HORMONAL HEALTH INSTITUTE
Executive Instruction for Medical Professionals

Female Hormone Therapy 101

Angela DeRosa, DO, MBA, CPE

1

Angela DeRosa, DO, MBA, CPE

Founder and President of Hormonal Health Institute

- Board Certified Internist
- Women's Health Specialist
- Author, Lecturer and Published Researcher
- Belmar Pharma Solutions, Medical Director and BOD
- MBA Amhurst Business College
- Founder and President of DeRosa Medical, DRM Integrative Health & Revive Wellness
- European Menopause and Andropause Society Advisory Board
- Board and Executive Committee, Past President, Arizona Osteopathic Medical Association
- 20+ years in advanced BHRT therapy and hormone optimization, treated more than 20,000 patients

2

Disclosure Statement

- Dr. DeRosa is the founder and CEO of the Hormonal Health Institute and the Medical Director for Belmar Pharma Solutions.
- All of the relevant financial relationships listed for Dr. DeRosa have been mitigated.

3

Objectives

1. Summarize the indications and contraindications for the use of estradiol, and progesterone and testosterone

2. Discuss clinical information for the use of estradiol, progesterone and testosterone in patients diagnosed with hormonal deficiencies and explain how to clinically apply this knowledge in clinical practice

3. Recall menopausal basics and how to properly identify and assess hormone deficiency in women

4. Review the evidence related to breast cancer and cardiovascular disease as well as other clinical outcomes related to hormone replacement in men and women

4

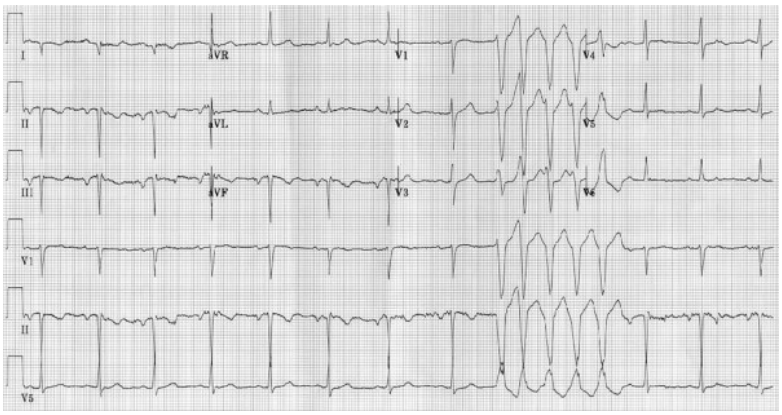
5

"The things you are passionate about are not random, they are your calling."

– Fabienne Fredrickson

6

27 Years Old and 2nd Year Resident



- Extreme Fatigue
- Insomnia
- Hot Flashes/Night Sweats
- Low Libido
- Anxiety/Depression
- Weight Gain
- Heart Palpitations, Pre-Syncope

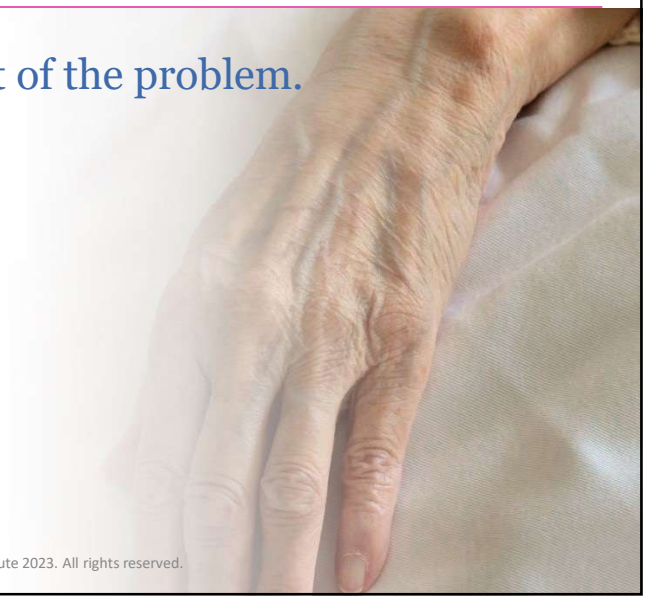
7

The medical profession failed me…

8

…and I was part of the problem.

