



MENOPAUSE: TIME TO TAKE PAUSE

DANIELLE WEISS, MD

OVERVIEW OF LECTURE

- ◉ Menopause Defined
 - ◉ Historical Perspective
 - ◉ Puberty vs Menopause
 - ◉ Symptoms and Signs of Menopause
 - ◉ Health Consequences of Menopause
 - ◉ Non-Hormonal Treatment Options
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- ◉ *Every woman goes through menopause, but no two have the same experience.*
 - ◉ *Care must be given on an individual basis.*



WHAT IS MENOPAUSE?

- ◉ Menopause can mean different things to different people:
 - Physiological event - ovulation ending
 - Psychological change - fertility to infertility
 - Hormone deficiency condition versus a natural process.
- ◉ It can be all of these and more!
- ◉ Each woman defines her own experience.

Menopause
The Musical™



WHAT IS MENOPAUSE?

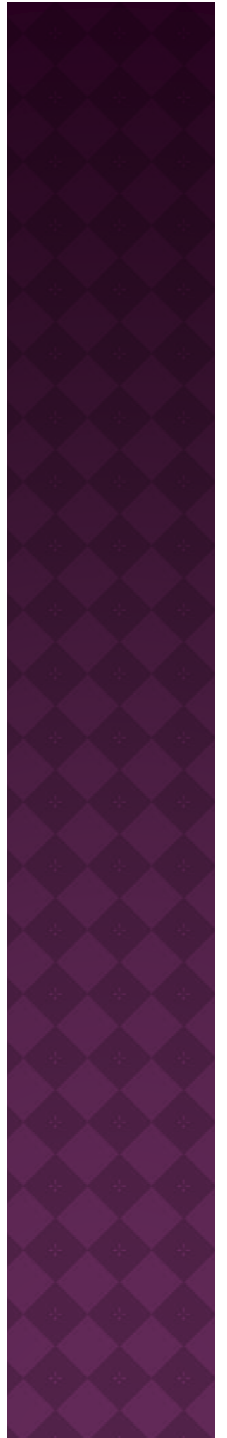
○ Medical Definition

- Perimenopause is the transition to menopause when periods become irregular (usually starting in the 40's).
- Menopause literally means the "end of monthly menstrual cycles"
- Postmenopausal is cessation of menses for >1 year

○ This is not a disease but a natural process...and a time to pause!

○ Pathophysiology

- Ovaries no longer release eggs and make less hormones (ie estrogen, progesterone)
- Causes: natural, medications, surgery, autoimmune
- Average age of menopause = 51yo
- Premature menopause = <40yo



MENOPAUSAL SYMPTOMS

○ Physical:

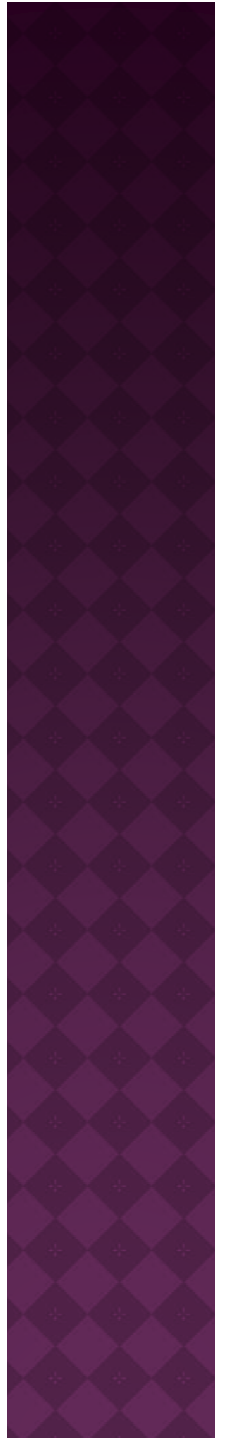
- Hotflashes, headaches, nightsweats, palpitations, joint and muscle aches, vertigo

○ Mental:

- Mood swings, agitation, depression, anxiety, insomnia, decreased libido

○ Urogynecological:

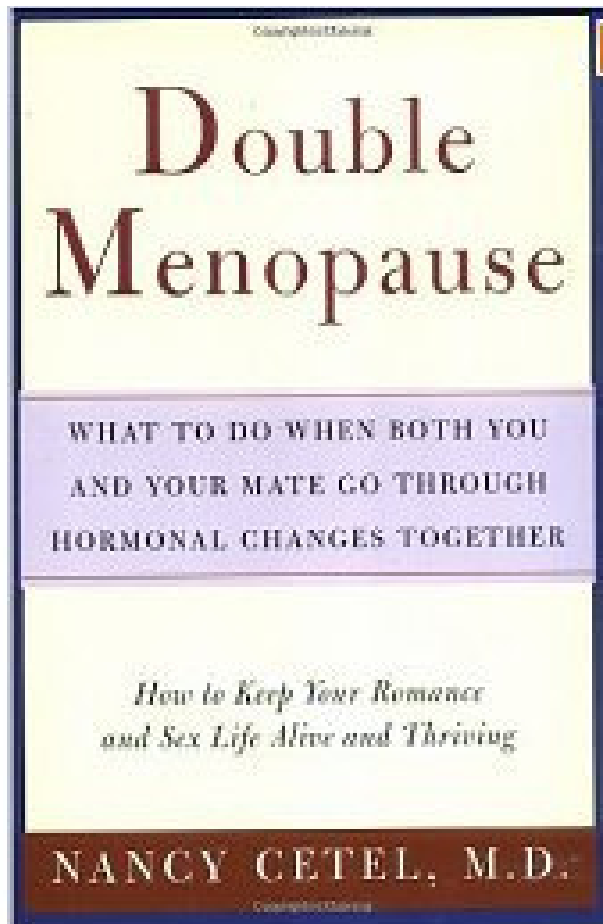
- Vaginal dryness and burning, pain with intercourse, urinary tract infections, frequent urination, urinary incontinence



HISTORICAL PERSPECTIVE

- ◉ In 1820, the average lifespan in the U.S. was 39!
 - Menopause did not exist unless you were lucky!
- ◉ Now, the average woman's lifespan is 82!
 -and the average age for menopause is 51yo!
 - We spend over 1/3rd of our life postmenopausal!

WE ARE NOT ALONE!



- ◉ Men go through Andropause
- ◉ Other animals go through menopause too!
 - rhesus monkeys
 - chimpanzees
 - elephants
 - pilot whales
 - rats
 - mice

HISTORICAL PERSPECTIVE

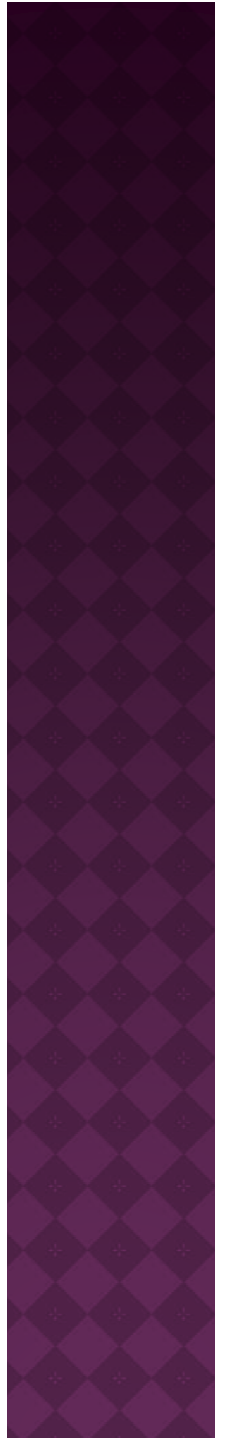
- ◉ In the 1930's, perimenopause "complaints" and experiences were thought to be largely psychological.
- ◉ The first therapy for menopause in the "modern era" was the early antiepileptic sedative, phenobarbital.

HISTORICAL PERSPECTIVE

- ◉ At the time estrogens were isolated and synthesized in the late 1930s, the idea of menopause changed again.
- ◉ Menopause began to be understood as a time of estrogen deficiency and menopausal symptom scores were developed for diagnosis and monitoring of treatment.

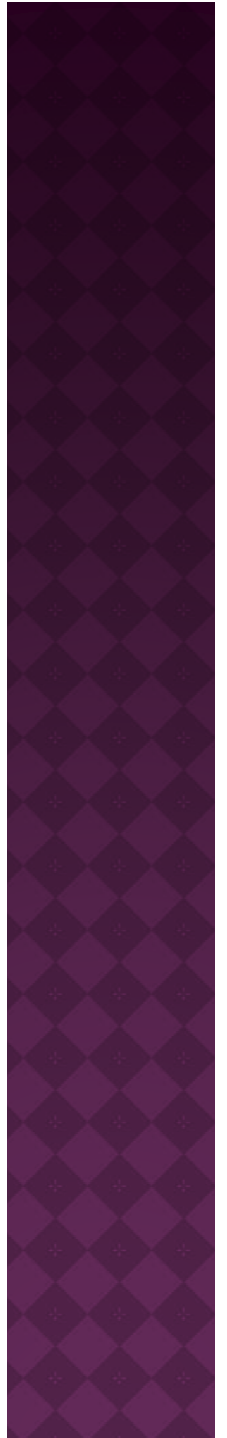
HISTORICAL PERSPECTIVE

- ◉ Interestingly, on these symptom scores perimenopausal and adolescent women just starting to menstruate shared many complaints:
 - ◉ weight gain, cold hands and feet, labile mood, and headaches.
- ◉ The increased production of sex hormones at menarche (1st period) and the volatile estrogen levels in perimenopause may account for this similarity in symptoms.



