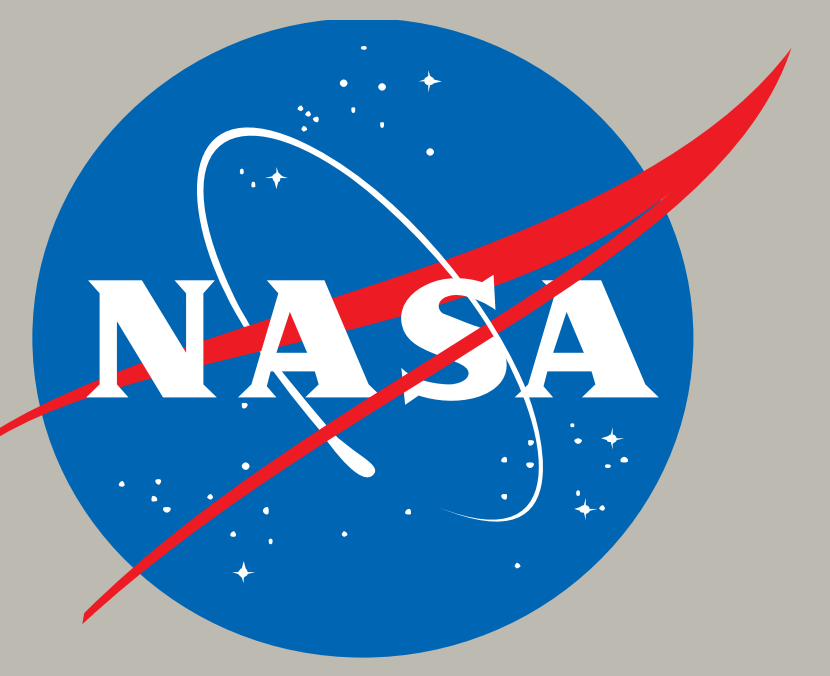


THE VISUAL IMPAIRMENT INTRACRANIAL PRESSURE SYNDROME IN LONG DURATION NASA ASTRONAUTS: AN INTEGRATED APPROACH



