MANAGEMENT OF GENITOURINARY SYNDROME OF MENOPAUSE (GSM) IN FEMALE CANCER SURVIVORS

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DISCLOSURES

Sprout Pharmaceuticals
Advisory board

Astellas
Speakers Bureau

No Off-Label and/or Investigational Uses
LEARNING OBJECTIVES

- Describe the hypoestrogenic effects of genitourinary syndrome of menopause (GSM) on female genitals and lower urinary tract
- Recognize the impact of cancer treatments on menopausal status and contribution to GSM
- Identify treatment options for GSM in female cancer patients
- Distinguish the risks and benefits of treatment modalities for GSM by cancer type
- Understand additional implications of GSM on sexual health

#transformWH
90%

- Among quality-of-life issues in cancer survivors, sexual health is listed in 90% of gynecologic, breast, lower abdominal, anal and colorectal cancers as a major concern.

CANCER TREATMENTS AND MENOPAUSE STATUS

• Drivers of the hypoestrogenic state
  Chemotherapy
  Radiation
  Surgery-Oophorectomy
  Endocrine hormone therapy
  Menopause
VAGINAL ATROPHY—GENITOURINARY SYNDROME OF MENOPAUSE (GSM)

- Only effects the vagina
- Is isolated to the vagina and urethra
- Has no impact on genital arousal
- Impacts risks for urinary tract infections

- Labia majora
- Clitoris
- Vestibule/introitus
- Vagina
- Urethra
- Bladder
THE ROLE OF ESTROGEN ON UROGENITAL HEALTH

- Vasoactive hormone
- Increases blood flow, increases transudative lubrication
- Supplies glycogen to the superficial and intermediate layers maintaining the acidic pH
- Supports collagen content of the vagina, maintains thickness and elasticity of the vaginal walls
- Supports the epithelium, connective tissue and smooth muscle of the vulva, vagina, urethra and bladder trigone
GSM: EFFECTS OF DIMINISHED ESTROGEN

Vulvovaginal dryness
Burning or irritation
Dyspareunia
Urinary symptoms- urgency, dysuria, recurrent UTIs
Usually, progressive

Vulva: thinning/loss of pubic hair
Fusion of the labia
Clitoral hood retraction

Vagina: introital retraction
Pallor
Loss of rugae
Ph>5

Urethra:
Prominence of urethral meatus/caruncle
GENITOURINARY SYNDROME OF MENOPAUSE

Vaginal estrogen is superior to placebo in the prevention of occurrence in postmenopausal women with an active diagnosis of recurrent UTIs.

Vaginal Estrogen for the Prevention of Recurrent Urinary Tract Infection in Postmenopausal Women: A Randomized Clinical Trial
Kimberly L. Ferrante, MD,* Erika J. Wasenda, MD,† Carrie E. Jung, MD,†
Female Pelvic Med Reconstr Surg 2019;00: 00-00
DIFFERENTIAL DIAGNOSIS

- Vaginitis
- Vulvar dermatitis
- Lichen sclerosus
- Lichen planus
- Vulvar HSIL
“IT HURTS TOO MUCH TO HAVE SEX. IT FEELS LIKE I’M BEING TORN.”

- **Acute reaction**: mucosal erythema and desquamation that is self-limiting (2-3 months)

  Normal structure and appearance may never return

- **Long-term (80%)**: vaginal wall thinning, adhesions, atrophy and fibrosis leading to decreased vaginal elasticity narrowing, shortening, decreased sensation, and possibly total vaginal stenosis leading to dyspareunia

- **Limited access for tumor surveillance**
45-YEAR-OLD WITH STAGE II ENDOMETRIAL CANCER

- Hysterectomy with bilateral salpingo-oophorectomy
- Completed External beam radiation 3 months ago
- The patient and her partner are struggling over sexual issues
- Failed a 12-week trial of vaginal moisturizers
- What else can you offer her?

- Continue Moisturizers?
- Add topical estrogen?
- Consider pelvic floor PT?
- Consultation with Sex Therapy?
- All of the above?
TOPICAL HORMONE THERAPY BY CANCER TYPE

- **Uterine cancer**
  - Type I and Type II
  - Carcinosarcoma
  - Leiomyosarcoma
  - Stromal sarcoma

- **Ovarian cancer**
  - High-grade serous
  - Endometroid
  - Germ Cell
  - Granulosa cell
TOPICAL HORMONE THERAPY BY CANCER TYPE

• Cervical Cancer
  - Squamous cell
  - Adenocarcinoma

• Vulvar/vaginal Cancer
  - Squamous cell
  - Adenocarcinoma

• Clear cell adenocarcinoma
  (cervical, vulvar or vaginal)

Crean-Tate 2020 ajog.org
50-YEAR-OLD WITH BREAST CANCER

- Lumpectomy with negative nodes
- Radiation
- Insertional and deep dyspareunia
- Lubricants offer minimal benefit during sexual activity
- Supportive partner
- Feeling guilty about her loss of desire
NONPHARMACOLOGIC: VAGINAL MOISTURIZERS

