Informational Briefing:

Risk of Microgravity-Induced Visual Impairment and Elevated Intracranial Pressure (VIIP)

Wednesday May 25, 2011.

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Outline

- Background
- Ocular Findings
- Cephalad Fluid Shift
- Current Assessment Methodologies
- Cases
- Contributing Structures of the Eye
- CSF Production
- CSF Resorption
- Exacerbating Factors
- Current Measures
- Draft Research Plan
- Opportunities for Partnership

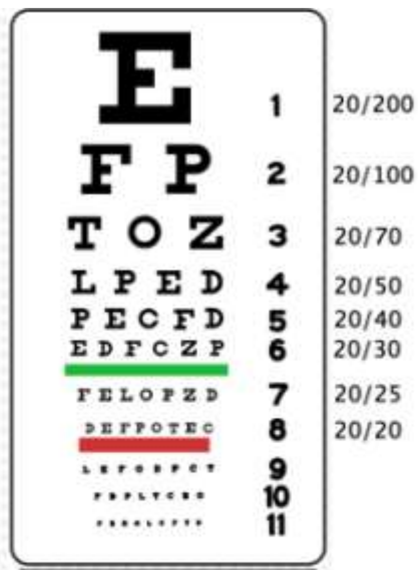
Background

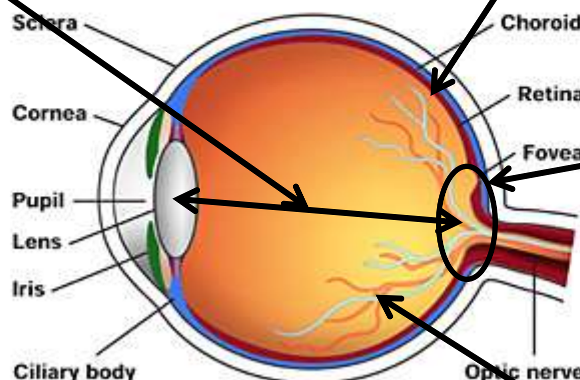
- Eight cases identified, represent 23.5% of the 34 crewmembers flown on the ISS, with inflight visual changes and pre-to-postflight refractive changes. In some cases, the changes were transient while in others they are persistent with varying degrees of visual impairment.
  - Decreased intraocular pressure (IOP) postflight was observed in 3 cases.
  - Fundoscopic exams revealed postflight findings of choroidal folds in 4 cases, optic disc edema in 5 cases and presence of cotton wool spots in 3 cases.
  - Optical coherence tomography (OCT) confirmed findings of choroidal folds and disc edema and documented retinal nerve fiber layer thickening (4 cases).
  - Findings from MRI examinations showed posterior globe flattening (5 cases) and optic nerve sheath distension (6 cases).
  - Opening cerebrospinal fluid (CSF) pressure was elevated in 4 cases postflight reflecting raised intracranial pressure.
- While the etiology remains unknown, hypotheses speculate that venous insufficiency or hypertension in the brain caused by cephalad fluid shifts during spaceflight are possible mechanisms for ocular changes in astronauts.

Risk Background - Ocular Symptoms

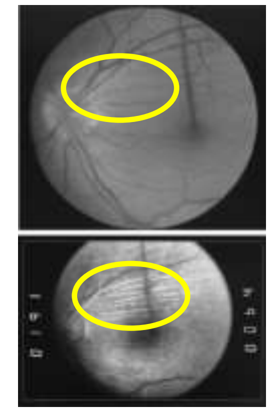
- 8 cases identified (23.5% of 34 long duration crew) with inflight visual changes and pre-to-postflight refractive changes.
  - Elevated Intracranial Pressure measured postflight

Hyperopic Shifts
Up to +1.75 diopters



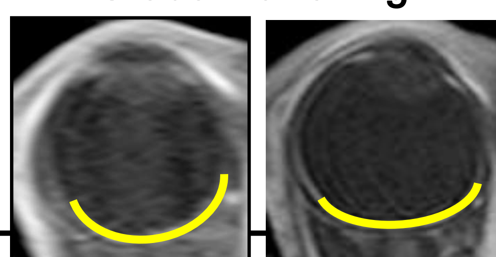


Choroidal Folds
parallel grooves in the posterior pole



Optic Disc Edema (swelling)

Globe Flattening

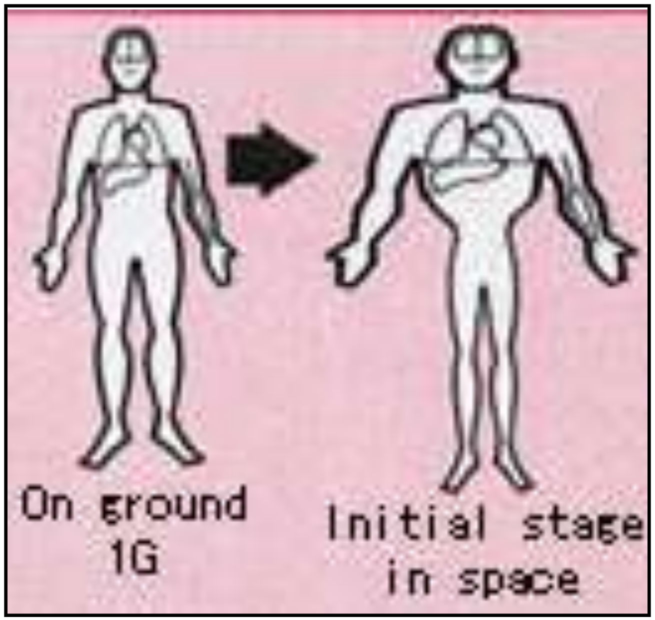


MRI Orbital Image showing globe flattening

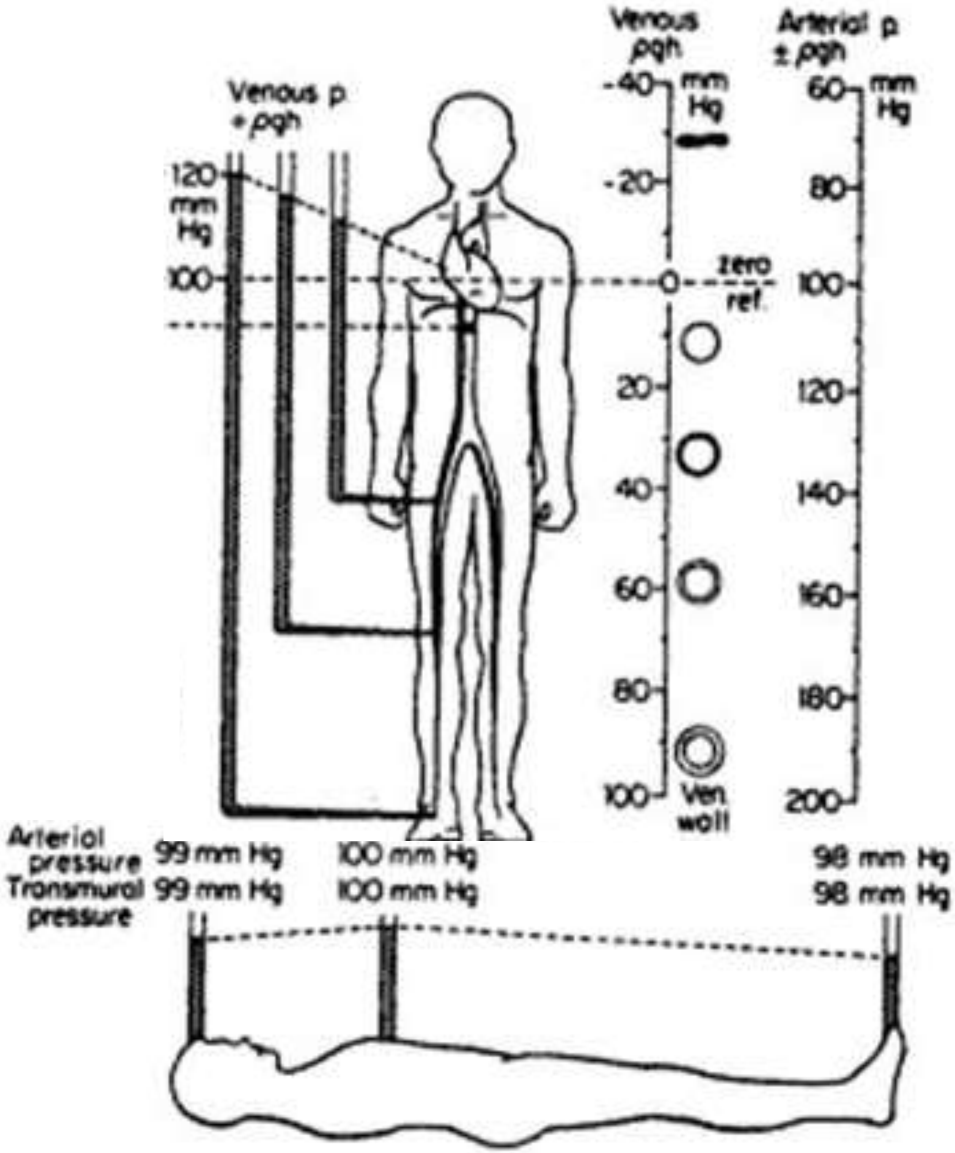
Normal   Flattened

Vision distortion
Cotton "wool" spots

Cephalad Fluid Shift



Hydrostatic Pressure Changes

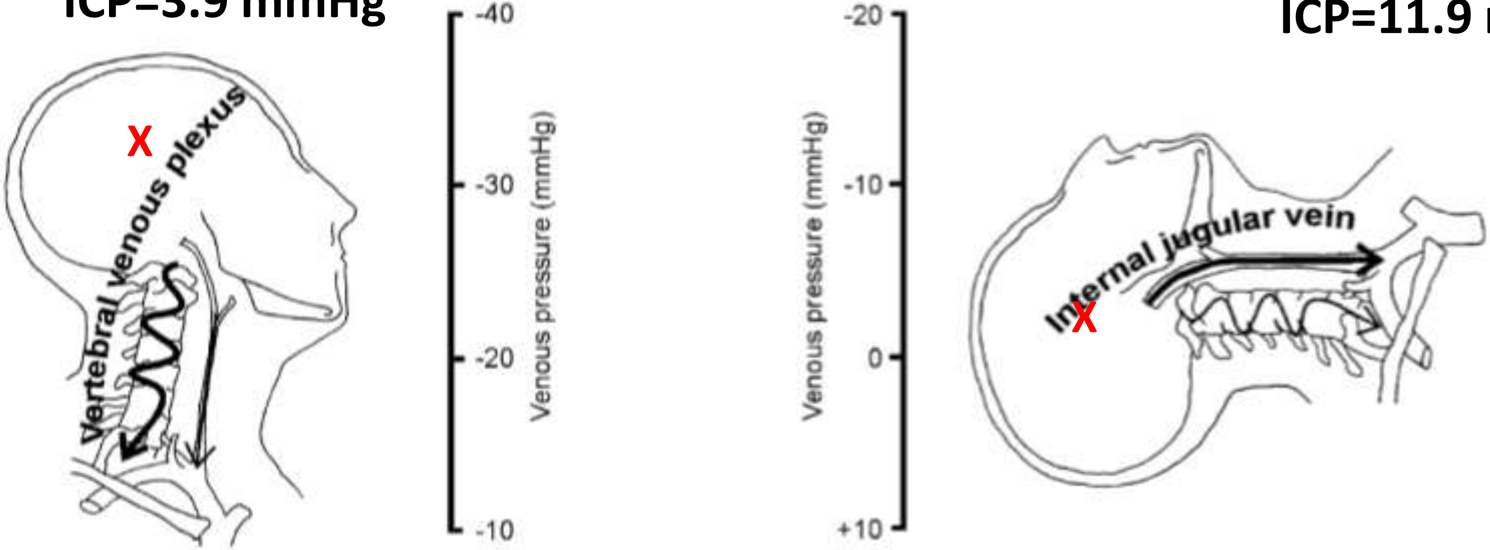


Rowell, 1988.

Venous Pressure & ICP Increases in Microgravity-Supine Model

ICP=3.9 mmHg

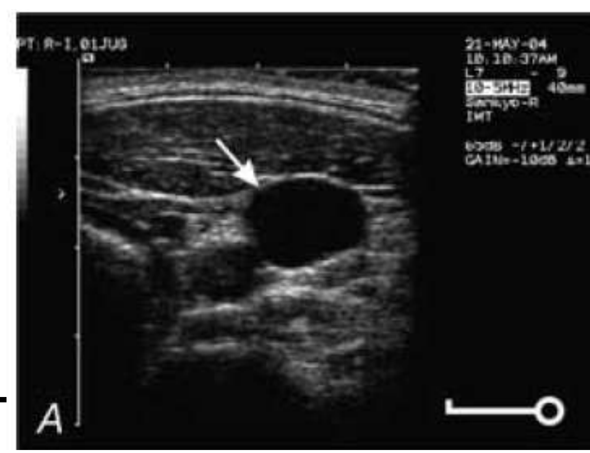
ICP=11.9 mmHg



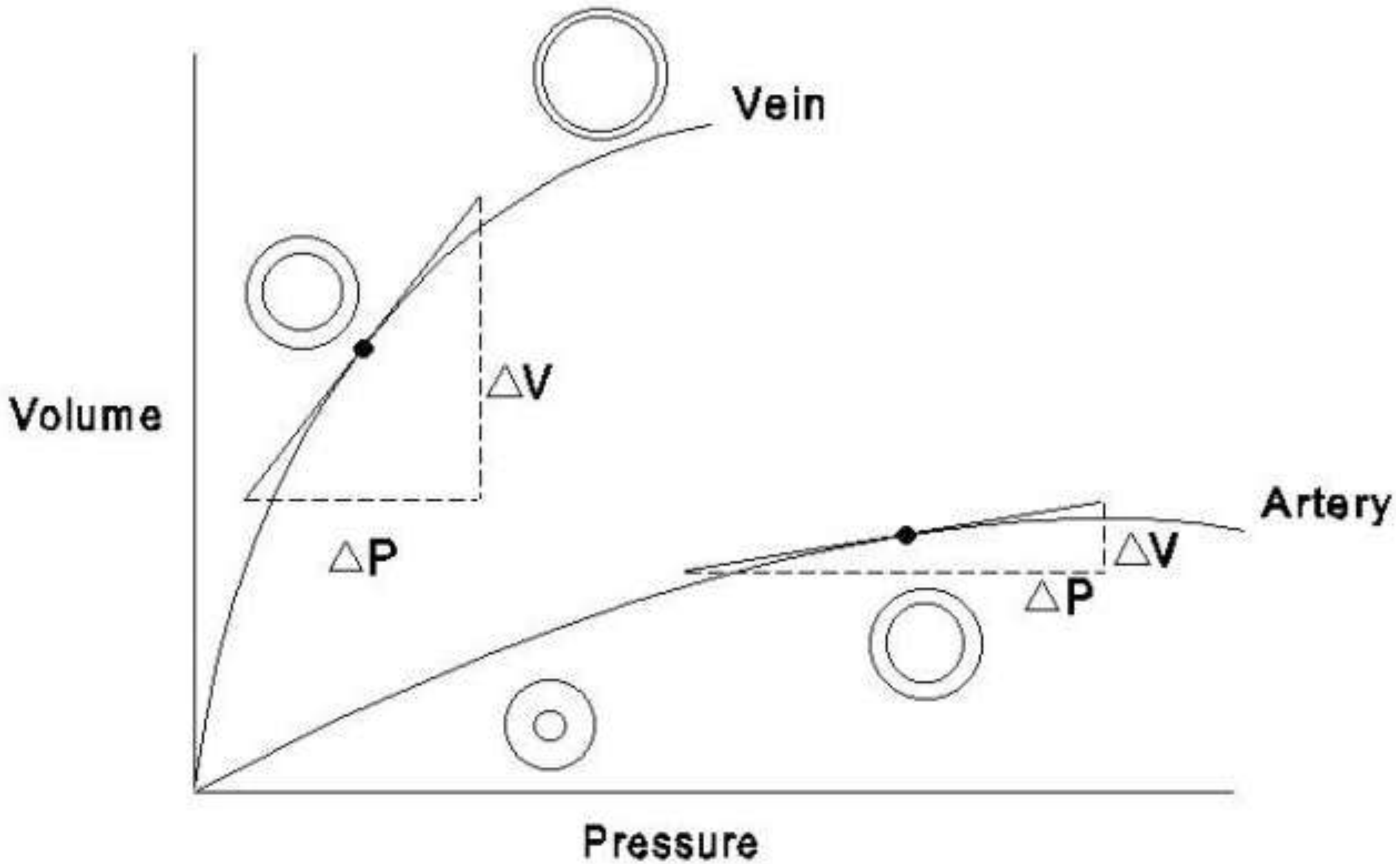
Standing

Internal Jugular
Vein Caliber

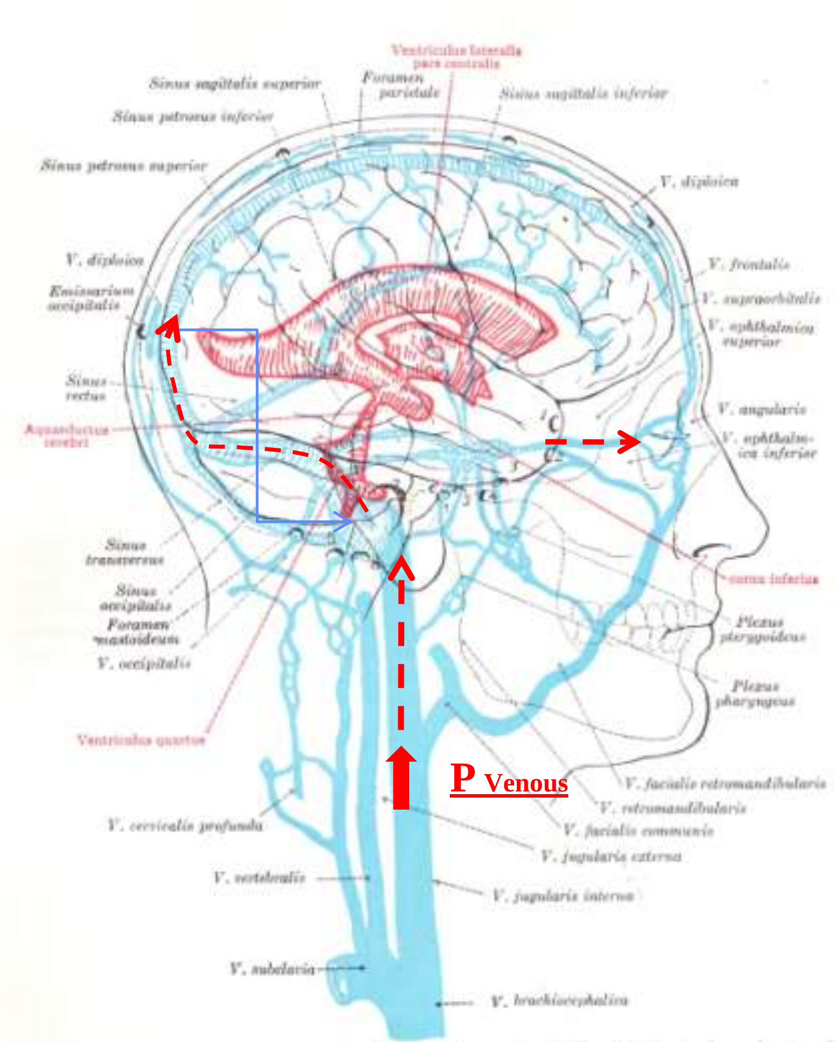
Supine



Increased Volume=Increased Pressure



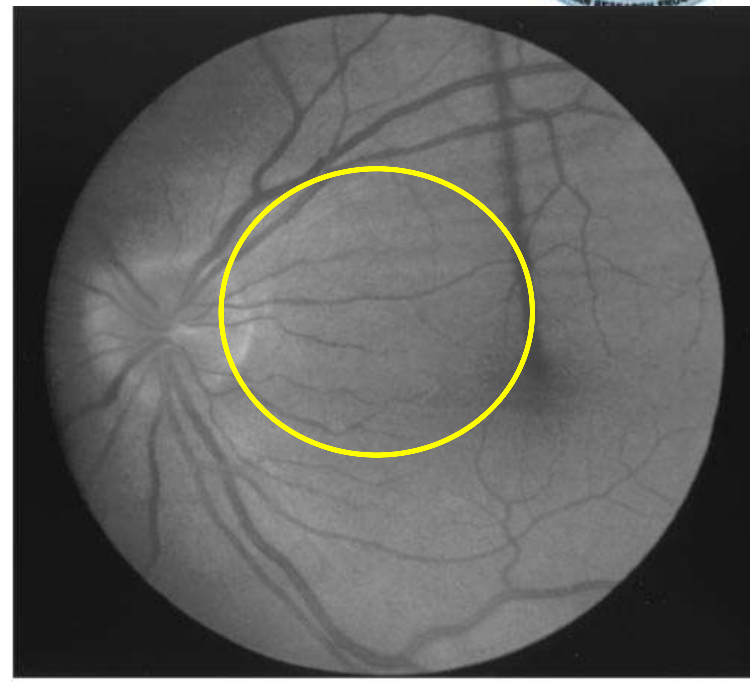
Risk Background – Intracranial Pressure

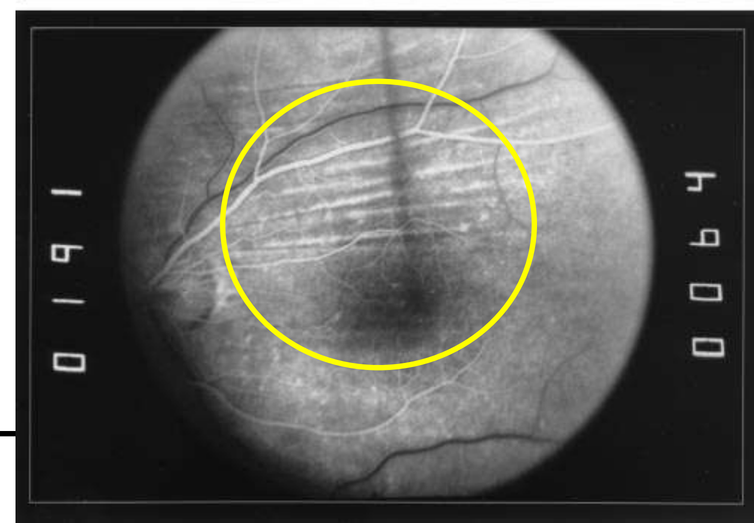


MRI Brain Venogram

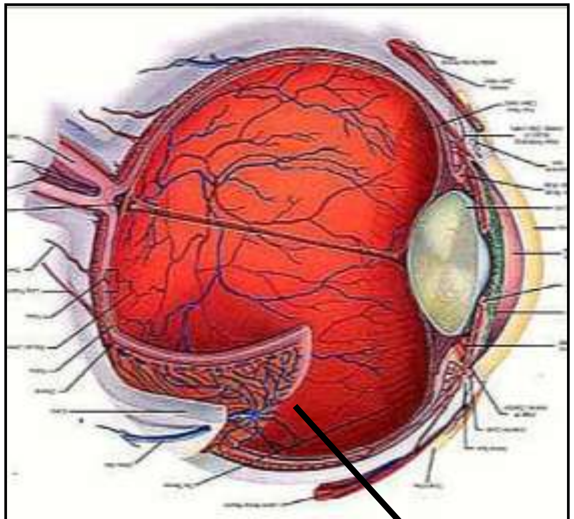
CHOROIDAL FOLDS

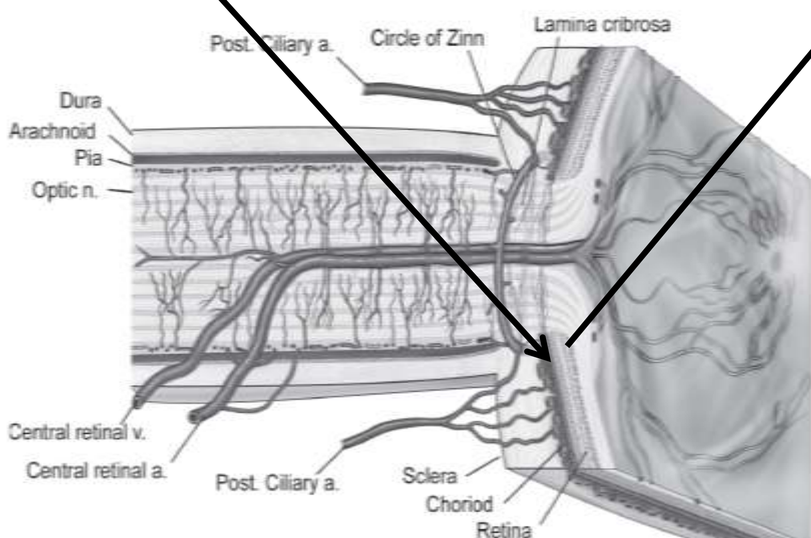
- Choroidal folds are parallel grooves or striae that involve the choroid in the posterior pole.
- They are usually horizontal but may be vertical, oblique, or irregular and are usually situated temporally, rarely extending beyond the equator.
- Their characteristic appearance on funduscopic examination, with the crests appearing yellow and less pigmented, is caused by the stretching and thinning of the retinal pigment epithelium, and the troughs appearing darker are caused by retinal pigment epithelium compression.
- Known causes of choroidal folds include orbital diseases or tumors, choroidal tumors, posterior scleritis, hypotony, chronic papilledema or optic nerve tumor, choroidal neovascular membrane, scleral buckle, and central serous

