No Financial Disclosures
Learning objectives

• Be able to counsel patients on bioidentical vs compounded hormone therapy
• Appreciate future cardiovascular risk associated with hypertension in pregnancy
• Understand options available for management of vasomotor symptoms
• Understand risks and limitations of screening average risk women for ovarian cancer
• Manage women with vulvovaginal atrophy appropriately
Case 1

- A 48-year-old woman, gravida 3, para 3 LMP 9 months ago
  - moderate hot flashes and night sweats
  - vaginal dryness.
  - heard about bioidentical hormone therapy
  - consulted another practitioner who performed salivary hormone levels and suggested individualized custom-compounded bioidentical hormone therapy
  - She seeks your advice regarding bioidentical hormone therapy
Question

Which **one** of the following statements would you include in your advice to her?

A. Custom compounded bioidentical HT has fewer risks than commercially available HT

B. Salivary hormone level testing will provide useful guidance

C. There are multiple options for FDA-approved bioidentical HT

D. Custom-compounded bioidentical HT products are submitted to the same safety standards as commercially available HT products

E. There is no role for the use of compounded bioidentical HT
Answer

C. There are multiple options for FDA-approved bioidentical hormone therapy
Bioidentical vs compounded hormone therapy

Bioidentical hormone versus

Compounded hormone therapy
FDA-approved bioidentical hormone therapy

- Multiple options for FDA-approved bioidentical HT that can be delivered via oral, transdermal, vaginal routes
Compounded hormone therapy

• Not regulated by FDA
  • Batch-to-batch variability
  • Purity
  • Labeling
  • Safety and efficacy
• Are they ever useful?
The naked truth about bioidentical hormones

“...with bioidentical hormones, I got my life back.”
- Suzanne Somers
More conducted a study sending 12 compounding pharmacies the same prescription.

Results: Estradiol 96-260%
Progesterone 60-80%

None would have met FDA standards (90-110%)
Salivary (and blood) hormone testing

- Levels variable (by the hour, from day to day)
- No well-established reference ranges
- No evidence that monitoring improves safety
- Levels don’t necessarily correlate with symptoms
- Current practice is to let symptoms rather than levels guide therapy
Clinical Pearl

For most women who are acceptable candidates for hormone therapy, a commercially available, FDA-approved, bioidentical option is appropriate, with therapy tailored to symptom relief rather than to hormone levels.
Case 2

- A 36-year-old woman presents for routine care. She reports no current concerns.
- Gravida 4, para 3 with hx of preeclampsia during her last two pregnancies.
- No personal history of hyperlipidemia, DM or tobacco use. Exercises by jogging 2x per week.
- No family history of premature coronary artery disease.
- Examination: overweight (BMI 27); BP 126/80. Heart, lung, abdominal and neurological examinations are normal.
Question

Given her history, there is an increased risk for all of the following except which one?

A. Stroke
B. Cancer
C. Cardiovascular disease
D. Future cardiovascular disease in her children
E. Venous thromboembolism
Answer

B. Cancer
Hypertension in pregnancy

• A female-specific risk factor for future cardiovascular disease (2-3 fold increased risk compared with 2-4 fold increased risk with tobacco use)

• Higher risk associated with
  • early onset (< 34 weeks)
  • more severe preeclampsia
  • recurrent disease (in multiple pregnancies)
Hypertension in pregnancy

It is unclear if underlying risk factors predispose to both placental disease and future vascular disease

Or

If damage to the vascular endothelium in the setting of preeclampsia establishes the framework for future vascular disease
Women with preeclampsia

• Have an increased risk of
  • Diabetes
  • Hypertension
  • Ischemic heart disease
  • Peripheral vascular disease
  • Venous thromboembolism
  • Stroke
• Offspring who may themselves be at increased risk of future cardiovascular disease
Women with preeclampsia

- Have no increased risk of cancer
- May benefit from regular, long-term follow up and vigilant attention to cardiovascular risk factor modification
Clinical Pearl

Pregnancy is a window to future cardiovascular disease risk in women. An obstetrical history is an important female-specific addition to cardiovascular risk assessment.
Case 3

A 54 year old gravida 3, para 3 with LMP 2 years ago

- 2 years of bothersome hot flashes and night sweats multiple times per day and waking her frequently at night. Feels unrefreshed upon awakening in the morning and has difficulty functioning at work.
- Also has vaginal dryness
- History of hypothyroidism treated with levothyroxine
- Exercises regularly and does not smoke
- PE unremarkable
- Negative cervical cancer screening and mammography within the last year
Question

What would you recommend as the most appropriate next step in the management of her menopausal symptoms?

