HORMONE REPLACEMENT THERAPY

UPDATE FOR THE PRIMARY CARE PHYSICIAN

PRESENTED BY: MARY LYNN PERRY, D.O. , FACOG
HIBISCUS WOMEN'S CARE
MELBOURNE, FL

GOALS OF PRESENTATION

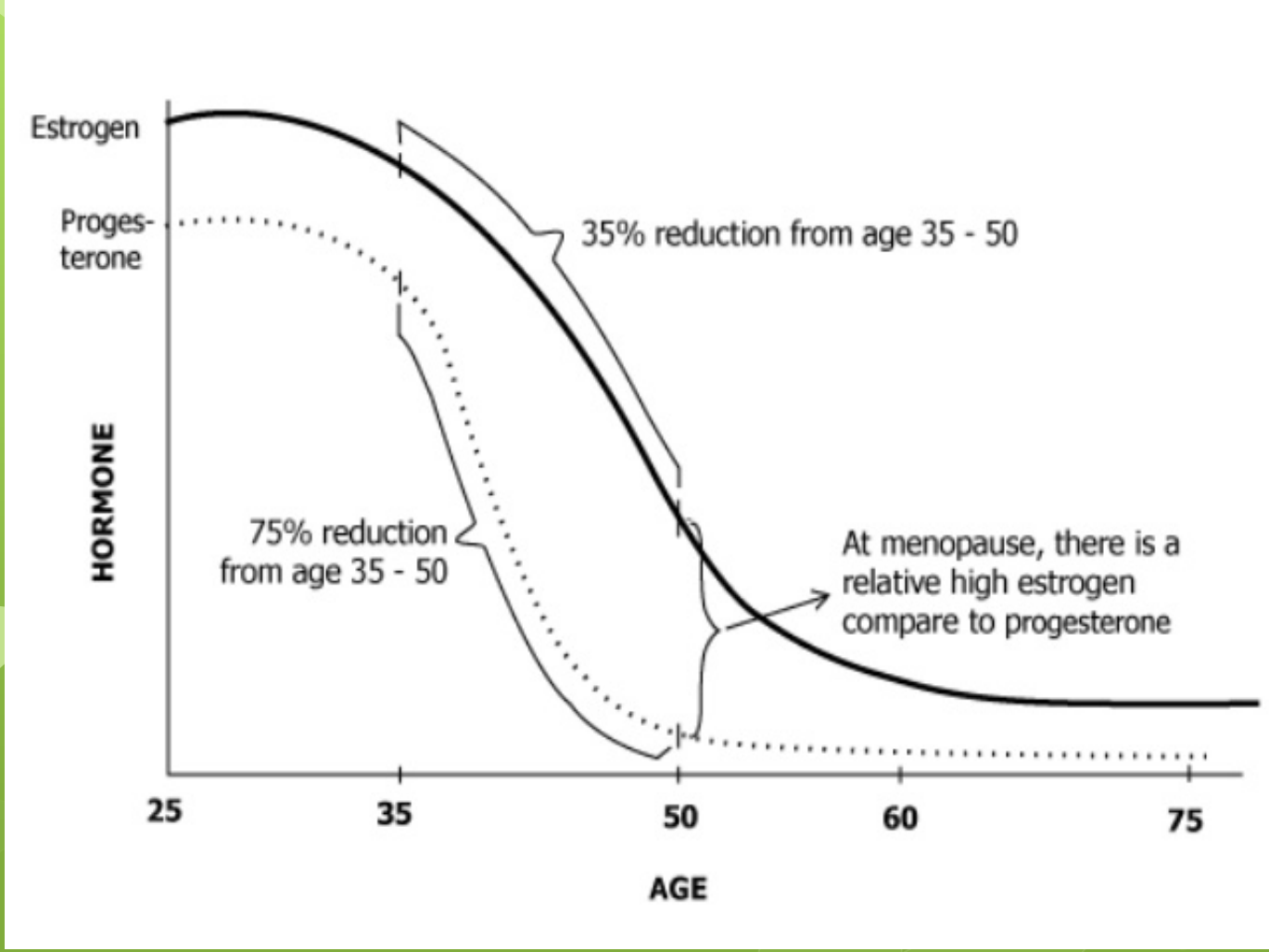
- IDENTIFY CHARACTERISTICS OF MENOPAUSAL TRANSITION
- DISCUSS WOMEN'S HEALTH INITIATIVE AND EXPLAIN HOW IT HAS CHANGED HORMONE REPLACEMENT THERAPY RECOMMENDATIONS AND TREATMENT
- PRESENT OPTIONS FOR SYSTEMIC AND LOCAL HORMONE REPLACEMENT THERAPY
- ADVISE ON ALTERNATIVES TO HORMONAL MEDICATIONS TO TREAT PERIMENOPAUSAL AND MENOPAUSAL SYMPTOMS
- DISCUSS "BIOIDENTICAL HORMONES"