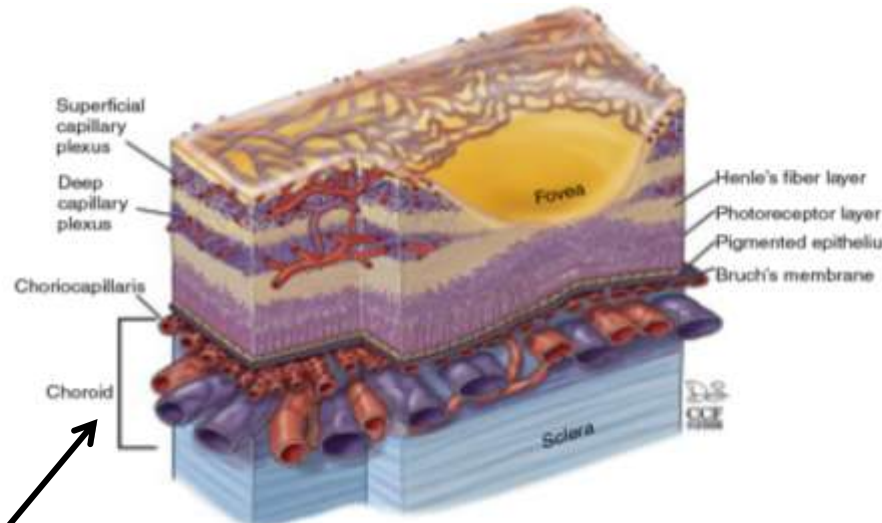




The Choroid

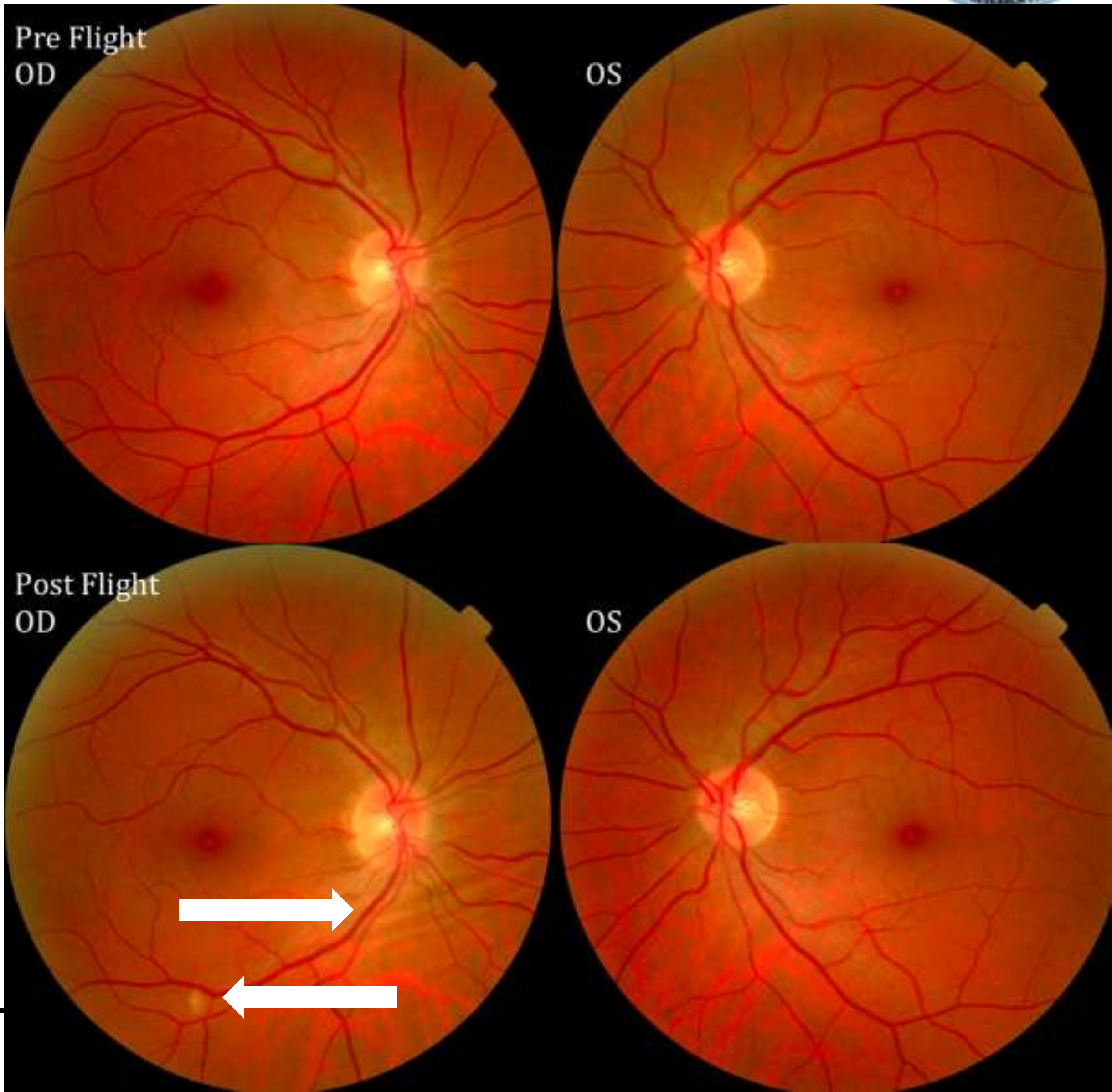






The choroid contains a dense vascular network terminating with the fenestrated choriocapillaris

Case Report 1: Pre & Post Flight Fundoscopy



[Top Pre Flight]

Fundoscopic images of the right and left posterior pole.

[Bottom Post Flight]

Fundoscopic images of the right and left posterior pole showing choroidal folds below the optic disc (top arrow) and a“ cotton--wool” spot (bottom arrow) in the inferior arcade in the right eye.

Optic disc imaging did not show presence of observable disc edema.

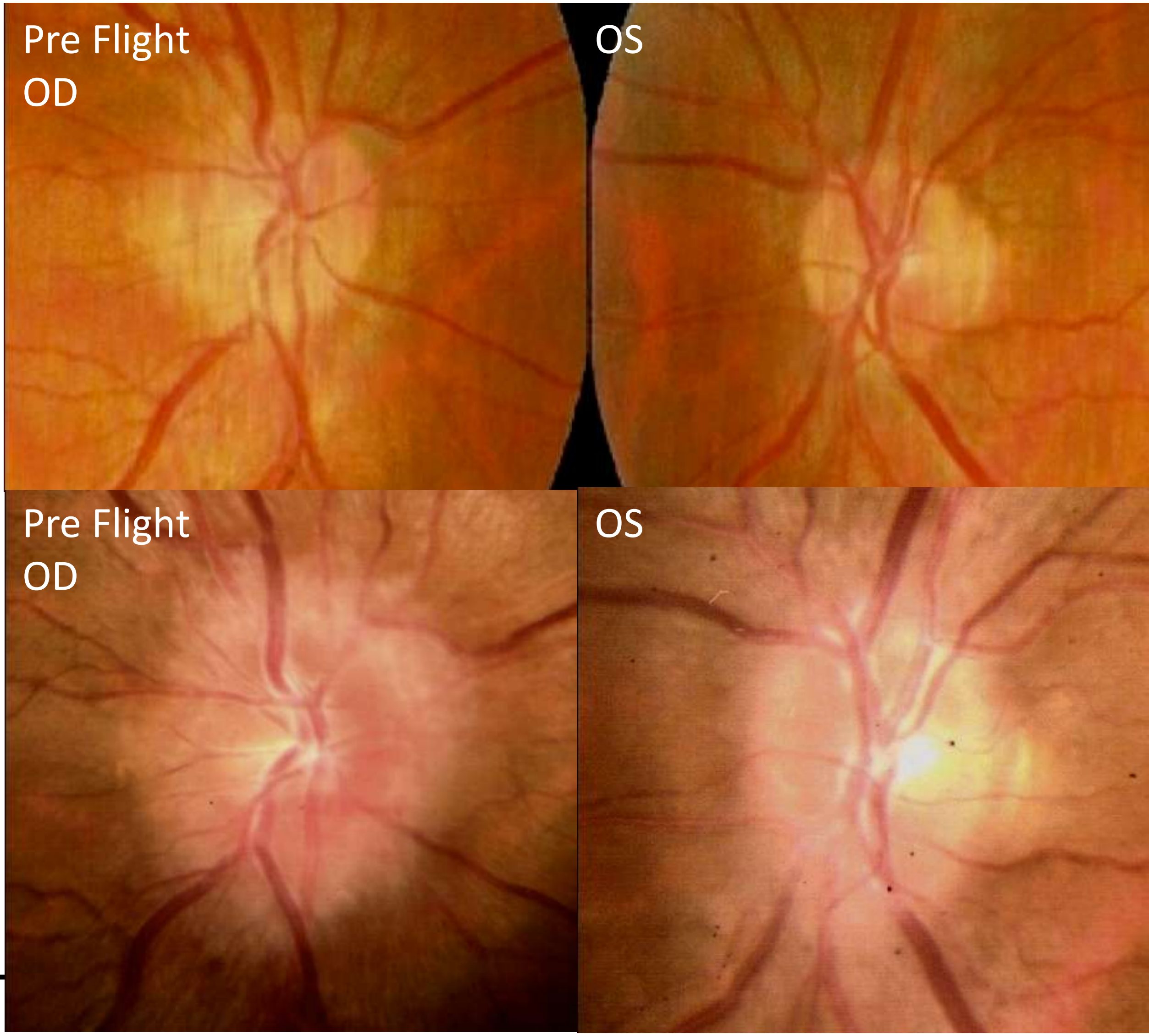
Case Report 3: Pre & Post Flight Fundoscopy

[Top Pre Flight]

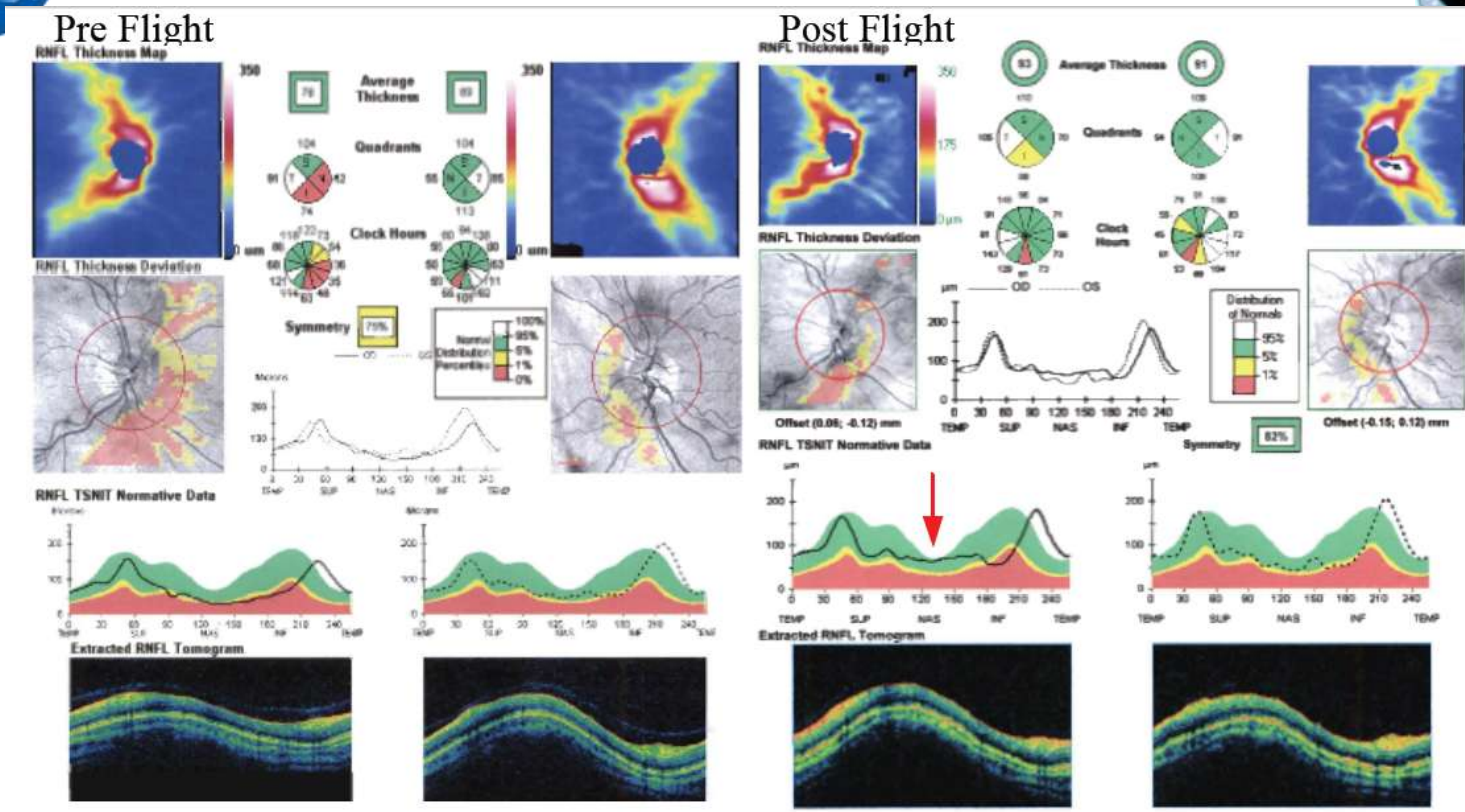
Fundoscopic images of the right and left optic disc.

[Bottom Post Flight]

Fundoscopic images of the right and left optic disc showing Grade 3 edema at the right optic disc and Grade 1 edema at the left optic disc. Fig.



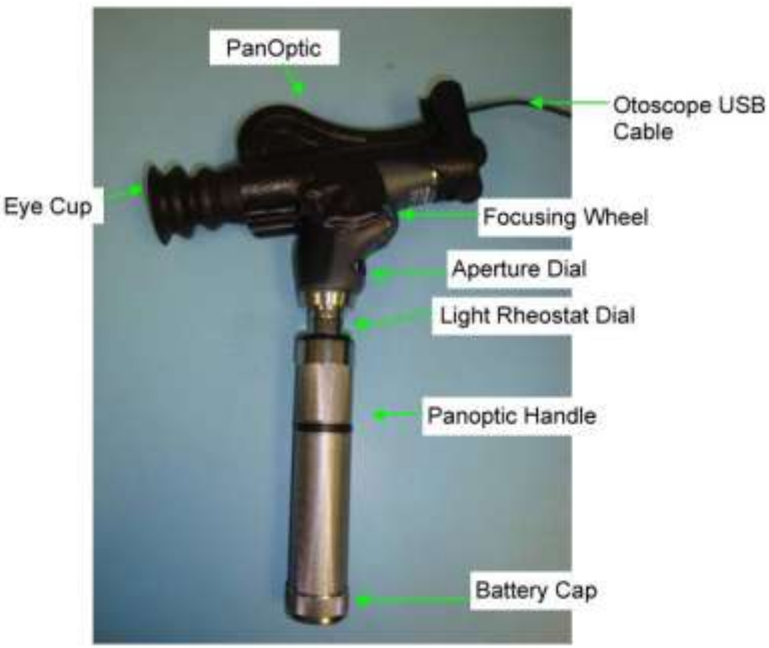
Case Report 5 - Continued

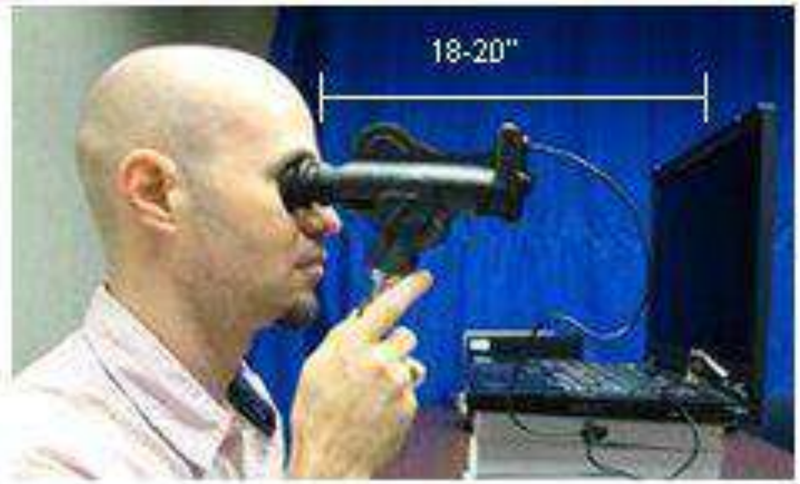


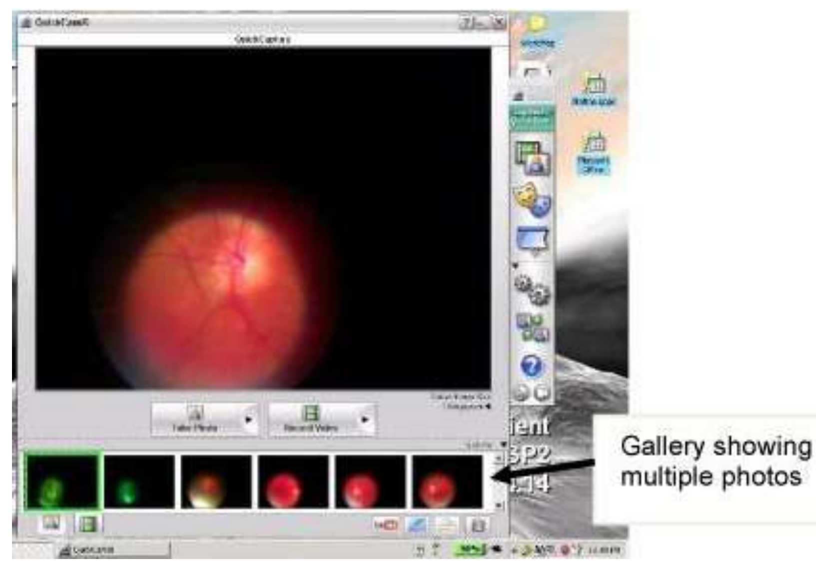
[Left] Pre flight Zeiss Cirrus OCT showing right and left NFL 'TSNIT' (temporal, superior, nasal, inferior and temporal curve).

[Right] Post flight Zeiss Cirrus OCT showing increased thickness of the nasal (red arrow) NFL. Greater increase is noted in the right eye in the nasal quadrant NFL thickness; 42µ pre flight to 70µ post flight. Fundus and optic disc imaging did not show presence of observable disc edema-choroidal folds may be an early sign of elevated ICP which precedes papilledema (important to obtain accurate in flight measurement of choroidal fold development-OCT)

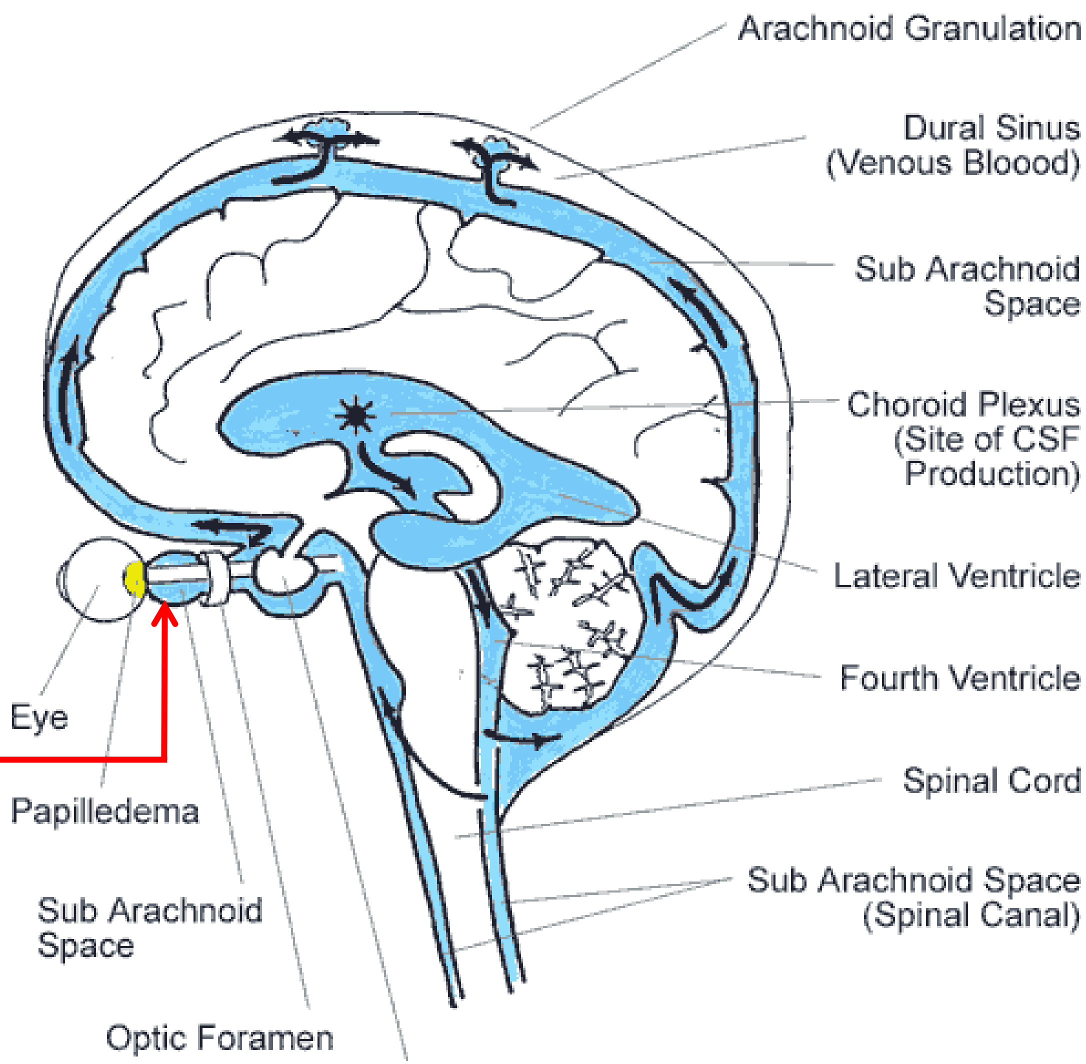
PanOptic Ophthalmoscope





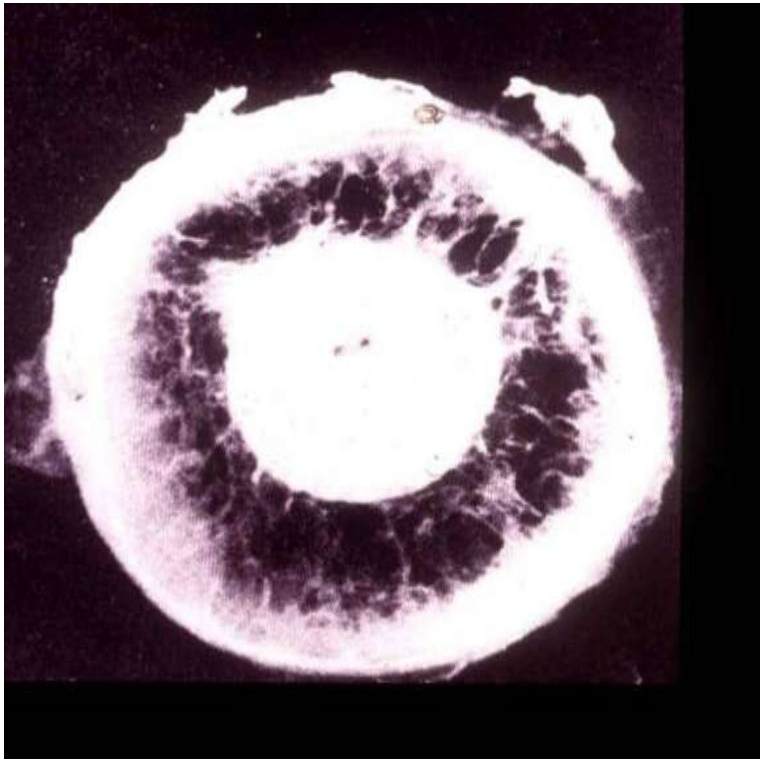


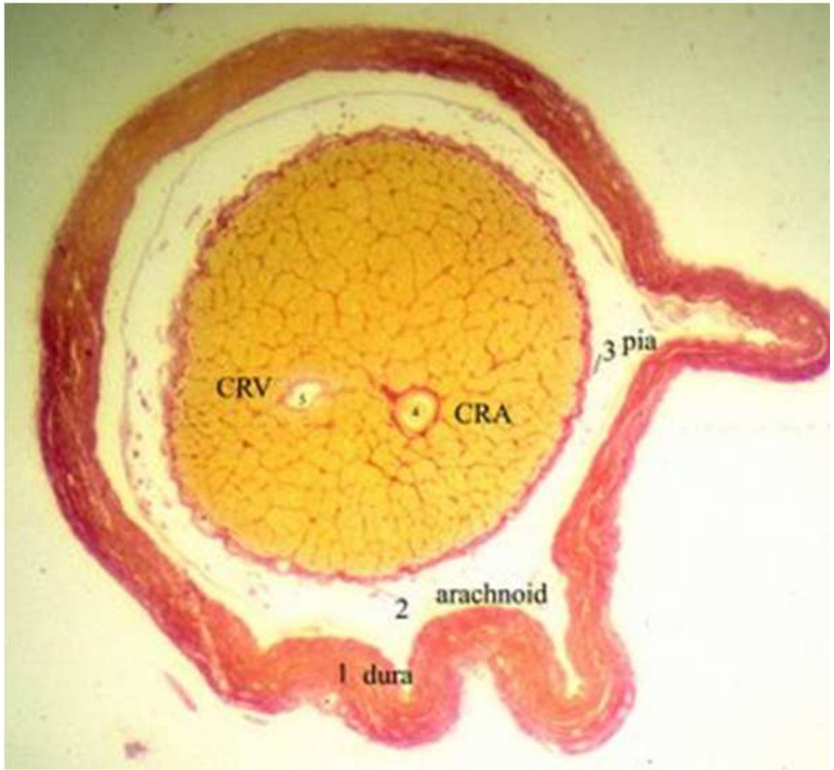
Raised Intracranial Pressure-Qualitative Measurement?



Elevated ICP transmitted to optic nerve

Cross -Sectional Area of Optic Nerve and Sheath





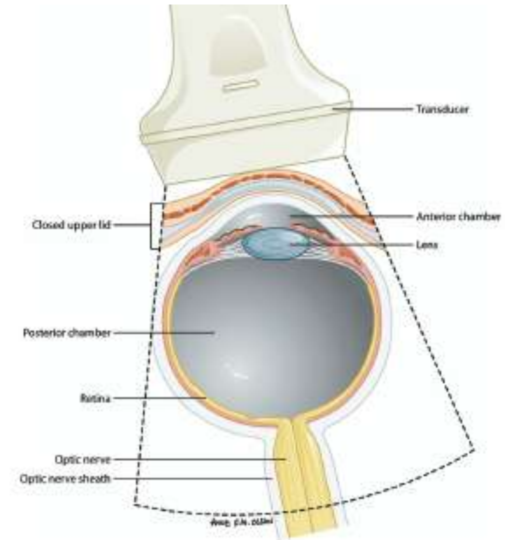
- Optic nerve x-section (post-mortem) from patient with papilledema.
- Large space, filled with web-like strands of arachnoid between nerve & nerve sheath.

