Menopause Management Update

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OBJECTIVES

- Describe theories of the mechanisms for vasomotor symptoms
- Elucidate algorithms for approaches to screening and treatment options
- Summarize the current guidelines for shared decision making for treatment approaches
- Describe the Over The Counter and pharmacologic treatment options for the menopausal transition

Menopause

- Normal & Natural Event
- Average age: 51
- Final menstrual period (FMP) = absence of menses for 12 consecutive months
- Permanent end of fertility
- Elevated FSH, Lowered Estradiol ($E_{2)}$ levels

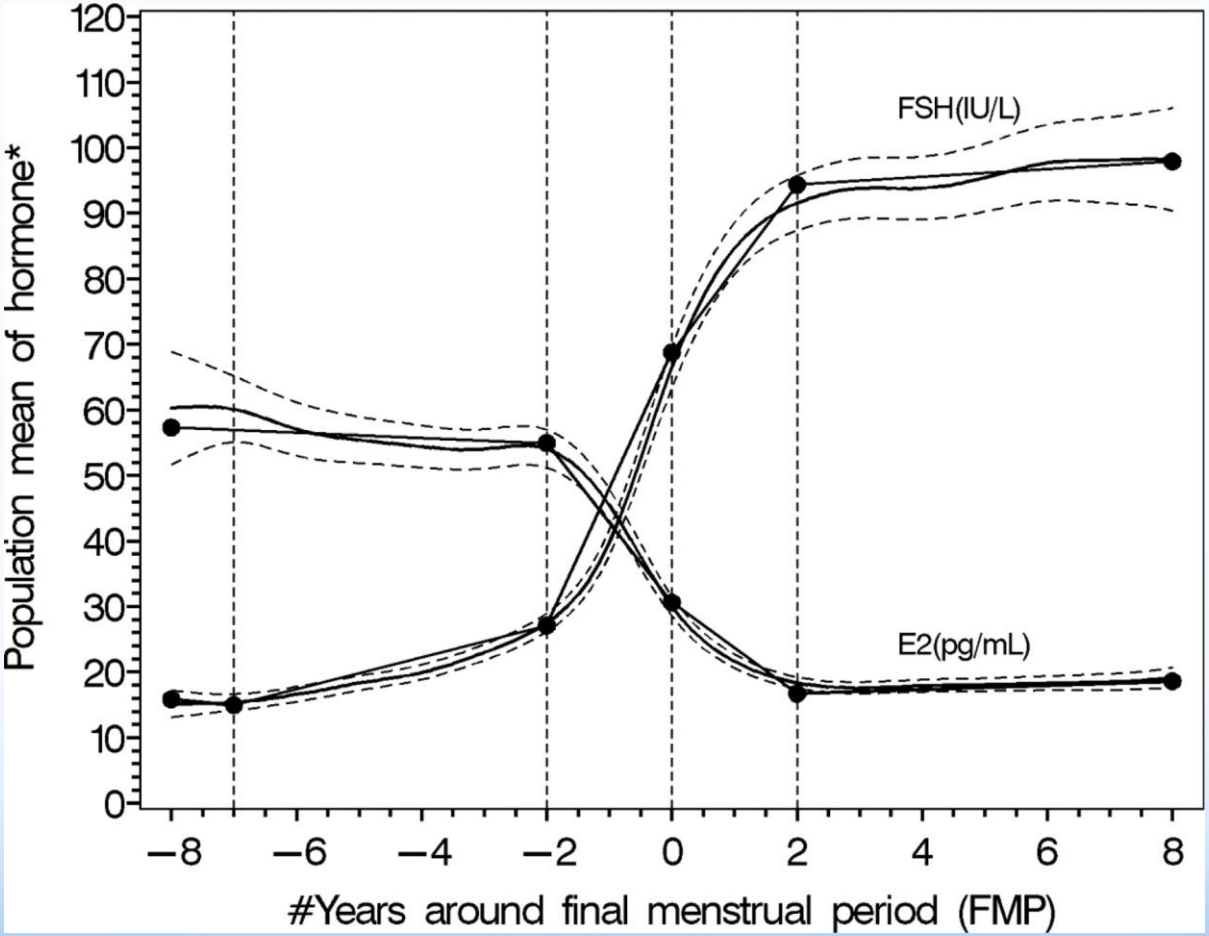
North American Menopause Society, 2017

There is no 1 universal menopausal syndrome

- Altered menstrual cycles in perimenopause
- Vasomotor symptoms = HF & NS
- Vulvovaginal symptoms, dyspareunia, low libido (60%)
- Sleep disturbances (80%), Weight gain (34%)
- Cognitive concerns (memory, concentration)
- Psychological symptoms (depression, anxiety, moodiness) (31%)

North American Menopause Society, 2017
Praire, B et al. *Journal of Women's Health*, 2014

Changes in Estradiol & FSH



* Harlow SD *Menopause* 2012;19:387-95 (reproduced with permission from Randolph JF *JCEM* 2011;96:746-54)

NAMS
The North American Menopause Society

Serum hormone levels at menopause

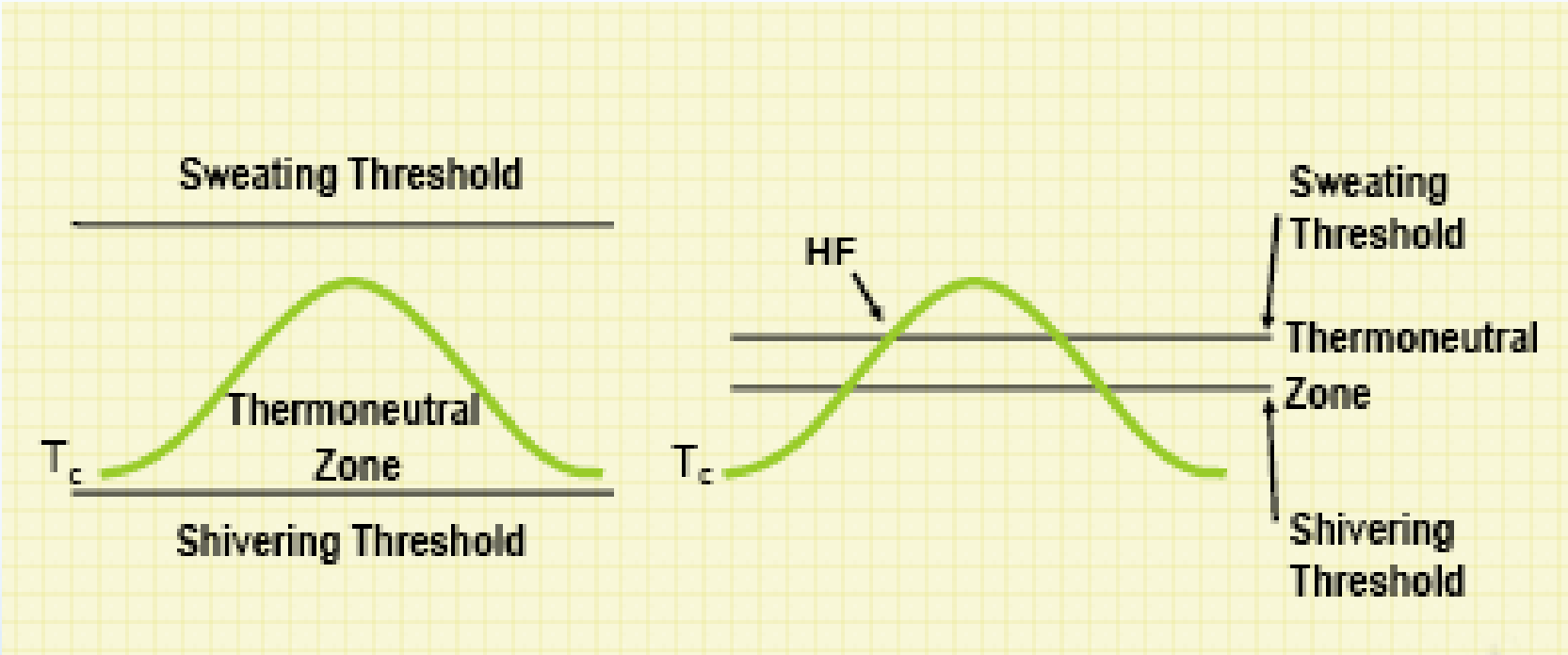
- ⬇ Circulating estrogens
- ⬇ Ratio of estrogen to androgen
- ⬇ Sex hormone-binding globulin secretion
- ⬆ Peripheral aromatization of DHEA to estrone
- ⇄ Reversal of estradiol (E_2) to estrone (E_1) ratio
- ↔ No significant change in testosterone levels