MENOPAUSAL TRANSITION

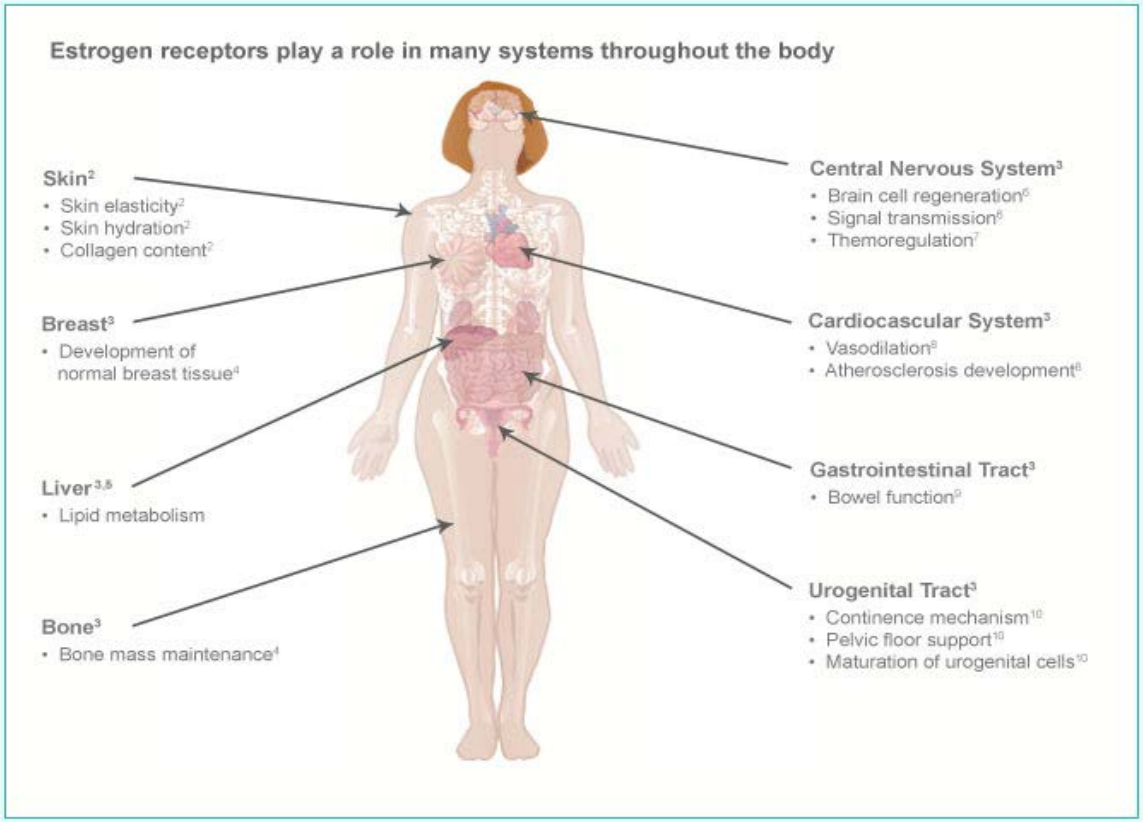
- MEDIAN AGE OF MENOPAUSE IS 51
- PHYSIOLOGIC CHANGES BEGIN TO OCCUR 3-5 YEARS BEFORE CESSATION OF MENSES
- MARKED BY FLUCTUATIONS IN HORMONE LEVELS
  - SERUM LEVELS OF ESTRADIOL AND PROGESTERONE DECLINE
  - FOLLICLE STIMULATING HORMONE LEVELS INCREASE

VASOMOTOR (HOT FLUSHES) AND VAGINAL SYMPTOMS ARE THE MOST CLOSELY ASSOCIATED CHANGES RELATED TO HORMONE DECLINE.

HORMONE LEVELS DECLINE WITH AGE



Effects of Estrogen on Female Body



The Effects of Menopause Are Wide-Spread

Estrogen receptors have been identified in the reproductive organs, breasts, bones, skin and most connective tissue, cardiovascular system, urogenital tract, liver and central nervous system.[11] These receptors bind with naturally occurring estrogen to assist in a wide range of physiologic activities and functions, including lipid metabolism and neural signal transmission.[4,5] While estrogen is not the only hormone or chemical utilized in these processes, estrogen has been shown to play an important role in many of them. With depleted levels of estrogen within a woman's body, many of these functions may be compromised before and after menopause.[4,5,6,7,8,9]

MENOPAUSE IS A CLINICAL DIAGNOSIS!!!...BUT SOME PATIENTS WANT THEIR HORMONES CHECKED

Laboratory Tests to Aid in the Differentiation of Menopause From Other Conditions

Test	*Notes*
Follicle-stimulating hormone	An elevated follicle-stimulating hormone level (>30 mIU/mL) is consistent with the diagnosis of menopause. In women under age 40 years, 2 to 3 levels may be needed to make the diagnosis; best done around day 3 of the cycle, if possible to time cycle (day 1 is the first day of bleeding)
Thyroid-stimulating hormone	To detect hypothyroidism or hyperthyroidism
Prolactin	To diagnose hyperprolactinemia, often accompanied by galactorrhea
Pregnancy test (BhCG)	Although unlikely in this age group, pregnancy can occur
Estradiol	May be useful in women using hormonal contraception; 7 d after discontinuation of oral contraceptives, a result of <20 pg/mL is consistent with menopause

BhCG = human chorionic gonadotrophin.

Table 1. Select Age-Related Changes in the Female Genital Tract

Components of steroid biosynthesis in the ovary
Before menopause (reproductive years): Maturing follicle, functioning corpus luteum, and stroma (supporting tissue of the ovary). ***After menopause:*** Stroma.
Changes in estrogen
Estradiol (17 ß-estradiol): The most potent estrogen produced and secreted by the ovary, in postmenopause its secretion is minimal; although blood levels are reduced by 90%, it has 10 times greater biological activity than estrone. Important role in maintaining tissues that are hormone-dependent.
Estrone: A metabolite of estradiol with about one-third the estrogenic potency of estradiol; it is the major postmenopausal estrogen. Generated primarily from conversion of androstenedione (produced in the ovaries and adrenal glands) in peripheral tissues. Postmenopausal levels are four times higher than in younger women.
Estriol: A metabolite of estradiol with significantly less potency than estradiol; does not play a significant role in postmenopause.
Anatomical changes
Cervix: More flush with the vaginal vault; squamocolumnar junction recedes into the endocervical canal.
Ovary: Reduction in size; sclerotic; loss of follicular activity; cysts may be present.
Pelvic Floor: Weakness; lack of support due to diminished collagen following the climacteric; nerve damage may be associated with parturition (childbirth) and uterovaginal prolapse.
Uterus: Marked reduction in size; fibrosis and thickened blood vessels in the myometrium; singular layer endometrium (cuboidal cells).
Vagina: Thinner, atrophic, less elastic; more vulnerable to trauma; reduced defenses against infection
Vulva: Shrinkage of tissue; sparse graying pubic hair; thinner and keratinized epidermis.

Source: References 1,13,15,19.

THE RESULT OF ESTROGEN DEFICIENCY!!!

WITH A LITTLE HUMOR…..

WOMEN'S HEALTH INITIATIVE

- RCT of healthy menopausal women aged 50-77
- Combined HT using Conjugated Equine Estrogen and Medroxyprogesterone Acetate demonstrated a slightly increased risk of:
  - Breast Cancer
  - Coronary Heart Disease
  - Stroke
  - Venous Thromboembolic Events

STUDY DESIGN

WHI OBJECTIVES

WHI RESULTS


Absolute Excess Risks and Absolute Risk Reductions per 10,000 Person-Years:
Women's Health Initiative
Difference in risk per 10,000 person-years
CHD events +7
Strokes +8
Pulmonary embolisms +8
Invasive breast cancer +8
Colorectal cancers −6
Hip fractures −5
Global index +19
Writing Group for the WHI Investigators. JAMA 2002;288:321-333.

