Objectives
At the end of this lecture, the attendee will:
1. List two common menopausal symptoms women experience
2. List one difference in oral versus transdermal estrogen therapy from the KEEPS trial
3. Discuss the current risks and benefits of hormone therapy for women in the early post menopause
4. Discuss treatment options for vasomotor symptoms including oral and transdermal estrogen

Disclosures
Advisory Board: Hologic
Advisory Board: LabCorp

An Historical Perspective on Hormone Therapy
From where have we come?

Hormone Therapy: Historical Perspective
> 1920’s: Estrogen isolated from the urine of pregnant women and made available
> 1940’s: Ayerst, a Canadian drug maker found a way to make it from pregnant mares and called it “Premarin”
> 1950’s: Massive campaign to promote Premarin as a rejuvenating agent and mood stabilizer for postmenopausal women
  – Premarin ads frequent in medical journals

> Mid 1960’s: Approximately 12% of postmenopausal women were taking estrogen
> 1975: New England Journal of Medicine published 2 studies showing that women taking estrogen had as much as 14 times the risk of endometrial cancer as women not on the drug
> Progestogen was added when women had a uterus
> 1992: Premarin was the most widely prescribed drug
Hormone Therapy: Historical Perspective

> 1998: Heart and Estrogen/Progestin Replacement study
  – Found that women who already had heart disease did not have prevention of MI’s
> Women’s Health Initiative (WHI)
  – Designed to answer the question of long term hormone therapy and prevention of heart disease
  – 2002: Prempro arm stopped early

The Study That Changed Everything!
What Have We Learned in more than 15 Years?!

1998 and 2002: Results from 2 large randomized controlled trials:
> The Heart and Estrogen/Progestin Replacement Study (HERS): a secondary prevention study
> The Women’s Health Initiative (WHI): a primary prevention study

Changed the widely accepted belief that hormone therapy was protective against cardiovascular disease!


Panic ensued….

> Increased risk of breast cancer
> Increased risk of cardiovascular disease (CHD)
> Increased risk of stroke
> Increased risk of pulmonary embolism (PE)

Change in Practice

> Women stopped taking hormone therapy
> Practitioners stopped prescribing hormone therapy
> Women who wanted hormone therapy couldn’t always get prescriptions
> Confusion increased further with the marketing of so called, “safer” and “bioidentical” products in the marketplace

Kronos Early Estrogen Prevention Study (KEEPS)

Effects of Oral Conjugated Estrogens vs. Transdermal Estradiol on Common Carotid Artery Intima Media Thickness (CIMT) and Coronary Artery Calcium (CAC)

First data reported: October 3rd, 2012

What About KEEPS?
What recent data has continued to change practice?
KEEPS

4-year randomized, double-blinded, placebo-controlled clinical trial of low-dose oral or transdermal estrogen and cyclic monthly progesterone

> Inclusion
  – Healthy women ages 42 to 59 (mean age 52)
  – Within 3 years after menopause

> Excluded women with evidence of cardiovascular disease

Key Goal of KEEPS

> To compare two formulations of hormones
  – Low dose oral conjugated estrogens
  – Transdermal estradiol
  – Both with cyclical micronized progesterone

> Both studied over 4 years in relationship to:
  – Atherosclerosis progression by noninvasive imaging
  – Carotid intima-media thickness
  – Coronary artery calcium

Main Differences in KEEPS From WHI

> WHI:
  – Mean age 65
  – More than 12 years past the onset of menopause

> KEEPS
  – Average age 52
  – Within 3 years of final menstrual period

> Doses, formulations and routes of delivery of hormones were different

> KEEPS trial much smaller with 727 women enrolled

What Are Some Concerns About WHI?

> WHI did change the approach of recommending hormone therapy as a prevention of cardiovascular disease for older women… BUT…

> The results were often extrapolated to newly menopausal women who were considering hormone therapy for distressing symptoms

Key Findings of KEEPS

> Favorable effects of estrogen in newly menopausal women
  – Reduction in vasomotor symptoms
  – Improvement in several parameters of sexual function
  – Improvement in bone mineral density
  – Oral estrogen: improvement in mood outcomes with decrease in depressive symptoms, anxiety and tension

> No significant increase in adverse events!

