Pharmacology During Spaceflight Missions

V. E. Wotring

24 March 2012

St. Louis MO

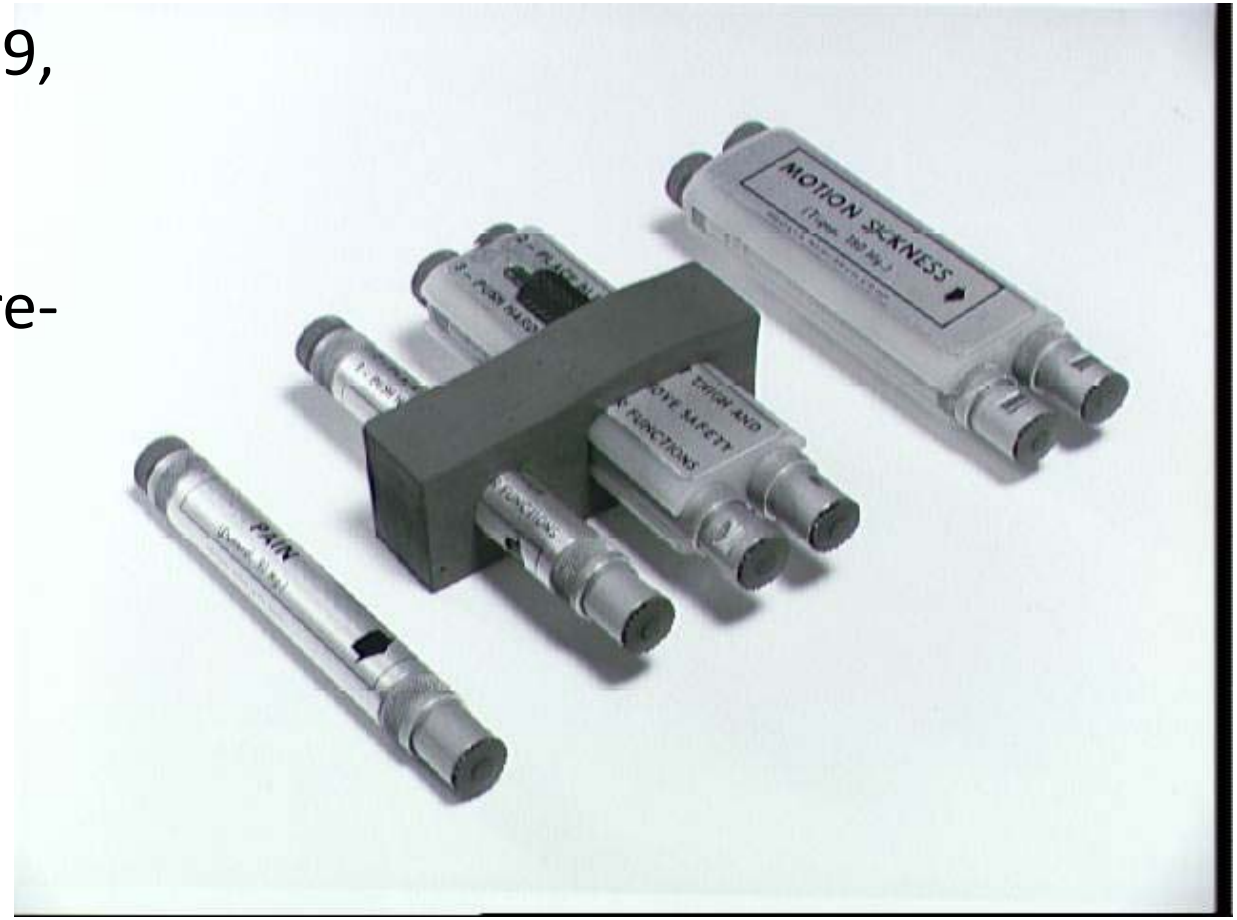
NASA has a Pharm lab?

First pharmaceuticals in US spaceflight

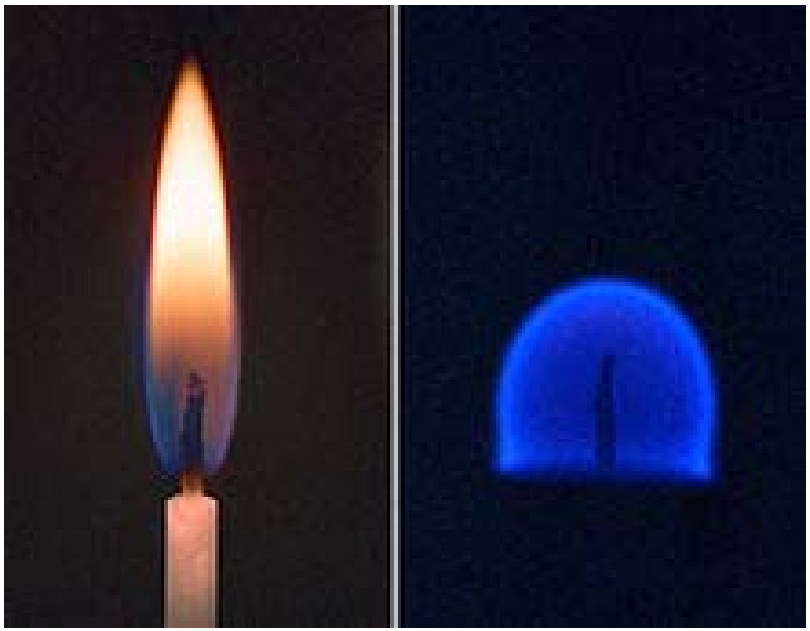
In 1963 on Mercury Atlas 9,
22 Earth orbits, 35 hours