Cardiovascular Outcomes

CHD Risk by Year of Follow-up: *WHI*

Year of Follow-up	CHD cases,* n (annualized %)		Hazard Ratio for CHD (95% CI)
	Estrogen + Progestin	Placebo	
1	42 (0.50)	23 (0.29)	1.81 (1.09–3.01)
2	38 (0.45)	28 (0.35)	1.34 (0.82–2.18)
3	19 (0.23)	15 (0.19)	1.27 (0.64–2.50)
4	32 (0.39)	25 (0.32)	1.25 (0.74–2.12)
5	29 (0.41)	19 (0.28)	1.45 (0.81–2.59)
≥6	28 (0.37)	37 (0.56)	0.70 (0.42–1.14)

*Acute MI requiring hospitalization, silent MI (ECG), CHD death

Manson JE et al. *N Engl J Med* 2003;349:523-534.

WHI CONCLUSIONS

Women's Health Initiative

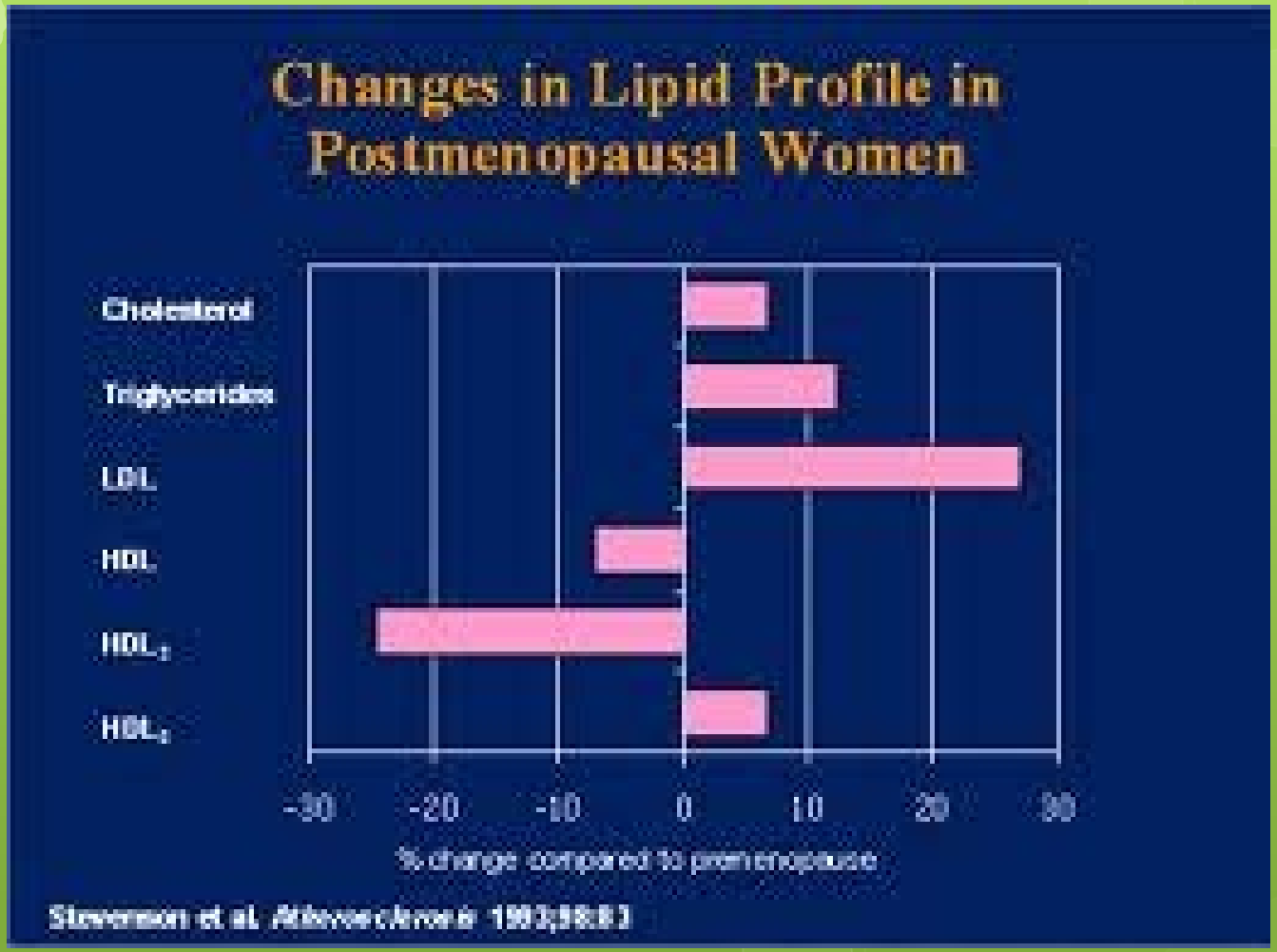
- REPORTED A LACK OF CARDIOPROTECTION
- SHOWED INCREASED RISK OF BREAST CANCER, VTE, AND STROKE WITH COMBINED HORMONE THERAPY
- SECONDARY ANALYSIS OF WHI CONTINUES
- WHI TRIAL HAD SEVERAL CHARACTERISTICS THAT LIMITED GENERALIZING THE FINDINGS TO ALL POSTMENOPAUSAL WOMEN
  - USED ONLY ONE ROUTE OF ESTROGEN (ORAL)
  - ONLY ONE FORM OF ESTROGEN (CEE) AND ONE PROGESTOGEN (MPA)
  - WHI ENROLLED GENERALLY HEALTHY POSTMENOPAUSAL WOMEN AGED 50-79

WHI REANALYSIS RELATED TO CHD AND VTE RISK

- ET MAY REDUCE CHD RISK WHEN INITIATED IN YOUNGER AND MORE RECENTLY POSTMENOPAUSAL WOMEN WITHOUT A UTERUS (AGES 50-59), HAZARD RATIO FOR CHD WAS .59 AND FOR TOTAL MI IS WAS .54
- WOMEN WHO INITIATE HT MORE THAN 10 YEARS BEYOND MENOPAUSE ARE AT INCREASED RISK FOR CHD AND THOSE WHO INITIATE HT WITHIN 10 YEARS TEND TO HAVE A LOWER RISK OF CHD
- IN THE TRIAL THE ABSOLUTE EXCESS VTE RISK WITH EPT OR ET WAS LOWER IN WOMEN WHO STARTED HT BEFORE AGE 60
  - THIS RISK WAS THREEFOLD GREATER IN OBESE WOMEN (BMI >30)

