Menopause
A Review of Systemic Impact and Current Treatment Guidelines

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Learning Objectives

- Explain the biological, physiological, and psychological impact of menopause
- Review current guidelines for hormone replacement therapy
- Discuss non-hormonal alternatives to menopausal associated conditions
Before Menopause (peri-menopausal)

- The months/years leading up to menopause
- Common symptoms:
  - Irregularity in menstrual cycles
  - Hot flashes/night sweats may start
  - Changes in mood, sleep, concentration
  - Vaginal dryness
  - Slowing of metabolism, weight gain

Menopause (Meno“stop”)

- Defined after the absence of a menstrual cycle for 12+ months OR lab values consistent with menopause (FSH typically >30 and estradiol typically <30)
- Ovaries are no longer producing estrogen and progesterone
  - However, estrogen is still produced and metabolized in estrogen-sensitive organs (i.e. adipose tissue) although at significantly lower levels (genetically driven)
  - Testosterone still produced by the adrenal glands
- Impacts multiple biological, physiological, and psychological functions
- Significant shift in overall quality of life
Menopause: A Review of Systemic Impact and Current Treatment Guidelines

Systemic Impacts

- Cardiovascular Disease
- Metabolic Changes
- Osteoporosis
- Dermal Changes
- Genitourinary Menopausal Syndrome
- Cognitive Decline
- Vasomotor Symptoms

Cardiovascular – Shift in Risk after Menopause

- Cardiovascular disease (CVD) is the leading cause of death and disability in postmenopausal women older than 50 years
  
- Rapid increase in prevalence of CVD is seen at the onset of menopause. With continuation of increase through the postmenopausal period
  
- The complex effects of hormones on the cardiovascular system result in different presentations of coronary heart disease in women:
  - Higher incidence of angina
  - Lower burden of obstructive coronary artery disease (CAD) on angiography
  - Poorer prognosis compared with men
  - More likely to develop heart failure with preserved ejection fraction

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Metabolic – Pear to Apple

- Shifts in hormones appear to accelerate fat accumulation, which appears to accumulate disproportionately in the abdominal area.
- This shift is associated with increased insulin resistance and dyslipidemia.
- In Women’s Health Initiative (WHI) Trials - hormone therapy significantly reduced the diagnosis of new-onset type 2 DM, but it is not FDA approved for this purpose.
- Hormone therapy may help attenuate abdominal adipose accumulation and the weight gains that are often associated with the menopause transition.


Osteoporosis

- As defined by the National Osteoporosis Foundation: chronic, progressive disease characterized by low bone mass, microarchitecture deterioration of bone tissue, bone fragility, and a consequent increase in fracture risk.
- High Prevalence: approx. 50% of white women will have an osteoporotic fracture in their lifetime.
- Consequences
  - Disability – 40% regain pre-fracture independence
  - Mortality – 10-20% increased mortality at 1 year
  - Longterm care – 20% of patients with a fracture require assisted care
  - Expensive! – projected to cost $25 billion by 2025
- Risks after menopause: lack of estrogen blockade on receptors allows for osteoclast-driven bone resorption and accelerated rate of bone remodeling.

Dermal Changes

- With menopause – skin integrity is impacted
  - Decrease in elasticity
  - Thinning of dermal layers
  - Poor wound healing

- Estrogen therapy (ET) may benefit wound healing through modifying inflammation, stimulating granulation tissue formation, and accelerating re-epithelialization. In studies, ET increased epidermal and dermal thickness, increased collagen and elastin content, and improved skin moisture, with fewer wrinkles.


Genitourinary Syndrome of Menopause (GSM)

- Symptoms
  - Genital dryness, burning, and irritation
  - Sexual symptoms of diminished lubrication and pain
  - Urinary symptoms of urgency, dysuria, and recurrent urinary tract infections (UTIs)

- Consequence of postmenopausal estrogen deficiency
  - Changes to the labia, vagina, urethra, and bladder
  - Atrophic vulvovaginitis
Cognitive Impact  
“I’m losing my mind!”

- Women experience varying degrees of cognitive impact
  - Mood changes (depression, anxiety)
  - Irritability
  - Sleep disruption
  - Lack of focus/concentration
- Dementia?
  - Inconclusive evidence when looking at affects of hormone replacement therapy (HRT) on developing dementia/Alzheimer's with some evidence of worsening if HRT initiated later in life


Hot Flashes  
“Do these ever go away?”

