



# WOMEN'S HEALTH: MENOPAUSE

Elyse Watkins, DHSc, PA-C, DFAAPA



# Disclosures

- I have no industry relationships
- I serve on the AAPA Commission on Continuing Professional Development and Education
- I am the President of the NCAPA



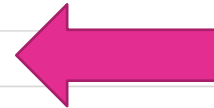
# Menopause

- **Definition: unintentional** cessation of menses after one year.
  - Surgical menopause: s/p bilateral oophorectomy
  - Premature: before age 40 years (also called premature ovarian insufficiency)



# Menopause<sup>1</sup>

Region or country	<i>n</i>	Number of studies	Mean age at menopause (95% CI)	Heterogeneity ( <i>I</i> -squared; %)
Africa	1,175	3	48.4 (48.1–48.6)	0.0
Asia	39,158	8	48.8 (48.1–49.4)	98.9
Australia	9,268	2	51.3 (49.8–52.8)	99.1
Europe	18,692	6	50.5 (50.0–51.1)	96.6
Latin America	18,073	3	47.2 (45.9–48.6)	99.1
Middle East	7,733	8	47.4 (46.9–47.8)	97.2
United States	15,690	6	49.1 (48.8–49.4)	94.6
Total	109,789	36	48.8 (48.3–49.2)	99.6



# Menopause

- **Perimenopause:** can occur 4 – 5 yrs before final menstrual period (FMP)
  - Irregular menses, vasomotor symptoms (VMS), sleep disturbances, mood/cognitive changes.
- **Postmenopause:** >1 yr after FMP
  - may complain of vaginal dryness, urinary changes due to genitourinary atrophy, skin changes, cognitive changes, sleep disturbances, and sexual dysfunction.