CARDIOVASCULAR DISEASE

- Estrogen is cardioprotective(antioxidant property also)
- After menopause→ **HDL↓,LDL↑, total cholesterol ↑,**
- Estrogen deficiency→atherosclerosis, ischemic heart disease, MI
- Risk factors: obese women with hypertension , previous thromboembolicepisodes


Changes in Lipid Profile in Postmenopausal Women
Cholesterol
Triglycerides
LDL
HDL
HDL2
HDL3
-30
-20
-10
0
10
20
30
% change compared to premenopause

WHI REANALYSIS RELATED TO BREAST CANCER RISK

- DIAGNOSIS OF BREAST CANCER INCREASES WITH EPT USE BEYOND 3-5 YEARS
- 8 ADDITIONAL BREAST CANCERS PER 10,000 WOMEN USING EPT FOR 5 OR MORE YEARS
- RISK MAY BE GREATER WITH CONTINUOUS USE OF PROGESTOGEN (VERSUS SEQUENTIAL OR ITERMITTENT USE)
- LONG TERM FOLLOW UP FOUND THAT THE RISK OF NEW DIAGNOSIS OF BREAST CANCER DISSPIATED IN THE 3 YEARS AFTER CESSATION OF EPT
- REANALYSIS OF DATA SHOWED THOSE STARTING EPT SHORTLY AFTER MENOPAUSE HAD AN HR OF 2.75 FOR BREAST CANCER WITH MORE THAN 5 YEARS OF USE, WHEREAS THOSE WITH A GAP TIME OF GREATER THAN 5 YEARS DID NOT. (THIS IS IN CONTRAST WITH THE FINDINGS ON CHD, STROKE, AND VTE)

ESTROGEN ONLY THERAPY AND BREAST CANCER RISK

NO DIFFERENCE IN INVASIVE BREAST CANCER COMPARED WITH PLACEBO

History of Hormone Therapy

- **2002 Women's Health Initiative (WHI) Study**
  - Lower doses = lower side effect profile
  - Estrogen + *Progestin* (Prempro) arm had a 22% increase in breast cancer vs. Estrogen alone arm
- **Resulting Hormone Prescribing Trends**
  - Start with the lowest effective dose
  - Progesterone (bioidentical) popularity over Progestins (non-bioidentical)
  - Bioidentical (exact molecular structure of human Estrogen and Progesterone) sales sky rocket

Risk factors for menopausal related problems are as follows:

- Early menopause
- Surgical menopause or radiation.
- Chemotherapy esp alkylating agents.
- smoking., caffeine, alcohol.
- Family history of menopausal diseases.
- Drugs related such as GnRH, heparin, corticosteroids and clomiphene(anti-oestrogen) when given over prolonged peiod can cause oestrogen deficiency.

VASOMOTOR SYMPTOMS

- SUDDEN SENSATION OF EXTREME HEAT IN UPPER BODY, PARTICULARLY THE FACE, NECK, AND CHEST
- TYPICALLY LAST 1-5 MINUTES
- MAY INCLUDE PERSPIRATION, FLUSHING, CHILLS, ANXIETY, AND OCCASIONALLY HEART PALPITATIONS
- MAY ALSO INTERFERE WITH SLEEPING AND CAUSE CHRONIC SLEEP DISRUPTION
- 87% OF WOMEN WHO REPORT HOT FLUSHES EXPERIENCE THEM DAILY, APPROXIMATELY 33% EXPERIENCE MORE THAN 10/DAY