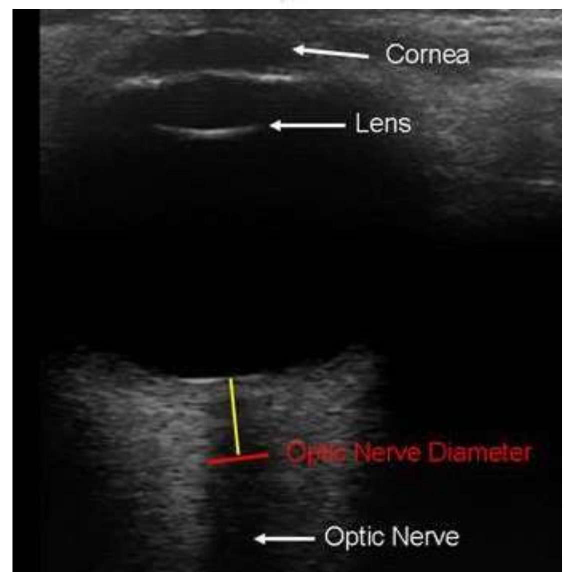
Ocular Sonography

- Image optic nerve and nerve sheath with ultrasound
- Optic nerve sheath diameter (ONSD) → ICP
- Gives broad sense of increased ICP versus normal
- No reliable linear relationship

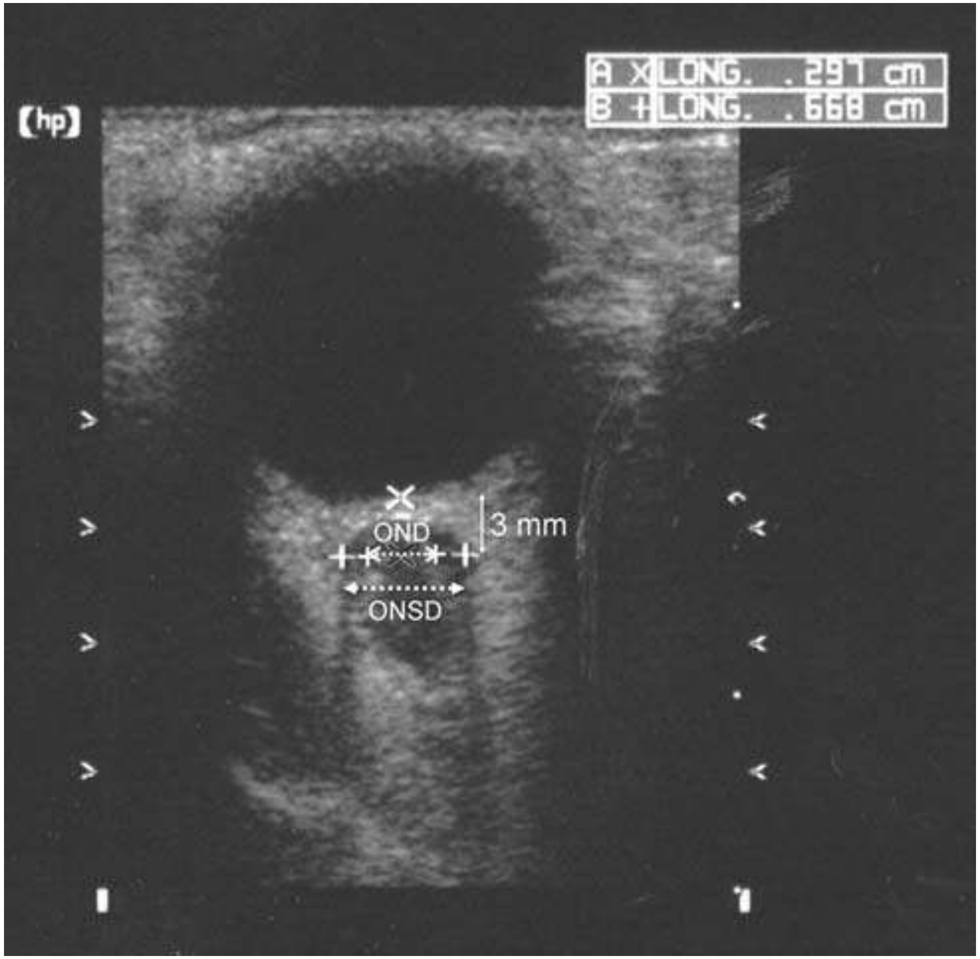
Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med 2008;15:201-4.

In Flight B-scan Ultrasound





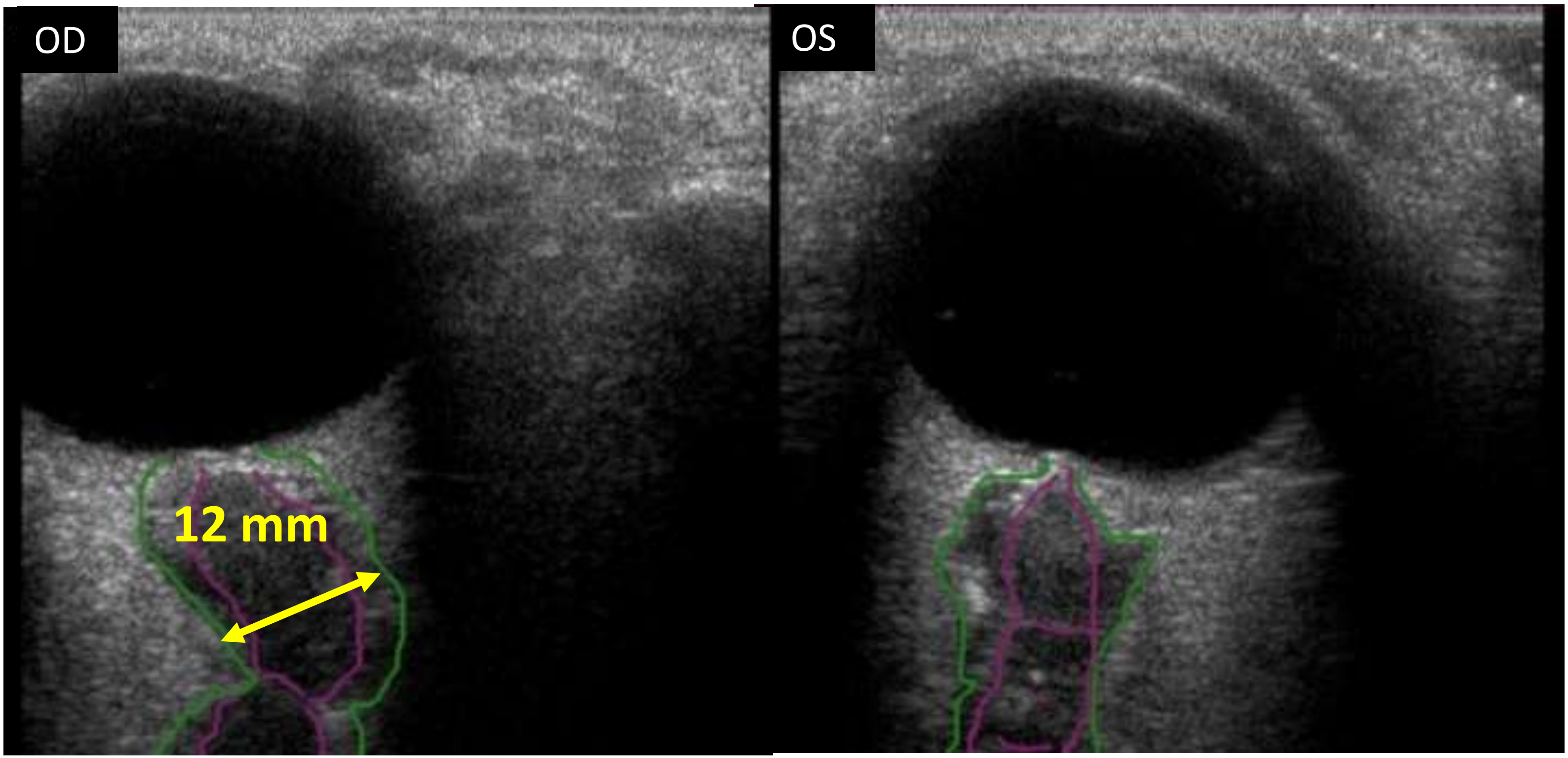
Optic Nerve Sheath Diameter



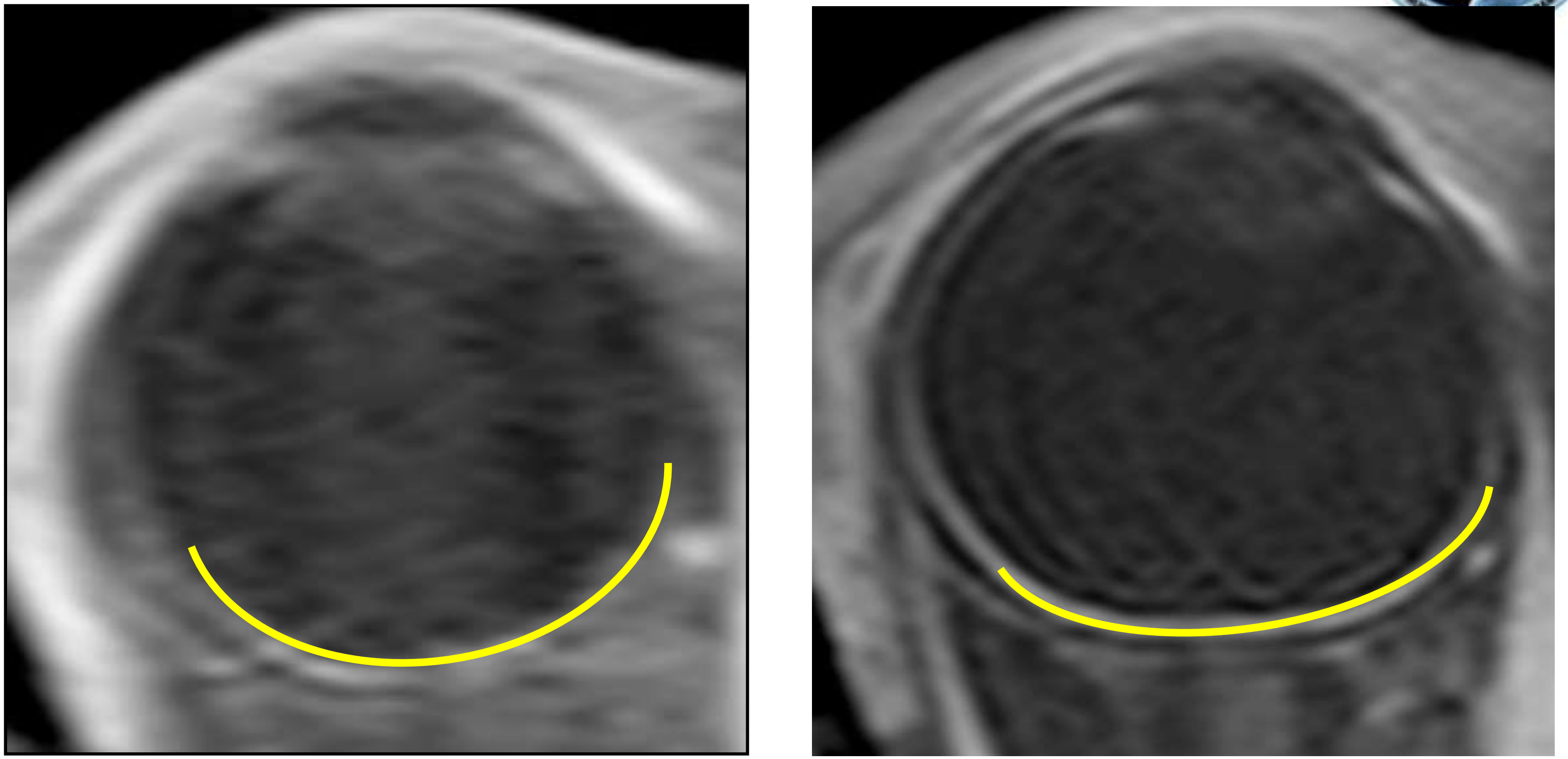
- Generally accepted that ONSD > 5 mm ≈ ICP > 20 cm H_2O

Geeraerts T, Merceron S, Benhamou D, Vigue B, Duranteau J. Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Med 2008;34:2062-7.

Case Report 4 - Increased Optic Nerve Sheath Diameter On-Orbit

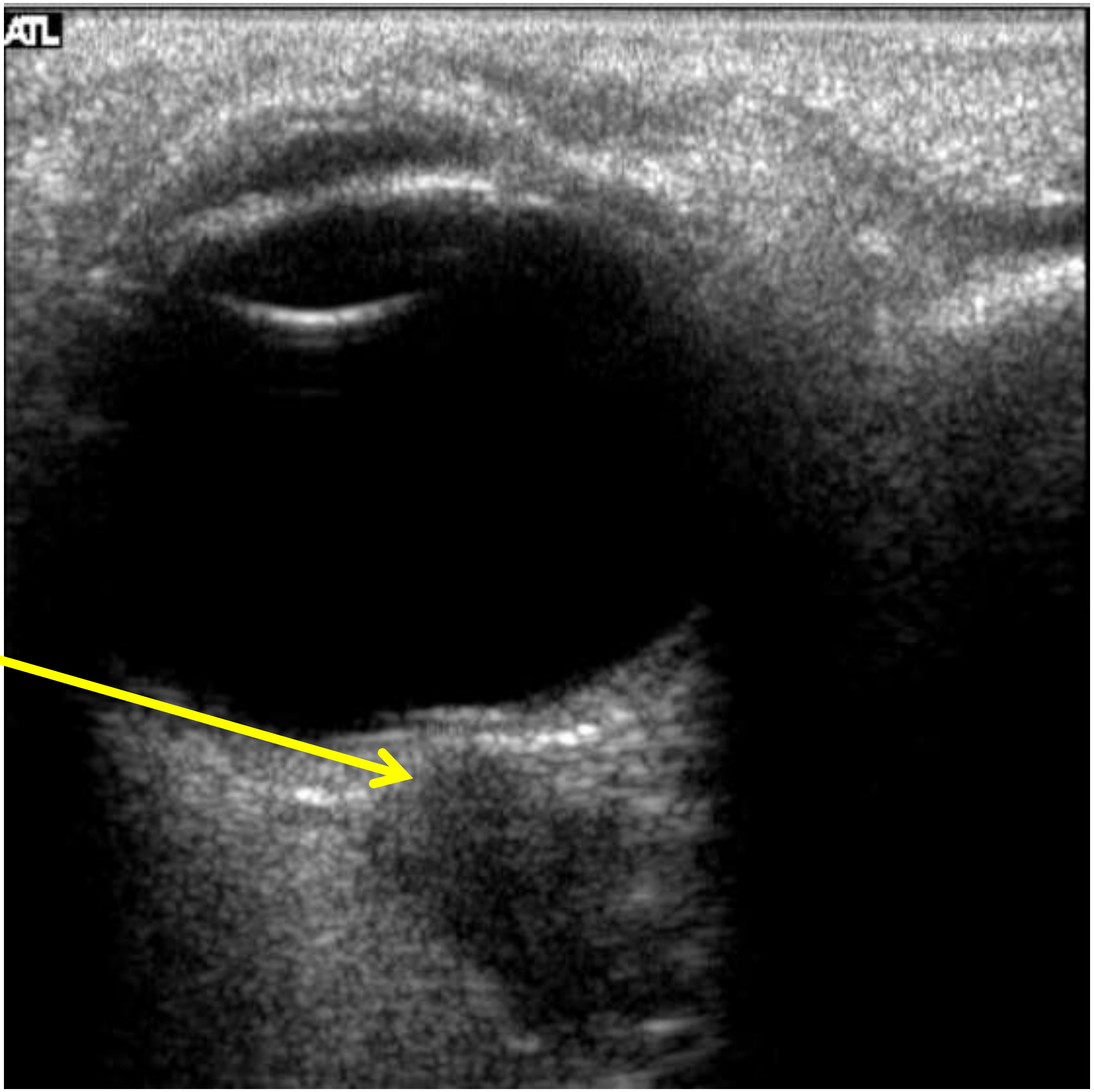


Case Report 5: MRI Globe Imaging



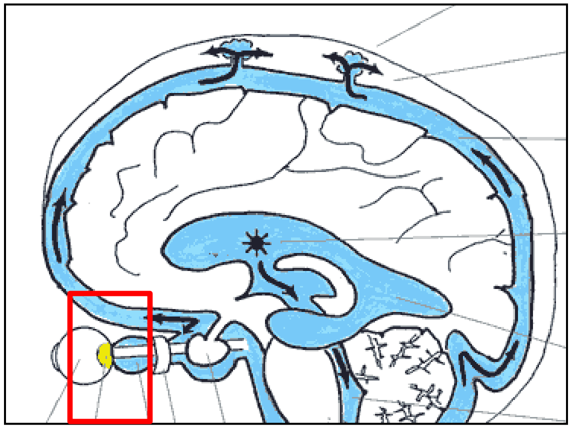
T1 MRI orbital imaging of the right eye. Pre flight (left) and Post flight (right) showing flattening of the posterior globe.

CASE Report 4 - Flattening of Posterior Wall - and Raised Optic Disk

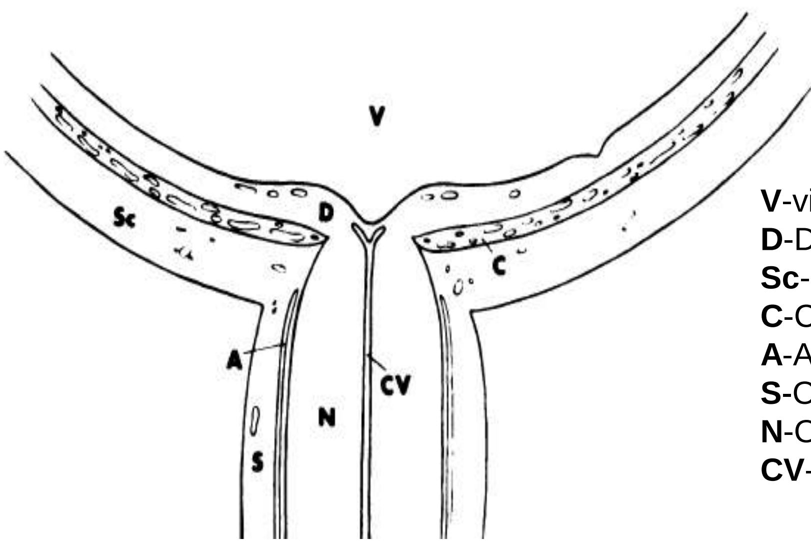


Elevation of optic disc

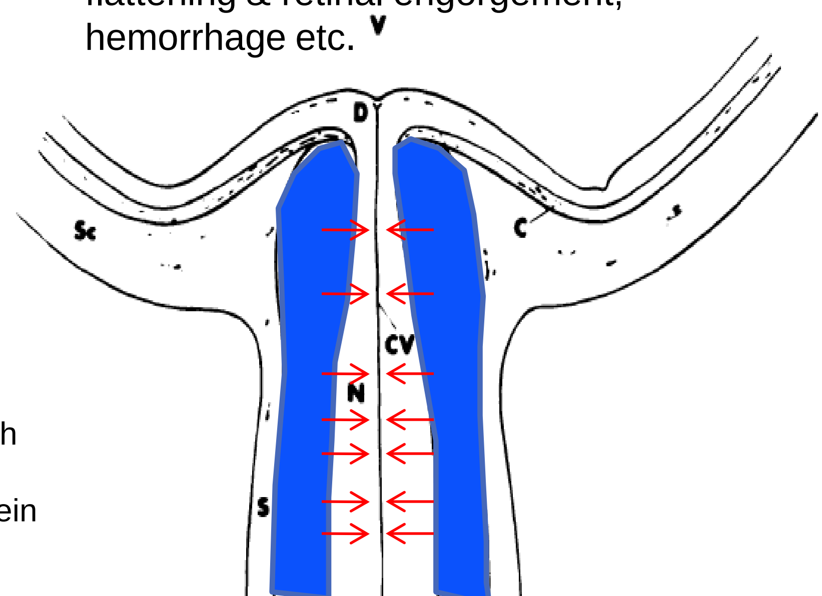
Ocular Venous Hypertension via Optic Nerve Compression



- ➢Increasing ICP transmitted to optic nerve via CSF space causes compression of central retinal vein
- ➢Arterial blood continues to flow into eye but venous drainage impaired
- ➢Result= venous hypertension, optic disc edema, disc protrusion, globe flattening & retinal engorgement, hemorrhage etc.



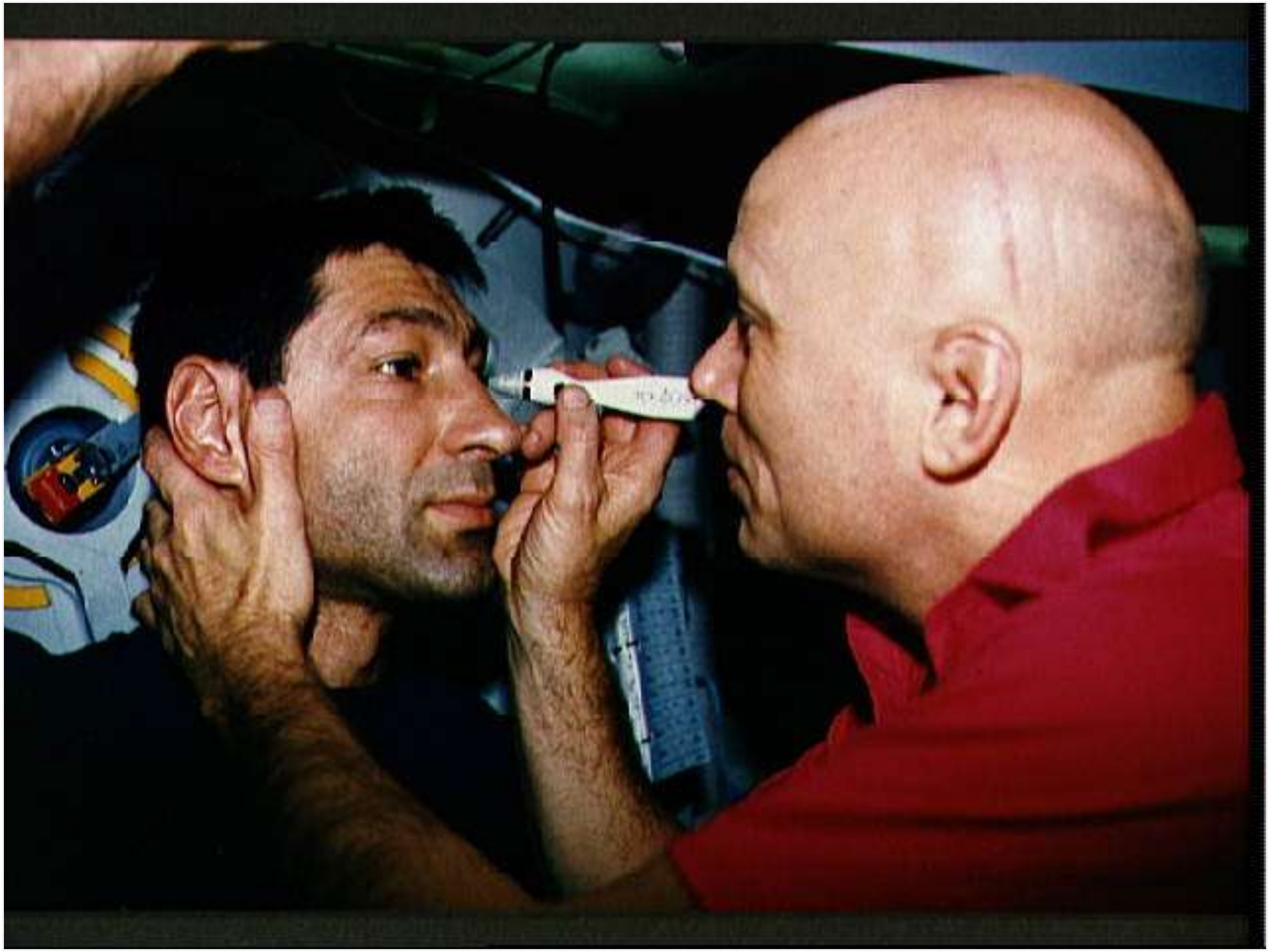
V-vitreous
D-Disc
Sc-sclera
C-Choroid
A-Arachnoid space
S-Optic nerve sheath
N-Optic Nerve
CV-Central retinal vein



A. Normal distal optic nerve/sheath complex & head in longitudinal cross section

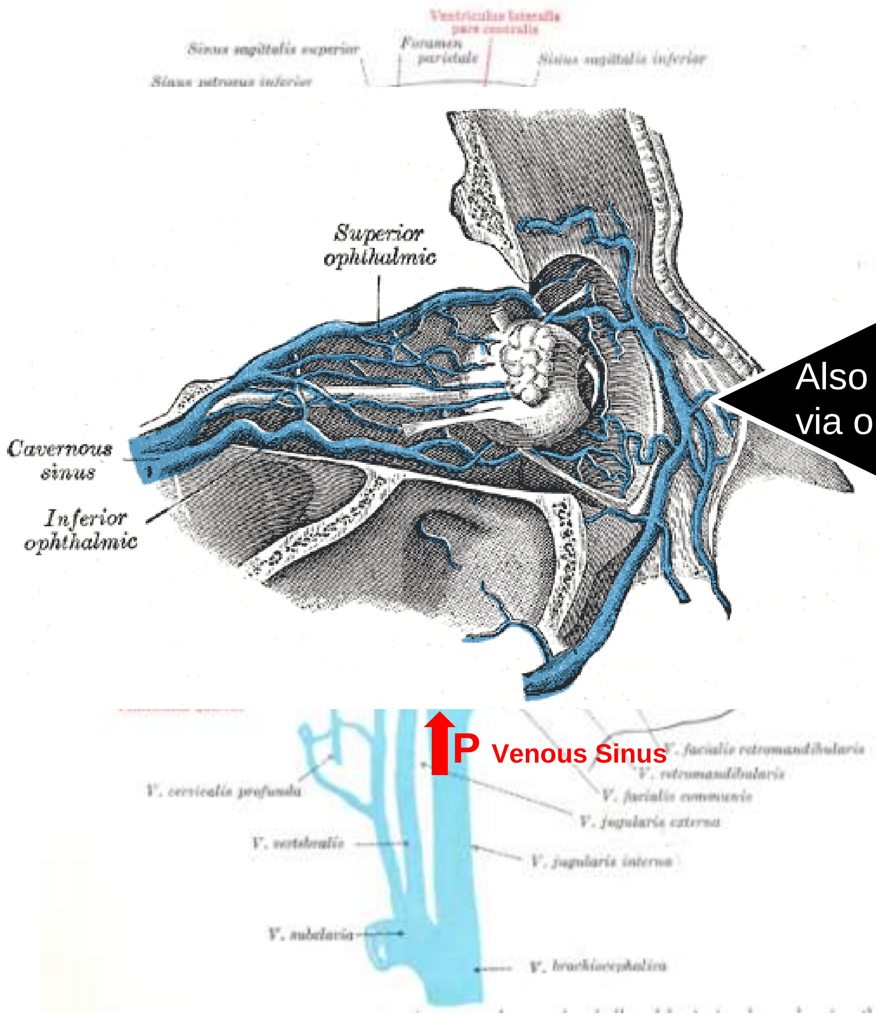
B. Papilledema showing enlargement of subarachnoid space & compression central retinal vein (CV)

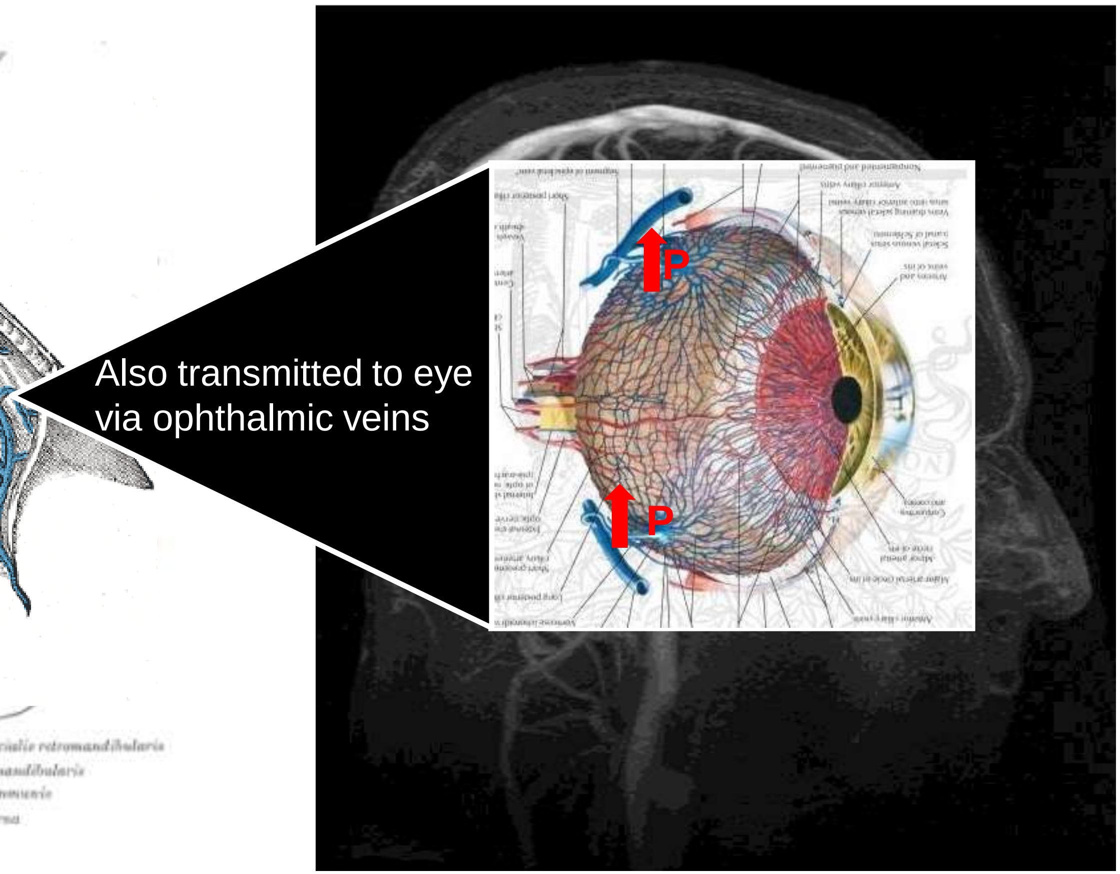
Measurement of Intraocular Pressure with Applantation Tonometry



Dr. Story Musgrave conducting tonometry on STS 44

Elevated ICP-Is it Transmitted to the Eye?