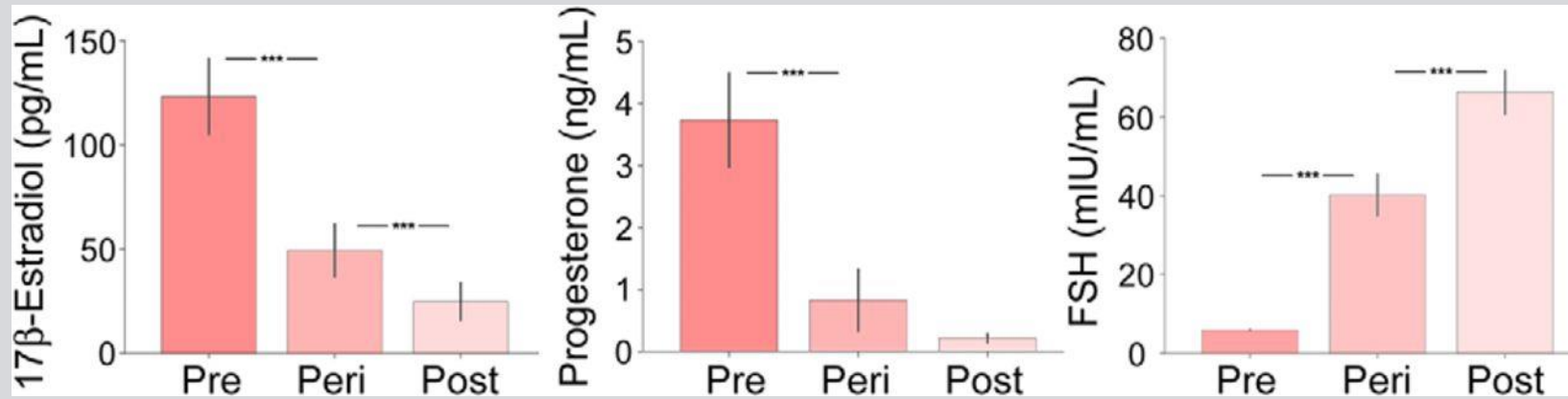


# Menopause<sup>2</sup>

Final Menstrual Period (FMP)							
▼							
<i>Stages:</i>	-5	-4	-3	-2	-1	+1	+2
<i>Terminology:</i>	Reproductive			Menopausal transition		Postmenopause	
	Early	Peak	Late	Early	Late	Early	Late
				Perimenopause			
<i>Duration of stage:</i>	variable			variable	1 yr <sup>a</sup>	4 yrs <sup>b</sup>	until demise
<i>Menstrual cycles:</i>	variable to regular	regular	regular	variable cycle length (>7 days different from normal)	≥ 2 skipped cycles and an interval of amenorrhea (≥60 days)	Amen. x 12 month	
<i>Endocrine:</i>	normal FSH	normal FSH	↑FSH	↑FSH		↑FSH	



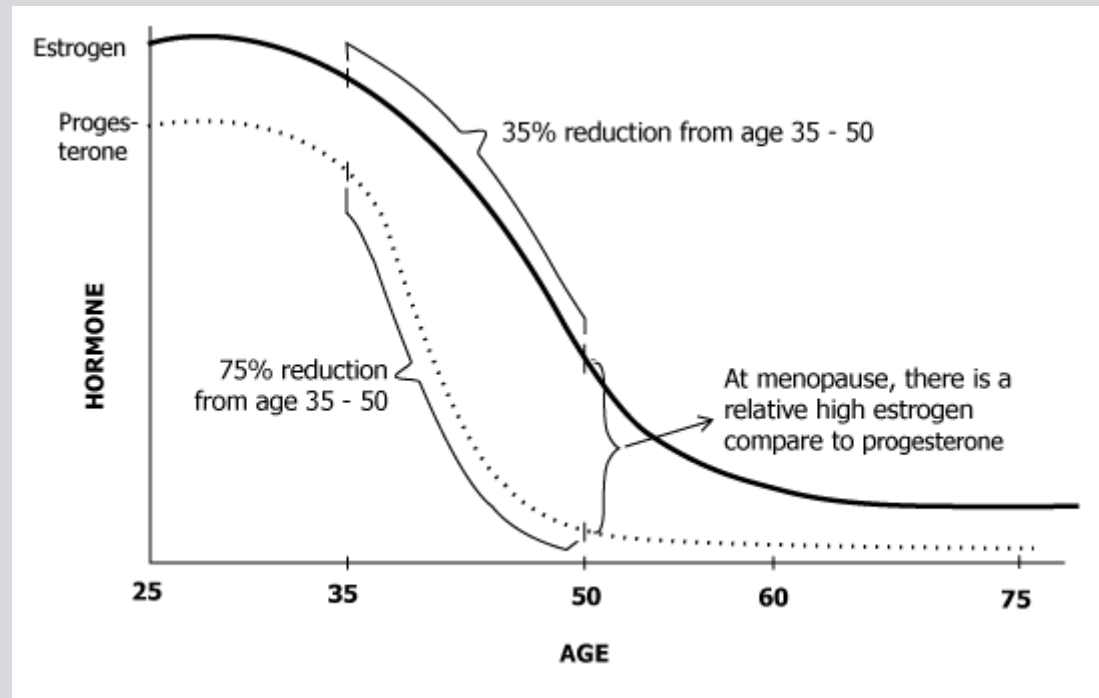
## Sex steroid and gonadotropin hormone concentrations by menopausal stage.



Emily G. Jacobs et al. *J. Neurosci.* 2016;36:10163-10173



# Menopause





# Case

- A 49 y/o G2P2 presents to the clinic with a chief complaint of “I need to get my hormones checked.” Her LMP was 2 months ago and she thinks she is in menopause.
- How do you diagnose menopause?