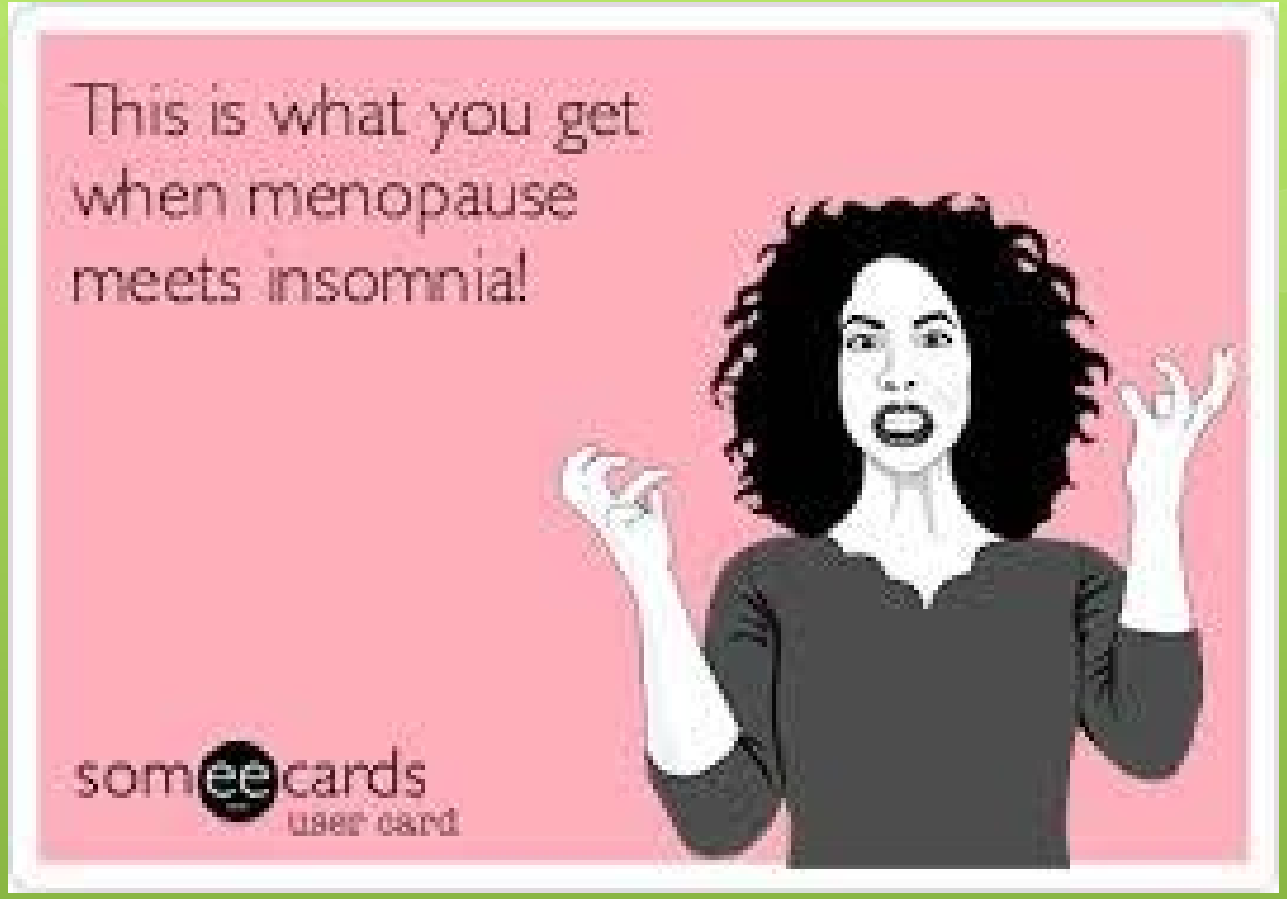

This is what you get when menopause meets insomnia!
someecards
user card

Table 1. Contraindications and Pretreatment Assessment in Prescribing Hormone Replacement Therapy

Contraindications*
Pregnancy
Unexplained vaginal bleeding
Active or chronic liver disease
History of breast or endometrial cancer‡
Recent vascular thrombosis
Informed patient refusal
Relative contraindications†
Hypertriglyceridemia
History of thromboembolic disease
Family history of breast cancer
Gallbladder disease
Migraine headaches
Uterine leiomyoma
Seizure disorder
Pretreatment assessment and medical record documentation before initiation of hormone replacement therapy*
Medical history consistent with the diagnosis of menopause
Assessment of contraindications and relative contraindications
Discussion of the risks and benefits of hormone replacement therapy
Physical examination, including blood pressure and breast and pelvic examinations
Results of cervical cytologic examination and screening mammography negative for malignancy
Baseline endometrial aspirate is not necessary

* Reference 11.

† Reference 21.

‡ Currently under debate. Some physicians prescribe hormone replacement therapy for survivors of breast cancer (12, 22–24). For survivors of endometrial cancer, most gynecologists prescribe estrogen in those who had stage I, grade I disease (11, 12).

Table 1

Recommendations Regarding ET/HT for Vasomotor Symptoms

Organization	Conclusions/Recommendations
American College of Obstetricians and Gynecologists	Estrogens are the most effective treatment for menopausal vasomotor symptoms. The use of ET and HT for alleviation of hot flashes and night sweats should be reassessed yearly. The lowest effective dose should be used for the shortest possible time to alleviate symptoms.
North American Menopause Society	Treatment of moderate to severe vasomotor symptoms remains the primary indication for systemic ET and HT. Every systemic product is government-approved for this indication.
American Society of Reproductive Medicine	Low-dose estrogen therapy remains a valid option for many seeking short-term relief from the symptoms of menopause. Women are advised that HT does not provide additional health benefits that would justify its use beyond the immediate relief of menopausal symptoms.
FDA	When these products are being prescribed solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered. Estrogens and progestins should be used at the lowest doses for the shortest duration to reach treatment goals, although it is not known at what dose there may be less risk of serious side effects.

ET: estrogen therapy; HT: hormone therapy.
Source: References 8, 21–23.


"H..has your hot flush gone yet, c..can we close the window now?"

Table 2. Available Systemic Estrogen Products, Equivalencies, and Dosages			
Steroidal Agent	**Equipotent Dose**	**Dosage Forms**	**Source**
Oral estrogen preparations:			
Conjugated equine estrogen, CEE (Premarin, Wyeth-Ayerst)	0.625 mg	Tablet: 0.3, 0.45, 0.625, 0.9, 1.25 mg	Urine of pregnant mares
Estradiol (Estrace, Warner Chilcot)	1 mg	Tablet: 0.5, 1, 2 mg	Soy/Yams
Estradiol (Gynodiol, Fielding)	1 mg	Tablet: 0.5, 1, 1.5, 2 mg	Soy/Yams
Esterified Estrogen (Menest, Monarch)	0.625 mg	Tablet: 0.3, 0.625, 1.25, 2.5 mg	Mexican yams
Esterified Estrogen (Estratab, Solvay Pharmaceuticals Inc.)	0.625 mg	Tablet: 0.3, 0.625, 1.25, 2.5 mg	Mexican yams
Esterified Estrogen (Ogen, Pharmacia)	0.75 mg	Tablet: 0.75, 1.5, 2.5 mg	Mexican yams
Esterified Estrogen (Ortho-Est, Women First Healthcare)	0.75 mg	Tablet: 0.75, 1.5 mg	Mexican yams
Synthetic conjugated estrogens (Cenestin, Elan)	0.625 mg	Tablet: 0.3, 0.45, 0.625, 0.9, 1.25 mg	Synthetic
Synthetic conjugated estrogens B (Enjuvia, Elan)	0.625 mg	Tablet: 0.625, 1.25 mg	Synthetic
Oral estrogen-progestogen preparations:			
CEE/medroxyprogesterone (Prempro, Wyeth-Ayerst)	0.625/2.5 mg	Tablet: 0.3/1.5, 0.45/1.5, 0.625/2.5, 0.625/5 mg	Urine of pregnant mares
CEE/medroxyprogesterone (Premphase, Wyeth-Ayerst)	0.625/5mg	Tablet: 0.625/5 mg	Urine of pregnant mares
Estradiol/norgestimate (Prefest, Duramed)	1/0.9 mg	Tablet: 1/0.9 mg	Soy/Yams
Estradiol/norethindrone acetate (Activella, Novo Nordisk)	1/0.5 mg	Tablet: 1/0.5 mg	Soy/Yams
Estradiol/drosperinone (Angeliq, Berlex)	1/0.5 mg	Tablet: 1/0.5 mg	Soy/Yams
Ethynl estradiol/norethindrone (FemHRT, Warner Chilcot)	5 mcg/1 mg	Tablet: 5 mcg/1 mg	Synthetic
Transdermal patches:			
Estradiol (Vivelle, Novartis)	50 mcg	Patch: 25, 37.5, 50, 75, 100 mcg/day	Soy/Yams
Estradiol (Estraderm, Novartis)	50 mcg	Patch: 50, 100 mcg/day	Soy/Yams
Estradiol (Climara, Berlex)	50 mcg	Patch: 25, 50, 60, 75, 100 mcg/day	Soy/Yams
Estradiol (Alora, Watson)	50 mcg	Patch: 25, 50, 75, 100 mcg/day	Soy/Yams
Estradiol (Esclim, Women First)	50 mcg	Patch: 25, 37.5, 50, 75, 100 mcg/day	Soy/Yams
Estradiol (Menostar, Bayer)	N/D	Patch: 14 mcg/day	Soy/Yams
Estradiol/norethindrone (Combi-Patch, Novartis)	50mcg/0.14mg	Patch: 50/0.14, 50/0.25 mcg/mg/day	Soy/Yams
Estradiol/levonorgestrel (Climara Pro, Berlex)	45/15 mcg	Patch: 45/15 mcg/day	Soy/Yams
Transdermal emulsion, gels, and spray:			
Estradiol 0.06% (EstroGel, Solvay)	0.75 mg	Gel: 0.75 mg/1.25 g pump	Soy/Yams
Estradiol 0.06% (Elestrin, Kenwood)	N/D	Gel: 0.52 mg/0.87 g pump	Soy/Yams
Estradiol 0.1% (Divigel, Upsher-Smith)	N/D	Gel: 0.25/0.25, 0.5/0.5, 1/1 mg/g pouch	Soy/Yams
Estradiol (Estrasorb, Novavox)	N/D	Emulsion: 4.35 mg/1.74 g pouch	Soy/Yams
Estradiol (EvaMist Spray, KV Pharmaceutical)	N/D	Spray: 1.5 mg/90 mcL spray	Soy/Yams
Intravaginal ring (systemic):			
Estradiol (Femring, Warner-Chilcott)	0.05 mg	Ring: 0.05, 0.1 mg/day over 3 months	Soy/Yams
Note: N/D, not determined due to the low-dose preparations that are not equipotent.			