Mechanism of Hot Flashes & Night Sweats

- Estrogen levels are ***EQUAL*** in symptomatic and asymptomatic women
- Estrogen levels alone ***NOT*** predictive of hot flash frequency or severity
- ***ARE*** caused by pulses of LH
- Perimenopause often much worse than postmenopause
- FSH ↑'s 2 years prior to FMP = ↓ E_2

Prague, J K, et. al, *The Journal of Clinical Endocrinology & Metabolism,* 2019

Thermoneutral Zone



Tc = core body temperature; HF = hot flash

Freedman RF. *Semin Reprod Med*. 2005.

Hot Flash Hypothesis

- Women with no hot flashes have wider TNZ than women with hot flashes[1]
  - 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 lab[2]
- Lowered Estrogen levels narrow the TNZ

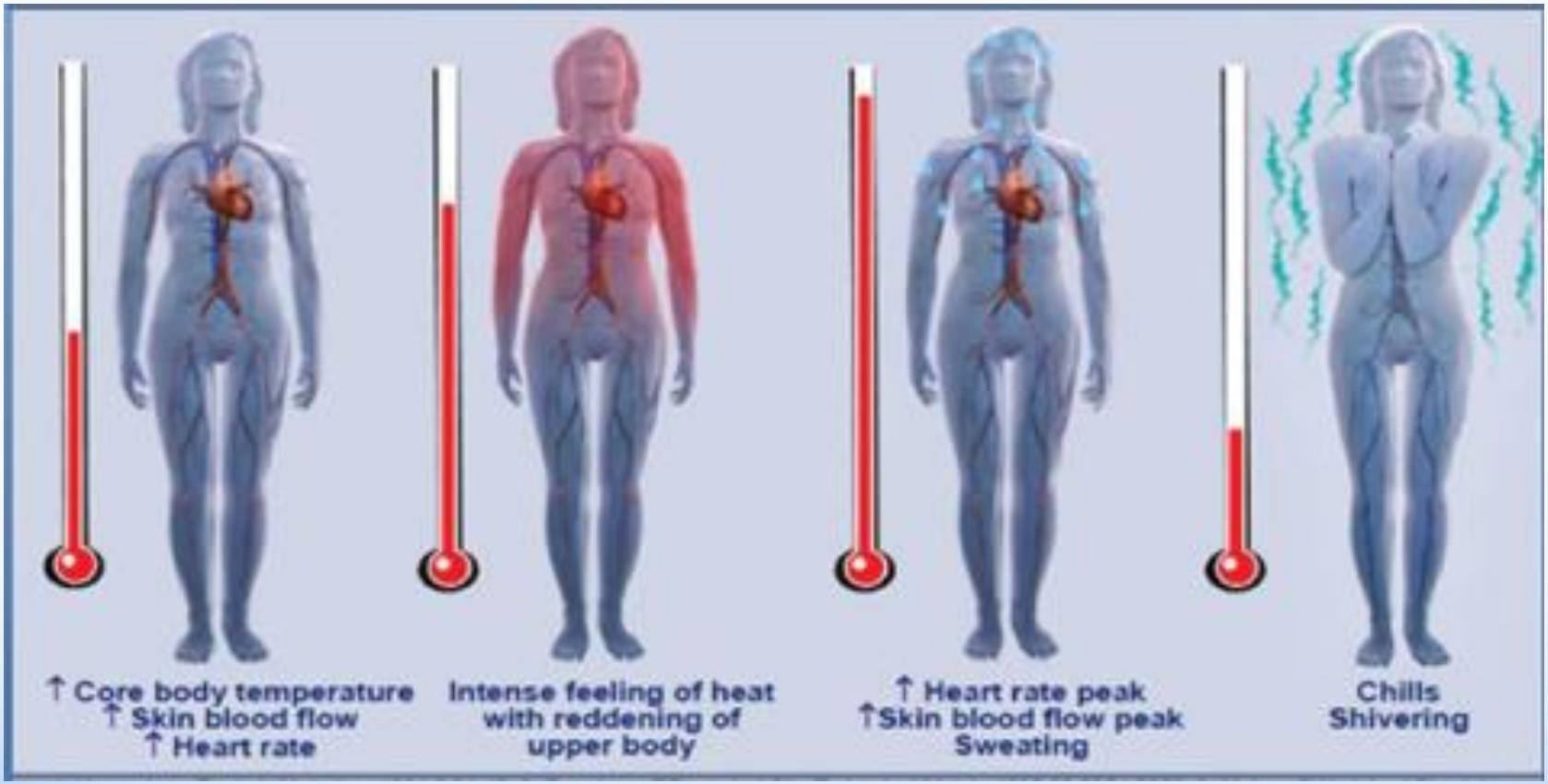
Freedman RF. *Semin Reprod Med*. 2005.

Hot Flash Triggers

- Warm environment, hot drinks, spicy food, cigarette smoking, alcohol
- Disease conditions including thyroid disease, autoimmune disorders, anxiety
- Hot showers, warm clothes
- Higher BMI
- Any level of Stress

Freeman, EW et al. *Obstet Gynecology,* 2011.

