



**University of
Nottingham**

UK | CHINA | MALAYSIA



Pharmacological Countermeasures

gg
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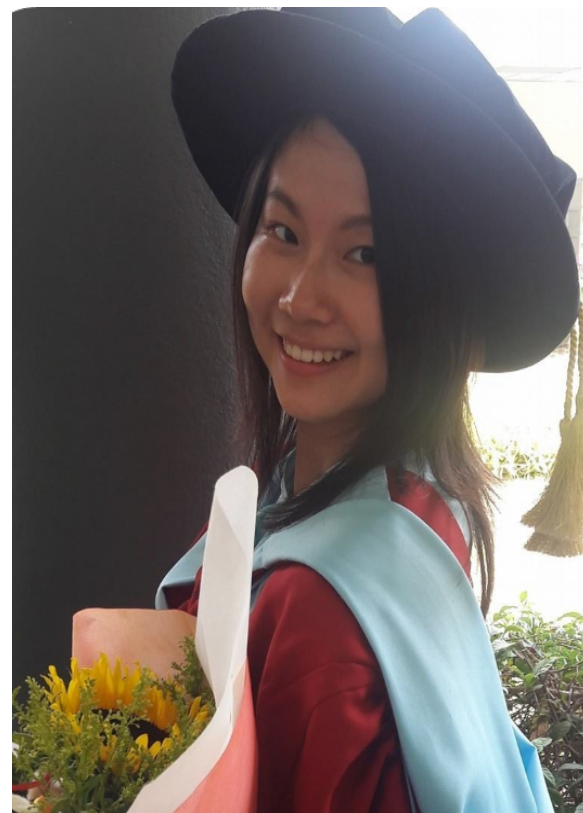
A little bit about me



- From: Malaysia
- Pediatrics leukemia pharmacist
- GP-based pharmacist



- Community pharmacist
- Lecturer in Australia

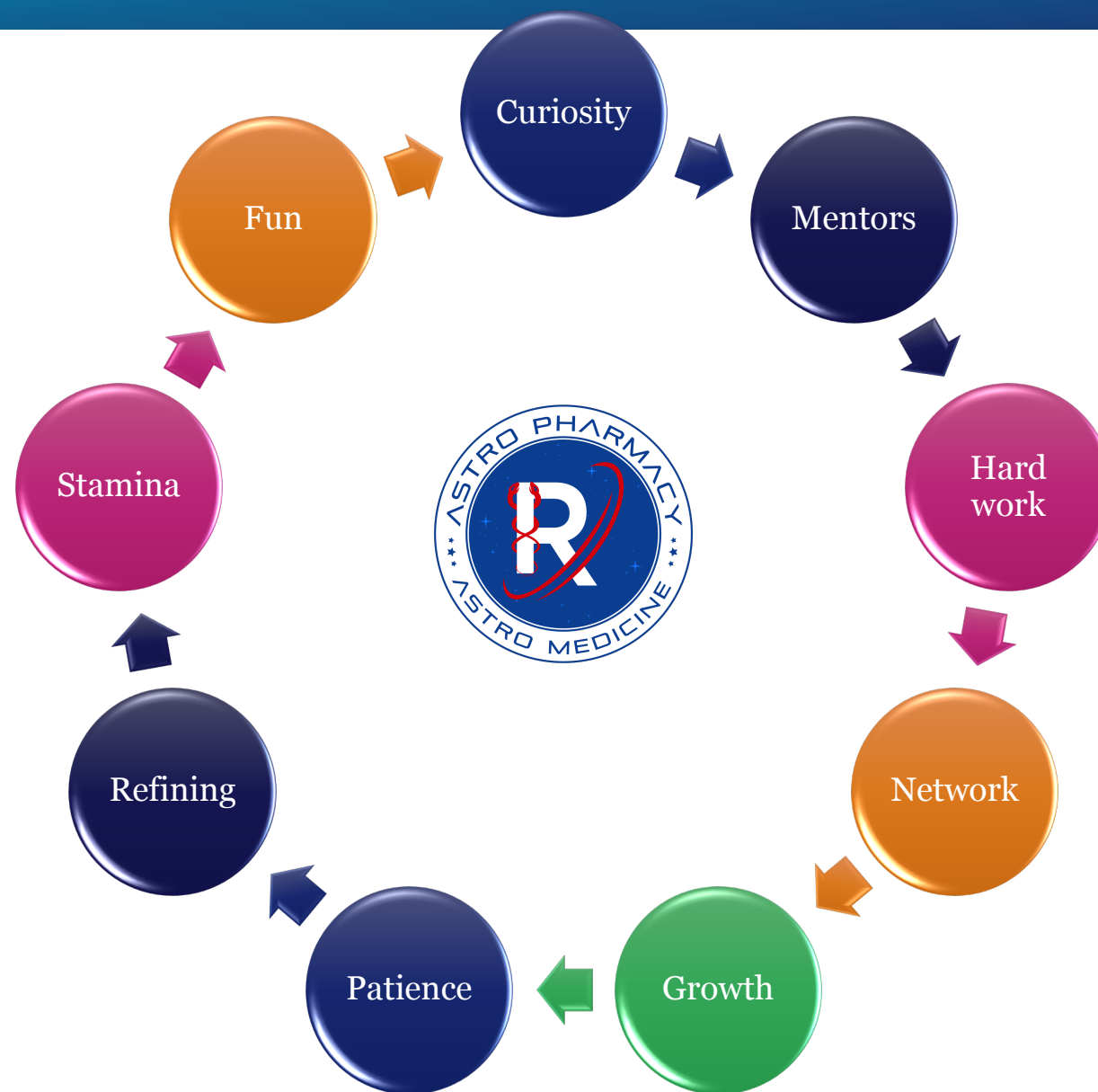


- Research expertise:
 - Improving medicines management
 - Improving healthcare services- Osteoporosis
 - Discrimination
 - Astropharmacy





The journey into Astropharmacy

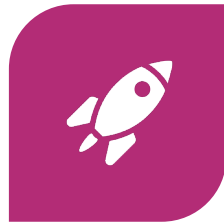




HEALTH
PROBLEMS IN
SPACE



TYPES OF SPACE
TRAVELERS



HOW TO BEGIN
RESEARCH



TYPES OF
PLATFORMS



EXAMPLE OF
RESEARCH



THE FUTURE AND
BENEFIT



Bone and muscular deterioration

- Bone density drops 1% per month
- Kidney stones
- Lack of vitamin D
- Usefulness of rehabilitation
- Risk of osteoporosis related fractures
- Muscle loss



Source:NASA

Biphosphonate

- Mechanism of action: Slow the rate that bone is broken down in your body.
- Types: Alendronic acid/Zoledronic acid etc
- Effect: 6-12 months
- Route: Oral or injection
- Administrations for oral:
 - Once weekly
 - Empty stomach with a full glass of water.
 - Stand or sit upright for 30 minutes after taking them.
 - Wait between 30 minutes and 2 hours before eating food or drinking any other fluids.
- Side effects:
 - Irritation to the foodpipe
 - Swallowing problems
 - Stomach pain
 - Osteonecrosis of the jaw (ONJ) (High doses)





Cyclizine

Hyoscine and Dexamfetamine

Sparingly used

Dimenhydrinate transdermal patch

Intramuscular promethazine



Antihistamine

Patch test

Topical and oral steroids



Melatonin

Sleep medications

- Zolpidem (a sedative)
- Zalpelon (sedative-hypnotic)
- Diphenhydramine (Benadryl- Over the counter anti-histamine)



Apollo Programme common medications taken from the summary report:

- All mission used skin cream
- Apollo 7- Actifed (Antihistamine)
- Apollo 8- Seconal (Sleeping tablet)
- Apollo 9- Seconal
- Apollo 10- Aspirin
- Apollo 11- Lomotil, Aspirin, Scopalamine/dextroamphetamine
- Apollo 12- Actifed & Seconal
- Apollo 13- Aspirin, Lomotil, Scopalamine/dextroamphetamine
- Apollo 14- Nose drops
- Apollo 15- Aspirin, nose drops
- Apollo 16- Seconal
- Apollo 17- Seconal, simethicone, Scopalamine/dextroamphetamine, Lomotil

Twentieth Century Fox



It is estimated that the rate of **significant illness or injury** (such as stroke, myocardial infarction, intracerebral haemorrhage, appendicitis, and bone fractures) **or death** on submarines, Antarctic expeditions, military aviation and **space flight is 0.06 cases-per-person-year**.

