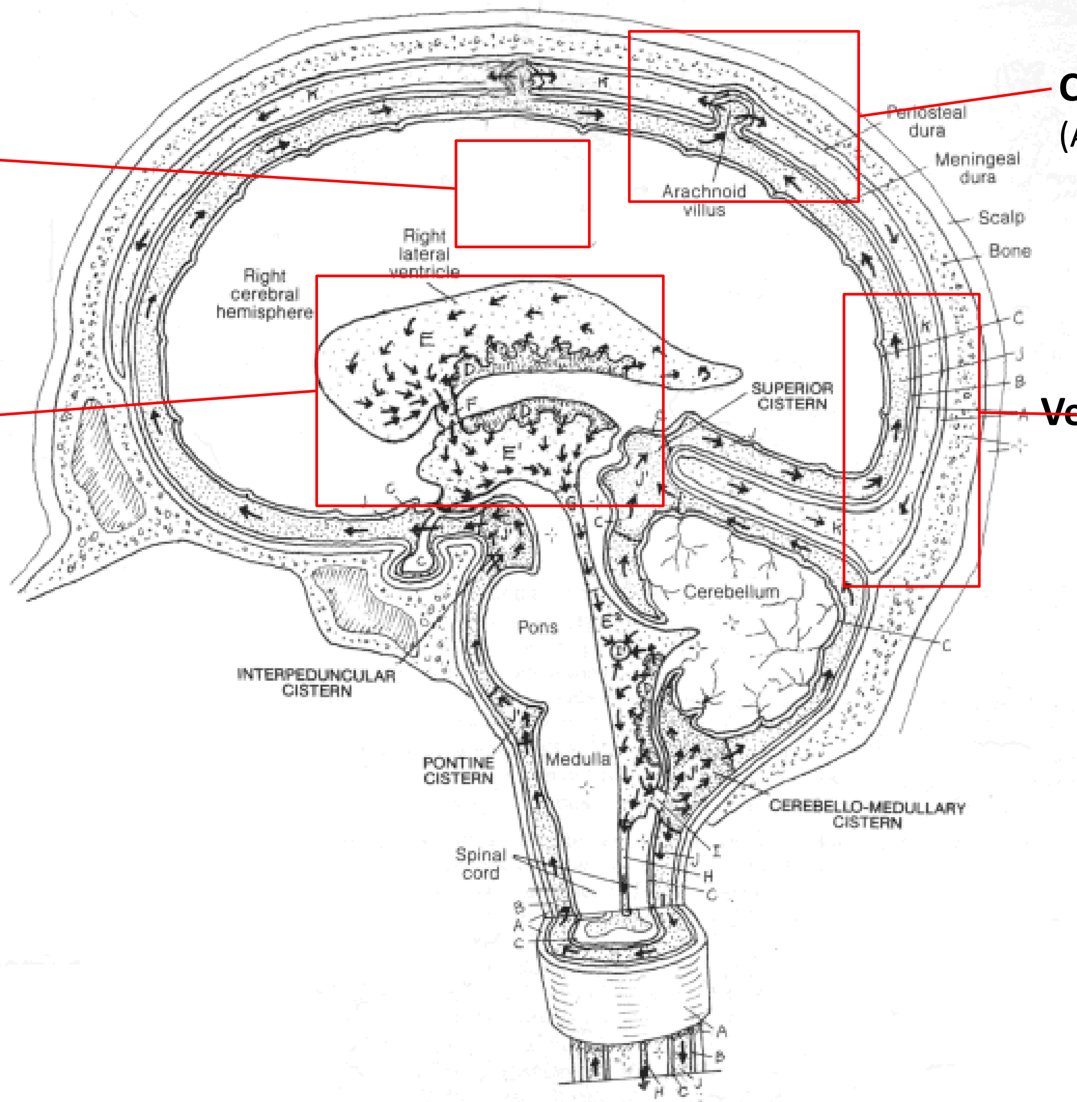
Key Brain Areas Potentially Affected by Fluid Shift