Anatomy of a hot flash



1. Kronenberg F. Ann N Y, *Acad Science,* 1990.
2. Freedman RF. *Semin Reprod Med*. 2005.

Focus on Quality of Life

- Hot Flashes & Night Sweats
- Sleep: Quality & Quantity
- Is she riding an emotional roller coaster?
- Fatigue
- Weight gain
- Cognitive changes
- Sexual & Urogenital symptoms
- Cardiovascular Concerns
- Bone loss

Estrogen Timing Hypothesis

- Younger, healthier women seem to do better
  - ***Reduced*** CV events if started *within* 10 years of FMP
  - *Increased* CV events if started 5+ years *after* FMP
- Oral Contraceptives OK until 55 (unless any contraindications)
- Improved quality of life across all measures
- Consider transdermal or newer oral bio-identicals to decrease risks

North American Menopause Society, 2017

Abrupt Menopause

- Women with Surgical Menopause or Premature Ovarian Failure Should be started on Hormone treatment until natural age of Menopause

North American Menopause Society, 2017

Combined Oral Contraceptives?

- Use in Perimenopause to smooth the hormonal transition
- Ok until 54 unless there are risk factors
- Lo Dose (20 mcg Estradiol)
- Reduces Night sweats, hot flashes, corrects anovulatory, irregular bleeding,

Oral Contraceptives

- Contraindications for women over 35:
- Smokers
- Migraine with Aura
- Hypertension
- Hx of clots
- Also consider: hyperlipidemia, diabetes, other risk factors for clots: family Hx, obesity

Menu of Treatment Options

- Do Nothing
- Yoga
- Accupuncture
- Soy & Flaxseed
- Other herbs
- Black Cohosh
- Relizen
- SSRIs, SNRIs, Gabapentin
- Hormones
  - Bio-Identical
  - Natural
  - Synthetic
  - Oral
  - Transdermal

Soy

- Differences in food, supplements and natural metabolite S-Equol
- Modest improvements in HF, NS
- Eating Soy foods - lower risk of breast and endometrial cancer in observational studies.
- Isoflavones – No improvement in BMD
- Substituting soy for animal protein can decrease total cholesterol and BP slightly.

Flaxseed

- Lignans are phytoestrogens
- No improvement in hot flashes or night sweats greater than what was seen with placebo
- Does help with GI issues

Herbs

- Dong Quai – no improvement over placebo
- Red Clover - no improvement over placebo
- Many Chinese herbalists use combinations that may be beneficial

Black Cohosh

- Does NOT exert estrogenic effects
  - No effects on FSH, LH, SHBG, Prolactin, E2
- Probably works on serotonin receptors
- Of 12 clinical trials, all but 1 showed improvement
- Postulated - some women have receptors and will improve

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 mixed results in reduction of HF and NS.
- 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

Relizen

- Deriative of flower pollen, non-allergenic
- May work as a mild SSRI
- No hormonal effects - No endometrial activity
- Sub pharmacologic levels of phytoestrogens
- RDB PCT of 54 women: 65% had decreased HF compared to 38% in control group
- Hot flash reduction of about 1/3 the # of HF, NS
- Dose: 2 per day

Paroxetine Mesylate

- Paroxetine Mesylate (*Brisdelle*) – only FDA approved SSRI
  - Molecule, dose & side effects different from Paroxetine Hydrochloride (*Paxil*)
  - 60% reduction in HF and NS
  - Improved sleep quality and other QOL
  - No sexual side effects
  - No weight gain

Brisdelle – Paroxetine Mesylate

- 7.5 mg at night
- Doesn’t induce sleep, however adds on average 30 extra minutes/night
- Reductions seen at 6 and 12 weeks
- Ok to use with Estrogen

SSRIs SNRIs & Gabapentin

- Other SSRIs and SNRIs are used off-label
- All have between 50-60% improvement
  - Sertraline, Venlafaxine, Desvenlafaxine
  - May work by increasing serotonin & by decreasing sympathetic response
- Gabapentin 300 mg/hs
  - Long acting Gabapentin 50% reduction in HF & NS, improves sleep

FDA-approved indications for hormone therapy

- First-line therapy for relief of vasomotor symptoms in appropriate candidates
- To prevent bone loss and reduce fractures in postmenopausal women at elevated risk of osteoporosis or fractures
- For women with hypogonadism, primary ovarian insufficiency, or premature surgical menopause without contraindication, hormone therapy is recommended for health benefits until the average age of menopause
- Low-dose vaginal estrogen therapy is recommended first line for isolated genitourinary syndrome of menopause to treat symptoms of vulvovaginal atrophy

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Differing risks of hormone therapy for women

- Depending on type, dose, duration, route of administration, and timing of initiation and whether a progestogen is needed
- Treatment should be individualized using best available evidence to maximize benefits and minimize risks
- Periodic reevaluation about the benefits and risks of continuing or discontinuing hormone therapy

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Endometrial protection

- For systemic estrogen, endometrial protection requires an adequate dose and duration of a progestogen or use of the combination conjugated equine estrogen with bazedoxifene (Level I)
- Progestogen therapy is ***NOT*** recommended with low-dose vaginal estrogen—1-year safety data
- Appropriate evaluation of the endometrium should be performed for vaginal bleeding (Level I)

The 2017 hormone therapy position statement of The North American Menopause Society. ***Menopause*****. 2017;24(7):728-753.**

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Concerns about compounded bioidentical hormone therapy

- Unique concerns about safety surround use of compounded bioidentical hormone therapy and it should be avoided
  - Lack of regulation and monitoring
  - Possibility of overdosing or underdosing
  - Lack of scientific efficacy and safety data
  - Lack of a label outlining risks
- No evidence to support use of routine serum or salivary hormone testing

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Hormone therapy and vasomotor symptoms

- Hormone therapy remains the gold standard for relief of vasomotor symptoms (VMS)
  - Estrogen-alone therapy is used for symptomatic women after hysterectomy
  - For symptomatic women with a uterus, combination therapy protects against endometrial neoplasia, either with a progestogen or a combination of conjugated equine estrogen and bazedoxifene
- The lowest dose that offers relief should be used and assessed periodically
- Progestogens relieve VMS
  - Micronized progesterone 300 mg nightly decreases VMS
  - Synthetic progestins have shown benefit
  - No long-term study results are available

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Hormone therapy, vasomotor symptoms, and sleep

- Hormone therapy is the most effective treatment for hot flashes
- During the menopause transition, women with hot flashes are more likely to report reduced sleep
- Hormone therapy improves sleep in women with bothersome nighttime hot flashes
  - Reduces nighttime awakenings
  - Improves duration, disruption, latency, and sleep cycles

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Hormone therapy and bone and joints

- Hormone therapy effectively prevents postmenopause osteoporosis and fractures
- Women in the estrogen-alone and estrogen-progestogen therapy overall cohorts in the Women's Health Initiative (WHI) had significant 33% reductions in hip fracture
- After treatment discontinuation in the WHI, beneficial effects on bone dissipated rapidly, but no rebound was seen
- Women in the WHI showed less joint pain or stiffness

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Trials of hormone therapy and coronary heart disease

