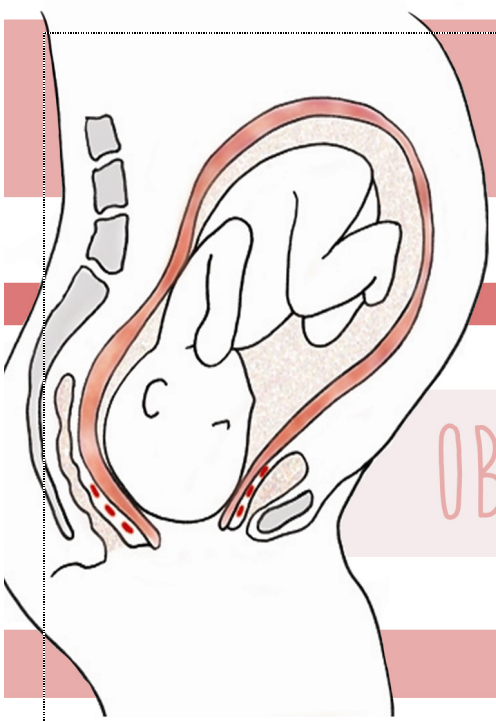

OBSTETRICS AND GYNECOLOGY

29- Menopause and Post-menopausal bleeding

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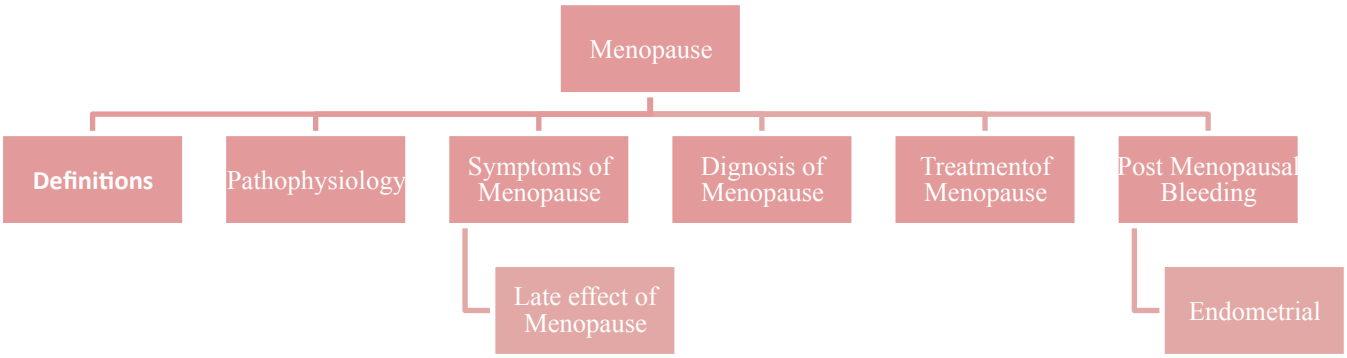
Doctor's note Team's note Not important Important 431 teamwork

Objectives:

Not given



Introduction

- The term menopause is derived from Greek Meno (months) and pause (cessation). The word means cessation of menstruation.

- Cliamacteric which is by dictionary definition is period of life when fertility and sexual activity decline. Transition from the productive to non-productive stage .It is a wide term leading to:

*Pre Menopause
*Peri Menopause
*Post Menopause

Definitions:

*** Perimenopause:**
- It is 3-5 years period before menopause with increase frequent irregular anovulatory bleeding followed by episodes of amenorrhea and intermittent menopausal symptoms.(like hot flush).

* **Menopause:**
- The point in time at which menstrual cycles permanently cease. It is a retrospective diagnosis after 12 months of ammenorrhea women classified as being menopause.
- Mean age – 51 years. (Mainly menopause starts at age of 40, if it's before that think about premature ovarian failure or induced menopause by chemotherapy, radiotherapy or surgeries).

Pathophysiology

- The number of primordial follicle decline even before birth but dramatic just before menopause.
- Increase FSH, LH from about 10 years before menopause.
- Close to menopause: There will be:
- Anovulation → inadequate Leuteal phase → decrease progesterone but not estrogen level → lead to DUB (dysfunctional uterine bleeding) and endometrial Hyperplasia. (Estrogen here is still produced which means, high estrogen without progesterone to stabilize the menstruation resulting in **irregular period**)

- At menopause:

- Dramatic decrease of estrogen →menstruation ceases and symptoms of menopause started.
- But still ovarian stroma produce →small androstenedione and testosterone but, main postmenopausal estrogen is **estrone** produced by Peripheral fat from adrenal androgen.

Symptoms:

1. Hot flushes "cutaneous vasodilation" due to alteration in hormones level which will affect the thermoregulation of the hypothalamus.

- Occurs only 1-5 minutes.
- occurs in 75% of women.
- More severe after surgical menopause.
- continue for 1 year.
- 25% continue more than 5 years.

2. Urinary Symptoms

- Urgency.
- Frequency.
- Nocturia.

3. Psychological changes "decreased level of central neurotransmitters"

- Depression
- Irritability
- Anxiety
- Insomnia
- Loss of concentration

So if patient after 40 and has psych symptoms, suspect menopause and investigate it before referring her to psychiatry.

4. Atrophic Changes

- Vagina

* vaginitis due to thinning of epithelium, ↓ PH and lubrication.
* dysparnue → due to decrease vascularity and dryness

-Decrease estrogen level lead to:

* Decrease size of cervix and mucus with retract of segumocolumnar (SC) junction into the endocervical canal.

* Decrease size of the uterus, shrinking of myoma & adenomyosis. (So if she has polyps, it will shrink with menopause, so don't treat if it is not causing problems like anemia)

* Decrease size of ovaries, become non palpable.
* Pelvic floor - relaxation →prolapse.
* Urinary tract → atrophy → lose of urethral tone →caruncle
* Hypertonic Bladder - detrusor instability
* Decrease size of breast and benign cysts (Like Fibroadenoma)

5- Skin Collagen
– ↓ collagen & thickness → ↓ elasticity of the skin.

6- Reversal of premenstrual syndrome.

Late effect of Menopause

A. Osteoporosis:

- Bone mass reach peak at the end of their 3rd decade of life.
- After 40 years bone resorption exceeds bone formation by 0.5% per year.
- This negative balance increase after menopause to a lose of 5% of bone per year.
- predisposes to fractures by slight causes, eg: pelvic fracture ➔ 50% may die.
- considered a cause of death in old ladies.

1- Risk factors:

- Gender: more in women (male to female ratio is 1:3)
- Race
  *high in white women
  *moderate in Asian women
  *lowest in Black women
- Family History +ve
- BMI, Life style, smoking, caffeine intake, alcohol, increase in protein diet, decrease in Calcium and Vit D intake.
- Steroid Medication
- Exogenous medication
- Cushing Syndrome

2- Diagnosis:

- (DEXA-Dual Energy X-ray Absorptiometry)
-for Assessment of bone densmetry to demonstrate if bone density above or below fracture threshold.

3- Prevention:

– improve lifestyle, regular exercise, eliminate smoking & alcohol. If the patient has low vit-D or calcium level → ask the patient to take enough Calcium and Vit-D supplements and expose to the sun twice a week at least for 10-20 mins

4- Medication:

a. ERT (Estrogen Replacement Therapy) (To treat vasomotor symptoms (severe hot flushes) only not for osteoporosis because it has very bad side effects like: thrombosis, breast cancer, etc …)
b. Biphosphonate (Fosamax) that inhibit osteoclastic activity & minimal S/E (give it for any women at the age of 45 complaining of irregular period and menopause symptoms. tell the lady to take it on an empty stomach(food and milk can interfere with its absorption)and don't lie down (it may cause heartburn and esophagitis). It has no contraindication)
c. Raloxifene (Evista) is selective estrogen receptors moderator [SERMs] that bind with a high affinity to estrogen receptors. It has some estrogen like effect **e.g. ↑ bone density, ↓LDL Cholesterol [cardioprotective]** but act as estrogen antagonist on endometrium and breast. (Good for patients with +ve family history of breast cancer, but has no effect on the vasomotor symptoms)
d. Calcitonin inhibit osteoclastic activity + analgesic effect of
e. Calcium Supplement & Vit D.

B. Cardiovascular Disease:

CVD is now the leading cause of death among post menopausal women
-before menopause, risk of heart attack is 1/3 of man
-after menopause increase in women become the same of man at an age of 70years.

Because of effect of oestrogen:

*Before menopause:

- increase HDL & decrease LDL.
- decrease Atherogenic plague formation by direct action on vascular endonelium.

*After menopause:

-HDL : LDL ratio become closer to male ratio.

-Observational Studies:
*HRT decrease mortality by 30%. But recent epidemiological studies do not show a beneficial effect of HRT on CHD but there is increase number of Breast Cancer when compared with non users HRT.

C. Urogenital System:

- Embryologically female genital tract & lower urinary system develop in close proximity from primitive urogenital sinus.

- The Urethra and vagina have a high concentration of estrogen receptors and there is significant evidence to support one use of estrogen in treatment of urogenital symptoms like: frequency and urgency in a 45 year-old lady with a negative urine culture we give estrogen here to relieve the symptoms (recurrent UTI, vaginitis and dyspareunia 'painful intercourse').