Table. Low-Dose Formulations of Estrogens and Estrogen-Progestin Combinations Available in the US

Estrogen type	Dose per day	Products available	Menopause-associated indication(s)[i]
Oral estrogens			
Conjugated equine estrogens (CEE)[ii]	0.3 mg and 0.45 mg	Premarin®; Prempro® (also contains a low-dose progestin [1.5 mg medroxyprogesterone])	• Treatment of mild to severe vasomotor symptoms • Prevention of osteoporosis • Treatment of vaginal and vulvar atrophy (0.45-mg dose)
Synthetic conjugated estrogens (SCE)	0.3 mg and 0.45 mg	Cenestin® (SCE-A),[iii] Enjuvia® (SCE-B)[iv]	• Treatment of mild to severe vasomotor symptoms • Treatment of vaginal and vulvar atrophy
Oral estradiol (E_2) (17β-estradiol)	0.45 mg or 0.5 mg depending on product	Activella® (also contains a low-dose progestin [0.1 mg norethindrone]), Estrace,[v] Femtrace®	• Treatment of mild to severe vasomotor symptoms • Prevention of osteoporosis
Ethinyl estradiol (EE_2)	2.5 mcg	Femhrt® (also contains a progestin [norethindrone])	• Treatment of mild to severe vasomotor symptoms • Prevention of osteoporosis
Esterified estrogens	0.3 mg and 0.45 mg	Menest®[vi]	• Vaginal and vulvar atrophy (0.3 mg) • Treatment of moderate to severe vasomotor symptoms (doses of 0.45 mg and higher recommended)
Transdermal estrogens			
E_2 patch	To deliver 0.025 mg/day To deliver 0.014 mg/day	Alora®, Climara®, Vivelle®, Vivelle-Dot® Menostar®	• Treatment of mild to severe vasomotor symptoms • Treatment of vaginal and vulvar atrophy • Prevention of osteoporosis • Prevention of osteoporosis
E_2 gel	To deliver 0.025 mg/d To deliver 0.003, 0.009, or 0.027 mg/d	Elestrin™ Divigel®[vi]	• Treatment of moderate to severe vasomotor symptoms • Treatment of moderate to severe vasomotor symptoms
E_2 spray	To deliver 0.021 mg/d	Evamist™[vii]	• Treatment of moderate to severe vasomotor symptoms

[i]Indications apply to the general type of estrogen listed, but within each class, specific indications may vary by product and dose. Consult each product's prescribing information for approved indication and dosing information.

[ii]CEEs contain a mixture of sodium estrone sulfate and sodium equilin sulfate and other components including sodium sulfate conjugates, 17α-dihydroequilin, 17α-estradiol, and 17β-dihydroequilin. Whereas the 0.45-mg dose is indicated for treatment of vulvar atrophy, the 0.3-mg dose [or higher] may be used for treatment of vasomotor symptoms or for prevention of osteoporosis. (Wyeth, 2006 74998 /id)

[iii]SCE-A contains a mixture of nine synthetic estrogenic substances: sodium estrone sulfate, sodium equilin sulfate, sodium 17α-dihydroequilin sulfate, sodium 17α-estradiol sulfate, sodium 17β-dihydroequilin sulfate, sodium 17α-dihydroequilenin sulfate, sodium 17β-dihydroequilenin sulfate, sodium equilenin sulfate and sodium 17β-estradiol sulfate. The 0.3-mg dose of SCE-A is indicated for treatment of vaginal and vulvar atrophy, whereas the 0.45-mg dose (or higher) of SCE-A is indicated for treatment of mild to severe vasomotor symptoms. (Duramed Pharmaceuticals, 2004 58556 /id)

[iv]SCE-B contains a mixture of ten synthetic estrogenic substances: sodium equilin sulfate, sodium 17α-dihydroequilin sulfate, sodium 17α-estradiol sulfate, sodium 17β-dihydroequilin sulfate, sodium 17α-dihydroequilenin sulfate, sodium 17β-dihydroequilenin sulfate, sodium equilenin sulfate, sodium 17β-estradiol sulfate, and sodium Δ8,9-dehydroestrone sulfate. (Enjuvia PI, Duramed)

[v]Higher doses (1-2 mg) are recommended in the Estrace prescribing information for treatment of vasomotor, vaginal, and vulvar symptoms (Estrace PI, Warner-Chilcott)

[vi]A mixture of sodium estrone sulfate (~75-85%) and sodium equilin sulfate (~6-15%) (Menest PI, Monarch)

[vii]Ackerman R, Hedrick R, Lambrecht L. Efficacy of 3 doses of estradiol gel 0.1% in the treatment of vasomotor symptoms and vulvar vaginal atrophy. Poster presented at the 18th Annual Meeting of The North American Menopause Society, October 3-6, 2007; Dallas, TX.

