To MENOSTEASE and BEYOND

ALEECE FOSNIGHT, MSPAS, PA-C, CSC-S, CSE, NCMP, IF
UROLOGY, WOMEN’S HEALTH, SEXUAL MEDICINE
SKIN, BONES, HEARTS, AND PRIVATE PARTS 2021
Objectives

- Discuss the stages of menopause and pathophysiology of organ changes.
- Apply hormone therapy options for women seeking menopause symptom relief.
- Identify risk factors associated with the menopause transition.
What is menopause?

Definitions of menopause:
- Menopausal transition
- Perimenopause
- Natural menopause
- Postmenopause

Additional definitions
- Primary ovarian insufficiency
- Induced (surgical vs cancer treatments) menopause
## Stages of Menopause

<table>
<thead>
<tr>
<th>Stages</th>
<th>-5</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>+1</th>
<th>+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terminology</td>
<td>Reproductive</td>
<td>Menopausal transition</td>
<td>Postmenopause</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Early</td>
<td>Peak</td>
<td>Late</td>
<td>Early</td>
<td>Late</td>
<td>Early</td>
<td>Late</td>
</tr>
<tr>
<td></td>
<td>Perimenopause</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of stage</td>
<td>Variable</td>
<td>Variable</td>
<td>1 yr</td>
<td>4 years</td>
<td>Until demise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual cycle</td>
<td>Variable to regular</td>
<td>Regular</td>
<td>Variable cycle length (&gt;7 days different from normal)</td>
<td>≥2 skipped cycles and an interval of amenorrhoea (≥60 days)</td>
<td>Amenorrhoea for 12 months</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>Normal FSH</td>
<td>Increasing FSH</td>
<td>Increasing FSH</td>
<td>Increasing FSH</td>
<td>Increasing FSH</td>
<td>Increasing FSH</td>
<td></td>
</tr>
</tbody>
</table>

Final menstrual period (FMP)
Pathophysiology of menopause organ changes

Sources: Lenz: Comprehensive Gynecology, 6E
Williams Textbook of Endocrinology, 12E

↓ Estradiol

CNS/Vasomotor instability
- ↑ norepinephrine
- ↑ serotonin
- Narrow thermoregulatory setpoint in hypothalamus
- Hot flashes
- Night sweats
- Sleep disturbance
  - Estrogen
- Depression
- Daytime fatigue

Urogenital mucosa
- ↓ collagen synthesis
- ↓ blood flow in vaginal epithelium
- Weakening of vaginal walls
- ↓ glycogen production
- ↓ energy source for lactobacillus
- ↑ secretions
  - ↑ vaginal pH
  - ↑ pelvic organ prolapse
- ↑ stress incontinence
- ↑ vaginal pH
- Epithelial atrophy
- ↑ vaginal pH
- ↑ infections
- Dyspareunia

Cardiovascular
- ↑ total cholesterol
- ↑ LDL
- ↓ HDL
- ↓ NO synthase
- ↑ ACE → ↑ Ang II
- Vasoconstriction
- Endothelial dysfunction
- ↑ risk of atherosclerosis

Bones
- ↑ osteoclast apoptosis (e.g., via ↓ TGF-β)
- ↓ OPG secretion by osteoblast
- ↑ RANK ligand
- ↑ osteoclast maturation and survival
- Bone resorption > formation
- Osteoporosis

- Estrogen
- SERM
- Estrogen Bisphosphonates
- Osteopenia
- Trabecular bone loss > cortical bone in early stages
- Vertebra: most easily fractured due to high trabecular bone turnover
- ↓ collagen synthesis contributes to osteoporosis as well
- Weight-bearing exercises, vitamin D, and calcium are important lifestyle factors in reducing osteoporosis
Vasomotor Symptoms

- AKA – hot flashes, hot flushes, night sweats
- Recurrent, transient episodes of flushing accompanied by a sensation of warmth to intense heat on upper body and face
- Adversely affect QOL
- 2nd most frequently reported perimenopausal symptom – 75% of women
- Start in late perimenopause and last 6-24 months
- Associated with circadian rhythm
- Penn Ovarian Aging Study - 6-20x severe hot flashes in those who smoked
- SWAN study – ethnic groups and BMI
- 47% of women with moderate to severe premenstrual complaints
Vasomotor Symptoms – WHY?

