Vulvovaginal Atrophy in Menopause: Counseling and Care Strategies for the Primary Care Clinician
Session 5: Vulvovaginal Atrophy in Menopause: Counseling and Care Strategies for the Primary Care Clinician

Learning Objectives
1. Utilize detailed interviewing and physical examination to identify symptoms of vulvovaginal atrophy.
2. Develop an individualized treatment plan for a postmenopausal woman whose most bothersome complaint is vulvovaginal atrophy.

Faculty
James A. Simon, MD, CCD, NCMP, FACOG
Clinical Professor
George Washington University
President and Medical Director
Women’s Health & Research Consultants
Washington, DC

James A. Simon, MD, is clinical professor of obstetrics and gynecology at the George Washington University in Washington, DC, and maintains a private practice of reproductive endocrinology and infertility. He is currently the Scientific Committee Chairman of the North American Menopause Society. Dr Simon’s clinical research focuses on menopause, particularly osteoporosis diagnosis, prevention, and treatment, and hormone replacement therapies, including complementary and alternative approaches. A short list of Dr Simon’s honors and achievements includes being selected to “Top Washington Physicians” and “The Best Doctors in America.” He has authored or coauthored more than 160 articles, chapters, and proceedings, including several prize-winning papers, as well as more than 150 published abstracts.

Faculty Financial Disclosure Statements
The presenting faculty reported the following:

Dr Simon serves as a consultant to and is on the advisory boards of Abbot Laboratories; Allergan; Alliance for Better Bone Health; Amgen Inc.; Ascend Therapeutics; Azur Pharma, Inc.; Bayer; BioSante; Boehringer Ingelheim; Concert Pharmaceuticals; Corcept Therapeutics Inc.; Depomed, Inc.; Fabre-Kramer; GlaxoSmithKline; Graceway Pharmaceuticals, LLC; KV Pharmaceutical; Lipocine, Inc.; Meditrina Pharmaceuticals; Merck; Merrion Pharmaceuticals; Nanman Tripharma/Trinity; NDA Partners, Inc.; Novo Nordisk; Novogyne; Pear Tree Pharmaceuticals; QuatRx Pharmaceuticals; Roche; Schering-Plough; Sciele; Solvay; Teva; Ther-Rx; Warner Chilcott; and Wyeth. He receives grant/research support from BioSante, Boehringer-Ingelheim, FemmePharma, GlaxoSmithKline, Nanma/Tripharma/Trinity, Novartis, Procter and Gamble, QuatRx Pharmaceuticals, and Teva. In addition, he is on the speakers’ bureaus of Amgen, Ascend, Bayer, Boehringer Ingelheim, GlaxoSmithKline, KV, Merck, Novartis, Novo Nordisk, Novogyne, Sciele, Teva, Ther-Rx, Warner Chilcott, and Wyeth.

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The content collaborators at Haymarket Medical Education have reported the following:

Faith Frankel, medical writer, and Krista Sierra, senior project editor, have no relevant financial relationships to report.

Drug List

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
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</thead>
<tbody>
<tr>
<td>estradiol vaginal cream</td>
<td>Estring, Femring</td>
</tr>
<tr>
<td>conjugated estrogen</td>
<td></td>
</tr>
<tr>
<td>vaginal cream</td>
<td></td>
</tr>
<tr>
<td>estradiol hemihydrate</td>
<td></td>
</tr>
<tr>
<td>vaginal tablet</td>
<td></td>
</tr>
<tr>
<td>estradiol vaginal ring</td>
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</table>
**Acronym List**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>VVA</td>
<td>vulvovaginal atrophy</td>
</tr>
<tr>
<td>UTI</td>
<td>urinary tract infection</td>
</tr>
<tr>
<td>ET</td>
<td>estrogen therapy</td>
</tr>
<tr>
<td>NAMS</td>
<td>North American Menopause Society</td>
</tr>
</tbody>
</table>

**Suggested Reading List**


Vulvovaginal Atrophy in Menopause: Counseling and Care Strategies for the Primary Care Clinician

Learning Objectives

At the conclusion of this educational activity, participants should be better able to:

- Utilize detailed interviewing and physical examination to identify symptoms of vulvovaginal atrophy
- Develop an individualized treatment plan for a postmenopausal woman whose most bothersome complaint is vulvovaginal atrophy

Pre-Test Question 1

For a menopausal patient whose most bothersome complaint is vulvovaginal atrophy, which of the following would you use as first-line therapy:

1. Increased consumption of soy, legumes, and other dietary phytoestrogens
2. OTC lubricants, vaginal moisturizers
3. Systemic hormone therapy
4. Localized hormone therapy
5. Transdermal hormone therapy

Pre-Test Question 2

I would offer menopausal hormone therapy to a woman who has a history of breast cancer...