- Long term aid for vaginal dryness
- Attaches to mucin and epithelial cells on the vaginal wall
- Carries up to 60 times its weight in water
- Holds water in place on the vaginal epithelial surface until it is sloughed off
- Requires 2-3 applications per week

12-week trial

Edwards D. Panay N. Climacteric, 2020
NONPHARMACOLOGIC TREATMENT: VAGINAL LUBRICANTS

Reduce friction and discomfort during penetrative sexual activity

- Women ages 18-68
  - 96% “greater sexual comfort”
  - 94% “greater sexual pleasure”
  - “Increased ease of orgasm”

ELEMENTS OF MOISTURIZERS AND LUBRICANTS

• Water, silicone based
  Paraben free, acidic pH (3.8-4.5), low osmolality <380 Osm), free of additives, flavors, glycerine,
  Recommend: Satin (organic), Good Clean Love, Luvena (probiotic)
  Avoid Astroglide, Ky Jelly with glycerine promoting candida; Replens low pH

• Hyaluronic acid gel-reduced symptoms in women with BC
  Releases water molecules into the tissues
  RCT-improvement in urinary incontinence, dryness, maturation index and composite of vaginal symptoms better than conjugated estrogen cream group. Jokar et al 2016

• Natural oils-may be associated with vaginal infections
SAFETY OF TOPICAL ESTROGEN IN BREAST CANCER SURVIVORS (BCS)

- Vaginal estrogen has not been found to increase primary breast cancer

  Finnish registry
  Women’s Health Initiative Observational Study
  Nurses Health Study

- **Recommendations for low dose vaginal estrogen in BCs**
  
  North American Menopause Society (NAMS): low dose vaginal estrogen if failed 12-week trial of nonhormonal treatment

  American Cancer Society/American Society of Clinical Oncology: low dose estrogen is discouraged in BCs on Aromatase Inhibitors
VAGINAL ESTROGEN IN BREAST CANCER SURVIVORS ON TAMOXIFEN OR AROMATASE INHIBITORS

- Nested case-controlled study-no increase in recurrence in female cancer survivors on tamoxifen or aromatase inhibitors after 3.5 years
  LeRay I Breast Cancer Res Treat 2012

- Systemic or Vaginal Hormone Therapy after Early Breast Cancer: A Danish Observational Cohort Study
  
  8461 women-9.8 years for recurrence, 15.2 years for mortality
  No vaginal or systemic hormone therapy prior to diagnosis
  No increase in recurrence or mortality with tamoxifen
  Increase in recurrence risk but not mortality with vaginal estrogen on aromatase inhibitors

  Cold S. JNCI J Natl Cancer Inst 2022
  Cathcart-Rake E, Ruddy KJ JNCI J Natl Cancer Inst 2022
VAGINAL ESTROGEN IN BREAST CANCER SURVIVORS ON AROMATASE INHIBITORS

• Prospective study-hormone levels in BCs on AIs
  2 weeks (n=7) of 25 mcg estrogen tablet, estradiol level increased 83%, at 10 weeks 66%  Kendall et al, Ann Oncol 2006

• Prospective study
  • AIs on vaginal estrogen (25 mcg tablet or ring) increased circulating E2 levels over 90 days  Wills et al. J Oncol Pract 2012

• Lopez DML. Management of genitourinary syndrome of menopause in breast cancer survivors: An update  World J of Clin Oncol 2022
## FACTORS TO CONSIDER PRIOR TO PRESCRIBING VAGINAL HORMONES IN BREAST CANCER PATIENTS

<table>
<thead>
<tr>
<th>More desirable candidates</th>
<th>Less desirable candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage of disease</strong></td>
<td>Stage 0-2, or metastatic with limited life expectancy</td>
</tr>
<tr>
<td><strong>Grade of disease</strong></td>
<td>Low-intermediate grade</td>
</tr>
<tr>
<td><strong>Lymph node involvement</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Hormone receptor status</strong></td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Endocrine therapy</strong></td>
<td>Tamoxifen</td>
</tr>
<tr>
<td><strong>Risk of recurrence</strong></td>
<td>Low</td>
</tr>
<tr>
<td><strong>Time since diagnosis</strong></td>
<td>Remote</td>
</tr>
<tr>
<td><strong>Symptom severity</strong></td>
<td>Severe</td>
</tr>
<tr>
<td><strong>Nonhormone therapies</strong></td>
<td>Failed</td>
</tr>
<tr>
<td><strong>Effect on quality of life</strong></td>
<td>Severe</td>
</tr>
</tbody>
</table>

Start with 12 weeks of vaginal moisturizers  
Faubion S. Consensus Recommendations. Menopause 2018
VAGINAL ESTROGEN

- **Potency**: CEE > estradiol > estrone > estriol
- **Amount**: Greater surface area > tablet or ring
- **Formulation**: Penetration enhancers > bioadhesive
- **Location**: Upper 2/3 vagina > lower 1/3 > vulvar skin and vestibule
- **Condition of the tissues**: More atrophied > less atrophied
VAGINAL ESTROGEN PREPARATIONS