- Chronic illness and comorbidities
- More medications
- Skyrocketing cost
- Non-compliance
- Managing to illness
- Slow march to death



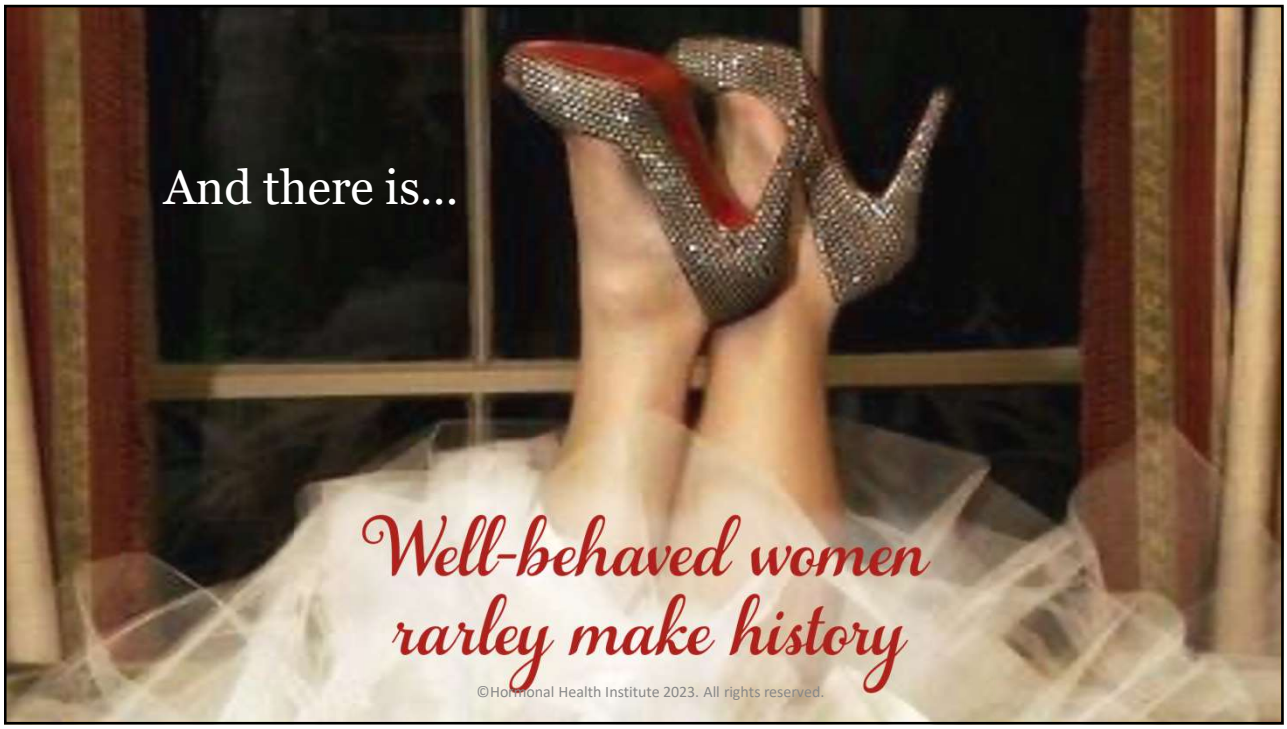
9

There had to be a better way.

"To find health should be the object of the doctor. Anyone can find disease."

– Andrew Taylor Still

10



11

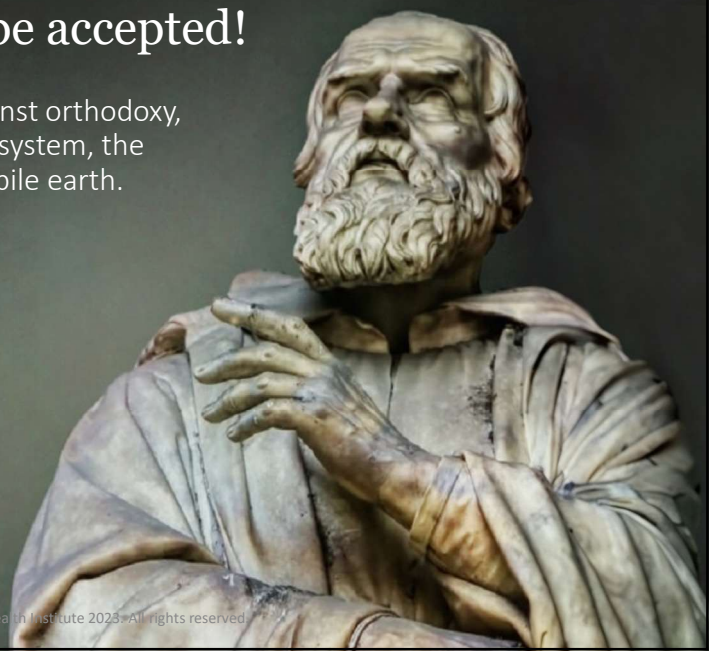
Current State of Affairs

- 20th Century and Population Growth
- 21st Century and Ageing
- Life Expectancy and Health Expectancy
- Health Care Burden and Costs
- Need for preventive, holistic osteopathic strategies
- Complimentary and integrative medicine which includes hormonal medicine is rapidly evolving, although not all providers and associations agree on its role in the treatment of our patients
- Many current guidelines diagnosis and treat to illness but do not make recommendations to treat to optimal health
- Modern scientific medicine prefers laboratory measurements rather than assessing patient's symptoms; regardless of the fact that it is the symptoms that make up syndromes

12

Medical dogma cannot be accepted!