# Menopause

Final Menstrual Period (FMP)							
▼							
<i>Stages:</i>	-5	-4	-3	-2	-1	+1	+2
<i>Terminology:</i>	Reproductive			Menopausal transition		Postmenopause	
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<i>Endocrine:</i>	normal FSH	normal FSH	↑FSH	↑FSH		↑FSH	





# DIAGNOSING MENOPAUSE



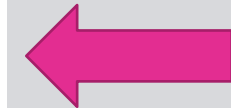
# Diagnosing menopause<sup>4</sup>

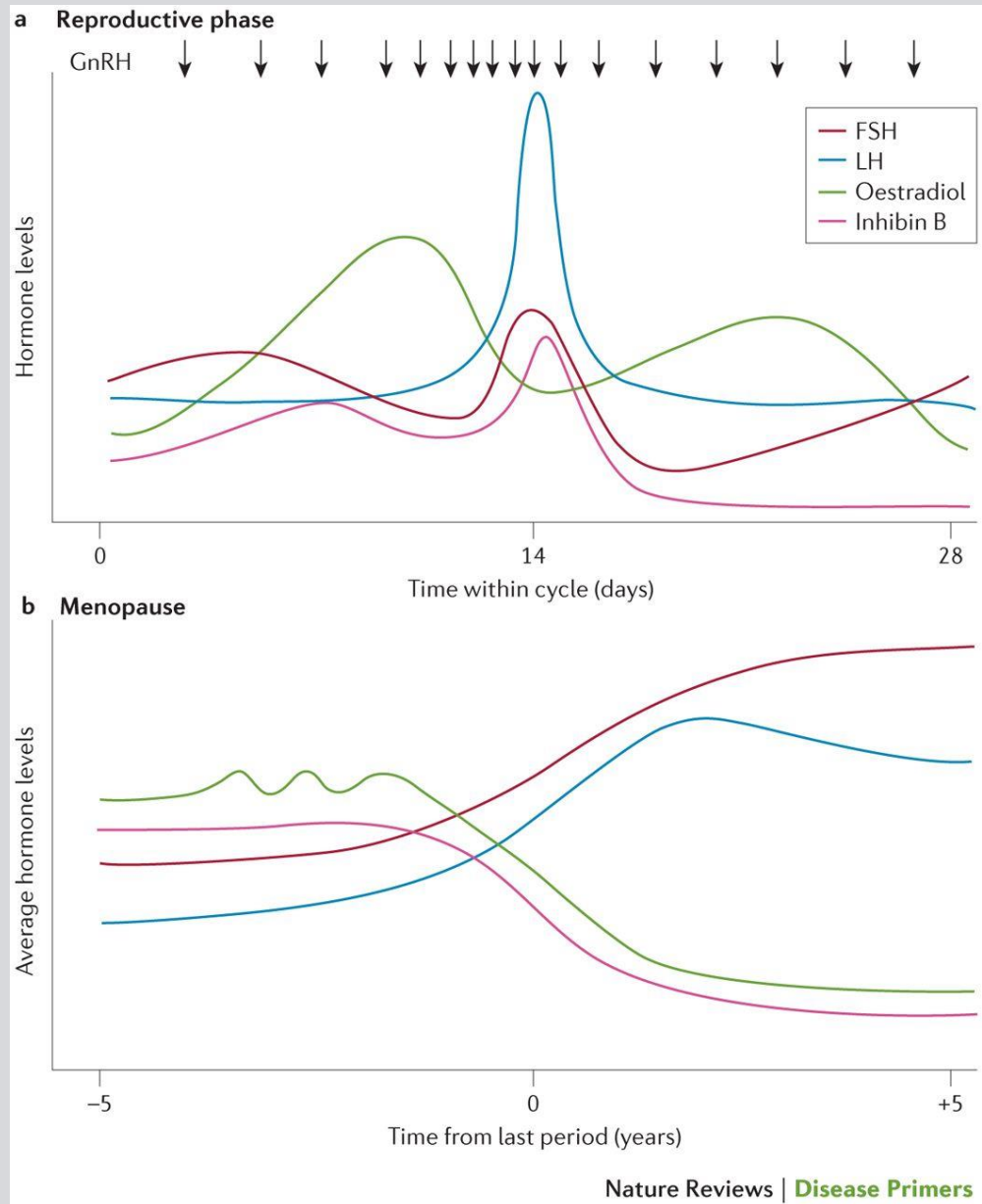
Age groups	20-29 (n=48)	30-39 (n=33)	40-49 (n=30)	p value*
Age (yr)	25.2±2.8	34.2±3.1	44.0±2.7	<0.001
LH (mIU/mL)	3.4±2.4	3.6±1.4	3.2±1.6	0.653
FSH (mIU/mL) <sup>†</sup>	4.3±1.4 <sup>a</sup>	5.9±2.4 <sup>a</sup>	8.9±5.8 <sup>b</sup>	<0.001
Estradiol (pg/mL)	51.3±19.4	50.1±16.7	60.7±30.2	0.119
IGF-I (ng/mL) <sup>†</sup>	463.8±111.4 <sup>a</sup>	347.3±105.7 <sup>b</sup>	263.7±70.8 <sup>c</sup>	<0.001
IGFBP-3 (ng/mL) <sup>†</sup>	4,495.1±6,38.9 <sup>a</sup>	4,348.2±703.9 <sup>a</sup>	3,965.9±631.0 <sup>b</sup>	0.003
AMH (ng/mL) <sup>†</sup>	4.8±3.0 <sup>a</sup>	2.8±2.2 <sup>b</sup>	1.2±1.2 <sup>c</sup>	<0.001
Inhibin B (pg/mL)	52.2±39.1	52.0±37.9	36.9±35.1	0.175