Interstitial fluid

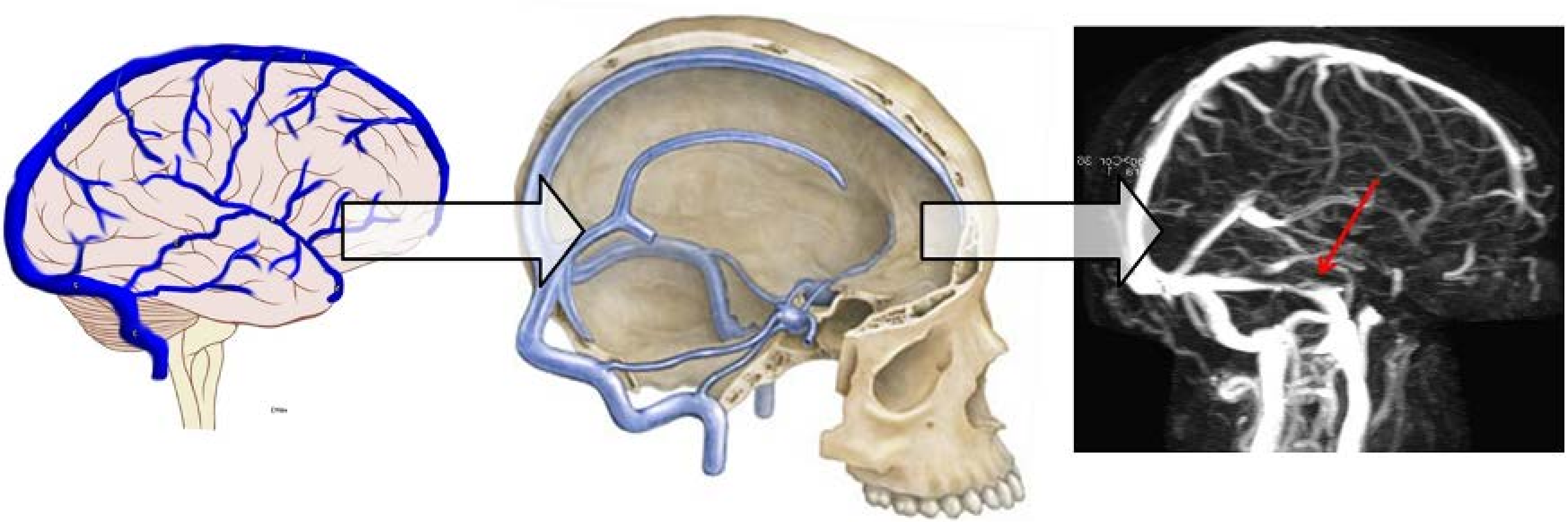
CSF Production

CSF Resorbtion
(AG-Venous/Lymphatic)