This is reminiscent of Galileo's fight against orthodoxy, to make the sun the center of the solar system, the heliocentric view, rather than an immobile earth.



13

Just the facts, ma'am.

14

What Is Menopause?

- The ovaries are officially retired
- Determined by:
  - Lack of Periods for 12 months
    - Ablation, OCP and IUDs complicate this prediction
  - Surgical removal of the ovaries
  - Chemical shut down of the ovaries
    - May be temporary
  - Laboratory assessment
- Does not usually happen overnight
  - Slow decline of ovarian function for a decade or more
  - Hormonal deficiency signs and symptoms usually present

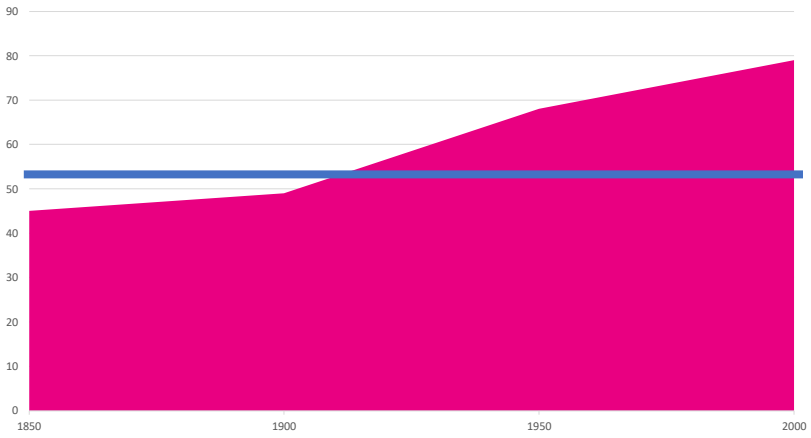
15

Statistics

- 51 years is the average age of menopause globally
- Premature Menopause is menopause before age 40
  - May happen naturally, surgically when both ovaries are removed, or be induced by chemotherapy or radiotherapy for malignancies
- Population shifts
  - 1998: ~ 477 million women in menopause
  - 2025: estimated 1.1 Billion women

