MENOPAUSE

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Overview[1,2]

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[1]

- 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.[1]
- Natural History: Sx last <7 years , but 15% remain symptomatic for >15years
- Clinical Features: manifest as sweating, palpitations, apprehension, and anxiety. It can be a significant contributor to sleep disturbances.
- Treatment:[1]
  - 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)[3,4]

Alternatives to HRT[5]

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

Vaginal Atrophy[1,2]

- 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[6]

- 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

Dr. Michael Evans developed the One-Pager concept to provide clinicians with useful clinical information on primary care topics

Management

Hormone Replacement Therapy (HRT)[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:[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[2,7]

HRT Regime	Estrogen Dose	Progestin Dose	Comments
Unopposed Estrogen	CEE 0.3mg - 0.625mg PO OD Estrace 0.5 – 1mg PO OD	None	If no uterus
Continuous		MPA 2.5mg PO OD Prometrium 100mg OD Norethindrone 0.1mg PO OD	Some breakthrough bleeding Early observational data with micronized progesterone shows no increased risk of breast cancer but need to be reviewed
Cyclic		MPA 5-10mg PO OD Prometrium 200mg (for days 1-14)	Monthly bleeding. Can cause PMS symptoms. No need for estrogen free period
Transdermal (Estraderm)	Patch (0.025-0.1mg twice weekly	MPA 2.5mg PO OD Prometrium 100mg OD Norethindrone 0.1mg PO OD	Less incidence of VTE than oral No increase in TG or BP
Combined (Angeliq)	1 tab OD (1 mg EE+ 1mg drospirenone)		Newly approved

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm