MENOPAUSE

Overview
Menopause: 12 consecutive months of amenorrhea with no other obvious pathological or physiological cause. Average age in Canada is 51 years old. Factors that play a role in age of onset include genetics, smoking, pelvic radiation, and chemotherapy.

Perimenopause: Includes the period prior to menopause when clinical features present as well as the first year after the last menses.

Premature Menopause: Menopause <40yo. Occurs in 1% of women. Can be idiopathic or due to toxic exposure, autoimmune disease, chromosomal abnormality etc.

Diagnostic Considerations
- Clinical features: irregular/anovulatory bleeding in perimenopause period, amenorrhea in menopause, vasomotor symptoms (i.e. hot flashes), urogenital changes, sleep disturbances, depression, etc.
- Usually retrospective diagnosis. No role for routine estradiol or FSH levels in women >45yo.

Vasomotor Symptoms
- Most frequent reason women seek medical treatment for menopausal Sx. Effects 60-80% of menopausal women.
- Natural History: Sx last <7 years, but 15% remain symptomatic for >15 years.
- Clinical Features: manifest as sweating, palpitations, apprehension, and anxiety. It can be a significant contributor to sleep disturbances.
- Treatment:
  - Mild symptoms: reducing core body temperature (e.g. layering, use of a fan, drinking cold beverages), regular exercise, weight management, smoking cessation, controlled breathing and avoidance of known triggers.
  - Moderate-Severe symptoms: Hormone Replacement Therapy is first line. Use alternatives if patient does not want HRT (see below).
  - No evidence for herbal remedies.
- Black cohosh 40–80mg OD and evening primrose oil 2–8g OD are most commonly used. Both have low risk for SE (GI upset/abdominal pain most common).

Alternatives to HRT

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Dosing</th>
<th>SE/Contraindications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNRI</td>
<td>Venlafaxine 37.5-75mg XR OD</td>
<td>SE: mouth dryness, anorexia, constipation</td>
<td>Good evidence, well tolerated</td>
</tr>
<tr>
<td>SSRI</td>
<td>Fluoxetine 20mg OD Escitalopram 10-20mg OD</td>
<td>May affect Tamoxifen metabolism</td>
<td>Less symptom relief compared to SNRI</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>titrate up to 300mg TID 300mg qhs for relief of night symptoms alone</td>
<td>SE: somnolence, dizziness</td>
<td>Similar efficacy to SNRI but may be less well tolerated</td>
</tr>
<tr>
<td>Progestin</td>
<td>Depot MPA (Depo-Provera) single dose 400mg</td>
<td>Well tolerated</td>
<td>Initial studies shows greater efficacy than SNRI</td>
</tr>
<tr>
<td>Progestin</td>
<td>Megestrol acetate 20-80mg OD</td>
<td>Transient increase in symptoms, weight gain</td>
<td>Adrenal insufficiency can occur after stopping</td>
</tr>
</tbody>
</table>

Vaginal Atrophy
- Urogenital tissue atrophy due to estrogen deprivation.
- Clinical Features: vaginal dryness, dyspareunia, pruritus, frequent UTIs, prolapse, post coital bleeding.
- Physicians should ask about Sx in all postmenopausal women as many will not volunteer.
- On Exam: vulvovaginal epithelium is pale, thin, and friable.
- Treatment:
  - Vaginal Lubricants: decrease immediate irritation during sexual activity.
  - Vaginal Moisturizer (e.g. Polycarbophil gel): equivalent symptomatic relief to local estrogen.
  - Local Estrogen therapy:
    - Estrogen cream (e.g. Premarin 0.5-2.0g daily for 2 weeks then twice weekly) - requires Progestin for 10 days each month due to systemic absorption.
    - Estradiol-containing vaginal ring (Estring 2 mg: replaced every 90 days) – no Progestin co-treatment.
    - Estradiol vaginal tablets (Vagifem 10 OD then twice weekly) – no Progestin co-treatment.
- Women may also experience urinary incontinence due to urogenital changes.
  - Treat stress incontinence with weight loss, pelvic floor exercises, pessaries.
  - Treat urge incontinence with lifestyle changes, bladder retraining, antimuscarinic agents.