- Normal thermoregulation
  - Upper limit – sweating
  - Lower limit – shivering
- Decreases in estrogen
  - Reduced or absent thermoneutral zone
  - Small elevations in core body temperatures → heat dissipation response
- Theory support
  - Triggered by peripheral heating (warm room)
  - Core body heating (hot drink)
  - Ameliorated by ambient and internal cooling
- Other causes = thyroid, epilepsy, infection, insulinoma, pheochromocytoma, carcinoid syndromes, leukemia, pancreatic tumors, autoimmune, new-onset hypertension, mast-cell disorders
- Drugs that block estrogen/inhibit estrogen biosynthesis, SSRIs/SNRIs
- Night sweats – tuberculosis and lymphoma
VMS Management

- 25% of women seek help
- Symptomatic relief only – there is no “cure”
- Treatment should be tailored to each individual
- Cancer survivors more likely to have severe VMS
- Nonpharmacological treatments
  - Lifestyle
    - Enhanced relaxation techniques – meditation, yoga, massage, lukewarm bath
    - Regular exercise and maintain a healthy body weight
    - No smoking
    - Paced respirations
    - Dress in layers, ice packs, avoid hot/spicy foods and caffeine/alcohol
  - Nonprescriptive remedies
    - Soy foods/phytoestrogens or isoflavone supplements
    - Black cohosh
    - Vitamin E and Omega-3 fatty acids
    - Ginseng root
- Complimentary/Alternative Treatments
  - Cognitive Behavioral Therapy (CBT)
  - Acupuncture
VMS Prescriptions

- Estrogen (ET) or Estrogen-Progesterone (EPT) Combo
  - Hysterectomy – ET only
  - Retains uterus – EPT
  - Start early, lowest dose, shortest duration
- Examples
  - Oral: Conjugated estrogens or human estrogens with/without progestins
  - Transdermal: Patches and creams/gels
  - First pass effects – oral vs. transdermal
    - Less effect on clotting factors, triglycerides, c-reactive protein, SHBG
Bioidentical vs Synthetic Hormones

- **Bioidentical = Replacement**
  - Identical to the hormone in the body
  - Derived from wild yams

- **Synthetic = Substitution**
  - Conjugated equine estrogens → Premarin
  - Progestins → Medroxyprogesterone
  - Prempro (combo – conjugated equine estrogens + medroxyprogesterone)

### Goals of bHRT

- Alleviate the symptoms caused by the natural decrease in production of hormones by the body
- Restore the protective benefits which were originally provided by naturally occurring hormones
- Re-establish a hormonal balance
Estrogens

**Estrone (E1)**
- Primary estrogen after menopause

**Estradiol (E2)**
- Most potent
- Treats hot flashes
- Increase in HDL
- Decrease in LDL/TG

**Estriol (E3)**
- Maintains pregnancy
- Protective in breast cancer
- Blocks estrone
Progesterone

- Protects against breast cancer
- Protects against endometrial cancer
- Protects against breast cysts
- Balances estrogen
- Helps thyroid hormone action
- Natural antidepressant
- Helps normalize blood sugar
- Normalizes blood clotting
- Normalized Zinc and Cu levels
- Maintains proper cell O2 levels
- Improves sleep (PO dosing)
- Lowers cholesterol and lipid profile
- Lowers blood pressure
- Improves Bone Mineral Density scores
# Prescription Therapies

## Oral Estrogen Therapy

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product Name</th>
<th>Dosage, mg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogens</td>
<td>Premarin</td>
<td>0.3, 0.45, 0.625, 0.9, 1.25</td>
</tr>
<tr>
<td>Synthetic conjugated estrogens</td>
<td>Cenestin</td>
<td>0.3, 0.45, 0.625, 0.9, 1.25</td>
</tr>
<tr>
<td></td>
<td>Enjuvia</td>
<td>0.3, 0.45, 0.625, 0.9, 1.25</td>
</tr>
<tr>
<td>Esterified estrogens</td>
<td>Menest</td>
<td>0.3, 0.625, 1.25, 2.5</td>
</tr>
<tr>
<td>17β-estradiol</td>
<td>Estrace (varying generics)</td>
<td>0.5, 1.0, 2.0</td>
</tr>
<tr>
<td>Estropipate</td>
<td>Ogen (varying generics)</td>
<td>0.625 (0.75), 1.25 (1.5), 2.5 (3.0)</td>
</tr>
</tbody>
</table>
## Prescription Therapies