MRI Brain Venogram

ISS Crew Member	*Mission Duration*	*Refractive Change*	*Intraocular Pressure (mmHg)*	*Fundoscopic Exam Postflight*	*Disc Edema (Frisén)*	*OCT Postflight*	*Eye MRI Postflight* *Globe Flattening*	*CSF Pressure Postflight (cmH2O)*
CASE 1	6 months	Preflight: OD: -1.50 sph OS: -2.25-0.25x135 Postflight: OD: -1.25 -0.25x005 OS: -2.50-0.25x160	Preflight: 15 OU Postflight: 10 OU	• Choroidal folds OD • Cotton wool spot OD	Edema: No disc edema	• Choroidal folds still visible inferior to the OD disc (R+ >5yrs)	MRI not performed Globe Flattening: Not assessed	Not measured
CASE 2	6 months	Preflight: OD: +0.75 OS:+0.75-0.25x165 Postflight: OD: +2.00 sph OS: +2.00-0.50x140	Preflight: 14 OU Postflight: 14 OU	• Bilateral disc edema OD>OS • Choroidal folds OD > OS • Cotton wool spot OS	Edema: Grade 1 OD and OS	• NFL thickening c/w disc edema	Optic nerve sheath distension OD and OS Globe Flattening: OD and OS	Elevated • 22 at R+66 days; • 26 at R+17 months; • 22 at R+19 months) • 23 at R+>5yrs
CASE 3	6 months	Preflight: OD: -0.50 sph OS: -0.25 sph Postflight: Plano Plano	Preflight: 10 OU Postflight: 10 OU	• Bilateral disc edema OD>OS • Small hemorrhage OD	Edema: Grade 3 OD Grade 1 OS	• Severe NFL thickening OD>OS c/w Disc edema	Optic nerve sheath distention OD Globe Flattening: None observed	Elevated • 21 at R+19 days
CASE 4	6 months	Preflight: OD: -0.75-0.50x100 OS: plano-0.50x090 Postflight: OD: +0.75-0.50x105 OS: +0.75-0.75x090	Preflight: 15/13 Postflight: 11/10	• Disc edema OD • Choroidal folds OD	Edema: Grade 1 OD	• Mild NFL thickening OD>OS c/w disc edema • Choroidal folds OD	Optic nerve sheath distention and tortuous optic nerves OD>OS Globe Flattening: OD > OS	Elevated • 28.5 at R+57 days
CASE 5	6 months	Preflight: OD: -5.75-1.25x010 OS: -5.00-1.50x180 Postflight: OD: -5.00-1.50x015 OS: -4.75-1.75x170	Preflight: 14/12 Postflight: 14/12	• Normal	Edema: No disc edema	• Subclinical disc edema • Mild/moderate NFL thickening OD	Optic nerve sheath distention and tortuous optic nerves Globe Flattening: OD and OS	Not measured
CASE 6	6 months	Preflight: OD: +0.25 OS: +0.25-0.50x152 Postflight: OD: +2.00-0.50x028 OS: +1.00 sph	Preflight: 14 OU Postflight: 14 OU	• Disc edema OD • Cotton wool spot OS	Edema: Grade 1 OD	• Mild NFL thickening c/w disc edema • Choroidal folds OD	Optic nerve sheath distention OD>OS Globe Flattening: OD > OS	Not Measured
CASE 7	6 months	Preflight: OD: +1.25 sph OS: +1.25 sph Postflight: OD: +2.75 sph OS: +2.50 sph	Preflight: 16 OU Postflight: 12/14	• Disc edema OU • Choroidal folds OD>OS	Edema: Grade 1 OD and OS	• Moderate NFL thickening c/w disc edema OD and OS • Choroidal folds OD and OS	Optic nerve sheath distention OD and OS Globe flattening: OD and OS	Elevated • 28 at R+12 days (with +SVP) • 19 at R+ days

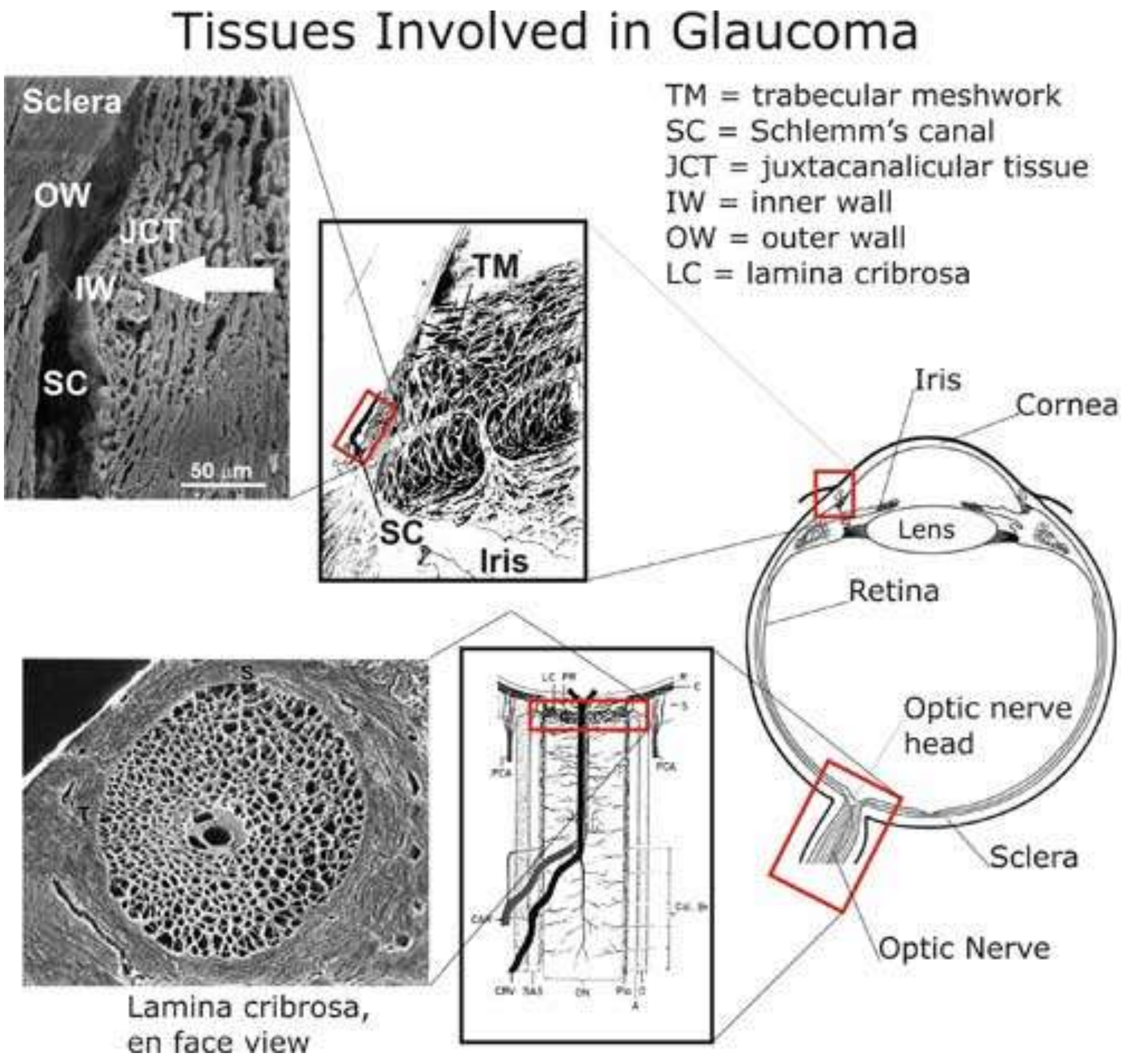
Impacts

- Elevated intracranial pressure and vision disturbance in spaceflight are serious health risks to the astronaut population.
  - Much longer missions are being planned that will subject personnel to even greater periods of microgravity and hence prolonged exposure to elevated IOP and/or ICP.
- VIIP Risk team formed with membership from Med Ops and HRP.
  - Current plan for HRP content is to work via project team within HHC.
- High-level research plan in development
- **What are the physiological causes?**

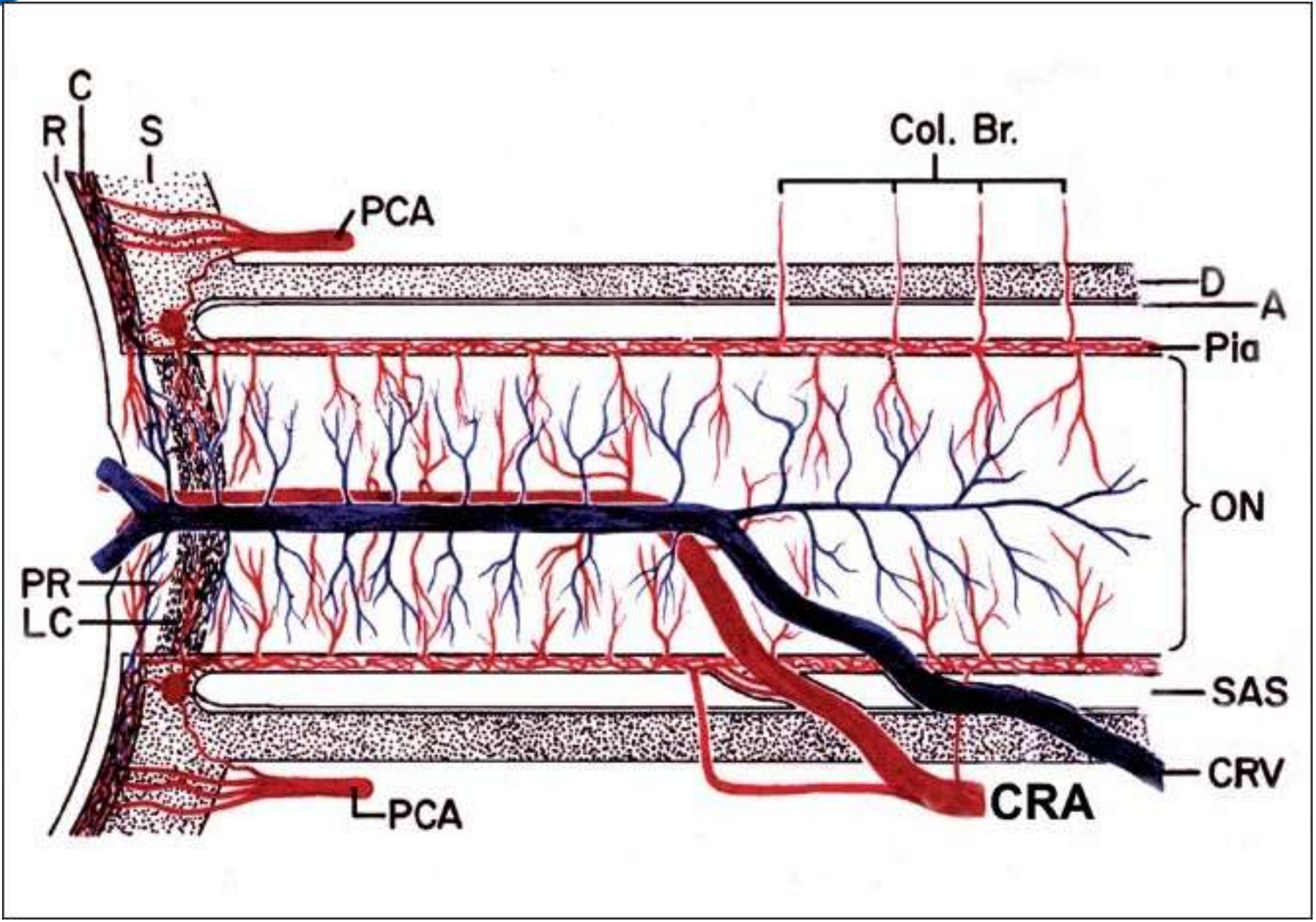
VIIP Risk – Med Ops and Research

- Summit held February 8-10 with national and international experts in ophthalmology, neuro-ophthalmology, neurosurgery, neurophysiology, and cardiology.
  - Obtained suggestions for current pre, in, and post-flight operations as well as research areas with respect to detection, monitoring, treatment, imaging, susceptibility, computer modeling, and/or use of analogs.
- Results from the summit further reinforced the existence of multiple contributing factors with no clear cause identified. While Medical Operations approaches from a clinical perspective, research is needed to further quantify and mitigate the risk.
- The NASA HRP has added this risk to its portfolio and established the VIIP Project within the Human Health Countermeasures Element.

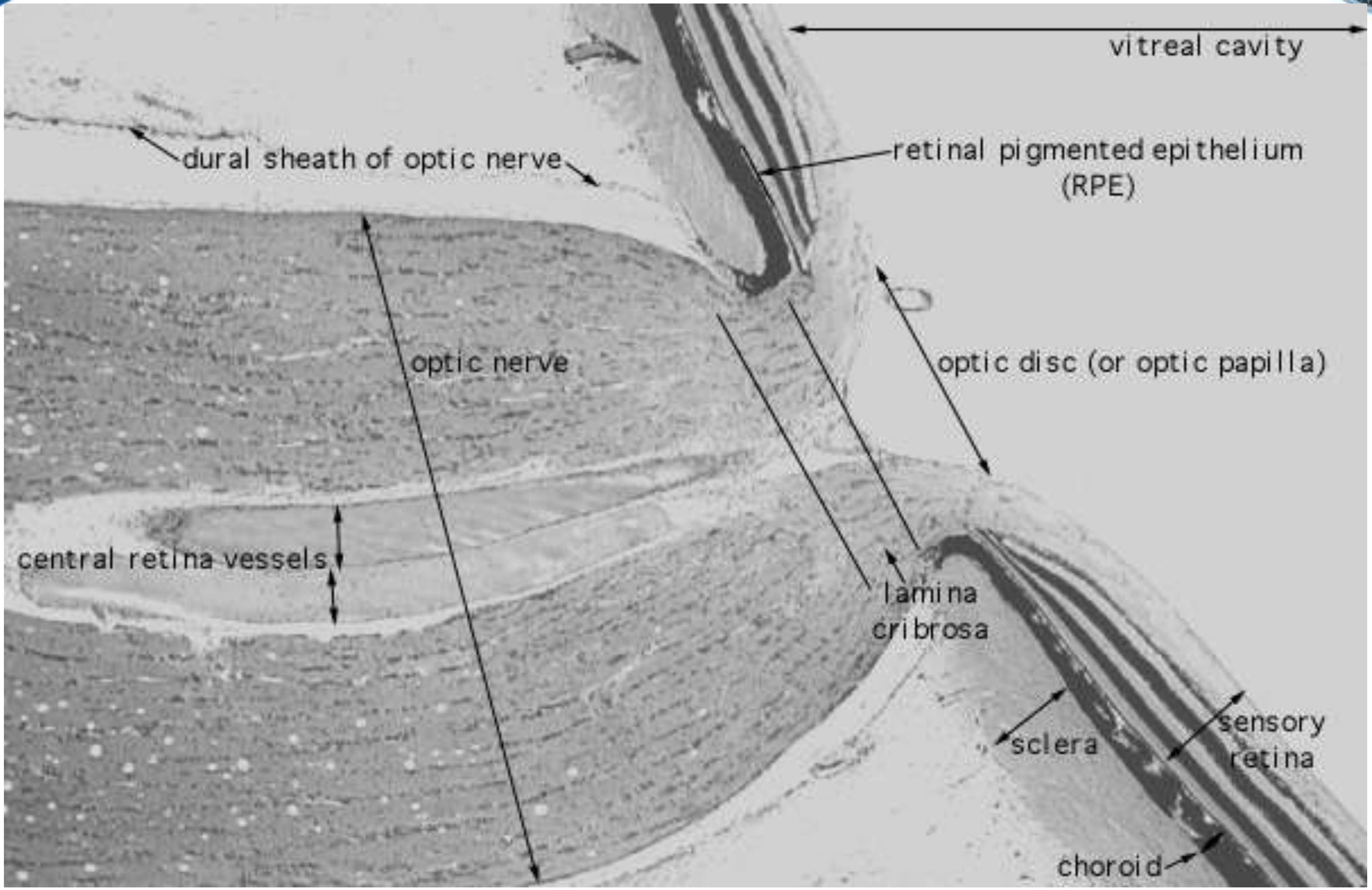
Glaucoma


Tissues Involved in Glaucoma
TM = trabecular meshwork
SC = Schlemm's canal
JCT = juxtacanalicular tissue
IW = inner wall
OW = outer wall
LC = lamina cribrosa
Sclera
OW
JCT
IW
SC
50 µm
TM
SC
Iris
Iris
Cornea
Lens
Retina
Optic nerve head
Sclera
Optic Nerve
Lamina cribrosa, en face view

Posterior Eye & Optic Nerve Anatomy

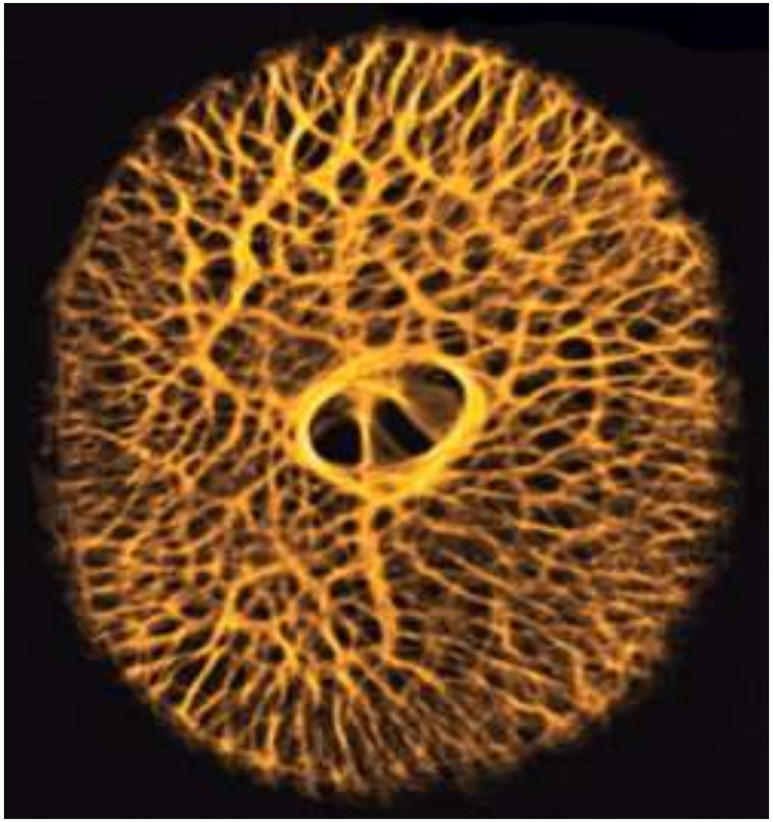


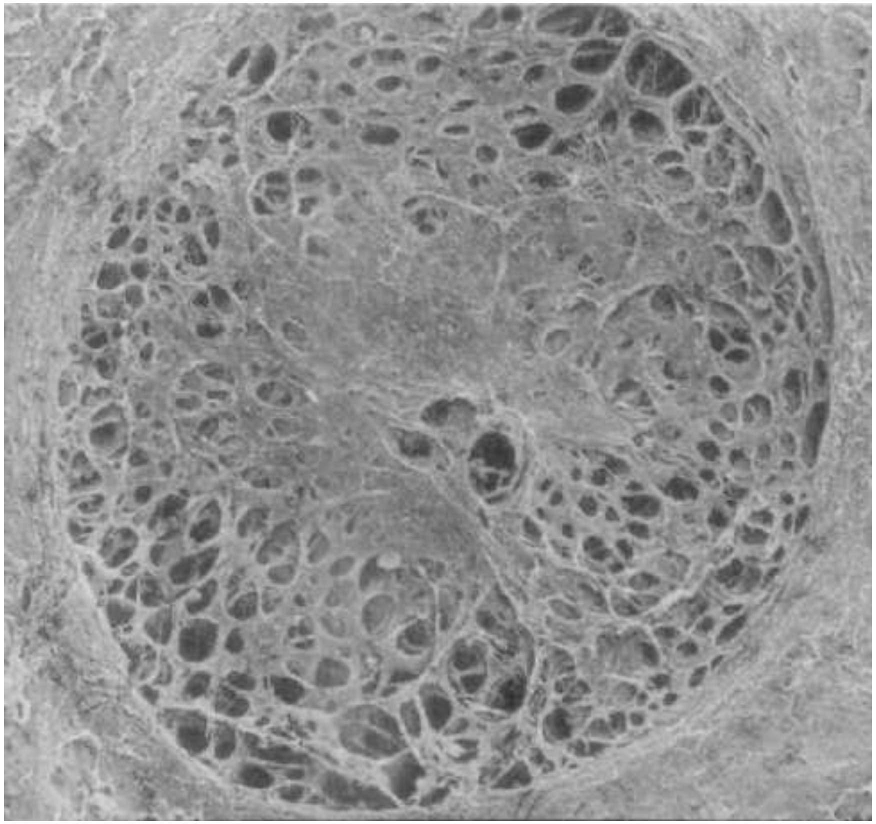
The Lamina Cribosa: Barrier Between the Intraocular Space and SAS



The LC serves as a barrier to separate the intraorbital space, with typically higher pressure, from the subarachnopid space, with typically lower pressure. The LC therefore prevents orbital contents from leaking into the subarachnoid space