Bone Health
- Screening: bone mineral density scan indicated for
  - All women age >65yo.
  - Post-menopausal women with a risk factor for fracture (previous fragility fracture, steroid use, parental hip fracture, vertebral fracture, high alcohol intake, current smoker, RA, low body weight, high risk medications).
- Osteoporosis prevention: for all postmenopausal women
  - Vitamin D supplementation: 400-1000IU OD for low risk, 800-1000IU OD for moderate risk.
  - Calcium intake: ensure 1200 mg of elemental calcium daily from all food/supplement sources.
  - Lifestyle: regular active weight bearing aerobic exercises, balance exercises (e.g. Tai Chi) smoking cessation, decrease coffee/alcohol intake.

Please see Osteoporosis for details on treatment.
Management
Hormone Replacement Therapy (HRT)\textsuperscript{2,7}

- Use the lowest effective dose of estrogen consistent with treatment goals
- Systemic progestogen is required for endometrial protection from unopposed estrogen therapy (ET). Transdermal progesterone is not recommended as part of estrogen-progestogen therapy (EPT)
- Indications:
  - Best treatment for vasomotor symptoms
  - Not recommended for treatment of hyperlipidemia, cardiovascular disease, or osteoporosis alone
- Contraindications: history of breast cancer, liver disease, DVT, abnormal vaginal bleeding
- Adverse effects:\textsuperscript{[8]}
  1. Cardiovascular risk (including coronary heart disease, stroke, and VTE)
     - Decreased risk of CHD with HRT use within 10yrs of menopause, increased risk when started >10yrs after onset. Increased risk of VTE with oral HRT. Risk highest in first 2 years of starting HRT, then excess risk decreases over time.
  2. Endometrial Cancer
     - Unopposed ET for >3yrs associated with 5x risk of endometrial CA (up to 10x risk with >10yrs use). This is mitigated by concomitant progesterone use.
  3. Breast Cancer
     - Diagnosis of breast cancer increases with EPT use greater than 3 -5yrs. In the WHI, this increased risk was 8 per 10,000 when using EPT for >5yrs.
     - Data indicates that ET use in breast cancer survivors has not been proven to be safe and may be associated with an increased risk of recurrence
  4. Ovarian Cancer
     - Meta-analysis shows increase in annual ovarian cancer risk of 1.11-fold for EPT use and 1.28-fold for ET.

Sample HRT Regimes\textsuperscript{2,7}

<table>
<thead>
<tr>
<th>HRT Regime</th>
<th>Estrogen Dose</th>
<th>Progestin Dose</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Unopposed Estrogen</td>
<td>CEE 0.3mg - 0.625mg PO OD</td>
<td>None</td>
<td>If no uterus</td>
</tr>
<tr>
<td>Continuous</td>
<td>Estrace 0.5 – 1mg PO OD</td>
<td>MPA 2.5mg PO OD</td>
<td>Some breakthrough bleeding. Early observational data with micronized progesterone shows no increased risk of breast cancer but need to be reviewed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prometrium 100mg OD</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Norethindrone 0.1mg PO OD</td>
<td></td>
</tr>
<tr>
<td>Cyclic</td>
<td></td>
<td>MPA 5-10mg PO OD</td>
<td>Monthly bleeding, Can cause PMS symptoms. No need for estrogen free period</td>
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<tr>
<td></td>
<td></td>
<td>Prometrium 200mg (for days 1-14)</td>
<td></td>
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<tr>
<td>Transdermal</td>
<td>Patch (0.025-0.1mg twice weekly</td>
<td>MPA 2.5mg PO OD</td>
<td>Less incidence of VTE than oral. No increase in TG or BP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prometrium 100mg OD</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norethindrone 0.1mg PO OD</td>
<td></td>
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<tr>
<td>Combined (Angeliq)</td>
<td>1 tab OD (1 mg EE+ 1mg drospirenone)</td>
<td></td>
<td>Newly approved</td>
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References can be found online at \url{http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project References.htm}