- What are hot flashes?
  - Due to thermoregulatory dysfunction
  - Sensations of heat, sweating, flushing, anxiety, or chills lasting for 1-5 minutes
  - Affects sleep, increased irritability, lack of concentration, and overall impacts quality of life
  - Lasts longer than we initially thought – median of 7.4 years\(^1\)
    - Asian women 5 years
    - White women 7 years
    - Hispanic women 9 years
    - Black women 10 years

Case Study - Janet

- 52-year-old black female; last menstrual period was at 50
  - Trying to “tough it out” but hot flashes are waking her up multiple times each night
  - Missing deadlines at work because she’s tired and can’t concentrate and is gaining weight
  - History of hypertension but is well controlled on medication
  - Partial hysterectomy at age 41 due to fibroids and heavy periods but kept her ovaries. She is wondering if she should take hormones but is afraid of getting cancer . . .

What would you recommend for Janet?

Hormones help, but are they safe?

Hormones Help…
  - Hot flashes
  - Sleep
  - Mood
  - Protect bones
  - Genitourinary issues
  - Metabolically

But . . . . Are they safe? . . . .
Hormones “Yea or Ney”?

- For years it was “observed” that post menopausal hormone replacement therapy could provide protection from cardiovascular disease and dementia
- The 2002 Women’s Health Initiative (WHI) – post menopausal women ages 50-79
  - 16,608 women with intact uterus randomized to receive Conjugated Equine Estrogen (CEE) (0.625mg) combined with MPA (2.5mg) or placebo
  - 10,739 women s/p hysterectomy randomized to receive CEE (0.625mg) alone or placebo
- Primary efficacy and safety endpoints: CHD (coronary heart disease) and invasive breast cancer
- Global index: CVA, PE, CRC, endometrial CA, hip fracture, deaths

CVA=cerebrovascular accident/stroke; PE=pulmonary embolism; CRC=colorectal cancer; CA=cancer


WHI Findings

- Study was stopped early due to evidence of increased risk – outweighing benefits
  - CEE/MPA arm stopped at 5.9 years (median)
    - Risks: CHD increased in treatment group (hazard ration HR of 1.18), also increased risk of invasive breast CA, CVA, PE and global index. Increased dementia in women > 65
    - Benefits: decreased hip fracture, improvement of vasomotor symptoms, reduced diabetes
    - Post intervention: most risks/benefits dissipated except some persistence of breast CA risk
  - CEE arm stopped at 7.2 years (median)
    - More balanced re CHD risk (hazard ration HR of 0.94)
    - Risks CVA, venous thrombosis
    - Benefits: decreased hip fracture, reduced diabetes
    - Post intervention: decrease in breast CA risk
- Neither regimen affected all cause mortality, mixed results on quality of life
- Were variations of risks based on age: 50-59 more favorable for all cause mortality, MI, global index but not for CVA and VTE (venous thromboembolism)
- Cumulative f/u of 13 years (September 30, 2010)

Additional Information re: CHD

- The impact of hormone therapy on CHD may vary depending on the woman’s age at start of treatment and/or how many years she has been in menopause
- Some observational data suggest a reduced risk of CHD in women who start therapy when <60 years old and/or who are within 10 years of menopause
- In women who start therapy >10 years from menopause onset, and even more so if >20 years, there is potential for increased risk of CHD
- In WHI both CEE alone and CEE/MPA increased risk of CHD, with potentially greater risk with CEE/MPA


So What Do We Do Now?

- Hormone therapy is approved by FDA for four indications:
  1. Symptomatic vasomotor symptoms
  2. Prevention of bone loss
  3. Hypoestrogenism (such as premature ovarian failure, surgical menopause)
  4. Genitourinary symptoms
- Recommendation – lowest therapeutic dose to effectively treat the indicated condition for the shortest period of time
- Benefits may outweigh risks when initiated in recently menopausal patients <60 years old

Goals of Treatment – The 4 “I”s

- **Identify** if a woman is experiencing conditions related to estrogen deficiency
- **Individualize** therapy – adjust dose to obtain clinical efficacy and maximize safety, choosing method of delivery tailored to patient
- **Initiation** of therapy (timing from start of menopause to start of therapy) to optimize its efficacy and minimize adverse events/risks
- **Inquire** – check-in with patient annually regarding their therapy – Is it still effective? Is it still needed? Is it still safe to take?