### Transdermal Estrogen Therapy

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product Name</th>
<th>Dosage, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>17β-estradiol matrix patch</td>
<td>Alora</td>
<td>0.025, 0.05, 0.075, 0.1 twice/wk</td>
</tr>
<tr>
<td></td>
<td>Climara</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1 once/wk</td>
</tr>
<tr>
<td></td>
<td>Menostar</td>
<td>0.014 once/wk (osteoporosis)</td>
</tr>
<tr>
<td></td>
<td>Minivelle</td>
<td>0.0375, 0.05, 0.075, 0.1 twice/wk</td>
</tr>
<tr>
<td></td>
<td>Vivelle</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1 twice/wk</td>
</tr>
<tr>
<td></td>
<td>Vivelle-Dot</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1 once or twice/wk</td>
</tr>
<tr>
<td>17β-estradiol reservoir patch</td>
<td>Estraderm</td>
<td>0.025, 0.05, 0.1 twice/wk</td>
</tr>
<tr>
<td>17β-estradiol transdermal gel</td>
<td>Divigel</td>
<td>0.25, 0.5, 1.0/d</td>
</tr>
<tr>
<td></td>
<td>EstroGel</td>
<td>0.75/d</td>
</tr>
<tr>
<td></td>
<td>Elestrin</td>
<td>0.52/d</td>
</tr>
<tr>
<td>17β-estradiol topical emulsion</td>
<td>Estrasorb</td>
<td>0.05/d (2 packets)</td>
</tr>
<tr>
<td>17β-estradiol transdermal spray</td>
<td>Evamist</td>
<td>0.021 mg per 90 μL spray/d</td>
</tr>
</tbody>
</table>
# Prescription Therapies

## Combination Estrogen-Progesterone Therapy

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product Name</th>
<th>Dosage/d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Continuous-cyclic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjugated estrogens (E) + medroxyprogesterone acetate (P)</td>
<td>Premphase</td>
<td>0.625 mg E + 5.0 mg P (E 1-14 days then E+P 15-28 days)</td>
</tr>
<tr>
<td><strong>Oral Continuous-combined</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjugated estrogens (E) + medroxyprogesterone acetate (P)</td>
<td>Prempro</td>
<td>0.3 or 0.45 mg E + 1.5 mg P</td>
</tr>
<tr>
<td>Ethinyl estradiol (E) + norethindrone acetate (P)</td>
<td>Femhrt</td>
<td>2.5 μg E + 0.5 mg P or 5.0 μg E + 1.0 mg P</td>
</tr>
<tr>
<td>17β-estradiol (E) + norethindrone acetate (P)</td>
<td>Activella</td>
<td>0.5 mg E + 0.1 mg P 1.0 mg E + 0.5 mg P</td>
</tr>
<tr>
<td>17β-estradiol (E) + drospirenone (P)</td>
<td>Angeliq</td>
<td>0.5 mg E + 0.25 mg P 1 mg E + 0.5 mg P</td>
</tr>
<tr>
<td><strong>Transdermal Continuous-combined</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17β-estradiol + norethindrone acetate (P)</td>
<td>CombiPatch</td>
<td>0.05mg E + 0.14 mg P twice/wk 0.05 mg E + 0.25 mg P twice/wk</td>
</tr>
<tr>
<td>17β-estradiol (E) + levonorgestrel (P)</td>
<td>Climara Pro</td>
<td>0.045 mg E + 0.015 mg P once/wk</td>
</tr>
<tr>
<td>Composition</td>
<td>Product Name</td>
<td>Dosage/d</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------</td>
<td>----------</td>
</tr>
<tr>
<td>Oral tablet - Progestin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>Provera (generics)</td>
<td>2.5 mg, 5 mg, 10 mg</td>
</tr>
<tr>
<td>Norethindrone</td>
<td>Micronor (generics)</td>
<td>0.35 mg</td>
</tr>
<tr>
<td>Norethindrone acetate</td>
<td>Aygestin (generics)</td>
<td>5 mg</td>
</tr>
<tr>
<td>Megestrol acetate</td>
<td>Megace (generics)</td>
<td>20 mg or 40 mg tab, 40 mg suspension</td>
</tr>
<tr>
<td>Oral capsule - Progesterone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronized progesterone (peanut)</td>
<td>Prometrium (generics)</td>
<td>100 mg or 200 mg</td>
</tr>
<tr>
<td>Intrauterine System - Progestin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>Mirena, Liletta, Kyleena, Skyla</td>
<td>20 μg/d release (52 mg for 5y), 19.5 μg/d release (52 mg for 5y), 17.5 μg/d release (19.5 mg for 5y), 6 μg/d release (13.5 mg for 3y)</td>
</tr>
<tr>
<td>Vaginal Progesterone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gel – Progesterone</td>
<td>Crinone 4% or 8%</td>
<td>45 or 90 mg applicator</td>
</tr>
<tr>
<td>Insert – Micronized progesterone</td>
<td>Endometrin</td>
<td>100 mg insert</td>
</tr>
</tbody>
</table>
Counseling for HRT

