Pharmacological Countermeasures

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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

- Curiosity
- Mentors
- Hard work
- Network
- Growth
- Patience
- Refining
- Stamina
- Fun
Weightlessness and its effects

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
Weightlessness and its effects

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 does)

Alternative? – Denosumab/Teriparatide?

Source: NASA
Medications for Space sickness

- Cyclizine
- Hyoscine and Dexamfetamine
- Sparingly used
- Dimenhydrinate transdermal patch
- Intramuscular promethazine
Medication for Allergies

- Antihistamine
- Patch test
- Topical and oral steroids
Non prescription and prescription sleep medications

Melatonin

Sleep medications

• Zolpidem (a sedative)
• Zalpelen (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
Key challenges

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)
and worse…

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.

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

- ISS 10x radiation
  - Cancer risk
  - CNS
  - N + V
  - Death

- Moon mission
  - Van Allen belts

- Solar flares

https://www.nasa.gov/hrp/bodyinspace
Final Fantasy V
Medication stability

• 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
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

- Your interest
- Read up literature
- Gaps
- Novel
- Important
- Skills
- Equipment
- Network
- Funding
Platforms/tools

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
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.
Methods

• Qualitative research - Social and policy science -> Exploratory study

• Individual interviews and focus group discussions with stakeholders

• 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

Total sample: 53 participants
All recruited from various geographical locations covering North America, Europe, Asia, Africa and Australia.

Space Sector

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

<table>
<thead>
<tr>
<th>Themes</th>
<th>Sub themes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication management</td>
<td>i.e. Medication optimization</td>
</tr>
<tr>
<td>Medication-related research</td>
<td>i.e. Pharmacokinetics/Pharmacodynamic</td>
</tr>
<tr>
<td>Awareness on health and medication in space</td>
<td>i.e. Improving space health and medication literacy</td>
</tr>
</tbody>
</table>

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*. ~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:

<table>
<thead>
<tr>
<th>Stages</th>
<th>Definition</th>
<th>Past exploration</th>
<th>Deep space exploration</th>
<th>Space tourism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturing and marketing</td>
<td>Ensuring that medicines are manufactured legitimately and safely, and that advertising complies with ABPI standards.</td>
<td>√</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Procurement</td>
<td>Ensuring medicines are purchased from a legitimate source.</td>
<td>√</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Selection</td>
<td>Making a choice about which medicines to use.</td>
<td>√</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Prescribing</td>
<td>Ensuring legal processes are adhered to for medicines particularly prescription only medicines.</td>
<td>probably</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Dispensing</td>
<td>Ensuring that medicines are dispensed correctly.</td>
<td>probably</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Sale or supply</td>
<td>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.</td>
<td>Sale-n/a Supply-√</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Patient use</td>
<td>How patients engage in medicine management eg, self-administration and adherence.</td>
<td>probably</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Disposal</td>
<td>Safe disposal of medicines that have not been used or have been partially used.</td>
<td>√ (Earth)</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
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-...

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 -

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

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

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 therapeutics

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

Tejasvi Shivakumar
CEST 1630 Stay tuned!
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”
Example 6

Pierre Boutouyrie and Audrey Derobertmasure

Next Talk! Stay tuned!
European Space Agency SpaceSci Roadmap 2021

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
“We came all this way to explore the moon, and the most important thing is that we discovered the Earth.”

William Anders, Apollo 8
Future of pharmacy and healthcare

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!