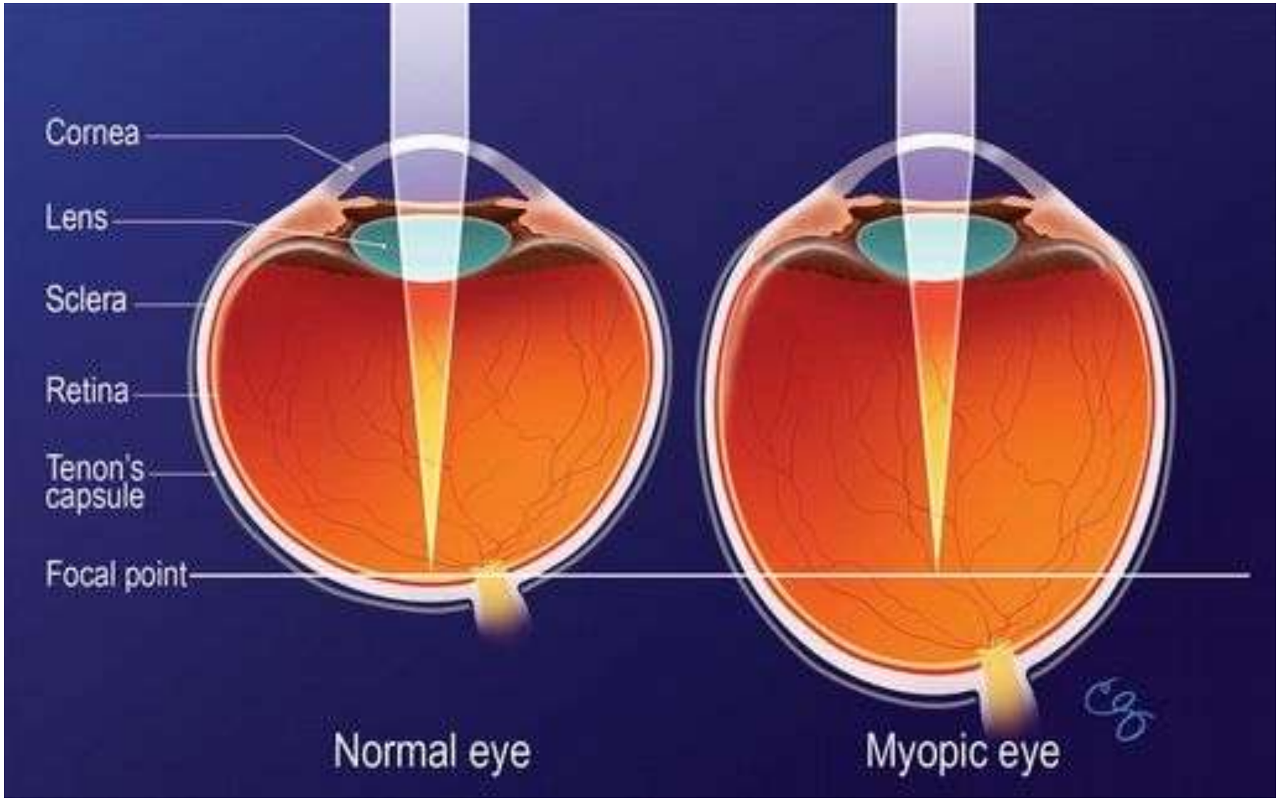
Lamina Cribosa Structure





- LC is a series of cribiform plates, with pores that line up to permit nerve axons to pass through
- LC cores are filled with fibrillar collagen and elastic fibres, during aging constituents are altered
- LC   becomes stiffer and thinner, thus ability to support nerve axons passing though is compromised especially around the ages of 40-50 years

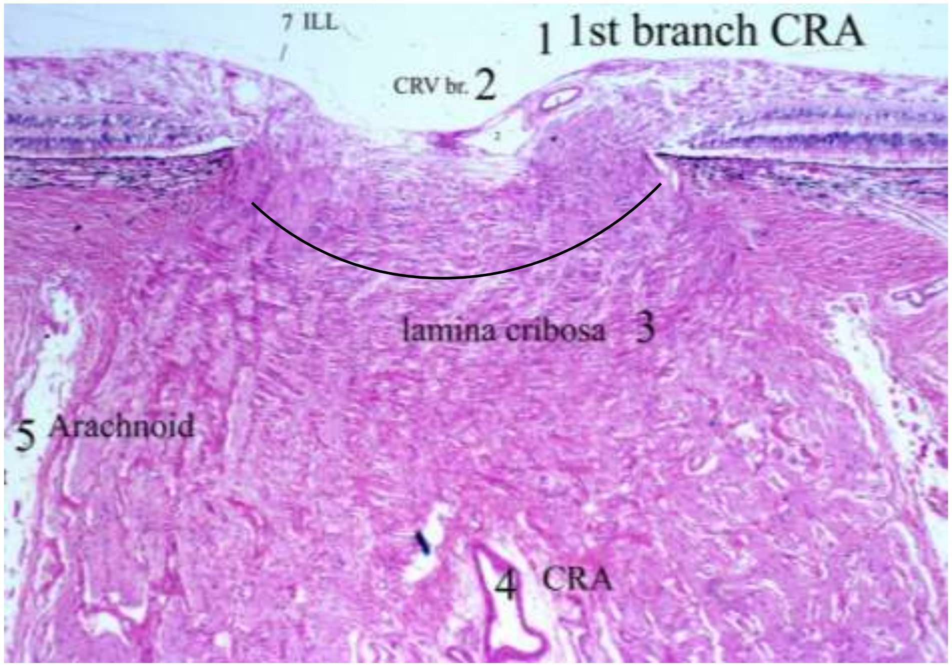
Myopes put Greater Shear Stress on LC Higher Risk for Glaucomatous Changes



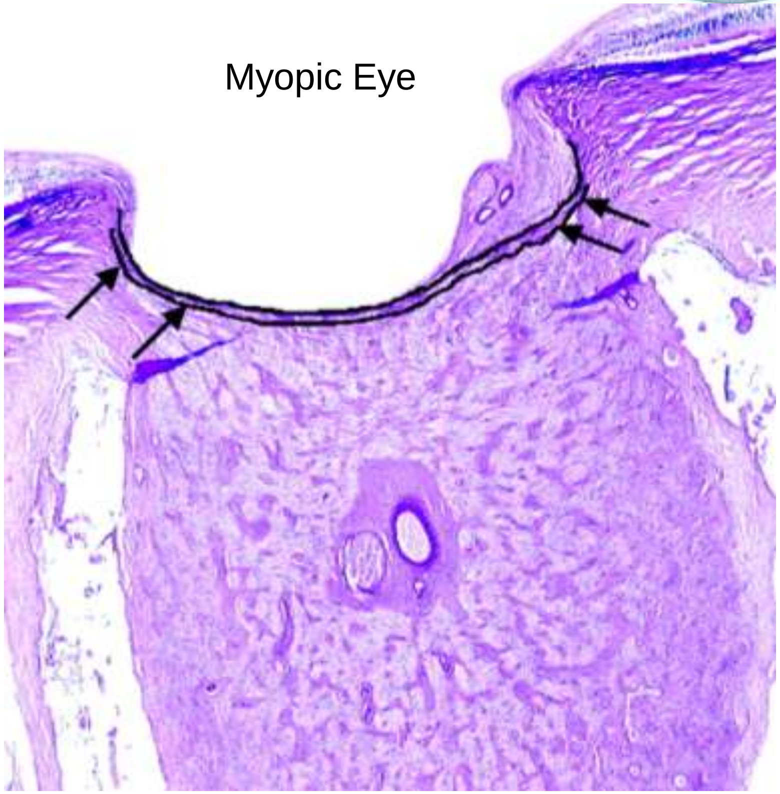
Stress on any part of ocular shell related to IOP and radius of structure: σ=PR/2t
σ=circumferential stress
P=IOP
R=radius of curvature at that part of the globe
T=thickness
Thus, in myopic eyes when LC is cupped, radius is larger, and stress is greater

Lamina Cribosa: Normal vs Myopic

Normal Eye

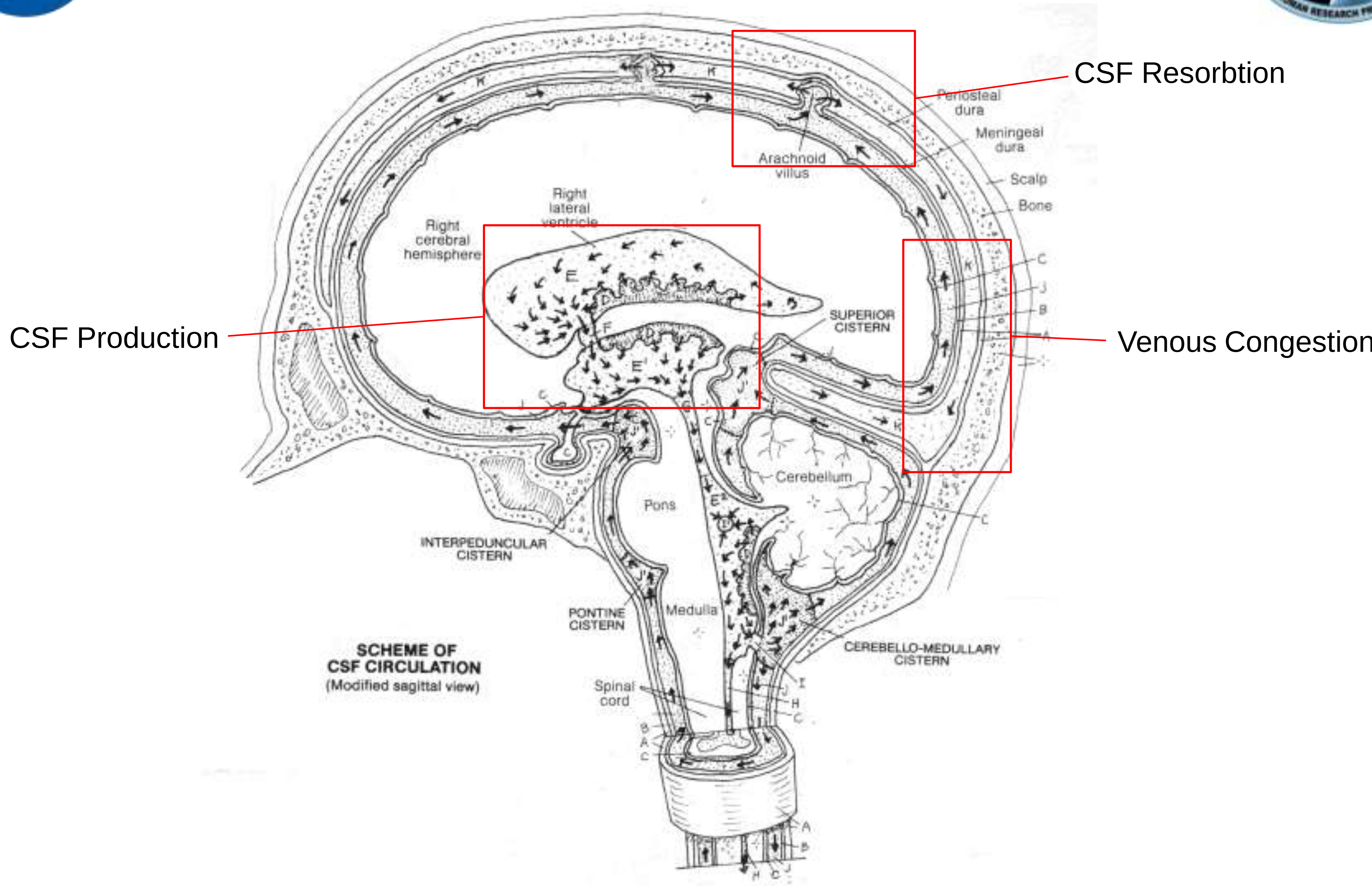


Myopic Eye

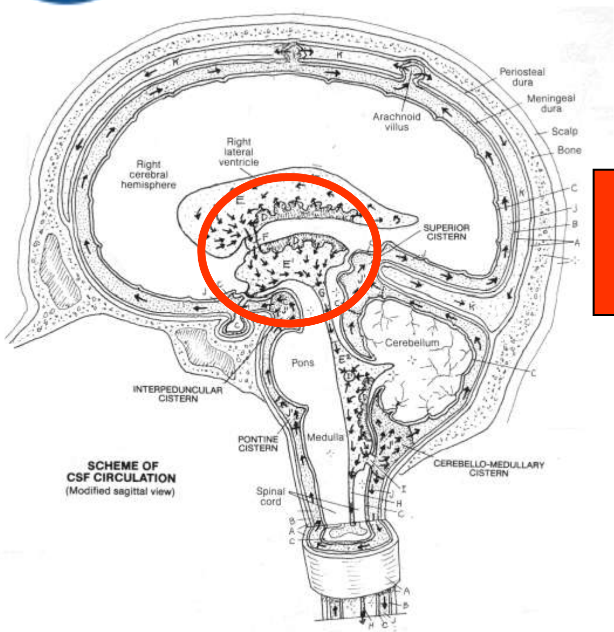


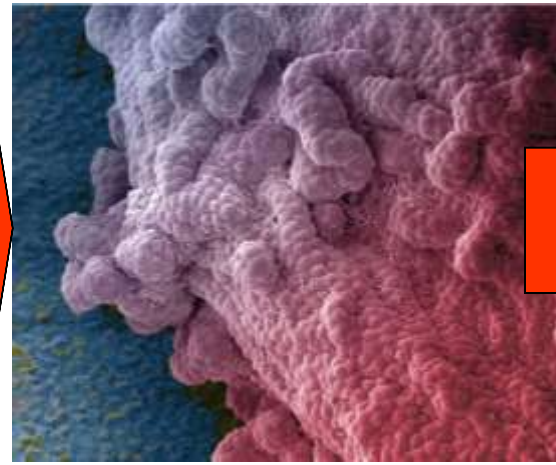
- Shear stresses are dominant, and maximal at the periphery owing to the greater curvature in myopic eye
- LC increases in stiffness with age=decreased compliance' means higher likelihood of permanent deformation and at lower pressures
- Change in mechanical compliance most marked after 40-50 years of age, same age incidence of glaucoma increases.
- Any elevation in deformation pressure, even transient, may result in permanent shape

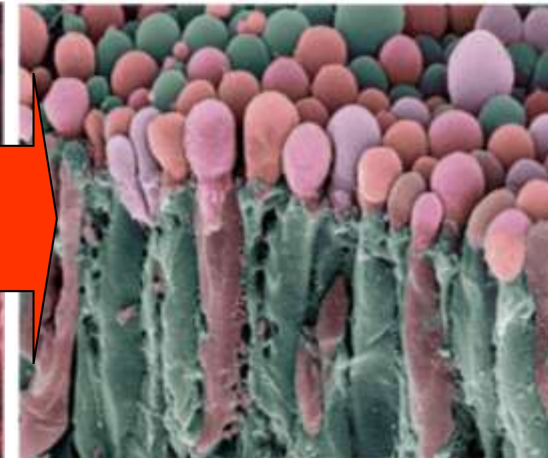
Key Brain Areas



CSF Production: Choroid Plexus

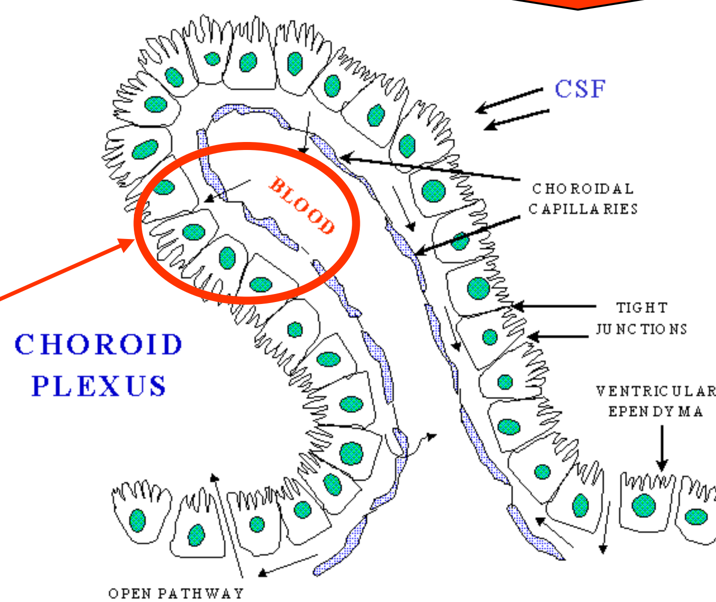






Choroid plexus in lateral, third & fourth ventricle produces 70-90% of CSF in brain

Increased filtration?



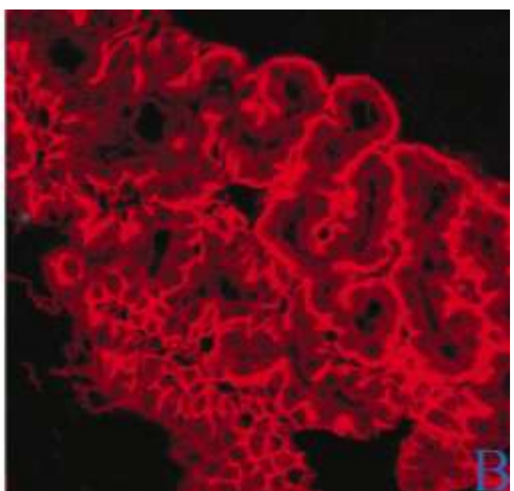
Choroidal Cell Responses in Microgravity-Atrial Naturietic Peptide

Normal Control Choroid Cell

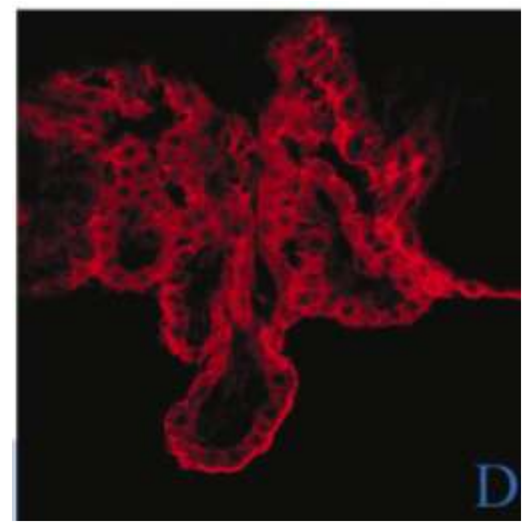
- ANP neurohormone
- In CNS when ANP activated, decreases CSF by inhibiting Na-K-ATPase proteins in cerebral capillaries
- Increased ANP binding sites 1.5-2.5x in HLU rat studies

Immunodetection of (red) Na-K-ATPase at the apical pole of choroid plexus
(B) in a control rat   (D) in a ground-based model simulating cephalad fluid shift

Ground Control 1G



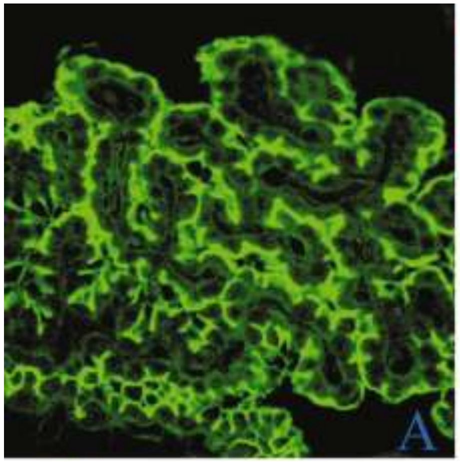
0G & Hind Limb Unloaded



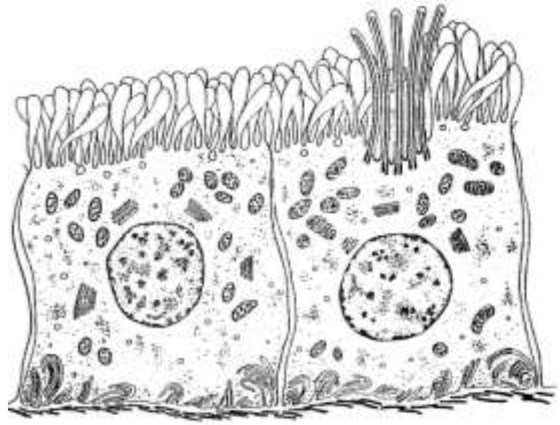
Gabrion et al. Choroidal responses in microgravity. Acta Astronautica. 1995

Choroidal Cell Responses in Microgravity-Aquaporin-1 Expression

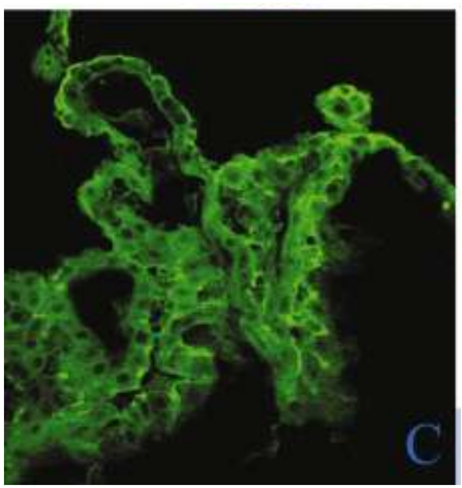
Ground Control 1G



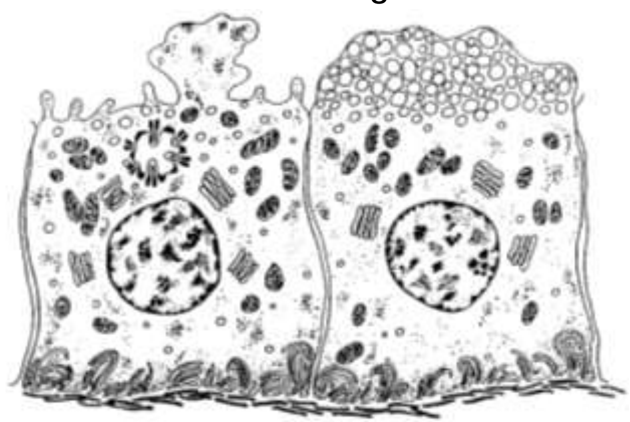
Normal Control Choroid Cell



0G & Hind Limb Unloaded



Abnormal 0G Analog Choroid Cell



Immunodetection of aquaporin 1 (in green) at the apical pole of choroid plexus,

(A) in a control rat (homogeneously covered with long bulbous apical microvilli, and tufts of kinocillia)

(C) in a model simulating cephalad fluid shift. AQP1 was reduced 64% after 14d spaceflight (STS-58), by 44% after 14 days HLU, and by 68% after 28d HLU.

A net decrease was noted at the epithelial cells, suggesting that CSF production was decreased.

Loss of microvilli, failure of exocytosis, loss of kinocillia

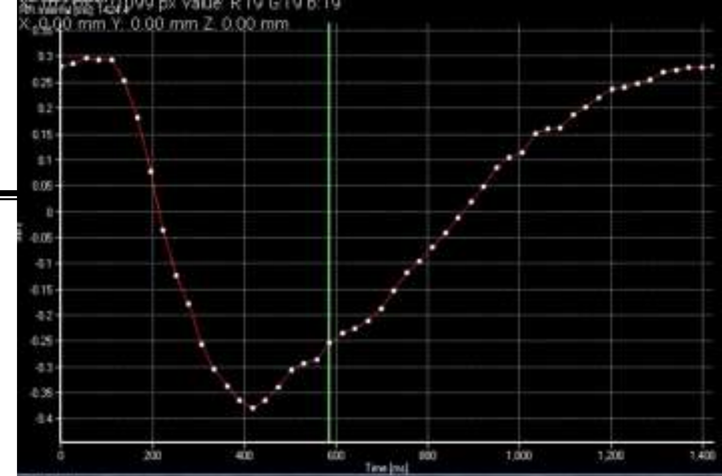
Suggests brain adaptation in microgravity with a reduction in CSF secretory activity.

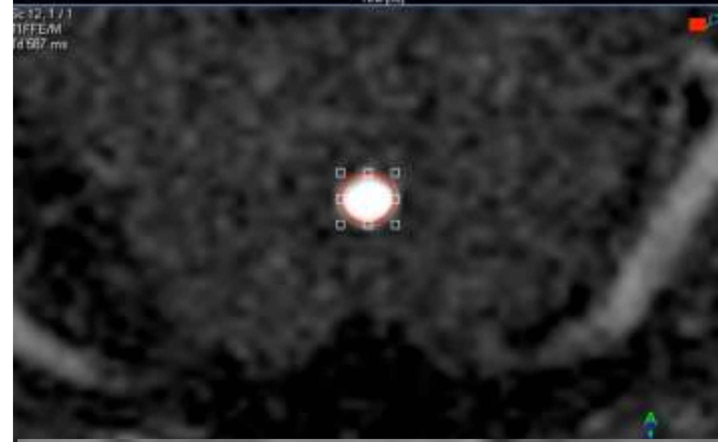
Gabrion et al. Choroidal responses in microgravity. Acta Astronautica. 1995

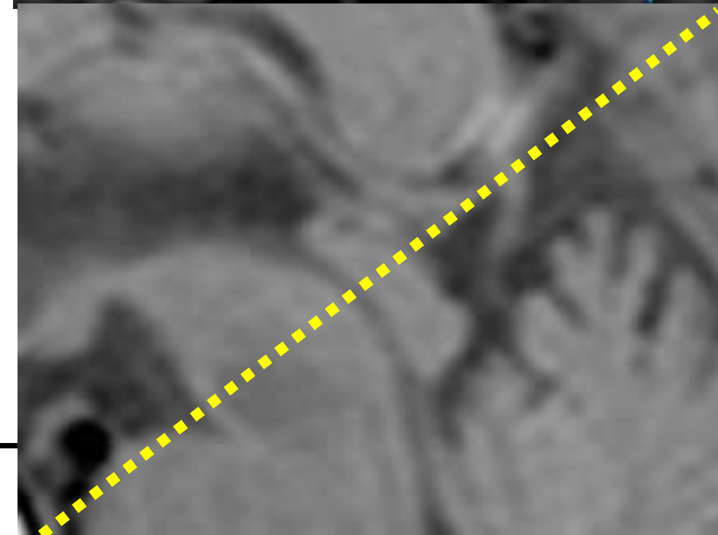
Overshoot of AQP-1: A Mechanism for Elevated ICP Post Flight?

- Once rats returned to 1G, at 2 days readaptation, AQP1 expression was 48% greater than control rats
- In the 14d HLU rats there was a 57% increased expression in AQP-1 after 6 hours readaptation, compared to controls
- Could over-expression of AQP-1 upon return to 1G be a mechanism for the persistently elevated ICP seen in some crew members?

