

M U N I
M E D

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Menopause and HRT

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Obstetrics and Gynecology - lectures

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Key words

Perimenopause (climacteric)

Menopause

Premenopause

Postmenopause

Induced menopause

Senium

Hormonal replacement therapy

Definition

Perimenopause (Climacteric)

- the period of transition between the fertile age of a woman and the onset of senium
- physiologically between 45 and 60 years
- **Premature ovarian failure (insufficiency)** – before 40 years

Menopause

- last menstrual bleeding
- defined retrospectively 12 months after the last menstrual bleeding
- Typically occurs between 49 and 51 years of age

Definition

Premenopause

- period of time within 12 months before menopause
- menstrual cycle (MC) is still preserved
- ovarian function is progressively decreasing
- symptoms of menopausal syndrome are already appearing
- MC can be irregular, decreasing number of ovarian cycles
- Decrease in progesterone levels, relative predominance of estrogen

Definition

Postmenopause

- begins 12 months after the last menstrual bleeding
- minimal estrogen production – hypergonadotropic hypoestrism
- estrogens of extragenital origin (adipose tissue)
- constantly elevated FSH level (40 IU/l and more)
- LH-FSH ratio <1 ; elevated LH (3-7x) and FSH level (4-10x)
- high levels for 2-5 let, then gradual decrease in gonatropin level
- with the end of postmenopause starts the **senium** – decline of secondary sex characteristics reduction of steroid production in adrenal glands after age of 60

Anatomic changes

- caused by **estrogen deficiency**, depletion of ovarian follicles
 - termination of ovarian function, atrophy
 - endometrium - premenopausal hyperproliferation
or glandular cystic hyperplasia
- postmenopausal atrophy
- vagina - loss of elasticity, shortening, thinning of the mucosa,
disappearance of lactobacilli,
- atrophy of the uterus, vulva, ligaments and pelvic floor muscles,
skin (dry, wrinkled), hirsutism, breast atrophy, change body weight
- pelvic floor – pelvic organ descensus and prolaps

Climacteric syndrome

Symptoms associated with climacterium

Climacteric (menopausal) syndrome

- vegetative
- organic
- metabolic

Climacteric syndrome vegetative

vasomotor symptoms

- hot flashes
- night sweats
- palpitation

changes in psychic

- mood changes, depression, anxiety, mournfulness, exhaustion
- memory impairment, loneliness, irritability,
- loss of libido, headache, sleep problems, loss of energy

Climacteric syndrome organic

- **estrogen deficiency**
- **estrogen receptors are present in the vagina, urethra, bladder trigon and pelvic floor muscles, in the skin**
- **atrophic vulvovaginitis, dyspareunia, pruritus, chronic vaginitis**
- **stress incontinence, urge incontinence**
- **atrophic senile urethritis, hypoestrogenic cystopathy**
- **thinning of the epidermis, faster skin aging, loss of elasticity**
- **decreasing estradiol level causes a decrease in SHBG - an increase in free testosterone levels (hirsutism)**

Climacteric syndrome metabolic

- **osteoporosis** loss of bone mass, disorder of bone architecture,
- tendency to fractures – compression fractures of the vertebrae, femoral neck and wrist
- **atherosclerosis**
- estrogens have a cardioprotective effect (prevents HDL degradation by inhibiting hepatic lipase)
- estrogen deficiency - decrease in HDL, increase in LDL, triglycerides
- and plasma cholesterol
- cardiovascular disease, ischemic heart disease

Osteoporosis

- loss of bone density, bone microarchitecture impairment, Increased susceptibility to fractures
- in the CR 7 % of population, almost 35% in postmenopausal women
- postmenopausal osteoporosis - caused by estrogen deficiency
- from the age of 30 begins a loss of bone mass of 0.1 - 1% per year
- in early postmenopause 1/3 of women: loss of bone density of up to 7% per year - **fast losers**
- significant estrogen deficiency in fertile age - after ovariectomy, loss of bone density up to 7% per year
- clinically: bone fracture, bone and joints pain

