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

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). \( \alpha_2 \text{R} \) = adrenergic \( \alpha_2 \)-receptor; CPG = central pattern generator; \( D_2 \text{R} \) = dopamine \( 2 \)-receptor; \( \Delta^8 \)-THC = \( \Delta^8 \)-tetrahydrocannabinol; DVC = dorsal vagal complex; 5-HT = serotonin; H = histamine; mR = cholinergic muscarinic receptor; NK = neurokinin; R = receptor.

Central neurocircuitry associated with emesis. [Hornby PJ](http://example.com).
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

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.
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.

Wotring  JSC NASA Pharmacology  24 March 2012
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
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.
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

Wotring
JSC NASA Pharmacology
24 March 2012
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
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
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/
NSBRI  http://www.nsbri.org/
Bedrest Study Info:  http://www.bedreststudy.com
Postdoctoral Opportunities  http://nasa.orau.org/postdoc/

Ginger  virginia.e.wotring@nasa.gov
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