- Meta-analysis of randomized, controlled trials (Boardman HM, et al. *Cochrane Database Syst Rev*. 2015.)
  - Hormone therapy initiated fewer than 10 years after menopause onset in postmenopausal women reduced coronary heart disease
    - Relative risk (RR), 0.52; 95% confidence interval (CI), 0.29-0.96
  - Significant increased risk of venous thromboembolism
    - RR, 1.74; 95% CI, 1.11-2.73
  - Death was significantly reduced
    - RR, 0.70; 95% CI, 0.52-0.95

Boardman Cochran Review 2015

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Hormone therapy and coronary heart disease: timing of initiation

- Hormone therapy (HT) represents a safe and effective option for the treatment of menopause symptoms when initiated in healthy postmenopausal women aged younger than 60 years or within 10 years of menopause onset
- The effects of HT on coronary heart disease may vary depending on when HT is initiated in relation to a woman's age and/or time since menopause onset

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Hormone therapy and stroke

- Meta-analyses of randomized, controlled trials
  - No increased risk if hormone therapy initiated within 10 years of menopause onset (observational trials mixed)
  - Increased risk in women more than 10 years from menopause onset
- In the Women's Health Initiative, increased risk with both conjugated equine estrogen + medroxyprogesterone acetate and conjugated equine estrogen alone in overall study cohort
  - Rare attributable risk if hormone therapy initiated in women aged younger than 60 years

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Low-dose vaginal estrogen and survivors of breast cancer with bothersome GenitoUrinary Syndrome of menopause (GSM

- Low-dose vaginal estrogen therapy (ET)
  - Minimal systemic absorption
    - Blood levels in postmenopause range
  - Based on limited data, minimal risk for recurrence of breast cancer (Level II)
- For survivors of breast cancer with bothersome genitourinary syndrome of menopause symptoms, low-dose vaginal ET may be an option
  - After a failed trial of nonhormone therapies
  - In consultation with an oncologist
  - Concern even with low-dose vaginal ET for women on aromatase inhibitors because of suppressed estradiol levels (Level III)

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Hormone therapy and prolonged duration

- Longer durations of therapy should be for documented indications such as persistent vasomotor symptoms or bone loss, with shared decision making and periodic reevaluation
- Good-quality information is lacking about prolonged duration with lower doses or transdermal products in women who initiate hormone therapy at younger ages or closer to menopause for risk of coronary heart disease or breast cancer
  - Risk may increase with longer durations of use or with age
- Recent observational data are positive
  - Finnish database (less coronary heart disease, no increased breast cancer)
  - May include healthy-user bias

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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No general rule to discontinue hormone therapy after age 65

- The recommendation to use the Beers criteria to routinely discontinue systemic hormone therapy after age 65 is not supported by data
- Decisions regarding whether to continue hormone therapy beyond the age of 60 years should be individualized
  - After appropriate evaluation
  - Counseling about potential benefits and risks
  - Ongoing surveillance (Level III)

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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The experts agree about hormone therapy

- Benefits are likely to outweigh risks for symptomatic women who initiate hormone therapy aged younger than 60 years or within 10 years of menopause onset (Level I)

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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The experts agree about who should not use hormone therapy

- For women who initiate hormone therapy more than 10 or 20 years from menopause onset
- Women aged 60 years and older, the benefit-risk ratio appears less favorable than for younger women
- Greater absolute risks
  - Coronary heart disease, stroke, venous thromboembolism, and dementia

The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24(7):728-753.

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Depression

Emotions – Increased rates of depression in women compared to men

In both women with previous hx and those without

- Aging and mortality issues
- Empty nesting
- Health and mobility
- Socio-economic
- Estrogen: Serotonin connection
- Sleep

Freeman, E W. *Women's Midlife Health*, 2015

Estrogen and Serotonins

- E2 increases the production of tryptophan – the precursor to serotonin
- E2 increases the amount of time serotonin stays in the synapse
- E2 Increases density, distribution of serotonin receptors
- E2 increases serotonin transporter sites

Why Women Seek Care

Photo purchased iStockPhoto

Weight Gain

- Seems to happen overnight
- Insulin resistance increases
- Increased deposition of abdominal fat
- Number of calories needed is drastically reduced
- Loss of skeletal muscle
- Need for more exercise - especially weight bearing

Why Women Gain Weight

- Change in BMR
- Change in Insulin Resistance
- Change in Abdominal Adiposity
- Lean muscle mass
- Same diet does not equal same weight

What can women do

- Decrease intake
- Increase exercise > 1 hour/day
- Intermittent Fasting
- Influence of GI Biome

Medications

- This *IS* the time to use them
- Phentermine -
- Belviq - Lorcaserin
- Qsymia – Phentermine/Topiramate
- Contrave – Naltrexon/Bupropion

Phentermine

- Sympathomimetic amine
- Schedule IV
- Suppresses appetite and increases BMR
- Side effects: Increased BP
- Dry mouth
- Nervousness
- Dizziness
- Sleeplessness
- Constipation

Indications

- Indicated for patients with initial (BMI) of:
- 30 kg/m2 or greater (obese) or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition:
  - hypertension, type 2 diabetes mellitus, or dyslipidemia

Belviq and Belviq XR- Lorcaserin

- 10 mg BID
- MOA – Serotonin 2C receptor agonist
- Decreases food consumption and promotes satiety by selectively activating 5-HT2C receptors in the hypothalamus

Adverse Reactions

- **Without diabetes:**
- Headache - 17%
- Dizziness – 9%
- Fatigue - 7%
- Nausea - 8%
- Dry mouth 5%
- Constipation 6%

- **In patients with diabetes:**
- Hypoglycemia – 29%
- Headache – 15%
- Back pain -12%
- Cough – 8%
- Fatigue -7%

Qysmia capsules

- Phentermine mg/ Topiramate mg extended release:
- • 3.75 mg/23 mg
- • 7.5 mg/46 mg
- • 11.25 mg/69 mg
- • 15 mg/92 mg
- Average of 24 pounds lost, 10% body wt
- Once daily

Qsymia adverse reactions

- Paraesthesia
- Dizziness
- Insomnia
- Constipation
- Dry mouth
- Difficulty concentrating

Contrave

- Naltrexone HCL/Buproprion HCL
- 8mg/90mg
- Works on the hypothalamus – appetite regulatory center
- Affects mesolimbic dopamine circuit and influences reward pathways

Adverse Reactions - Contrave

- Nausea -32.5%
- Constipation - 19.2%
- Headache - 17.6%
- Vomiting 10.7%
- Dizziness - 9.9%
  Insomnia - 9.2%
- Dry mouth - 8.1%
- Diarrhea 7.1%

Skin changes

- 30% decline in skin collagen in the first 5 years after menopause
- ~2% per year decline over next 20 years
- Greater correlation between skin thickness and collagen content to yrs since menopause *versus* chronologic age
- Estrogen receptors are present in significant numbers in skin

Verdier-Sevrain S *Exp Dermatol* 2006.