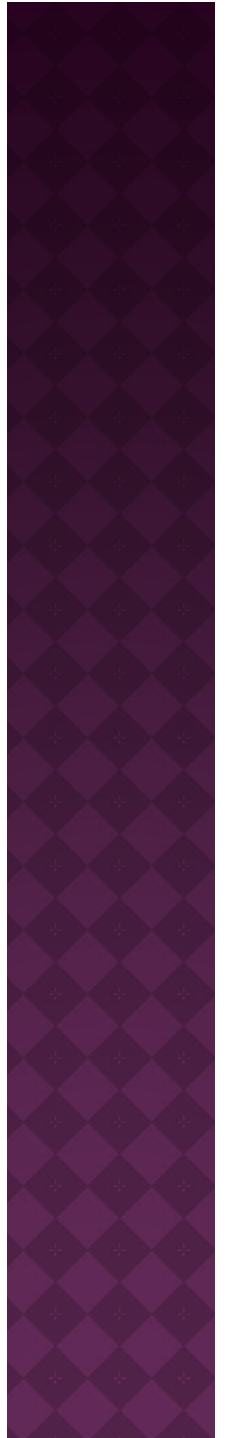
PUBERTY

- The onset of puberty is associated with pulses of gonadotropin releasing hormone (GnRH) that come from the hypothalamus in the brain
- GnRH stimulates the pituitary sex hormones: luteinizing hormone (LH) and follicle stimulating hormone (FSH).
- LH and FSH stimulate maturation of the uterus and ovaries.



PUBERTY

- It is not clear what initiates the GnRH pulse.
- Leptin (a fat cell hormone) appears to play a role in initiating puberty since individuals who lack leptin fail to start puberty.
- Genetics and environmental factors (nutrition and social) also influence timing of puberty.



PUBERTY: STAGES OF SEXUAL DEVELOPMENT

- **Adrenarche:**
 - adrenal gland development (androgens, DHEA)
~age 7
- **Gonadarche:**
 - ovary/testicular development ~age 8
- **Thelarche:**
 - breast development ~age 11
- **Pubarche:**
 - pubic hair growth ~age 12
- **Menarche:**
 - start of menses ~age 12.5 (range 9-16)
 - anovulatory and irregular for ~2yrs

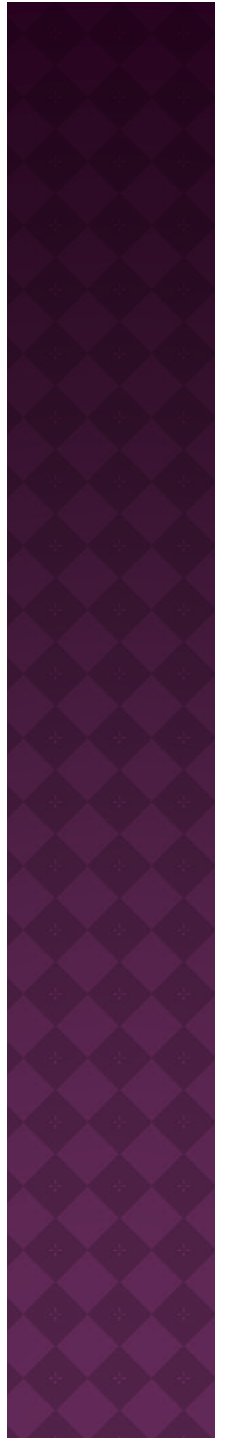
PUBERTY VS PERIMENOPAUSE

- ◉ Elevated and fluctuating estrogen levels
- ◉ Fluctuating mood
- ◉ Short and long menstrual cycles
- ◉ Anovulatory cycles (no egg released)
- ◉ Timing partially based on genetics



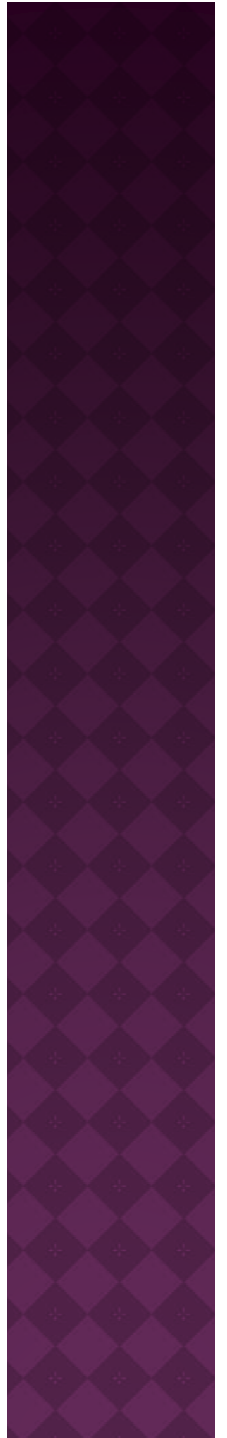
PUBERTY VS PERIMENOPAUSE

- Estrogen, testosterone and other hormones effect the growth and function of:
 - Brain (cognition and mood)
 - Bones and Muscle
 - Blood
 - Skin
 - Hair
 - Breasts
 - Fat distribution
 - Sex organs