Crew of 6

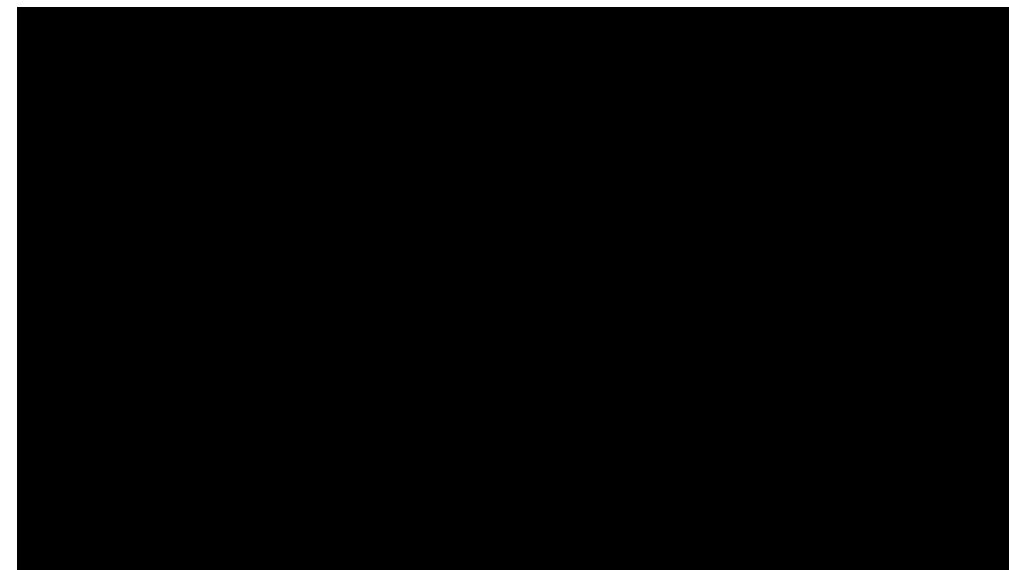
36 month trip

0.06 serious incidents per person per year

Probability of a serious incident?

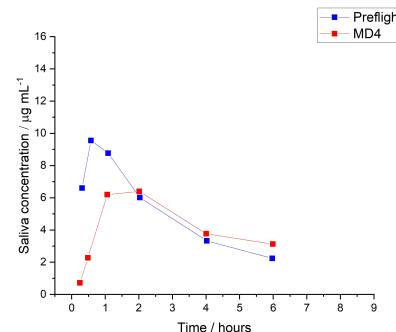
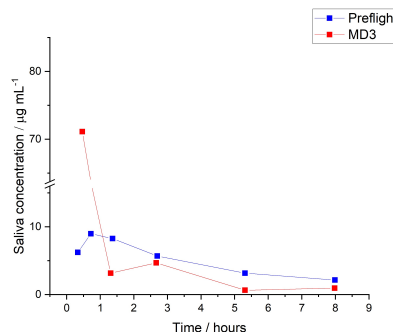
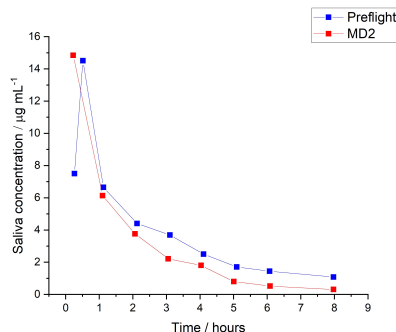
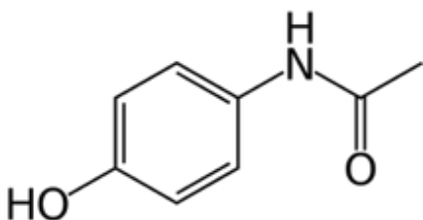
67% ! That's not good

(38% chance of only one, 20% of two, 7% of three)



Twentieth Century Fox

Drug regimens (dosage, rate of release, etc.) will have to be altered, or specifically tailored to individuals depending on their time in space or other adaptations.

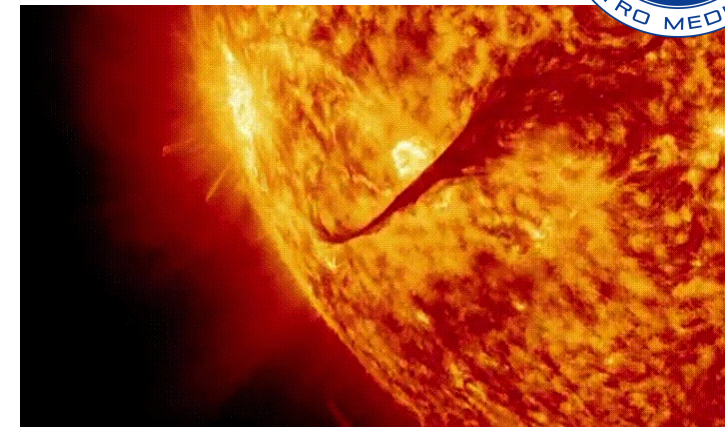


Universal Pictures

Changes in PK/PD are difficult to predict and subject dependent.



- ISS 10x radiation
 - Cancer risk
 - CNS
 - N + V
 - Death
- Moon mission
 - Van Allen belts
- Solar flares





- 87% flown to ISS have shelf lives of less than 24 months – limits exploration
- Only opportunistic studies > 550 days no control
 - Degradation and impurities found in
 - Aspirin
 - Ibuprofen
 - Loratadine
 - Zolpidem
- Antibiotic medications studied:
 - Augmentin (most unstable)
 - Imipenem/cilastatin -- flown in original commercial packaging



3.001 MEDICAL KIT- CONTENTS AND REFERENCE
(MED CL/SpX-6 - ALL/FIN/T) Page 2 of 27 pages

Table 1. Convenience Medication Pack (White)

