

# 2022 Update on Management of the Menopausal Patient

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# Disclosures

- ▶ I have no financial disclosures
- ▶ I have presented this topic both before and after menopause
- ▶ The presentation could have changed to reflect personal experiences, BUT
- ▶ I have always tried to present the facts without bias



# Learning Objectives

- ▶ Define menopause and perimenopause
- ▶ Outline genitourinary vs vasomotor symptoms
- ▶ List benefits of estrogen and progestogen treatment in normal menopause
- ▶ Outline treatment of patients with premature ovarian insufficiency



# Definitions

- ▶ Menopause—cessation of menses for 12 months
- ▶ Average age 51.5 years
- ▶ Perimenopause—three years before and two years after cessation of menses
- ▶ Laboratory markers can be wrong
  - ▶ FSH > 25 mIU/ml, estradiol < 50 pmol/L




# Definitions

- ▶ Early menopause before age 45
- ▶ Premature ovarian insufficiency before age 40
  - ▶ May be surgical
- ▶ 20% have no symptoms, 20% have severe symptoms




# Menopause

- ▶ Cluster of symptoms and health problems
  - ▶ Need to address at wellness visit
  - ▶ Provider may have to begin the conversation
- 




# Vasomotor Symptoms (VMS)

- ▶ Affect 80% of patients, may last up to 10 years
  - ▶ Thermoregulatory zone in hypothalamus
  - ▶ More common in African-Americans, less common in Asian- American population
- 



# VMS

- ▶ Affect patient's quality of life
  - ▶ Interferes with sleep
- 






# VMS Triggers

- ▶ Red wine
- ▶ Hot liquids
- ▶ Spicy foods
- ▶ Warm sleeping environment
- ▶ Long sleeved clothing



# VMS Triggers

- ▶ No good literature to support
- ▶ Patients will refute that however



## Genitourinary symptoms of menopause (GSM)

- Prior to 2014 referred to as vulvovaginal atrophy (VVA), atrophic vaginitis, or urogenital atrophy.



# GSM

- ▶ Loss of lactobaccilus or decrease in colonization when estrogen is lost
- ▶ Higher ph, change in bacteria
- ▶ More prone to UTI and vaginitis
- ▶ Urethral caruncle, stenosis, prolapse



# GSM

- ▶ Vaginal dryness, itching
- ▶ Labial atrophy, prolapse, introital stenosis
- ▶ Irritation, pain with intercourse
- ▶ May have bleeding with intercourse



# GSM

- ▶ Affects quality of life
- ▶ Interferes w/ sexual functioning and relationships
- ▶ Body image “feel old”



# Other menopausal symptoms

- ▶ Mood swings
- ▶ Cognitive dysfunction
- ▶ Depression
- ▶ Resurgence of symptoms, worsened by sleep deprivation
- ▶ Musculoskeletal achiness



# Other menopausal changes

- ▶ Weight gain 5-8 lb.
- ▶ 50% of women of menopausal age are OBESE
- ▶ Increased risk of metabolic syndrome in this population
- ▶ Even without weight gain, there is often a change in body appearance
- ▶ Fat distribution, change in abdominal girth





# Other menopausal changes

- ▶ Tired
  - ▶ Change in libido
- 



# Other health problems

- ▶ Osteoporosis
- ▶ Increase heart disease risk
- ▶ Cognitive changes



# Treatment Options

Let's discuss GSM treatment first



# Treatment of GSM

- ▶ Topical estrogen at lowest dose to be effective
- ▶ Available in creams, vaginal tablets, patches
- ▶ No need for progestogen
- ▶ Endometrial surveillance not necessary unless bleeding develops



# Vaginal estrogen for GSM

- ▶ Help reverse atrophic changes while minimizing systemic exposure
- ▶ Increase in the vaginal rugae
- ▶ Increase in the number of lactobacilli
- ▶ Does not alleviate VMS or reduce risk of osteoporosis



## Other GSM rx--Prasterone

- ▶ A synthetic equivalent of DHEA available in vaginal tablet form
- ▶ Improves vaginal epithelial cells, vaginal pH, parabasal cells
- ▶ Improves vaginal symptoms
- ▶ Serum levels of estradiol and testosterone remain wnl
- ▶ Do not use in pts who had ER+ breast cancer or are on estrogen modulators (tamoxifen)



