437 Team: Obstetrics and Gynecology

Menopause

Objectives:

- Define menopause and describe changes in the hypothalamic-pituitary-ovarian axis associated with perimenopause/menopause.
- Describe symptoms and physical exam findings related to perimenopause/menopause.
- Discuss management options for patients with perimenopause/menopausal symptoms.
- Counsel patients regarding the menopausal transition.
- Discuss long-term changes associated with menopause.

References:

- Kaplan USMLE step 2 CK - Obstetrics and Gynecology
- Online Meded videos
- Team 435

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Color index: Important | Notes | Meded | Video-Case

Editing file link

What is the menopause?

- Menopause is a retrospective diagnosis and is defined as 12 months of amenorrhea. associated with elevation of (FSH, LH)
- The mean age is **51 years** is genetically determined and unaffected by pregnancies or use of steroid contraception.
- Menopause occurs due to the programmed loss of ovarian follicles .
- Women are born with between 1.5 and 2 million oocytes (primary ovarian follicles) and reach menarche (first menstruation) with about 400,000 potentially responsive eggs.
- The perimenopause refers to the (several years of more gradually decreasing ovarian function that may be associated with the symptoms of reduced estrogen levels).
- The signs and symptoms of the perimenopause and menopause are related to progressively decreasing secretion of estrogen from the ovarian follicle .
- Smokers experience menopause up to two years earlier.

Premature menopause: :

Occurs at 30-40 and is mostly idiopathic, but can also occur after radiation therapy or surgical oophorectomy.

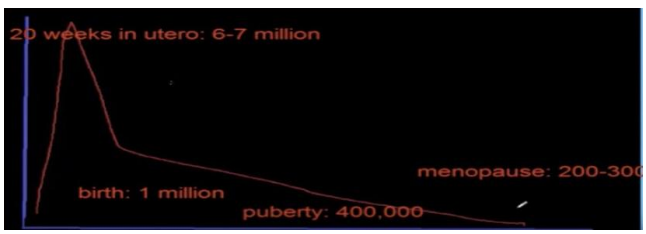
Premature ovarian failure :

Occurs at < 30 and may be associated with autoimmune disease or Y chromosome mosaicism.

Pathophysiology :

The hypothalamus produces GnRh which ⟶ stimulates the anterior pituitary to produce FSH and LH ⟶ this stimulates the ovary to produce estrogen .
With advancing age as the oocyte number decline ➜ estrogen levels decline . The remaining oocytes become increasingly resistant to FSH and FSH plasma concentrations increase.
Both FSH and LH are very high in menopause but FSH increase first and thus it is a better marker and we can detect it earlier (important)
At the time of menopause FSH concentrations > 30 mIU/m

Changes occur in the menstrual cycle (beginning at age 40) :
● Shortening or lengthening of menstrual cycle.
⟶ The luteal phase stays the same at 13-14 days.
⟶ Variation in cycle length is related to follicular phase.
⟶ women may notice that their cycle is now 21 days.



The number of the oocyte (germ cells)

Clinical Findings :

The majority of menopausal symptoms and signs are caused by a lack of estrogen.

Amenorrhea (most common symptom is secondary amenorrhea)	menses typically become anovulatory and decrease during a period of 3–5 years known as perimenopause.
Hot flashes (75% of menopausal women)	unpredictable profuse sweating and sensation of heat, probably mediated through the hypothalamic thermoregulatory center. Obese women are less likely to undergo hot flashes, owing to peripheral conversion of androgens to estrone in their peripheral adipose tissues. • Women describe the sudden sensation of extreme heat in the upper body particularly the face, neck, and chest . • The episodes typically last for 1-5 minutes . • For many women the hot flushes are tolerable and do not require any medical treatment .However 33% of women experience > 10 hot flushes/ day. • the hot flushes can be associated with many significant adverse outcomes such as hampered job in productivity, and sleep deprivation.
Reproductive tract	Low estrogen leads to : • Decrease vaginal lubrication. • Increase vaginal pH. • Increase vaginal infections. 40% of women will experience one or more symptoms of vaginal atrophy . May present with (itching and burning , loss of vaginal rugae and elasticity can cause narrowing and shortening of the vagina). Vaginal atrophy and vaginal dryness can be symptomatic during intercourse and an cause significant dyspareunia. Vaginal lubrication and vaginal estrogens can provide symptom relief.
Urinary tract	Low estrogen leads to increased urgency, frequency, nocturia, and urge incontinence. Frequent UTIs
Psychic	Low estrogen leads to mood alteration, emotional lability, sleep disorders, and depression. Irritability and mood swings
Cardiovascular disease (most common cause of mortality (50%) in postmenopausal women) Screen by LDL, give statin if required	
Osteoporosis: high in lean pt and low in fat body mass Screen by dexa, give bisphosphonates if indicated.	a disorder of decreased bone density, leads to pathologic fractures when density falls below fracture threshold. Bone density decreases postmenopausally by 1-2% per year compared to 0.5% per year in peri-menopausal women. Lifestyle modifications (exercise) , Ca and vitd supplements are important at this point

Other Symptoms:

- **Mood disturbance:** Low estrogen leads to mood alteration, emotional lability, sleep disorders, and depression.
- **Sleep disturbances:** Decline in estrogen levels can induce a change in women's sleep cycles independent of hot flushes. Sleep disturbances are one of the most common and disabling effects of menopause.
- **Pelvic organ prolapse and atrophic urethritis:** Occurs when the paravaginal tissue that supports the bladder and rectum becomes atrophic .

