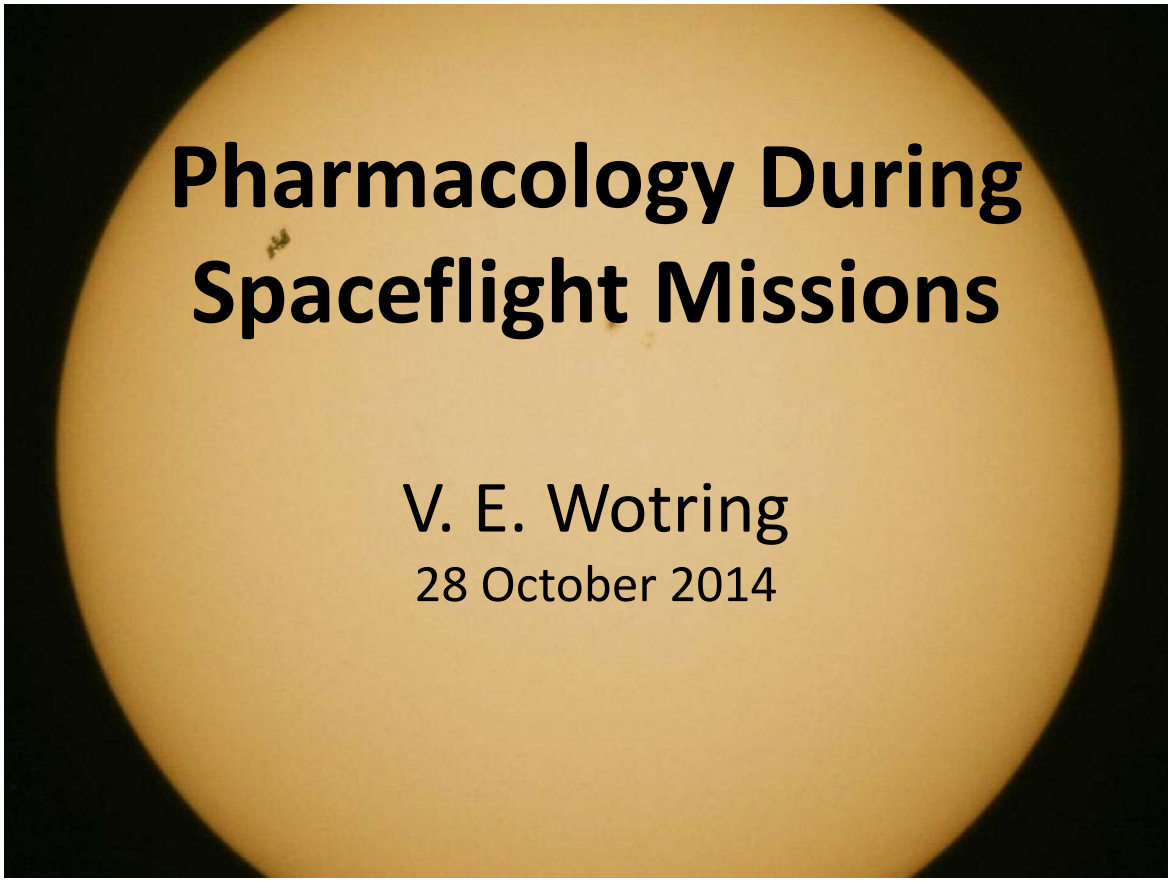


Pharmacology During Spaceflight Missions

V. E. Wotring

28 October 2014

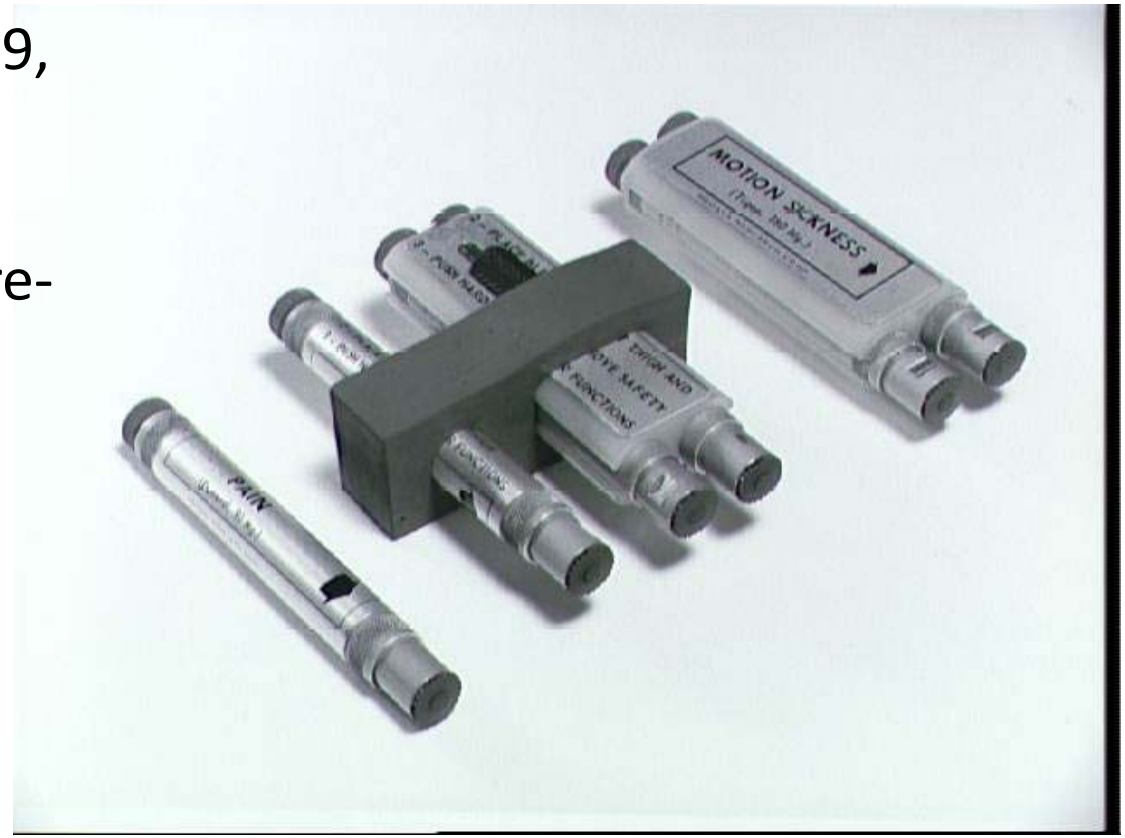
NASA has a Pharm lab?