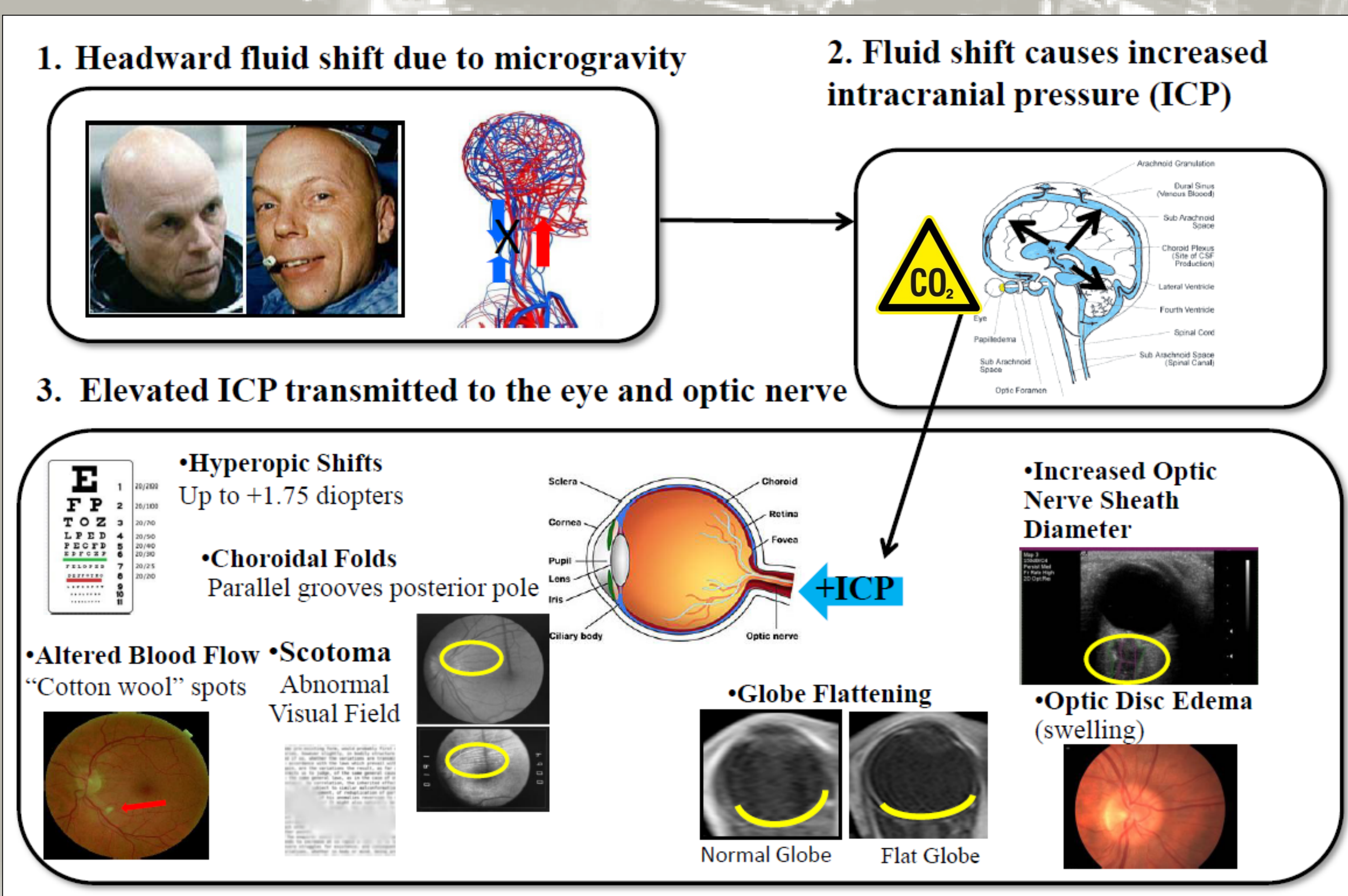
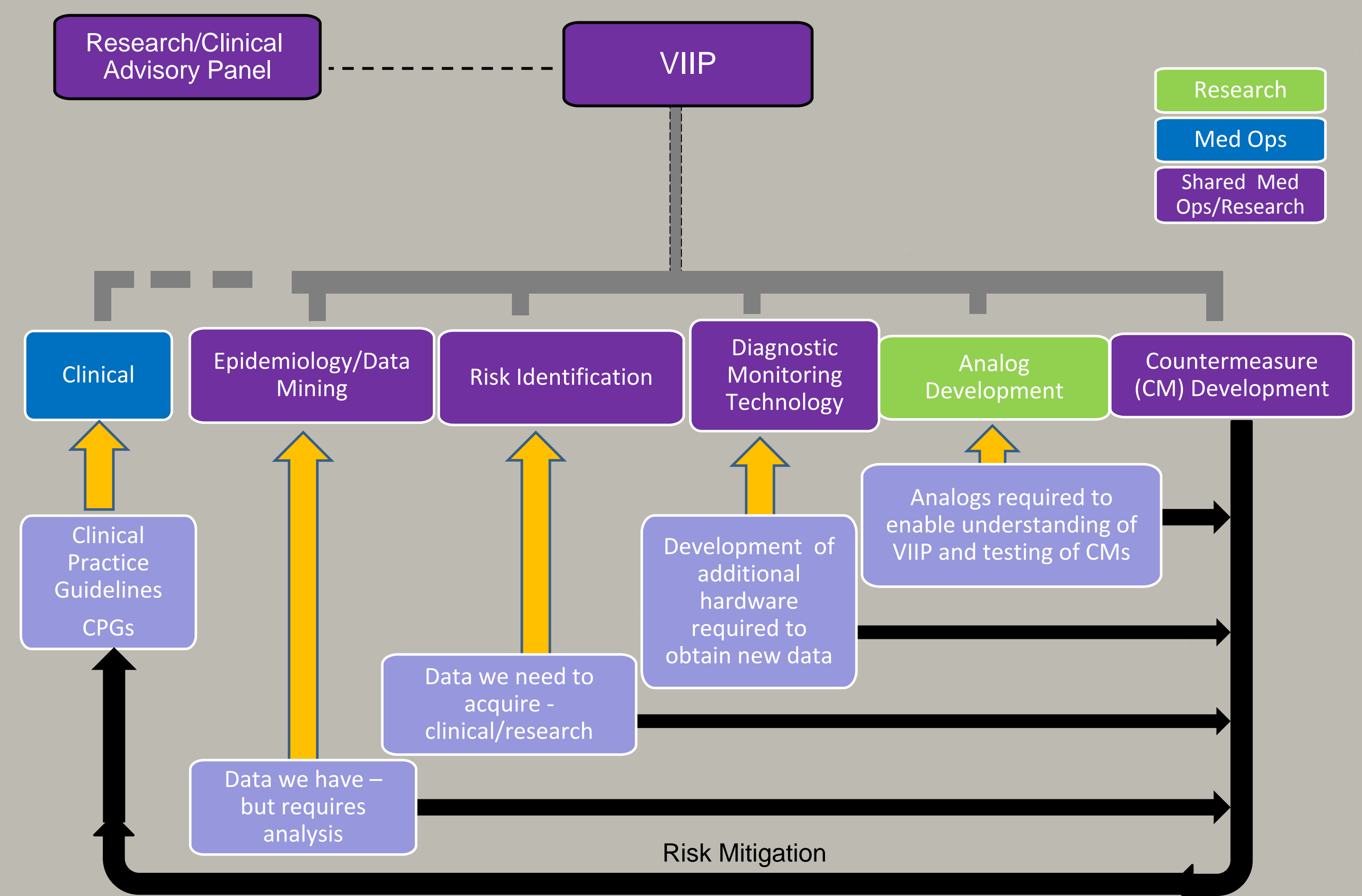
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INTRODUCTION