[viii]Buster JE, Kaltun WD, Pascual ML, et al. Low-dose estradiol spray to treat vasomotor symptoms: a randomized controlled trial. Obstet Gynecol 2008;111:1343-51.

ORAL VS TRANSDERMAL THERAPY

ORAL	TRANSDERMAL
• LARGEST TOTAL DOSES OF ESTROGEN (CEE & 17 B-ESTRADIOL) • ABSORBED FROM GI TRACT AND DELIVERED DIRECTLY TO LIVER • PRODUCE ESTRONE AND ESTRADIOL RATIONS 5X HIGHER THAN IN MENSTRUATING WOMEN • INCREASES TGLS, C-REACTIVE PROTEIN, CLOTTING FACTORS, AND SHBG	• SMALLEST TOTAL ESTROGEN DOSES • ABSORBED DIRECTLY INTO CIRCULATION VIA SKIN • PRODUCE ESTRONE/ESTRADIOL RATIONS SIMILAR TO THOSE IN MENSTRUATING WOMEN • NO STIMULATION OF HEPATIC PROTEINS AND ENZYMES

ACOG Recommends:

- Healthcare providers should individualize care on a patient by patient basis
- Women should be treated with the lowest effective dose for the shortest duration that is needed to relieve vasomotor symptoms.

NON-HORMONAL THERAPY FOR VASOMOTOR SYMPTOMS

- SELECTIVE SEROTONIN REUPTAKE INHIBITORS (PAROXETINE 7.5MG IS THE ONLY SSRI THAT IS FDA APPROVED FOR VMS)
- SELECTIVE SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS (DESVENLAFAXINE/ PRISTIQ 100MG/D OR VENLAFAXINE/ EFFEXOR 37.5-75MG/DAY)
- ALPHA 2 AGONIST (CLONIDINE .1MG/DAY)
- GAMMA AMINOBUTYRIC ACID ANALOGUE (GABAPENTIN 900MG/DAY)
- THESE MEDICATIONS ARE COMMONLY USED IN PATIENTS WHO HAVE CONTRAINDICATIONS TO ESTROGEN THERAPY WHICH IS SUPERIOR IN ALL STUDIES IN ALLEVIATING VASOMOTOR SYMPTOMS

- Neuroactive agents, such as selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors and gabapentin, appear to have efficacy, but larger, long-term, randomized, placebo-controlled trials are needed.
- The most promising agents appear to be venlafaxine, desvenlafaxine, paroxetine extended release and clonidine (oral or transdermal).
- Nonprescription remedies, such as black cohosh or soy, have been tested short term with little-to-mild efficacy over placebo. Trials are limited by variation in products, menopause populations and inclusion criteria.
- Homeopathy, magnetic therapy, reflexology, dong quai, ginseng, evening primrose oil and vitamin E have not been demonstrated to be clinically significant compared with placebo.

Nonhormonal options

- Lifestyle modifications: layering clothing and avoiding triggers
- Paced respiration: randomized, controlled trials show benefit
- Yoga: pilot trials show benefit
- Exercise: no conclusive evidence; sweating increases vasomotor symptoms
- Homeopathy: no benefit over placebo
- Magnetic therapy: no benefit
- Reflexology: no benefit

Nonhormonal prescription options demonstrating the benefits over placebo

- Venlafaxine: benefit over placebo
- Densvenlafaxine: benefit over placebo
- Paroxetine and other selective serotonin reuptake inhibitors: benefit over placebo
- Gabapentin: benefit over placebo
- Clonidine: benefit over placebo
- Progesterone: benefit over placebo

Hormonal therapy

- Standard, low and ultra-low dose: benefit over placebo depending on degree of symptoms, age and time since menopause.

Future

- FDA-approved nonhormonal medications, such as desvenlafaxine and gabapentin
- Lower dose vaginal estrogen
- Selective estrogen receptor modulators in combination with estrogen
- Estrogen receptor-β agonist MF-101

Medscape


Copyright 1997 by Randy Glasbergen. www.glasbergen.com
"Having nine lives is cool, but if I have to go through menopause again, forget it!"

VAGINAL ATROPHY

- RESULTS IN ANATOMIC AND PHYSIOLOGIC CHANGES IN UROGENITAL TRACT
- 10-40% OF WOMEN WILL EXPERIENCE ONE OR MORE SYMPTOMS OF VAGINAL ATROPHY
  - SYMPTOMS INCLUDE DRYNESS, ITCHING, BURNING, DYSPAREUNIA, DISCHARGE

COLLECTIVELY THESE SYMPTOMS MAY HAVE A DELETERIOUS EFFECT ON A WOMAN'S QUALITY OF LIFE, SELF-ESTEEM, AND SEXUAL INTIMACY

MENOPAUSAL VAGINAL SYMPTOMS TREATMENT

- ET IS THE MOST EFFECTIVE THERAPY FOR MODERATE TO SEVERE VULVAR AND VAGINAL ATROPHY
- WHEN ET IS CONSIDERED SOLELY FOR TREATMENT OF VAGINAL ATROPHY, LOCAL ET IS ADVISED
- PROGESTOGEN IS NOT GENERALLY INDICATED WHEN ET AT RECOMMENDED LOW DOSES ARE ADMINISTERED
- ANY UTERINE BLEEDING MUST BE FULLY EVALUATED IF USING LOCAL ET

VAGINAL ESTROGEN PREPARATIONS

- US FDA-approved vaginal ET products
  - Estradiol vaginal cream (Estrace)[a]
  - Conjugated estrogen vaginal cream (Premarin)[a]
  - Estradiol vaginal ring (Estring)
  - Estradiol acetate vaginal ring (Femring)[b]
  - Estradiol hemihydrate vaginal tablet (Vagifem)
- All are effective at recommended doses
- Choice depends on clinical experience and patient preference

LOCAL ESTROGEN THERAPY

Table 2. Topical Estrogen Dosage Forms

Vaginal cream (Estrace, Premarin, others) Inserted directly into the vagina with an applicator usually at bedtime daily for the first few weeks and then 2-3 times a week thereafter; more immediate relief than other vaginal forms of estrogen; can be messy.
Vaginal ring (Estring) Inserted into the upper part of the vagina by patient or health care provider; soft, flexible ring releases a consistent dose of estrogen; needs to be replaced about every 3 months; convenient.
Vaginal tablet (Vagifem) Inserted, via disposable applicator, in vagina usually daily for the first 2 weeks and then twice a week thereafter.