Flow analysis of CSF through the aqueduct

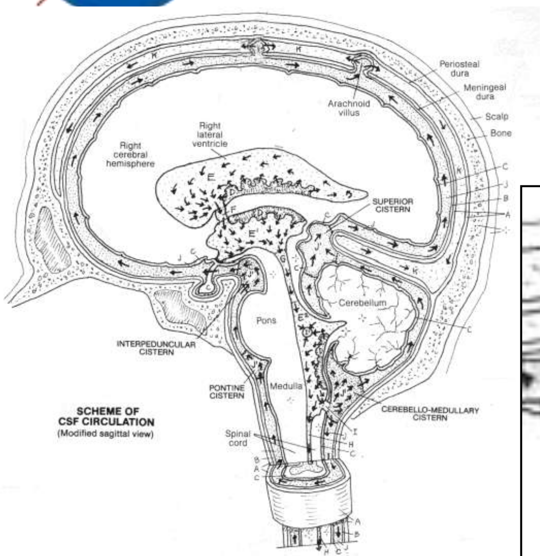






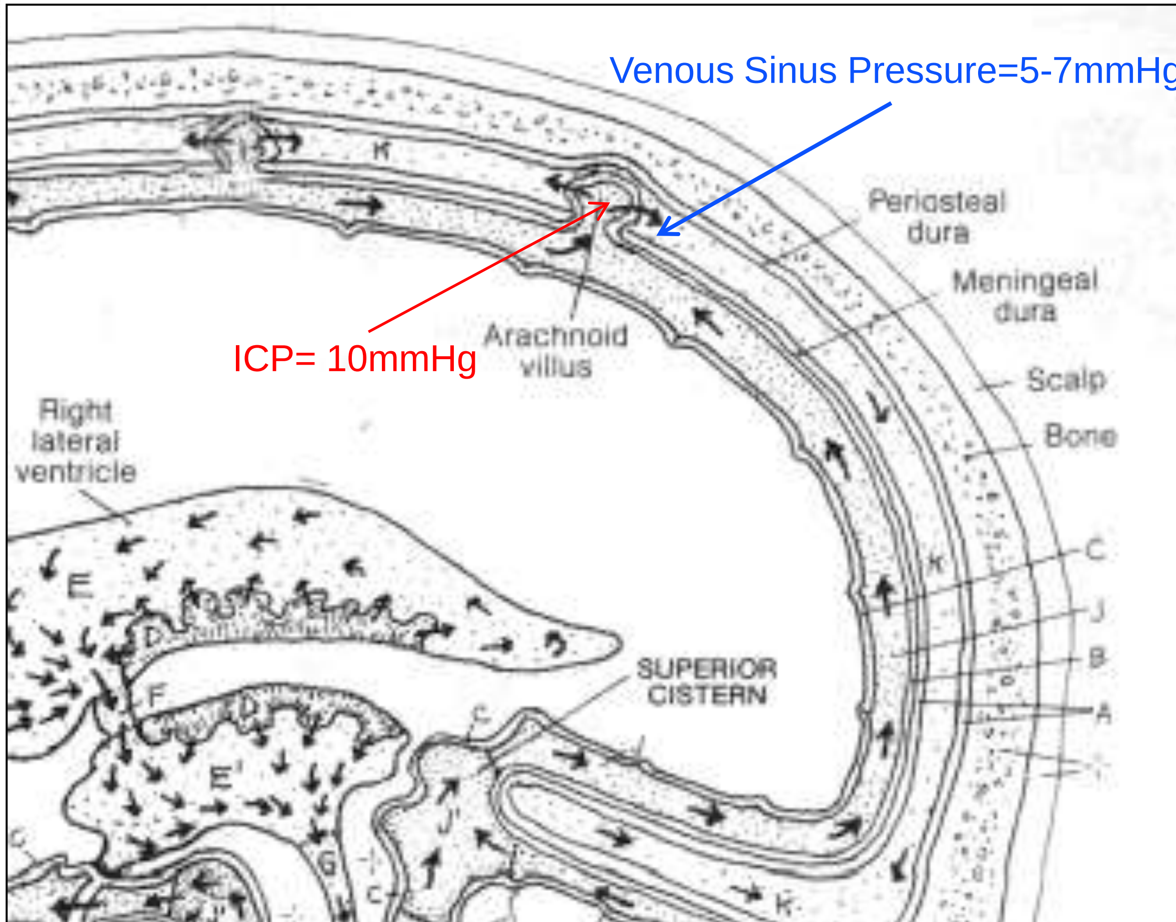
- The flow analysis of CSF through the aqueduct (axial oblique section noted as dashed line --Bottom).
- A CINE phase contrast sequence obtained perpendicular to the mid cerebral aqueduct showing velocity versus time after the QRS wave (graph --- top left) Case #5:
  - R+30: CSF production rate=**305** ul/min
    - CSF peak velocity=**3.65**cm/s
  - R+57: LP opening pressure=28.5
  - R+180:CSF production rate=**682** ul/min
    - CSF peak velocity=**7.80**cm/s
  - Normal CSF production 150-270 ul/min
- Cross sectional image through the mid cerebral aqueduct (Middle) showing the area of flow analysis
- T1 weighted mid sagittal image (Bottom) showing plane of section through the mid cerebral aqueduct
- There is no obvious narrowing of the cerebral aqueduct. CSF production rate is approximately one standard deviation above average in several cases

Normal CSF Diffusion Gradient



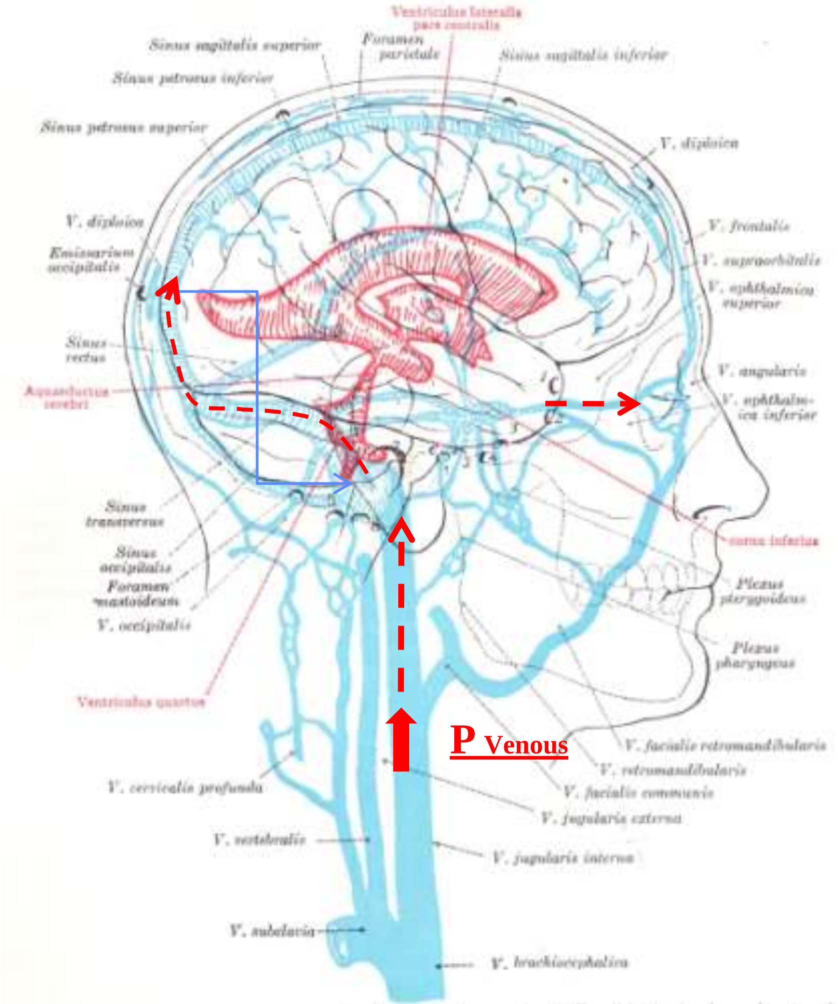
Normal SSVP:CSFP= 0.60

Therefore delta driving pressure only~3-5mmHg



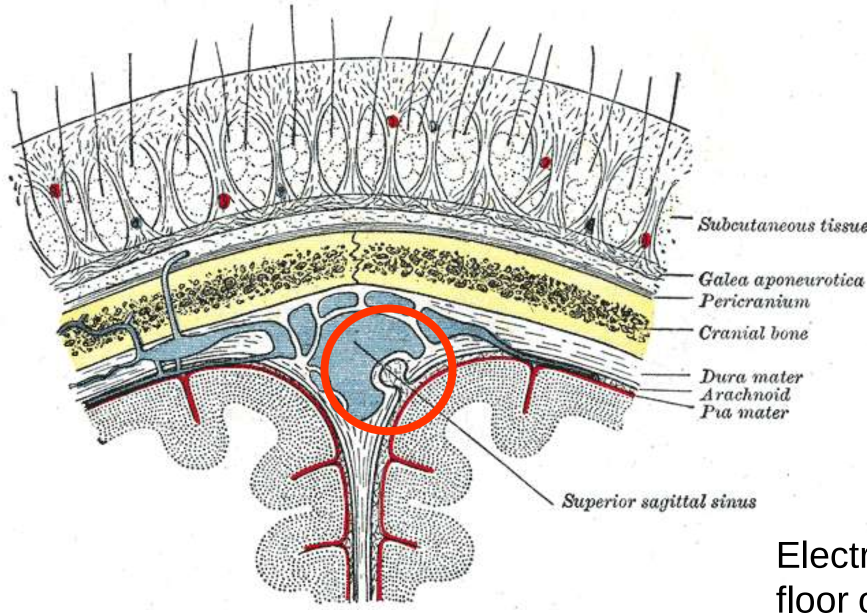
Risk Background - Intracranial Pressure

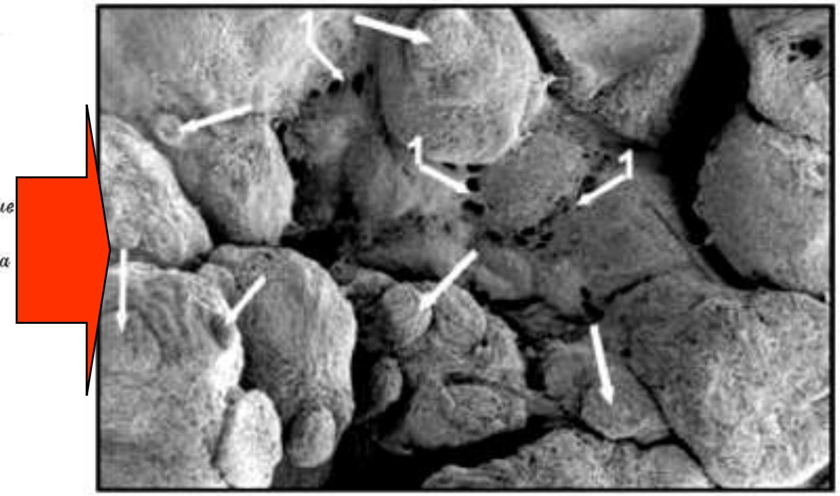
As SSVP:CSFP increases, approaches 1.0
Driving pressure falls<3-5mmHg and decreased CSF absorbtion



MRI Brain Venogram

CSF Resorption: Arachnoid Granulations

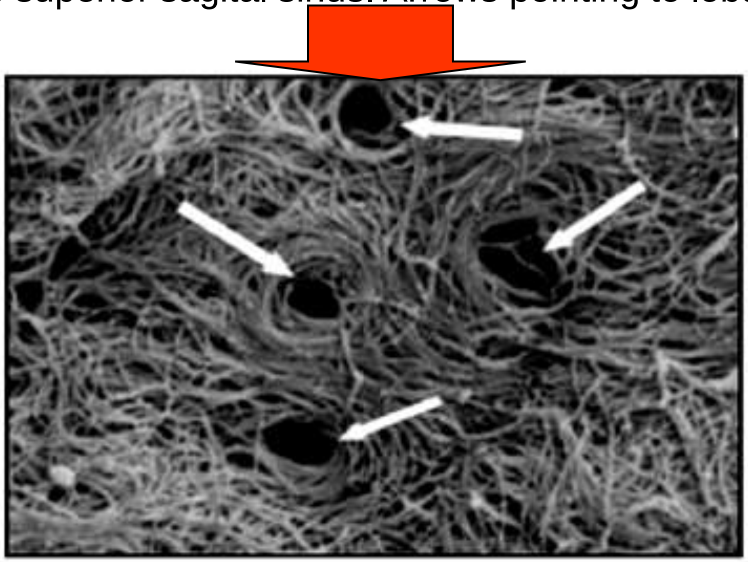




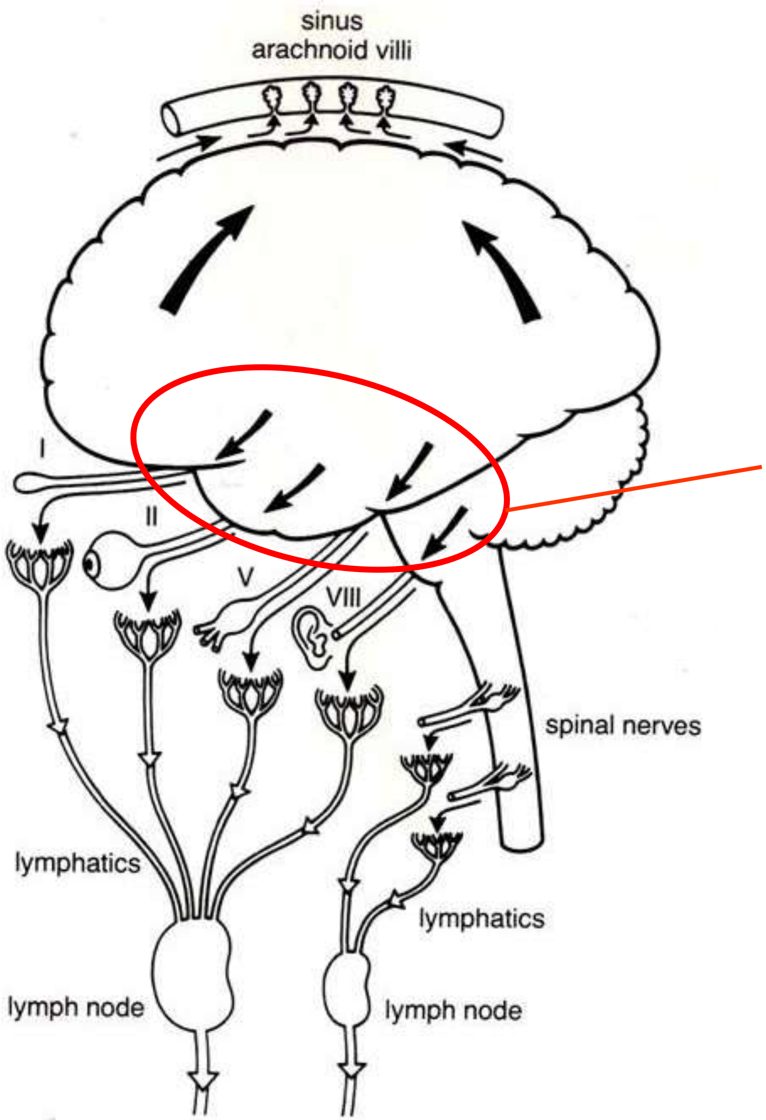
Electron Micrograph of clustered arachnoid granulations from the floor of the superior sagital sinus. Arrows pointing to lobules

Inflammation of the arachnoid villi as one mechanism inhibiting resorption?

Electron micrograph of outer arachnoid granulation- apical region- showing collagen fibers surrounding the pores and linking the granulations



Blocked Lymphatic Drainage of CSF



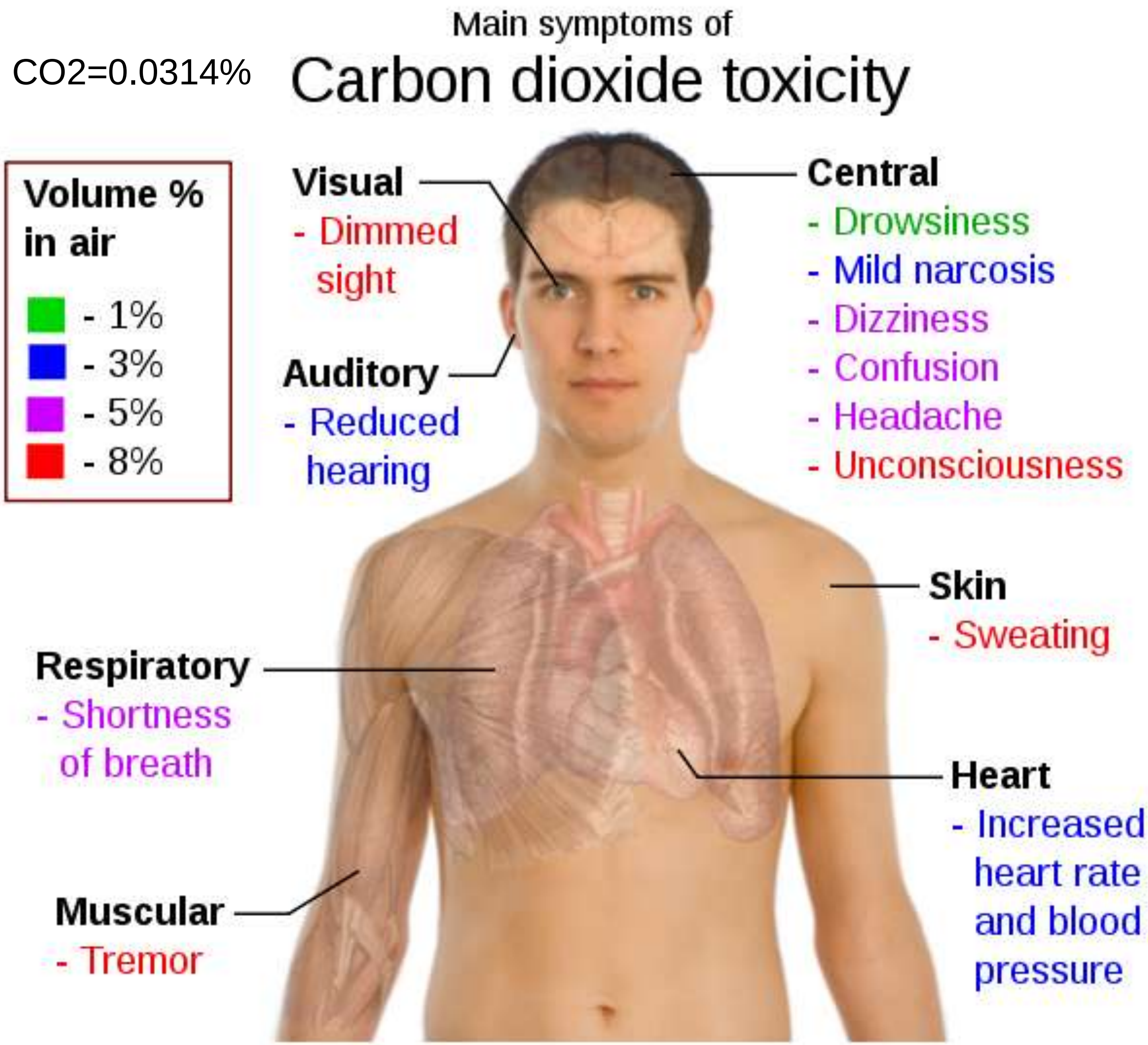
Perineural pathways along cranial nerves for subarachnoid CSF-lymphatic connections may become congested decreasing absorbtion (thin curved arrows)
Low pressure system

Exacerbating Factors?

Strength training may cause potentially damaging transient spikes in ICP

Carbon Dioxide

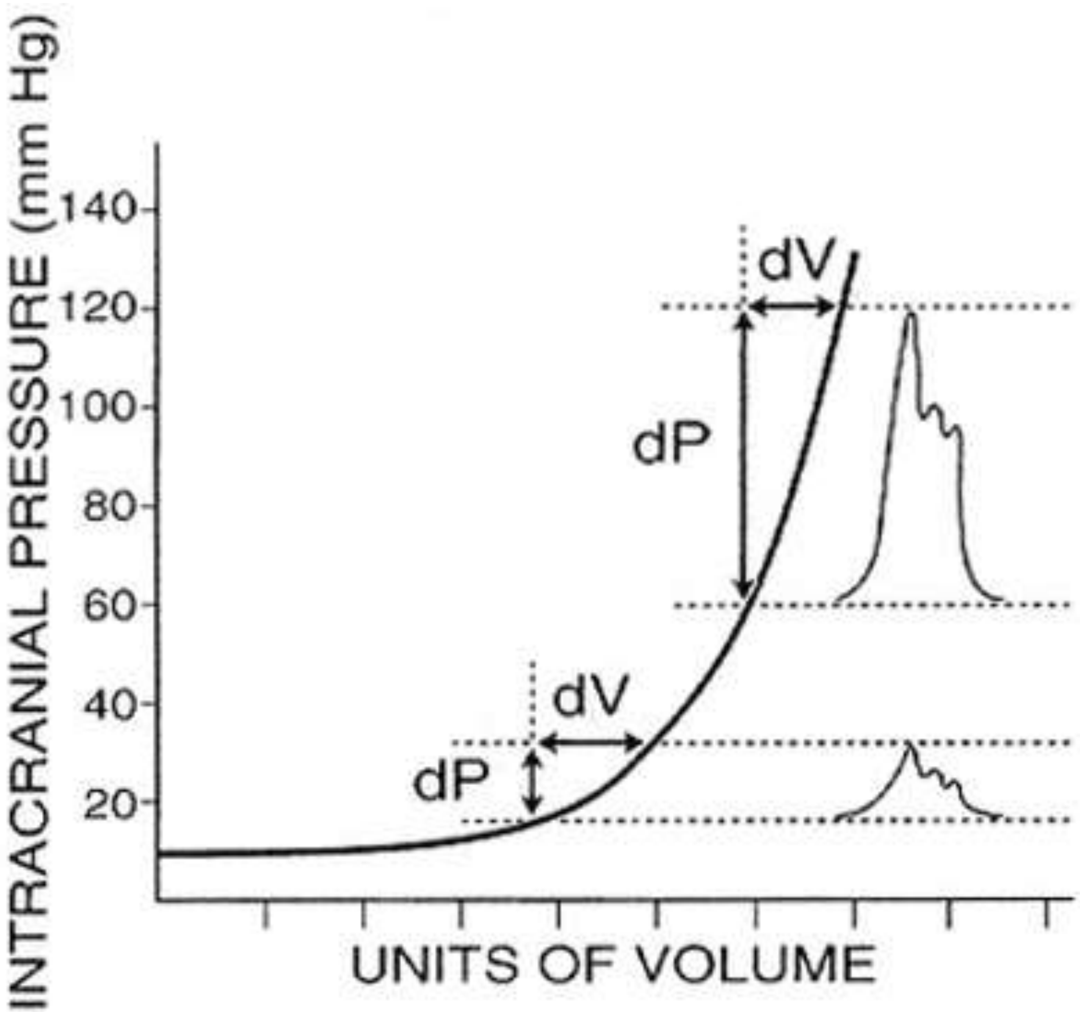
Normal Sea Level CO_2=0.0314%



CO2 on ISS

- CO2 level mission average=3.56mmHg (0.33%)
  - Ten times normal atmospheric
  - (Normal sea level atmospheric CO2=0.0314%)
- No mission under 2.0mmHg
- Average Peak CO2=8.32mmHg (0.7%)
- CO_2 potent vasodilator
- Cerebral CO_2 autoregulation not changed in microgravity.[1]
- Causes increased blood flow
  - Every 1mmHg increase PaCO2=4% increase in cerebrovascular dilation
  - Problem-cerebral blood vessels are already congested
  - Thought to be contributory to the symptoms occurring at lower levels.
  - Causes increased CSF production.

Compliance: Intracranial



CO2 Symptoms in Space

- Symptom onset 1.3-1.6mmHg
- Primarily noted to be headache and visual changes.
- When CO2 level dropped headaches dissipate
- Noted onset at levels far lower than terrestrially i.e.
- Mission Control personnel noticed behavioral changes had occurred at lower levels in crewmembers. Procedural errors, unwarranted comments from crewmembers, and increased “aggravation”
- EVA crewmembers “felt better” post initiation of Oxygen pre-breath and donning the suit (100% O_2 and 4.3 psi environment).

Pre-Flight MRID 1.10 (L-180 - L-30)
All Long Duration crew members

Previous

- Refraction
- Near and far visual acuity
- Tonometry
- Automated visual fields
- Dilated Fundoscopy
- Contact lens/spectacle storage plan
- Amsler Grid
- Retinal photography
- Extraoccular muscle examination
- Spectral domain optical coherence tomography (OCT)
- Pupil reflex
- Biomicroscopy
- A-Scan Ultrasound

Additional

- PanOptic video fundoscopy baseline and training
- 3T orbital MRI with contrast
- 2-D imaging ultrasound baseline and training

Red = currently performed as per existing MRID
Blue = currently performed, but are added to new MRID

In-Flight MRID 1.10 (L+30, R-30, L+100)
All Long Duration crew members

Previous

- None previously required per MRID

Additional

L+30 and R-30, potentially at L+100

- **Near and far visual acuity**
- **Amsler grid**
- **Questionnaire**
- **Tonometry**
- **Dilated PanOptic video fundoscopy exam**
- **Remotely guided HRF eye ultrasound**

Post-Flight MRID 1.10 (R+ 0- R+3 or ASAP) All Long Duration crew members

Previous

- Near and far visual acuity
- Tonometry
- Pupil reflex
- Extraoccular muscle examination
- Biomicroscopy
- Questionnaire
- Amsler Grid
- Dilated Fundoscopic exam
- Automated visual fields
- Refraction
- Retinal photography
- Spectral domain optical coherence tomography (OCT)
- A-Scan Ultrasound

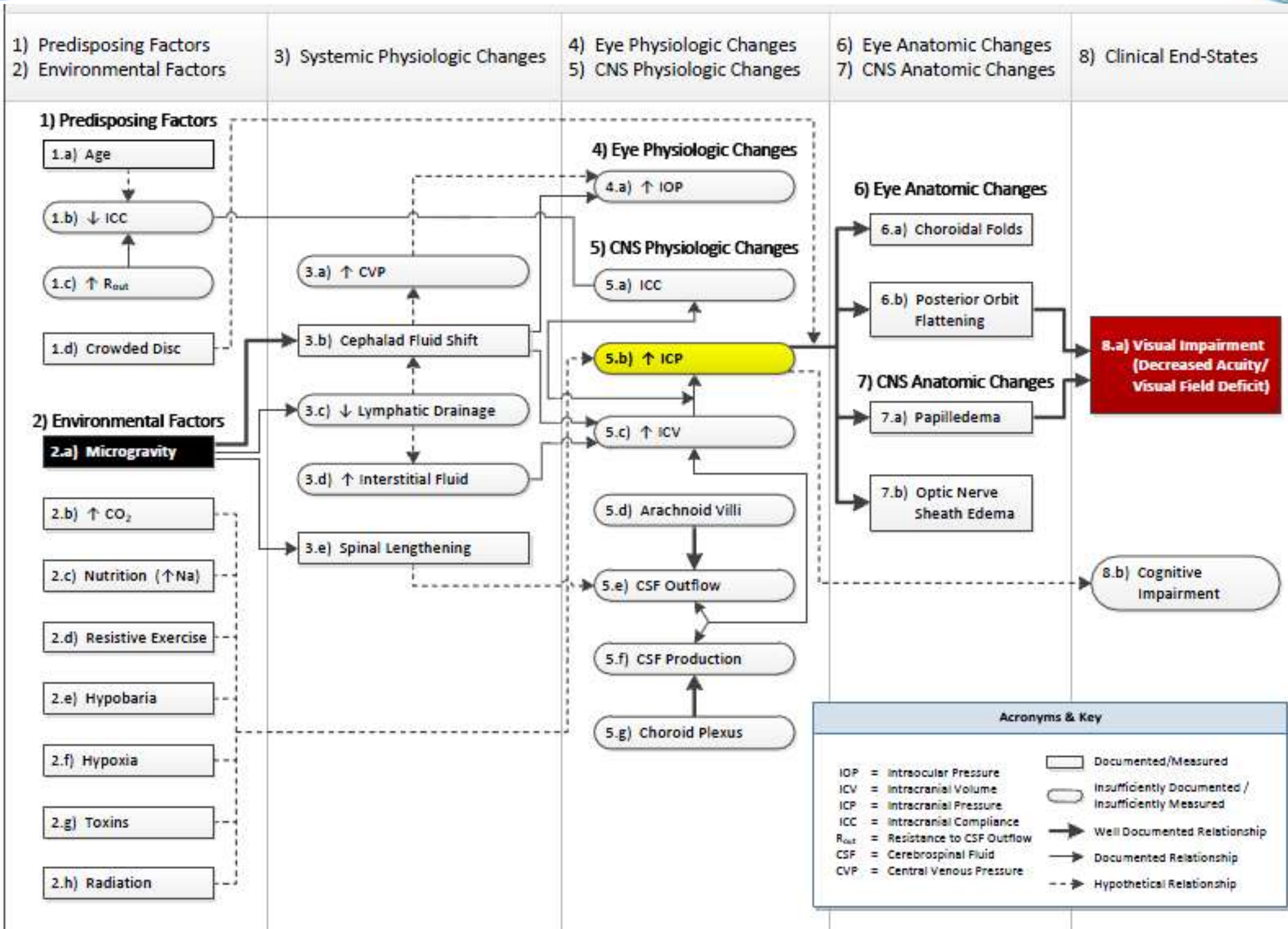
Red = currently performed as per existing MRID