16

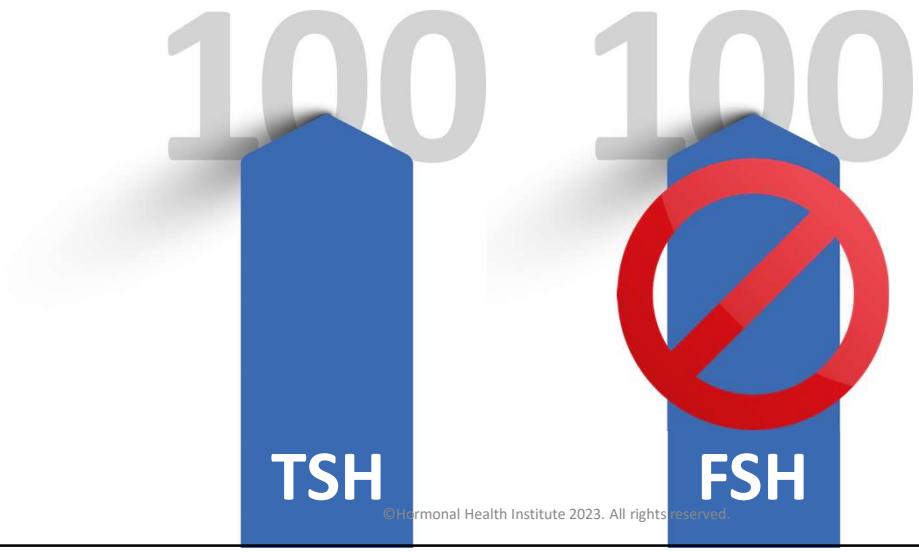
Life Expectancy and Menopause



J Am Geriatric Soc 1982;30:548

17

TSH versus FSH

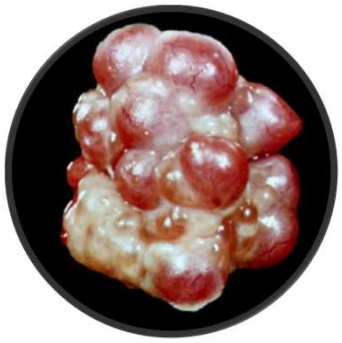


18

Ovarian Hormonal Secretion

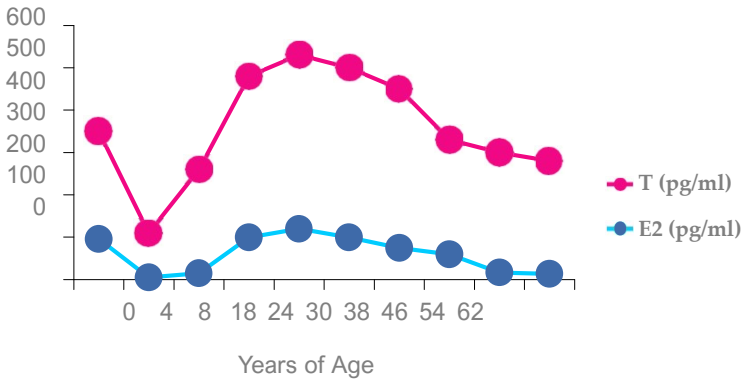
Estradiol
100%

Testosterone
95%



Testosterone > Estradiol levels

Throughout the entire female lifespan



Dimitrakakis 02

Symptoms of Estrogen Deficiency

Hot Flashes • PMS Worsening • Night Sweats

Irritability • Dry Itchy Skin • Insomnia • Depression

Mood Swings • Forgetfulness • Vaginal Dryness

Heart Palpitations • Increased Allergies

Dry Hair and/or Hair Loss • Vision Changes

Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives.
Woods NF, Mitchell ES
Am J Med. 2005;118 Suppl 12B:14.

Symptoms of Testosterone Deficiency

Low Libido • Weight Gain • Loss of Focus

Anxiety • Depression • Muscle Pain

Mood Swings • Memory Loss • Migraine Headaches

Sugar Cravings • Fatigue • Belly Fat

Lobo RA. Androgens in postmenopausal women: production, possible role, and replacement options. Obstet Gynecol Surv. 2001 Jun;56(6):361-76.

Long Term Consequences of Hormone Deficiencies

- HTN
- Insulin Resistance and Diabetes
- Hypercholesteremia
- Cardiovascular Disease
- Osteoporosis
- Cancer
- Dementias

23

Role of Progesterone

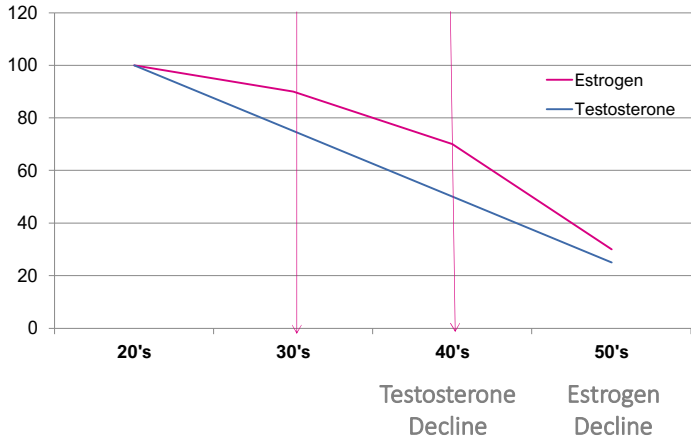
- Prepares the Body for Pregnancy

Goletiani NV, Keith DR, Gorsky SJ. Progesterone: review of safety for clinical studies. Exp Clin Psychopharmacol. 2007 Oct;15(5):427-44

24

Hormonal Peak to Decline

Estrogen = Cash and Savings
Testosterone = Cash Only



Special Consideration: Surgical Menopause

HYSTERECTOMY

With one ovary removed

- Reduction in E2 & T1 levels by at least 50%

Without ovary removal

- Increases risk for early E2 &T1 deficiency due to disruption of blood supply to ovaries from the surgery

The Best Way…

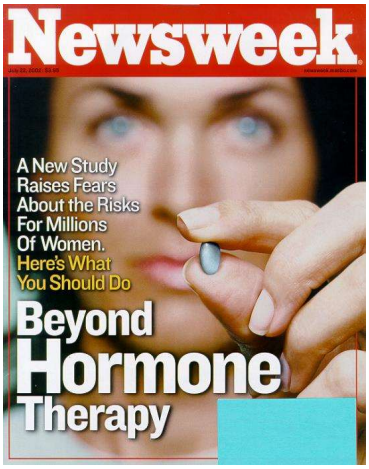
…to manage symptoms of menopause is to optimize or replace

27

So… If hormones are so great, why aren't more women taking them?

28

Media Message



"Hormone therapy resulted in a 26% increase in breast cancer risk and a 29% increased risk in heart disease."

29

Interpreting Data

When it comes to "data" one must have a high level of skepticism and an ability to understand the information presented.

30

Statistical Homicide

"The Triumph of Long Odds Over Common Sense."

31

What Are The Biggest Risks In Life?

- Driving
- Boating
- Smoking
- Drinking
- Household chores

32

What Worries The Public?