1. Always
2. Sometimes
3. Never

Pre-Test Question 3

What is the FDA’s current position on hormone therapy for menopause symptoms?

1. Hormone use in any form is acceptable when vulvovaginal atrophy is the chief complaint.
2. Use lowest hormone dose for the shortest possible duration, consistent with treatment goals and risks for the individual woman.
3. Based on the results of the Women’s Health Initiative, hormone therapy should be reserved for prevention of osteoporosis.

Vulvovaginal Atrophy: Scope of the Problem

- Average age of menopause is 51 years
- By 2020, >50 million U.S. women will be >age 51
- Symptomatic vaginal atrophy will affect 10% to 40% of menopausal women
  - Without therapy, prevalence and severity increase

Up to 85% of Women Experience Symptoms of Menopause*

<table>
<thead>
<tr>
<th>Vasomotor</th>
<th>Urogenital</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hot flushes/night sweats</td>
<td>• Vaginal dryness/itching/pain</td>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Insomnia/disrupted sleep</td>
<td>• Dyspareunia</td>
<td>• Mood changes: anxiety, irritability, depression</td>
</tr>
<tr>
<td>• Headache</td>
<td>• Reduced sexual desire/arousal</td>
<td>• Cognitive difficulties</td>
</tr>
<tr>
<td>• Palpitations</td>
<td>• Urinary frequency, dysuria, urgency</td>
<td>• Backache/stiffness</td>
</tr>
<tr>
<td></td>
<td>• Increased susceptibility to urinary tract infection</td>
<td>• Skin changes</td>
</tr>
</tbody>
</table>

* Not all of these symptoms are “officially” accepted symptoms of menopause.


Estrogen Loss and Manifestation of Health Risks Over Time

Development of subclinical disease

<table>
<thead>
<tr>
<th>Short-Term Symptoms</th>
<th>Long-Term Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flushes, sleep, mood</td>
<td>Osteoporosis</td>
</tr>
</tbody>
</table>

Age (years)


Female Urogenital Anatomy: Rich in Estrogen Receptors

Ovary — Fallopian tube — Uterus — Bladder — Rectum — Cervix — Vagina — Urethra

Source: American Medical Association

Vaginal Maturation Index

Mature Squamous Epithelium — Atrophic Epithelium


Maturation Index

• Maturation index:
  - Proportion of parabasal cells increased
  - Proportion of superficial cells decreased

VAGINAL EPITHELIUM

<table>
<thead>
<tr>
<th>Premenopause</th>
<th>Postmenopause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial cells</td>
<td>15%</td>
</tr>
<tr>
<td>Intermediate cells</td>
<td>80%</td>
</tr>
<tr>
<td>Parabasal cells</td>
<td>5%</td>
</tr>
</tbody>
</table>


pH Confirms VVA

• Premenopausal vaginal luminal pH is acidic
  - pH 4.5–6.0
  - ~6.5 before ovulation
• Estrogen loss → more alkaline pH
  - pH 6.5–7.0
• pH test: Medicare eligible

Differential Diagnosis: What is Not VVA?

Vaginal candidiasis

Photo courtesy of Phototake

Lichen sclerosis et atrophicus

Photo courtesy of Visuals Unlimited

Differential Diagnosis: What is Not VVA? (cont’d)

Vulvar Cancer

Photo courtesy of Phototake

Case 1

Connie, age 50

- ~3 years post final menstrual period
- Divorced 4 years ago, dating 42-year-old man
- Afraid of intimacy
  - Vulvovaginal symptoms: “Feel old”
  - Only menopausal symptom is vaginal dryness

Case Vignette 1

Goals of VVA Treatment

- Relieve symptoms
- Reverse anatomic changes
- Improve sexual function and quality of life

Nonhormonal Therapeutic Options

- Moisturizer: Long-term
  - Gel or cream
  - Used regularly
  - Maintains hydration; relieves dryness
- Lubricant: As needed
  - Moistens vaginal epithelium
  - Short duration of action
  - Facilitates medical exam or intercourse

Pharmacologic Options: Systemic Estrogen Therapy?