A. Soy supplement
B. Trial of acupuncture
C. Vaginal estrogen cream twice weekly
D. Systemic hormone therapy
E. Venlafaxine
Answer

D. Systemic hormone therapy
Treatment of vasomotor symptoms

Non-hormonal options

• Soy-derived isoflavones
  • May have modest effect
  • Generally safe

• Acupuncture
  • Mixed results, some studies reveal modest effect
  • Safe in the hands of a trained provider
Treatment of vasomotor symptoms
Non-hormonal options

• Others
  • stress management techniques (meditation, yoga, qigong, tai chi, biofeedback, massage)
  • maintaining healthy weight and regular exercise
  • paced-respirations
  • staying cool; avoidance of alcohol, tobacco, hot food/beverages, and caffeine; dressing in layers
Treatment of vasomotor symptoms
Non-hormonal prescription treatments

• Useful in women who cannot or prefer not to take HT
  • SSRI/SNRI
    • paroxetine (Paxil/Brisdelle) first non-hormonal FDA approved drug for VMS-6/28/13
    • venlafaxine (Effexor)
    • escitalopram (Lexapro)
  • Gabapentin
  • Sleeping medications
Treatment of vasomotor symptoms

Hormonal options

• Systemic hormone therapy
  • Still the most effective treatment for moderately severe vasomotor symptoms
  • Use a progestogen to protect the endometrium in women with a uterus
  • Use the lowest possible dose for the shortest amount of time to control symptoms
  • Individualize treatment, taking into account risks, benefits, and personal preferences
Treatment of vasomotor symptoms
Hormonal options

• Vaginal estrogen therapy is useful for treatment of vulvovaginal atrophy, but does not treat vasomotor symptoms
Clinical Pearl

Systemic hormone therapy remains the most effective treatment for menopausal symptoms
Case 4

A 57 year-old woman, G1,P1 presents for her annual examination. She reports no current symptoms. She tells you of concerns she has about ovarian cancer as a good friend recently died of the disease. She requests screening for ovarian cancer.

• no family history of breast or ovarian cancers
• physical examination is unremarkable
Question

All of the following are true regarding ovarian cancer screening except which one?

A. The risks of ovarian ca screening outweigh the benefits in average risk women

B. There is no clear mortality benefit to screening high-risk women with CA-125 and trans-vaginal US

C. Screening with CA-125 and trans-vaginal US is not associated with significant harm

D. Screening with CA-125 and trans-vaginal US does not reduce ovarian ca mortality in average risk women

E. Most women with a positive screening test for ovarian ca will have a false-positive result
Answer

C. Screening with CA-125 and trans-vaginal US is not associated with significant harm
Ovarian Cancer Screening

- Rare disease with lifetime risk of 1.4% in general population
- 5th leading cause of cancer death in women
- Highest mortality rate of all gynecologic cancers
- Prevalence is low, positive predictive value of screening also low, so most women with positive screening test will not have the disease (false-positive screening test)
- No available screening test is proven effective and accurate for early detection
Ovarian Cancer Screening

• No mortality benefit to screening average-risk, asymptomatic women with CA-125 and transvaginal US (not recommended by USPSTF, ACOG or ACS)

• No data to suggest these tests reduce mortality in higher risk women though balance of risk and potential benefit less well established-USPSTF
  • ACOG and ACS “may include TV US and CA-125 for high-risk individuals”
Who is “high risk”?  

- BRCA1 and 2 mutation carriers  
- Lynch syndrome (hereditary nonpolyposis colon cancer)  
- Family history of ovarian cancer (consider genetic counseling to evaluate risk)  
  - 2 or more first- or second-degree relatives with ovarian ca or combination of breast and ovarian cancers  
  - Ashkenazi Jewish descent-a first-degree relative (or 2 second-degree relatives on same side) with breast or ovarian cancer
Potential harms associated with ovarian cancer screening

• PLCO trial
  • 10% false positive rate in screening group
  • 1/3 of women with false + had oophorectomy
  • 20 surgeries to find 1 screen-detected ovarian cancer
  • 21 major complications per 100 surgeries done for + screen
    • Infection, blood loss, bowel injury, cardiovascular/pulmonary event
Clinical Pearl

Ovarian cancer screening with CA-125 and transvaginal ultrasound does not reduce ovarian cancer deaths in average risk, asymptomatic women and is associated with considerable harms.
Case 5

A 56 year-old woman, G2P2 with LMP age 53, presents to your office with a two year history of progressive vaginal dryness and dyspareunia; hx of 3 UTIs in the last year.

