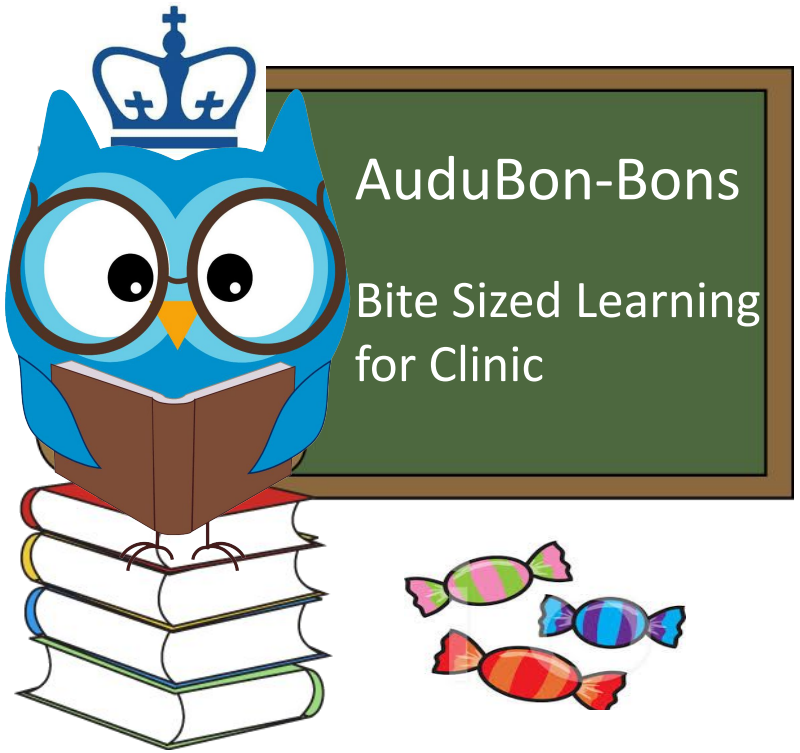
MANAGEMENT OF MENOPAUSAL SYMPTOMS



Week 9

Prepared by: **Devon Rupley, MD**

Reading Assignment:
ACOG, PB #141, Management of Menopausal Symptoms

LEARNING OBJECTIVES

- To understand the common symptoms of the menopausal transition
- To review options for treatment of symptoms of menopause
- To be able to counsel patients on risks and benefits of HRT

CASE VIGNETTE

- Ms. Hot Flash is a 49 yo G3P3 presenting with complaints of severe hot flashes, sleep disturbances and irritability.

- She notes her last menstrual cycle was approximately 14 months ago, with no bleeding since. Denies abnormal discharge, or pelvic pain.

FOCUSED HISTORY

What elements of the patient's history are most relevant?

- **PMH:** Seasonal allergies
- **PSH:** Adenoidectomy as a child
- **POBH**: NSVD x 2, CD x 1 for NRFHT
- **PGYNH:** Regular menses prior to menopause. Denies abnormal paps or STIs. Denies history of fibroids or cysts.
- **MEDS:** Claritin PRN
- **All:** NKDA
- **FH:** Mother has T2DM
- **SH:** Lives with partner. Adult children nearby. Denies tob, drug, EtOH use. Denies IPV. Works as a middle school English teacher. Accepts blood products.

PERTINENT PHYSICAL EXAM FINDINGS

What elements of the patient's physical exam are most relevant?

- **General:** Well appearing woman, VSS
- **Pulm:** CTAB
- **CV:** RRR
- **Breast:** Examined in 2 positions. No visual or palpable masses, no skin retraction or dimpling, no LAD.
- **Abd:** Soft, non-tender, no masses
- **Pelvic:** Normal external genitalia, pale mucosa c/w atrophy, no blood in vault, nl cervix without lesions, no abnl discharge
- **Ext:** WWP

MENOPAUSE

Definition

- **Permanent cessation of menstruation that occurs after the loss of ovarian activity. >12 months after last menstrual cycle**

- Median age of 51 in US

- Menopausal transition/ Perimenopause
  - The years preceding cessation of menses
  - Caused by decreasing estradiol and progesterone, and elevations of FSH

SYMPTOMS OF MENOPAUSE

Vasomotor symptoms:

- 75% of women undergoing menopause
- Hot flush: last 1-5 mins, extreme heat of upper body
- From daily to 10+ times
- Can interrupt sleep
- Median duration of 4 years, but can vary 6 months to 10 years
- Varies by race with Black populations experiencing most, Asian experiencing least

Vaginal atrophy:

- Experienced by 10-40% of menopausal women
- Caused by hypoestrogenic state
  - Loss of superficial epithelial cells --> thinning of epithelium, shortening/ narrowing of vagina
  - Loss of subcutaneous fat of labia majora
  - Increased pH
  - Decreased vaginal secretions
- Can lead to dysparuenia

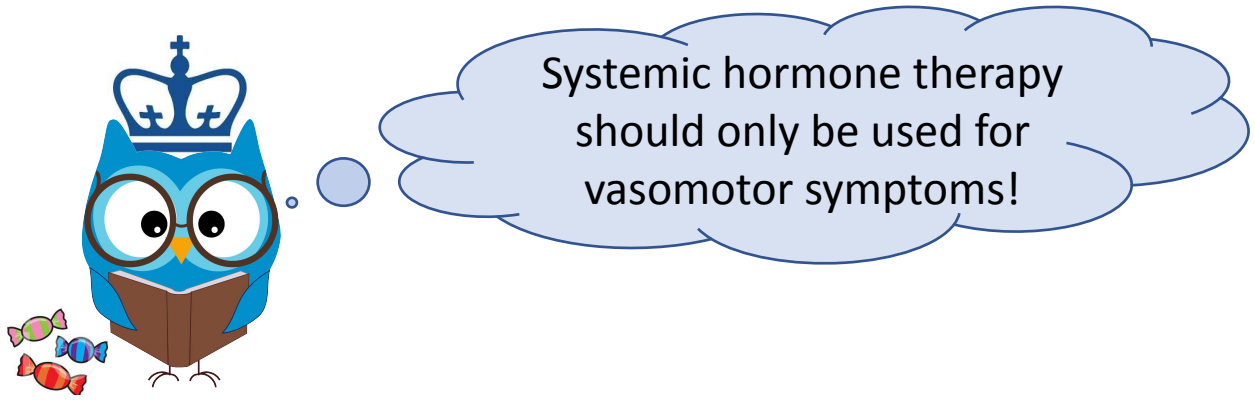
HORMONAL THERAPY

What are the options for HRT?

- **Systemic estrogen therapy (ET)**
- **Systemic estrogen-progesterone therapy (EPT)**
- **Topical estrogen**

When do you use each?

- **Vasomotor symptoms in patients without a uterus**
- **Vasomotor symptoms in pts with a uterus**
- **Vaginal atrophy**



HRT FORMULATIONS

Table 1. Treatment Options for Menopausal Vasomotor Symptoms ⇦

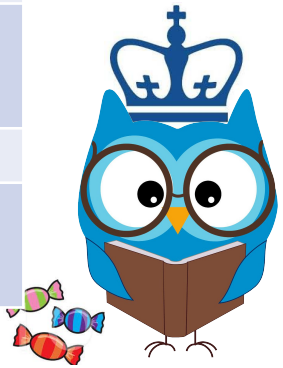
Treatment	Dosage/Regimen	Evidence of Benefit*	FDA Approved
	Hormonal		
Estrogen-alone or combined with progestin			
• Standard Dose	Conjugated estrogen 0.625 mg/d	Yes	Yes
	Micronized estradiol-17β 1 mg/d	Yes	Yes
	Transdermal estradiol-17β 0.0375–0.05 mg/d	Yes	Yes
• Low Dose	Conjugated estrogen 0.3–0.45 mg/d	Yes	Yes
	Micronized estradiol-17β 0.5 mg/d	Yes	Yes
	Transdermal estradiol-17β 0.025 mg/d	Yes	Yes
• Ultra-Low Dose	Micronized estradiol-17β 0.25 mg/d	Mixed	No
	Transdermal estradiol-17β 0.014 mg/d	Mixed	No
Estrogen combined with estrogen agonist/antagonist	Conjugated estrogen 0.45 mg/d and bazedoxifene 20 mg/d	Yes	Yes
Progestin	Depot medroxyprogesterone acetate	Yes	No
Testosterone		No	No
Tibolone	2.5 mg/d	Yes	No
Compounded bioidentical hormones		No	No

https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2014/01/management-of-menopausal-symptoms