Hair changes

- Increase in the ratio of androgen to estrogen may influence hair changes in some women
- Female pattern hair loss (thinning on crown) most common diagnosis
- Hair width can thin
- Large “rogue hairs” can appear on the chin, neck, upper lip around menopause
- Loss of pubic hair, eyebrows, eyelashes

Riedel-Baima A *Endocr Regul* 2008.

Pharmacology - unwanted hair

- Vaniqa – Eflornithine
- It does not remove the hair but rather slows its growth
- The cells responsible for hair growth depend upon polyamines, proteins which require an enzyme ornithine decarboxylase (ODC)
- Eflornithine blocks ODC

Pharmacology for Eyelashes/Brows

- Eyelashes and Eyebrows – Latisse
- Bimatoprost ophthalmic solution 0.03% increases eyelash growth, including length, thickness, and darkness.
- Prolongs the active growth phase—or anagen phase

Minoxidil 2%

- Prolongation of growth or anagen phase and increase in follicle hair size
- 20% of women will see moderate hair growth
- More will see hair loss slow or stop
- May see more hair fall out in first 4 weeks as new hair pushes out old hair

Finasteride - Propecia

- Finasteride is *NOT* FDA - indicated for women
- 5 alpha-reductase inhibitor for male pattern baldness (androgenic alopecia) which decreases DHT
- 1 mg q day
- >60% of men saw increase in hair
- 80% of men had a decrease in hair loss
- May cause reduction in libido

Muscle Aches

- Many women experience an increase in muscle aches during the menopausal transition
- Hands, knees, hips, lower back and shoulders
- Not well understood, could be correlated with decreased collagen levels and loss of muscle fibers with aging

Midlife sleeplessness

- Both men and women report an increase in sleep disturbances at midlife
- About 46% of US women ages 40-54 and 48% ages 55-64 report sleep problems
- Sleep disturbances are associated with fatigue, irritability, chronic illness (CVD), mood disorders, depression and anxiety.

Parry BL *Menopause* 2007.

A Cascade Effect

Night sweats

Interrupted sleep

Fatigue

Irritability, mood changes

Kronenberg. *Ann NY Acad Sci*. 1990.

Sleep Fragmentation

- Multiple “mini-awakenings”
- Person may or may not be aware
- Move out of Delta (restorative wave sleep) into lighter sleep multiple times
- Wake up *NOT* feeling refreshed

Causes of sleeplessness

- Night sweats typically occur in first half of night
- Advancing age early awakening more common
- Sleep disorders
  - 53% have sleep apnea, restless legs, or both
- Stress/depression
- Pain: muscle aches, joint pain, arthritis
- Other conditions: GERD, SOB, CVD, allergies
- Medications

Freedman RR *Menopause* 2007.

Treating sleep problems

- Essential to do a complete evaluation
- Complex condition
- Sleep specialist instead of Sleep study
- Multi-disciplinary approach
  - CPAP not helpful if in the closet
  - CBT, mindfulness, treating anxiety
  - Treat Night sweats
  - Avoid Addictive medication

Sleep hygiene helps

- Use cool, dark, quiet room
- Use bedroom only for sleep and sexual activities
- Use lightweight sleepwear
- Avoid heavy evening meals
- Avoid alcohol, caffeine, nicotine, chocolate
- Exercise daily, but not close to bedtime
- Use relaxation techniques
- Have regular sleep schedule, even on weekends

Mood Changes

- Interrupted sleep
- Memory loss
- Distractibility, Irritability
- Feeling out of control over how body works
- Inability to predict how she'll feel from 1 day to the next
- It is NOT in her head
- DO CHECK THE TSH LEVELS AND THYROID ANTIBODIES IF YOU SUSPECT HASHIMOTO'S

Potential stressors at midlife

- Aging
- Loss of fertility
- Sleep problems
- Medical problems, fatigue
- Divorce or widowhood
- Empty nest
- “Sandwich generation” (care of both children & elders)
- Career issues
- Tsunami of physical changes including HF & NS

Mood disorders

- May be caused by fluctuating hormone levels that perturb neural systems
- Feelings of upset, loss of control, irritability
- Estrogen is part of the Dopamine/Serotonin pathway
- Women with hx of PMS, significant stress, HF, NS sexual dysfunction, physical inactivity vulnerable
- Medications, CBT, Mindfulness, Stress Reduction

References

- Bachmann GA In: *Treatment of the Postmenopausal Woman* Philadelphia: Lippincott, Williams & Wilkins, 1999.
- Caufriez, A *et al.* Progesterone Prevents Sleep Disturbances and Modulates GH, TSH, and Melatonin Secretion in Postmenopausal Women *Clin Endocrinol Metab* 2011;96:E614-23.
- De Villiers, et al. Global Consensus Statement on Menopausal Hormone Therapy. Climacteric, 2013. Vol. 16, Iss. 2.
- Freedman RR. Pathophysiology and treatment of menopausal hot flashes: a contemporary approach to the menopause. Semin Reprod Med 2005;23:117–25.
- Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of Menopausal Hot Flushes and Associated Risk Factors. *Obstetrics and gynecology*. 2011;117(5):1095-1104.
- Harlow SD *Menopause* 2012;19:387-95 (reproduced with permission from Randolph JF *JCEM* 2011;96:746-54).
- Kronenberg F. Hot flashes: epidemiology and physiology. Ann N Y Acad Sci 1990;592:52–86; discussion 123–33.
- North American Menopause Society Global Position Statement on Hormone Treatment, 2017.

References

- Nappi, RE, Kokot-Kierepa, M. Vaginal Health: Insights, Views & Attitudes (VIVA) - results from an international survey. Climacteric. 2012 Feb;15(1):36-44
- Parry, BL. Sleep disturbances at menopause are related to sleep disorders and anxiety symptoms. Menopause. 2007 Sep-Oct;14(5):812-4.
- Prague, J K, et.al. , Determining the Relationship Between Hot Flushes and LH Pulses in Menopausal Women Using Mathematical Modeling, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 9, September 2019, Pages 3628–3636.
- Prairie BA, Klein-Patel M, Lee M, Wisner KL, Balk JL. What Midlife Women Want from Gynecologists: A Survey of Patients in Specialty and Private Practices. *Journal of Women's Health*. 2014;23(6):513-518.
- Prairie BA, et al. Symptoms of Depressed Mood, Disturbed Sleep, and Sexual Problems in Midlife Women: Cross-Sectional Data from the Study of Women's Health Across the Nation. *Journal of Women's Health*. 2015;24(2):119-126.
- 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.
- Sitka, CS, Atrophic vaginitis. Dermatol Ther. 2010 Sep-Oct;23(5):514-22.
- Verdier-Sévrain, et al. Biology of estrogens in skin: implications for skin aging. Exp Dermatol. 2006 Feb;15(2):83-94.

GSM
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

1. Stika CS *Dermatol Ther* 2010.
2. Bachmann GA In: *Treatment of the Postmenopausal Woman* Philadelphia: Lippincott, Williams & Wilkins, 1999.