Contraindications to using HRT

- Active liver disease
- Active or recent arterial thromboembolic disease (i.e. angina, MI)
- Current, past, or suspected breast cancer
- Known hypersensitivity to HRT
- Known or suspected estrogen-sensitive malignant condition
- Porphyria cutanea tarda (absolute contraindication)
- Previous idiopathic or current VTE (DVT, PE)
- Undiagnosed genital bleeding
- Untreated endometrial hyperplasia
- Untreated hypertension

### Hormone Replacement Options

#### Estrogen Only

<table>
<thead>
<tr>
<th>Estrogen Only</th>
<th>Route</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (multiple brand formulations)*</td>
<td>Transdermal patch, injection, gel, vaginal cream, skin cream, vaginal insert, vaginal ring, oral tablet, transdermal skin spray, vaginal tablet, injection</td>
<td>Micronized estradiol – 17β Estradiol acetate Estradiol Valerate</td>
</tr>
<tr>
<td>Conjugated Estrogen (Premarin)</td>
<td>Oral pill, vaginal cream, injection</td>
<td></td>
</tr>
<tr>
<td>Estropipate (Ogen, Ortho-Est)</td>
<td>Oral pill, vaginal cream</td>
<td></td>
</tr>
<tr>
<td>Esterified Estrogen (Menest)</td>
<td>Oral pill</td>
<td></td>
</tr>
<tr>
<td>Synthetic Conjugated Estrogen (Cenestin, Enjuvia)</td>
<td>Oral pill</td>
<td></td>
</tr>
<tr>
<td>Osremifene (Osphena) (Tissue selective estrogen agonist/antagonist)</td>
<td>Oral pill (FDA approved for dyspareunia)</td>
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#### Progesterone Only

<table>
<thead>
<tr>
<th>Progesterone Only</th>
<th>Route</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micronized Progesterone (Prometrium)</td>
<td>Oral pill</td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate (Provera)</td>
<td>Oral pill</td>
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</tr>
</tbody>
</table>

Other options (not FDA approved) – may include progesterone containing IUDs or topical progesterone creams

## Hormone Replacement Options

<table>
<thead>
<tr>
<th>Combination Estrogen and Progesterone</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol/norethindrone acetate (Activella, Combipatch)</td>
<td>Oral pill, Transdermal patch</td>
</tr>
<tr>
<td>Estradiol/drospirenone (Angeliq)</td>
<td>Oral pill</td>
</tr>
<tr>
<td>Estradiol/levonorgestrel (Climera Pro)</td>
<td>Transdermal patch</td>
</tr>
<tr>
<td>Norethindrone acetate/ethinyl estradiol (Femhrt)</td>
<td>Oral pill</td>
</tr>
<tr>
<td>Estradiol/norgestimate (Prefest)</td>
<td>Oral pill</td>
</tr>
<tr>
<td>Conjugated estrogen/medroxyprogesterone (Prempro)</td>
<td>Oral pill</td>
</tr>
<tr>
<td>Conjugated estrogen/bazedoxifene (Duavee) (Combination Estrogen/Selective Estrogen Receptor Modulator)</td>
<td>Oral tablet</td>
</tr>
</tbody>
</table>


## Conjugated Estrogen vs Estradiol

- The different formulations vary in content, pharmacokinetics, and pharmacodynamics
  - Conjugated Equine Estrogens (CEE) “partially natural”
  - Micronized 17beta Estradiol (E2) “completely natural”
  - Ethinyl Estradiol (EE) “synthetic”
- The variations are further affected by dosage and route of administration – although the full impact is not clearly understood
- Serum lab testing – not reliable – does not measure all active/bioavailable components, levels vary over time, does not correlate with response
- Base adjustment of dose, type, delivery method based on response

Conjugated Estrogens/Bazedoxifene

- FDA approved for the treatment of moderate to severe vasomotor symptoms associated with menopause and prevention of postmenopausal osteoporosis
- Dosing: 0.45mg/20mg tablet taken once daily with or without food
- Bazedoxifene is a selective estrogen receptor modulator:
  - Stimulates estrogen receptors in bone
  - Antagonistic effects in the breast and uterus
- In clinical trials showed statistically significant improvements in:
  - Sexual functioning
  - Menopause-related quality of life
  - Sleep quality
  - Maintenance or slight increase in bone mineral density in lumbar spine and hip – effect on vertebral, hip, or overall fracture rate is unknown

