Menopause Management

Tiffany Weber, MD
Assistant Professor
University of Utah OB/GYN Department
DISCLOSURES

• No financial disclosures

• I have not yet experienced menopause
HISTORY OF MENOPAUSE

• Described by Aristotle, but not defined until 1820s
• AKA “hysteria”

• Wide variety of treatments: opium, cannibus, ground up animals ovaries, “testicular juice”, vaginal solutions, oophorectomy, hysterectomy, clitoridectomy

• 1930s, estrogen and progesterone identified and a more medical understanding of menopause began to develop
MENOPAUSE BACKGROUND

• Women spend about 1/3 of their life after menopause
• “Grandmother hypothesis”
MENOPAUSE DEFINITION

• Definition: permanent cessation of menstruation

• Median age in the US is 51 years

• Due to loss of ovarian function
Perimenopause

Estrogen decreases as ovaries run out of eggs

Ovulation becomes irregular

Progesterone not produced if ovulation doesn’t occur

Thickness of uterine lining varies according to hormone level

Periods become irregular

Postmenopause

Very little estrogen released

Ovulation does not occur

Progesterone is not produced

Uterine lining does not thicken

Periods do not occur
ESTROGEN

Heart
Protects from cholesterol

Liver
Reduces cholesterol in blood

Ovary
Produced from growing eggs

Uterus
Monthly preparation for pregnancy or menstrual cycle

Vagina
Makes it moist
Protect from infection

Brain
Helps adjust body temperature
Increases memory
Adjusts libido

Breast
Grows and shapes breast
Prepare breast for feeding

Skin
Makes skin young

Bone
Strengthens bone and
Increase its density
MENOPAUSE: HORMONES

- Estradiol
- Progesterone
- FSH
- Androgens
MENOPAUSE

- Amenorrhea
- Vasomotor symptoms
- Dyspareunia
- Sleep Disturbance
- Weight redistribution
- Mood lability

- Osteoporosis
- Vaginal atrophy
- Urinary incontinence
- Heart disease
- Poor skin elasticity, muscle tone
- Cognitive changes?
TREATMENT

• YES
  • Vasomotor symptoms
  • Osteoporosis
  • Vaginal atrophy

• NO
  • Weight gain
  • Cognitive changes
  • Heart Disease
VASOMOTOR SYMPTOMS

• Of women with hot flushes:
  – 87% of women who experience these symptoms experience on a daily basis
  – 33% have more than 10 episodes per day
  – How long do these symptoms last?
    • WHO KNOWS! (reported 6 months to 10 years)
VASOMOTOR SYMPTOMS TREATMENT

- GOLD STANDARD: Systemic estrogen
- Low dose
- Decreases frequency and severity of hot flushes
VASOMOTOR SYMPTOM TREATMENT-NONHORMONAL

- Lifestyle changes
- Supplements
- Paxil (only FDA approved non hormonal treatment)
- Clonodine
- Gabapentin
VASOMOTOR SYMPTOMS AFTER HRT

• 50% of women have vasomotor symptoms return
OSTEOPOROSIS

- WHI statistically significant reduction with HRT
- 33-36% reduced risk of hip and vertebral fractures with ET or Combined ET/PT
- HRT approved for prevention of osteoporosis
- Benefit is dose related
- Bone mineral density due to HRT is lost within 1-2 years after discontinuing treatment (so may need to transition to alternate treatment)

ACOG Practice Bulletin “Osteoporosis”
VAGINAL ATROPHY (GENITOURINARY SYNDROME OF MENOPAUSE)

- Symptoms: dyspareunia, vaginal dryness, discharge, itching
- Due to: loss of superficial epithelial cells, decreased subcutaneous fat, tissue is fragile
VAGINAL ATROPHY TREATMENT

- Lubricants/moisturizers
- Estrogen
  - Local (cream, ring or tablet)
  - Systemic
- Ospemifene
- Vaginal dilators
WEIGHT GAIN

• Cochrane review:
  • No difference in weight gain, BMI
    – Unopposed estrogen
    – Combined estrogen and progesterone
    – Non-HRT users
  • Insufficient data for: fat distribution, waist hip ratio
COGNITIVE CHANGES

• SWANS, Nurses Health Study and WHI:
• Does not support decline in cognitive function
• Increase in anxiety and depression which are independent risk factors for negative cognitive changes
• Dementia risk
INITIATING HRT

• What to start?
• When to start?
• How to discuss risks with patient
HORMONE REPLACEMENT THERAPY

- Estrogen
- Progesterone
- Testosterone
ESTROGEN REPLACEMENT THERAPY

• Systemic
  – Oral, transdermal (patch, gel, sprays)

• Vaginal
ESTROGEN REPLACEMENT THERAPY

• Low dose
  – 0.3-0.45mg/d oral conjugated equine estrogen
  – 0.5mg/d oral micronized estradiol
  – 5mcg/d oral ethinyl estradiol
  – 0.025-0.075mg/wk of transdermal estradiol patch

• Other topicals: gels, creams, spray
VAGINAL ESTROGEN

• Do not need progestin treatment
• Cochrane metanalysis: vaginal estrogen not associated with increased risk for endometrial hyperplasia
• No endometrial surveillance required in asymptomatic women
VAGINAL ESTROGEN AND HISTORY OF BREAST CANCER

• Non-hormonal approaches are the first line choice
• Symptoms often worsened by anti-estrogen treatments
• RISK VS BENEFIT
• Several studies have shown low dose vaginal estrogen have minimal systemic absorption
  – Systemic levels do not exceed the normal menopausal range (cream has greater variability compared to ring or tablet)
PROGESTIN REPLACEMENT THERAPY

• NECESSARY if they have a uterus to prevent endometrial hyperplasia
• May help vasomotor symptoms
• Safety? No great studies looking at unopposed progestin use
TESTOSTERONE REPLACEMENT THERAPY

• No benefit for vasomotor symptoms
• May improve sexual function and number of satisfying sexual episodes

• Risks:
  – dyslipidemia
  – clitoromegaly, hirsutism, acne, hair loss
HORMONE REPLACEMENT THERAPY

• RISKS

  – THROMBOEMBOLIC DISEASE
  – BREAST CANCER
  – HEART DISEASE?
HRT AND THROMBOEMBOLIC RISK

• Oral Estrogen
  – 1.2-1.5 fold increased risk of VTE

• Risk per 100,000
  – 40s: 54
  – 50s: 62-122
  – 70s: 300-400
  – 80s: 700
HRT AND THROMBOEMBOLIC RISK

• Transdermal estrogens
  – little or no effect in elevating prothrombotic substances
• The estrogen and thromboembolism risk study (Case control)
  – OR oral: 4.2, transdermal: 0.9
• Progestins
  – natural progesterone no increased risk
  – synthetic progestins increased risk
HRT AND THROMBOEMBOLIC RISK

• WHI
  – 41% increase risk of stroke
    • 21 to 29 per 10,000 woman-years
  – These risks were noticed within 1-2 years of initiation
HRT AND THROMBOEMBOLIC RISK

- Cochrane review

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>VTE</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Risk Increase per 1000</td>
<td>6</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>NNTH</td>
<td>165</td>
<td>118</td>
<td>242</td>
</tr>
</tbody>
</table>
HRT AND BREAST CANCER RISK

• Collaborative Group on Hormonal Factors in Breast Cancer:
  – 52,705 women with BC, 108,411 women without breast cancer
  – Each year a women uses HRT, risk of BC increases 2.3% (did not differentiate between ET and ET/PT)

• WHI
  – in ET/PT there were 8 excess cases per 10,000 women years
  – No statistical difference between placebo and ET
HRT AND HEART DISEASE

• WHI study terminated early due to cardiovascular events (and worsened global index)
• 29% increase in cardiovascular events  
  – but no significant difference in CHD deaths
• 30/10,000 woman-years to 37/10,000 woman-years
HRT AND HEART DISEASE

• “Timing hypothesis”
• WHI: Average age of participants was 63
• Subsequent WHI analysis:
• Women age 51-59 showed reduced total mortality (decreased 30%) with HRT within the first 10 years after menopause
HRT AND HEART DISEASE

• Timing hypothesis (RE-EVAL of WHI)
  – 1000 women under 60 years old start HRT:
  – 6 fewer deaths
  – 8 fewer cases of CHD
  – 5 additional VTE
HRT AND HEART DISEASE

• Cochrane review subanalysis

• Timing theory (<10 years from menopause)
  – Increased risk of VTE
  – Lower mortality
  – Lower CHD
  – No statistical significance on stroke
HRT AND HEART DISEASE

• Heart and Estrogen/Progestin Replacement Study (HERS) and follow up (HERSII)
  – RCT: conjugated equine estrogen and medroxyprogesterone acetate
  – CHD risk among women with CHD
• Tx group: 52% increase in CHD events in the 1st year
HRT AND HEART DISEASE

• HRT should not be used for primary or secondary cardiac disease prevention
HRT AND THE PATIENT

• Know the benefits for the patient

• Discuss the risks for the patient

• Determine the goals of treatment with the patient
BIG PICTURE IDEAS

• Do use HRT for treatment for vasomotor symptoms (in appropriate patients)
  – Lowest dose and shortest duration to control symptoms
• Do use HRT for vaginal atrophy
• Do NOT use HRT for CV protection
• HRT is probably safest when initiated at the onset of menopause
REFERENCES

- Compounded bioidentical menopausal hormone therapy. ACOG Committee Opinion #532, Aug 2012
- Postmenopausal Estrogen Therapy: route of administration and risk of venous thromboembolism. ACOG Committee Opinion #556, April 2013
- Hormone therapy and heart disease. ACOG Committee Opinion #565, June 2013
- Dodin, et al. Acupuncture for menopausal hot flushes. Cochrane database of systematic reviews 2013, issue 7, Art No CD 007410
- Osteoporosis. ACOG Practice Bulletin #129, Sept 2012