Blue = currently performed, but are added to new MRID

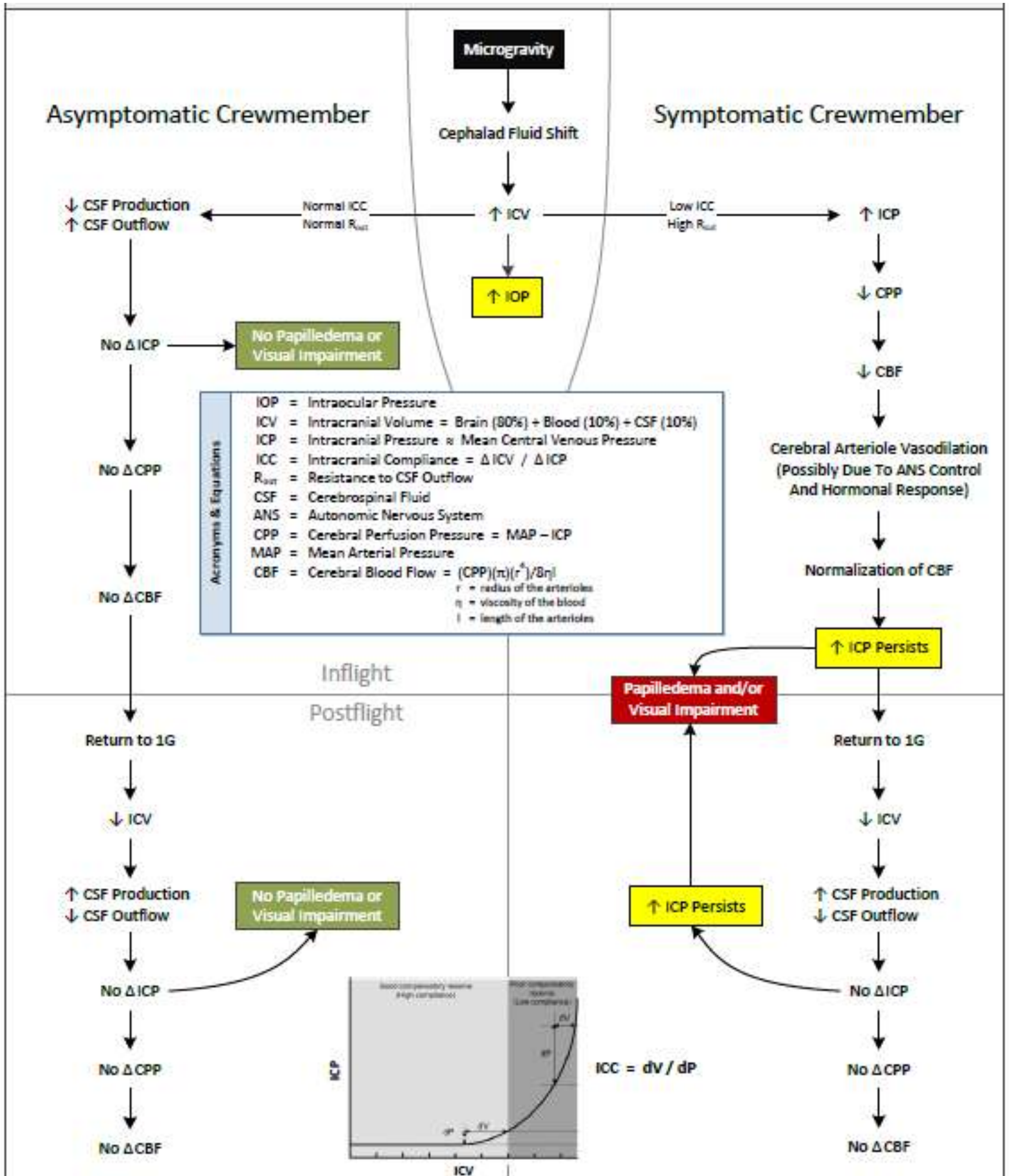
Additional

- 3T orbital MRI with contrast
- 2-D imaging ultrasound

Visual Impairment and Intracranial Pressure Flow Chart



Hypothesized Mechanisms of Cerebral Blood Flow Autoregulation Inflight and Postflight for Asymptomatic and Symptomatic Crewmembers



VIIP Knowledge Gaps

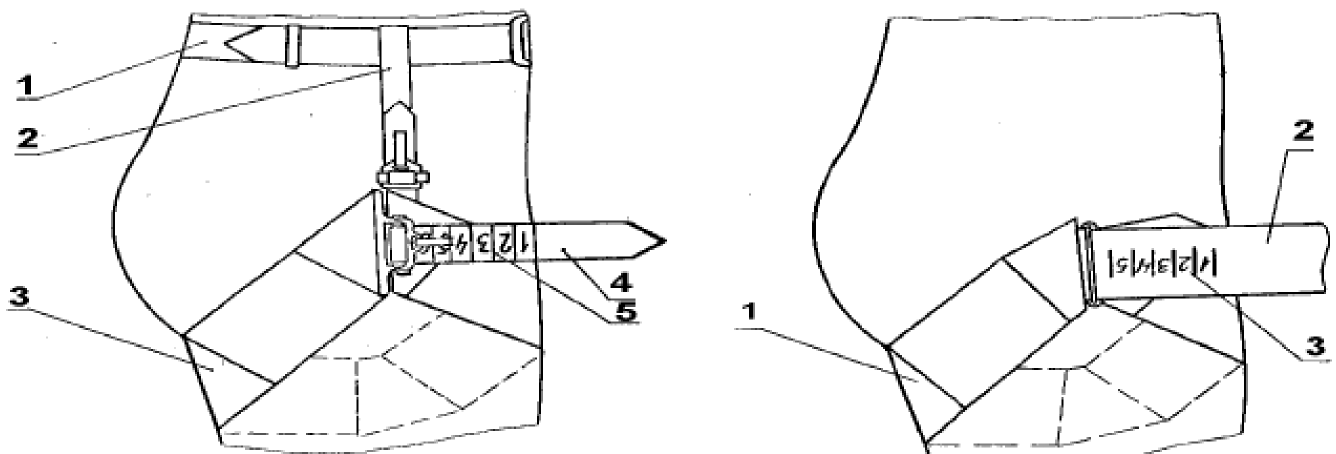
- Gaps (VIIP1) What is the etiology of visual acuity and ocular structural and functional changes seen in-flight and post-flight?
- Gap (VIIP2) Does exposure to microgravity cause changes in visual acuity, intraocular pressure and/or intracranial pressure? Are the effects related to mission duration?
- Gap (VIIP3) What in-flight diagnostic tools are needed to measure changes in intraocular pressure and intracranial pressure?
- Gap (VIIP4) Are changes in visual acuity related to changes in chronic choroidal engorgement, elevated intraocular pressure and/or intracranial pressure? Gap
- (VIIP5) Do multiple or cumulative exposures to spaceflight increase the risk of changes in visual acuity, intraocular pressure or intracranial pressure?
- Gap (VIIP6) How do changes in vascular compliance/pressures influence intraocular pressure or intracranial pressure?
- Gap (VIIP7) Is intracranial hypertension and visual impairment an all or nothing phenomenon or a continuum of severity that occurs in all individuals during spaceflight?

VIIP Knowledge Gaps

- Gap (VIIP8) What is the role of the ISS environment (e.g. high salt diet, CO_2 pockets, pharmaceutical use, exercise countermeasures) on ocular structure and function and intracranial pressure?
- Gap (VIIP9) What is the time course for recovery of intracranial hypertension and visual impairment and do anatomical structures of the eye recover? What factors determine the rate of recovery?
- Gap (VIIP10) Are asymptomatic crewmembers with anatomic eye changes or low grade intracranial hypertension at risk for future visual impairments?
- Gap (VIIP11) Does long-term, low grade intracranial hypertension predispose individuals to disease processes other than what manifests in the eye?
- Gap (VIIP12) Are there suitable ground-based analogs to study this spaceflight-associated phenomenon?
- Gap (VIIP13) Can safe and effective countermeasures be designed (in-flight and post-flight) to mitigate changes in visual acuity, intraocular pressure and intracranial hypertension if a problem it exists?

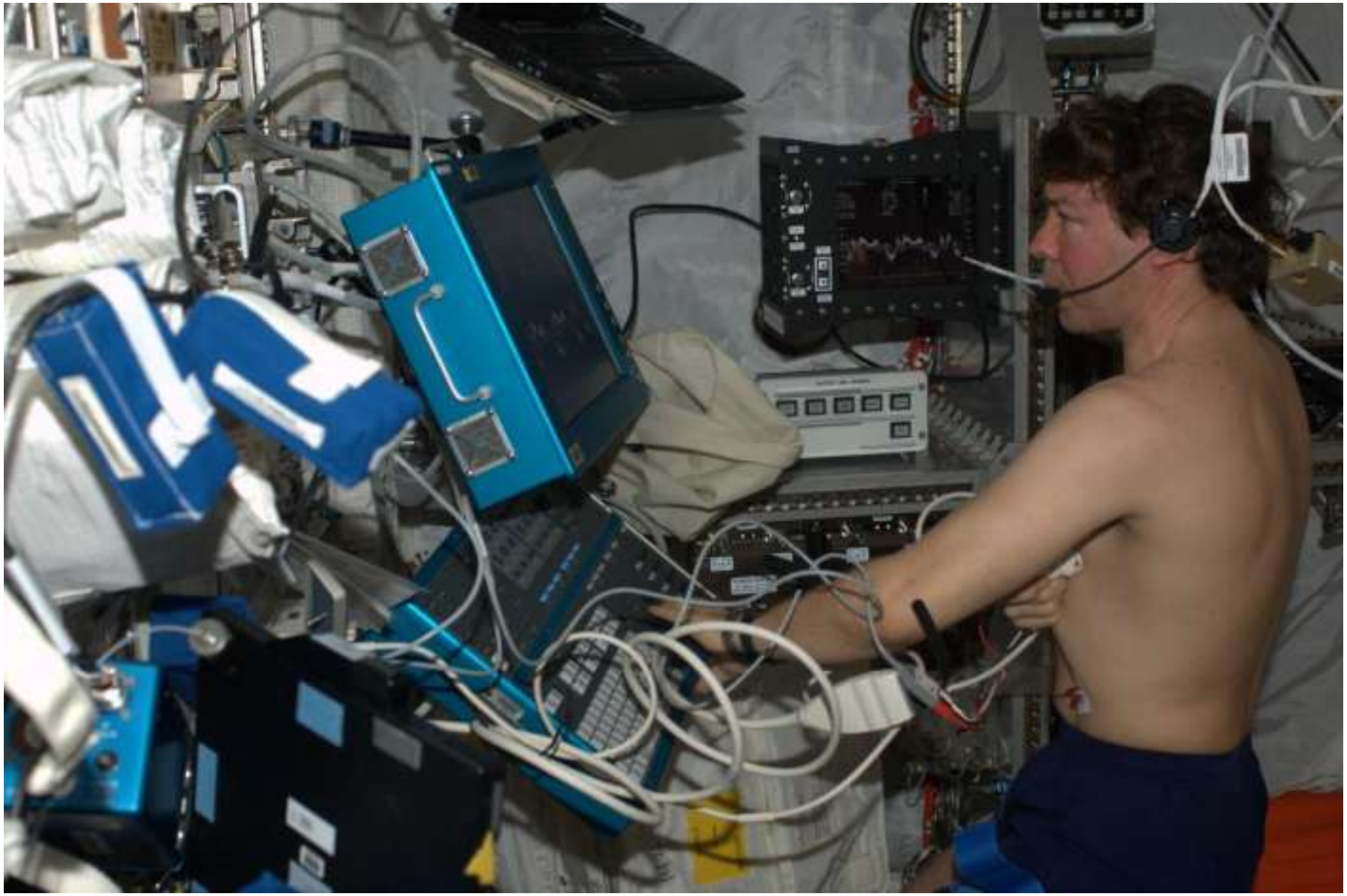
Forward Research-Possible Countermeasures: Braslet

Рис. 3.12 Браслет-М

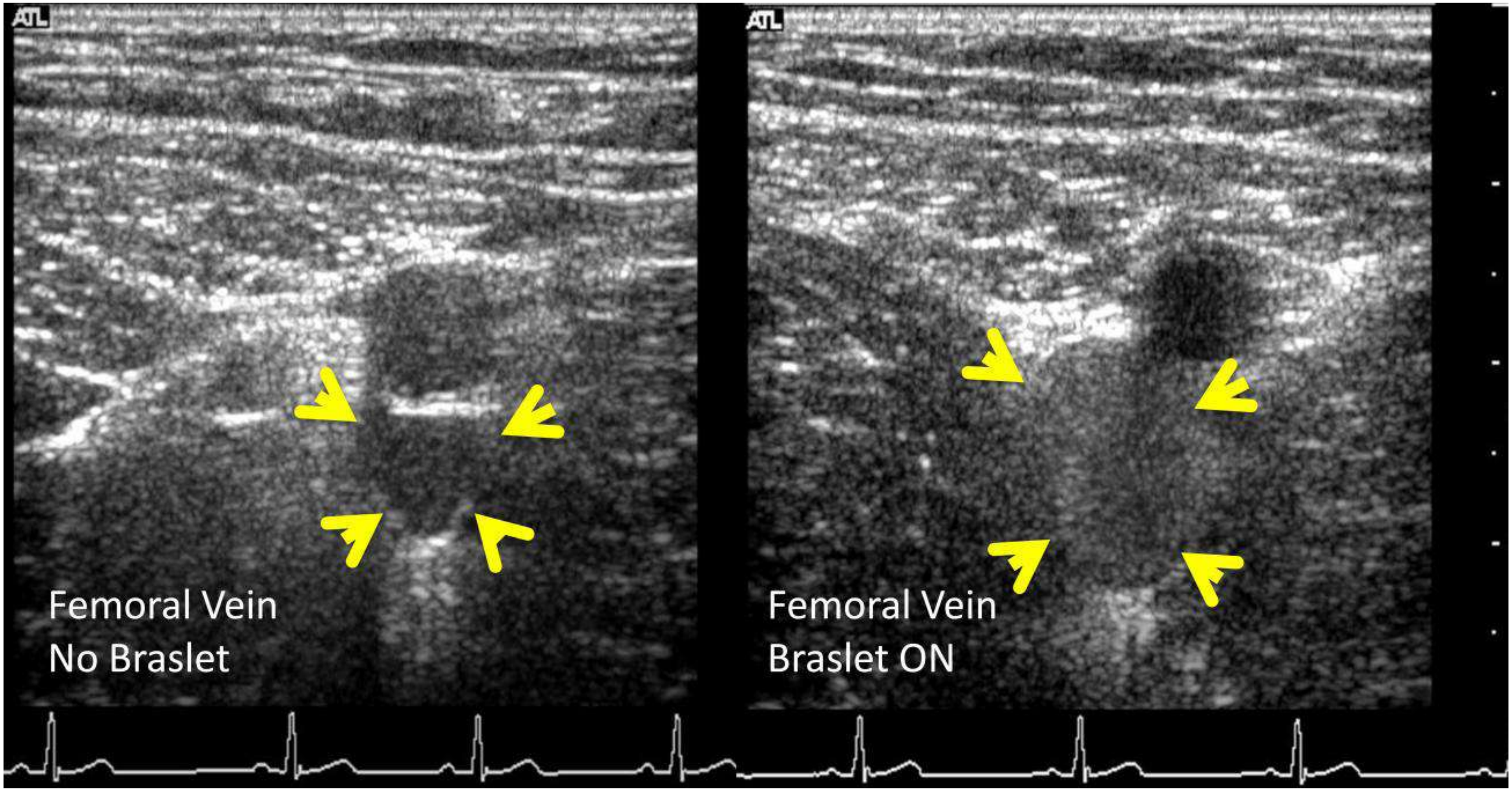


Braslet (left): 1 – belt; 2 – pull-up strap; 3 – compression cuff; 4 – tightening strap; 5 – compression scale
Braslet-M (right): 1 – compression cuff; 2 – tightening strap; 3 – compression scale

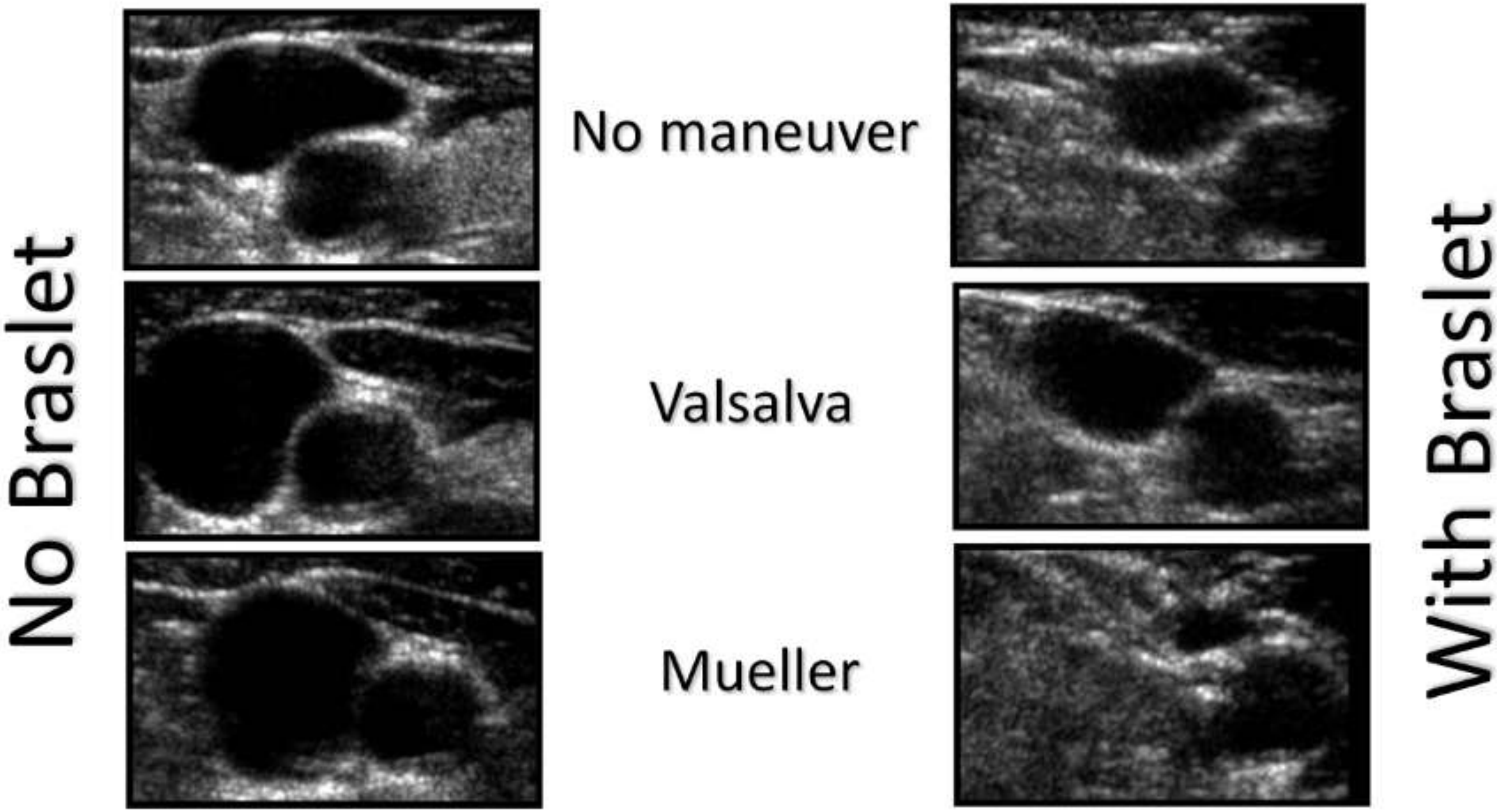
Russian-US ISS Braslet Study



Femoral Vein Images with and without Braslet Applied



Internal Jugular Vein vs Breathing Manouvers With & Without Braslet



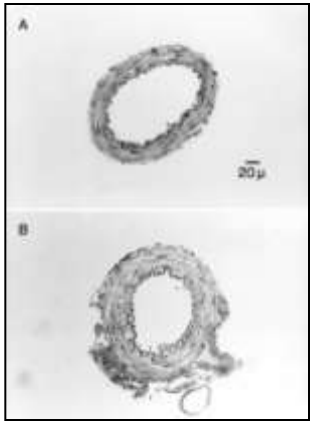
Internal jugular vein cross sections with and without Braslet applied, with breathing maneuvers: With Braslet application the internal jugular vein responds to Valsalva with smaller changes, and with Mueller maneuver the vein almost completely collapses.

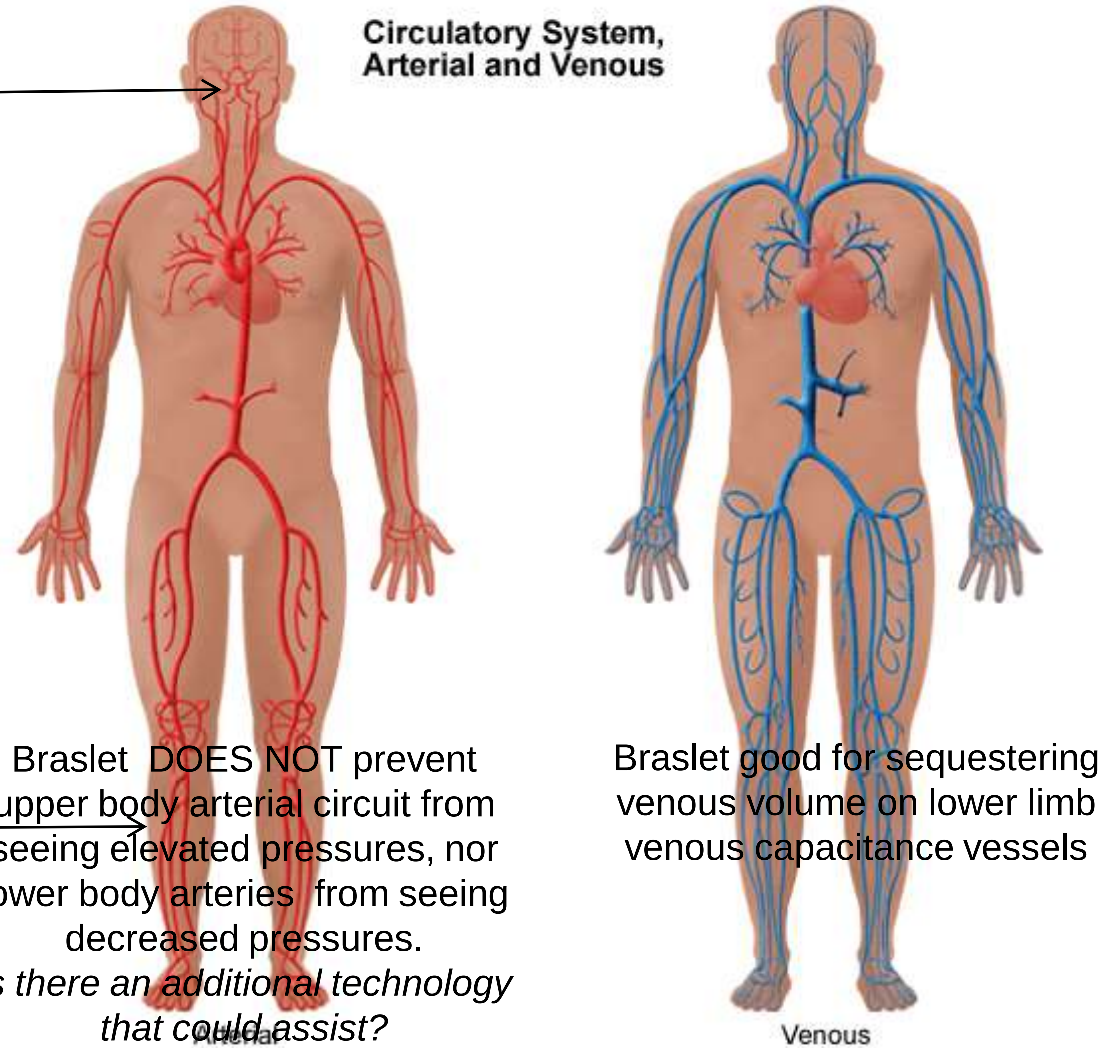
Combining Countermeasures?

Aerobic exercise may be protective as it draws cephalad fluid caudally into lower limbs

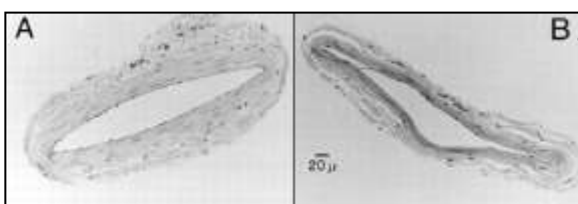
Countermeasures for Arterial *and* Venous Circuits?

Rat Basilar Artery:
A. Control
B. 14d Hindlimb Unloaded
Cerebral artery Hypertrophies with Cephald fluid shift





Rat Hindlimb Skeletal Artery:
A. Control
B. 14d Hindlimb Unloaded
Hindlimb skeletal artery artrophies with Cephald fluid shift



Braslet DOES NOT prevent upper body arterial circuit from seeing elevated pressures, nor lower body arteries from seeing decreased pressures.
Is there an additional technology that could assist?

