2013 DECADAL STUDY
The Impact of Sex & Gender on Adaptation to Space

A Joint Study by the National Aeronautics and Space Administration and the National Space Biomedical Research Institute

Reproduction Workgroup
Working Group Members and Affiliations

- **Marjorie Jenkins MD FACP (Presenter/Co-Chair)**
  Professor of Medicine, Chief Science Officer, Laura W Bush Institute for Women's Health; Rush Endowed Chair for Excellence in Gynecology Oncology, Texas Tech University Health Sciences Center

- **April E. Ronca, PhD (Co-Chair)**
  Scientist, Space Biosciences, NASA Ames Research Center; Adjunct Professor of Obstetrics & Gynecology, Former Research Program Director, Women Center of Excellence, Wake Forest School of Medicine

- **Ellen S. Baker, MD, MPH**
  Retired, NASA Medical Officer and Astronaut, Johnson Space Center

- **Tamara G. Bavendam, MD, MS**
  Senior Scientific Officer, Program Director, Women's Urologic Health, NIH/NIDDK

- **Kevin D. Beck, PhD**
  Associate Professor of Neurology & Neurosciences, New Jersey Medical School

- **Virginia M. Miller, PhD**
  Professor of Physiology; Surgery, Mayo Clinic

- **Joseph S. Tash, PhD**
  Former Director of the Interdisciplinary Center for Male Contraceptive Research and Drug Development; Professor of Molecular and Integrative Physiology; Professor of Urology; University of Kansas Medical Center; President, American Society for Gravitational and Space Research
Approach to Evaluation of Sex and Gender on Reproductive and Genitourinary Health

- Unique Organ System
- Spermatogenesis, Ovulation, Menstruation, Menopause
- Reproductive Biology

- Shared Organ Systems
  - Endocrine
  - With Unique Features

- Shared Organ System
  - Voiding Renal Ca⁺ Excretion

- Environmental
  - Sleep Deprivation/Stress
  - Microgravity
  - Radiation

- Biology

- Behavioral

- Anatomy

- Physiology

- Roles
## Reproductive System: Effects of Radiation

### Gonads Top the Table of Radiation Tissue Sensitivity*

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Single Dose (Gy)</th>
<th>Fractionated Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovary</strong></td>
<td>2–6</td>
<td><strong>Testes</strong></td>
</tr>
<tr>
<td>Bone marrow</td>
<td>2–10</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong></td>
<td>2–10</td>
<td></td>
</tr>
<tr>
<td>Eye (lens)</td>
<td>2–10</td>
<td></td>
</tr>
<tr>
<td>Mucosa</td>
<td>5–20</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5–10</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>7–10</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>Vasculoconnective tissue</td>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>15–20</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>15–20</td>
<td></td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>15–20</td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>15–20</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>15–25</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>18–20</td>
<td></td>
</tr>
<tr>
<td>Bone and cartilage</td>
<td>&gt;30</td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>&gt;70</td>
<td></td>
</tr>
</tbody>
</table>

Are there sex differences in altered estrogen signaling in the space-flight affected/aging systems?

- Ground-based studies have identified age-related alterations in estrogen receptor signaling in many major organ systems.
- A body of animal research has indicated several of these same systems are also altered in space flight (which is known to accelerate some aging processes).

*Estrogen-regulated systems known to be affected by space flight & aging*
Consideration of the Impact of Sex & Gender on Reproductive Biology of Astronauts

Stress:
- impacts gonadal hormone levels
- increases inflammatory markers
- activates the HPA axis
  - can lead to disrupt ovarian function
- increases risk and prognosis of CVD and events

Future Reproduction:
Prior flight vs post flight fertility
(Spermatogenesis, IVF, spontaneous abortions, term pregnancy, pregnancy associated complications)
Unique Organ System
Reproductive/Endocrine

• **Terrestrial**
  – HPG Axis
    • Dysregulation alters sleep quality
    • *Age* and *Sex*-related differences in reproductive hormones exert known effects
  – HPA Axis
    • Stressor exposure increases pituitary and adrenal hormone release
    • Stronger correlation of increased cortisol levels to male performance
    • OC usage is associated with stress-induced cortisol release

• **Space Travel**
  – ACTH and cortisol are have been shown to be following some missions
  – Longer duration travel has significantly increased duration of exposure relative to normal reproductive cycle lengths

• **Future Exploration**
  – Prospectively examine whether OC usage alter the space-flight and recovery profiles of HPA-axis tone
  – Examine sex differences in cortisol levels and performance during and post-flight
Shared Organ System
Urogenital Systems

• **Terrestrial**
  – Urinary tract stones are more prevalent in Caucasian men
  – Urinary tract infections are more common in women
    • Emerging data regarding normal urinary microbiome
  – There is no data on sex differences in spontaneous urinary retention
  – Incidence on post-operative urinary retention is not different between men and women

• **Space Travel**
  – Incidence of urinary tract stones is equivalent between sexes
  – Incidence of urinary tract infections is greater in women
  – Urinary retention requiring catheterization has occurred only in women
    • Unless there is evidence of more anti-emetic use in women or more dehydration, this likely represents adaptation to new voiding behavior

• **Future Exploration**
  – Studies of urinary tract manipulation in low gravity environment
  – Better understanding of risk factors for UTI
## Demographics of Astronauts

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Age during 1st transit</td>
<td>42.4 yo</td>
<td>44.5 yo</td>
</tr>
<tr>
<td>% with at least 1 child</td>
<td>38%**</td>
<td>67%</td>
</tr>
<tr>
<td># of Children</td>
<td>1.6</td>
<td>2.5</td>
</tr>
<tr>
<td>% Married</td>
<td>69%</td>
<td>76%</td>
</tr>
</tbody>
</table>

### Societal Roles (Gender)

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>More likely to be primary caregiver</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hiatus from career due to parental role</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

### Biological Factors (Sex)

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cessation of Reproductive Capacity</td>
<td>Menopause</td>
<td></td>
</tr>
<tr>
<td>Thromboembolic Risk with OCPs</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Bone loss with certain types of contraception</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

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Sex and Gender in Space Adaptation: Past - Present - Future

- 2013 Report on Sex, Space and Environmental Adaptation
  - Approach
    - Organized the work around applicable unique and shared organ systems and the major space travel components likely to alter these systems
  - Updated Content
    - Outlines sex differences in genitourinary health
    - Includes both Sex-based and Gender-based issues such as the impact of sex and gender on healthy aging in conjunction with astronaut health
  - Considerations to Enhance the Research Infrastructure
    - Discussion of further development of ground-based analogs
    - Pre-, During, and Post-flight longitudinal de-identified data collection
    - Tandem space and ground-based studies
    - “Space originated’ cells, systems and organisms across generations
    - Emphasizes threading sex and gender throughout health research platforms
Thank you