- Cell phones
- PCB's
- High voltage lines
- Pesticides
- Ozone depletion
- E. coli contaminated beef
- Nuclear accidents
- Breast implants
- SARS
- IUDs
- Air Travel
- Mad cow disease
- Gluten
- **Hormone Therapy**

33

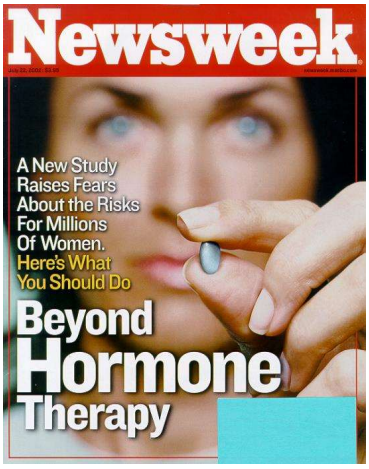
34

Medical War Waged Against Women (And Hormones)

- What works again against women in medicine
  - Gender Bias
  - Politics
  - Pharmaceutical Companies
  - Money
  - Lack of Research
  - Media and Celebrities
  - **Fear**

Fear of breast cancer fuels the debate about hormone therapy.

Media Message



"Hormone therapy resulted in a 26% increase in breast cancer risk and a 29% increased risk in heart disease."

Women's Health Initiative

- NIH wanted to assess effect of Hormones on CVD and breast cancer and spent $700 million to do so
- Two hormone trials
  - 16,000 women with a uterus
    - PremPro (Estrogen and Progestin) versus placebo
- 10,000 women after hysterectomy
  - Premarin (Estrogen alone) versus placebo
  - 16,000 women with a uterus
    - PremPro (Estrogen and Progestin) versus placebo
- To reduce expense and time they enrolled women up to age 79
- 2/3 of the women in the trial were over 60 years old
- Trial was stopped early due to concerns about breast cancer and increased cardiovascular risk

The Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701-12

Original WHI Findings: PremPro Arm

Condition	Reduces Risk	Insufficient Evidence	Increases Risk
Breast Cancer			8
CHD			7
VTE			18
Stroke			8
Fractures	44		
Colon Cancer	6		

Actual Number of Women Per 10,000

Revised WHI Findings: PremPro Arm

Condition	Reduces Risk	Insufficient Evidence	Increases Risk
Breast Cancer		✓	
CHD	✓ Women Age 50-62		
VTE			✓
Stroke			✓
Fractures	✓		
Colon Cancer	✓		

Actual Number of Women Per 10,000

Roger Lobo, "Where are we 10 years after the Women's Health Initiative"
J Clin Endocrinol Metab, May 2013, 98(5):1771–1780

39

Original WHI Findings: Premarin Arm

Condition	Reduces Risk	Insufficient Evidence	Increases Risk
Breast Cancer	✓		
CHD		✓	
VTE			✓
Stroke			✓
Fractures	✓		
Colon Cancer	✓		

Actual Number of Women Per 10,000

40

Revised WHI Findings: Premarin Arm

Condition	Reduces Risk	Insufficient Evidence	Increases Risk
Breast Cancer	✓		
CHD	✓ Women Age 50-62		
VTE			✓
Stroke			✓
Fractures	✓		
Colon Cancer	✓		

Actual Number of Women Per 10,000

Roger Lobo, "Where are we 10 years after the Women's Health Initiative"
J Clin Endocrinol Metab, May 2013, 98(5):1771–1780

41

In the Women's Health Initiative randomized, placebo controlled trial evaluating conjugated equine estrogen (N=10.739), ER-positive, PR-negative cancers were statistically significantly reduced in the intervention group (hazard ratio, 0.44; 95% CI, 0.27 to 0.74) and deaths from breast cancer were reduced 40% (P= 0.04).

…These findings suggest that reexamination of breast cancer risk reduction strategies and clinical practice is needed.

* R. Chlebowski et al. "Breast Cancer Prevention: Time for Change" JCO Oncology Practice
Volume 17, Issue 12 page 709-716

42

What Did the WHI Actually Find?

- Neutral risk of breast cancer in the PremPro arm
- Decreased risk of breast cancer in Premarin arm
- Decreased risk of CVD in women 50-59 years old both arms
- Women on Premarin not only had a risk reduction in breast cancer but also a 40% reduction in all cause mortality from breast cancer
- Women 10 years from menopause greatly benefit from HRT
- Older women with CVD should use caution when starting hormones

Pandering

Media Headlines pandering to women's greatest fear—breast cancer — spread the word of the study like wildfire and ensured the conversation was driven by emotion and politics rather than science!