Contraindications
- Undiagnosed abnormal genital bleeding
- Known, suspected, or history of breast cancer
- Known, suspected, or history of estrogen-dependent neoplasia
- Active or history of DVT and/or PE
- Active or history of arterial thromboembolic disease (CVA or MI)
- Liver dysfunction or disease
- Known or suspected pregnancy
- Known hypersensitivity to ET or EPT
- Smoking/tobacco use and >35 years

Potential Adverse Effects
- Uterine bleeding (starting or recurrence)
- Breast tenderness and sometimes enlargement
- Nausea
- Abdominal bloating
- Fluid retention in extremities
- Changes in shape of cornea (possible contact lens intolerance)
- Headache (including migraine)
- Dizziness
- Mood changes
Other Therapies

- Paroxetine 7.5mg – first nonhormonal medication approved for VMS
- Bazedoxifene (BZA) 20 mg + Conjugated Estrogen (CE) 0.45 mg and 0.625 mg – first SERM for menopausal symptoms and osteoporosis
- SSRIs
  - Escitalopram 10 mg or 20 mg per day
- SNRIs
  - Venlafaxine 37.5 mg to 75 mg per day
  - Desvenlafaxine 100 mg to 150 mg per day
- Eszopiclone – nighttime hot flashes
- Gapabentin – start with 300 mg daily QHS, increase as needed
- Clonidine – 0.05 mg BID or 0.1 mg BID (taper slowly with higher dose)

Adverse effects – nausea and sexual problems, caution after breast cancer
What about testosterone?

- Did you know that women need testosterone too?
- Produced by the ovaries and adrenal glands
- Reasons for female low T
  - Declining sex steroid hormones secondary to menopause and aging
  - Problems with ovaries, pituitary gland, adrenal glands, thyroid gland
- Diagnostic testing – labs (total testosterone and SHBG)
  - [http://www.issam.ch/freetesto.htm](http://www.issam.ch/freetesto.htm) (Normal = 0.6 to 1.0 ng/dL)
- Treatment options?
  - No FDA approved formulations
  - 1/10 of male dose, compounded, DHEA
  - Caution in supraphysiological levels
  - Side effects – acne, mood changes, hirsutism,

**Symptoms**

- Sluggishness
- Muscle weakness
- Fatigue
- Depressed mood
- Hot flashes
- Weight gain
- Fertility issues
- Irregular menstrual cycles
- Sleep disturbances
- Low libido
- Orgasm concerns
- Vaginal dryness
- Loss of bone density
Androgens in Females

Figure adapted from: Glaser R, Dimitrakakis C. Maturitas. 2013;74(3):230-234

Table 1. Key take-away messages
- Androgens, including testosterone, are essential hormones for development and maintenance of female sexual anatomy and physiology and modulation of sexual behavior.
- Testosterone has many physiological actions in women, directly through its cell-specific receptor, by non–receptor-mediated actions, and by conversion to 5α-DHT and estrogens.
- There is no testosterone level for diagnosis of HSDD or for use as a treatment target.
- Total testosterone concentration is the best practical assay.
- Total testosterone and SHBG should be measured before initiating therapy.
- Proper dosing should attain and maintain total testosterone levels in the premenopausal physiological range.
- If an approved female formulation is not available, one-tenth of a standard male dose of 7% transdermal testosterone or about 300 mcg/day can usually achieve the normal premenopausal physiological range.
- Compounded testosterone, pellets, IM injections, and oral formulations are not recommended.
- Additional testing and alternative strategies may be required to assess failure to respond to typical testosterone treatment, particularly when testosterone or SHBG levels are high.