First pharmaceuticals in US spaceflight

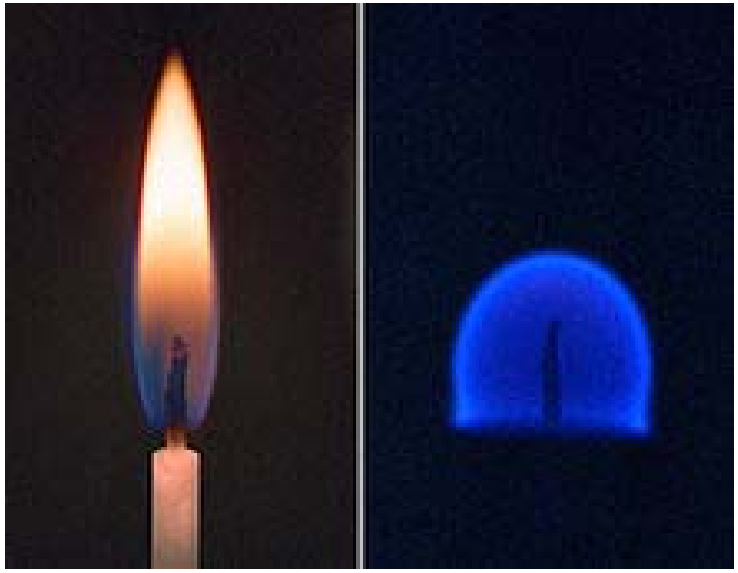
In 1963 on Mercury Atlas 9, 22 Earth orbits, 35 hours

Gordon Cooper carried pre-loaded drug injectors in space suit pocket

Demerol – pain relief
Tigan - motion sickness



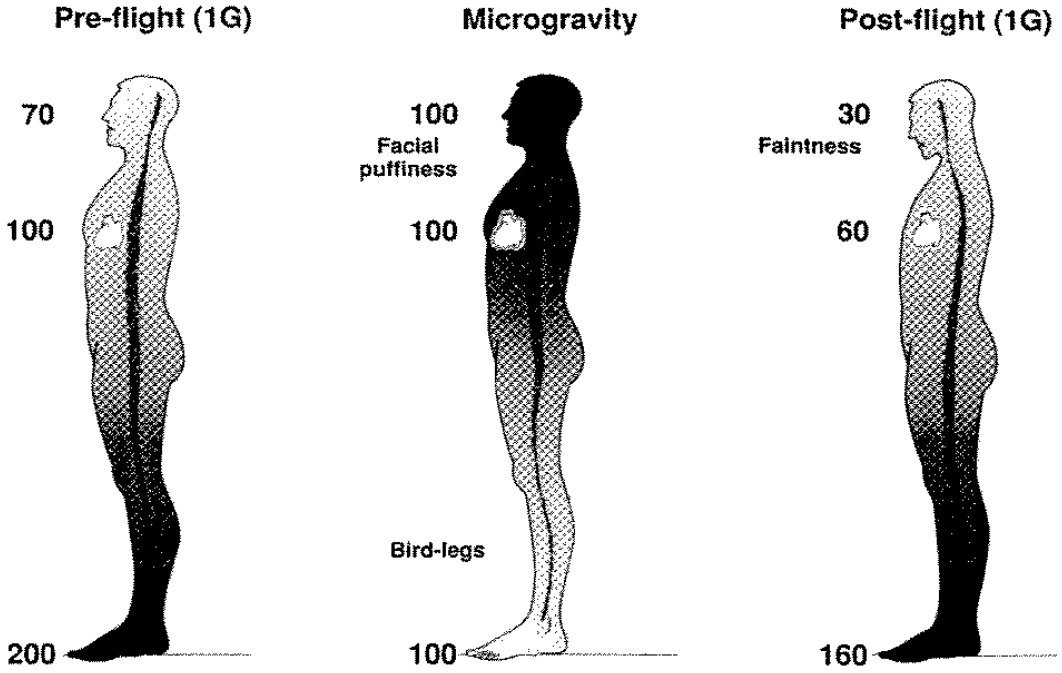
Things are different in microgravity



Things are different in microgravity. Even people.