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

Demerol – pain relief
Tigan - motion sickness

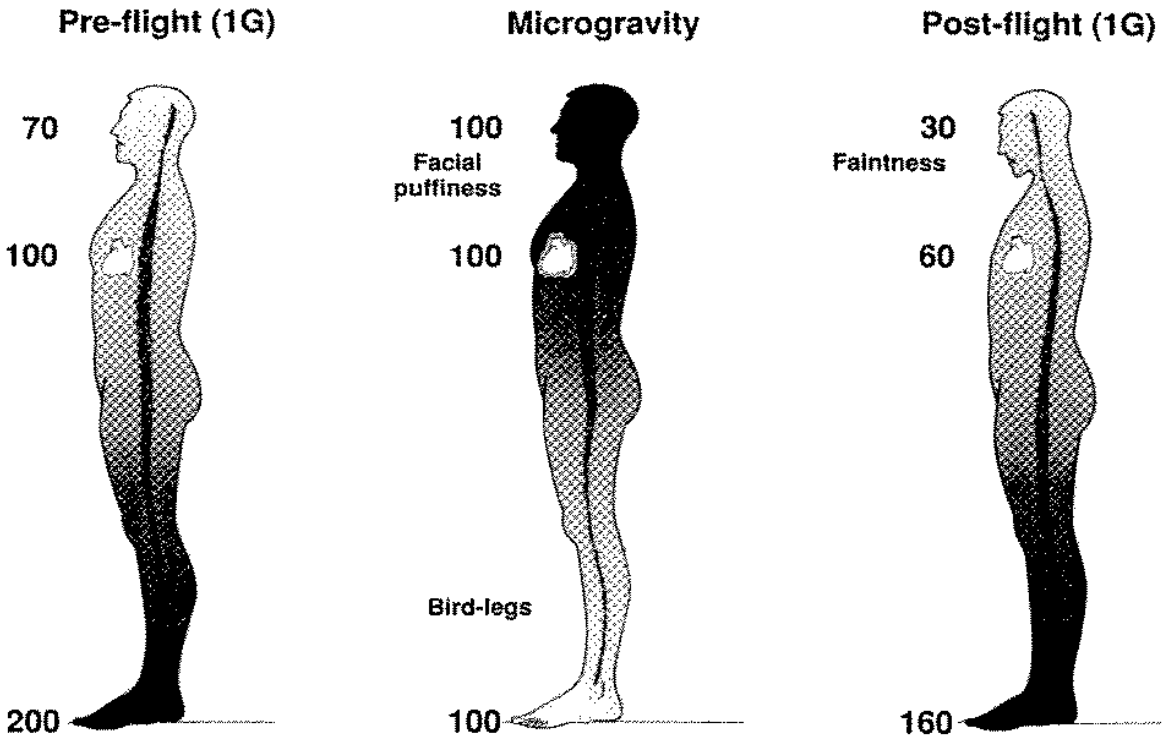


Things are different in microgravity



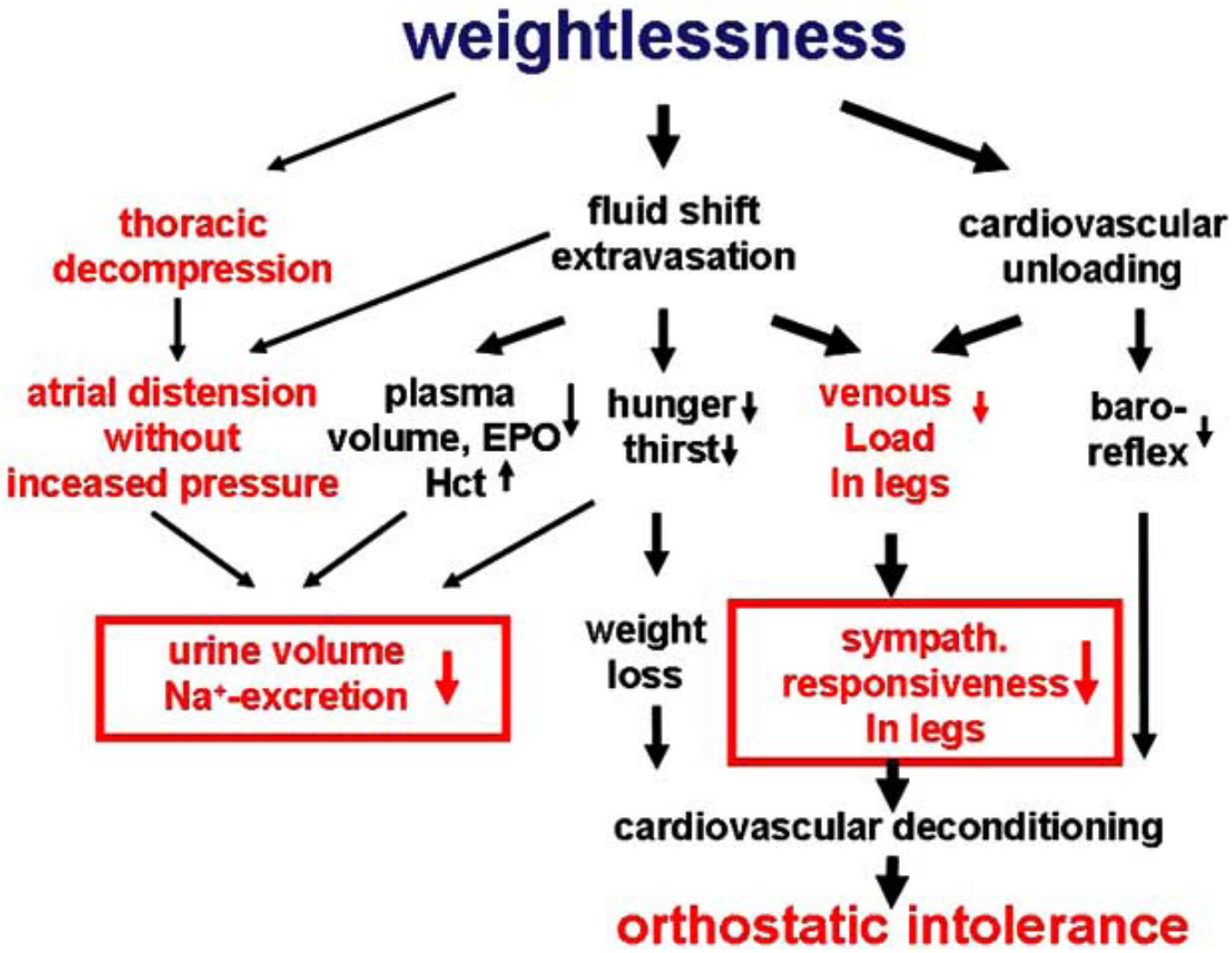
Things are different in microgravity. Even people.