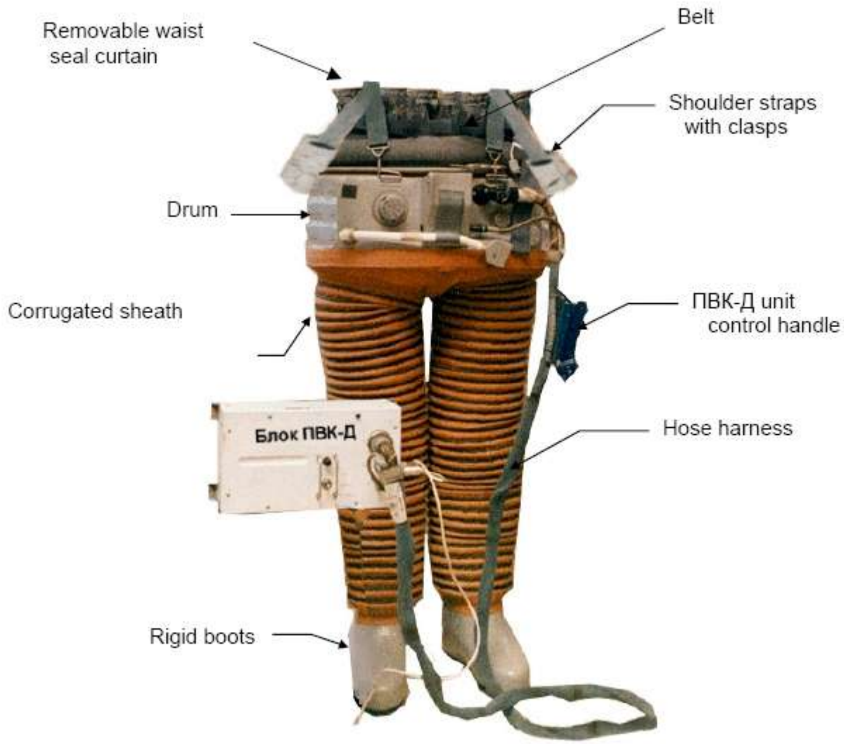
Braslet good for sequestering venous volume on lower limb venous capacitance vessels

Chibis LBNP Device

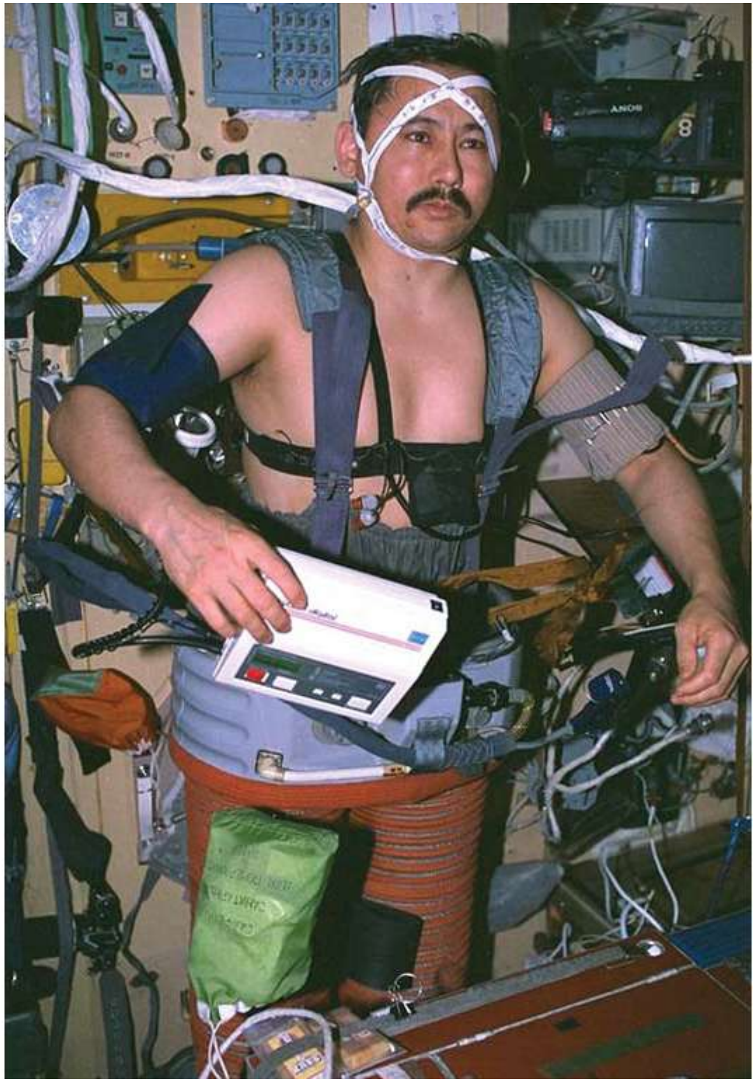
ISS008E21918

Chibis LBNP Device

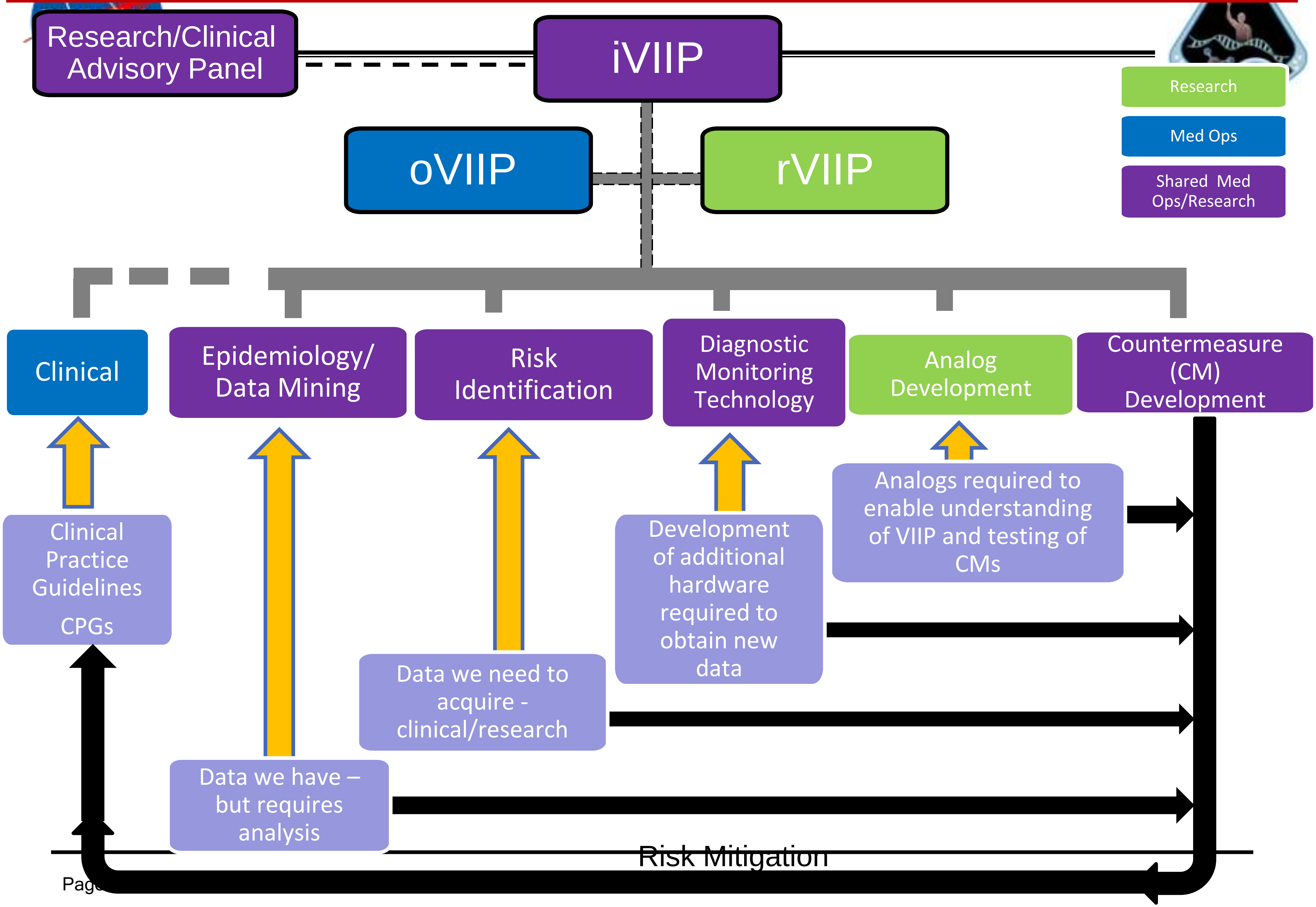
Components:
- Chibis suit (ПВК-1)
- Chibis suit pressure control unit (ПВК-Д)
- Hose harness in kit
- ПВК-1 removable waist seal curtain in kit



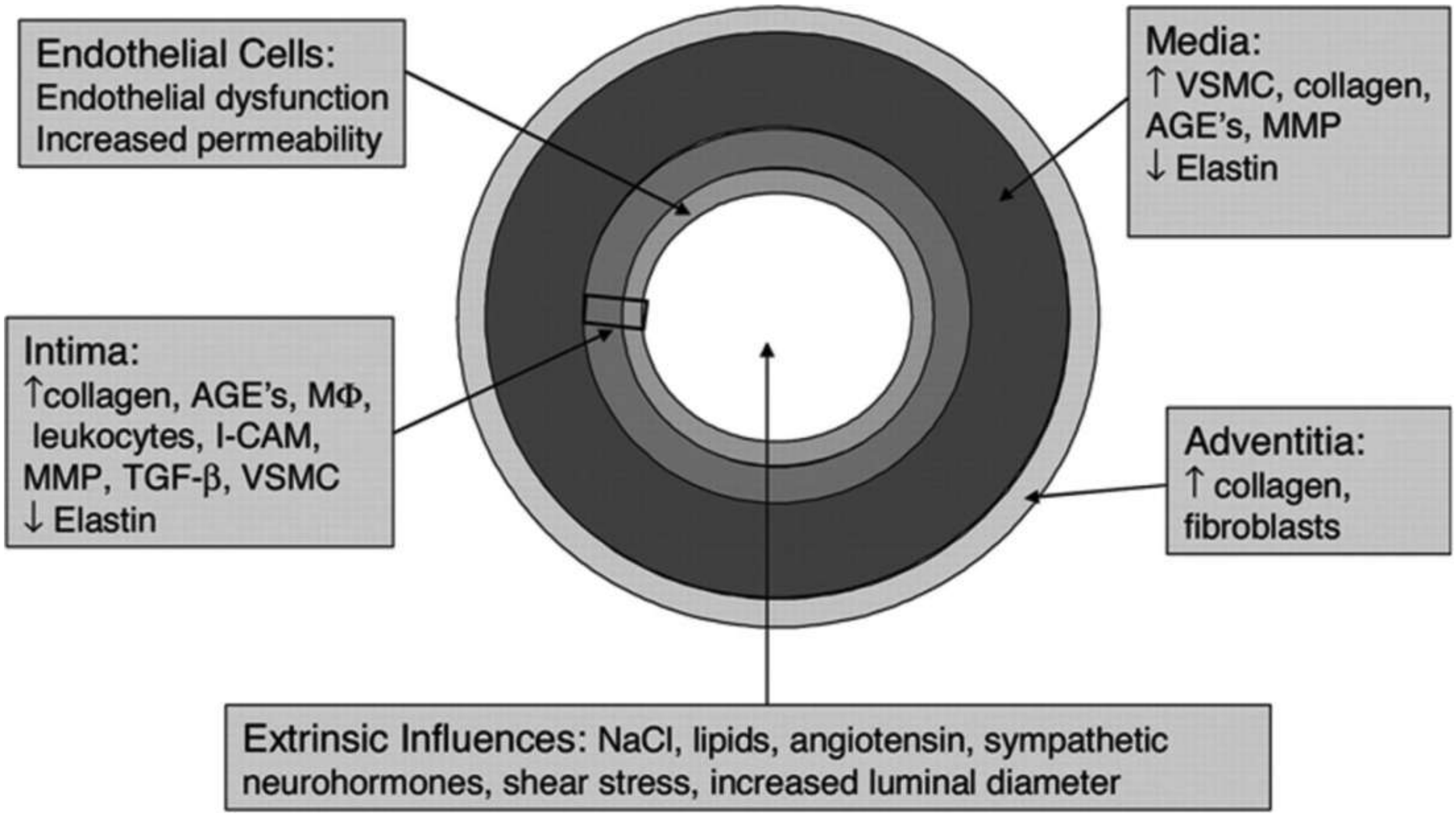
Chibis Suit (ПВК-1)



VIIP Project Structure

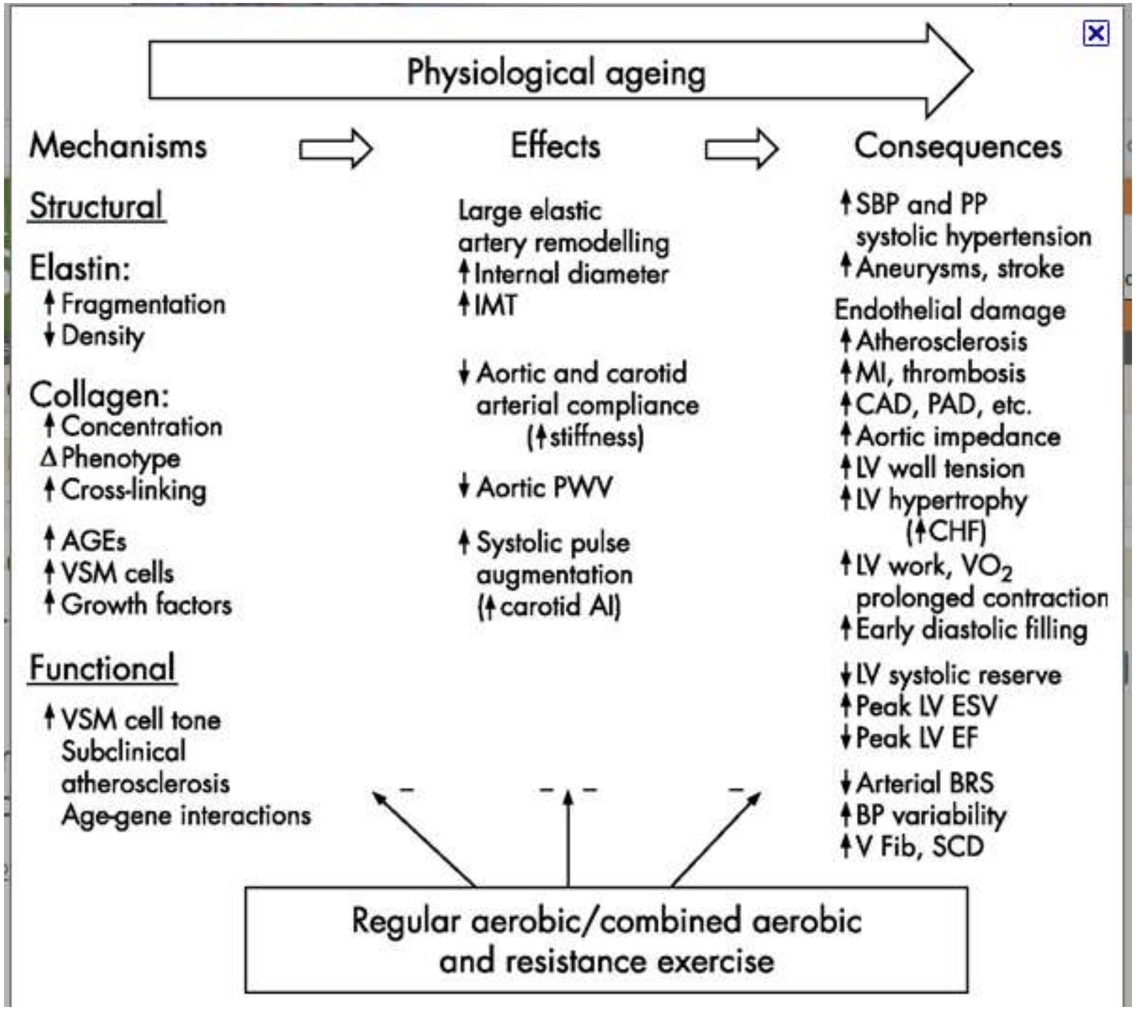


Compliance: Vascular

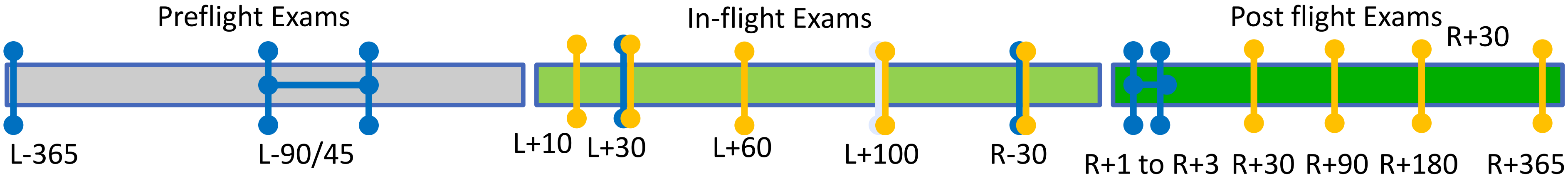


Preliminary review of data for affected crew members reveals that blood pressure, serum lipids and homocysteine may be elevated compared to those non-affected. Also, maximal aerobic oxygen uptake may be lower in those affected.

Exercise Protective?



Proposed Pre/In/Post-Flight VIIP Research Testing



New Tests for consideration

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
- Vascular Compliance

L+30 & R-30, L+100 if requested (+/- 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)

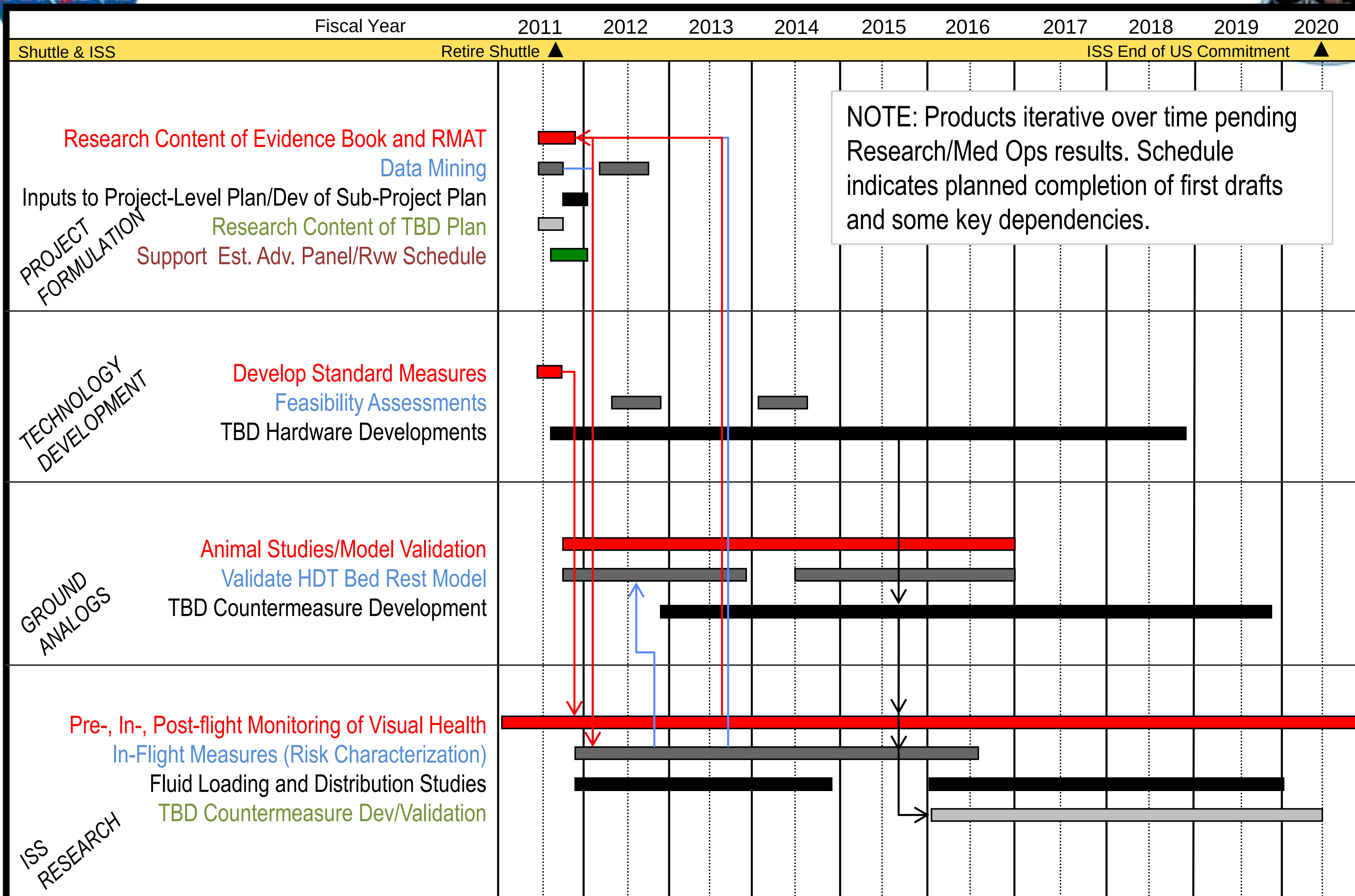
- MRI Of Brain and Orbits Without Contrast
- Ultrasound Eye/Orbit
- Vascular Compliance
- Fundoscopy - PanOptic Ophthalmoscope
- Tonometry
- Visual Acuity Including Amsler Grid Testing
- Other Tests - biomicroscopy (slit lamp), high resolution retinal photography, OCT (high resolution), and

Proposed In-Flight VIIP Data Collection Sequence Per Increment Time Point

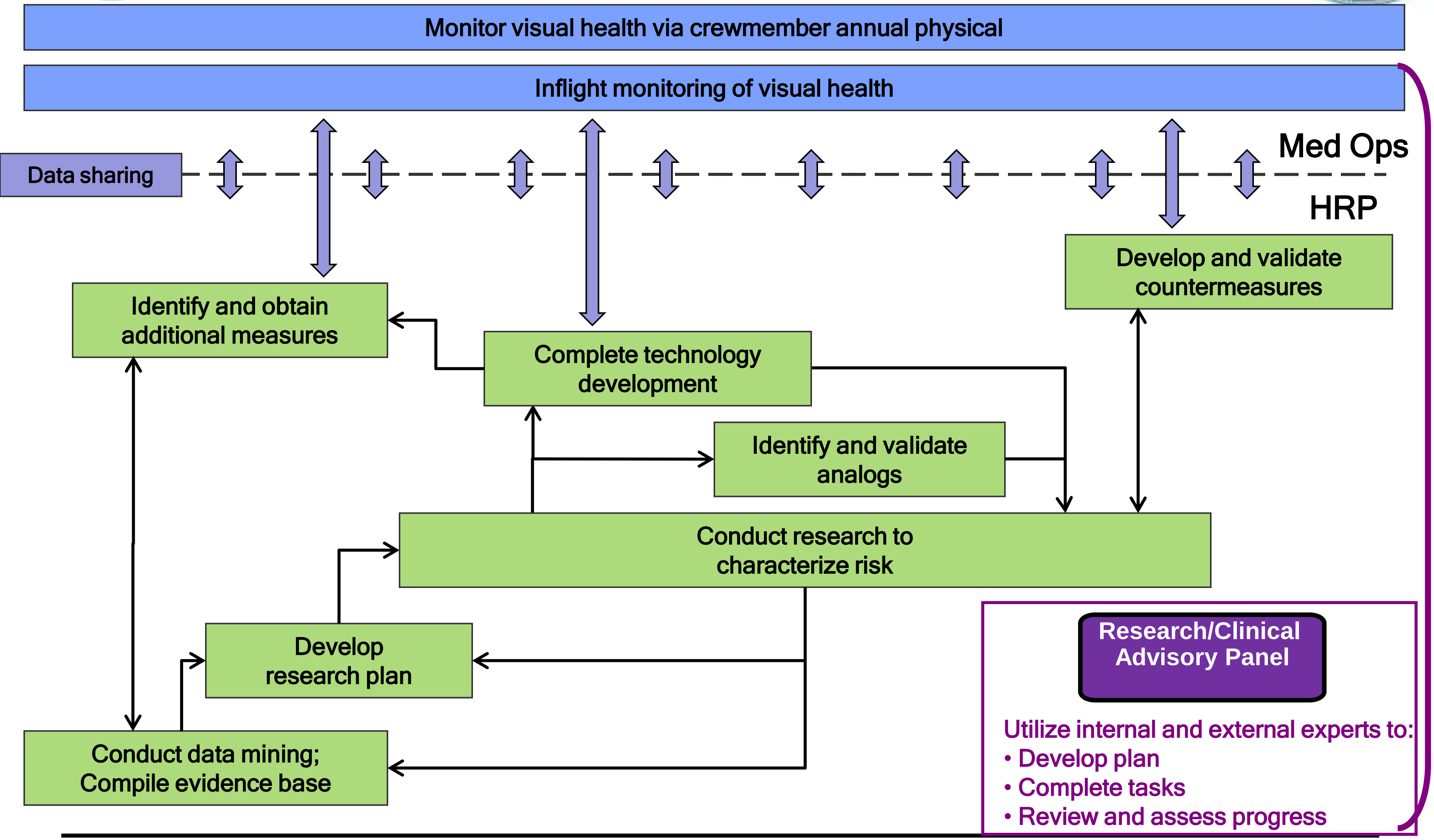
	Data Collection Per Increment Time Point (L+10, L+30, L+60, L+100, L-30)			
	Day 1	**Time**	**Day 2 or 3**	**Time**
Data Collection Measures	ManualCuff BP	7min	ManualCuff BP	7 min
	Visual Acuity	5 min	Visual Acuity	5 min
	Amsler Grid	5 min	Amsler Grid	5 min
	PanOptic Retinal Imaging	45 min	IOP Tonometry	20 min
			ManualCuff BP	7 min
			Cardiac Echo measures	5 min
			Ocular Ultrasound	35 min
	Total Time:	1:02 Hours	Total Time:	1:24

Real-time Guidance

VIIP Schedule Summary



VIIP Risk - Research Approach



Summary

- Background
- Ocular Findings
- Cephalad Fluid Shift
- Current Methodologies
- Cases
- Contributing Structures of the Eye
- CSF Production
- CSF Resorption
- Exacerbating Factors
- Current Measures
- Draft Research Plan
- Opportunities for Partnership

Informational Briefing:

Risk of Microgravity-Induced Visual Impairment and Elevated Intracranial Pressure (VIIP)

Wednesday May 25, 2011.

Christian Otto, M.D., VIIP Project Scientist