# Diagnosing menopause<sup>4</sup>

	Pre-MP (n=111)	Post-MP (n=33)	<i>p</i> value
Age (yr)	31 (20-49)	56 (50-59)	<0.001
LH (mIU/mL)	3.1 (0.8-14.1)	15.8 (6.8-55.9)	<0.001
FSH (mIU/mL)	5.0 (1.6-29.2)	51.9 (11.3-116)	<0.001
Estradiol (pg/mL)	49 (17-140)	20 (12-36)	<0.001
IGF-I (ng/mL)	363 (87-767)	179 (35-388)	<0.001
IGFBP-3 (ng/mL)	4,254 (2,796-6,071)	4,070 (2,539-6,301)	0.141
AMH (ng/mL)	2.54 (ND-12.2)	ND (ND-0.80)	<0.001
Inhibin B (pg/mL)	44.2 (ND-189)	All ND	<0.001





# Diagnosing menopause

- Ultimately, it is a clinical diagnosis!





# MENOPAUSE

What happens when estrogen levels decline?





# Menopause

- Brain
- Bones
- Cardiovascular
- Skin
- Uro-Genital





# THE BRAIN



# Menopause - Brain

- Vasomotor symptoms
- Cognitive changes
- Mood changes
- Sleep changes



# Brain

- Females with VMS have more white matter hyperintensities – ischemic lesions deep within the brain (found on MRI)
- A **three-fold increased risk of stroke** and a **two-fold increased risk of dementia** and death in individuals with white matter hyperintensities<sup>6</sup>
- Blood flow through the middle cerebral artery decreases during a hot flash<sup>7</sup>



# Menopause - Brain

- Raloxifene (a SERM): associated with cognitive improvements in otherwise healthy postmenopausal women and in schizophrenia
  - (we'll revisit this relationship...)



# Brain

- Lower estradiol was related to poor performance on a **memory** task<sup>8</sup>
- Estradiol has a direct effect on **mood** by affecting norepinephrine activity and serotonin response and uptake<sup>9</sup>
- **Sleep:** most common complaint is night-time awakenings<sup>10</sup>
  - May be due to lower estrogen, VMS but evidence is weak