Breast Cancer (BC) Studies Summarized

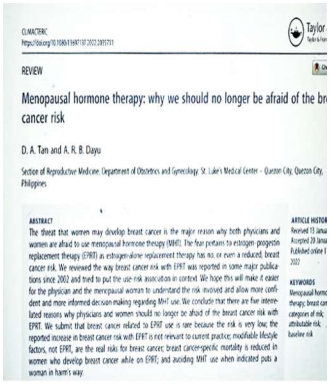
WHI: CCE alone	• CEE 0.625mg/d alone vs placebo • Treatment for 7.2 years • 18 Follow up years	• Typical PMP female, no previous MHT • Decreased BC incidence, 45% BC mortality reduction
WHI: CEE + MPA	• CEE o.625mg/d + MPA 2.5mg/d placebo • Treatment for 5.6 years • 18 Follow up years Randomized to the placebo arm had a lower BC incidence than all other WHI RCT	• Typical PMP female, no previous MHT • Neutral effect on BC incidence and BC mortality • Older PMP females, who had previously used MHT prior to randomization, those placebo groups and the WHI-OS comparator group

WHI 2020 update	• CEE alone vs placebo, 7.2 treatment years
	• CEE + MPA vs placebo, 5.6 treatment years
	• 20 follow-up years
		• CEE alone-vs placebo: decreased BC incidence and mortality
		• CEE + MPA previous MHT: null effect on BC mortality (like placebo group) but because of faulty analysis that was never corrected, still reporting increased BC incidence (See Hodis and Sarrel WHI 2018 reanalysis)
		  • Placebo arm had a lower BC incidence than all other placebo groups in WHI studies
		  • CEE + MPA no previous MHT: no SS difference when compared to placebo

WHI: WHI-OS	• CEE 0.625mg/d (18.5 years treated) • CEE <0.625mg/d (17.4 years treated) • TD E2 dose and delivery unknown (14 years treated) • 8.2-year follow-up study	• PMP females s/p hysterectomy • CEE 0.625mg/d vs CEE <0.625mg/d: no difference in invasive BC risk • Cee 0.625mg/d vs TD E2 with a non-significant decreased BC risk • Time since menopause had no effect on invasive BC risk
FINNISH-OS	• O-E2 1 or 2md/d • TD E2 0.025 -0.1mg/d patches • TD E2 0.5-1.5mg/d gels • Progestins used in PMP females with a uterus • Placebo	• All MHT users (even when combined with a progestogen had an up to 54% BC mortality reduction • E2 alone had the greatest mortality reduction, regardless of age • Females 50-59 years old had the greatest mortality reduction • With E2 BC mortality 1 in 20 females, whereas without E2 BC mortality 1 in 10 females
Million Women's	• CEE, 0-2, TD E2, pellets: doses unknown • Never users (comparator)	• All increased BC "relative risk" and "relative" mortality risk • Increased BC and BC mortality occurred in females who likely had undiagnosed BC • Comparator group had a lower BC incidence than the general population, skewing the data
E3N	• Primarily TD E2 • Some used 0-E2 • Never users (comparator)	• Increased BC "relative risk" • Data not clean: large percentage in the TD E2-only group used combined therapy and large percentage in the TD E2 + OMP group used progestin

45

The Pendulum is Swinging


REVIEW

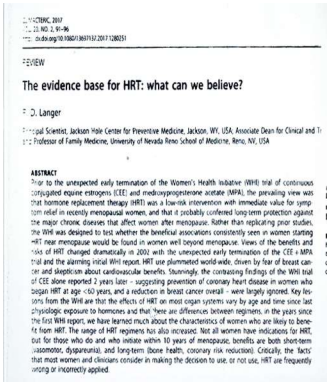
Menopausal hormone therapy: why we should no longer be afraid of the br
cancer risk

D. A. Tan and A. R. B. Dayu

Section of Reproductive Medicine, Department of Obstetrics and Gynecology, St. Luke's Medical Center – Quezon City, Quezon City, Philippines

ABSTRACT

The threat that women may develop breast cancer is the major reason why both physicians and women are afraid to use menopausal hormone therapy (MHT). The fear pertains to estrogen-progesta replacement therapy (EPRT) as estrogen-alone replacement therapy has no, or even a reduced, breast cancer risk. We reviewed the way breast cancer risk with EPRT was reported in some major publica tions since 2002 and tried to put the use-risk association in context. We hope this will make it easier for the physician and the menopausal woman to understand the risk involved and allow more confi dent and more informed decision-making regarding MHT use. We conclude that there are five interre lated reasons why physicians and women should no longer be afraid of the breast cancer risk with EPRT. We submit that breast cancer related to EPRT use is rare because the risk is very low, the reported increase in breast cancer risk with EPRT is not relevant to current practice, modifiable lifestyle factors, not EPRT, are the real risks for breast cancer, breast cancer-specific mortality is reduced in women who develop breast cancer while on EPRT, and avoiding MHT use when indicated puts a woman in harm's way.