CE/Bazedoxifene: Safety

- When compared to CE/MPA formulation CE/Bazedoxifene results in less vaginal bleeding
- Boxed warning:
  - Increased dementia in women >65
  - Endometrial CA
  - CVA
  - DVT (Deep Vein Thrombosis)
- Should not be used in the following patients:
  - Abnormal uterine bleeding
  - Breast CA or other estrogen-dependent neoplasia
  - Venous or arterial thromboembolism
  - Liver disease
  - Thromboembolic disorders

Back to Case Study - Janet

- 52-year-old black female whose last menstrual period was at age 50
  - Hot flashes are waking her up multiple times each night
  - Missing deadlines at work because she is tired and can’t concentrate
  - Gaining weight
  - Controlled hypertension
  - No uterus
  - Worried about cancer risk

  “I heard natural hormones were safer”

Compounded Bio-identical Hormones

- Compounded formulation claim to be identical in structure to human hormones (in many cases this has not been biochemically sustained)

- Compounded bioidentical HT presents safety concerns:
  - Minimal government regulation and monitoring
  - Overdosing or underdosing
  - Presence of impurities or lack of sterility
  - Lack of scientific efficacy and safety data (can’t say better or worse)
  - Lack of a label outlining risks
New Case Study – Mary

- 60-year-old Asian, postmenopausal woman
  - Been on combined estrogen/progesterone HRT 0.45mg/1.5mg daily since she started menopause 6 years ago
  - Recently diagnosed with stage II ER/PR+ invasive breast cancer
  - She is coming to you to discuss what she can expect when stopping hormones and options to keep her feeling “normal” ...

Non-Hormonal Treatment for Vasomotor Symptoms of Menopause

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Route</th>
<th>Effective dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-adrenergic blocking agents – Clonidine (Catapres)</td>
<td>Oral daily tablet/Transdermal weekly patch</td>
<td>0.1 mg per day</td>
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<tr>
<td>Gabapentin (Neurontin)</td>
<td>Oral tablet</td>
<td>900mg/day in divided doses</td>
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<tr>
<td>Lifestyle modifications</td>
<td>Relaxation: yoga, meditation</td>
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<tr>
<td></td>
<td>Fans/AC</td>
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<tr>
<td></td>
<td>Light/loose clothing</td>
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<tr>
<td>Pollen Extract (Relizen, Femal)</td>
<td>Oral tablet</td>
<td>2 tablets daily (minimum of 2-3 months to start seeing benefit)</td>
</tr>
<tr>
<td>Phytoestrogens</td>
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<tr>
<td>- Black Cohash</td>
<td>Oral capsule</td>
<td>40mg daily for black cohosh (avoid in patients with estrogen sensitive neoplasia)</td>
</tr>
<tr>
<td>- Soy</td>
<td>Various sources</td>
<td></td>
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<tr>
<td>SSRIs</td>
<td></td>
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</tr>
<tr>
<td>- Fluoxetine (Prozac)</td>
<td>Oral tablet/Capsule daily</td>
<td>- 20mg</td>
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<tr>
<td>- Paroxetine (Brisdelle, Paxil)</td>
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<td>- 7.5 (Brisdelle)</td>
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<tr>
<td></td>
<td></td>
<td>- 12.5-25mg (Paxil CR) or 20mg (Paxil)</td>
</tr>
<tr>
<td>SNRIs</td>
<td></td>
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</tr>
<tr>
<td>- Venlafaxine (Effexor)</td>
<td>Oral tablet/Capsule</td>
<td>37.5-75mg XR formulation daily</td>
</tr>
</tbody>
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Complimentary & Alternative Medicine (CAM) to treat Menopause

- 51% of women report using CAM
- 60% of these women report perceived benefit
- Evidence is mixed with regards to safety and efficacy
- Patients often don’t openly discuss with providers
- Important we address integrative approaches to reduce undertreatment and risk

Mind-Body Practices

- **Hypnosis for Hot Flashes**: RCT showed equally as effective when compared to venlafaxine 75mg (50% reduction in vasomotor symptoms (VMS) compared to 25% placebo)
  - Recommended by the North American Menopause Society (NAMS) for the treatment of menopausal symptoms and poses little risk
- **Cognitive Behavioral Therapy (CBT)**: when compared to placebo – reduction in VMS interference but not in frequency
  - Recommended by NAMS for reduction of bothersome symptoms but not for frequency
- **Relaxation & Biofeedback**: conflicting evidence – may provide some benefit but more evidence is needed to draw conclusions
- **Meditation**: Mindfulness-Based Stress Reduction (MBSR) – variety of exercises including meditation/yoga etc – low risk, may reduce stress/anxiety and improve sleep but no evidence in reduction in VMS
- **Aromatherapy**: may be helpful when combined with massage (stress relief) but no evidence of benefit alone
### Natural Products

**Herbals, Vitamins, Dietary Supplements**

- **Black Cohosh** (*Cimicifuga racemosa*): Side effects may include gastrointestinal problems, rash, and acute hepatitis.
- **Wild Yam** (*Diascorea*).
- **Dong Quai** (*Angelica sinensis*): Safety concerns exist regarding *A. sinensis*, including interactions with other medications and herbs, photosensitization, anticoagulation, and possible carcinogenicity.
- **Maca** (*Lepidium meyenii*).
- **Pollen Extract**.
- **Evening Primrose Oil** (*Oenothera biennis*).
- **Phytoestrogens**.
- **Vitamin E**

Consensus: more studies needed to draw conclusions.

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### Whole System Approach

(Mind-Body Practices + Natural Products)

- **Traditional Chinese Medicine**
- **Reflexology**
- **Acupuncture**
- **Homeopathy**

Consensus: more studies needed to draw conclusions.
Back to Mary

- 60-year-old, Asian female
- Menopausal x 6 years
- On HRT – recently diagnosed with ER/PR+ breast CA
- What do we expect? What can we offer?

Considerations:
- Age
- Treatment for Cancer?
- Race
- Other disease states (bones?)

Case Study – Beth (Libido)
Don’t they make Viagra for women?

- 50-year-old white female experiencing irregular menstrual cycles for past 7 months
  - Started noticing periodic hot flashes and night sweats but tolerable
  - More concerning is it’s become painful when she has intercourse and has had 3 UTIs in the past 6 months
  - Just doesn’t feel like having sex anymore – not interested
  - Happily married for 26 years and wants to get her “mojo” back!
GSM – Recap From Earlier

- Symptoms
  - Genital dryness, burning, and irritation
  - Sexual symptoms of diminished lubrication and pain
  - Urinary symptoms of urgency, dysuria, and recurrent urinary tract infections (UTIs)
- Consequence of postmenopausal estrogen deficiency
  - Changes to the labia, vagina, urethra, and bladder
  - Atrophic vulvovaginitis

What can we do to help??

Options for GSM Treatment

- Topical Estrogen – vaginal cream, tablet
- Ospemifene (Osphena) – oral tablet
- Prasterone (DHEA) (Intrarosa) – 6.5mg intravaginal insert QHS
- Hyaluronic Acid (Revarée) – vaginal insert 2-3 nights/week
- Over the counter lubricants
- Pelvic physical therapy
- Laser therapy
- Radiofrequency therapy
### Vaginal Estrogen Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Route</th>
<th>Effective dosage</th>
</tr>
</thead>
</table>
| **Vaginal Cream**  | Intravaginally with applicator frequency varies – often higher dose nightly initially then tapering down to lower dose 2-3 nights per week for maintenance | - 0.1mg/g (1-4 grams)  
  - 1.5mg/g (2-4 grams)  
  - 0.625mg/g (0.5-2 grams) |
| - Estradiol (Estrace) |                        |                                   |
| - Estropipate (Ogen)  |                        |                                   |
| - Conjugated estrogen (Premarin) |                  |                                   |
| **Vaginal Ring**   | Inserted Vagina – inserted 1 ring every 90 days | - 2mg/day  
  - 0.05mg/day or 0.1mg/day |
| - Estradiol (Estring) |                        |                                   |
| - Estradiol acetate (Femring) |                |                                   |
| **Vaginal Tablet** | Tablet inserted nightly for 2 weeks then decrease to maintenance dose of 2 nights/week | 10mcg/tablet |
| - Estradiol (Vagifem) |                        |                                   |

### Ospemifene 60mg Oral Tablet Daily

- An estrogen agonist/antagonist FDA approved in 2013 for:
  - The treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause
  - The treatment of moderate to severe vaginal dryness, a symptom of vulvar and vaginal atrophy, due to menopause

- **Adverse Reactions:** hot flush, vaginal discharge, muscle spasms, headache, hyperhidrosis, vaginal hemorrhage, night sweats

- **Drug-drug interaction**
  - Fluconazole (increase serum concentration of ospemifene)
  - Rifampin (decrease serum concentration of ospemifene)