Diagnosis :

- Mostly a clinical diagnosis, especially if at the common age
- The laboratory diagnosis of menopause is made through serial identification of elevated gonadotropin (FSH and LH) and low estrogen. Ultrasound will show no follicles, but not done routinely, unless premature menopause.

Management :

There are both benefits and risks associated with menopausal replacement therapy.

Benefits	Risks
Both hormonal therapy (estrogen and progestin) and estrogen therapy only have decreased osteoporotic fractures and lower rates of colorectal cancer.	• Both HT and ET groups in WHI were found to have small increases in deep vein thrombosis (DVT). • The HT group also had increased heart attacks and breast cancer, but these were not increased in the ET group.

Indications For Use MHT:

- **Vasomotor symptoms** : most effective treatment for vasomotor symptoms associated with menopause at any age, but benefits are more likely to outweigh risks for symptomatic women age <60 or within 10 years after menopause.
- **Vaginal dryness** : Local low-dose estrogen therapy is preferred for women whose symptoms are limited to vaginal dryness or associated discomfort with intercourse.
- **Premature menopause** : In women with premature ovarian insufficiency, systemic MHT is recommended at least until the average age of the natural menopause.

Benefits of MHT but Not Indications For Use.

- **Osteoporosis** : effective and appropriate for the prevention of osteoporosis related fractures in at-risk women age <60 or within 10 years after menopause.
- **Coronary heart disease** : Findings depend on the kind of MHT used :
  - ❏ Estrogen-alone (ET) may decrease coronary heart disease and all-cause mortality in women age <60 and within 10 years of menopause.
  - ❏ Estrogen plus progestin (HT) in this age group shows a similar trend for decreased mortality but no significant increase or decrease in coronary heart disease has been found

Risks of MHT

The risk of **venous thromboembolism (VTE)** and **ischemic stroke** increases with oral MHT but the absolute risk is rare age <60.
The risk of **breast cancer in women age >50** -> associated with the addition of a progestin to estrogen therapy (HT) and related to the duration of use.
The women's health initiative was a large randomized placebo, control trail.
• Estrogen + Progesterone **increases** ⬆️ risk of (coronary heart disease, breast cancer, stroke and Venous thromboembolic events).
• Estrogen + Progesterone **decreases** ⬇️ risk of (colon cancer, fractures).
• Estrogen only **increase** ⬆️ risk of (stroke and Venous thromboembolic events)

Contraindications for MHT

- include personal history of an estrogen-sensitive cancer (breast or endometrium), active liver disease, active thrombosis, or unexplained vaginal bleeding.

Administration of Menopausal Hormone Therapy (MHT).

- Estrogen can be administered by oral, transdermal, vaginal cream (especially for vaginal atrophy) , or parenteral routes.
- The most common current regimen is oral estrogen and progestin given continuously.

Uterus present or absent

Estrogen as a single systemic agent (ET) is appropriate in women after hysterectomy, but additional progestogen (HT) is required in the presence of a uterus to protect her from endometrial cancer.

Individualized management

The option of MHT is an individual decision in terms of quality of life and health priorities, as well as personal risk factors such as age, time since menopause, and risk of venous thromboembolism, stroke, ischemic heart disease, and breast cancer.

Dose and duration

Dose and duration of MHT should be consistent with treatment goals and safety issues, and thus should be individualized.

Other treatment options

- Bioidentical hormones: Limited evidence on their safety, potency and efficacy ,not preferred over traditional hormone therapy.
- SSRI/SNRI's: Reduce hot flushes by 50-62% .
- Herbal therapy: Have not been shown to be superior to placebo.

Estrogen alternatives :

- In patients with contraindications to estrogen-replacement therapy, SERMs can be used.
- These are medications with estrogen agonist effects in some tissues and estrogen antagonist effects on others.
- Although protective against the heart as well as bone, these medications do not have much effect on hot flashes and sweats.

❖ Tamoxifen is a SERM with endometrial and bone agonist effects, but breast antagonist effects.
❖ Raloxifene has bone agonist effects, but endometrial antagonist effects.

Choosing the medication is dependent on:

- Her age
- Symptoms (affecting her life or not)
- Risk factors
- Duration of menopause (for how long has she been in menopause.

