Pharmacology During Spaceflight Missions

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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). $\alpha_2$R = adrenergic $\alpha_2$-receptor; CPG = central pattern generator; $D_2$R = dopamine $D_2$-receptor; $\Delta^2$-THC = $\Delta^2$-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 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

- Spinal cord
- Bone
- Vertebral disk
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

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
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
The Human Exploration Research Analog (HERA) 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
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.
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

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