- tried vaginal moisturizers and lubricants w/o relief
- mild hot flashes, improved with regular exercise
- hx hypertension treated with hydrochlorothiazide
- family hx of breast ca maternal aunt age 54
Question

All of the following are true regarding the use of local vaginal ET except which one?

A. Treatment with local vaginal ET should be limited to 3-5 years

B. Local vaginal ET is at least as effective as systemic ET for management of VVA

C. The use of a progestogen for endometrial protection is generally not needed when using low-dose local ET

D. Treatment with local vaginal ET is associated with improved OAB sx and a reduced risk of recurrent UTI

E. Vaginal ET is not contraindicated in patients with a FHx of breast cancer
A. Treatment with local vaginal estrogen should be limited to 3-5 years of therapy
Vulvovaginal Atrophy

• Affects almost 50% of postmenopausal women and over 60% of breast cancer survivors

• Unlike vasomotor symptoms, VVA progresses without treatment

• Symptoms—vaginal dryness, irritation, itching, dyspareunia, reduced sexual responsiveness, urinary urgency, frequency, dysuria, recurrent UTI, urge incontinence

• Significant impact on QOL, sexual function, relationship with partner
Vulvovaginal Atrophy

- Loss of labial/vulvar fullness
- Pallor of urethral/vaginal epithelium
- Decreased vaginal moisture/fissures
- Pain with palpation
Atrophic change: Estrogen deficiency trumps age

53 yo woman not on ET, not sexually active

79 yo woman on ET
Vulvovaginal Atrophy-NAMS recommendations

- Local vaginal estrogen therapy is at least as effective as systemic therapy
  - Cream, vaginal tablet, ring
- Progestogen not indicated for women using local low-dose estrogen
- Endometrial surveillance not recommended in asymptomatic women at low risk for endometrial hyperplasia
- Can be continued as long as symptoms remain
Replacing Vaginal Estrogen in Postmenopausal Women

- Increases pelvic blood flow, lubrication, elasticity
- Protects against clitoral fibrosis
- Improves coital satisfaction, genital tactile perception and sensation
- Reduces vaginal pH, risk of UTI
# Vaginal Estrogens Available for Postmenopausal Use in the US

<table>
<thead>
<tr>
<th>Composition</th>
<th>Name</th>
<th>Dosing</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Vaginal cream</td>
<td>Estrace®</td>
<td>Initial 2-4 g/d for 1-2 wk Maintenance: 1 g/d (0.1 mg active ingredient/g) 0.5-1.0 g (0.625 mg active ingredient/g) 3x weekly</td>
<td>Premarin® is also indicated for dyspareunia</td>
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<tr>
<td>Estradiol</td>
<td>Premarin®</td>
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<tr>
<td>Conjugated estrogens</td>
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<tr>
<td>Vaginal ring</td>
<td>Estring®</td>
<td>Device containing 2 mg releases 7.5 μg/d for 90 d</td>
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<tr>
<td>Estradiol acetate</td>
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<tr>
<td>Vaginal tablet</td>
<td>Vagifem®</td>
<td>Initial: 1 tablet/d for 2 wk Maintenance: 1 tablet twice/ wk (tablet 10.3 μg of estradiol hemihydrate equivalent to 10 μg of estradiol)</td>
<td>The 10 mcg dose is the only available formulation of the drug available in the US</td>
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<tr>
<td>Estradiol hemihydrate</td>
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2. www.eMPR.com.
Ospemifene: A newly approved (oral) SERM for VVA

• Novel SERM differentiated from other SERMS by its favorable effect on the vagina and antagonistic activity on endometrial and breast tissues

• Phase 3 clinical trial demonstrated it to be effective and well tolerated for symptoms of dyspareunia and dryness for up to 12 weeks

• Longer term safety data at 52 weeks of f/u revealed no clinically meaningful endometrial changes; no VTE; AE hot flashes up to 7.2% with 60 mg dose vs 2% with placebo
Treatment of VVA in breast cancer survivors

• Use of local vaginal ET is controversial
  • Increase E2 levels reported in women with breast ca on aromatase inhibitors using E cream/vaginal tablet
  • No studies have shown an increased risk of breast ca recurrence with the use of local vaginal ET in breast ca survivors

• Family history of breast cancer is not a contraindication to the use of local vaginal ET
Clinical Pearl

Local vaginal ET is at least as effective as systemic ET for treatment of vulvovaginal atrophy and avoids many of the concerns associated with systemic estrogen use.
Thank You!