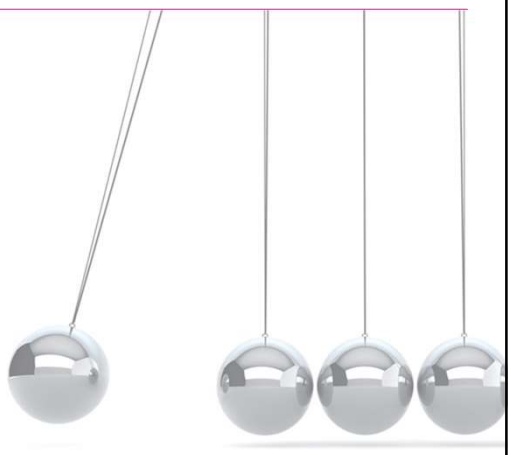

REVIEW

The evidence base for HRT: what can we believe?

D. Langer

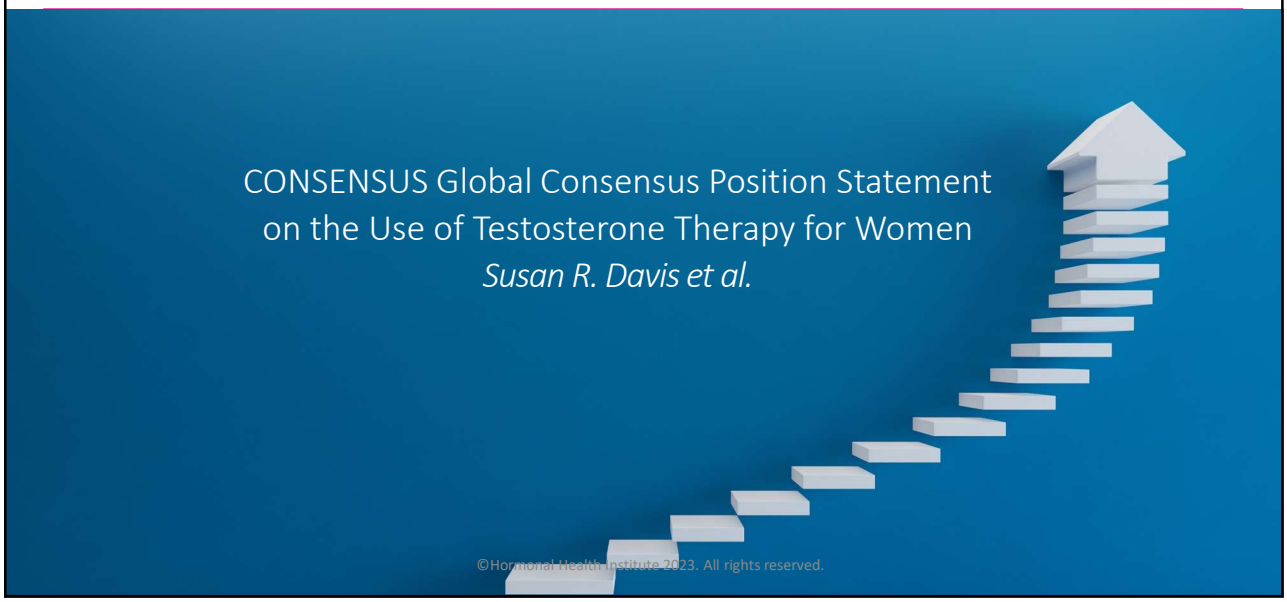
ABSTRACT

Prior to the unexpected early termination of the Women's Health Initiative (WHI) trial of continuous conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA), the prevailing view was that hormone replacement therapy (HRT) was a low-risk intervention with immediate value for symp tom relief in recently menopausal women, and that it probably conferred long-term protection against the major chronic diseases that affect women after menopause. Rather than replicating prior studies, the WHI was designed to test whether the beneficial associations consistently seen in women starting HRT near menopause would be found in women well beyond menopause. Views of the benefits and risks of HRT changed dramatically in 2002 with the unexpected early termination of the CEE + MPA trial and the alarming initial WHI report. HRT use plummeted world-wide, driven by fear of breast can cer and skepticism about cardiovascular benefits. Stunningly, the contrasting findings of the WHI trial of CEE alone reported 2 years later – suggesting prevention of coronary heart disease in women who began HRT at age <60 years, and a reduction in breast cancer overall – were largely ignored. Key les sons from the WHI are that the effects of HRT on most organ systems vary by age and time since last physiologic exposure to hormones and that there are differences between regimens, in the years since the first WHI report, we have learned much about the characteristics of women who are likely to bene fit from HRT. The range of HRT regimens has also increased. Not all women have indications for HRT, but for those who do and who initiate within 10 years of menopause, benefits are both short-term (vasomotor, dyspareunia), and long-term (bone health, coronary risk reduction). Critically, the facts that most women and clinicians consider in making the decision to use, or not use, HRT are frequently wrong or incorrectly applied.



46

A Step Forward?