5α-DHT = 5α-dihydrotestosterone; HSDD = hypoactive sexual desire disorder.
<table>
<thead>
<tr>
<th>Symptom</th>
<th>E</th>
<th>P</th>
<th>TH</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrocystic Breast</td>
<td>↑</td>
<td>↓</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Weight Gain</td>
<td>↑</td>
<td>↓</td>
<td>P</td>
<td>↓</td>
</tr>
<tr>
<td>Heavy/Irregular Menses</td>
<td>↑</td>
<td>E</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Hot Flashes</td>
<td>↓</td>
<td>E</td>
<td>↑</td>
<td>E</td>
</tr>
<tr>
<td>Dry Skin/Hair</td>
<td>↓</td>
<td>E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>↑</td>
<td>E</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Depression</td>
<td>↓</td>
<td>E</td>
<td>↑</td>
<td>P</td>
</tr>
<tr>
<td>Night Sweats</td>
<td>↓</td>
<td>E</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Vaginal Dryness</td>
<td>↓</td>
<td>E</td>
<td>↓</td>
<td>T</td>
</tr>
<tr>
<td>Headaches</td>
<td>↓</td>
<td>E</td>
<td>↑</td>
<td>P</td>
</tr>
<tr>
<td>Irritability</td>
<td>↑</td>
<td>E</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Mood Swings</td>
<td>↑</td>
<td>E</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Breast Tenderness</td>
<td>↑</td>
<td>E</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Sleep</td>
<td>↓</td>
<td>P</td>
<td>↓</td>
<td>E</td>
</tr>
<tr>
<td>Cramps</td>
<td>↓</td>
<td>P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluid Retention</td>
<td>↓</td>
<td>P</td>
<td>↑</td>
<td>E</td>
</tr>
<tr>
<td>Breakthrough Bleeding</td>
<td>↓</td>
<td>P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>↓</td>
<td>T</td>
<td>↓</td>
<td>TH</td>
</tr>
<tr>
<td>Loss of Memory</td>
<td>↓</td>
<td>T</td>
<td>↓</td>
<td>E</td>
</tr>
<tr>
<td>Bladder Symptoms</td>
<td>↓</td>
<td>E</td>
<td>↓</td>
<td>T</td>
</tr>
<tr>
<td>Arthritis</td>
<td>↓</td>
<td>T</td>
<td>↓</td>
<td>P</td>
</tr>
<tr>
<td>Harder to Reach Climax</td>
<td>↓</td>
<td>T</td>
<td>↓</td>
<td>E</td>
</tr>
<tr>
<td>Decreased Sex Drive</td>
<td>↓</td>
<td>T</td>
<td>↑</td>
<td>E</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>↑</td>
<td>T</td>
<td>↑</td>
<td>TH</td>
</tr>
</tbody>
</table>

E = Estrogen  
P = Progesterone  
T = Testosterone  
C = Cortisol  
TH = Thyroid  
↓ = Caused by Low Level  
↑ = Caused by High Level  
↓↑↑ = Caused by Fluctuating Levels

**Chart obtained with permission from Innovation Compounding Pharmacy.**
Sexual Function

- PRESIDE Study
  - At least 40% of women and 12% have personal distress
  - A third to half perimenopauseal/postmenopausal women experience one or more concerns with sexual functioning

- Decrease in ovarian function
  - Loss of testosterone – key player!
  - Sex drive $\rightarrow$ motivation, desire, and sexual sensation

- Non-hormonal causes at midlife and beyond
  - Psychological, sociocultural, and interpersonal
North American Menopause Society Questionnaire

Are you currently sexually active?
- If yes, are you currently have sex with men, women, both? History of partners?
- If no, why not?

How long have you been with your current partner?
- Is the relationship committed, monogamous?
- Safe sex practices
- Any sexually transmitted infections?