HRT FORMULATIONS

Type	Composition	Product name	Commonly usedstarting dose	Commonly usedmaintenance dose	Typical serumestradiol level(pg/mL)
Vaginalcreams	17B-estradiol 0.01% (0.1 mg activeingredient/g)	Estrace vaginalcream[a]	0.5-1 g/d for 2 wk	0.5-1 g 1-3 times/wk	Variable
	Conjugated estrogens (0.625 mg activeingredient/g)	Premarin vaginalcream	0.5-1 g/d for 2 wk	0.5-1 g 1-3 times/wk	Variable
	Estrone 0.1% (1 mg active ingredient/g)	Estragyn vaginalcream[b]		0.5-4 g/d, intended forshort-term use;progestogen recommended	Variable
Vaginal inserts	17B-estradiol inserts	Imvexxy[a]	4 or 10 µg/d for 2 wk	1 insert twice/wk	3.6 (4 µg) 4.6 (10 µg)
	Estradiol hemihydratetablets	Vagifem Yuvafem	10 µg/d for 2 wk	1 tablet twice/wk	5.5
	Prasterone (DHEA) inserts	Intrarosa	6.5 mg/d	1 insert/d	5
Vaginal ring	17β-estradiol	Estring	2 mg ring releasesapprox 7.5 µg/d	Replace ring every 90 days	8
Oral tablet	Ospemifene	Osphena[a]	60 mg/d	1 tablet by mouth/d	N/A

Products not marked are available in both the United States and Canada.
[a]Available in the United States but not Canada
[b]Available in Canada but not the United States



The NAMS 2020 Genitourinary Syndrome of Menopause Position Statement Editorial Panel. *Menopause.* 2020;27(9):976-992.

RISKS OF HRT

Risks

- VTE (18 additional cases/10,000 women-years)
- Breast cancer (1 additional case per 1000 women)
- CHD with women starting HRT >10 years after menopause
- Risks minimized with estrogen therapy only*

Benefits

- Decreased CRC
- Decreased fracture

In most symptomatic women aged 50-59, benefits outweigh the risks for HRT!

CONTRAINDICATIONS TO SYSTEMIC HRT

What are the contraindications to systemic HRT?

- Breast cancer
- CHD
- Previous VTE or stroke or TIA
- Active liver disesase
- Unexplained vaginal bleeding
- Endometrial cancer

CESSATION OF HRT

Goal is to use HRT for the shortest amount of time for symptom control

- Requires frequent re-evaluation

When should you stop HRT?

- Individualized
- Can continue beyond age 65

Do you need to taper therapy?

- No, no difference seen between taper vs abrupt cessation

What percentage of women will experience symptom recurrence?

- 50%

NON-HORMONAL TREATMENT OPTIONS

What are non-HRT based treatment options?

		Evidence of benefit	FDA Approved
Nonhormonal			
SSRIs and SSNRIs		No	No
Paroxetine	7.5 mg/d	Yes	Yes
Clonidine	0.1 mg/d	Yes	No
Gabapentin	600–900 mg/d	Yes	No
Phytoestrogens		No	No
Herbal Remedies		No	No
Vitamins		No	No
Exercise		No	No
Acupuncture		No	No
Reflexology		No	No
Stellate-ganglion block		Yes	No

Abbreviations: FDA, U.S. Food and Drug Administration; SSRIs, selective serotonin reuptake inhibitors; SSNRIs, selective serotonin norepinephrine reuptake inhibitors.