Item	Strength, Volume	Route of Use	Qty in Pack	Unit	Possible Side Effects	Comments	Location
Antibiotic							
Bacitracin	500 units/gm, 0.9 gm	Topical	30	unit dose pack	No significant side effects		Spine
Antidiarrheal							
Loperamide (Imodium)	2 mg	Oral	40	tablet	Abdominal discomfort, nausea, vomiting, constipation, drowsiness, dizziness, dry mouth	Use for nonbloody diarrhea. No more than 8 tablets every 24 hours.	B2
Antihistamine							
Fexofenadine (Allegra)	180 mg	Oral	100	tablet	Headache, vomiting, fatigue, somnolence, dizziness, fever, pain, drowsiness, diarrhea, nausea, upset stomach, muscle aches, back pain, pain in extremities	Do not use with other antihistamines. Do not drink grapefruit juice 1 hour before or 2 hours after taking the medication.	B2
Loratadine (Claritin)	10 mg	Oral	375	tablet	Headache, drowsiness, dizziness, fatigue, dry mouth		A2
Olopatadine (Pataday)	0.2 %, 2.5 mL	Eye	6	bottle	Blurred vision, eye pain, stinging, burning, headache	Remove contact lenses before use. After instilling drops, wait at least 10 minutes before inserting contact lenses.	A3

A medical emergency and the necessary pharmaceutical intervention of an astronaut in Earth orbit can be accommodated by an aborted mission and early return



Other space travelers



Astronauts



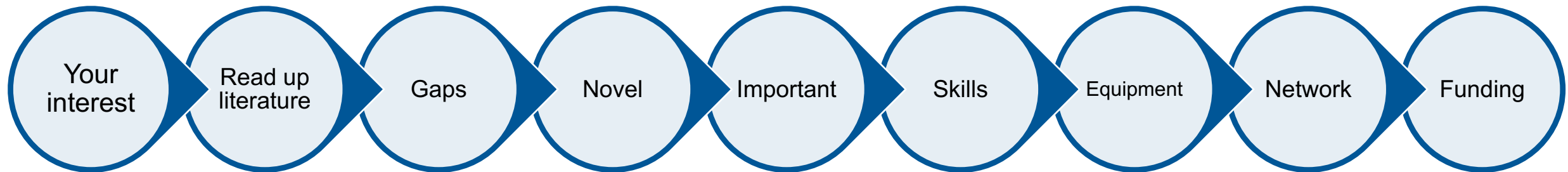
Space tourists



Commercial workers-
engineers, miners etc

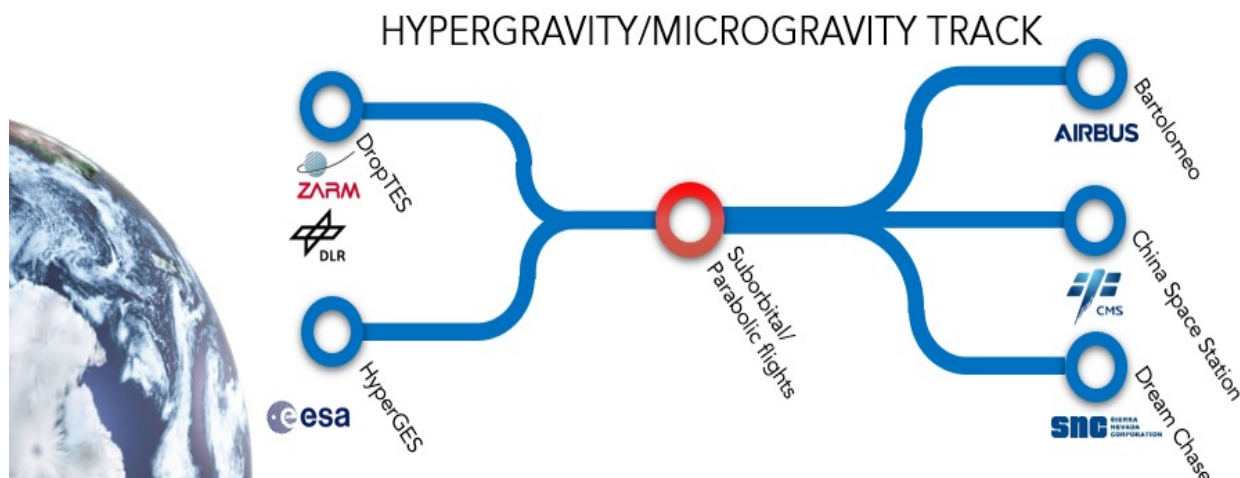


How experiments are developed





1. ISS
2. Payloads
3. Sounding rockets
4. Analogue- Bed rest studies, mice etc
5. Social and policy science
6. Adapting current research methods and applying to space





Example 1: Social and policy science in space



The aim: To explore stakeholder perspectives towards the role of
Astropharmacy in the space sector

Astropharmacy addresses the question of how
pioneers and explorers are to receive effective
medical and pharmaceutical care.