The Visual Impairment Intracranial Pressure (VIIP) syndrome is currently NASA's number one human space flight risk. The syndrome, which is related to microgravity exposure, manifests with changes in visual acuity (hyperopic shifts, scotomas), changes in eye structure (optic disc edema, choroidal folds, cotton wool spots, globe flattening, and distended optic nerve sheaths). In some cases, elevated cerebrospinal fluid pressure has been documented postflight reflecting increased intracranial pressure (ICP). While the eye appears to be the main affected end organ of this syndrome, the ocular affects are thought to be related to the effect of cephalad fluid shift on the vascular system and the central nervous system. The leading hypotheses for the development of VIIP involve microgravity induced head-ward fluid shifts along with a loss of gravity-assisted drainage of venous blood from the brain, both leading to cephalic congestion and increased ICP. Although not all crewmembers have manifested clinical signs or symptoms of the VIIP syndrome, it is assumed that all astronauts exposed to microgravity have some degree of ICP elevation in-flight. Prolonged elevations of ICP can cause long-term reduced visual acuity and loss of peripheral visual fields, and has been reported to cause mild cognitive impairment in the analog terrestrial population of Idiopathic Intracranial Hypertension (IIH). These potentially irreversible health consequences underscore the importance of identifying the factors that lead to this syndrome and mitigating them.

VIIP Project Structure



Images courtesy of NASA.

Suspected pathophysiological mechanisms leading to VIIP clinical manifestations.

- 1) Cephalad fluid shifts and loss of gravity assisted venous drainage from the brain leads to:
- 2) increased ICP, which is manifested with:
- 3) Structural and functional changes to the eye.

Current U.S. ISS VIIP Incidence:

51 U.S. ISS astronaut missions:
 - Unclassified astronauts N=15 (No MRI, OCT or ocular US)
 - Known non-cases: N= 9 (26%)
 - Confirmed cases: N= 27 (75%)

Classification of Cases:
 - Class One: 6%
 - Class Two: 50%
 - Class Three: 8%
 - Class Four: 11%
 - Disc edema cases