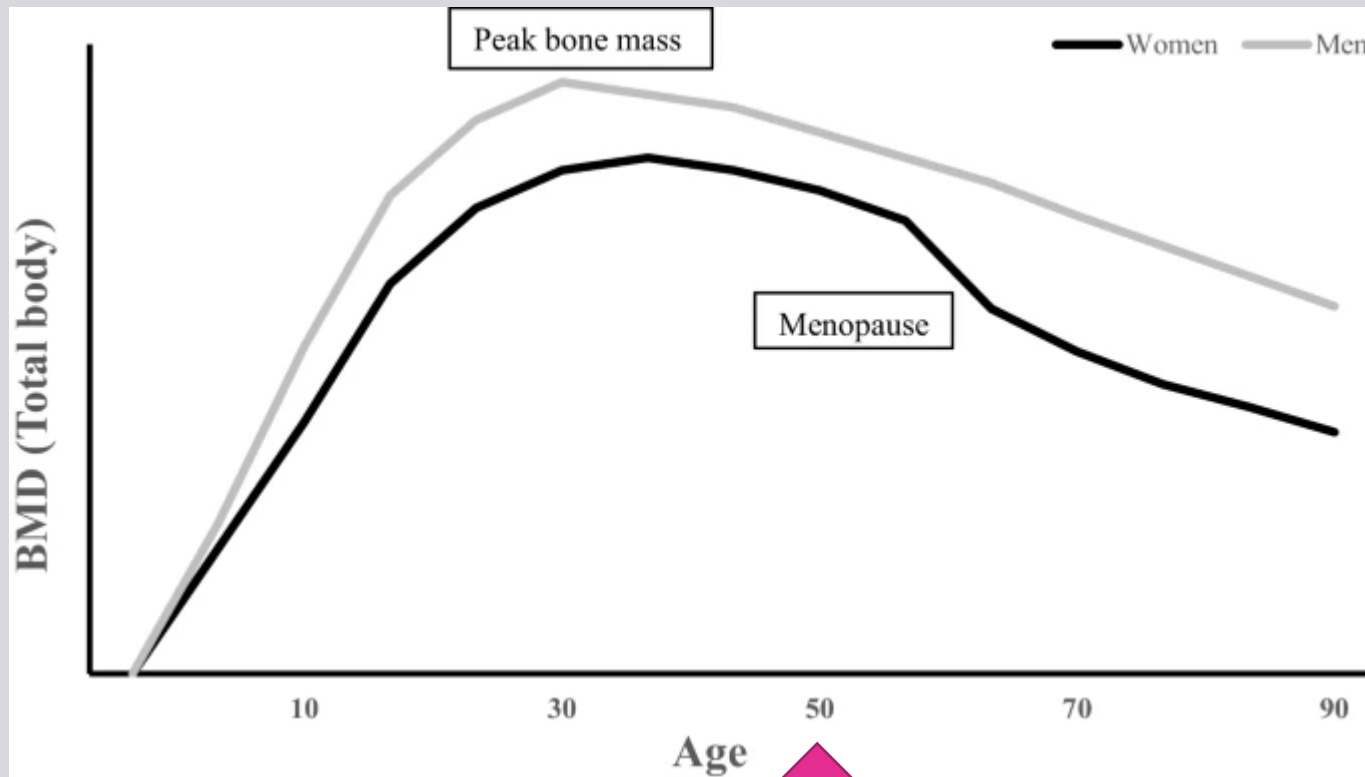




# BONES



# Menopause – Bones<sup>11</sup>



This is why it is important to talk to your patients BEFORE they go through the transition!





# Menopause - Bones

**Table I** World Health Organization's definition of osteoporosis based on bone mineral density

Classification	T-score
Normal	$\geq -1.0$
Low bone mass (osteopenia)	Between $-1.0$ and $-2.5$
Osteoporosis	$\leq -2.5$
Severe or established osteoporosis	$\leq -2.5$ with one or more fractures

**Note:** Data from Kanis et al.<sup>19</sup>

## ➤ DEXA scan

- T-score: measures how closely bone density compares to that of an average 30-year-old of the same sex
- Z-score: compares an individual to others their own age and sex