D. AL Zheimer's Disease:

-prevalence of Dementia as high 50% by age 85 years.
-Alzheimer's disease account for 60-65% of cases.
-Observation studies –decrease risk of Al Zheimer's by 1/3 among women taking HRT.
-it has beneficial effect on brain function but no randomized studies to confirm observational data.

Diagnosis of Menopause

- The Triad of:
-Hot flushes
-Amenorrhea for 12 months
-increase FSH > 15 i.u./L

- Before starting treatment: You should perform:

-breast self examination

-mammogram

-pelvic exam (Pap smear) (to check for any cancers, because HRT will promote their growth).

-weight, Blood pressure

- No indication to perform

-bone density (but if she has multiple fractures or a family history of osteoporosis, you should do it)

-Endometrial Biopsy

But any bleeding should be investigated before starting any treatment.

Treatment of Menopause

- Estrogen – a minimum of 2mg of oestradiol is needed to maintain bone mass and **relief symptoms of menopause** (hot flushes).
- Women with uterus – add progestin at last 10 days to **prevent endometrial Hyperplastic.**
- **Sequential Regimens** used in patient **close to menopause**.

Oestrogen – in the first ½ of 28 day per pack

& Oestrogen & Progetin in 2nd 1/12 of 28 day pack.

(Patient will have monthly bleeding, given if patient desires it so she can feel she's still young).

- Combined continuous therapy **who has Progesterone everyday** is useful for women who are few years past the menopause and who do not to have vaginal bleeding.

- There is evidence that **increase risk of endometrial cancer** with sequential regimens for > 5 years while on combined continuous regimens **decrease risk of Cancer**.

1- Benefits of HRT:

*Vagina-↑ vaginal thickness of epithelium →↓ dyspareunia & vaginitis.

*Urinary tract – enhancing normal bladder function.

*Osteoporosis – decrease fractures by more than 50%

*CVS – decrease by 30% by observation studies but recent studies shows no benefits.
*Colon Cancer decrease up to 50% (due to estrogen effect).

2-Confirmed Risk:

* Endometrial CA eliminated by

1. Add Progesterone
2. Using selective estrogen receptors modulators (SERMS), because it works as an estrogen antagonist on the breast and uterus.

* Gall Bladder Disease

ERT:
*↑ triglyceride
*↑ total cholesterol
* increase risk of Gall stone

* Breast Cancer risk with long term HRT adds

-2/1000 after 5 years – 6/1000 – 10years
-12/1000 after 15 years – background risk 45/1000 between the age of 50 and 70 not taken HRT

3- Contraindication to HRT: (same as OCP)

* Undiagnosed vaginal bleeding
* Acute liver disease.
-chronic impaired liver functions
* Acute vascular thrombosis
* Breast Cancer

Post Menopausal Bleeding:

Vaginal bleeding occurs after 12 months of Amenorrhea in middle age women who are not receiving replacement therapy. It can never be dysfunctional or anovulatory in nature (with lose of functional ovarian follicle bleeding from normal ovulatory cycle is impossible).

*** Post-menopausal bleeding? R/O endometrial cancer unless she's taking HRT or Heparin.**

*** Bleeding in young age? Think about ectopic pregnancy**.

Causes:

- **Upper Reproductive Tract Causes:**

- Atrophic Endometritis
- Endometrial Polyp (degenerated submucous fibroid)
- Endometrial Hyperplasia (specially obese and PCO patients)
- Endometrial Ca
- Ovarian (granulosa cell tumor) or tubal Ca (bleeding with watery discharge)

- **Lower reproductive tract:**

- vaginitis vaginal or vulvar tumors, varicose veins, cervical polyp or tumors

- **GIT causes**:

- hemorrhoids, anal fissures or colorectal CA

Endometrial Ca as cause of post Menopausal Bleeding:

-The most common Gynecological malignancy.
-Endometrial neoplasia can progress from simple hyperplasia to invasive Ca caused by unopposed estrogen.
-The mechanism of many End. Ca. is prolonged estrogen stimulation of the endometrium unopposed by progesterone.