- **Black box warning**
  - Endometrial cancer (increased risk)
  - Cardiovascular Disorder (CVA/DVT increased risk)

Osphena prescribing information: [https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/203505s015lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/203505s015lbl.pdf)
**Prasterone 6.5mg (DHEA)**

- A steroid indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause
- FDA approved 2019
- Intravaginal insert – dosed nightly at bedtime
- Contraindicated in undiagnosed vaginal bleeding
- Caution in patients with history of breast cancer (DHEA converted to estrogen in the body)
- Side effect – vaginal discharge

Intrarosa prescribing information: [https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208470s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208470s000lbl.pdf)

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**Hyaluronic Acid Sodium Salt 0.25%**

- Through the creation of new blood vessels, hyaluronic acid can improve the vaginal epithelium’s ability to repair itself and reverse vaginal atrophy without exhibiting any hormonal effects
- In a randomized, controlled, 30-day head-to-head clinical trial of 144 women: Hyaluronic acid demonstrated comparable efficacy to topical estrogen in relieving vaginal atrophy
  - At 9 days and at 30 days hyaluronic acid significantly improved multiple symptoms of vaginal atrophy (P<0.05)
  - No significant difference versus estrogen cream (P>0.05)
- Vaginal Suppository – inserted at bedtime 2-3 nights per week

Procedural Options – “Vaginal Rejuvenation”

- Uses energy to heat the vaginal tissue
  - Stimulates collagen formation
  - Improve circulation through stimulation of new blood vessel formation
  - Improve tightness
  - Improve lubrication
- Not typically covered by insurance – treatments can be expensive
  - In Orange County, CA ranges from $1800-$2500 for series of 3 treatments
- CO₂ laser treatment: heats up the superficial tissue resulting in collagen production in deeper layers
  - MonaLisa Touch®, FemTouch™ and FemiLift
- Radiofrequency (RF): Electromagnetic waves are used in RF devices
  - Geneveve by Viveve and ThermiVa

Libido – Physiological Component

- Physiologic
  - The female sexual response involves the production of Endothelial Nitric Oxide Synthase (eNOS)¹
  - eNOS converts arginine and citrulline into nitric oxide (NO)
  - NO increases genital tissue circulation
  - eNOS decreases with age and hormonal changes²,³
  - Rose hips extract, a potent antioxidant, has been shown to significantly reduce free radicals and improve oxidative stress after 8 weeks, supporting overall sexual function.¹,⁴
  - Replacing estrogen seems to have little effect on sexual function in menopausal women (small improvement with transdermal formulation)⁵

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Ristela

- In three randomized controlled trials across a total of 236 women: Ristela showed statistical improvement of patients’ overall Female Sexual Function Index scores at 4 weeks and 8 weeks (P<0.05)\(^1,2,3\)
- Ristella contains: Pycnogenol (pine bark extract) shown to increase eNOS; L-Arginine, L-Citrulline, and Rose Hips extract
- Dosing: 2 tablets once daily
- Effective pre, peri, and postmenopausally\(^1,2,3\)
- In postmenopausal women: 59% Improvement over one month  
  61% Improvement over two months\(^3\)


Back to Beth

- 50 years old
- Perimenopausal
- Vasomotor symptoms tolerable
- Biggest concerns:
  - Dyspareunia
  - UTIs
  - No Libido

Suggestions??
Summary of Case Studies

- Janet
  - Good candidate for low dose, short term use of approved HRT for her primary complaint of vasomotor symptoms

- Mary
  - Pursue non hormonal options for appropriate conditions
    - Bones
    - Mood/sleep

- Beth
  - Address both physiologic and psychologic aspects of “libido” in the postmenopausal woman

Summary

- Menopause occurs when the ovaries cease to produce estrogen and progesterone
- Impacts multiple biological, physiological, psychological functions
- Can significantly impact a woman’s quality of life
- Hormone therapy is approved by FDA for four indications:
  1. Symptomatic vasomotor symptoms
  2. Prevention of bone loss
  3. Hypoestrogenism (such as premature ovarian failure, surgical menopause)
  4. Genitourinary symptoms
Summary cont.

- Recommendation – lowest therapeutic dose to effectively treat the indicated condition for the shortest period of time
- Benefits may outweigh risks when initiated in recently menopausal patients <60 years old
- There are effective non-hormonal treatment options for those women who are unable to choose not to take hormones
- Therapy should be individualized based on symptoms, risks, desire to treat