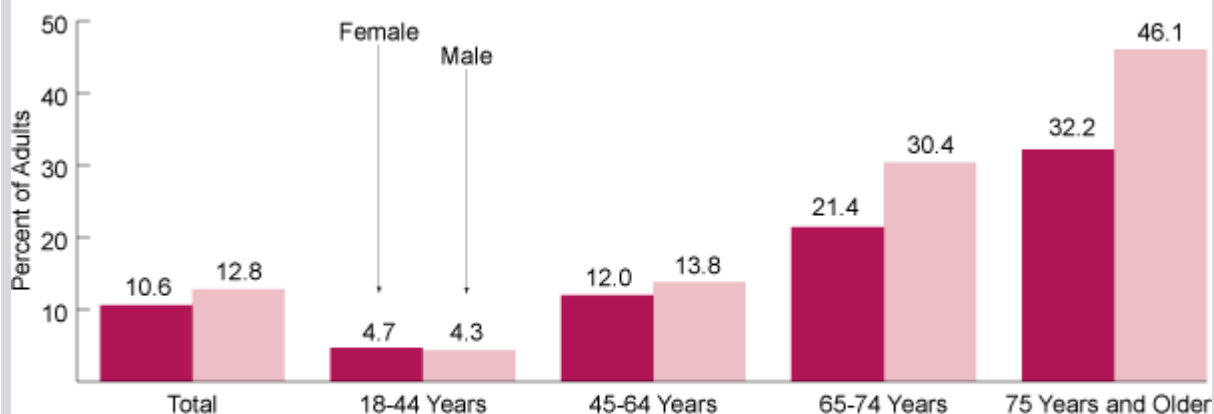


# CARDIOVASCULAR



# Cardiovascular health

Heart Disease\* Among Adults Aged 18 and Older, by Age and Sex, 2008–2010



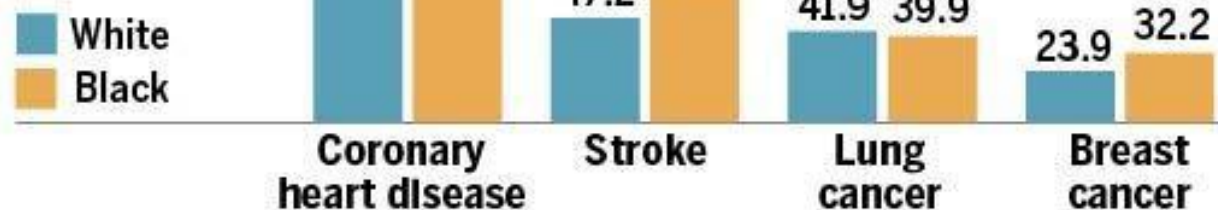
\*Reported a health professional had ever told them that they had coronary heart disease, angina pectoris, heart attack, or any other heart condition or disease; total estimates are age-adjusted.

Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey with multiply imputed poverty data, 2008-2010. Analysis conducted by the Maternal and Child Health Bureau.