- Primary indication is treatment of moderate to severe vasomotor symptoms
- Used to treat urogenital symptoms as part of a constellation of symptoms

FDA Guidelines: Estrogen

- Effective for treating vasomotor symptoms and vaginal dryness, preventing osteoporosis
  - Use topical therapy for vaginal dryness alone
  - Second-line for osteoporosis prevention alone
  - Use lowest dose and shortest duration possible consistent with treatment goals

FDA, American Association of Clinical Endocrinologists

When hormone therapy is being used solely to treat “symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.”

NAMS Position Statement on Local ET for Vaginal Atrophy

“Randomized controlled trials, albeit limited, have shown that low-dose, local vaginal estrogen delivery is effective and well tolerated for treating vaginal atrophy.”

Condom Compatibility: Types of Lubricants

<table>
<thead>
<tr>
<th>Base</th>
<th>Ingredients</th>
<th>Safe with latex</th>
<th>Staining?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Deionized water, glycerin, propylene glycol</td>
<td>Yes</td>
<td>No</td>
<td>Rarely causes irritation but drys out with extended activity</td>
</tr>
<tr>
<td>Petroleum</td>
<td>Mineral oil, petrolatum jelly, baby oil</td>
<td>No; do not use</td>
<td>Yes</td>
<td>Irritating to vagina</td>
</tr>
<tr>
<td>Natural oil</td>
<td>Avocado, olive, peanut, corn</td>
<td>Yes</td>
<td>Yes</td>
<td>Safe (unless peanut allergy)</td>
</tr>
<tr>
<td>Silicone</td>
<td>Silicone polymers</td>
<td>Yes</td>
<td>No</td>
<td>Nonirritating to vagina, long-lasting and waterproof</td>
</tr>
</tbody>
</table>

Harrison’s Chapter on Estrogen

- Main focus: systemic estrogen
  - Authors agree with FDA, medical society guidelines
  - "For genitourinary symptoms, the efficacy of vaginal estrogen is similar to that of oral or transdermal estrogen"

Discontinued Estrogen Therapy 3 Years Previously

Using Estrogen Therapy

Comparison of 2 sexually active 65-year-old women

Topical Estrogens

**Vaginal Estrogen Therapy for Postmenopausal Use in the United States**

<table>
<thead>
<tr>
<th>Composition</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal creams 17β-estradiol</td>
<td>Initial: 2-4 g/d for 1-2 wk. Maintenance: 1 g/d (0.1 mg active ingredient/g) 0.5-2 g/d (0.625 mg active ingredient/g)</td>
</tr>
<tr>
<td>Conjugated estrogens (formerly conjugated equine estrogens)</td>
<td></td>
</tr>
<tr>
<td>Vaginal ring 17β-estradiol</td>
<td>Device containing 2 mg released 7.5 µg/d for 90 d</td>
</tr>
<tr>
<td>Estradiol vaginal rings</td>
<td></td>
</tr>
<tr>
<td>Estradiol vaginal tablet</td>
<td></td>
</tr>
<tr>
<td>Estradiol hemihydrate</td>
<td>Initial: 1 tablet/d for 2 wk. Maintenance: 1 tablet twice/wk (tablet 16.3 mcg of estradiol hemihydrate equivalent to 10 mcg of estradiol)</td>
</tr>
</tbody>
</table>

FDA-Approved Products for Vaginal Changes of Menopause Include:

- Estradiol vaginal cream
- Conjugated estrogens vaginal cream
  - Also indicated for dyspareunia
- Estradiol hemihydrate vaginal tablet
- Estradiol vaginal rings
  - Can deliver systemic dose; also indicated for vasomotor symptoms

Restored Normal Physiology

- Influence of Estrogen
  - Vaginal epithelium thickens
  - Normal lactobacilli produce lactic acid
  - Acidic vaginal pH maintained
  - Mucous membrane maintained