Decreased gravity makes body fluids shift upward



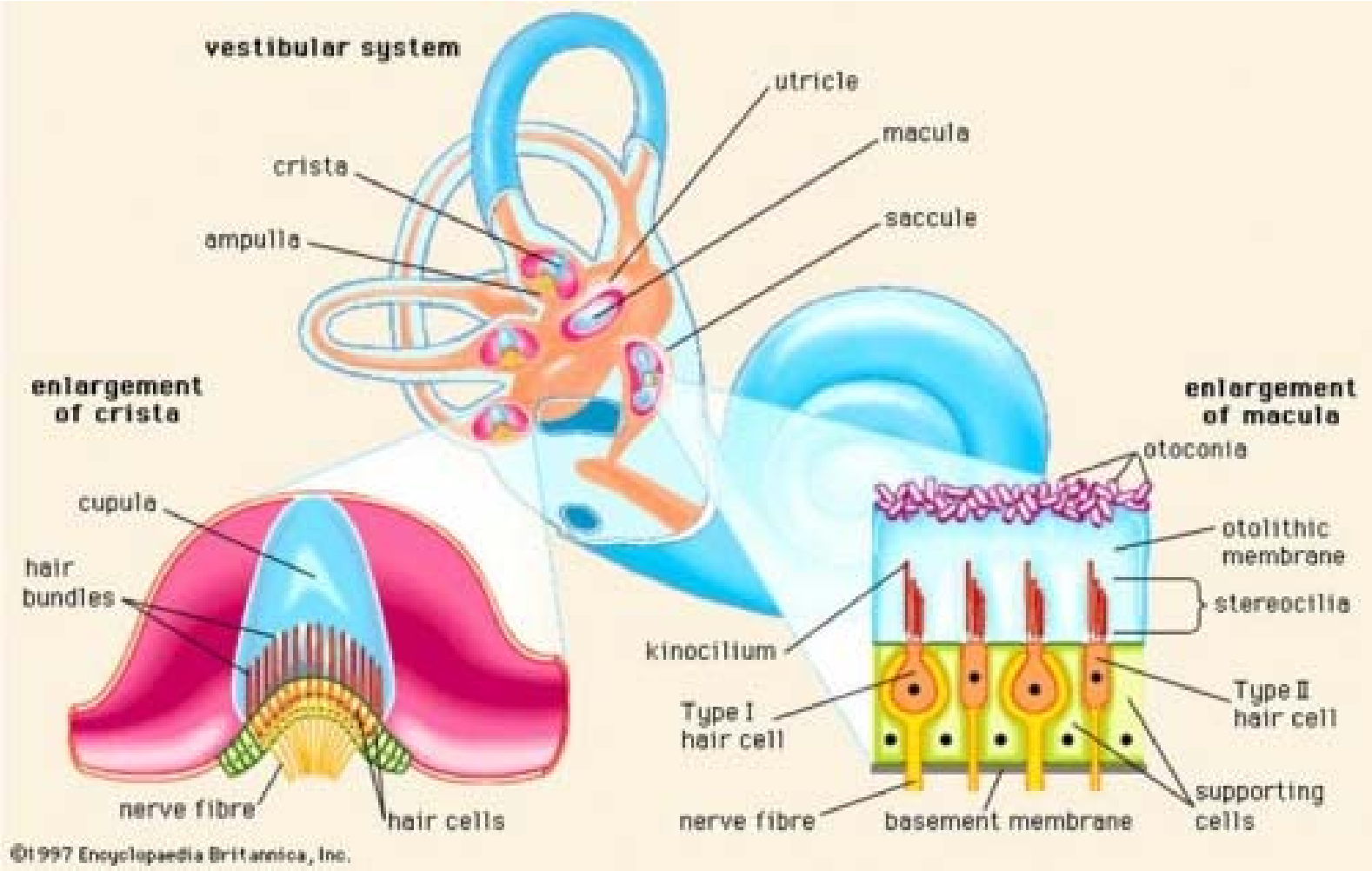
Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight☆

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)