Source: References 1,2.

ATROPHIC VAGINITIS THERAPY

- LOCAL THERAPY IS ADVISED
- CAN BE ADMINISTERED IN CREAMS, RING, AND TABLET FORMULATIONS
- LOW DOSE 10MCG VAGINAL ESTRADIOL TABLETS IMPROVE VAGINAL SYMPTOMS
- STUDIES INDICATED THAT THE 3 MONTH VAGINAL RING IS PREFERRED TO CREAM BECAUSE OF GREATER COMFORT, EASE OF USE, AND SATISFACTION
- USE OF LOCAL ESTROGEN THERAPY DOES NOT REQUIRE ENDOMETRIAL SURVEILLANCE UNLESS WOMEN EXPERIENCE POSTMENOPAUSAL BLEEDING WHICH WOULD REQUIRE DIAGNOSTIC EVALUATION
- ADDITION OF PROGESTIN IS GENERALLY NOT INDICATED WITH LOCAL THERAPY

ADDITIONAL THERAPY FOR TREATING VAGINAL ATROPHY SYMPTOMS

- VAGINAL LUBRICANTS
  - NONESTROGEN WATER BASED OR SILICONE BASED LUBRICANTS
    - RELIEVE FRICTION DYSPAREUNIA RELATED TO VAGINAL DRYNESS
    - THERE ARE INSUFFICIENT DATA TO SUPPORT THE USE OF HERBAL REMEDIES OR SOY PRODUCTS FOR THE TREATMENT OF VAGINAL SYMPTOMS
    - OSPEMIFENE 60MG/D (OSPHENA) AN ESTROGEN AGONIST AND ESTROGEN ANTAGONIST IMPROVES VAGINAL ATROPHY WITHOUT STIMULATING THE ENDOMETRIUM
      - ADVERSE EFFECTS INCLUDE HOT FLUSHES, VAGINAL DISCHARGE, MUSCLE SPASMS, AND SWEATING
        - RALOXIFENE AND TAMOXIFEN ARE NOT EFFECTIVE IN THE TREATMENT OF MENOPAUSAL VAGINAL SYMPTOMS

VAGINAL ESTROGEN THERAPY AND BREAST CANCER

- Symptoms of VVA are common among women with breast cancer, especially those on endocrine treatments or aromatase inhibitors
- For women with a nonhormone-dependent cancer, VVA management is similar to that for women without cancer
- For women with a hormone-dependent cancer, VVA management depends on each woman's preference in consultation with her oncologist

“BIOIDENTICAL HORMONES”

- PLANT DERIVED HORMONES THAT ARE CHEMICALLY SIMILAR TO THOSE PRODUCED BY THE BODY
- INCLUDE COMMERCIALLY AVAILABLE PRODUCTS APPROVED BY THE FDA SUCH AS MICRONIZED PROGESTERONE AND ESTRADIOL
- ALSO INCLUDE COMPOUNDED PREPARATIONS THAT ARE NOT REGULATED BY THE FDA
  - THE PURITY, POTENCY, AND QUALITY OF COMPOUNDED PREPARATIONS ARE A CONCERN
    - ACOG STATES THAT CONVENTIONAL HT IS PREFERRED GIVEN THE AVAILABLE DATA

“BIOIDENTICAL HORMONES”

- SOME OF THE HORMONES ARE NOT FDA APPROVED (ESTRIOL)
- SALIVARY TESTING HAS BEEN PROVEN TO BE INACCURATE AND UNRELIABLE
  - THE FDA STATES THAT THERE IS NO SCIENTIFIC BASIS FOR USING SALIVA TESTING TO ADJUST HORMONE LEVELS
- PRODUCT INFORMATION IS NOT CONISISTENTLY PROVIDED TO WOMEN ALONG WITH THEIR PRESCRIPTION
- FOR MOST WOMEN FDA APPROVED HT WILL PROVIDE APPROPRIATE THERAPY WITHOUT THE RISKS OF CUSTOM PREPARATIONS


SOME DAY THEY'LL HAVE HOT FLASHES AND THEIR BODIES WILL CHANGE, TOO...
offthemark.com

TAKE HOME MESSAGES!!

- INDIVIDUALIZATION IS OF KEY IMPORTANCE IN THE DECISION TO USE HORMONE REPLACEMENT THERAPY
- SHOULD INCORPORATE THE WOMAN'S HEALTH AND QUALITY OF LIFE PRIORITIES AS WELL AS HER PERSONAL RISK FACTORS SUCH AS RISK OF VTE, CHD, STROKE AND BREAST CANCER
- DURATION OF EPT IS LIMITED BY INCREASED RISK OF BREAST CANCER AND SHOULD BE LIMITED TO 3-5 YEARS
- ET HAS A MORE FAVORABLE BENEFIT/ RISK PROFILE WHICH WAS OBSERVED DURING A MEAN OF 7 YEARS OF USE AND 4 YEARS OF FOLLOW-UP GIVING GREATER FLEXIBILITY IN OVERALL DURATION OF USE
- ET IS THE MOST EFFECTIVE TREATMENT FOR VULVAR/ VAGINAL ATROPHY

TAKE HOME MESSAGES

- WOMEN WITH PREMATURE OR EARLY MENOPAUSE, CAN USE HT AT LEAST UNTIL MEDIAN AGE OF NATURAL MENOPAUSE (AGE 51)
- ALTHOUGH ET DID NOT INCREASE BREAST CANCER RISK IN THE WHI, THERE IS A LACK OF SAFETY DATA SUPPORTING THE USE OF ET IN BREAST CANCER SURVIVORS
- BOTH TRANSDERMAL AND LOW DOSE ORAL ESTROGENS HAVE BEEN ASSOCIATED WITH LOWER RISKS OF VTE AND STROKE THAN STANDARD DOES OF ORAL ESTROGEN, RCT ARE PENDING

THE END!!!!!


It is a known fact that we just keep getting HOTTER with AGE . . .
HOT MAMA