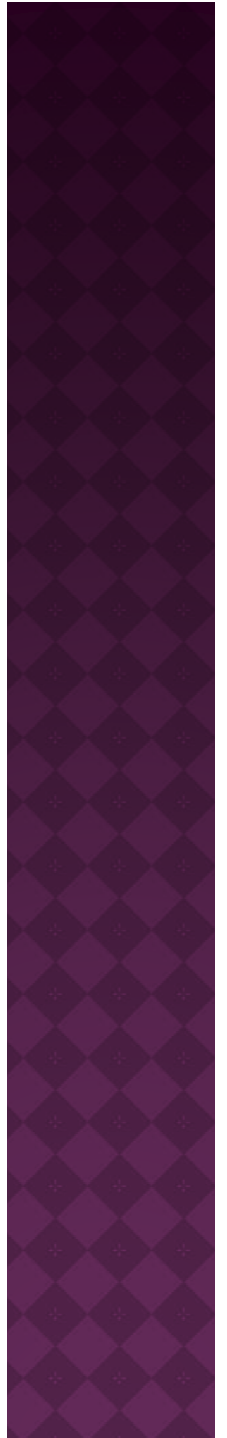
“HOT FLASH” PATHOPHYSIOLOGY

- A hot flash, or flush, is the spontaneous sensation of warmth, often associated with perspiration, palpitations, and anxiety, resulting from a vasomotor response to decreasing estrogen levels.
- 50-80% of peri/postmenopausal women experience this for <1yr to >10yrs.



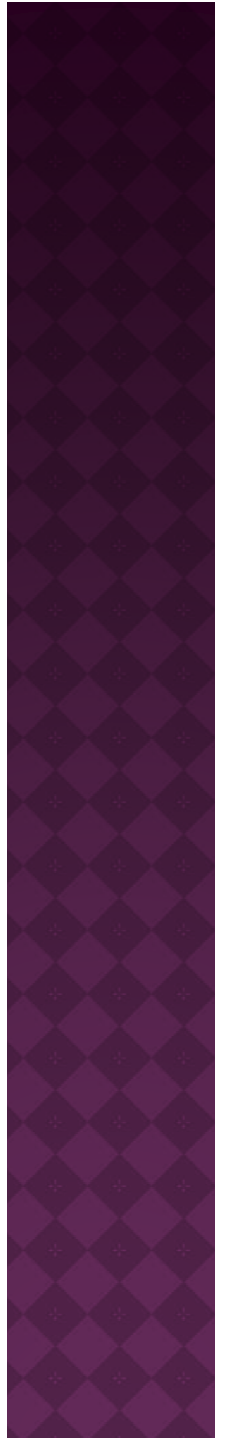
“HOT FLASH” PATHOPHYSIOLOGY

- It is hypothesized that declining estrogen production enhances release of norepinephrine and serotonin in the hypothalamus.
- This lowers the set point in the thermoregulatory nucleus (ie thermostat) and leads to inappropriate heat-loss mechanisms (ie sweating, vasodilation).



OTHER HEALTH CONSEQUENCES OF MENOPAUSE

- ◉ Osteoporosis
- ◉ Heart Disease
- ◉ Metabolic Dysfunction (ie diabetes)
- ◉ Urinary tract Infections
- ◉ Change in fat distribution
- ◉ Cognition



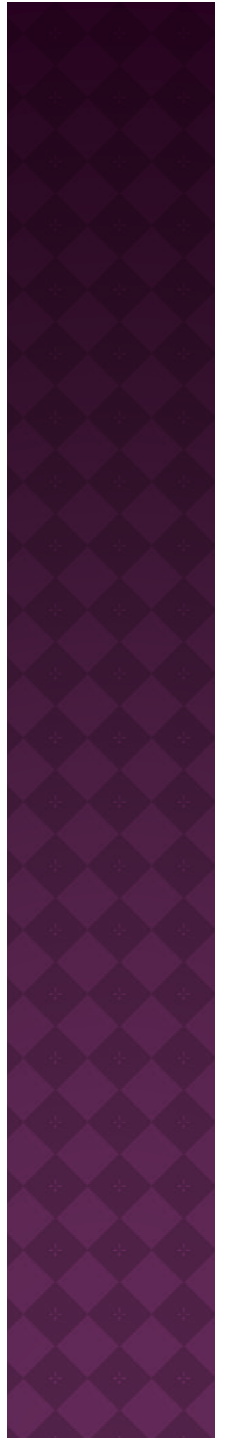
MENOPAUSAL TREATMENT OPTIONS

○ Hormonal

- Estrogen
- Progesterone
- DHEA
- Testosterone

○ Non-Hormonal

- Lifestyle/behavior/exercise
- Culture
- Supplements/herbs
- Accupuncture
- Biofeedback
- Stress management
- Diet
- Non-Hormonal Pharmaceuticals



MENOPAUSAL TREATMENT OPTIONS

- ~50% of women use alternative non-hormonal therapies to manage menopausal symptoms
- Estrogen is the most effective way to treat menopausal symptoms (ie hotflashes) but prescriptions declined by >60% after the Women's Health Initiative (WHI) study.
- Every woman is a unique individual and management of menopause must be individualized as well!

NON HORMONAL MENOPAUSAL SYMPTOM TREATMENTS

○ Vaginal Dryness

- Using over-the-counter water-based vaginal lubricants (Astroglide®, K-Y®) or moisturizers (Replens®, Vagisil®).
- Staying sexually active also helps with dryness.

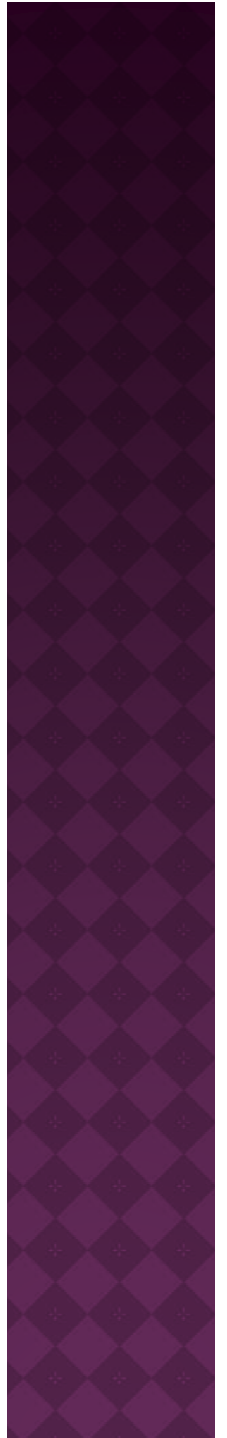
○ Urinary Symptoms

- Incontinence: Kegel exercises:
 - Consists of contracting and relaxing the muscles of the pelvic floor.
 - For example, imagine stopping the stream of urine mid way through urination.
- Urinary Tract Infection:
 - D-Mannose, probiotics

NON HORMONAL MENOPAUSAL SYMPTOM TREATMENTS

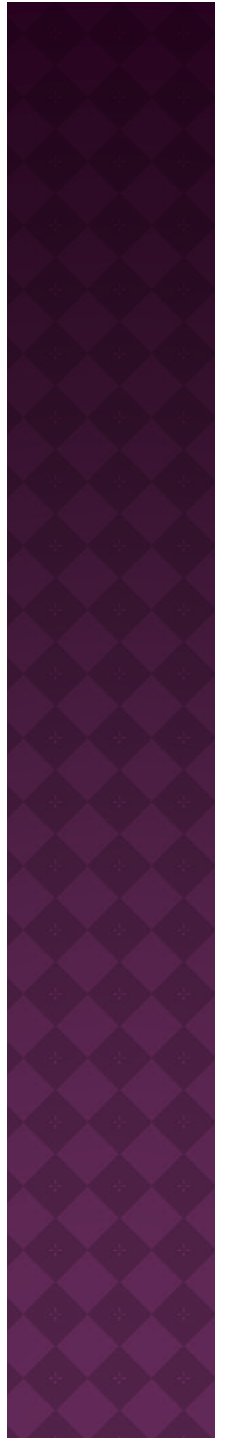
○ Insomnia

- Avoid caffeine in the afternoon/evening.
- Exercise during the day and not prior to bed.
- Relaxation techniques: deep breathing, etc.
- No TV watching or computer/bright light use 1hr prior to bed.
- Consider Valerian root and/or melatonin.
- Consider sleep study to see if you have restless leg syndrome, obstructive sleep apnea or another reason for insomnia.
- Keep room cool and dark.
- Wear earplugs.



LIFESTYLE: EXERCISE

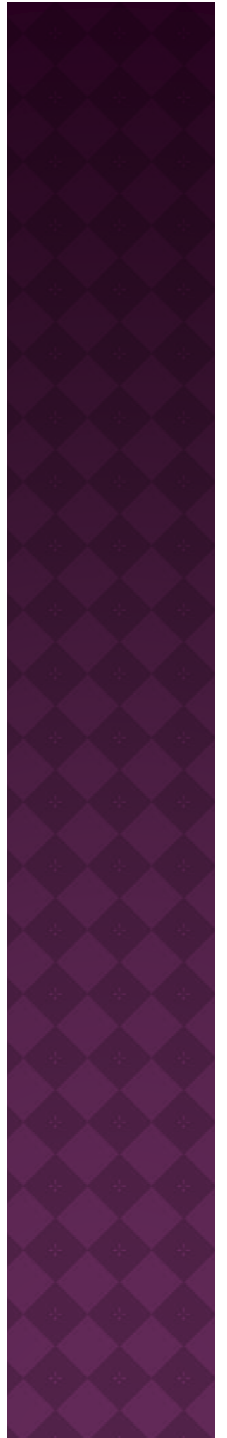
- **Reduced stress.**
 - Menopause can often lead to depression, anxiety and stress. Exercise is proven to help reduce stress and improve your mood.
- **Increased bone mass.**
 - Strength training and impact activities (walking, dance, running) can help strengthen the bones, improve balance and prevent osteoporosis.
- **Reduced risk of high blood pressure, heart attacks and strokes.**



LIFESTYLE: EXERCISE/WEIGHT

◉ **Weight loss.**

- It has been noted that people who exercise have less hot flashes.
- Those who are overweight (by ~10lbs) have more hotflashes.
- Exercise can help create a calorie deficit (muscle burns more calories than fat) to assist with weight loss.

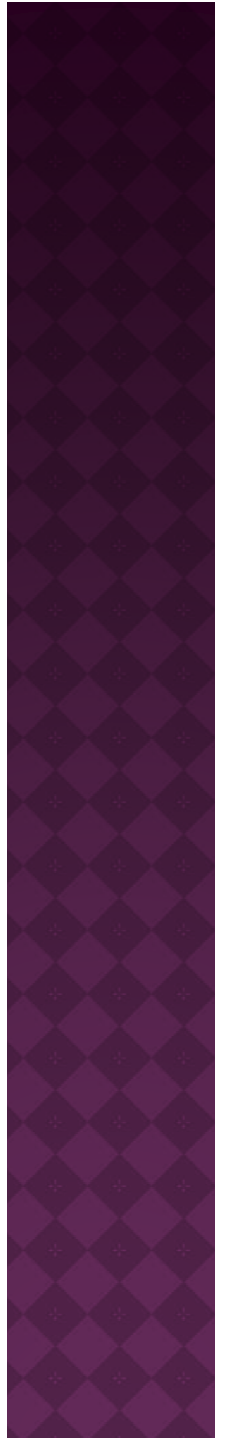


LIFESTYLE: EXERCISE/WEIGHT

- Hot flashes diminish with weight loss (~10lbs).
- Hot flashes may also improve as exercise increases β -endorphins which may stabilize the thermoregulatory center.
- Increases in endorphins may be related to exercise intensity.

LIFESTYLE: ENVIRONMENT

- ◉ Fan/flowing air
- ◉ Cool clothes
- ◉ Cool water/food
- ◉ Reduce triggers

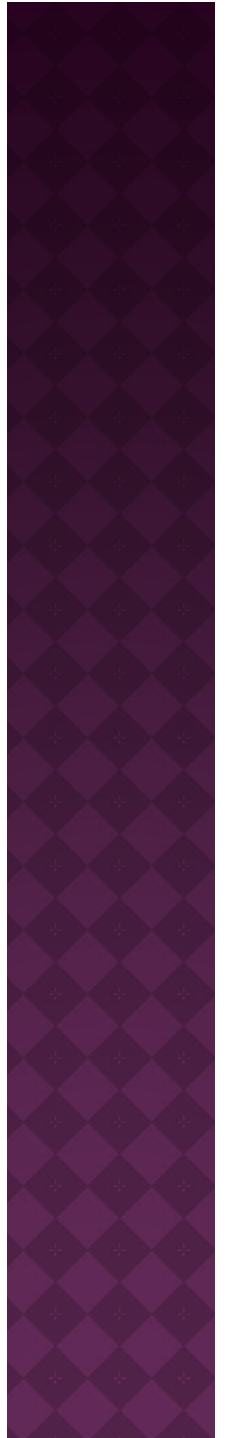


LIFESTYLE: CULTURE

- Cultural vs personal perceptions and expectations.
- ~70% of women report having hot flashes, yet <10% considered them bothersome.
- Asian women report suffering the least amount of menopausal symptoms.
- British women suffer the most.
- Americans are somewhere in between.
- Factors that effect this:
 - having a good health status (physical activity, diet)
 - high perceived control
 - higher educational level
 - Genetics?

LIFESTYLE: BEHAVIOR

- Relaxation response training /Paced breathing
 - Hypnotherapy & Biofeedback
 - Exercise
 - Reduce stress/triggers
 - Stop smoking (for hot flashes & osteoporosis)
-
- These lifestyle changes may be beneficial through decreasing stress hormones and increasing endorphins.



