Vaginal Atrophy Related to Estrogen Deficiency

By: Deanna Benner, MSN, WHNP
Prevalence

• Estimated 10-45% postmenopausal women suffer from symptoms associated with vaginal atrophy.

• 61.5% of postmenopausal breast cancer survivors

• But only 20-25% seek treatment
Symptoms: Vaginal

- Dryness
- Pain
- Itching
- Burning
- Discharge
- Difficulties with intercourse
  - Sexual pain
  - Difficulty in achieving orgasm
  - Decreased perception of sexual attractiveness
  - Difficulty in achieving orgasm
Urinary symptoms

- Frequency
- Dysuria
- Hematuria
- Urethral discomfort
- Urinary tract infections
- Stress Incontinence
Causes of Estrogen Deficiency

• Menopause
  • Leading cause

• Non-menopausal causes:
  • Radiation therapy/Chemotherapy
  • Spontaneous premature ovarian failure
  • Immunologic disorders
  • Bilateral Oophorectomy
  • Postpartum

• Side effects of anti-estrogen medications
  • Provera
  • Tamoxifen
  • Danazol
  • Lupon
  • Synarel
Pathophysiology

• Vaginal and urinary tract originate from same embryologic tissue that are both estrogen dependent.
• Estrogen helps main the collagen content to the tissue which affects thickness and elasticity of the tissue.
• Estrogen keeps epithelial surfaces moist and ensures optimal genital blood flow.
• Creates thick rugated glycogen rich vaginal epithelium
• Lactobacilli use sloughed-off glycogen rich vaginal walls to convert glucose into lactic acid which is responsible for creating the acidic environment of the vagina.
• Lower pH of 3.5- 4.5 is essential for protection from vaginal and urinary tract infections from bacteria and fungi.
Lack of Estrogen

Causes thinning of vaginal epithelial cells

- Vaginal walls thinner, Less elastic
- Reduced nerve fibers= decreased sensation
- Decreased blood flow to vagina
- Vaginal walls shorten and narrow
- Decreased secretions

- Decreased sloughing off of epithelial cells
- Less glucose produced
- Less lactic acid produced by lactobacilli
- Increased pH
- Overgrowth of bacteria, fecal flora, other pathogens

All these changes increase the risk of trauma, infection, and pain
Assessment, Ask about...

- Urogenital symptoms
- Vaginal dryness
- Sexual difficulties
- Spotting, bleeding abnormalities
- Discharge
- Pruritus
- Burning
- Medications
- Interventions the patient has tried
Physical Exam

• **External genitalia**
  - Sparse pubic hair
  - Dry labia
  - Decreased labial fat
  - Clitoris will appear larger and protuberant while urethral meatus will be slightly lower and appear more reddened
  - Fusion of labia minora
  - Vulvar dermatoses, vulvar lesions
  - Urethral caruncel
  - Pelvic organ prolapse
Physical exam

**Internal exam:**

- Decreased rugae
- Dry vaginal epithelium that may appear smooth, and shiny
- Pale vagina and cervix
- Vaginal vault is likely to be shortened, less elastic, narrower.
- Petechiae, fissures, bleeding with minor trauma
Diagnosis

• Made on symptoms and physical exams. Laboratory tests unnecessary.
  • pH >5 in absence of infection, blood, or semen.

• Maturation index:
  • Premenopausal women:
    • 40-70% intermediate cells
    • 30-60% superficial cells
    • No parabasal cells
  • Postmenopausal women with vaginal atrophy:
    • Increase in parabasal cells and decrease in superficial cells.

• Measurement of serum hormone levels unnecessary.
Treatment

Primary goal: Lessen the severity of symptoms and reverse the atrophic changes as much as possible.
Non-hormonal Moisturizers and Lubricants

- **Vaginal moisturizers**
  - Replenish vaginal moisture by adhering to the vaginal wall.
  - May be used regularly every 2-3 days.

- **Lubricants**
  - Reduce friction and discomfort from dryness during intercourse without causing irritation or damage to diaphragms or condoms.
Moisturizers
Lubricants
Sexual activity

• Women who participate in regular intercourse have fewer symptoms of vaginal atrophy and less evidence of stenosis and shrinkage on physical exam.

• These benefits are from improved blood flow and increased androgens, which help to preserve vaginal elasticity and prevent introital stenosis.
Vaginal Estrogen Therapy

Indicated for postmenopausal women with moderate to severe vaginal symptoms not relieved by 1\textsuperscript{st} line, non-hormonal therapies.
Benefits of Vaginal Estrogen Therapy

- Reduces friability and thinning of vagina, lessens severity of symptoms within 12 weeks
  - Increased blood flow
  - Thickens and revascularizes the epithelium
  - Restores normal pH
  - Increased vaginal secretions.
- Decreased incidence of urinary tract infections.
- Reduces vaginal symptoms related to estrogen deficiency better than systemic estrogen therapy with fewer adverse effects.
Contraindications

• Undiagnosed vaginal bleeding
• Current breast cancer
• History of endometrial cancer
• Pregnant or breast feeding
• Caution with liver disease
• History of thromboembolic disorder
So how do you choose what type of estrogen...

- Need to individualized.
- Risk of systemic absorption, patient preference, convenience and cost should guide decision.