Osteoporosis – risk factors

- age, premature menopause, ovariectomy, GnRH analogues
- anorexia, malabsorption, low weight
- immobility, smoking, alcoholism
- long-term use of corticoids
- hyperparathyroidism (PTH increases bone resorption)
- metabolic syndrome, diabetes, hepatopathy, nephropathy, chronic gastrointestinal inflammation
- rheumatoid arthritis

Osteoporosis - diagnostics

- **anamnesis** - risk factors, family history, the age of menopause, fractures, drugs, diseases
- **Somatic examination** – weight, loss of height, ability to get up and walking
- **X-ray examination** - side image of Th and LS spine densitometry
- **Densitometry** – measuring of bone mineral density (bone loss)
- **Quantitative computed tomography (QCT)**
- **Heel ultrasound bone scans** – less accurate
- **Biochemical blood analysis**, vitamin D level, markers of **bone resorption** (carboxy-terminal telopeptide CTx) and **bone formation** (alkaline phosphatase and osteocalcin)

Densitometry

- Principle: X-ray absorption in bone mass
- Vertebrae L1 – 4, proximal femur including neck, distal forearm
- Degree of decalcification is assessed according to deviation from the average values in healthy young people of the same sex – **T-score**
- **normal T-score -1,0 and higher**
- **osteopenia T-score -1,0 to -2,5**
- **osteoporosis T-score -2,5 and lower**
- Repeated measurements at intervals of 1-2 years on the same machine
- Indicated in women at high risk of osteoporosis – long-term corticoid treatment, age over 65 years, thyreopathy

Densitometry

Hopital Carrebeau - CHU de Nîmes
Service de Médecine Nucléaire du professeur P.O. Kotzki
Rue du Pr Debré
30000 Nîmes

Telephone : 04 66 68 32 44

E-Mail :

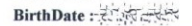
Fax : 04 66 27 32 85

Patient : 

Sex : Male

Patient ID :

Ethnic : Caucasian

BirthDate : 

Rachis

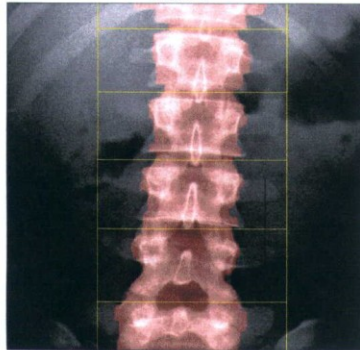


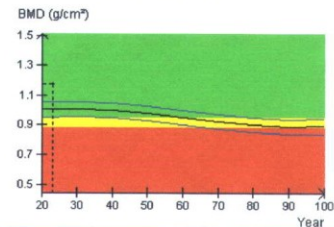
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Scan Information :

Physician : INCA
Exam Date : 11-28-2001
Exam hour : 4:34:28 pm
Printing date : 01-09-2002
Print Hour : 3:49:26 pm
Height : 175 cm
Weight : 66 kg
District : Rachis

R.O.I	Densitometry Data				
	BMD (g/cm ³)	BMC (mg)	Area (cm ²)	ZScore	Tscore
L1	1.179	0.141	119.27	3.37 (16%)	3.38 (16%)
L2	1.203	0.152	126.29	3.86 (19%)	3.88 (19%)
L3	1.266	0.171	135.11	5.13 (25%)	5.14 (25%)
L4	1.072	0.167	155.31	1.23 (6%)	1.25 (6%)
Total	1.176	0.158	134.00	3.31 (16%)	3.33 (16%)

Reference curve



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Telephone : 04 66 68 32 44

E-Mail :

Fax : 04 66 27 32 85

Patient : 

Sex : Male

Patient ID :

Ethnic : Caucasian

BirthDate : 

Left Femur



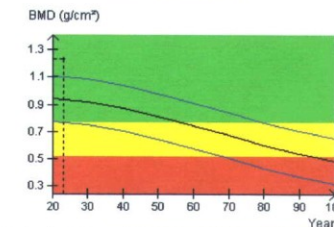
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Scan Information :

Physician : INCA
Exam Date : 11-28-2001
Exam hour : 4:39:12 pm
Printing date : 01-09-2002
Print Hour : 3:49:52 pm
Height : 175 cm
Weight : 66 kg
District : Left Femur