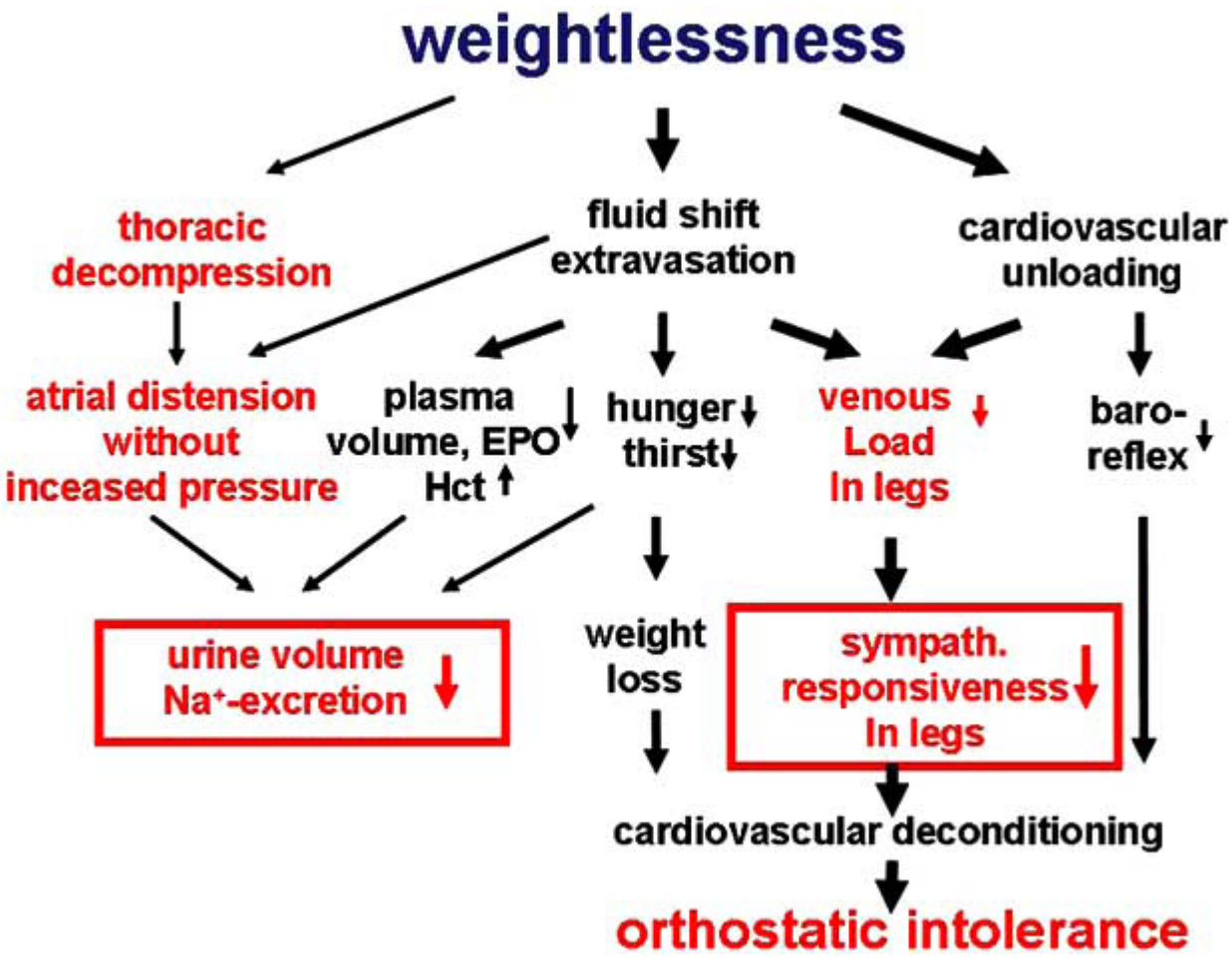
Human Health and Performance
NASA JOHNSON SPACE CENTER
Exploring Space | Enhancing Life

Decreased gravity makes body fluids shift upward



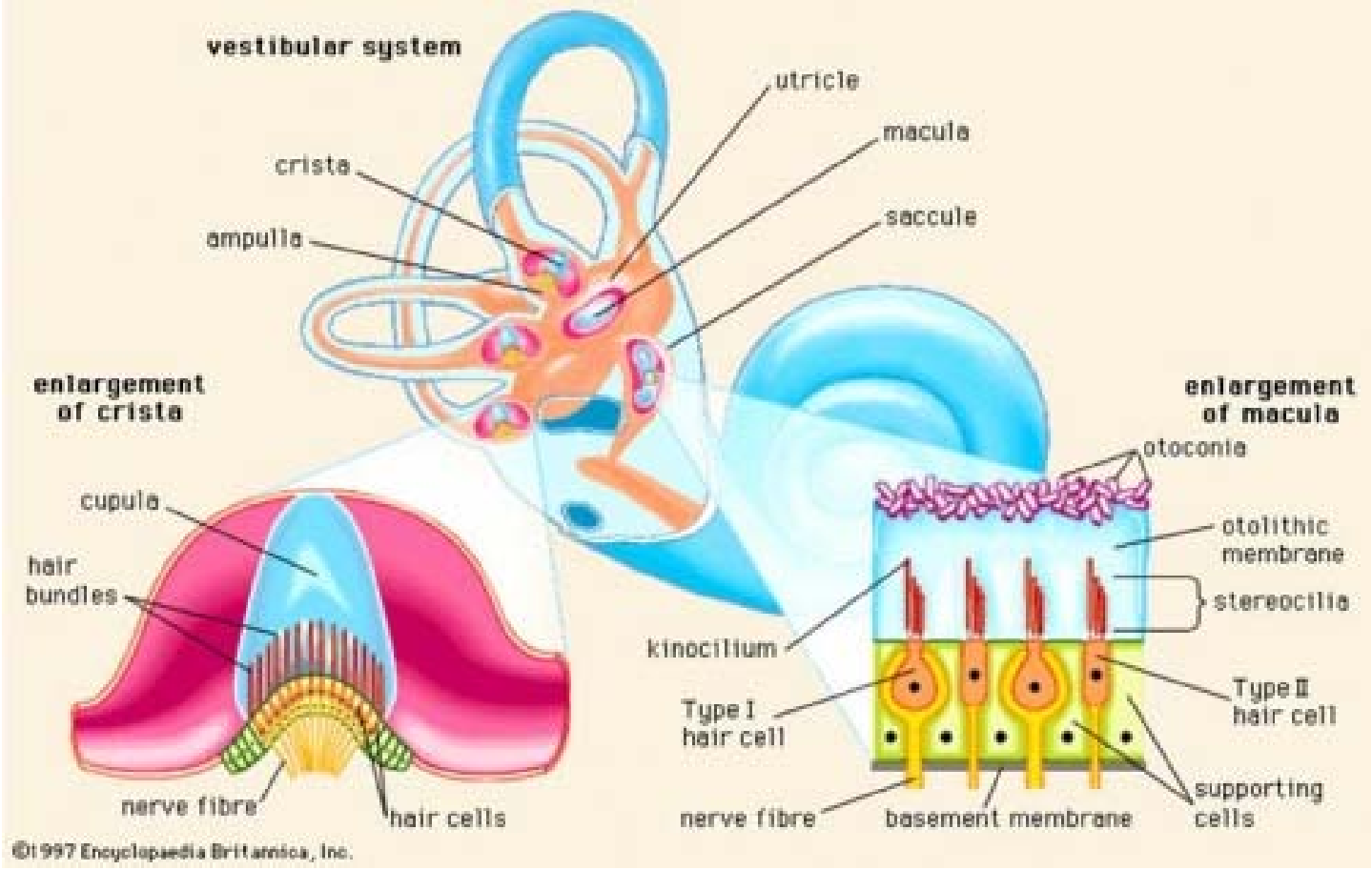
Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight☆

Alan R. Hargens[a,*], Sara Richardson[b] *Respiratory Physiology & Neurobiology 169S (2009) S30–S33*



Regulation of Body Fluid and Salt Homeostasis – from Observations in Space to New Concepts on Earth. R. Gerzer* and M. Heer *Current Pharmaceutical Biotechnology, 2005, 6, 299-304 299*

Decreased gravity disrupts the sense of balance



http://www.skybrary.aero/index.php/Vestibular_System_and_Illusions_(OGHFA_BN)

Space Motion Sickness

(Space Adaptation Syndrome)