- Qualitative research- Social and policy science-> Exploratory study
- Individual interviews and focus group discussions with stake holders



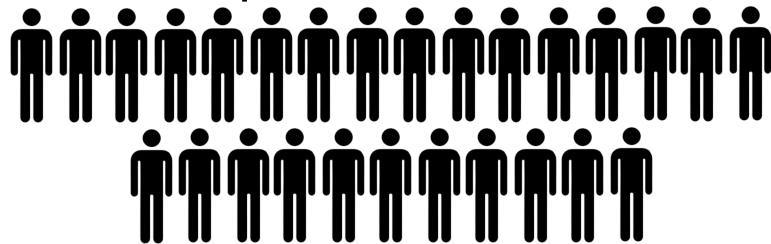
- Transcribe verbatim
- Thematic analysis
 - Step 1: Become familiar with the data,
 - Step 2: Generate initial codes,
 - Step 3: Search for themes,
 - Step 4: Review themes,
 - Step 5: Define themes,
 - Step 6: Write-up.



Sample Details

Pharmacy

Hospital, community, industry,
primary care, entrepreneurs,
governing bodies, academic, future
pharmacists



Space Sector

Space agency leads, private
astronauts, commercial space
companies, space tourists,
academics, Space journalism, Space
law, aerospace doctors, space
related field students



Total sample: 53 participants

All recruited from various geographical locations covering North America,
Europe, Asia, Africa and Australia.



Themes	Sub themes
Medication management	i.e. Medication optimization
Medication-related research	i.e. Pharmacokinetics/Pharmacodynamic
Awareness on health and medication in space	i.e. Improving space health and medication literacy

Full paper coming soon!



Medicines management:

*The **clinical, cost effective and safe** use of medicines to ensure patients get the **maximum benefit** from the medicines they need, while at the same **time minimising potential harm** ~
Medicines and Healthcare Products Regulatory Agency (MHRA) 2004~*

Medicines optimisation:

*Helps the **right patients** to get the **right medicines** at the **right time**. It examines how patients may stop or start their medicines, how they use them over time and how lifestyle changes or non-medical therapies might reduce the need for medicines ~Royal Pharmaceutical Society~*

Medication optimization focuses on outcomes and patients rather than process and systems.

Activities which promote safe and effective medicines management occur at each stage of the medicines journey and aim to improve outcomes for the patient. The stages of the journey include:

Stages	Definition	Past exploration	Deep space exploration	Space tourism
Manufacturing and marketing	Ensuring that medicines are manufactured legitimately and safely, and that advertising complies with ABPI standards.	✓	?	?
Procurement.	Ensuring medicines are purchased from a legitimate source.	✓	?	?
Selection	Making a choice about which medicines to use.	✓	?	?
Prescribing	Ensuring legal processes are adhered to for medicines particularly prescription only medicines.	probably	?	?
Dispensing	Ensuring that medicines are dispensed correctly.	probably	?	?
Sale or supply	Medicines that are available over the counter either as over the counter medicines or in pharmacies, pharmacy only medicines. The supply of medicines is medicines that are supplied to a patient in a pre-dispensed form, for example over labelled medicines, and are given to the patient directly by the clinician.	Sale-n/a Supply-✓	?	?
Patient use	How patients engage in medicine management eg, self-administration and adherence.	probably	?	?
Disposal	Safe disposal of medicines that have not been used or have been partially used.	✓ (Earth)	?	?



Medication management- Medication optimization



I think a pharmacist could really **think about the comfort of participants** in ways that I know a lot of the other researchers are not...

An experienced pharmacist could sit down and say “ok I’ve worked with 12 astronauts, I know that many of them felt discomfort during this part of the transition... this percentage of them felt like they had a head cold until they chose to medicate, you know here are the things you can do prophylactically in advance, here’s the fast-acting solution for you know when you find yourself in trouble, and then here’s something for maintenance” –SS19-

A telepharmacy would be useful for all types of space travel! – SS10-



Drug review... before they leave, after they leave, during the period while they are up there... long-term –PH3-

You’ve got an individual that might be taking a medication regime... preferably it’s by a pharmacist who’s the expert in medicines and therefore can understanding from a **pharmacodynamic and pharmacokinetic perspective** how the medicines (work)... because really what we’re talking about is **do their current medications need to change in the context of being in space.** –PM1-PH11 -

There could be a drug that it’s seemingly harmless to us down here but once ingested up in space it gets us high or like a zombie –SS2-