Teaching case (video case)

A 53-year-old, G3P3 woman, whose last menstrual period was 4 months ago presents to the office with hot flushes, emotional lability, and insomnia. She experiences hot flushes 2-3 times per day and occasionally at night. She has been having trouble sleeping and is extremely fatigued. Since age 14, her periods have been regular until 2 years ago, when they began to space out to every 2-3 months. She is sexually active and recently has noted some dyspareunia. The patient rarely exercises. She smokes 2 packs of cigarettes a day and drinks alcohol socially. She recently started taking a soy supplement. She does not have any pertinent gynecological, medical or surgical history. Her family history is significant for her mother sustaining a hip fracture at age 60 and a sister with breast cancer and high cholesterol. On examination, she has normal vital signs. She is 5'4" tall and weighs 123 lbs. On pelvic examination, she has decreased vaginal rugae and a pale, small cervix. No masses or tenderness are palpated on bimanual exam.

Questions

1. What are the symptoms of perimenopause and menopause?

• Hypoestrogenism is the basis for the common changes of menopause.

• The common signs and symptoms of menopause include amenorrhea (of 12 months duration), hot flashes, memory changes, sleep difficulty, decreased libido, dyspareunia, urinary symptoms, breast changes. Symptoms start 3-5 years before amenorrhea but it varies some women will get it after.

Variation in: (These variation are due to variation in the remaining estradiol level in different women).

- onset (perimenopausal, menopausal)
- Age of onset (average is 51y)
- Duration of symptoms
- Length
- severity of symptoms

There is overlapping of symptoms.

2. How do you make the diagnosis of menopause?

• Menopause is the permanent cessation of menses and usually occurs between the ages of 50 and 55, with an **average of 50-52 years**.

• The definition of menopause is the absence of menses for 12 consecutive months. It is, therefore, a retrospective diagnosis.

• Perimenopausal symptoms usually begin **3 to 5 years before amenorrhea** or postmenopausal levels of hormones. To diagnose someone with menopausal symptoms complaint you need amenorrhea for 12 months consecutively.

3. What are the patient's risk factors for osteoporosis?

• This patient's risk factors include menopause, family history of osteoporosis, cigarette smoking, and sedentary lifestyle. Family Hx is a very imp. risk factor and previous personal Hx of fracture.

• Additional risk factors for discussion include age at menopause or oophorectomy, white or Asian origin, small body frame or low BMI, high risk for osteoporosis related fracture per FRAX tool, vitamin D3 deficiency, poor calcium intake, alcohol and caffeine intake, and corticosteroid use.

4. How do you diagnose and treat atrophic vaginitis?

• Patients commonly have vaginal dryness, vulvar irritation, pruritus, and dyspareunia.
• Associated urinary symptoms may be present.
• Examination shows vulvar erythema.
• Excoriation may be present. Loss of vaginal rugae, a pale vaginal mucosa, with patches of erythema and even superficial blood vessels are consistent with atrophy.
• The pale or yellow discharge has a pH of 5.5 or higher.
• Basal cells replace superficial vaginal epithelial cells and can be seen on a saline wet prep or Pap test.
• Treatment is topical estrogen (allow 4 to 6 weeks for symptomatic relief).

5.How do you counsel a patient regarding estrogen and alternative therapies?

• Risks and benefits of therapy should be reviewed (WHI and other studies).
• Contraindications should be discussed.
• Treatment options for menopausal symptoms and osteoporosis should be outlined.
• Bio-identical (compounded) hormones do not have an inherent advantage over standard therapies and may vary in their potencies.
• Micronized progesterone and estradiol are bio-identical by definition.
• Any patient on systemic HT with an intact uterus needs a progestogen.
• Transdermal estrogen administration is preferable due to a beneficial effect on lipid balance and thromboembolism risk.
• Lifestyle modifications including smoking cessation should be stressed.
• The importance of evaluating any postmenopausal bleeding should be discussed.
• Acknowledge frequent use of complementary and alternative treatments.
• SSRI antidepressants can be used as an alternative in women who are not candidates for HT
•Herbal use counseling. (the doctor didn't say if it's okay or not, but in the video case they said "Have not been shown to be superior to placebo".

6. What laboratory and diagnostic tests would you order for this patient?

Laboratory and diagnostic tests should focus on the patient's history and symptoms, as well as preventive screening. For example, a TSH and lipid panel is appropriate given her fatigue and family history. General health maintenance/screening test guidelines (i.e. colonoscopy at age 50, bone density at age 65,etc.) should be discussed. Tests include a mammogram, bone density (given patient's smoking and family history of fracture), colonoscopy. Discuss new cervical cytology screening recommendations.

When do you start screening for colon ca? 50y
Bone density? 65y unless she has risk factor then you should do it before 65y.
How frequent Pap smear screening? Every 5y if the last one was -ve, but if it was the first you should do it after 3y then if it was -ve it would be every 5y.