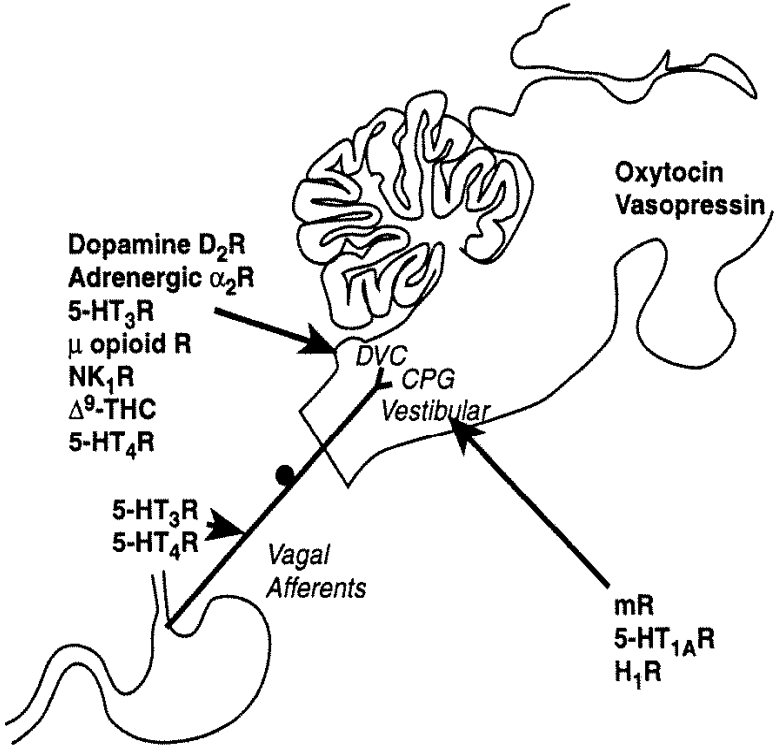


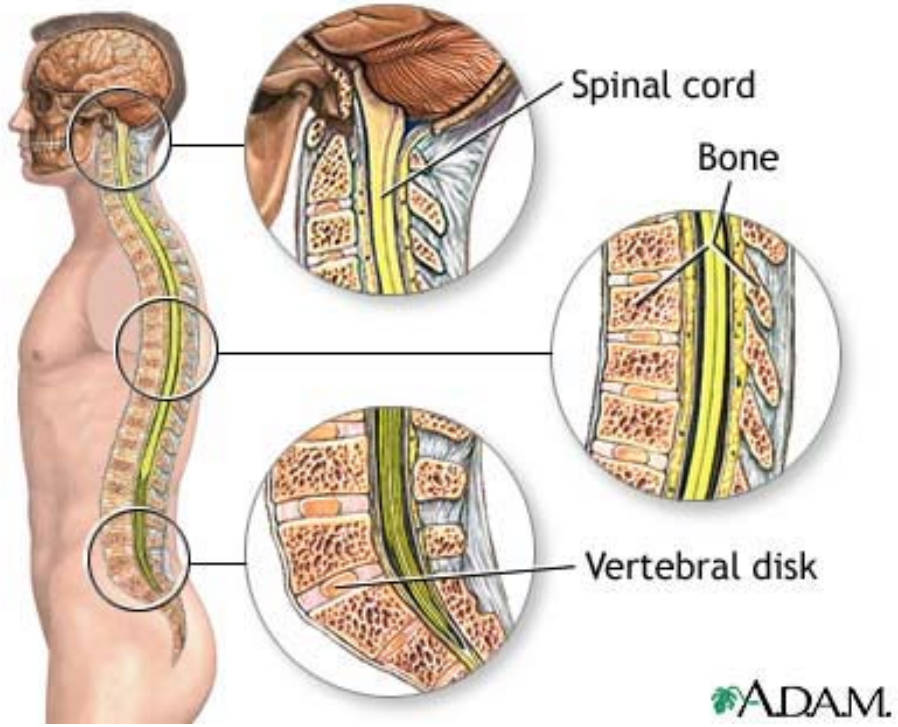
Figure 3. Selected drugs that affect emesis and their site(s) of action (if known). α_2R = adrenergic α_2-receptor; CPG = central pattern generator; D_2R = dopamine$_2$-receptor; Δ^9-THC = Δ^9-tetrahydrocannabinol; DVC = dorsal vagal complex; 5-HT = serotonin; H = histamine; mR = cholinergic muscarinic receptor; NK = neurokinin; R =receptor.

Am J Med. 2001 Dec 3;111 Suppl 8A:106S-112S.
Central neurocircuitry associated with emesis. Hornby PJ.

Loss of Bone Mineral Density

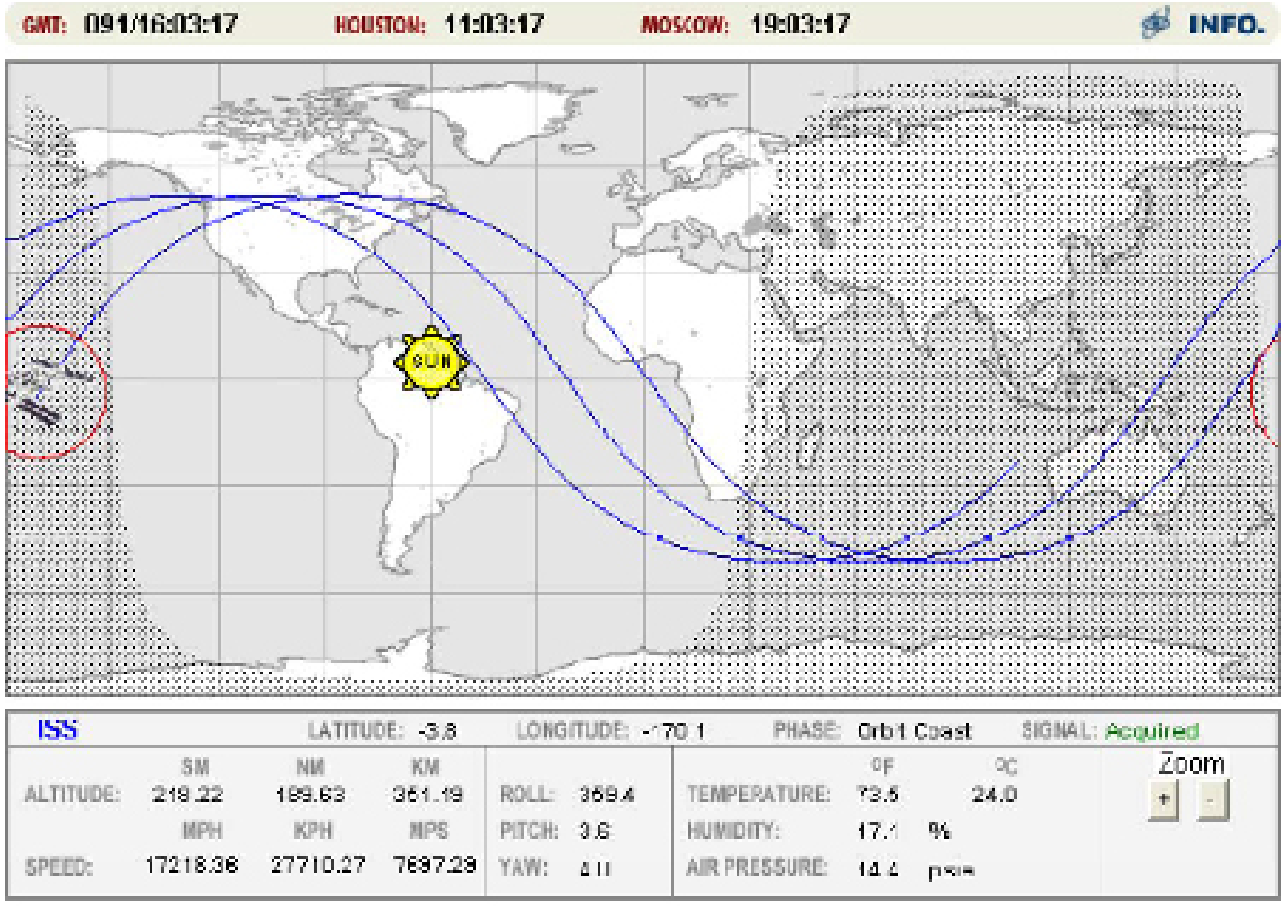
Russian staff and doctors carry Italian ESA astronaut Roberto Vittori to the medical tent upon his arrival to the town of Arkalyk, northern Kazakhstan, early Monday, April 25, 2005. [AP]