A Cochrane review of results from 16 clinical studies, concluded that estrogen vaginal cream, tablets and rings all equally effective for relief of vaginal atrophy symptoms.
Adverse events

- Generally, creams associated with larger risk of adverse events due increased likelihood of patient applying higher than recommended dosing with creams. However, Cochrane review reported no significant differences among 3 delivery methods with regard to endometrial thickness or adverse events.

1. Breast pain
2. Vaginal bleeding
3. Systemic absorption
4. Endometrial hyperplasia

Clinical trials have not followed local estrogens greater than 1 year.
Vaginal Creams

• **Conjugated Estrogen (Premarin 0.625mgCE/1g cream)**
  - Dosages range 0.5-2.0 g of cream= 0.3mg to 1.25 mg CE.
  - Low dosing
    - 0.5g (0.3mg CE) administered nightly x 2 weeks then 3 x/weekly for 12 weeks.

• **Estradiol (Estrace: 100mcg estradiol/1g cream)**
  - Dosages range from 1-4 g of cream= 100 to 400mcg of estradiol.
  - Loading dose 2-4 g/d for 2 weeks and then reduce to half the dose for 2 weeks, then maintenance dose of 1 gram for 1-3x/week.
  - (NOTE: 2.0 g produced premenopausal estradiol ranges and should not be used long term without endometrial protection and/or endometrial assessment).
Cream

• Studies have shown that twice weekly use of low does CE cream 0.3 mg is as effective as daily application for treatment of moderate to severe vaginal atrophy.
• No cases of endometrial hyperplasia or carcinoma found during the 52 week study period.
• Twice weekly had better compliance than daily use.
• Creams more soothing for women suffering from vulvar atrophy, fissures can be applied directly to vulva. When symptoms improve—may change to another preparation

Advantages:
• Able to be applied directly over vulva and vaginal area
• Flexibility in dosing
<table>
<thead>
<tr>
<th>Composition</th>
<th>Product name</th>
<th>Dosing as per labeling</th>
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<tbody>
<tr>
<td>Estradiol</td>
<td>Estrace Vaginal Cream(^a)</td>
<td>Initial: 2.0-4.0 g/d for 1-2 wk</td>
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<td>Maintenance: 1.0 g/d (0.1 mg active ingredient/g)</td>
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<tr>
<td>Conjugated</td>
<td>Premarin Vaginal Cream</td>
<td>0.5-2.0 g/d (0.625 mg active ingredient/g)</td>
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<td>estrogens</td>
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<td>Estradiol acetate</td>
<td>Estricon (^b)</td>
<td>Device containing 2 mg</td>
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<tr>
<td></td>
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<td>releases 7.5 μg/d for 90 d</td>
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<tr>
<td>Vaginal tablet</td>
<td>Vagifem</td>
<td>Systemic-dose device containing 12.4 or 24.8 mg estradiol</td>
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<tr>
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<td>acetate releases 50 or 100 μg/d estradiol for 90 d</td>
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<td>hemihydrate</td>
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\(^a\) Available only in the United States, not in Canada.
\(^b\) Delivers systemic dose.

NAMS 2007 Position Statement: The role of local vaginal estrogen for treatment of vaginal atrophy in postmenopausal women.
Ring- (Estring)

- Flexible silicone ring (Contains 2mg micronized estradiol) with estradiol that delivers a set dose of estradiol into vaginal for 90 days
  - Released 7.5 mcg of estradiol every 24 hours.
  - Rests on pelvic floor muscles in horizontal position
  - Usually not noted by patient or partner during intercourse.
  - Studies indicate that women who undergone hysterectomy may have difficulty retaining ring
- Vaginal ring produced similar endometrial proliferation as 0.625mg CE cream but less than 1.25mg CE cream.
- Not to be confused with Femring (50-100mcg per day)
Tablet- 10 mcg of estradiol (Vagifem)

- Inserted in vagina daily for first two weeks and then twice weekly after.
- Studies show results achieved after 14 days of local administration and result sustained until week 52.
  - Increased thickness of vaginal epithelium.
  - Less prone to bleeding
  - Increased cell secretion and lubrication
- Within week 2- pH shifted to more acidic.
  - Decreased mean vaginal pH by -2.7 from baseline after 3 weeks and sustained throughout 12 week assessment period.
Women with a History of Cancer

- For women diagnosed with non-hormone dependent neoplasm: management should be same as women without cancer experiencing vaginal atrophy.
- For women with history of hormone dependent cancers-
  moisturizers and lubricants are recommended as 1\textsuperscript{st} line.
  - Data lacking regarding safety of low dose localized estrogen.
  - Women reporting moderate to severe atrophy who have been unresponsive to 1\textsuperscript{st} line treatment should discuss with their gyn provider and oncologist about risk/benefits of low dose local estrogen.
Key Points

• Progesterone not indicated for low dose vaginal estrogen therapy for endometrial protection.
• Vaginal estrogen should be used for as long as vaginal symptoms bothersome.
• Lack of data regarding endometrial surveillance for asymptomatic women, after 1 year.
• Vaginal therapy not sufficient for relief of vasomotor symptoms or prevention or treatment of osteoporosis
• No evidence that routine endometrial surveillance is warranted in asymptomatic women receiving low dose vaginal estrogen.
• Ring and tablet provide lowest dose routes for vaginal estrogen.
For further information...

- Menopause.org
References

- Bachmann, G., & Santen, R. Clinical manifestations and diagnosis of vaginal atrophy., 2/25/2013.