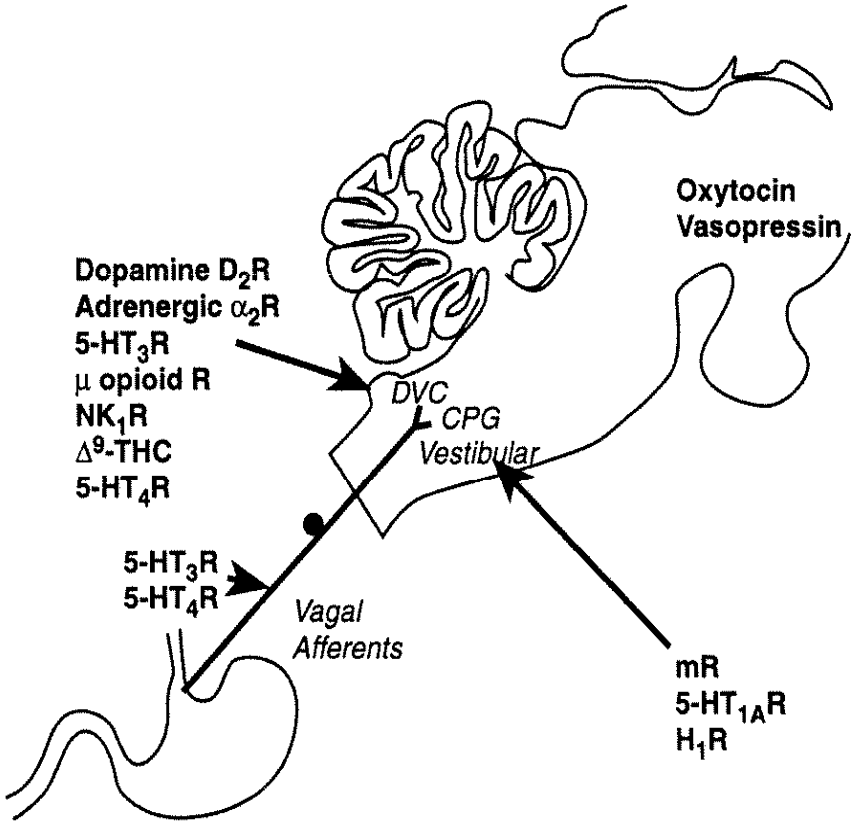


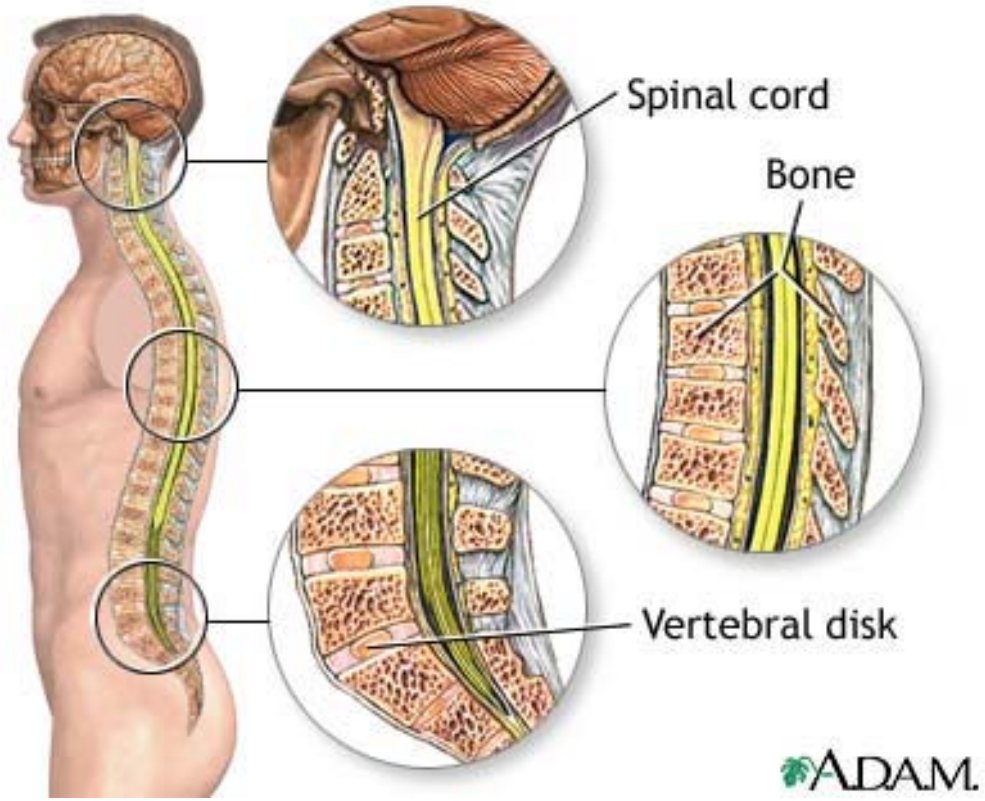
Figure 3. Selected drugs that affect emesis and their site(s) of action (if known). α_2R = adrenergic α_2-receptor; CPG = central pattern generator; D_2R = dopamine$_2$-receptor; Δ^9-THC = Δ^9-tetrahydrocannabinol; DVC = dorsal vagal complex; 5-HT = serotonin; H = histamine; mR = cholinergic muscarinic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

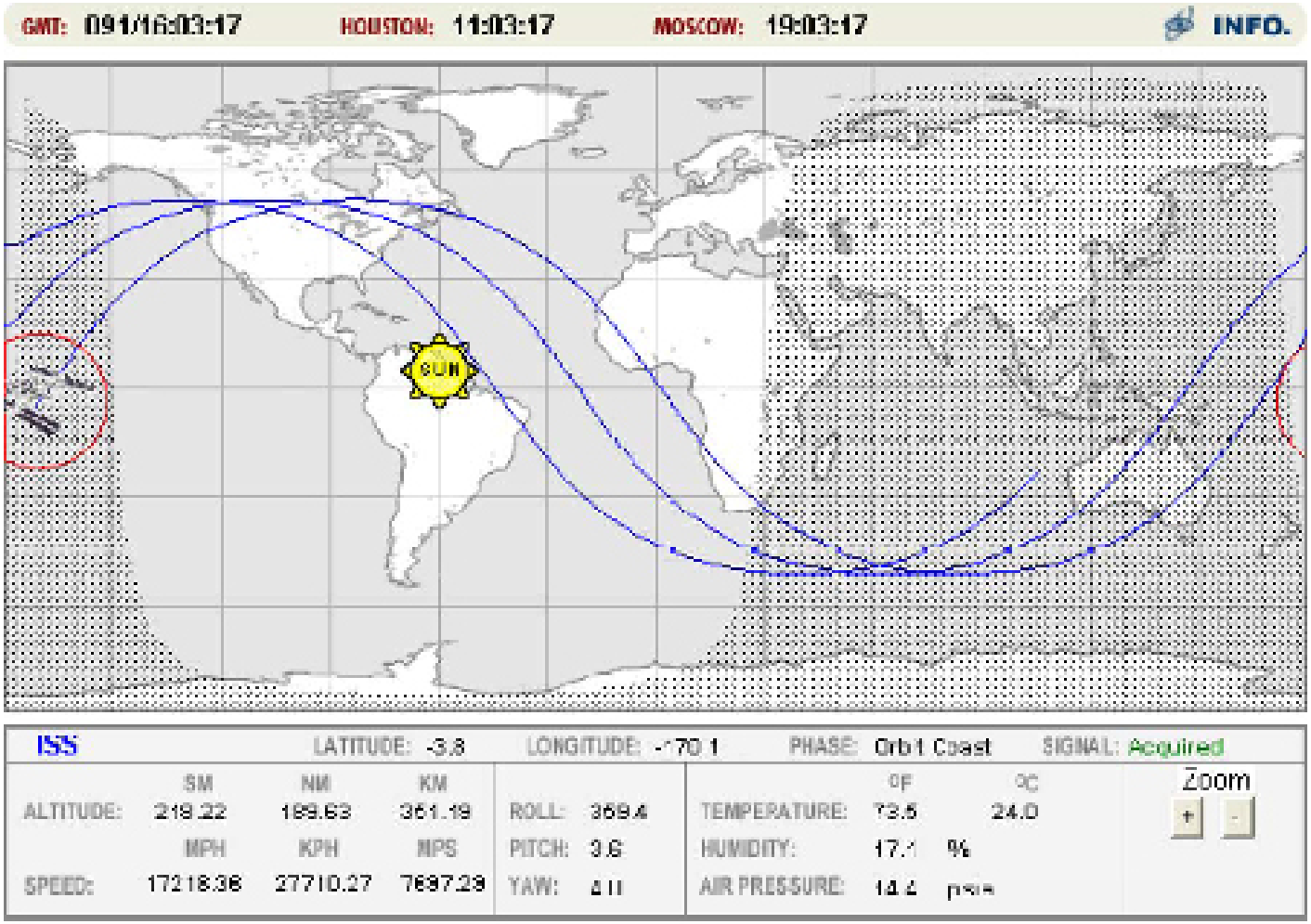
Russian ground personal members and doctors carry Italian ESA astronaut Roberto Vittori to the medical tent upon his arrival to the town of Arkalyk, northern Kazakhstan, early Monday, April 25, 2005. [AP]