Body Pain



Head Congestion

Circadian Rhythm Disruption



Medical Complaints in Space

Based on ISS Missions:

Anorexia
Space motion sickness
Fatigue
Insomnia
Dehydration
Dermatitis
Back pain
Upper respiratory infection
Conjunctival irritation
Subungual hemorrhage
Urinary tract infection
Cardiac arrhythmia
Headache
Muscle strain
Diarrhea
Constipation

From Clement , Fundamentals of Space Medicine, 2003

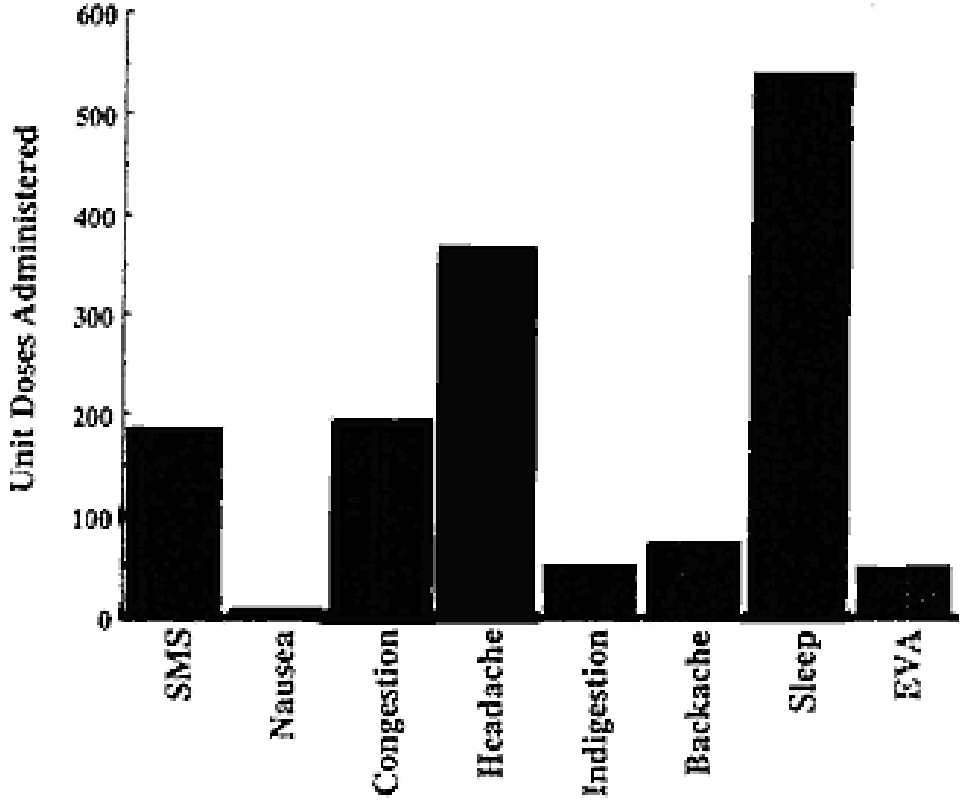
Based on Space Shuttle,

1988- 1995

Facial Fullness
Headache
Sinus congestion

Dry skin, irritation, rash
Eye irritation, dryness, redness
Foreign body in eye
Sneezing/coughing
Sensory changes
Upper respiratory infection
Back muscle pain
Leg/foot muscle pain
Cuts
Shoulder/trunk muscle pain
Hand/arm muscle pain
Anxiety/annoyance
Contusions
Ear problems (usu. Pain)
Neck muscle pain
Stress/tension
Muscle cramp
Abrasions
Fever, chills
Nosebleed
Psoriasis, folliculitis, seborrhea
Low heart rate
Myoclonic jerks

Pharmaceutical Use on Shuttle



PUTCHA L, BERENS KL, MARSHBURN TH, ORTEGA HJ, BILLICA RD. *Pharmaceutical use by U.S. astronauts on space shuttle missions.* Aviat Space Environ Med 1999; 70:705–8.

So, NASA has a Pharm lab.