Key Differences Between Oral and Transdermal Therapy

> Oral
  – Benefits for mood, depressive symptoms, anxiety and tension
  – LDL lowering and HDL increase
  – Subset of women with low cardiovascular risk
    • Cognitive benefit in terms of memory and verbal learning

> Transdermal
  – Greater reduction in insulin resistance
  – Improvement in libido-related aspects of sexual function
The Early VS Late Intervention Trial with Estradiol (ELITE)

- Included 643 Postmenopausal women
- Stratified according to time since menopause
  - < 6 years (Early postmenopause)
  - ≥ 10 years (Late postmenopause)
- Randomized to either 17 Beta Estradiol (1mg per day), plus progesterone (45mg) vaginal gel administered sequentially (for women with a uterus) and with placebo (for women without a uterus)

Primary outcome
- Rate of change in carotid-artery intima-media thickness (CIMT)
  - Measured every 6 months

Secondary outcome
- Assessment of coronary atherosclerosis by cardiac computed tomography (CT)

Women's Health Initiative and All-cause Mortality

Subgroup analyses in the Women's Health Initiative
- Showed that women in their 50's tended to do better for heart disease and all-cause mortality and global index than women who were older
- Reassuring news for women in early menopause who are are considering hormone therapy for vasomotor symptoms
  - Absolute risk of adverse cardiovascular events in women close to menopause are low
  - All cause mortality effects are neutral or even favorable for younger menopausal women

It's Time to Rethink, Reboot and Review: Hormone Therapy
Advocacy for women to live with quality
Different Approaches: Individualization of Care....

Disclaimer: Presenting an approach that supports evidence based practice and position statements for practice:

“One goal of The North American Menopause Society (NAMS) is to develop position statements and other reports about clinical issues pertinent to women at midlife and beyond.”

Perimenopause

> The time around the FMP, also called “the menopause transition”
> Begins with variation in the menstrual cycle length
> Associated with a rise in follicle-stimulating hormone (FSH) and ends 1 year after the FMP
> Often the most symptomatic phase for women

What is menopause?

> Menopause is a normal, natural event, defined as the final menstrual period (FMP), confirmed after 1 year of no menstrual bleeding
> Represents the permanent cessation of menses resulting from loss of ovarian follicular function, usually due to aging

When Is Menopause?

> Naturally (spontaneously) average age 51
> Prematurely from medical intervention (eg, bilateral oophorectomy, chemotherapy, radiation)
> At any time from impaired ovarian function
> Premature menopause occurs before age 40

Serum Hormone Levels At Menopause

1. Circulating estrogens
2. Ratio of estrogen to androgen
3. Sex hormone-binding globulin secretion
4. Peripheral aromatization of DHEA to estrone
5. Reversal of estradiol (E₂) to estrone (E₁) ratio
6. No significant change in testosterone levels
Standardization of Stages of Menopause

Stages of Reproductive Aging Workshop (STRAW)

In 2001, the Stages of Reproductive Aging Workshop (STRAW) established a nomenclature for reproductive aging.

In 2011, STRAW+10 updated and modified the model.

What is the Problem?

Menopause Symptoms

Menopausal symptoms & signs

Classic symptoms:
> Change in menstrual cycle pattern (during perimenopause)
> Vasomotor symptoms (hot flashes & night sweats)
> Vulvovaginal symptoms, dyspareunia
> Sleep disturbances

Other symptoms sometimes associated with menopause:
> Cognitive concerns (memory, concentration)
> Psychological symptoms (depression, anxiety, moodiness)
> There is no one universal menopausal syndrome

Managing Menopausal Symptoms

In the Age of KEEPS
Vasomotor Symptoms
Hot Flashes & Night Sweats

Frequency
- As many as 75% of perimenopausal women in US report hot flashes
- Number of episodes vary
- Few to multiple episodes daily
- Highest occurrence during perimenopause and first 2 years of postmenopause

Mechanism of Hot Flashes
- Estrogen levels are **EQUAL** in symptomatic and asymptomatic women
- Estrogen levels alone **NOT** predictive of hot flash frequency or severity
- **NOT** caused by pulses of LH
- Perimenopause often much worse than postmenopause
- FSH ↑'s 2 years prior to FMP = ↓ E₂

