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WOMEN'S HEALTH CONSIDERATIONS FOR EXPLORATION SPACEFLIGHT

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WOMEN'S HEALTH CONSIDERATIONS OUTLINE

- ► ABNORMAL UTERINE BLEEDING
- ► ANEMIA
- ► BONE MINERAL DENSITY
- OVARIAN CYSTS
- VENOUS THROMBOEMBOLISM
- ► CONTRACEPTION
- ► FERTILITY
- ► HEALTH MAINTENANCE

ABNORMAL UTERINE BLEEDING BACKGROUND

- Affects 14-25% of reproductive-aged women in the US
- Etiology can be structural and non-structural
 - PALM: polyps, adenomyosis, leiomyomas, malignancy/neoplasia
 - COEIN: coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic, not otherwise classified
- Unknown how the space environment affects AUB
 - Simulated microgravity (hind-limb unloading) affects estrous cycling
 - Bed rest studies have not affected the menstrual cycle

ABNORMAL UTERINE BLEEDING PRE-FLIGHT CONSIDERATIONS - STRUCTURAL

- Pre-flight TVUS (transvaginal US) recommended for all female astronauts with AUB
- Can consider diagnostic ± therapeutic hysteroscopy if any concern for endometrial or intramural pathology
 - ► If polyp \rightarrow polypectomy \rightarrow LNG IUD
 - ► If adenomyosis \rightarrow LNG IUD vs. hysterectomy
 - ► If leiomyomas \rightarrow myomectomy \rightarrow LNG IUD
 - ▶ If malignancy/neoplasia \rightarrow mgmt depends upon pathology

ABNORMAL UTERINE BLEEDING PRE-FLIGHT CONSIDERATIONS – NON-STRUCTURAL

- Screening for PCOS, thyroid dysfunction, prolactinoma
- Screening for personal/family history of bleeding disorders
- Screening and treatment of iron deficiency
- Management of non-structural AUB:
 - Progesterone-only or progesterone/estrogen therapy
 - LNG IUDs are first line agents for treating new-onset AUB and preventing recurrence
- Screening for inherited thrombophilias

ABNORMAL UTERINE BLEEDING PRE-FLIGHT CONSIDERATIONS – MENSTRUAL SUPPRESSION

- Combined Hormonal Contraceptives (CHCs) and LNG-IUD achieve highest rates of amenorrhea
 - LNG-IUD:
 - no risks/side effects of systemic estrogen
 - ▶ Remains efficacious for 5-7 years
 - ► Function is not dependent upon strict daily compliance

► CHCs:

- ► May be associated with less BMD loss
- ► Can suppress ovarian cyst formation
- Avoids IUD-associated migratory risks
- More cumulative spaceflight experience

ABNORMAL UTERINE BLEEDING IN-FLIGHT CONSIDERATIONS

- No perfect modality of inducing amenorrhea or preventing AUB in-flight
- Advanced surgical options likely unavailable ->
 pharmacologic management = mainstay of treatment
- CMOs should have some pre-flight training in digital pelvic examination
- Speculums are not currently available
- Point-of-care lab tests may include CBC, pregnancy test
- ► TAUS (TVUS if available)

ABNORMAL UTERINE BLEEDING IN-FLIGHT CONSIDERATIONS

► New-onset AUB in-flight:

- Continue LNG-IUD or current CHC
- Consider adding a burst taper of CHCs
- GnRH agonists/antagonists

Non-hormonal pharmaceuticals that can be considered include:

- ► TXA: prevents fibrin/clot degradation w/o increasing VTE risk
- NSAIDs: shown to decrease duration and volume of menses
- Doxycycline: low risk adjunctive medication to hormonal modalities

Extreme scenarios

BONE MINERAL DENSITY PRE-FLIGHT/IN-FLIGHT CONSIDERATIONS

Estrogen

Shown to be protective against cortical / cancellous BMD loss in microgravity analogs and spaceflight

Evidence is inconclusive for LNG-IUD

Recommend vitamin D and calcium supplementation

Recommend resistive exercise

May consider bisphosphonate

OVARIAN CYSTS PRE-FLIGHT CONSIDERATIONS

Ovarian cyst production is common following ovulation Present in 5-7% of reproductive-aged females. Most will resolve spontaneously Theoretically, large cysts can prompt ovarian torsion Pre-flight management of cyst: Observation vs. laparoscopic management for simple cysts ► Work-up for malignancy if concern

OVARIAN CYSTS IN-FLIGHT CONSIDERATIONS

- Acute abdominopelvic pain during flight:
 - Consider torsion
 - ► TAUS (or TVUS if available) may be diagnostic
- Management of Torsion:
 - Terrestrially: surgical emergency for preservation of ovarian tissue and prevention of rare but severe morbidities
 - In-flight management: conservative measures including of pain control and management of sequelae
 - ► Long term risks likely low

VENOUS THROMBOEMBOLISM PRE-FLIGHT/IN-FLIGHT CONSIDERATIONS

Risk factors during flight

- Microgravity: relative lower limb immobility
- Altered hydration status and fluid distribution increased upper extremity congestion, potential for VTE
- Exogenous hormone use
 - Cyclical use of estrogen is associated with 4-6X risk of VTE
 - Unclear risk profile with continuous suppression
- Recently reported sentinel event of VTE during flight (Marshall-Goebel 2019)
 - In-flight management of VTE is a subject of current discussion in operational medical group

ENDOMETRIOSIS PRE-FLIGHT/IN-FLIGHT CONSIDERATIONS

- Endometriosis affects 10% of reproductive-aged women
- Gold standard diagnosis: Laparoscopy
- ► Therapeutic options:
 - Continuous CHCs
 - High-dose progestins
 - GnRH agonists/antagonists with add-back estrogen

HEALTH MAINTENANCE PRE-FLIGHT/IN-FLIGHT CONSIDERATIONS

- Screening for STIs / Pap Smear within 12 months of flight
 Chlamydia, Gonorrhea, Trichomonas, Syphilis, HSV, HIV, HPV
- HSV suppression during flight if affected, consider prophylaxis?
- HPV vaccine encouraged for all astronauts
 Early colposcopic management if necessary

HEALTH MAINTENANCE PRE-FLIGHT/IN-FLIGHT CONSIDERATIONS

- Screening for peri-menopausal symptoms, urogynecologic symptoms, vulvar/vaginal dermatoses prior to flight
- Screening for family history of gynecologic/breast cancers as well as familial cancer syndromes (i.e BRCA, HNPCC, Cowden's)
- Annual clinical breast exams

Diagnostic mammograms ± US/MRI PRN starting at age 35

PRE-FLIGHT-POST-FLIGHT CONSIDERATIONS

- Routine pregnancy testing with final pre-flight pregnancy test performed ~10 days prior to flight
- Discuss fertility desires and timing before mission assignment
 - Discuss age-related risks associated with advanced maternal age if delaying parity
 - Fertility outcomes have not been robustly studied post-flight
 - Consider assessment of ovarian reserve and oocyte/embryo banking
- Discuss contraceptive modalities, the risk of pregnancy inflight is > 0%

AREAS OF INTEREST PRE-FLIGHT-POST-FLIGHT CONSIDERATIONS

- Long-duration spaceflight will introduce continued and novel challenges for maintenance of gynecological and reproductive health
- The impact of the space environment outside of LEO of women's health remains unknown
- There is a driving need for increased data collection and analysis to properly characterize and mitigate women's health risks in future spaceflight

IMPORTANT LINKS / REFERENCES

Steller et al 2020 Marshall-Goebel 2019 Blue 2019