Our Mission at the JSC Pharmacology Lab…

…is to ensure that flight surgeons have good information about how administered pharmaceuticals will work in the extreme conditions of spaceflight

…which means that we have to understand the physiological changes caused by living in the spaceflight environment

…as well as the effect of the spaceflight environment on the stored drugs themselves

…as well as the pharmaceuticals' mechanism of action

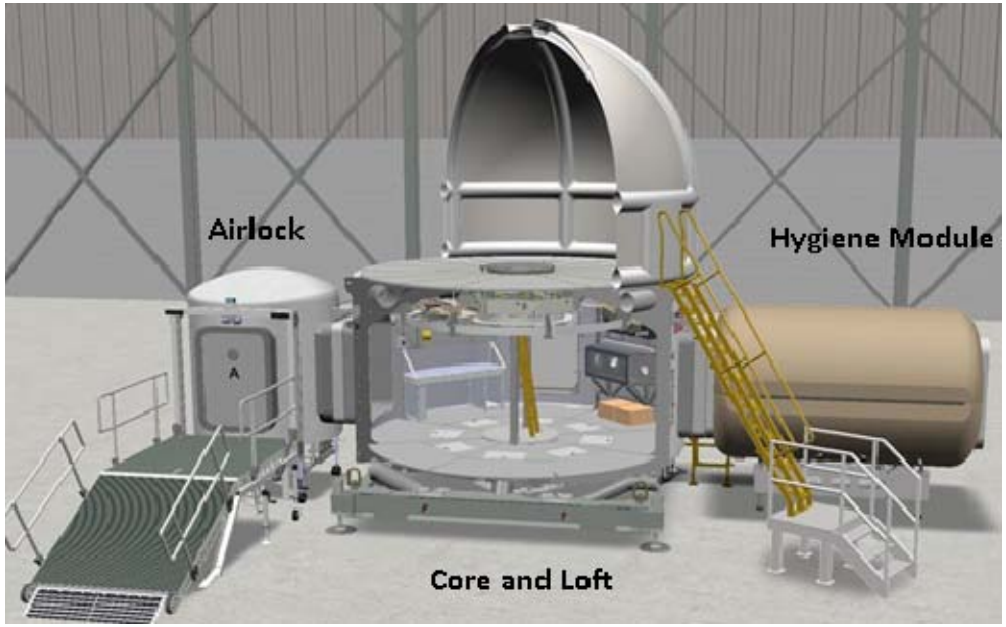
NASA Flight Analogs Project
Bedrest Study

Head-down Tilt Bed Rest

- serves as a model for studying the physiological changes that occur during spaceflight under controlled conditions;
- provides a platform for comparison between bed rest and spaceflight;
- provides a mechanism for testing certain countermeasures prior to being used in flight.

http://www.bedreststudy.com
Pillownaut blogs

Human Exploration Research Analog (HERA)



The Human Exploration Research Analog is a two-story, four-port habitat unit. It is cylindrical with a vertical axis, and connects to a simulated airlock and hygiene module

Duration: 4-60 days
Room Temperature: 72° F. (+/- 5 degrees)
Light/Dark Cycle: Lights on 0600, lights out 2130, 7 days per week, no napping is permitted
Monitoring of study operations 24 hours a day

Motion sickness is used to model space motion sickness

The rotating chair has a maximum velocity up to 360 degrees/second .
www.graybiel.brandeis.edu/.../facilities.html

Culture systems are used to measure changes at the cellular level

Dr. Cheryl Nickerson is studying the effects of simulated low-g on a well-known pathogen, Salmonella typhimurium, a bacterium that causes two to four million cases of gastrointestinal illness in the United States each year. While most healthy people recover readily, S. typhimurium can kill people with weakened immune systems. Thus, a simple case of food poisoning could disrupt a space mission. Using the NASA rotating-wall bioreactor, Nickerson cultured S. typhimurium in modeled microgravity. Mice infected with the bacterium died an average of three days faster than the control mice, indicating that S. typhimurium's virulence was enhanced by the bioreactor. Earlier research showed that 3 percent of the genes were altered by exposure to the bioreactor.

Limitations of Spaceflight Experiments:

Non-invasive methods best

Non-toxic

Lightweight and small equipment

No degassing, explosion or fire risk

Low power consumption

Low impact on crew schedule

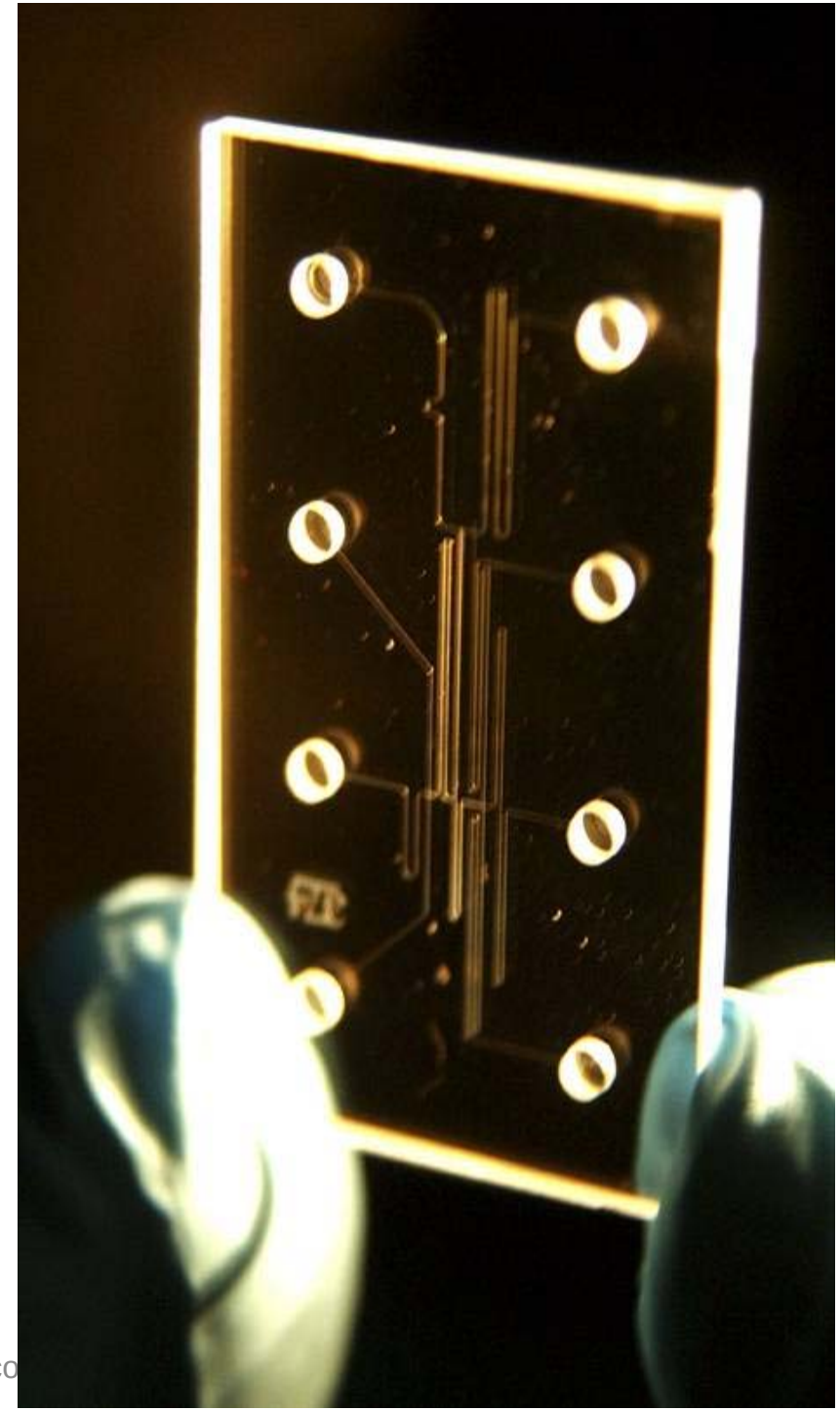
N will be small (~500 people have flown to space)

Inside the science module aboard the Earth-orbiting Space Shuttle Columbia, Astronaut David A. Wolf draws blood from payload specialist Martin J. Fettman, DVM. Blood samples from crew members are critical to Life Sciences investigations


ISS013E64639

ISS commander and science officer Leroy Chiao performs a scan on the eye of flight engineer Salizhan Sharipov Durin during ISS Expedition 10.

The eight holes on this chip are ports that can be filled with fluids or chemicals. Tiny valves control the chemical processes by mixing fluids that move in the tiny channels that look like lines, connecting the ports.



Before 1988, there were limited pharmacological countermeasures - fluid loading and g suits were used.
Shuttle missions lasted less no more than 7 days.
In 1988 Congress approved funds to expand missions to 16 days. Countermeasure development began in earnest.
Currently, 6 months on the ISS is routine and the first 1 year mission begins soon.
We are starting to think about longer duration missions, and the countermeasures that will be required to maintain crew health over periods of years.

Research in JSC Pharmacology

Pharmaceuticals

- Usage tracking
- Stability

Pharmacokinetics

- Absorption/Distribution
- Metabolism/Excretion

Pharmacodynamics

- all the reasons medications are used

Medication Usage

How are medications used on spaceflight missions?

1. Retrospective Analysis of Medication Usage During Long Duration Spaceflight – an analysis of medication uses on past missions, conducted with JSC Pharmacy
2. *Dose Tracker* Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions – an iPad app for crew to record their medication uses inflight

Stability

How long is a medication safe and effective?

1. Analysis of flight-aged medications (in-house and in collaboration with FDA & academic experts; working with JSC Pharmacy)
2. Evaluating packaging materials & methods to increase useful lifespan (working with JSC Pharmacy)
3. Low Gravity Drug Stability Analyzer (PI: Farquharson, SBIR)

Pharmacokinetics

Does the spaceflight environment

(radiation, microgravity, etc)

alter PK?

- Inflight pharmacokinetic and pharmacodynamic responses to medications commonly used in spaceflight (PI: Wotring)

Bone

How can medications be used to prevent or reduce spaceflight-induced bone loss?

- Watching new osteoporosis treatments, denosumab, teriparatide, various others …

Antimicrobial Efficacy

Are the antimicrobials carried aboard effective against spaceflight-altered microorganisms?

- Pilot study in rotating culture model in collaboration with JSC Microbiology and Arizona State University showed small differences in sensitivity of some microorganisms to medications that could be used for treatment of infection, only at low concentrations.

Space Adaptation Syndrome

How can medications be used to treat or prevent space adaptation syndrome?

- Can a training protocol permit reduced dependence on medication? (PI: Young)

Vision and Intracranial Pressure Changes

New issue – hasn't been well defined yet

- Are medications involved in vision and intracranial pressure changes seen in spaceflight? (Data mining study in progress, PI Wotring)
- Investigating treatment options

Muscle Atrophy

How can medications be used to prevent or reduce spaceflight-induced muscle atrophy?

- Watching selective androgen receptor modulators, mostly in pre-clinical trials

Radioprotectants

How can medications be used to prevent or reduce physiological effects of radiation exposure?

- Watching antioxidants, as well as other more selective compounds, in pre-clinical trials.

More information?

http://humanresearch.jsc.nasa.gov/

http://humanresearchroadmap.nasa.gov/evidence/reports/Pharm.pdf

virginia.e.wotring@nasa.gov