## Cardiovascular disease vs. cancer in women

Cardiovascular disease, not cancer, is the leading cause of death in women

Deaths per 100,000 population



Source: American Heart Association

DAN AGUAYO/STAFF

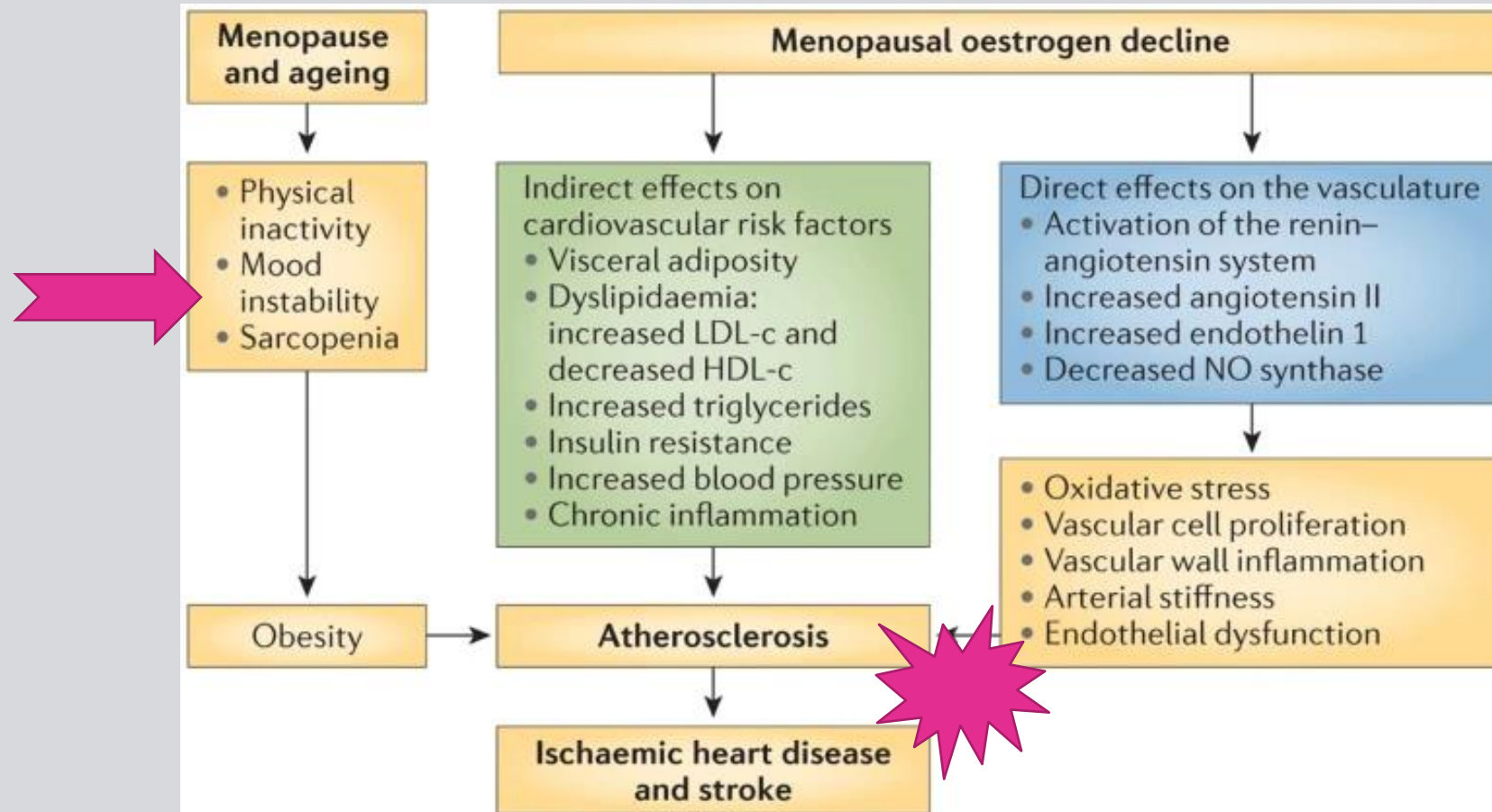


# Cardiovascular health

- A prospective cohort study of 11,725 women followed for 14 yrs found a **two-fold increase in CHD** in those women who reported having vasomotor sx's frequently compared with women having no VMS<sup>12</sup>



# Cardiovascular health<sup>13</sup>



# Cardiovascular health

- Screening: old methods, new methods
- **Ultrasonography of the ophthalmic artery<sup>14</sup>**
- 





# SKIN/GUSM



# GUSM: Genitourinary syndrome of menopause

- Vaginal atrophy due to estrogen loss
- Cystocele/rectocele/uterine prolapse
- Loss of elasticity of skin, collagen decreases





# GUSM: Genitourinary syndrome of menopause

- Dyspareunia + vaginal dryness and atrophy + urinary symptoms = **Libido issues**
- Consider this dx in any menopausal female with “recurrent UTI” or “recurrent yeast infection”