Do you have any concerns about your sex life?
- Loss of interest in sexual activities? Libido? Desire?
- Loss of arousal? Loss or diminished orgasm?
- Any pain with sexual activity? Intercourse? Outercourse?
  - If yes, when did the pain start? Does it happen every time?
PLISSIT Model

**Permission**
- Gives the patient permission to discuss their concern
- Example: “Most women going through menopause have a sexual health concern, is this a concern for you?” Expand with – Tell me more.

**Limited Information**
- The provider can provide a small amount of information of the concern and normalize the situation.
- Example: Pathophysiology of disease.

**Specific Suggestions**
- Provide specific suggestions to improve the patient’s concern.
- Example: Communication skills, literature, OTC, Rx’s, PFPT, sensate focus, masturbation, position modification, lubricants, dilators, etc.

**Intensive Therapy**
- Referral to sex therapy or sex counseling.
- Example: Long standing conflict within the relationship, unresolved trauma/abuse, infidelity/affairs
1 in 3 women will die of heart disease regardless of race or ethnicity

Does estrogen play a role? Controversial and Confusing

Early menopause (especially due to oophorectomy) are at increased risk of coronary heart disease than compared to age-matched premenopausal women

Increase in total cholesterol and low-density lipoprotein cholesterol (LDL-C)

SWAN Study
  - Association between earlier changes in lipids and the menopause transition

Despite abundance of evidence for cardiovascular benefit, it is the opinion that estrogen therapy NOT be prescribed for the purpose of heart disease prevention
  - No randomized trials of HRT and primary prevention of heart disease
  - No benefit of hormone therapy for secondary prevention of recurrent clinical events or atherosclerosis progression among women diagnosed with heart disease

Remember...initiation of hormone therapy for women between 50-59 years of age or within 10 years of menopause has not been shown to increase risk of CVD events
So what can you do?

- Identify risk factors:
  - Pericardial fat accumulation and elevated coronary calcium
  - Age, smoking, hypertension, DM, abnormal plasma lipids, FHx of premature CVD, poor exercise capacity on stress test, metabolic syndrome
- Monitoring lipids should be primary prevention of CVD
- No support is performing ECG
- Calculated risk-assessment tools
  - Framingham Heart Study, www.uptodate.com

- ACOG guidelines for women with history of preeclampsia
  - Annual blood pressure
  - Fasting glucose
  - Fasting lipids
  - BMI – metabolic syndrome
- Individualized counseling and plan
Osteoporosis

- AKA: “porous bone”
- Significant health threat for aging postmenopausal women with increased risk of fracture
- Bone strength = bone quantity and bone quality → bone mineral density (BMD)
- Peak bone mass is peaked at a woman’s third decade of life
- ACOG recommendation for DEXA or BMD test annually starting at age 65
- Z-score = secondary osteoporosis and is always used for children, young adults, women who are pre menopausal and men under age 50
- T-score = bone mass differs from a healthy 30 year old
  - Total hip, femoral neck, lumbar spine
- Categorized
  - Primary = age-related
  - Secondary = disease or medication related
  - Idiopathic = no known cause (young)
- Primary goal of management is to reduce fracture risk
- Prevalence
  - 19% of women 65 to 74 years
  - >50% of women 85 years and older
Osteoporosis – Treatment

- World Health Organization’s Fracture Risk Assessment Tool
  - http://www.shef.ac.uk/FRAX/index.aspx
- Conservative
  - Weight-bearing, balance, and resistance exercises
- Serum vitamin D3 levels >30 ng/mL
- 1200 mg calcium daily
- ACOG recommends postmenopausal women take 600 IU of vitamin D3 daily
- NOF recommends women >50 years 800-1000 IU of vitamin D3
- Counsel on smoking cessation and limit alcohol intake

Medications

- Bisphosphonates
  - Fosamax 70mg qweekly 30 min prior to food/drink taken with full glass of water
  - Actonel 35mg qweekly 30 min prior to food/drink taken with full glass of water
- Raloxifene (SERM) 60mg PO daily
- Miacalcin Nasal 200 IU 1 spray one nostril each day
- Miacalcin 100 units SQ/IM qod-qd
- Forteo 20 mcg SQ daily
- Prolia 60 mg SQ q6months
- Reclast 5mg IV q12months
Mental Health