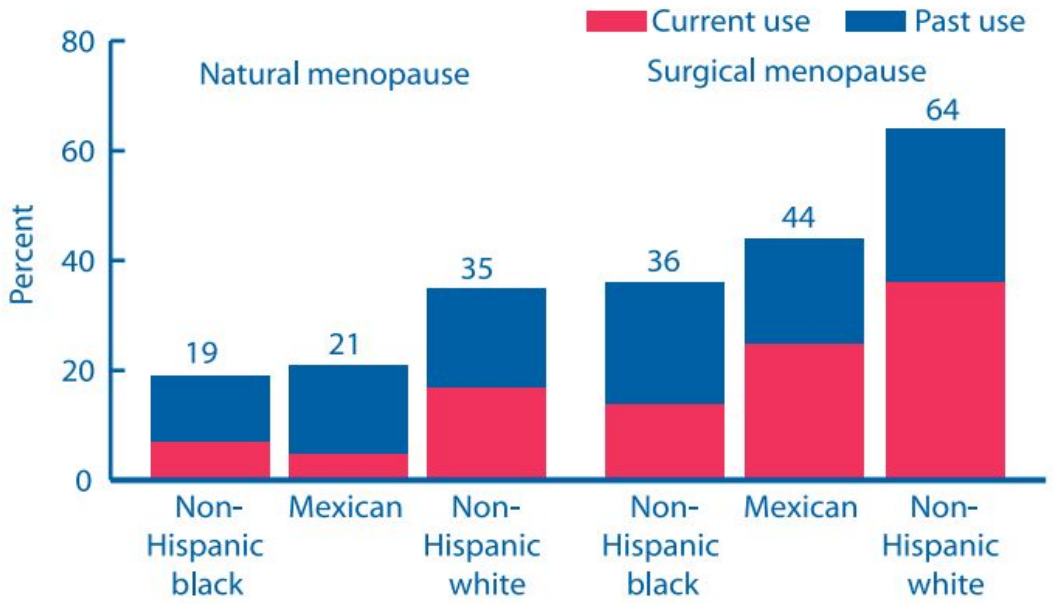
*Compared with placebo.

https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2014/01/management-of-menopausal-symptoms

SOCIAL DETERMINANTS OF HEALTH

White patients are more likely than other races to be prescribed or take HRT

Figure 5. Age-adjusted Hormone Replacement Therapy use by race/ethnicity



SOURCE: CDC/NCHS: NHANES III.

In order to provide best care, we must screen all patients routinely for menopausal symptoms and make recommendations for treatment!

EPIC .PHRASE

.BBonMenopause

Description: Counseling on management options for menopausal symptoms

The changes and associated symptoms of the perimenopausal state were discussed with the patient including vasomotor symptoms and vaginal atrophy. It was explained that vasomotor symptoms typically peak around 1 year after LMP, but can extend for variable length of time with median length of 6 years. The goals of treatment were outlined including relief of vasomotor and vaginal symptoms.

Risks and benefits of HRT were discussed including protective benefit against fracture and colon cancer, but slightly increased risk of breast cancer, CVD, and VTE. The patient ***has/does not have a uterus, ***requiring/not requiring endometrial protection with progestin therapy in the setting of systemic HRT.

We discussed treatment options and will begin with *** (lifestyle modifications, systemic ET, systemic EPT, topical ET, nonhormonal therapies including paroxetine and gabapentin).

Recommendations were made to continue HRT for the shortest amount of time which is effective for symptom resolution.

CODING AND BILLING

- **ICD-10 Code**
  - N90.5
    - Atrophy of vulva
  - N95.1
    - Menopausal and female climacteric state
  - N95.2
    - Postmenopausal atrophic vaginitis
  - N95.9
    - Unspecified menopausal and perimenopausal disorder

EVIDENCE

- ACOG Practice Bulletin No. 141: management of menopausal symptoms. *Obstetrics & Gynecology.* 2014 Jan;123(1):202-216.
- Marko KI, Gaba NE, Klatt TE. Medical Management of Menopausal Symptoms. SASGOG. Pearls of Exxcellence. 2020. Accessed on Feb 2, 2020. https://www.exxcellence.org/media/103281/medical-management-of-menopausal-symptoms-posted-2020-11.pdf
- The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone position statement of The North American Menopause Society. *Menopause.* 2017 Jul;24(7):728-753.
- Brown AF, et al. Ethnic differences in hormone replacement prescribing patterns. *J Gen Intern Med.* 1999 Nov; 14(11): 663-669.
- National Health and Nutrition Examination Survey. Use of hormone replacement therapy among postmenopausal women in the United States 1988-1994. CDC. 2003. Accessed on Feb 2, 2020, https://www.cdc.gov/nchs/data/nhanes/databriefs/hrtinwomen.pdf