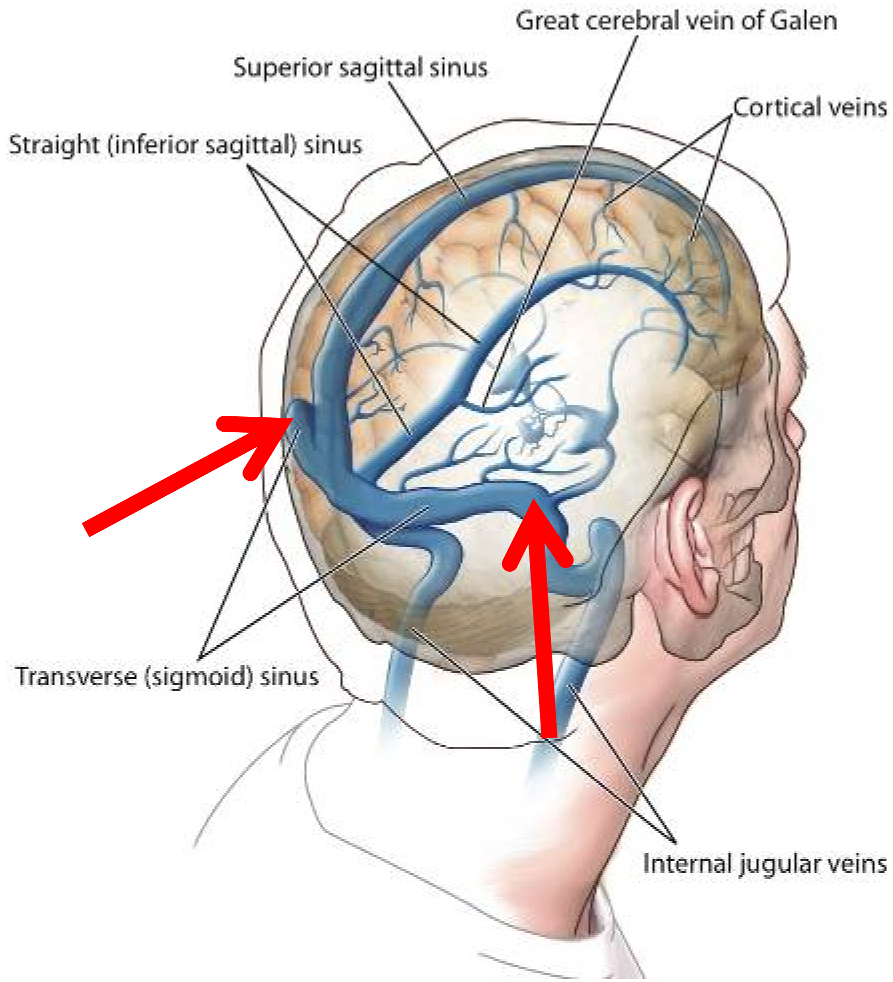
Venous Congestion



The Brain is an Expansile Vascular Organ Within a Rigid Cranium: An swollen brain can impair blood flow to itself



Expanding Brain Parenchyma & Cerebellum Compresses Transverse Sinus



Vision Impairment & Intracranial Pressure Risk Update

Case Definition for Spaceflight-Induced Intracranial Hypertension

Least Severe Symptoms

Class 0

- < .50 diopter cycloplegic refractive change
- No evidence of papilledema, nerve sheath distention, choroidal folds, globe flattening, scotoma or cotton wool spots compared to baseline.

Class 1

- Refractive changes ≥ .50 diopter cycloplegic refractive change and/or cotton wool spot
- No evidence of papilledema, nerve sheath distention, choroidal folds, globe flattening, scotoma compared to baseline.
- CSF opening pressure (if measured) ≤ 25 cmH2O

Treatment: repeat OCT & visual acuity in 6 weeks

Class 2

- Class 1 plus:
- Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma
- No evidence of papilledema
- CSF opening pressure ≤ 25 cm H2O (if measured)

Treatment: Repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every 4 -6 weeks x 6 months, repeat MRI in 6 months

Most Severe Symptoms

Class 3

- Class 2 plus:
- Papilledema of Grade 0-2.

Treatment: repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every 4 -6 weeks x 6 months, repeat MRI in 6 months

Class 4

- Class 3 plus:
- Papilledema Grade 2 or above.
- Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations
- CSF opening pressure >25 cm H2O

Institute treatment protocol as per CPG – LP, repeat MRIs, pharmaceutical intervention

Integrated Pre/In/Post-Flight VIIP Medical and Research Testing

Preflight Exams | In-flight Exams | Post flight Exams

L-365 | L-90/45 | L+10 | L+30 | L+60 | L+100 | R-30 | R+1 to R+3 | R+30 | R+90 | R+180 | R+365

New Research Protocol

Acceptable up to L-365 days

MRI
Of Brain and Orbits Without Contrast

L-90/45 days

Ultrasound
Eye/Orbit

Fundoscopy -
PanOptic Ophthalmoscope

Tonometry

Visual Acuity
Including Amsler Grid Testing

Other Tests -
biomicroscopy (slit lamp), high resolution retinal photography, OCT (high resolution), and A-Scan.

L+30 & R-30,
L+100 <u>if requested</u>
(+/- 7 days) &
as clinically indicated

Ultrasound
Eye/Orbit

Fundoscopy -
PanOptic Ophthalmoscope

Tonometry

Visual Acuity
Including Amsler Grid Testing

L+10, 30, 60, 100
& R-30,
(+/- 7 days)

Ultrasound
Eye/Orbit

Fundoscopy -
PanOptic Ophthalmoscope

Tonometry

Visual Acuity
Including Amsler Grid Testing

Blood Pressure

Vascular Compliance

R+1 to R+3
(or as soon as possible) <u>30, 90, 180, 365</u>

MRI
Of Brain and Orbits Without Contrast

Ultrasound
Eye/Orbit

Fundoscopy -
PanOptic Ophthalmoscope

Tonometry

Visual Acuity
Including Amsler Grid Testing

Other Tests -
biomicroscopy (slit lamp), high resolution retinal photography, OCT (high resolution), and A-Scan.