- Estrogen is neuroprotective
- No support with use of estrogen solely for cognitive benefits
  - Some supportive evidence in younger women undergoing surgical menopause
- Mind-body therapies – mindfulness, yoga
- Combo conjugated equine estrogen and medroxyprogesterone acetate in >65 years increases risk for dementia
  - Without medroxyprogesterone DID NOT increase risk
- Early intervention of estrogen in women <65 or within 10 years of LMP can decrease risk of Alzheimer dementia
- Objective decline in verbal recall, verbal fluency, and regional brain activation
- Approx 20% of women experience depression
  - Later transition = less risk of depression
  - Consider Paroxetine for treatment
  - Mini-mental screening and suicide screening
Other considerations

- Genitourinary syndrome of menopause (GSM)
- Urinary concerns and pelvic floor muscles
- Body image
- Weight gain
- Skin changes
- Hair changes
- Mood changes and depression
- DEI concerns and impact
44-year-old white cisfemale presents c/o hot flashes over past year
- Laparoscopic hysterectomy at age 27 secondary to large fibroid, retains ovaries
- Hot flashes are worse at night and causes sleep disturbances
- PMH: osteoarthritis, osteoporosis, recent lumbar spine fusion
- Denies any dyspareunia, low libido, or vaginal dryness
- Meds: flavoxate, duloxetine, aloe vera 600mg BID, 2000 IU Vit D3, MVI

What do you want to do next?
Case Study #1

- Let’s look at her hormonal labs

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Normal Values</th>
<th>Plan</th>
<th>Follow up in 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>&lt;0.1 ng/dL</td>
<td>start on 100mg micronized progesterone orally at bedtime</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>220.00 pg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone, T</td>
<td>&lt;75.0 ng/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHBG</td>
<td>70.6 nmol/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Free & Bioavailable Testosterone calculator**

These calculated parameters more accurately reflect the level of bioavailable testosterone than does the sole measurement such as albumin. The SHBG-bound fraction is biologically inactive because of the high binding affinity of SHBG for testosterone.

- Albumin: 4.3 g/dL
- SHBG: 70.6 nmol/L
- Testosterone: 13.3 ng/dL

- Free Testosterone: 0.142 ng/dL (1.07 %)
- Bioavailable Testosterone: 3.33 ng/dL (25 %)

**Normal Values**

- Testosterone: 0.6-1.0 ng/dL
Case Study #2

- 64-year-old white cisfemale c/o menopausal symptoms
- Would like to discuss hormone options
- Final menstrual period at age 51
- Tried testosterone pellets in the past (supraphysiological levels) and progesterone cream (caused depression)
- Brain fog, difficulty with memory recall and processing, dullness, flatness, fatigue, loss of vibrancy
- Less intense orgasms, vaginal dryness (estradiol tablet PV twice weekly), dyspareunia
- Medications: OTC vitamins and supplements
- What do you want to do next?
Case Study #2

- Pelvic Exam
- Hormone Labs

Plan = start on transdermal testosterone gel
(1.25mg daily x two wks then increase to 2.5mg daily)
Start on prasterone supp vaginal nightly

http://www.issam.ch/freetesto.htm
Case Study #2

- Follow up 6 weeks later
- Improved libido, energy, brain fog, vibrancy, less dryness
- Continues to have difficulty with memory recall
- Labs

Plan = increase transdermal testosterone gel to 3.75mg daily
Continue with prasterone supp vaginally as directed
Referral to pelvic floor physical therapy
Case Study #3

- 54-year-old black cisfemale presents to your clinic c/o severe hot flashes, starting about 5 years ago and worsening over the past 9 months, mild GSM symptoms
- Final menstrual period was at age 52 (retains uterus and ovaries)
- PMH: hypertension and hyperlipidemia, former cigarette user (quit 10 yrs ago)
- FMH: mother had diabetes and CVD
- Goal = maximize symptom control while minimizing potential for harm
- **What would you like to do next?**
Case Study #3

- Would you do a pelvic exam?
- Would you perform labs?
- What VMS treatment option would you like to try?
  - Systemic HRT therapy
  - Non-hormonal therapy
  - Local vulvovaginal hormone therapy

Plan = non-hormonal therapy to start secondary to risk factors
Add local hormone therapy as well.

Remember...if a trial of one or more nonhormonal strategies fails, systemic hormonal therapy remains an option
Counsel on risks vs benefits to help patient make an informed decision.

She has a uterus – protect it with progesterone 😊


Thank you!

Questions?

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