Body Pain



Head Congestion

Circadian Rhythm Disruption



Medical Complaints Associated with Spaceflight

Weight loss
Bone loss
Muscle atrophy

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

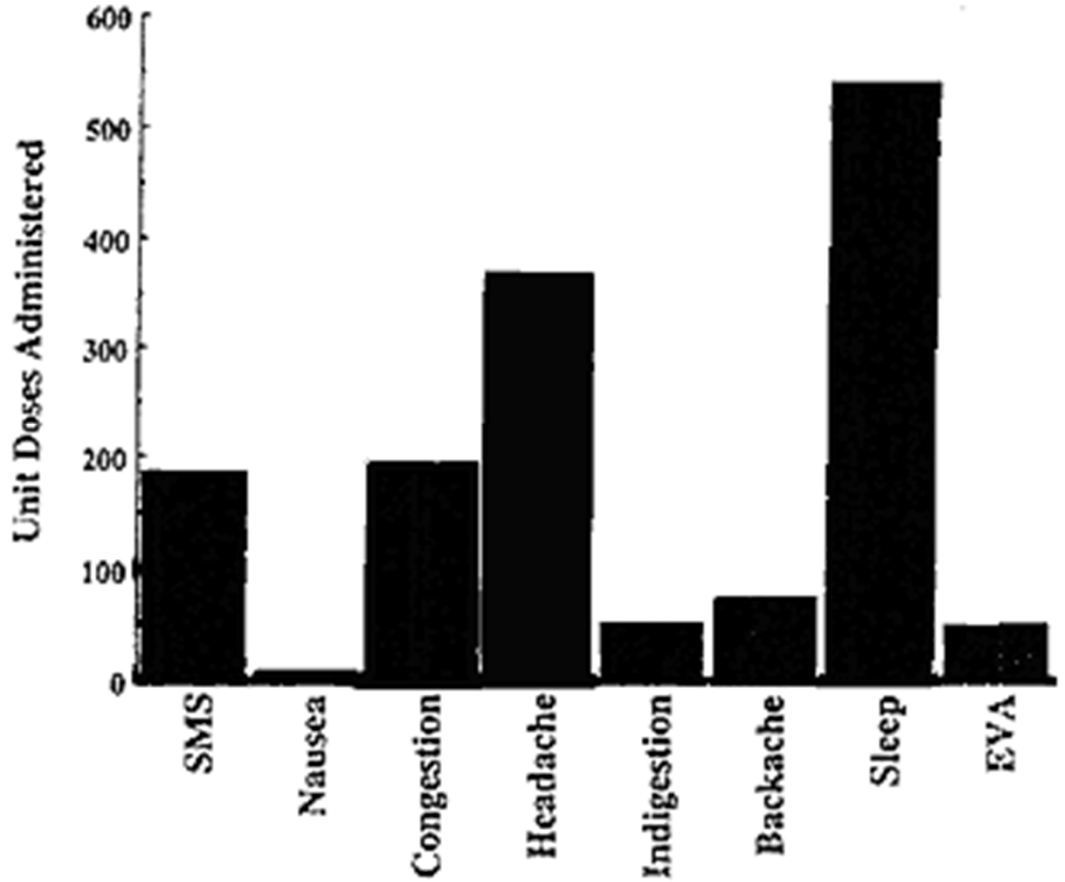
Based on Space Shuttle,

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

1. Design experiment to answer the scientific question.
2. Book the appropriate time in NASA's top-secret low-gravity chamber on Earth.
3. Analyze results and make recommendations to flight medicine.

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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 countermeasures prior to being used in flight.

http://www.bedreststudy.com
Pillownaut blogs

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

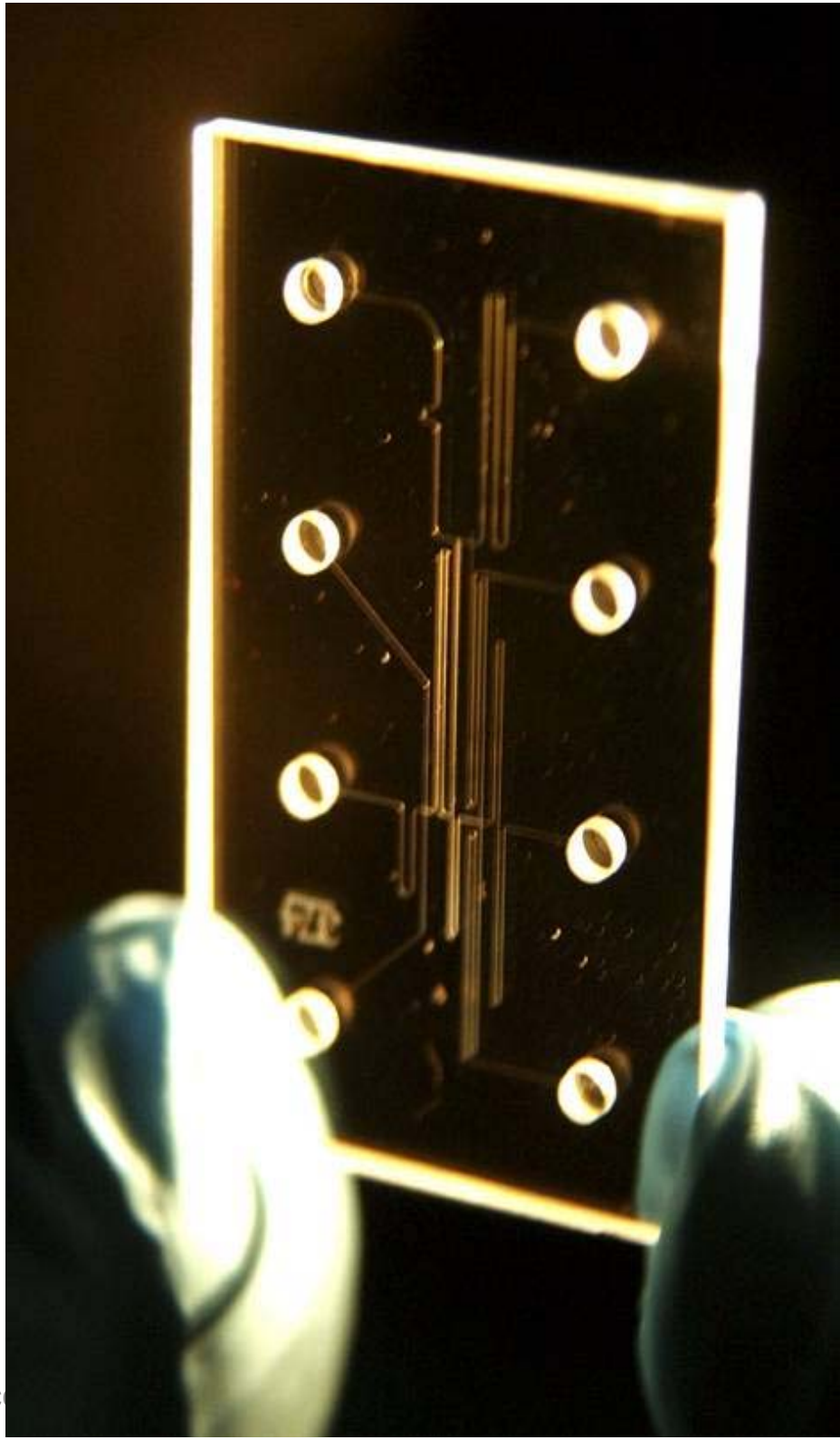
N will be small (~350 people have flown to space)