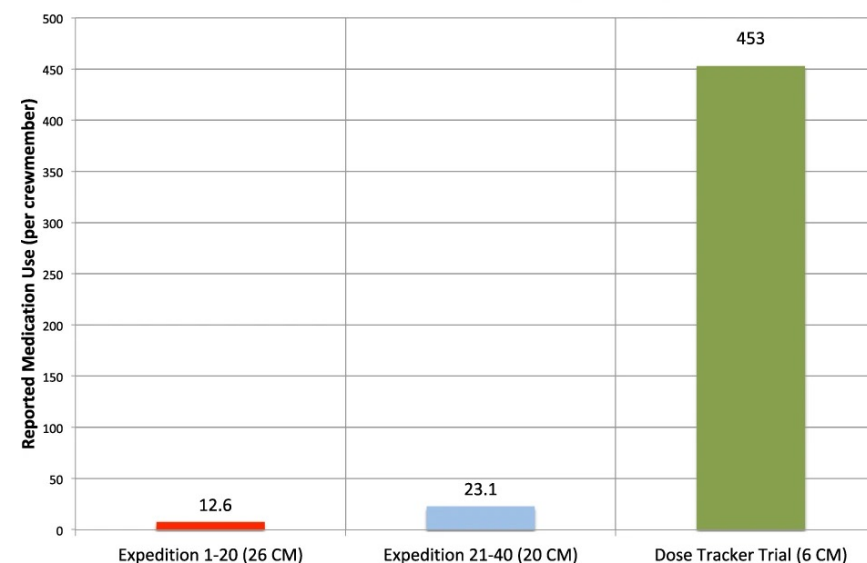


Example 2: Medication use and performance during space flight

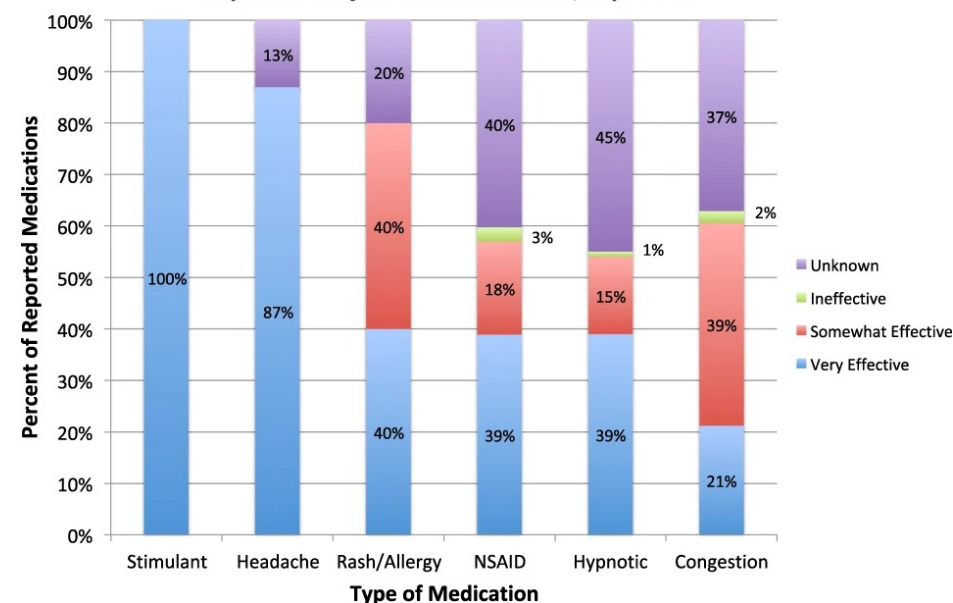


- Not comprehensively monitored
 - Crew time demand
 - Avoid onerous tracking
 - Crew able to take medication without discussing with flight surgeon
 - OTC rarely recorded
 - Poor documentation
 - Low priority as able to resupply

Reporting of Medication Use During Spaceflight



Reported Subjective Effectiveness, Exp 21-40



Example 3: Astromedicine and Astropharmacy



Bacterial and immunological crosstalk in space flight



Liposomes mimicking halophilic archaea cell membrane for antibacterial therapy in space



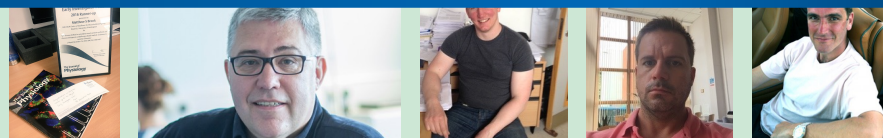
UoN Astrobiology CubeSat design and development



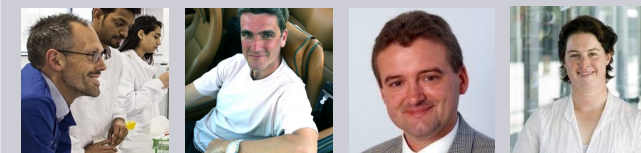
Synthetic biology for on-demand production of therapeutic



Tejasvi Shivakumar
CEST 1630 Stay tuned!