SUPPLEMENTS/HERBS: PHYTOESTROGENS

- Phytoestrogens are plant-derived compounds that are structurally similar to estrogen and may display both estrogenic and anti-estrogenic effects.
- There are three major classes of phytoestrogens:
 - Isoflavones - found in high concentration in soybean, soybean products (e.g. tofu) and red clover.
 - Lignans - mainly found in flaxseed.
 - Coumestans - found in split peas, pinto beans, lima beans, and especially alfalfa and clover sprouts.

SUPPLEMENTS/HERBS: PHYTOESTROGENS

- ◉ Fermentation and digestion (need the right intestinal flora) effect the potency.
- ◉ Phytoestrogens (especially genistein and S-equol) are the most helpful if used in women with mild to moderate vasomotor symptoms in early natural menopause. 35-135mg decreased hotflashes 15% \geq placebo (~35%).
- ◉ Other beneficial effects:
- ◉ Isoflavones (90mg/day) may minimize bone loss of the spine in menopausal women.
- ◉ Long-term intake of soy proteins lower blood pressure and cholesterol.

SUPPLEMENTS/HERBS (CONT'D)

- ◉ Boron - may increase estrogen levels but more research is needed in humans
- ◉ Belladonna - not shown to be effective
- ◉ Black cohosh (aka Remifemin)
NIH study showed no benefit
?liver toxicity
- ◉ DHEA (precursor to male and female sex hormones) - mixed

SUPPLEMENTS/HERBS (CONT'D)

- ◉ Dong quai - contains phytoestrogens. Not effective alone but appears to be helpful with other herbs (ie ginseng)
- ◉ Evening primrose oil - not shown to be effective but more studies needed
- ◉ Ginseng - mixed
+wellbeing, - hotflashes
- ◉ Green tea, black tea, and oolong tea may be helpful

SUPPLEMENTS/HERBS (CONT'D)

- ◉ Hops - estrogen like activity - may help
- ◉ Milk thistle - no clinical trials
- ◉ Pomegranate - no clinical trials
- ◉ Rhubarb (rhaponticin, extract ERr731, Phytoestrol) - may help hot flashes
- ◉ Sage - one study showed significant improvement in hot flashes

SUPPLEMENTS/HERBS (CONT'D)

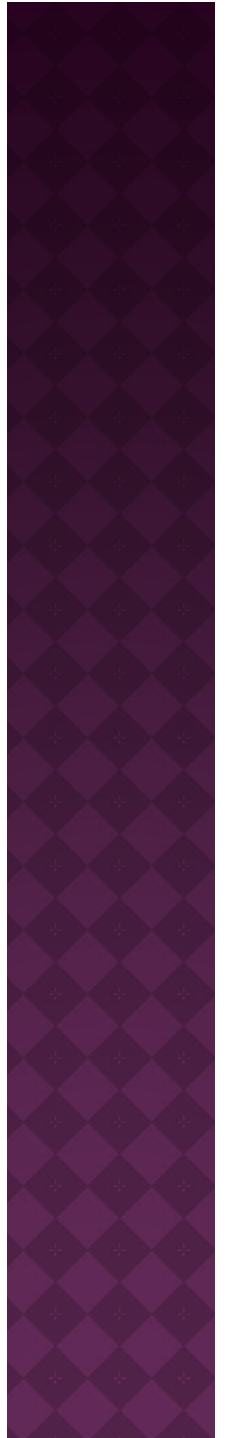
- ◉ S-adenosylmethionin (SAME) - no information on menopausal symptoms
- ◉ St. John's Wort - not enough information, interacts with metabolism of other drugs
- ◉ Valerian root- mixed
- ◉ Vitex/Chasteberry - mixed
- ◉ Wild Yam - ineffective

SUPPLEMENTS (CONT'D)

- ◉ Look for products with the US Pharmacopeia Verified Mark. USP sets standards for quality, purity, identity, and strength of medicines, food ingredients and dietary supplements.
- ◉ www.ConsumerLab.com This company performs independent testing at the manufacturer's request and expense.
- ◉ Botanicals are more tightly regulated in Europe and products from Germany, Switzerland and the United Kingdom offer more consistent quality.

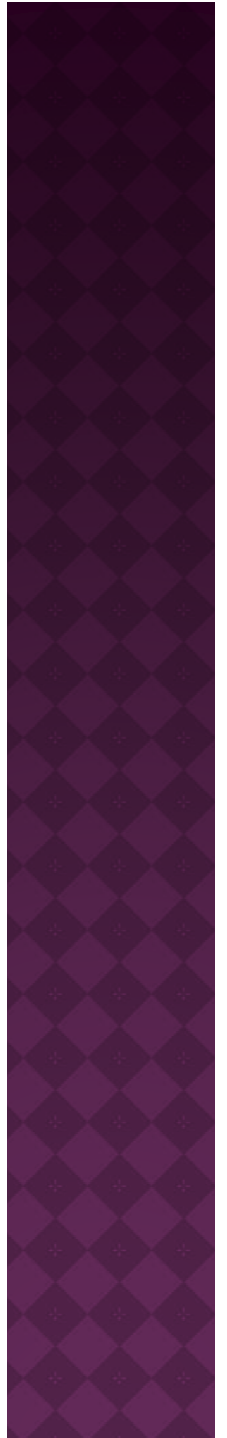
ACCUPUNCTURE

- ◉ Mixed results (poor quality trials , 1 trial showed it to be effective).
- ◉ Accupuncture appears to be helpful for menopausal symptoms when used in addition to other interventions.