VIVA Trial 2011

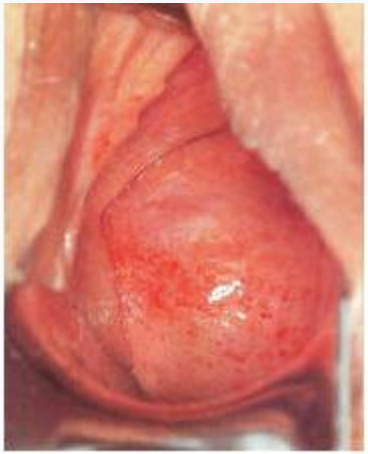
- Vaginal Health: Insights, Views & Attitudes
- Survey of 3250 Menopausal women from North America & Northern Europe
- 75% felt atrophy had a neg impact on quality of life
- 30% would consider vaginal estrogen
- Concluded **women had a low understanding of urogenital atrophy**

Nappi & Kokot-Kierepa, *Climacteric*. 2012

GSM = VVA

- REVIVE 2013 Survey n= 3046 found:
- Only 7% talked with HCP about VVA
- 59% reported that VVA interfered with sex
- 85% experienced “loss of intimacy” w partner
- 47% felt VVA affected their relationships
- 29% said VVA caused negative impact on sleep
- 27% reported a negative impact on their general enjoyment of life

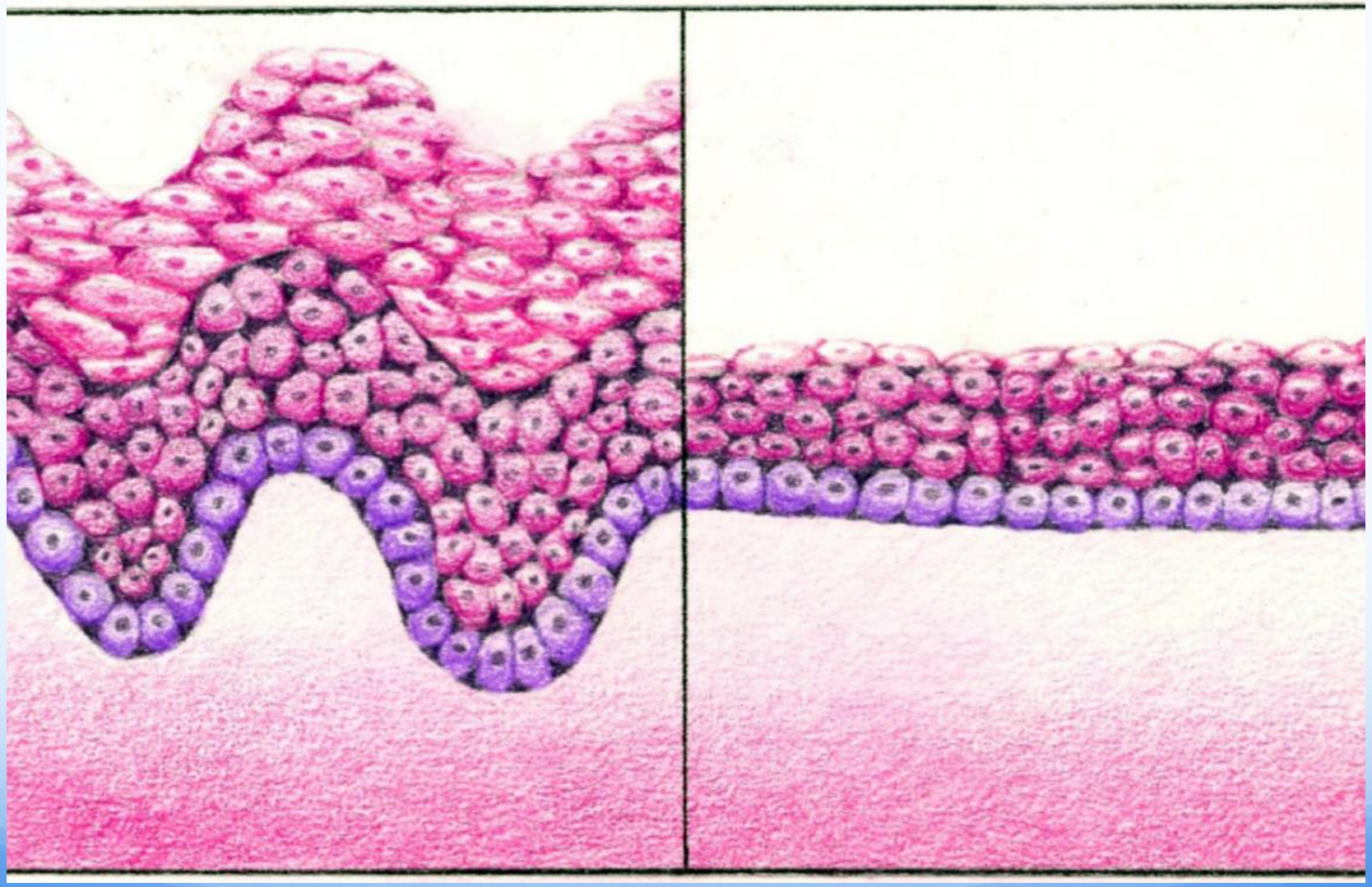
Urogenital Atrophy



- Physiology:
  - Early stages associated with thin dry, erythematous vaginal epithelium
  - Later, loss of labial fat pad, labia majora pendulous, labia minora less distinct
  - Prepuce covering clitoris decreases, clitoris may appear larger
  - Tissues of vulva become pallid, thin, dry
  - Increased tenderness of vestibule

Well-estrogenized
Premenopausal State

Low-estrogen
Postmenopausal State

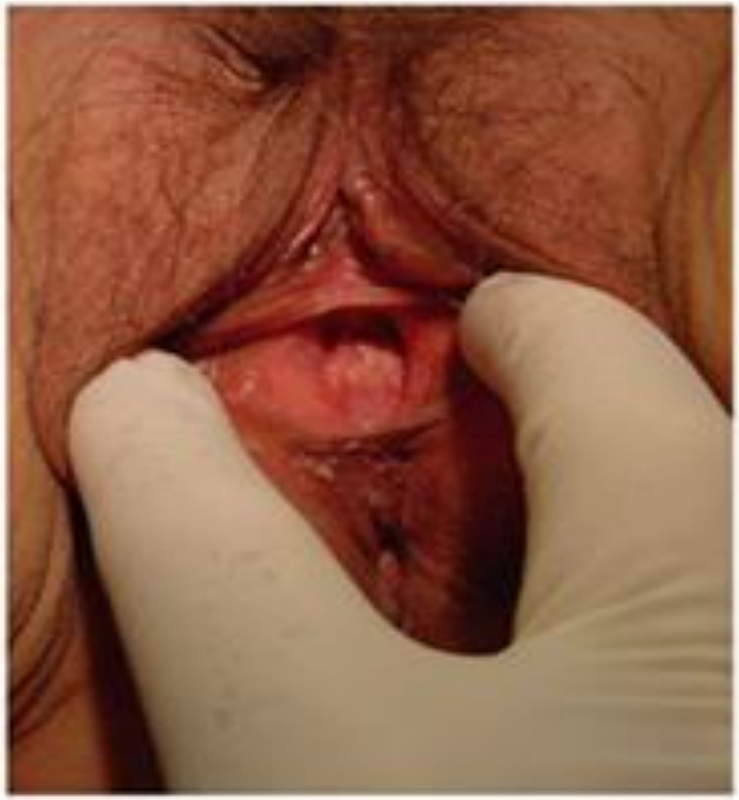


Courtesy of the Graphic Courtesy Dr. Diane Todd Pace NP from the North American Menopause Society