56% Class 1&2
 19% Class 3&4

Increasing severity

Current VIIP Incidence as a % of U.S. ISS astronauts tested= 75%

Males: 81%; Females: 56%

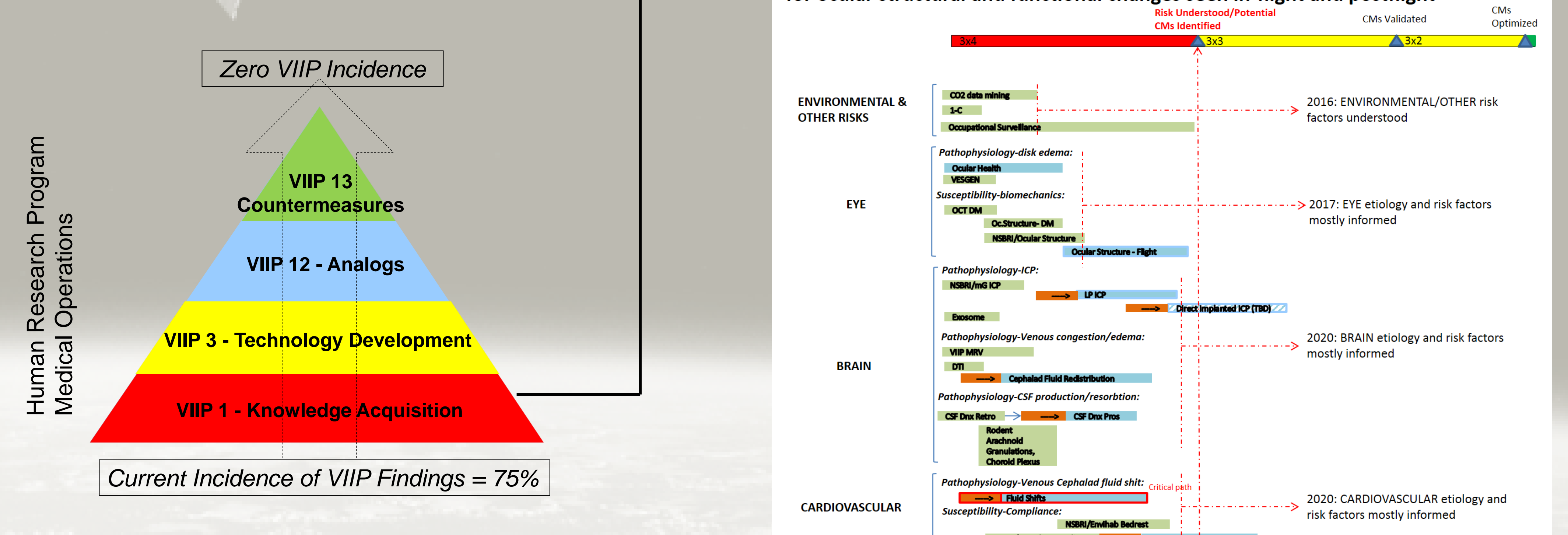
Additionally findings appear less severe in females

VIIP Research Case Definition

- Class 1** ≥ .50 diopter cycloplegic refractive change and/or cotton wool spot
- Class 2** ≥ .50 diopter cycloplegic refractive changes or cotton wool spot
 • Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma
- Class 3** ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot
 • Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma
 • Papilledema of Grade 0-2
- Class 4** ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot
 • Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma
 • Papilledema Grade 2 or above
 • Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations
 • CSF opening pressure >25 cm H₂O