## Other GSM rx--Ospemifene

- ▶ Selective estrogen receptor modulator
- ▶ Reduces severity of dyspareunia
- ▶ Beneficial effects for vaginal dryness and bone health
- ▶ Anti-estrogenic effects on breast tissue



## Other GSM rx

- ▶ Lubricants—water based stains less, ph4.5
- ▶ Hyaluronic acid
- ▶ Laser rx
- ▶ Pelvic floor exercises and dilators





# GSM rx--breast cancer patients

- ▶ ER – on tamoxifen, MAY consider low dose vaginal estrogen
- ▶ Triple negative breast cancer survivors may be candidates for vaginal estrogen



# Treatment Options

Vasomotor Symptoms



## VMS rx

- ▶ Hormonal therapy is the most effective treatment for VMS AND the prevention of osteoporosis
- ▶ First hormonal therapy was approved in 1942
- ▶ Widely used 1960's-1990's



# VSM rx--nonhormonal prescription

- ▶ SSRI, SNRI low doses, monitor for SE such as weight gain, loss of libido
- ▶ Gabapentin taken at bedtime, low dose 300 mg
- ▶ Clonidine
- ▶ Pregabalin



## VMS rx--soy

- ▶ Weak plant estrogens called isoflavones
- ▶ May have SERM-like properties or may stimulate breast tissue
- ▶ Large placebo effect in most studies



## VMS rx--CAM

- ▶ Mind-body such as meditation, CBT, biofeedback
  - ▶ Less negative side effects
  - ▶ Seem to be safe treatment and should be considered
- ▶ Herbal supplements
  - ▶ Insufficient evidence to support use
- ▶ Acupuncture, reflexology



## VMS rx--Black Cohosh

- ▶ Systematic review of 16 RCTs showed insufficient evidence to support the use for menopausal symptoms
- ▶ Combined with St. John's Wort, there was some improvement in depression



# Menopausal Hormone Therapy

What happened and what's new?





# Menopausal Hormone Therapy (MHT)

- ▶ Widely used 1960's-1990's
- ▶ The Women's Health Initiative changed all that
- ▶ Now we must relook at the data



# Women's Health Initiative (WHI)

- ▶ Enrolled 160,000+ women ages 50-79 in a set of clinical controls
- ▶ Low fat diet
- ▶ Calcium and vitamin D
- ▶ Estrogen only if no uterus
- ▶ Estrogen and progestogen if uterus present



# WHI

- Evaluating several points
- Heart disease
- Breast cancer
- Colorectal cancer
- Fractures



# WHI

- ▶ Conjugated equine estrogens (CEE) if no uterus
- ▶ Cee and medroxyprogesterone (MPA) for pts w/ uterus
- ▶ One of the questions was “ Does hormone therapy help prevent coronary artery disease?”



# WHI

- ▶ Terminated early after average 5.2 years
- ▶ Risks exceeded benefits in CEE/MPA arm of study
- ▶ FDA put black box warnings on ALL estrogen and progestogen products



# WHI

- ▶ We changed our practices
- ▶ Our patients were scared
- ▶ Our patients' health problems did not change
- ▶ New look at the data



# MHT

- ▶ Risk differs depending on type, dose, duration of use,
- ▶ route of administration, timing of initiation,
- ▶ and whether progestogen is used.



# MHT

- ▶ Treatment should be individualized
- ▶ Use the best available evidence to maximize benefits and minimize risks
- ▶ Periodic re-evaluation of benefits and risks





# MHT--estrogens

- ▶ Oral estrogen products: conjugated equine estrogen or estradiol
- ▶ Transdermal products are estradiol
- ▶ Transdermal products may have lower risk of DVT



# MHT-estrogens

- ▶ Contraindications
  - ▶ Blood clots
  - ▶ Liver disease
  - ▶ Breast cancer
  - ▶ High triglycerides
- ▶ Gallstones are a common side effect



## MHT—oral estrogens

- ▶ Enjuvia (conjugated estrogen)
- ▶ Estrace (estradiol)
- ▶ Menest (esterified estrogen)
- ▶ Premarin (conjugated estrogen)



# MHT—transdermal estrogens

- ▶ Alora
- ▶ Climara (once weekly)
- ▶ Minivelle
- ▶ Vivelle dot



# MHT--progestogens

- ▶ Progestogens must be used in combination with oral or transdermal
- ▶ estrogens if there is an intact uterus
- ▶ to prevent endometrial hyperplasia or carcinoma