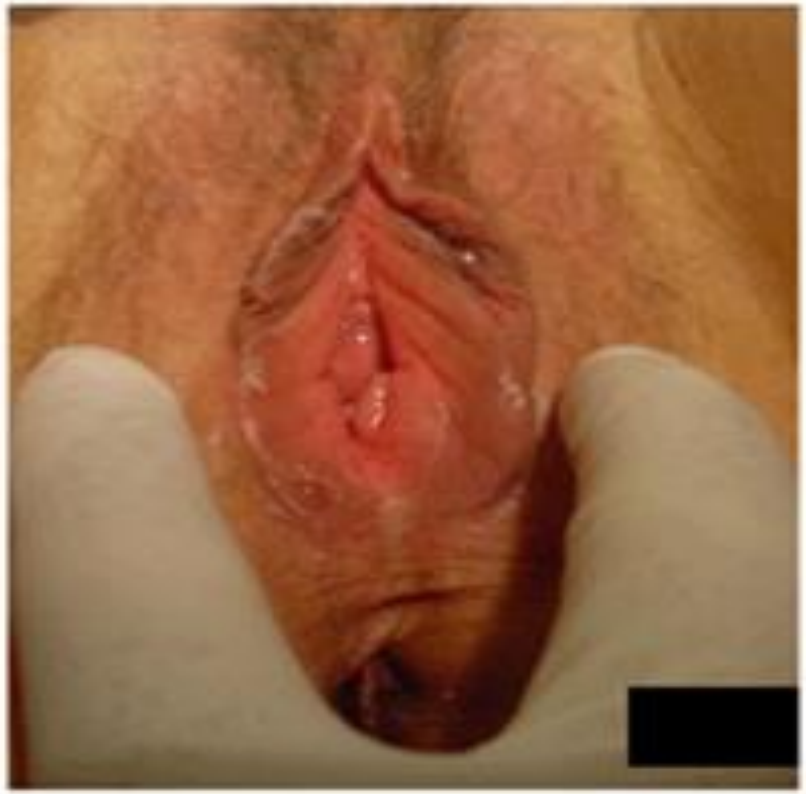
Loss of Estrogen

- 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, AIs)

Comparison of 2 sexually active 65 yr old women



Patient A stopped estrogen therapy 3 years previously



Patient B remained on therapy

Courtesy Dr. Murray Freedman

Medscape

Nonhormonal treatment

- ***Use it or Lose It***
- Regular sexual activity promotes blood flow
- Water-based vaginal lubricants and moisturizers
- Masturbation or use of a vibrator to maximize stimulation
- Cleansing with water but not soap

Stika CS *Dermatol Ther* 2010

Prevention & Treatment

- Estrogen has been proven to restore vaginal blood flow, decrease vaginal pH, and improve the thickness and elasticity of vulvovaginal tissue

- Low-dose, local, prescription vaginal ET:
  - Is effective and well tolerated
  - Has limited systemic absorption
  - No need for progestins
  - No evidence of increased risk of Br Ca

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Rahn, DD et al, Obstetrics and Gynecology, 2014.

Vaginal Estrogens

- Low-dose, local, prescription vaginal ET products FDA-approved for treating vaginal atrophy include:
  - estradiol vaginal cream (Estrace Vaginal Cream)
  - CE vaginal cream (Premarin Vaginal Cream)
  - estradiol vaginal ring (Estring)
  - estradiol hemihydrate vaginal tablet (Vagifem)

  - Discuss black box warning

DHEA Intravaginal ovules

- Labrie, et al, (2009) (n=216) phase lll
- DHEA ovules .25%, .5%, 1% applied daily
- After 2 wks, ↑'d parabasal cells
- ↑❼ d vaginal secretions, color, epithelial integrity
- No change in endometrial histology
- No increase in serum sex steroids
- Not FDA App/Need to be compounded at this time, $40.00 month