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 an ADUM 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. Scientists at NASA's Marshall Space Flight Center in Huntsville, Alabama designed this chip to grow biological crystals on the ISS. These chips, the size of dimes, could be loaded on a rover looking for biosignatures of past or present life. Other types of chips could be placed in handheld devices used to **monitor microbes** in water or to quickly conduct medical tests on astronauts. (NASA/MSFC/D.Stoffer)



Before 1988, there were no countermeasures except fluid loading and g suits.

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.

We are starting to think about longer duration missions, and the countermeasures that will be required to maintain crew health over periods of years.

Current Life Sciences Experiments on the ISS

Assessment of Endurance Capacity by Gas Exchange and Heart Rate Kinetics During Physical Training
Behavioral Issues Associated with Long Duration Space Missions: Review of Astronaut Journals
Biomechanical Analysis of Treadmill Exercise on the International Space Station
Biomedical Analyses of Human Exposed to a Long Term Space Flight
Cardiac Atrophy and Diastolic Dysfunction During and After Long-Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capacity & Risk of Cardiac Arrhythmias
Cardiovascular Health Consequences of Long-Duration Space Flight
Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Space Flight and Recovery
Effect of Gravitational Context on EEG Dynamics: A Study of Spatial Cognition, Novelty Processing and Sensorimotor Integration
Evaluation of Maximal Oxygen Uptake and Submaximal Estimates of VO2max Before, During, and After Long Duration International Space Station Missions
Integrated Resistance and Aerobic Training Study
Long Term Microgravity: A Model for Investigating Mechanisms of Heart Disease
Nutritional Status Assessment
Physiological Factors Contributing to Postflight Changes in Functional Performance
Psychomotor Vigilance Test on ISS
Scaling Body-Related Actions in the Absence of Gravity
Sodium Loading in Microgravity
Thermoregulation in Humans during Long-Term Space Flight
Validation of Procedures for Monitoring Crewmember Immune Function
Vascular Echocardiography

Research in JSC Pharmacology

Pharmaceuticals

- Usage tracking
- Stability

Pharmacokinetics

- Absorption/Distribution
- Metabolism/Excretion

Pharmacodynamics

- all the indications that people treat

Stability

How long is a medication safe and effective?

1. Collaboration with FDA on flight-aged medications (pilot)
2. Data sharing with pharmaceutical manufacturers
3. Evaluating packaging materials & methods to increase useful lifespan.

leading up to …

Comprehensive stability testing of all ISS meds

PK

Does the spaceflight environment

(radiation, microgravity, etc)

alter ADME?

1. Spaceflight effects on metabolism – gene & protein expression
2. Feasibility of salivary sampling for PK studies

leading up to …

In-flight PK, administration & analysis

Bone

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

1. Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss; PI LeBlanc
2. Watching denosumab and teriparatide …

Antimicrobial Efficacy

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

1. Pilot study in rotating culture model.

leading up to …

Comprehensive testing in culture and flight

SMS

How can medications be used to treat or prevent space motion sickness?

1. Analog testing of medications

Leading up to…

1. Flight testing of medications

Vision and Intracranial Pressure Changes

New issue – hasn't been defined yet

1. Are medications involved in vision and intracranial pressure changes seen in spaceflight?
2. Investigating treatment options

Muscle Atrophy

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

1. Watching selective androgen receptor modulators

Want to be involved?

Connect NASA to your group

Invite a speaker.

Work with NASA Scientists

We need external expertise!

Apply for a NASA or NSBRI grant

Collaborate with a NASA researcher

Review grants or programs for NASA

Opportunities for Students

K-12 educational opportunities (nasa.gov)

Internships for college students (Space Grant)

Graduate student rotations

Post-doctoral fellowships

What can the pharmaceutical industry do for astronauts?