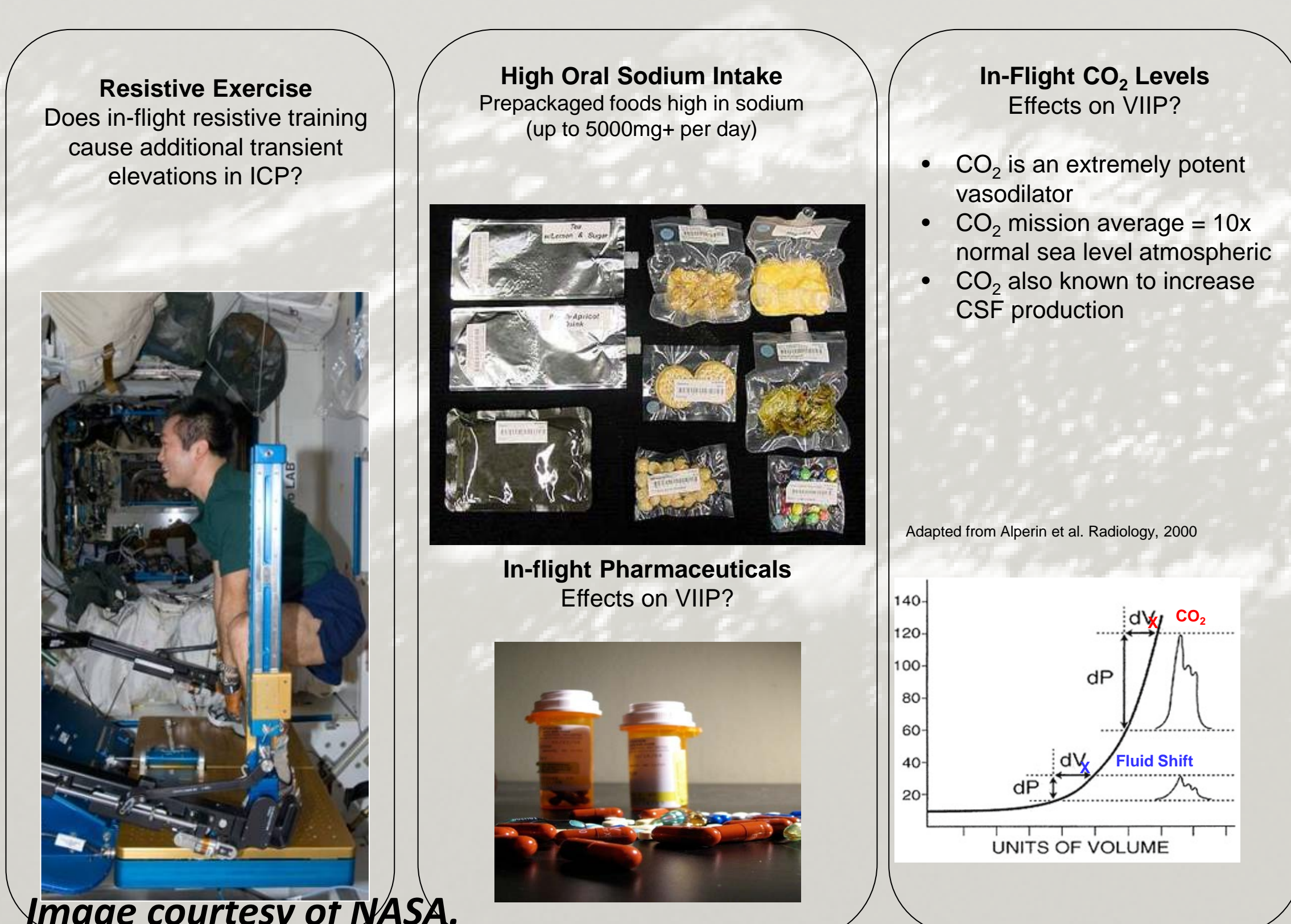
NASA's Human Research Program, via the Human Health and Countermeasures Element, has established the VIIP Research Project, which is investigating etiology, technology, analogs, and potential countermeasures encompassing over 70 current, planned, and completed studies, of which about 25 are currently in progress. These studies are aimed at understanding the interaction of the microgravity environment with the ocular, cardiovascular, and central nervous systems.