• **Creams**
  - Premarin 0.3mg = 0.5gm (1/8 applicator)
  - Estrace 50mcg = 1.0gm (1/4 applicator)
    - Daily dosing for 1-2wks, then 2 times weekly

• **Inserts**
  - Vagifem 10mcg
    - Daily for 2wks, then 2 times weekly
  - Imvexxy 4mcg or 10mcg
    - Daily for 2wks, then 2 times weekly

• **Low dose vaginal ring**
  - Estring 2mg (6-9mcg absorbed daily)
    - Vaginal ring placed every 3 months

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4-ug inserts, 10-ug inserts and tablets, vaginal ring (7.5 ug estradiol daily)

Faubion, et al. Menopause 2018
VAGINAL DHEA

- Plain moisturizers (PM) and DHEA improved vaginal symptoms at 12 weeks. However, vaginal DHEA, 6.5 mg, significantly improved sexual health.

- DHEA resulted in increased hormone concentrations, though still in the lowest half or quartile of the postmenopausal range, and provided more favorable effects on vaginal cytology, compared to PM.

- **Estrogen concentrations in women on AIs were not changed.**

  Barton DL. Support Care Cancer (2018)

  Barton DL. Support Care Cancer (2018)
LASER THERAPY

• Quick AM, et al. JCMJ. Clin. Med. 2022,
Breast cancer survivors treated with fractional CO2 laser therapy have sustained improvement in sexual function two years after treatment completion, suggesting potential long-term benefit.

• LIGHT Randomized Clinical Trial
Prospective double-blind sham-controlled trial in 84 breast cancer patients on aromatize inhibitors
Both groups-moisturizers and vaginal vibration therapy-5 weekly session fractional carbon dioxide laser or sham
6-month follow-up-safe but no difference in efficacy
  Mension E. JAMA 2023
OTHER CONSIDERATIONS

- Vaginal autologous platelet-rich plasma (A-PRP)
  20 patients with BC improved Vaginal Health Index after 6 months of treatment
- Smoking cessation
- Vaginal lidocaine
- Ospemifene-safety with concomitant use of other SERMS not studied—not recommended
THERAPEUTIC VIBRATORS

https://sexualityresources.com/
https://sexualityresources.com/content/tips-first-time-vibrator-users
Rullo JE. Genital vibration for sexual function and enhancement: best practice recommendations for choosing and safely using a vibrator. Sexual and Relationship therapy.
PELVIC FLOOR THERAPY

PELVIC FLOOR MUSCLE PT
Core stabilization
Internal release
Graduated dilators
Thera wand home program

http://aptapelvichealth.org
http://hermanwallce.com
### Sexual Health Products

- **Lubricants**: Designed to simulate your natural moisture.
- **Silicone Dilators**: Made of food-grade silicone for comfort and safety.
- **Silicone Personal Massagers**: Relieve stress and enhance relaxation.
- **Lubricants**: Suitable for use with latex condoms.

### Silicone Personal Massagers
- Lelo Ogi 2
  - A petite personal massager for intimate relief.
  - Provides soothing vibration and relaxation.
- Lelo Sona 2
  - A rechargeable clitoral massager.
  - Perfect for intimate self-care.

### Silicone Vaginal Dilators
- **Pure Romance Vaginal Dilator Set**: Offers adjustable dilators for vaginal training.
- **Soul Source Dilators**: For enhanced personal satisfaction.

### Lubricants
- Good Clean Love
  - **Almost Naked**: Non-sticky, non-greasy.
  - **Bio-Natural**: Water-based, biodegradable.

### Moisturizers
- Good Clean Love
  - **No-Nonsense**: A soothing, non-greasy formula.
  - **Bio-Natural**: A natural moisturizer for intimate use.

These products are available at the Mayo Clinic Store online at [MayoClinic.com/store](MayoClinic.com/store).
ROLE OF SEX THERAPY

• Maintaining intimacy
• Nonpenetrative sex guidance
• Introduction of sex aids

www.aasect.org
www.sstarnet.org
www.isswsh.org
LONG TERM CONSEQUENCES OF CANCER ON SEXUAL HEALTH

• N=2195 (men and women) in both non-sexuality and sexuality related cancers
• 57% suffered substantial SH deterioration even 5 years after diagnosis
• Younger women who received chemotherapy and radiation had a higher likelihood of SH deterioration
• Deterioration of Sexual Health (SH) in Cancer Survivors Five Years after Diagnosis: Data from the French National Prospective VICAN Survey
• Breast cancer-SH deterioration linked to endocrine therapy
  Sequin. Cancers 2020
CONCLUSION

- Cancer effects urogenital health
- Type of cancer and ongoing treatment plays a role in the safety of vaginal hormone utilization
- Consider Pelvic Floor PT, vibrator use and referral to a Sex Therapist
- You are an important part of their cancer survivorship!!
Thank you!
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