R.O.I	Densitometry Data				
	BMD (g/cm ³)	BMC (mg)	Area (cm ²)	ZScore	Tscore
Neck	1.156	0.044	38.41	1.42 (26%)	1.27 (22%)
Ward	0.994	0.008	7.83	0.46 (8%)	0.31 (5%)
G.T	0.979	0.095	96.81	0.37 (6%)	0.22 (3%)
InterTro	1.412	0.241	170.49	2.94 (54%)	2.79 (49%)
Total	1.237	0.097	78.39	1.90 (34%)	1.75 (31%)

Reference curve



Osteoporosis - therapy

- physical activity, nutrition (dairy products, fish), stop smoking
- **calcium** - the recommended daily calcium intake in postmenopausal women is 1200mg (dairy products)
- **vitamin D** - the target level of vitamin D is 50 -75 nmol/l, dose of 800 IU/day in combination with calcium reduces the risk of fracture
- **HRT** – reduces bone loss, increases the risk of breast cancer

Osteoporosis - therapy

- **Tibolon** – STEARs (selective tissue estrogenic activity regulator), comparable effect to HRT, does not increase breast density, does not stimulate the endometrium to grow
- **Bisphosphonates** - inhibition of osteoclastic resorption
- **Osteoanabolic treatment** – a derivative of PTH hormone Teriparatide
- **Raloxifen** – SERM (Selective estrogen receptor modulator), an estrogen receptor agonist in bone, does not affect the endometrium

Pharmacotherapy in menopause

- **non-hormonal** – phytoestrogens – soy (Estrovone), red clover (Fytofem), Alfalfa (*Medicago sativa*), *cimicifuga* (Fytofem), bee products (Sarapis)
 - SSRIs - antidepressants
- **hormonal** - ovarian hormone replacement
 - HRT** - estrogens + progestins
 - ERT** - estrogens
 - Tibolon** – steroid analogue, does not affect endometrium, the drug of choice in patients with a history of endometriosis, has a protective effect on bone mass (Livial, Ladybon)

HRT indication

- **menopausal syndrome – vasomotor symptoms**
– mental problems
- **estrogen deficiency syndrome – organic (urogenital atrophy)**
– metabolic (osteoporosis)
- **anticipated effects of long-term use– prevention of Alzheimer's and Parkinson's disease, prevention of senile macular degeneration, senile blindness, tooth loss and colon cancer (contrary to long-term use)**

HRT contraindication

- **breast cancer, estrogen dependent tumors**
- **endometrial cancer, unclear uterine (vaginal) bleeding**
- **active hepatopathy, severe liver disease**
- **thromboembolic disease - pulmonary embolism, phlebothrombosis**
- **arterial thromboembolism - myocardial infarction, angina pectoris**

Examination before HRT

- **Anamnesis**
- **Gynecological examination, ultrasound**
- **Gynecologic Cancer Prevention**
- **Mammography**
- **Blood pressure and weight check**
- **Densitometry – in women with risk of osteoporosis**

HRT side effects

- **Brest tension and pain, fluid retention**
- **nausea and headache, lower limb cramps**
- **thromboembolic complication**
- **uterine bleeding**

General principles of HRT

premenopause

- Gestagen substitution, intrauterine hormonal system(IUS)
- low-dose monophasic contraception

perimenopause

- combined sequential estrogen - gestagen therapy
- low-dose therapy, if not effective, increase the dose
- Period maintenance – according to the patient 's wishes (up to 52 yo)

postmenopause

- combined continuous estrogen - gestagen therapy

General principles of HRT

- In women **with uterus** – **ALWAYS** combined substitution with **gestagens!**
 - long-term administration of estrogens without gestagens increases the risk of endometrial cancer
- In women without uterus (after hysterectomy) only estrogen therapy
- HRT should be discontinued 4-6 weeks before surgical procedure
- early start - start of treatment no later than 5 years after menopause
- duration of therapy 5-10 years
- individual approach

HRT

therapeutic regimes

- cyclic – 3 weeks of application, one week break with withdrawal bleeding
- sequential – continuous application of estrogen with the addition of progestin in the second half of the menstrual cycle
- continuous – application without break

Application forms

- oral, transdermal, percutaneous, intramuscular, intranasal, subcutaneous and local (vaginal)