Thermoneutral Zone
Tc = core body temperature; HF = hot flash

Hot Flash Hypothesis
- Women with no hot flashes have wider TNZ than women with hot flashes¹
  - Includes women in peri and post menopause
- Tiny ↑ in Temp leads to hot flash
- A rise of 0.05 °C leads to 70% of hot flashes in the lab²
- Lowered Estrogen levels narrow the TNZ

Treatment of Hot Flashes
- **Treatment based on symptom severity, a woman’s risk factors, and her personal preferences**
- **Serum estrogen levels are not predictive of hot flash frequency or severity**
- Many government-approved formulations of HT
- Off-label use of various non hormonal prescription therapies and various dietary supplements and complementary and alternative options
COGNITIVE CONCERNS

There is evidence that psychomotor speed and to a lesser extent verbal memory can decline slightly in perimenopause. Although depression and anxiety are related to cognitive decline, neither mood nor age account for these cognitive changes experienced by some women. Any transient issue with cognition appears to resolve after menopause.

Cognitive changes

VULVOVAGINAL SYMPTOMS

Symptoms such as vaginal dryness, vulvovaginal irritation/itching, and dyspareunia are experienced by ~10%-40% of postmenopausal women. Unlike vasomotor symptoms, which abate over time, vaginal atrophy can be progressive and is unlikely to resolve on its own. Treatments include: regular sexual activity, lubricants and moisturizers, and local vaginal estrogen.

Vulvovaginal symptoms

MENOPAUSAL HORMONE THERAPY

PERIMENOPAUSE

GENITOURINARY SYMPTOMS OF MENOPAUSE: GSM

Treatments include: regular sexual activity, lubricants and moisturizers, and local vaginal estrogen.

Hormonal Management of Perimenopause

Oral Contraceptive
- Treat menorrhagia
- Treat anovulatory bleeding
- Contraception
- Prevention of bone loss
- Treat vasomotor symptoms
- Increase DVT/PE

Transition Off Hormonal Contraception or to HRT
- Should be done as soon as is appropriate
- Consider a women’s need for contraception when making this transition
- Timing of discontinuation or switch is often difficult
  - Cessation of menses is not observed

BEWARE THE SPORADIC OVULATION OF THE PERIMENOPAUSAL WOMAN!

Transition Off Hormonal Contraception or to HRT
- Some clinicians choose age 51: median age of menopause
- Some choose 53 to cover those women who reach menopause later than the average age
- Measure of FSH
  - Off hormonal contraception for 2 weeks prior to measurement, with non-hormonal contraception
  - If FSH level is consistently above 30mIU/mL, menopausal and transition can be safely made
- Hormonal method may be held, with non-hormonal contraception and observation for menses

MENOPAUSE AND POSTMENOPAUSE

Menopause Management
- There is no indication for hormone measurements for determining management
- Management is based on severity of symptoms
- Hormone therapy decisions are not based on levels of hormones from any measurement such as saliva testing
- There is no benefit in using potions and lotions of non FDA approved products!
- KEEPS addresses some differences in oral versus transdermal therapy

Bioidentical hormones
- Many well-tested, government-approved HT products contain bioidentical hormones
- Usually refers to compounded formulations
- Compounded HT not tested for efficacy, safety, batch standardization, or purity
- Some compounders make unsubstantiated claims about safety and effectiveness

NAMS Menopause 2012;19:257-71
American College of Obstetricians and Gynecologists (ACOG)

> Because such preparations have not been rigorously tested, only FDA-approved HT formulations are recommended.

NAMS Practice Pearl

What Are the Concerns About Custom-Compounded “Bioidentical” Hormone Therapy?

Released August 8, 2014

JoAnn V. Allen, M.D., NCMP
(University of Virginia Health System, Charlottesville, VA)

Bioidentical hormones, a marketing term not recognized by the US Food and Drug Administration (FDA), refers to estrogen hormones biochemically similar to those produced within the body and includes 17p-estradiol (predominantly estrogen from menopause), estrone (predominant estrogen after menopause), estriol (from placenta), progesterone (ovaries, placenta, and adrenal glands), testosterone (ovaries and adrenal glands), and their conjugates. These are not FDA approved.

Use of Hormone Therapy

Estrogen/Progestogen (EPT)
Estrogen (ET)

A Decade After The Women’s Health Initiative—The Experts Do Agree

This statement was published in the journals of The North American Menopause Society (Menopause), the American Society for Reproductive Medicine (Fertility and Sterility), and The Endocrine Society (Journal of Clinical Endocrinology and Metabolism)

*Report of the study follows in blue


Five Major Points of Agreement

For younger women

> HT is an acceptable option for treating moderate to severe menopausal symptoms in relatively young (up to age 59 or within 10 years of menopause) and healthy women
> Individualization is key in the decision to use HT

Women With Vaginal Symptoms Only

> The preferred treatments are low doses of vaginal estrogen

Women with a uterus

> Women who still have a uterus need to take a progestogen (progesterone or a similar product) along with the estrogen to prevent cancer of the uterus
> Women who have had their uterus removed can take estrogen alone

Risk of blood clots/stroke

> Both estrogen therapy and estrogen with progestogen therapy increase the risk of blood clots in the legs and lungs
> Although the risks of blood clots and strokes increase with either type of HT, the risk is rare in the 50-59-year-old age group

Risk of breast cancer

> An increased risk in breast cancer is seen in 3-5 years of continuous estrogen/progestogen therapy
> The risk decreases after HT is stopped

Living Life is a Continuous Risk/Benefit Analysis

This is no different in helping women make decisions regarding hormone therapy!

Shared Decision Making

Advocacy for helping women make informed choices
The Nuts and Bolts
Of Hormone Therapy

Your Treatment Algorithm
> How bothersome are symptoms to her?
> Preference - non-hormonal, hormonal or step approach?
> Years since LMP (5 or more? No hormones)
> Risk factors? DVT, Migraine with Aura?
> Risks and benefits

Considerations
> Clinician preference:
  – Start low and work up?
  – Mid-range? Titrate up or down
> Pt preference for frequency? Ease of use? Remembering to take/change
> Anticipatory Guidance for expected side effects, bleeding, when to call

Practical Pearls for Prescribing HT
> Oral estrogen
  – Increases triglycerides by 15%
  – Increases HDL by 10%
  – Decreases LDL by 10%

Practical Pearls for Prescribing HT
> If transdermal is used for hormone therapy, oral progesterone may be used at HS
> Combination estrogen/progestin patch available
> Start low and increase dose as necessary???
> Start average dose and decrease as symptoms come under control???
> Two products= two copays!!
> Generic products for transdermal patch, oral estrogen and combined estrogen/progestin

Estrogen Therapy
Estrogen/Progestogen Therapy
Primary indication for ET/EPT is to treat moderate to severe menopause symptoms (vasomotor)
> When symptoms are controlled or cease, may be continued though risks and benefits must be weighed
> Approved for prevention but not treatment of osteoporosis
> NAMS and ACOG recommend use of ET/EPT at the lowest effective dose for the shortest time period consistent with treatment goals
Practical Pearls for Prescribing HT

> Route of estrogen impacts risk of thromboembolic events, though data is not extensive
  - Oral estrogen has a first pass through the liver
    - May increase the risk of blood clot compared to transdermal
  - Transdermal estradiol had a 30% lower incidence of VTE than those who took oral estrogen only in a study reported in 2011.

Protect the Endometrium

> Unopposed Estrogen causes an 8 fold increase in the risk of endometrial hyperplasia
> Add progestogens to the cycle
  - Daily
  - Cyclic
  - IUDs – haven’t been studied as extensively

EPT Regimens

> Systemic progestogen required for endometrial protection
> Multiple approved dosing options available
> Current data support minimizing progestogen exposure
> Insufficient evidence regarding endometrial safety to recommend:
  - Off-label use of long-cycle regimens
  - Vaginal administration of progestrone
  - Levonorgestrel-releasing intrauterine system
  - Low-dose estrogen without progestogen

Progestogen Regimens

> Progestosterone can not be absorbed by the skin
> Can be absorbed in Vagina
  - Crinone – Micronized progesterone
  - 4% twice weekly
> Oral medications
  - Prometrium = Bio Identical
  - Provera = Medroxyprogesterone Acetate
  - Aygestin = Norethindrone

Progestin Regimens

> Daily oral reduces BTB
> No need to cycle for menses
> Progestogen must be at least 12 days/month
> Little data to support q 3 month use
  - Is associated with more BTB

Dosage of Hormone Therapy

> Improvement of vasomotor symptoms from low-dose and ultra-low dose preparations:
  - Not as well studied as standard-dose
  - May improve symptoms in many women, though not as effective as standard dose
> Recommended that health care providers individualize care
> Treat with lowest effective dose for the shortest duration
**Dosage of Hormone Therapy**

> **Standard Dose**
> - Conjugated estrogen 0.625mg/d
> - Micronized estradiol-17 Beta 1 mg/d
> - Transdermal estradiol-17 Beta 0.0375-0.05

> **Low Dose**
> - Conjugated estrogen 0.3-0.45mg/d
> - Micronized estrogen-17Beta 0.5mg/d
> - Transdermal estradiol-17Beta 0.025mg/d

**Dosage of Hormone Therapy**

> **Ultra-Low Dose**
> - Micronized estradiol-17Beta 0.25mg/d
> - Transdermal estradiol-17Beta 0.014mg/d

> **Estrogen combined with estrogen agonist/antagonist**
> - Conjugated estrogen 0.45mg/d and bazedoxifene 20mg/d
> - For post-menopausal women only. Do not add additional estrogens, progestogens, or estrogen agonists/antagonists.

**Dosage of Hormone Therapy**

> **Systemic HT, with estrogen alone or in combination with progestin, is the most effective therapy for vasomotor symptoms**

> **Low-dose and ultra-low dose systemic doses of estrogen are associated with a better adverse effect profile than standard dose and may reduce vasomotor symptoms in some women**

**Duration of Use**

> **Some experts recommend keeping duration of treatment short**
> - For many women vasomotor symptoms are a long term concern

> **Penn Ovarian Aging Study**
> - Median duration of moderate to severe VMS was more than 10 years
> - For many women, short-term use (3-5 years) will not be sufficient to control symptoms

**Duration of use (continued)**

> **Extending EPT use is acceptable for:**
> - Women who request it and are aware of its risks
> - Prevention of osteoporosis for women at high risk of osteoporotic fracture when alternate therapies are not appropriate
Duration of Hormone Therapy Use
NAMS 2012 Position Statement

“...extending EPT use with the lowest effective dose is acceptable under some circumstances, including for the woman who has determined that the benefits of menopause symptom relief outweighs risks, notably after failing an attempt to stop EPT”.

Use of HT to Treat Menopausal Symptoms: ACOG Guidance

“...ACOG recommends against routine discontinuation of systemic estrogen at age 65 years. As with younger women, use of HT and estrogen therapy should be individualized based on each women’s risk-benefit ratio and clinical presentation.”

Continuation of Hormone Therapy

> Requires individualized assessment of HT benefits and risks
> Shared decision making

Discontinuation of Systemic Therapy

> VMS may recur in as many as 50% of women
> Does not appear to vary between abrupt and tapered discontinuation
> Women may be reluctant to reduce their dose or to stop therapy
> Recommend a 3 month trial off with the understanding that therapy could be restarted

Age and Hormone Therapy
Is 65 too old to continue??

NAMS Statement and Writetiel on Continuing Systemic Hormone Therapy After Age 65


In response to the continuing inclusion of systemic HT on the NAMS list, NAMS states:

* HT is the most effective treatment for symptoms of menopause
* HT is the only treatment that can reduce the risk of osteoporosis and fracture
* HT is the only treatment that can reduce the risk of cardiovascular disease
* HT is the only treatment that can reduce the risk of colon cancer
* HT is the only treatment that can reduce the risk of Alzheimer's disease
* HT is the only treatment that can reduce the risk of dementia
* Use of HT should be individualized and not discontinued based solely on a woman's age

Because of the lack of alternative treatments that are not on the NAMS list, exceptions should be made in terms of quality of care metrics for menopausal women, as this care recommendation should be placed in the “Use with caution” category.
American College of Obstetricians and Gynecologists (ACOG)

Because some women aged ≥65 might still need systemic HT for VMS, HT should not be routinely discontinued at age 65, but, as in younger women, should be individualized.

ACOG Practice Bulletin 141

HT formulation, route of administration, and timing of initiation produce different effects

Individual benefit-risk profiles are essential

Absolute risks in healthy women ages 50-59 are low

Long-term use or HT initiation in older women, however, has greater risks

Breast cancer risk increases with EPT beyond 3-5 years

ET can be considered for longer duration of use due to its more favorable safety profile

Genitourinary Symptoms of Menopause

The Vulvovaginal symptoms

> Symptoms such as vaginal dryness, vulvovaginal irritation/itching, and dyspareunia are experienced by ~10%–40% of postmenopausal women
> Unlike vasomotor symptoms, which abate over time, vaginal atrophy can be progressive and is unlikely to resolve on its own
> Treatments include: regular sexual activity, lubricants and moisturizers, and local vaginal estrogen

2. Bachmann GA In: Treatment of the Postmenopausal Woman Philadelphia:

Loss of Estrogen

- Vagina loses elasticity, shortens, narrows, easily traumatized and irritated
- Loss of rugae, fornices become obliterated, cervix flush with vaginal vault
- Petechiae may be present
- pH greater than 5.0, parabasal cells dominate
- Repopulation with diverse vaginal flora leads to frequent UTIs
- Worse for women on chemo (tamoxifen, aromatase Inhibitors)

Vaginal Estrogens

- Low-dose, local, prescription vaginal ET products FDA-approved for vaginal atrophy
- 17β Estradiol Vaginal cream (Estrace)
- Conjugated EE vaginal cream (Premarin)
- Estradiol vaginal ring (Estring)
- Estradiol hemihydrate vaginal tablet (Vagifem)

Discuss the black box warning
Practical Pearls for Prescribing Vaginal Therapy

> Vaginal estrogen: Cream, ring and tablet
  – Cream may be less expensive
  – Ring is convenient and left in for 3 months before changing
  – Tablet is convenient and less messy
> Opposition of vaginal estrogen by progestin is not required

Treatment for Dyspareunia

Oral ospemifene 60mg
> FDA approved for the treatment of dyspareunia associated with vulvovaginal atrophy
> Estrogen agonist/antagonist (SERM)
> NAMS
  – The estrogen agonist/antagonist ospemifene is an oral agent for the treatment of moderate to severe dyspareunia due to GSM/VVA. (Level I)

(Level I based on good and consistent scientific evidence).

Intrarosa (Prasterone)

Vaginal DHEA for moderate to severe dyspareunia
> FDA approved 11/16
> Once daily vaginal insert
> Two 12 week trials showed reduction in the severity of pain during sexual intercourse compared to placebo
> Most common adverse reactions were vaginal discharge and abnormal Pap tests
> The product was not studied in women with breast cancer

Intrarosa (package insert). Quebec City, Quebec, Canada: Endoceutics Inc., 2016.

Fractional Laser Treatment for Vulvovaginal Atrophy

The North American Menopause Society (NAMS) and the American Congress of Obstetricians and Gynecologists (ACOG) agree:
> Further research is needed before this procedure can be recommend for treatment of VVA
> Although the technology is marketed as being FDA approved for broad indications, it is not cleared by the FDA for the specific indication of treating VVA.
Moisturizers & Lubricants

- Vaginal moisturizers – Non-hormonal, no prescription, attracts moisture to vagina, improves pH. Use 2-3 times/week for maintenance
- Lubricants – Water or silicon based, use with sex to help with gliding, also helps with arousal

Nonhormonal prescription options

- Nonhormonal prescription drugs (off-label use):
  - Antidepressant
    - SSRIs: fluoxetine, paroxetine, escitalopram
    - SNRIs: venlafaxine and desvenlafaxine
  - Hypnotic
    - Eszopiclone
  - Anticonvulsant
    - Gabapentin
  - Antihypertensive
    - Clonidine
  - Neuropathic pain drug
    - Pregabalin

Prescription Nonhormonal Remedies

- Selective serotonin reuptake inhibitors (SSRIs)
  - Fluoxetine
  - Paroxetine
  - Escitalopram
- Serotonin–norepinephrine reuptake inhibitors (SNRIs)
  - Venlafaxine
  - Desvenlafaxine