The source may be:
a. Exogenous Estrogen (E2) (ERT)
b. Peripheral Aromatization of Androstendione to estrone – obesity or PCO
c. Estrogen (E2) producing tumor (like granuloza cell ovarian tumor)
d. Tamoxifen (use in some cases of breast cancer, which are sensitive to estrogen) causes **Stimulation of Endometrium** (so you should follow up the patient by ultrasound)

1-Risk Factors of endometrial Ca:

- No pregnancy
-Prolonged Reproductive Life – late menopause
-Unopposed estrogen
-Triad of diabetes, hypertension & obesity
-Tamoxifen

2- Diagnosis:

***GIT Aitology:**

-rectal exam
-stool for occult blood
-Proctosigmoidoscopy

***Lower Reproductive Tract Causes – can be identified by:**

-Pelvic Exam
-Pap Smear & appropriate Biopsy
-Colposcopy and cervical biopsy

***Upper Reproductive Tract Causes Can be Identified only by:**
Tissue Diagnosis Obtained by Endometrial Evaluation

- First US:
  * If endometrial thickness <5mm no more investigation if bleeding stop.
  * If it's > 5mm do more investigation.

1. **Endometrial Biopsy**

- Inaccurate for diagnosis of Polyp & miss a sufficient number of hyperplasia.

2- Hysterosonography

- **-** is performed by **infusion saline** in the uterine cavity to identify endometrial polyps.
- Endometrial thickness <10mm indicate risk of hyperplasia→tissue should be obtained for histological studies.

3. Pipelle sampling for endometrial biopsy

- If +ve → refer to oncology(and perform hysterectomy).
- If –ve → continue investigation (hysteroscopy) because it's a blind procedure.

4. Fractional dilation and curettage (D&C)

-is the good standard for evaluating post menopausal bleeding. It is performed in 2 stages:
a. Initially **endocervical canal** is curretted obtaining the first specimen to rule out invasion of Cervix by Ca.
b. Then **uterine cavity** is curreted obtaining second specimen to assess endometrial neoplasia or malignancy.
-Done if no hysteroscopy.
-If negative: still it's not diagnostic

5.Hysteroscopy[best facility, diagnostic]:

- Performed at the time of D&C for Polyp & operative resection.

6- Pap Smear

- have poor sensitivity for endometrial cancer. **Only 40% cases are identified. "MCQ"**

7. MRI

* Treatment:

1- Atrophic vaginitis, cervicitis, endometritis may need local estrogen preparations.
2- Malignant cervical, uterine or ovarian pathology will require specific treatment.

Summary

* **Menopause is** the point in time at which menstrual cycles permanently cease.

*** Symptoms of menopause** is hot flush, urinary, Psychological, Atrophic Changes, skin changes and Reversal of premenstrual syndrome

*** Diagnosis of menopause:** Hot flushes, Amenorrhea, increase FSH.

***Treatment of menopause**: HRT: Sequential or Combined.

MCQ's: pre-test

1) You see five postmenopausal patients in the clinic. Each patient has one of the conditions listed, and each patient wishes to begin hormone replacement therapy today. Which patient would you start on therapy at the time of this visit?

A. Mild essential hypertension

B. Liver disease with abnormal liver function tests

C. Malignant melanoma

D. Undiagnosed genital tract bleeding

E. Treated stage III endometrial cancer

2) Which of the following is a true statement regarding the psychological symptoms of the climacteric?

A. They are considerably less important than hormone levels

B. They commonly include insomnia, irritability, frustration, and malaise

C. They are related to a drop in gonadotropin levels

D. They are not affected by environmental factors

1. They are primarily a reaction to the cessation of menstrual flow

3) Osteoporosis is least likely in which of the following women?

A. Asian

B. White

C. Smokers

D. Sedentary

E. Obese

1) **The answer is a.** Absolute contraindications to postmenopausal hormone replacement therapy include the presence of estrogen-dependent tumors (breast or uterus), active thromboembolic disease, undiagnosed genital tract bleeding, active severe liver disease, or malignant melanoma. Past or current history of hypertension, diabetes, or biliary stones does not automatically disqualify a patient for hormone replacement therapy.

2) **The answer is b.** Psychological symptoms during the climacteric occur at a time when much is changing in a woman's life. Steroid hormone levels are dropping, and the menses is stop- ping. However, studies show these two factors to be unrelated to emotional symptoms in most women. Many factors, such as hormonal, environmental, and intrapsychic elements, combine to cause the symptoms of the climacteric such as insomnia; vasomotor instability (hot flushes, hot flashes); emotional lability; and genital tract atrophy with vulvar, vaginal, and urinary symptoms.

3) **The answer is e.** A major menopausal health issue is osteoporosis, which can result in fractures of the vertebral bodies, humerus, upper femur, forearm, or ribs. Patients with vertebral fractures experience back pain, gastrointestinal motility disorders, restrictive pulmonary symptoms, and loss of mobility. There may be a gradual decrease in height as well. Although all races experience osteoporosis, white and Asian women lose bone earlier and at a more rapid rate than black women. Thin women and those who smoke are at increased risk for developing osteoporosis. Physical activity increases the mineral content of bone in postmenopausal women.