Foods for Space: Late stage customization of food materials in extreme environments



Lucia Morbidelli, PhD

Lab of Pharmacology of Angiogenesis and microcirculation
Det. Life Sciences, University of Siena (I)

Pharmacology in space & for space

Relevant activities for space biology

- Long lasting collaboration on microgravity effect on endothelial and stromal cells with Prof. Monica Monici (Univ Florence)
- Impact of microgravity on wound healing and sutures. Development of pharmacological and biological countermeasures

Funded projects

2014-2016: ASI "Tissue repair in microgravity - RITMI

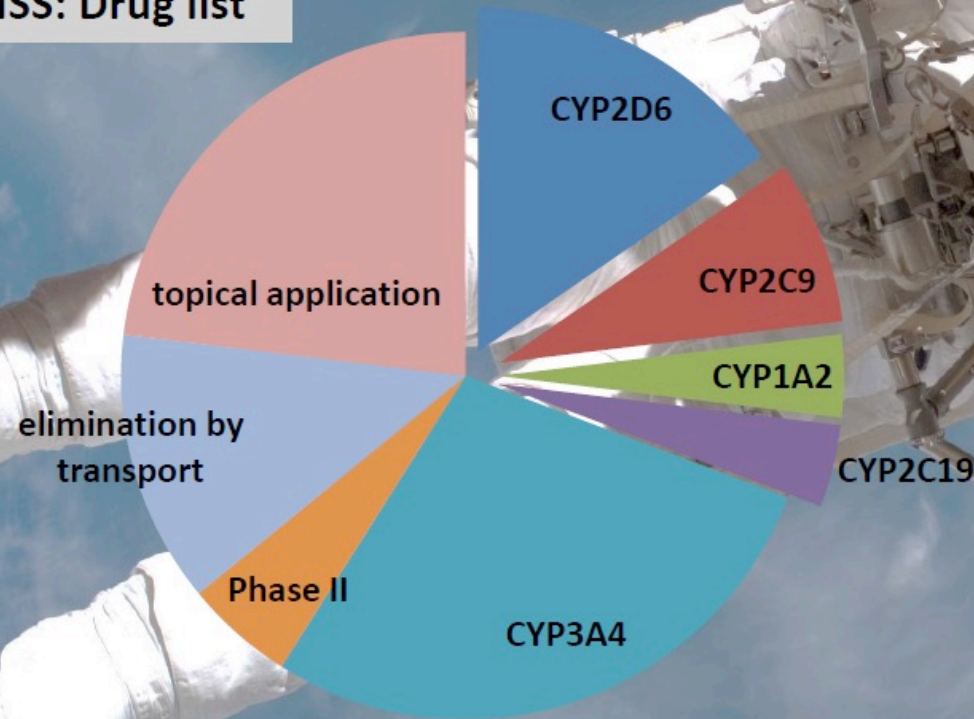
2018-2021 ASI, "Wound healing and sutures in unloading conditions-
SUTURE"

2020-2023: ESACORA MAP project "Wound Healing In Space: Problems and Prospects for Tissue Engineering and Regeneration - WHISPER"

Where Failure Is Not an Option –Personalized Medicine in Astronauts

Julia C. Stingl^{1,2*}, Susanne Welker¹, Gunther Hartmann³, Volker Damann⁴, Ruppert Gerzer⁵

ISS: Drug list



PLOS ONE 10(10): e0140764. <https://doi.org/10.1371/journal.pone.0140764>

Table 1. Polymorphic CYP substrates within the ISS drug list: Information about involvement of polymorphic drug metabolism labels or from evidence-based pharmacogenetic guidelines. Among the drugs listed in the ISS repository, specific warnings or effects have been identified in the label section of 14 drugs. For six drugs on the list, specific therapy modifications (alternative drug or dose) are proposed in existing evidence-based guidelines.