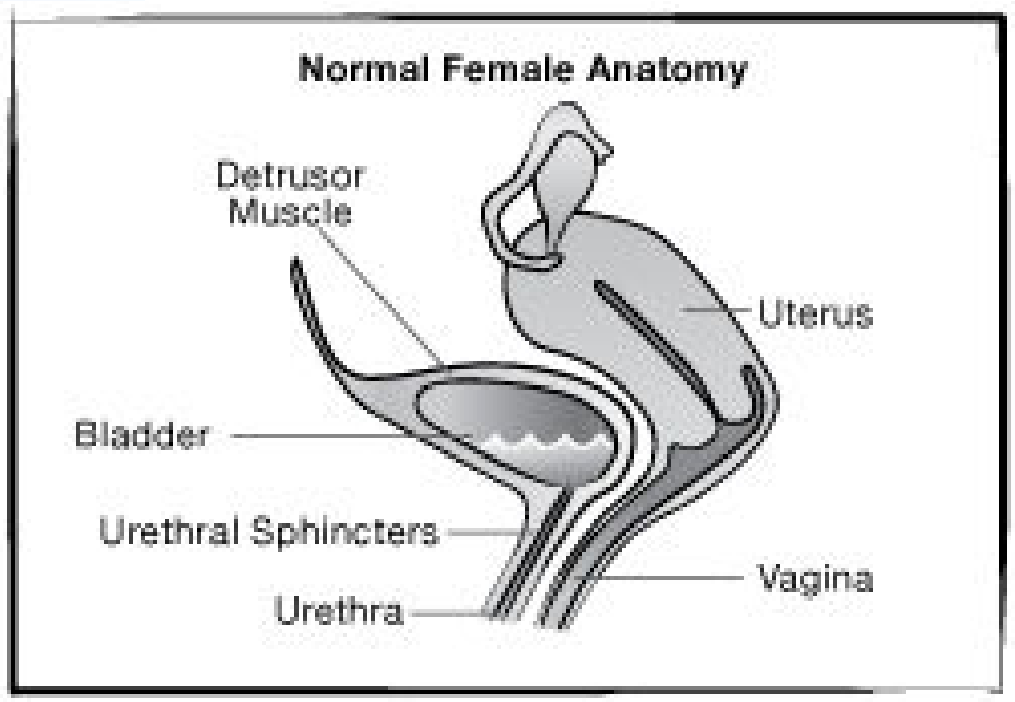
Lubricants & New Devices

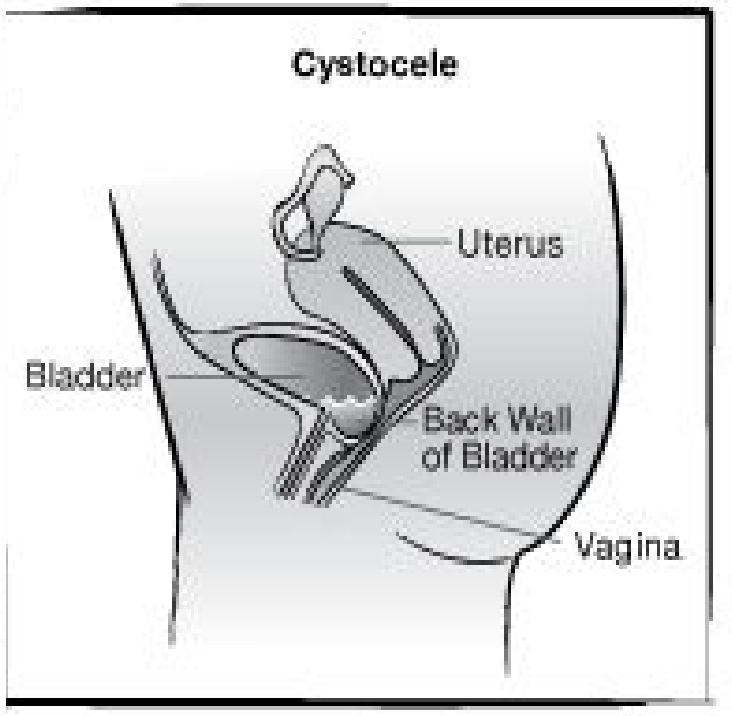
- Water based
- Silicon based
- Oils
- New devices

Urinary complaints

- Incontinence is the most common complaint
  - Among 3,302 women, mean age 46 years, 57% reported incontinence with 15% moderate and 10% severe symptoms
- Other complaints include frequency, urgency, dysuria
- Mechanical and Gravitational forces at play
- Loss of Estrogen changes muscle tone
- Urethral sphincters out of position
- Weight & Neuropathies influence

Gravity is NOT our Friend





Illustrations used with permission from The Hot Guide to A Cool Sexy Menopause, by Barbara Dehn NP.
Illustrator: Andrea Kelley

Treating urinary incontinence

- Kegels
- Pelvic Floor PT
- OAB meds have side effects but may be effective at reducing # of trips to bathroom
- Systemic Estrogen
- Local Estrogen
- Weight loss

References

- Bachmann GA In: *Treatment of the Postmenopausal Woman* Philadelphia: Lippincott, Williams & Wilkins, 1999.
- Caufriez, A *et al.* Progesterone Prevents Sleep Disturbances and Modulates GH, TSH, and Melatonin Secretion in Postmenopausal Women *Clin Endocrinol Metab* 2011;96:E614-23.
- De Villiers, et al. Global Consensus Statement on Menopausal Hormone Therapy. Climacteric, 2013. Vol. 16, Iss. 2.
- Freedman RR. Pathophysiology and treatment of menopausal hot flashes: a contemporary approach to the menopause. Semin Reprod Med 2005;23:117–25.
- Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of Menopausal Hot Flushes and Associated Risk Factors. *Obstetrics and gynecology*. 2011;117(5):1095-1104.
- Harlow SD *Menopause* 2012;19:387-95 (reproduced with permission from Randolph JF *JCEM* 2011;96:746-54).
- Kronenberg F. Hot flashes: epidemiology and physiology. Ann N Y Acad Sci 1990;592:52–86; discussion 123–33.
- Munro MG, et al. The flexible FIGO The Flexible classification concept for underlying causes of abnormal uterine bleeding. Semin Reprod Med. 2011 Sep;29(5):391-9.

References

- Nappi, RE, Kokot-Kierepa, M. Vaginal Health: Insights, Views & Attitudes (VIVA) - results from an international survey. Climacteric. 2012 Feb;15(1):36-44
- Parry, BL. Sleep disturbances at menopause are related to sleep disorders and anxiety symptoms. Menopause. 2007 Sep-Oct;14(5):812-4.
- Prague, J K, et.al. , Determining the Relationship Between Hot Flushes and LH Pulses in Menopausal Women Using Mathematical Modeling, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 9, September 2019, Pages 3628–3636.
- Prairie BA, Klein-Patel M, Lee M, Wisner KL, Balk JL. What Midlife Women Want from Gynecologists: A Survey of Patients in Specialty and Private Practices. *Journal of Women's Health*. 2014;23(6):513-518.
- Prairie BA, et al. Symptoms of Depressed Mood, Disturbed Sleep, and Sexual Problems in Midlife Women: Cross-Sectional Data from the Study of Women's Health Across the Nation. *Journal of Women's Health*. 2015;24(2):119-126.
- 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.
- Sitka, CS, Atrophic vaginitis. Dermatol Ther. 2010 Sep-Oct;23(5):514-22.
- Verdier-Sévrain, et al. Biology of estrogens in skin: implications for skin aging. Exp Dermatol. 2006 Feb;15(2):83-94.

Thank You

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References

- Bachmann GA In: *Treatment of the Postmenopausal Woman* Philadelphia: Lippincott, Williams & Wilkins, 1999.
- Caufriez, A *et al.* Progesterone Prevents Sleep Disturbances and Modulates GH, TSH, and Melatonin Secretion in Postmenopausal Women *Clin Endocrinol Metab* 2011;96:E614-23.
- De Villiers, et al. Global Consensus Statement on Menopausal Hormone Therapy. Climacteric, 2013. Vol. 16, Iss. 2.
- Freedman RR. Pathophysiology and treatment of menopausal hot flashes: a contemporary approach to the menopause. Semin Reprod Med 2005;23:117–25.
- Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of Menopausal Hot Flushes and Associated Risk Factors. *Obstetrics and gynecology*. 2011;117(5):1095-1104.
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- Nappi, RE, Kokot-Kierepa, M. Vaginal Health: Insights, Views & Attitudes (VIVA) - results from an international survey. Climacteric. 2012 Feb;15(1):36-44
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- Prague, J K, et.al. , Determining the Relationship Between Hot Flushes and LH Pulses in Menopausal Women Using Mathematical Modeling, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 9, September 2019, Pages 3628–3636.
- Prairie BA, Klein-Patel M, Lee M, Wisner KL, Balk JL. What Midlife Women Want from Gynecologists: A Survey of Patients in Specialty and Private Practices. *Journal of Women's Health*. 2014;23(6):513-518.
- Prairie BA, et al. Symptoms of Depressed Mood, Disturbed Sleep, and Sexual Problems in Midlife Women: Cross-Sectional Data from the Study of Women's Health Across the Nation. *Journal of Women's Health*. 2015;24(2):119-126.
- 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.
- Sitka, CS, Atrophic vaginitis. Dermatol Ther. 2010 Sep-Oct;23(5):514-22.
- Verdier-Sévrain, et al. Biology of estrogens in skin: implications for skin aging. Exp Dermatol. 2006 Feb;15(2):83-94.