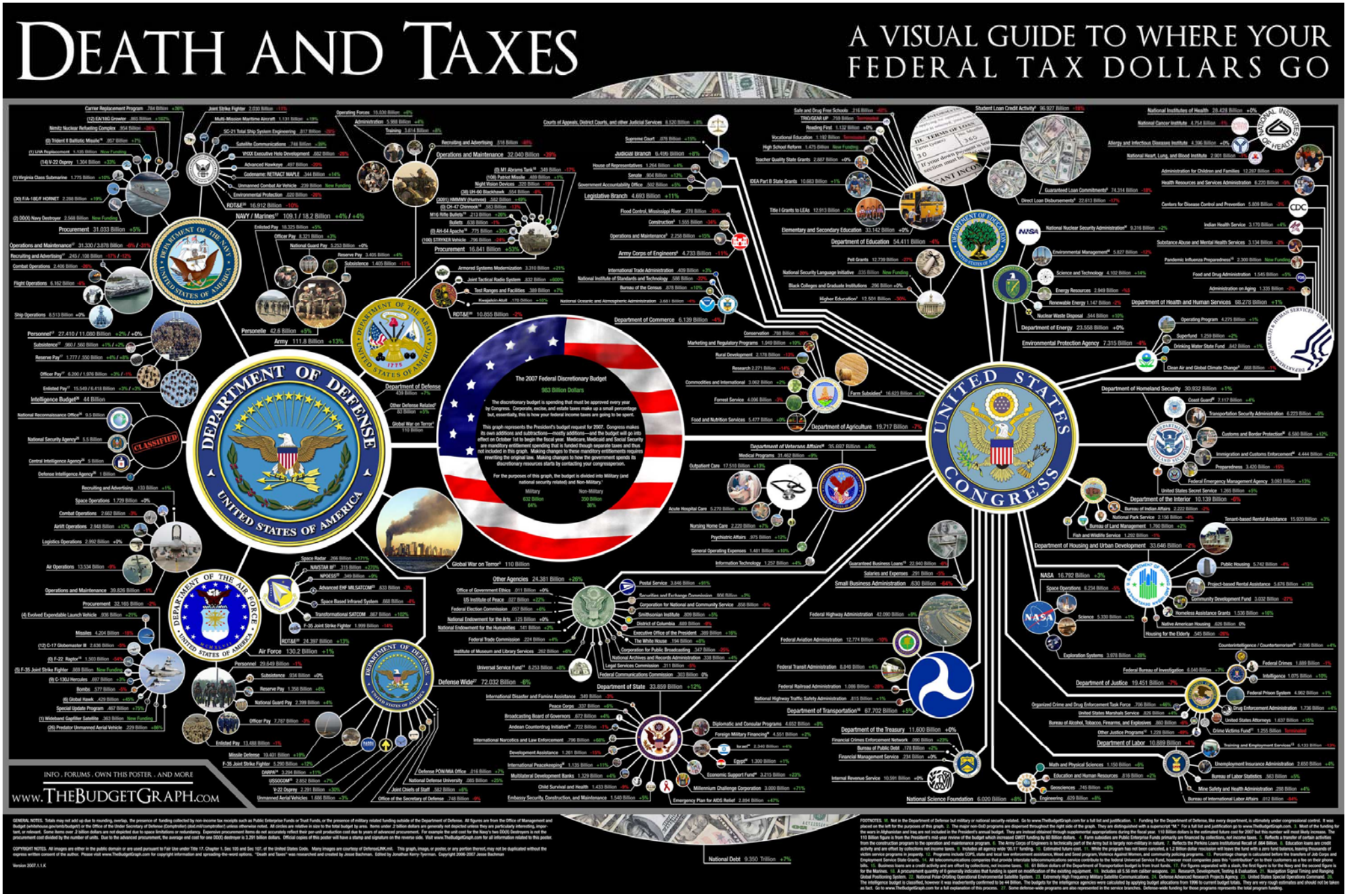
Are you a packaging or stability expert?

Do you have products that would apply to any of the spaceflight concerns?

Is your company willing to work with NASA?

Are you developing analytical instruments that might work in microgravity?

Email Ginger. virginia.e.wotring@nasa.gov


DEATH AND TAXES
A VISUAL GUIDE TO WHERE YOUR FEDERAL TAX DOLLARS GO
The 2007 Federal Discretionary Budget
963 Billion Dollars
Military
632 Billion
66%
Non-Military
350 Billion
36%
DEPARTMENT OF DEFENSE
UNITED STATES OF AMERICA
CONGRESS
Department of Defense
Army 111.8 Billion +13%
NAVY / Marines 109.1 / 18.2 Billion +4% / +4%
Air Force 130.2 Billion +1%
Defense Wide 72.032 Billion -6%
Department of Agriculture 19.717 Billion -7%
Department of Commerce 6.139 Billion -4%
Department of Education 54.411 Billion -6%
Department of Energy 23.558 Billion +0%
Environmental Protection Agency 7.315 Billion -8%
Department of Health and Human Services 68.278 Billion +1%
Department of Homeland Security 30.932 Billion +1%
Department of Housing and Urban Development 33.646 Billion -2%
Department of the Interior 10.139 Billion -6%
Department of Justice 19.451 Billion -7%
Department of Labor 10.889 Billion -4%
Department of State 33.859 Billion +12%
Department of Transportation 67.702 Billion +5%
Department of the Treasury 11.600 Billion +0%
Department of Veterans Affairs 35.697 Billion +8%
Other Agencies 24.381 Billion +26%
National Debt 9.350 Trillion +7%
Global War on Terror 110 Billion
Intelligence Budget 44 Billion
CLASSIFIED
Judicial Branch 6.496 Billion +8%
Legislative Branch 4.693 Billion +11%
Farm Subsidies 16.623 Billion +3%
Student Loan Credit Activity 96.927 Billion -18%
Guaranteed Loan Commitments 74.314 Billion -19%
Direct Loan Disbursements 22.613 Billion -12%
National Institutes of Health 28.428 Billion +0%
NASA 16.792 Billion +3%
National Science Foundation 6.020 Billion +6%
INFO . FORUMS . OWN THIS POSTER . AND MORE
www.THEBUDGETGRAPH.com

The NASA budget is about $17B.

Half a penny of every tax dollar goes to NASA.

NIH budget is about $30B.

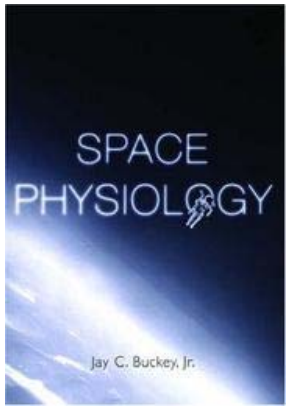
The National Retail Federation projected that Americans will spend nearly $18 billion on Valentine's Day 2012.

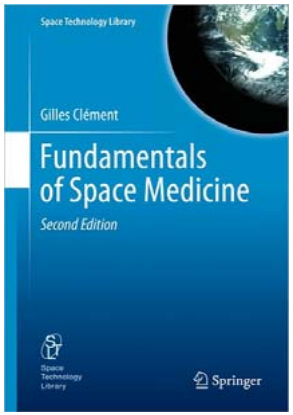
According to the National Coffee Association, Americans spend $18 billion on coffee every year.

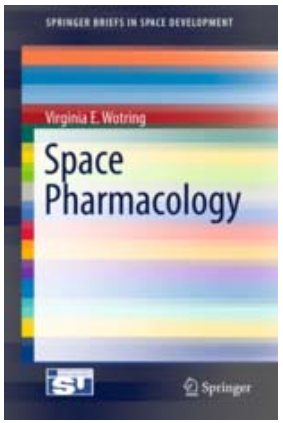
Americans spend more on pizza ($27B) than on the space program.