# MHT—oral progestogens

- ▶ Medroxyprogesterone acetate
- ▶ Micronized progesterone (Prometrium)
- ▶ Norethindrone
- ▶ Drospirenone



# MHT—endometrial protection options

- ▶ Levonorgestrel IUD
- ▶ SERM may be used
- ▶ Duavee is conjugated estrogen/bazedoxifene combination
  - ▶ Currently not available



# MHT--progestogen

- ▶ Combination estrogen/progestogen therapy can be cyclic or continuous
- ▶ Continuous often causes irregular bleeding followed by amenorrhea
- ▶ WHI showed no increased risk of mortality from breast cancer





## MHT—oral combinations available

- ▶ Activella (estradiol/norethindrone acetate)
- ▶ Angliq (estradiol/drospirenone)
- ▶ Duavee (CEE/bazedoxifene) not available
- ▶ Femhrt (estradiol/norethindrone acetate)



# MHT—oral combinations available

- ▶ Prefest (estradiol/norgestimate)
- ▶ Premphase (CEE/MPA)
- ▶ Prempro (CEE/MPA)



# MHT—transdermal combinations

- ▶ Climara Pro (estradiol/levonorgestrel)
- ▶ Combipatch (estradiol/norethindrone acetate)



# Premature ovarian insufficiency (POI)

- ▶ Hormone therapy recommended until at least the median age of menopause, about 52
- ▶ Observational studies suggest that benefits outweigh the risks for effects on bone, heart, cognition,
- ▶ GSM, sexual function and mood
- ▶ Decision to continue after age 52 will be individualized w/ patient



## Other rx--bioidentical hormones

- ▶ Patients think these are safer
- ▶ Compounded products do not have FDA safety sheets
- ▶ Rely on salivary hormonal testing which has been shown to be unreliable



## Other rx--androgens

- ▶ NO FDA approved testosterone for women
- ▶ Risk of cardiovascular disease and breast cancer unknow
- ▶ Acne, lipid and liver function abnormalities



But what are the  
recommendations?



## USPSTF

- No beneficial effect of estrogen for prevention of cardiovascular disease
- Reduce risk of osteoporosis
- Mild reduction in diabetes





# North American Menopause Society 2021 recommendations

- ▶ MHT is indicated for women for women > 45 years of age to manage menopausal and GSM symptoms
- ▶ MHT can also be considered in the management of perimenopausal or recently postmenopausal women with risk factors for OSTEOPOROSIS



# NAMS position statement

- ▶ Women younger than 60 or who are within 20 years of menopause onset and have no contraindications, the benefit-risk ratio is most favorable for treatment of bothersome VMS and for those at higher risk for bone loss or fracture
- ▶ If older than 60 or more than 10 years after menopause, there is higher absolute risk of coronary artery disease, stroke, dementia, thromboembolic event




# Other health problems

What do we know?



# MHT and heart disease

- ▶ The WHI was looking at this question
  - ▶ Problem was that many women were started on MHT years after menopause
  - ▶ In fact 20% of those enrolled were 70-79 years old
  - ▶ Potential increased risk in women > 10 years after menopause
  - ▶ HERS trial showed no increase in CV events in patients on MHT
- 



## MHT and breast cancer (WHI data)

- ▶ Use of CEE alone, compared w/ placebo— lower breast cancer incidence and lower breast cancer mortality
- ▶ CEE/MPA, compared w/ placebo, significantly higher breast cancer incidence (9 per 10,000 years of rx)



## MHT and breast cancer (WHI data)

- ▶ Attributable risk less than 1 additional case per 1,000 users annually
  - ▶ That is less than risk of 2 glasses of wine/day, obesity, low physical activity on breast cancer risk
- ▶ No significant increase in breast cancer mortality



## MHT and VTE

- ▶ Increased risk across all ages w/ CEE or CEE/MPA in WHI
- ▶ Transdermal has lower risk in observational studies
- ▶ Consider personal or family hx when making decision



# Okay now when do we stop MHT?

- ▶ Individualize “appropriate dose for appropriate duration”
- ▶ Most would suggest 5-10 years of rx
- ▶ Some women will accept the risk and ask for longer rx
- ▶ “Shared decision making”





# Interesting studies

- ▶ Melbourne midlife women's study
- ▶ Penn ovarian aging study
- ▶ These studies enrolled women in their early 40's and study symptoms and hormone levels yearly

Questions?