NON-HORMONAL VS HORMONAL TXS

- Protective, neutral, or adverse effects of hormones depend on:
 - Time of initiation
 - Type of hormone(s)
 - Duration of treatment
 - Dose
 - Route (transdermal, oral, vaginal)
 - Baseline body composition/health
 - Baseline physical activity/fitness
 - Symptoms you are treating
 - Personal/family history of breast cancer, osteoporosis, blood clots, etc.



NON-HORMONAL PHARMACEUTICALS

- The Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin-norepinephrine reuptake inhibitor (SNRIs), clonidine, and gabapentin trials provide evidence for efficacy.
- However, effects are less than for estrogen (which reduces the frequency of hot flashes by ~75% in most patients).
- Individualize treatment options:
 - High blood pressure?
 - Depression/anxiety?
 - Insomnia?
 - Pain?

NON-HORMONAL PHARMACEUTICALS

- ◉ Serotonin-norepinephrine reuptake inhibitor (SNRIs):
 - Duloxetine (Cymbalta)
 - Venlafaxine (Effexor, Effexor XR)
 - Desvenlafaxine (Pristiq)
- ◉ Selective Serotonin Reuptake Inhibitors (SSRIs):
 - Fluoxetine (Prozac)*
 - Paroxetine (Paxil)*
 - Citalopam (Celexa)
 - Escitalopram (Lexapro)

*can effect how tamoxifen is metabolized and thus decrease its effect.

NON-HORMONAL PHARMACEUTICALS

- Hot flashes are thought to be partly due to excess norepinephrine
- Clonidine reduces norepinephrine and is used to treat hypertension.
- Studies on clonidine for the treatment of hot flashes have been mixed.
- It reduces hot flashes by ~1 hot flash per day.
- Side-effects:
 - dry mouth, insomnia, drowsiness.
 - It does not cause hypotension at doses to treat hot flashes.

NON-HORMONAL PHARMACEUTICALS

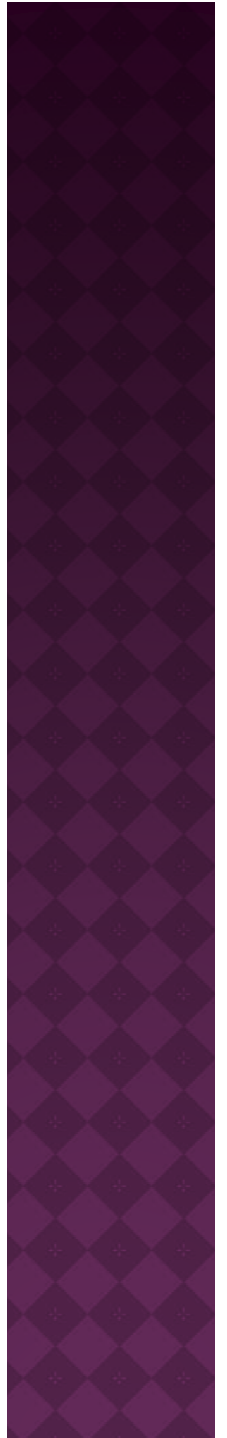
- ◉ Gabapentin binds to calcium channels in the brain's thermoregulatory center
 - This is thought to make the thermostat less sensitive and decreases hot flashes
- ◉ Gabapentin (neurontin) 900 mg/d reduced hot flash frequency 45% vs 29% for placebo.
- ◉ ~-1 hot flash per day
- ◉ Side-effects:
 - Somnolence, fatigue, dizziness, rash, heart palpitations, and peripheral edema.

NON-HORMONAL PHARMACEUTICALS

- Lunesta (eszopiclone)
- Helped with:
 - Sleep onset
 - Anxiety
 - Mood
 - Night time hot flashes (-1.5)
- Not thought to be due to direct effect on hot flashes but reduces reports because the women slept through them!

CONQUERING MENOPAUSE

- Perspective/Culture/Environment
 - Behavior: stress management
 - Lifestyle: diet, exercise
 - Supplements/herbs
 - Accupuncture
 - Non-Hormonal Pharmaceuticals
 - Hormonal treatments
-
- No one else is quite like you!
 - Your treatment plan must be customized for you as an individual.





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