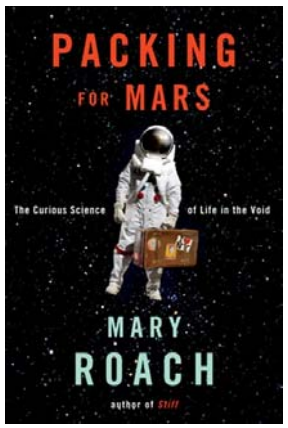
Need more ?

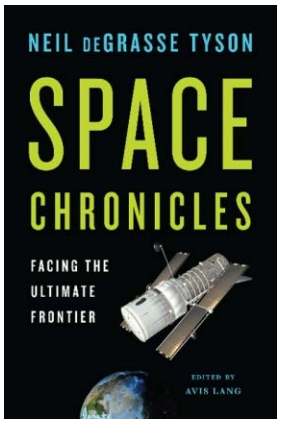
General NASA info:	http://www.nasa.gov
Human Research at NASA:	http://humanresearch.jsc.nasa.gov/
NASA Research Grants	http://nspires.nasaprs.com/external/
NSBRI	http://www.nsbri.org/
Bedrest Study Info:	http://www.bedreststudy.com
Postdoctoral Opportunities	http://nasa.orau.org/postdoc/
Don Pettit's Blog	http://blogs.airspacemag.com/pettit/
Ginger	virginia.e.wotring@nasa.gov

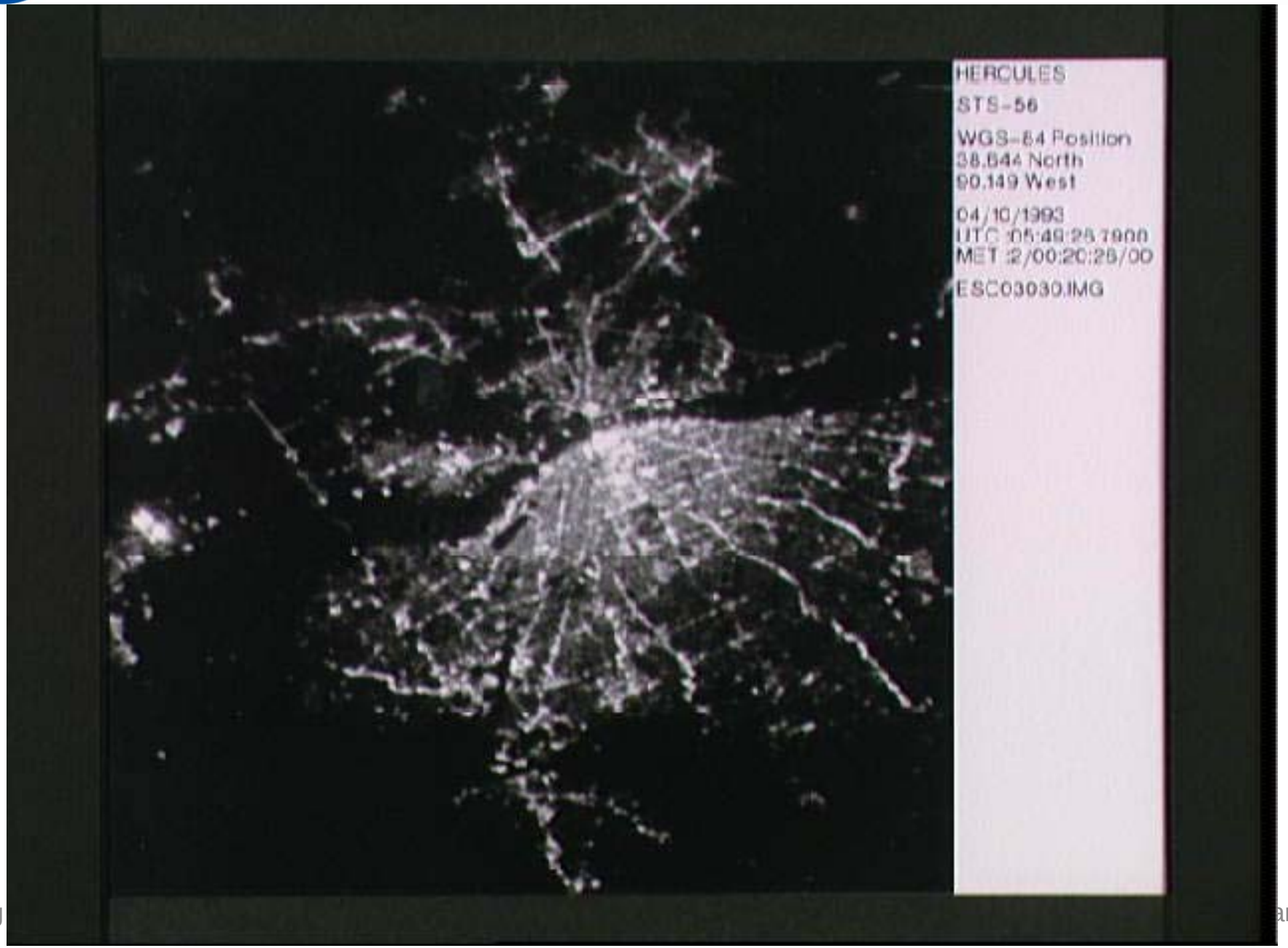








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Backup slides

If the U.S. hands orbital travel to private companies, then that means orbital travel is no longer a frontier. What NASA needs is steady funding for big science…

interview of Neil deGrasse Tyson by Laura Conaway Maddow Blog, March 3, 2010

"I tell you, NASA is a force of nature. They're like no other agency. When NASA dreams big, the country dreams big, and when the country dreams big, kids dream big. It attracts the kid biologists, the kid engineers, the kid chemists. It gets them in the pipeline, because it's worthy of their ambitions and their intellect. These are the people who make tomorrow come, who make the tomorrow we want to see."

Neil deGrasse Tyson

The JSC Workplace

The JSC Workplace

Aug 3, 1969 Apollo 11

Aldrin, Collins & Armstrong

in a quarantine area during their first post-flight debriefing

The JSC Workplace

The Apollo Quarantine area has been re-purposed as the Life Sciences conference room.

The JSC workplace