None of the above are government approved for hot flashes, so use would be considered off-label

FDA Approved Non-Hormonal Treatment

Paroxetine 7.5 mg capsule
- Low dose SSRI
- Indication: Used to treat moderate to severe hot flashes of menopause
- Most common side effects
  - Headache, nausea, vomiting

Non-Hormonal, Non-Estrogenic Supplement

Relizen
- Swedish flower pollen extract product
- Randomized, double-blind, placebo controlled trials show significant reduction in hot flashes and improved “quality of life” parameters
- No estrogenic effects
- Does not show inhibition of the CYP2D6 enzyme which is necessary for tamoxifen metabolism
Yoga

> Regular yoga practice did not show any improvement in HF or NS
  - No difference at baseline, 3, 6 and 12 weeks
> 249 women randomized
> Did show improvement for insomnia
> Other studies have shown about a 36% reduction about the same as placebo

Newton, KM. Menopause, 2014.

Acupuncture

> Multiple RCTs with various study designs have shown efficacy in reduction of HF and NS of 35-70%
> Is it possible that Acupuncture reduces neural activity in the hypothalamus and helps regulate temperature
> A systematic review did not show any benefit over sham acupuncture
  - 6 trials reviewed did not show any benefit

Lee, MS et al. Climacteric, 2009

Case #1

45 yo non-smoker, healthy, normal weight, normal blood pressure, normal lipid profile, has been on birth control pills for twenty years. She is sexually active and requires birth control. She sees you for her annual well woman visit.

Will you continue her birth control pill?

Case #2

54 yo c/o severe hot flashes both day and night. She is a non-smoker, BMI 28. F.H. Mother: osteoporosis, on Benicar 40 mg a day for HTN. Lipids: Mild elevated LDL, Low HDL

Is she a candidate for HT? Would you suggest oral or transdermal? What about endometrial protection? Would you start at the average, middle or lowest dose of therapy? What is the patient’s desire?

Case #3

63 yo smoker, has HTN, obesity, and type 2 diabetes. c/o trouble sleeping, mood concerns and a few hot flashes a day.

Is she a candidate for hormone therapy? Would you offer other therapy for her menopausal symptoms? What is her risk for endometrial cancer, osteoporosis?
Case #4

58 yo with severe day and night time hot flashes. She has a BMI of 32, exercises regularly, has normal blood pressure. She had a hysterectomy for fibroids and excessive bleeding at age 45. History of metabolic syndrome with insulin resistance.

Is she a candidate for hormone therapy? What route of therapy would you recommend? Would you start with an average, middle or low dose of estrogen?

Case #5

59 yo woman with c/o severe vaginal dryness and dyspareunia. She has occasional hot flashes, but does consider them manageable.

What therapy would you recommend? Would you offer vaginal cream, ring or tablet insert? Would you prescribe progesterone?

Case #6

69 yo patient is new to your practice. She has been on estrogen and progestin therapy for 20 years. She is on a statin and one medication for HTN. She states that she has tried stopping the hormones, but she is not willing to tolerate the severity of her hot flashes.

Will you continue to prescribe her HT? What will you tell her about risk and benefit? What about long term use?

Menopause Management

> Hormone therapy appears to have favorable effects on symptom management and quality of life in newly menopausal women
> Individualization of care is important
> There may be some advantages of transdermal therapy for some women and advantages of oral therapy for others
> Clinical decisions should be based on:
  - The woman’s symptoms
  - Underling risk factors
  - Personal preferences
  - Priorities for treatment

Conclusion: NAMS 2016 HT Position Statement

“Decisions about duration of HT require individualization, including consideration of personal preferences, balancing potential ongoing benefits and risks, and decisions to continue HT for preventative and/or quality of life purposes”

Shared decision making helps our patients make sound choices

QUESTIONS?
References

- Harlow SD Menopause. 2012;9;276.7-23.
- Riedel-Baima B1, Riedel A. Female pattern hair loss may be triggered by low oestrogen to androgen ratio. Endocr Regul. 2008 Mar;42(1):13-6.