# TREATMENT



# Menopause - Treatment

- Women's Health Initiative
- Estrogens
  - Conjugated equine vs. estradiol
- Progestins
  - Progestins vs progesterone



# Menopause - Treatment

- **Estrogens**

- Transdermal, oral, injectable, vaginal

- **Progestins**

- Oral

- **Progesterone**

- Oral

- **New combined estradiol/progesterone**

- **Conjugated equine estrogen/bazedoxifene**

- **SSRIs/SNRIs**

- **Others:** alternative/complementary

- **Neurokinin-3 antagonist:** (in clinical trials)<sup>15</sup>



# Menopause – Treatment

- **ACOG guideline<sup>16</sup>**
  - Dose
  - Route of administration
  - Risk/benefit
  - “Shared decision-making”



# GUSM Treatment Options

- Vaginal estrogens
- SERM (Ospemifene)
- DHEA vaginal insert
- Hyaluronic acid
- Laser tx



# Menopause

- **Health maintenance/anticipatory guidance**
  - Consider the whole body!





# CASES/QUESTIONS





# Case 1

A 45 y/o female presents with a chief complaint of “possible menopause.” She states her menses are regular, but is having hot flashes and emotional changes. Which of the following would be the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a detailed H&P
- D. Refer to counseling



# Case 1

A 45 y/o female presents with a chief complaint of “possible menopause.” She states her menses are regular, but is having hot flashes and emotional changes. Which of the following would be the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a comprehensive H&P**
- D. Refer to counseling



# Case 2

A 49 y/o female presents for “menopause.” She states her LNMP was 3 months ago, and prior to that it was regular. She states she otherwise feels fine. Which of the following is the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a detailed H&P
- D. Refer to counseling



# Case 2

A 49 y/o female presents for “menopause.” She states her LNMP was 3 months ago, and prior to that it was regular. She states she otherwise feels fine. Which of the following is the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a detailed H&P**
- D. Refer to counseling



# Case 3

A 39 y/o female presents for amenorrhea. She states her LNMP was about 3 months ago, and prior to that it was sporadic for about a year. She states she is having hot flashes, night sweats, and anxiety. Which of the following would be the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a detailed H&P
- D. Order a beta-hCG



# Case 3

A 39 y/o female presents for amenorrhea. She states her LNMP was about 3 months ago, and prior to that it was sporadic for about a year. She states she is having hot flashes, night sweats, and anxiety. Which of the following would be the most appropriate next step?

- A. Order an FSH
- B. Order a serum estradiol
- C. Perform a detailed H&P\***
- D. Order a beta-hCG



# Case 4

A 70 y/o female presents to discuss hormones. She states she had a hysterectomy at age 36 years. She was watching The View and they were talking about hormones and she is interested in trying them. Which of the following is the most appropriate intervention?

- A. Prescribe oral estradiol
- B. Prescribe oral estradiol and progestin
- C. Administer an injection of estradiol
- D. Engage in a risk/benefit discussion



# Case 4

A 70 y/o female presents to discuss hormones. She states she had a hysterectomy at age 36 years. She was watching The View and they were talking about hormones and she is interested in trying them. Which of the following is the most appropriate intervention?

- A. Prescribe oral estradiol
- B. Prescribe oral estradiol and progestin
- C. Administer an injection of estradiol
- D. Engage in a risk/benefit discussion**





# Case 5

A 52 y/o female presents with a chief complaint of painful intercourse. Her LMP was about one year ago. Which of the following is the most appropriate next step?

- A. Prescribe vaginal estrogen
- B. Prescribe vaginal DHEA
- C. Prescribe oral estrogen and progestin
- D. Perform a detailed H & P



# Case 5

A 52 y/o female presents with a chief complaint of painful intercourse. Her LMP was about one year ago. Which of the following is the most appropriate next step?

- A. Prescribe vaginal estrogen
- B. Prescribe vaginal DHEA
- C. Prescribe oral estrogen and progestin
- D. Perform a detailed H & P**



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# The End

Thank you!