**NAMS Guidelines Endorsed By:**

- National Association of Nurse Practitioners in Women’s Health (NPWH)
- Healthy Women (formerly the National Women’s Health Resource Center)
- Asociación Mexicana para el Estudio del Climaterio (AMEC)
- Society of Obstetricians and Gynaecologists of Canada (SOGC)
- The Endocrine Society
- American Medical Women’s Association (AMWA)


Women's Health Initiative (WHI): Safety of HT

May increase risk of:
- Blood clots
- Breast cancer
- Heart disease
- Stroke


WHI Results: Overall Relative Risk

<table>
<thead>
<tr>
<th>Event</th>
<th>Overall HR</th>
<th>95% nCI</th>
<th>95% aCI</th>
<th>Overall HR</th>
<th>95% nCI</th>
<th>95% aCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>1.24</td>
<td>1.00–1.54</td>
<td>0.97–1.60</td>
<td>0.91</td>
<td>0.75–1.22</td>
<td>0.72–1.15</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>1.24</td>
<td>1.01–1.54</td>
<td>0.97–1.59</td>
<td>0.77</td>
<td>0.59–1.01</td>
<td>0.57–1.06</td>
</tr>
<tr>
<td>Dementia**</td>
<td>2.05</td>
<td>1.21–3.48</td>
<td>1.49</td>
<td>0.83–2.66</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.31</td>
<td>1.02–1.68</td>
<td>1.39</td>
<td>1.10–1.77</td>
<td>0.97–1.99</td>
<td></td>
</tr>
<tr>
<td>VTE</td>
<td>2.11</td>
<td>1.58–2.82</td>
<td>1.26–3.55</td>
<td>1.33</td>
<td>0.99–1.79</td>
<td>0.86–2.08</td>
</tr>
<tr>
<td>PE</td>
<td>2.13</td>
<td>1.39–3.25</td>
<td>0.99–4.56</td>
<td>1.34</td>
<td>0.87–2.06</td>
<td>0.70–2.55</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>0.56</td>
<td>0.38–0.81</td>
<td>0.33–0.94</td>
<td>1.08</td>
<td>0.75–1.55</td>
<td>0.63–1.86</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>0.67</td>
<td>0.47–0.96</td>
<td>0.41–1.10</td>
<td>0.61</td>
<td>0.41–0.91</td>
<td>0.33–1.11</td>
</tr>
</tbody>
</table>

Total fractures 0.76 0.69–0.83 — 0.70 0.63–0.79 0.59–0.83

Shaded text indicates statistical significance.

VTE = venous thromboembolism; PE = pulmonary embolism.

*Only in women ≥ 65 years of age at baseline.


Which Product to Use?

- Products are equally effective at doses recommended in labeling
  - Significant subjective symptom relief
  - Signs (pallor, dryness, friability, petechiae) also improved
- Clinician experience and patient preference drive choice of product


How Soon Is Response Evident?

- Typically within a few weeks
  - May take up to 6 weeks
- 80% to 90% report subjective improvement


Case 2
Virginia, age 70

- 15 years postmenopause
- Widowed for 10 years
- Not sexually active
- Recurrent bladder infections
- Ongoing vulvovaginal atrophy
  - Diminishes quality of life
  - Patient thinks nothing can be done

Case Vignette 2
**Is Virginia a Candidate for Topical Estrogen Therapy?**

1. No – Her age and celibacy indicate that moisturizers are the most acceptable option
2. Yes – Her symptoms are bothersome and estrogen treatment could improve her quality of life

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**Estrogen Loss Increases UTI Susceptibility**

- **Estrogen-replete vagina:**
  - Acidic—pH 4.5-6.5
  - Favors lactobacillus, discourages pathogens
- **Estrogen-deprived vagina:**
  - Alkaline—pH 6.5-7.0
  - Permits colonization by pathogens that can migrate to the urinary tract
  - Many patients have recurrent UTIs
- Local estrogen application can restore vaginal pH to ~5.5


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**NAMS Position Statement on HT for UTI**

- Only vaginal therapy has been demonstrated to be effective in reducing the risk of recurrent UTI
  - No systemic HT product is indicated for urinary health