The VIIP Research Plan

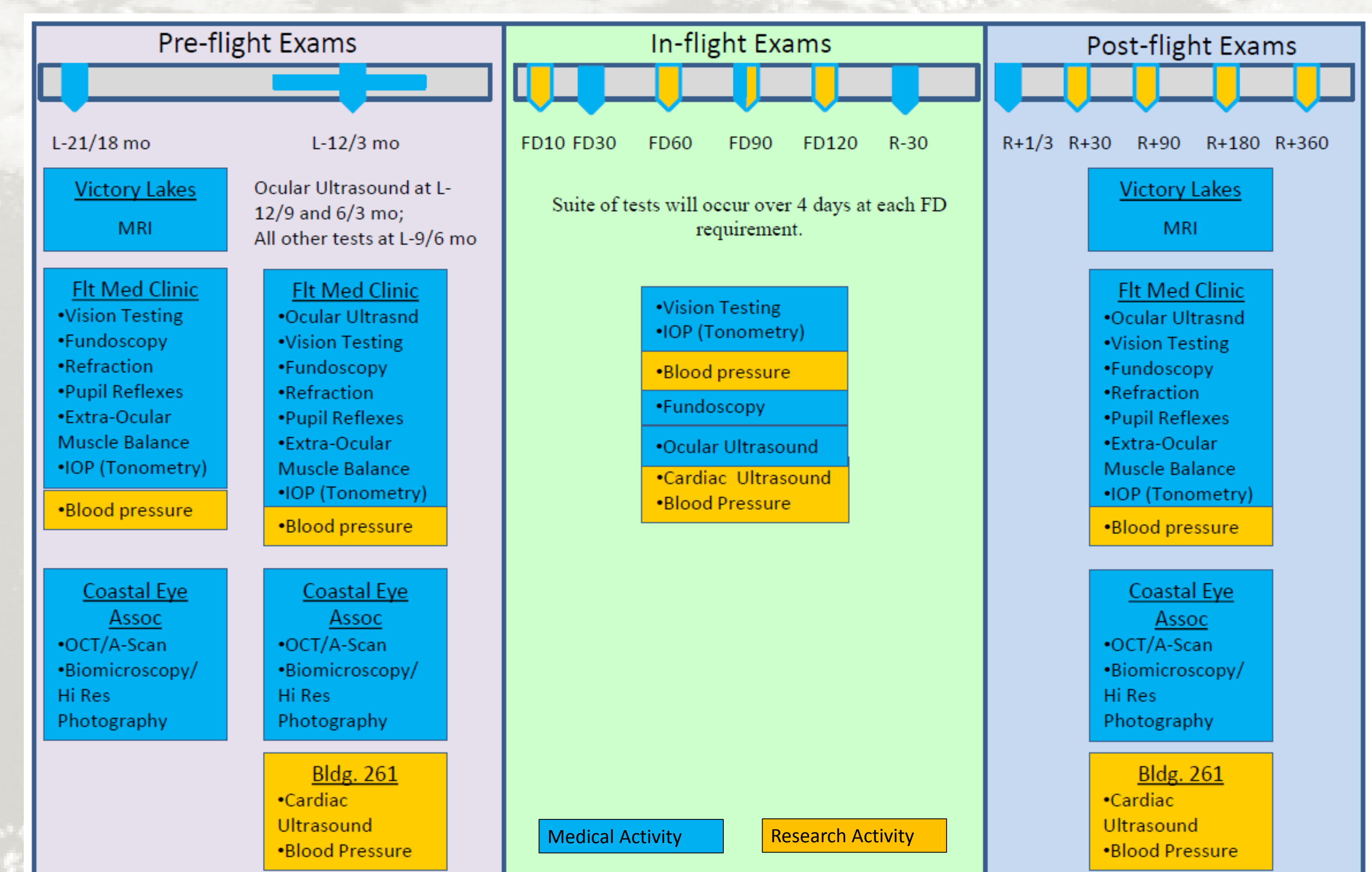


The operational and research communities at NASA are working collaboratively in an effort to understand the mechanisms causing the VIIP syndrome and to provide mitigation and countermeasures. The Medical Operations division (MedOps) has instituted extensive preflight, in-flight and postflight testing as part of occupational surveillance. Pre- and postflight tests include functional eye exams (vision testing), structural eye exams (fundoscopy, ocular ultrasound, optical coherence tomography [OCT] and biomicroscopy), intraocular pressure (tonometry), and eye, brain, and cerebrovascular anatomy via magnetic resonance imaging (MRI). The Ocular Health study, a prospective investigation, aims to define the temporal pattern for the appearance of signs and symptoms, delineate the association between duration of weightlessness and severity of symptoms (i.e., the dose-response), establish preflight baseline characteristics, characterize the nature of in-flight changes, and document changes from pre to postflight. The study expands upon in-flight medically required data collection with the addition of additional time points, cardiovascular compliance (via ultrasound with concurrent ECG and blood pressure), and noninvasive intracranial pressure (via pulsatility index, measured by transcranial Doppler [TCD]).

The integrated VIIP program that has been developed includes efforts to decrease environmental contributing factors such as elevated carbon dioxide levels onboard the ISS and sodium levels in space foods (operational efforts), development of Clinical Practice Guidelines for guiding diagnosis and treatment of affected crewmembers (clinical efforts), data mining of previously collected data to find patterns of susceptibility to VIIP development (occupational surveillance efforts), and a research program which includes flight studies, bed rest studies, animal studies, and studies on analogous terrestrial populations to elucidate the underlying mechanisms leading to VIIP, evaluate technologies to allow safe invasive and noninvasive intracranial pressure measurements, and test potential countermeasures (research efforts).



Potential In-Flight Exacerbating Factors



The Prospective Observational Study of Ocular Health in ISS Astronauts



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