HRT drugs

estradiol valerate + levonorgestrel

- Klimonorm EV 2mg + LNG 0,15mg cyclic (not available in CR)

estradiol valerate + medroxyprogesterone acetate

- Divina EV 2mg + MPA 10mg cyclic (not available in CR)
- Indivina EV 1mg + MPA 2,5mg, EV 2mg/ MPA 5mg continuous

estradiol valerate + cyproterone acetate

- Climen 2mg/1mg cyclic, sequential

estradiol valerate + dienogest

- Velbienne EV 1mg + dienogest 2mg continuous

HRT drugs

estradiol benzoate + testosterone

- Folivirin EB 5mg + T 50mg intramuscular every 4 – 6 weeks

estradiol hemihydrate

- Estrofem 2mg, 1mg
- Estrimax 2mg
- Estrahexal skin patch 2mg, 4mg
- Dermestril 25, 50 skin patch 2mg, 4mg
- Oestrogel – gel
- Vagifem – vaginal suppositories
- Linoladiol – vaginal cream
- Lenzetto – 1,53mg/dose, transdermal spray

HRT drugs

estradiol hemihydrate + drospirenone

- **Angeliq E 1mg + drospirenone 2mg continuous**

estradiol hemihydrate + norethisteronacetate

- **Activelle E 1mg + NETA 0,5mg continuous**
- **Gynovel E 1mg + NETA 0,5mg continuous**
- **Kliogest E 2mg + NETA 1mg continuous**
- **Novofem E 1mg + NETA 1mg sequential continuous, withdrawal bleeding**
- **Trisequens E 2mg 22 days/E 1mg 6 days + NETA 2mg 10 days sequential continuous, withdrawal bleeding**

Preparáty HRT

estradiol hemihydrate + dydrogesterone

- Femoston E 1mg, E 1mg + dydrogesteron 10mg sequential continuous
- Femoston E 2mg, E 2mg + dydrogesteron 10mg sequential continuous
- Femostin conti E 1mg + dydrogesteron 5mg continuous
- Femoston conti mini E 0,5mg + 2,5mg dydrogesteron continuous

Estriol

- Ovestin – 1mg/g vaginal suppositories, 1mg tbl., 0,5mg vag supp

Tibolon

- Livial 2,5mg
- Ladybon 2,5mg

HRT risks

- **long-term use of HRT (over 10 years) increases the risk of breast cancer by 10 - 30%**
- **estrogens can be cancer promoters**
- **increase of breast tissue density by up to 8% - decrease of mammography sensitivity**
- **using unopposed estrogens in women with a uterus: the relative risk of endometrial cancer is 2.3-9.5%, the risk increases with the duration of drug administration**
- **in compliance with the rules of therapy - the benefits outweigh the risks**
- **individual approach**

**Thank you
for
your
attention**

Menopause. It's like being a testy human volcano with PMS. Only sweat pours out instead of hot lava. But people still run from you in fear of their lives.

somee cards
user card



Questions

1. Menopause

- A) starts 12 months after the last menstrual bleeding
- B) is defined 12 months after the last menstrual bleeding
- C) starts 12 months before the last menstrual bleeding
- D) is a period of time with irregular menstrual cycles

2. Postmenopause is characterised by

- A) hypergonadotropic hypoestrinism
- B) hypogonadotropic hyperestrinism
- C) hypergonadotropic hyperestrinism
- D) estrogen overproduction

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Questions

3. Climacteric (menopausal) syndrome is not characterised by

- A) vasomotor disorders
- B) estrogen deficiency
- C) atrophic vulvovaginitis
- D) estrogen overproduction

4. HRT is not contraindicated in case of

- A) breast cancer
- B) estrogen dependent tumors
- C) osteoporosis
- D) arterial thromboembolism

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Questions

5. Principles of HRT

- A) in women with a uterus, we choose only estrogen therapy
- B) in women without uterus, we choose only gestagen therapy
- C) in women with a uterus, we choose combined estrogen-gestagen therapy
- D) All answers are correct

Questions

5. Principles of HRT

- A) in women with a uterus, we choose only estrogen therapy
- B) in women without uterus, we choose only gestagen therapy
- C) in women with a uterus, we choose combined estrogen-gestagen therapy**
- D) All answers are correct