CYP2D6 substrates on ISS drug list	Indication	Information about polymorphic enzymes in the drug label	Dosing Guidelines: CPIC/ GWPG	R
Metoprolol	Heart failure, hypertension	FDA: warnings about pharmacogenetics and drug interactions	PM: 75% UMT; up to 250%	[1]
Diphenhydramine	Vomiting, allergic rhinitis	Warning about drug interactions with drugs metabolized by CYP2D6		[1]
Cetirizine	Vomiting, allergic rhinitis	Information about drug metabolism via CYP2D6		[1]
Loratadine	Vomiting, allergic rhinitis, urticaria	Information about drug metabolism via CYP2D6		[1]
Meclozine	Vomiting, allergic rhinitis	Information about drug metabolism via CYP2D6		[1]
Ondansetron	vomiting	Information about drug metabolism via CYP2D6		[1]
Promethazine	Rhinitis, urticaria, Sickness, vomiting	Information about drug metabolism via CYP2D6		[1]
Tamsulosin	Prostate hyperplasia	Information about drug metabolism, high exposure in PM as compared to EM		[1]
Acetaminophen	Pain, fever	Warning about interaction potential with CYP2D6 substrates		[1]
Hydrocodone	Pain	CYP2D6 involved in activation; PMs less efficacy		[1]
Venlafaxine	Depression	Metabolism of venlafaxine to the active metabolite, total active moiety not affected by polymorphism	80% in PMs 170% in UM or select an alternative drug. Cardiovascular risk higher in PMs	[1]
Aripiprazole	Psychosis	Dose recommendations in FDA label, and interaction warning	Reduce dose in PMs to 67% UM; no recommendation	[1]
CYP2C19 substrates				
Diazepam	Sleep disturbances	Information about drug metabolism and interaction via CYP2C19		[1]
Setraline	Depression	Information about drug metabolism via CYP2C19	Reduce PM dose to 50% UM; no recommendation	[1]
Omeprazole	Reflux	Drug interactions	UM dose 100–200% increased	[1]
CYP2C9 substrates				
Ibuprofen	Pain, Fever	CYP2C9 and CYP2C8 involved in metabolism	CYP2C8 and 9 combined genotype involved in GI bleeding side effects	[1]
Phenytoin	Epilepsy, seizures	PMs: enhanced risk of toxicity	PMs: 50% higher risk for skin toxicity; IMs: 75% of dose	[1]
Ketamine	Anesthesia, pain	Minor enzyme involved in metabolism		[1]
Acetylsalicylic acid	Pain, fever, cardiovascular	Minor enzyme, Drug interactions	CYP2C8 PM higher risk for urticaria	[1]
Sulfamethoxazole	Antibiotic	Information about m via CYP2C9	Risk of hemolysis in Glucose 6-phosphate dehydrogenase deficiency	[1]
Loperamide	Diarrhea	Interaction warning		[1]
CYP1A2				
Melatonin	Daytime sleep, insomnia	Metabolism, Interactions		[1]
Caffeine	Sleepiness	Metabolism, Interactions		[1]
Udocaline	Anaesthetic	Interactions		[1]

* Level of evidence: 1: in vitro data only, 2: in vivo pk data, 3: clinical data on efficacy and/or side effects



Example 6



Pierre Boutouyrie and Audrey Derobertmasure

Next Talk! Stay tuned!



Effects of Space-Altered Physiology

Changes in pharmacokinetics (PK)

Changes in pharmacodynamics (PD)

Changes in Drug Interactions

Mitigating medication-related problems

Medication use

Medication supply

Long acting/personalized dosage forms

Coping with Emerging Hazards

Deep space radiation

Planetary hazards

Newly recognized risks to humans in space

Optimization of Existing PCMs

Pharmacogenomics

Update per new terrestrial treatments



on, and the most important

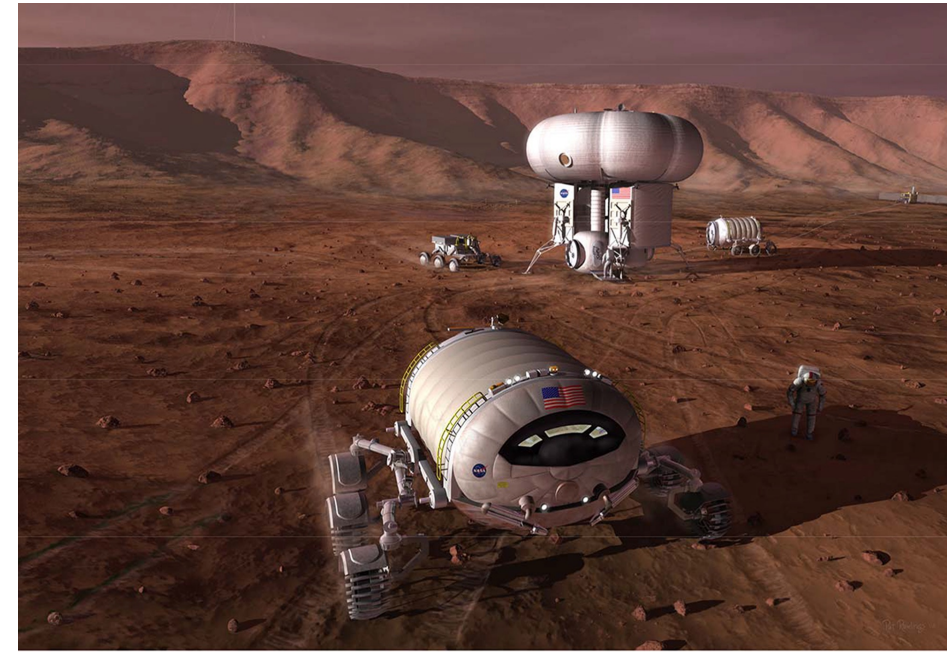
William Anders, Apollo 8





Mars as early as 2024

- More professionals to assist in medication management:
 - Preparing medical kits for Mars
 - Diseases or disorders that may arise later in life
 - Consider how space travel affects certain diseases or side effects to medications as well.
 - Colonization on Mars occurs- influx of humans wanting to travel to Mars, not just astronauts.
 - Manufacturing of medications



World's first

Could it be you?

Special thanks

Academics!

Scientist!

UK Space Agency!

European Space Agency!