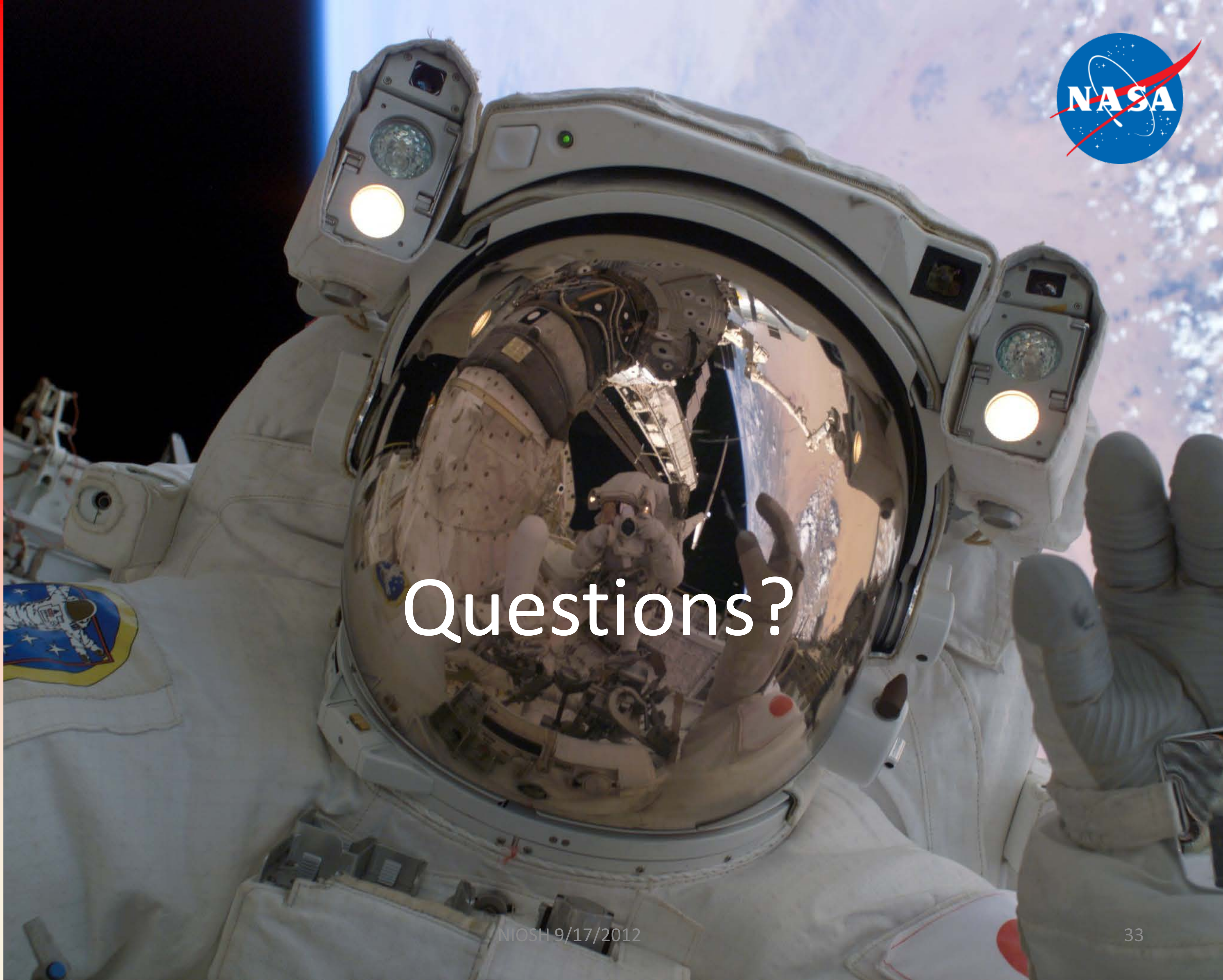
Vascular Compliance

Research

Medical Ops

Clinical Implications

- Potential disability secondary to vision loss in astronauts susceptible to optic disc edema or choroidal folds
- Potential for long-term sequelae due to optic nerve cells ischemia (visual field defect or loss)
- Potential effect on white matter (senility, dementia, etc.)
- Decreased functional ability due to IIH
- Unknown contribution to space motion sickness, asthenia, or functional impairments
- Potential to worsen with repetitive flights or long term space missions



Questions?