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**Case 3 Doris, age 62**

- Happily married
- History of breast cancer
- Complaints:
  - Depression
  - Dyspareunia

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**Vaginal Atrophy and Sexual Function**

- ↓ relaxation
- ↓ vaginal vault size
- ↓ blood flow
- ↓ lubrication
- ↓ tissue elasticity

**Vaginal Atrophy and Sexual Function (cont’d)**

- Cross-sectional, population-based study of
  - 1,480 sexually active, postmenopausal women
  - 57% had vulvovaginal atrophy
  - 55% had female sexual dysfunction
  - Women with sexual dysfunction ~4X more likely to also have vulvovaginal atrophy
- Conclusion: Reducing symptoms of one condition may also relieve symptoms of the other


**Use It or Lose It!**

- Continued sexual activity via coitus or masturbation increases blood flow to pelvic organs


**Is Doris a Candidate for Topical Estrogen Therapy?**

1. No – history of breast cancer is an absolute contraindication
2. Topical estrogen is OK
3. Maybe – the jury is still out

**Breast Cancer Hx: How to Handle?**

- Topical estrogen (off-label)?
  - Controversial
  - Individualized therapy decision is key

Consult with/refer patient to gynecologist or oncologist to confirm/discuss treatment decision

**Patient Management**

- How and when to follow up?
  - Ongoing assessment of symptoms, pH, vaginal morphology
  - Special cases: more frequent follow-up
- How long should therapy continue?
  - As long as needed
  - Continuous or intermittent therapy?


**Do You Need Progesterone When Using Local Therapy?**

- Progesterone not usually necessary, even if uterus is intact
- Ultrasound study shows no significant endometrial changes after local therapy
- Safety data on unopposed local estrogen come from studies of ≤6 months

Is Annual Endometrial Biopsy or Ultrasound Necessary?

- Insufficient data to recommend routine annual endometrial surveillance in women using low-dose, vaginal ET
- Possible exceptions:
  - Elevated risk for endometrial cancer
  - Higher dose of vaginal ET
  - Spotting, breakthrough bleeding, other concerning symptoms

Overcoming Barriers to Care

- Patient silence
  - 75% of women with symptomatic vaginal atrophy do not seek treatment
  - 68% fear that discussing sexual problems would embarrass clinician
- Clinician silence
  - Reluctance to offend patient
  - Concern about time constraints
  - Feeling uncomfortable or inadequately trained to discuss sexuality with patients

Overcoming Barriers to Care (cont’d)

- Diagnosis requires increased clinical suspicion
  - Be alert to signs and symptoms of vaginal atrophy
  - Be willing to initiate discussion, maintain open environment
- Support informed decision making
  - Patients’ wishes should always be respected

Strategies to Improve Sexuality Assessment, Counseling

- Understand sexuality from a quality-of-life perspective
- Provide information even if patients don’t ask
- Address causes of discomfort with discussion of sexuality
- Be an objective listener
- Avoid making assumptions
- Encourage questions

Online Resources, Guidelines, and Recommendations

- NIH State-of-the-Science Conference on Menopause-Related Symptoms
- NAMS
- ACOG
- NPWH
- Cochrane Collaboration
- International Menopause Society
- Association of Reproductive Healthcare Professionals

List of URLs, along with other Tools and Resources, on CD in your folder.

Post-test Question 1

For a menopausal patient whose most bothersome complaint is vulvovaginal atrophy, which of the following would you use as first-line therapy:

1. Increased consumption of soy, legumes, other dietary phytoestrogens
2. OTC lubricants, vaginal moisturizers
3. Oral hormone therapy
4. Vaginal hormone therapy
5. Transdermal hormone therapy
**Post-test Question 2**

I would offer menopausal hormone therapy to a woman who has a history of breast cancer.

1. Always
2. Sometimes
3. Never

**Post-test Question 3**

What is the FDA’s current position on hormone therapy for menopause symptoms?

1. Hormone use in any form is acceptable when vulvovaginal atrophy (VVA) is the chief complaint.
2. Use lowest hormone dose for shortest possible duration, consistent with treatment goals and risks for the individual woman.
3. Based on the results of the Women’s Health Initiative, hormone therapy should be reserved for prevention of osteoporosis.

**Q&A**