47

The True Experts

- Testosterone is NOT a male-exclusive hormone. It is the most abundant gonadal hormone throughout a woman's life.
- Serum testosterone levels do not correlate with symptoms of testosterone deficiency in women. Optimal ranges of serum testosterone levels in women have not been established.
- Female testosterone insufficiency is a clinical syndrome that may occur during any decade of adult life.
- Testosterone therapy may be breast protective.
- Testosterone insufficiency in women negatively affects sexuality, general health, and quality of life. Supplementation may positively influence sexuality, general health, and quality of life.
- Testosterone insufficiency may be associated with an increased risk of cardiovascular disease in women.
- Testosterone optimization may be brain protective and may enhance cognitive function.
- Testosterone optimization may be a key component for improved bone health.
- Testosterone therapy in women has no adverse effects on lipids and/ or cardiovascular risk.
- Studies of testosterone supplementation show benefits exceed the risk and that consistent purity and potency can be achieved

Donovitiz et al. "Testosterone insufficiency and treatment in women"
International Expert consensus. Medicina Salud Public Sept. 4th, 2019

48

Gender Bias At Its Finest!!!

Gender Bias in the Treatment of Menopausal Women:
I am Hot as Hell and Not Going to Take It Anymore
Part 1 and 2
Dr. Angela DeRosa
International Journal Of Pharmaceutical Compounding
Vol. 24 No. 6 Nov/Dec 2020
Vol. 25 No. 1 Jan/Feb 2021

49

Proper Intake for Hormonal Assessment

Female

50

Female Hormonal Intake

Patient is a (age) G___ P____ female with a PMHX of _____.
TAH/BSO (or has ovaries) or uterine ablation? If so, why?

She presents today for_____.

Is she still menstruating? If so, are her periods regular or irregular? LMP?
Or is she in menopause? If so, how long since her last period?

Is she UTD on paps, mammo, DXA, colonoscopy? Any abnormal or history of abnormal?

Important Clinical History

- Hormonal symptoms (next slide)
- Past or current treatment with hormones:
  - Current HRT regimen
  - +/_ effects
- Previous gynecologic issues including infertility, irregular periods, OCP, other birth control
- Other endocrine issues/treatments
- Previous work up or diagnoses by other providers
- Any significant meds and why they are being used

Hormonal Symptoms

Estrogen Deficiency	Testosterone Deficiency
• Hot flashes, night sweats • Vaginal dryness, dyspareunia • Mental fogginess/forgetfulness • Insomnia • Dry skin and hair/saggy skin • Heart palpitations	• Low libido • Mid-section weight gain • Irritability, impatience • Anxiety/depression/mood disorders (new or worsening) • Migraine headaches (new) • Muscle aches and pains • Decreased endurance and work out recovery
Estrogen Excess	**Testosterone Excess**
• Breast fullness or tenderness • Water retention • Weight gain • Crying spells/depression • Pelvic fullness	• Acne • Nipple pain • Hypersexual • Clitoral enlargement • Voice deepening • Excess hair
Progesterone Excess	
• Breast fullness or tenderness • Water retention	• Weight gain • Crying spells/depression (new)

Important Clinical Physical Exam Clues

- Obesity especially increase in mid- section
- Thin hair/dry hair
- Very dry skin, paper thin skin, yellowish hue to skin
- Saggy jowls
- Vaginal atrophy/vaginitis

Consider Depression Screening, such as PHQ-9

53

Menopause Rating Scale (MRS)

Which of the following symptoms apply to you at this time? Please mark the appropriate box for each symptom. For symptoms that do not apply, please mark 'none'.

SYMPTOMS	NONE	MILD	MODERATE	SEVERE	VERY SEVERE
SCORE	0	1	2	3	4
Hot flushes, sweating (episodes of sweating)	❑	❑	❑	❑	❑
Heart discomfort (unusual awareness of heartbeat, heart skipping, heart racing, tightness)	❑	❑	❑	❑	❑
Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early)	❑	❑	❑	❑	❑
Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings)	❑	❑	❑	❑	❑
Irritability (feeling nervous, inner tension, feeling aggressive)	❑	❑	❑	❑	❑
Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration)	❑	❑	❑	❑	❑
Sexual problems (change in desire, in activity, and satisfaction)	❑	❑	❑	❑	❑
Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence)	❑	❑	❑	❑	❑
Dryness of vagina (sensation of dryness or burning in the vagina difficulty with sexual intercourse)	❑	❑	❑	❑	❑
Join & muscular discomfort (joint paint, rheumatoid complaints)	❑	❑	❑	❑	❑

54

Contraindications to Hormones

55

Absolute Contraindications!

- Pregnancy/breast feeding
- Breast Cancer Active
  - E2 only
  - T1 ok with Oncology approval
- Gynecologic Cancer Active
- Acute Thromboembolic disorder
- Acute Myocardial Infarction
- Severe Liver Disease
- Severe Cardiac Disease
- Severe Renal Disease

Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline.
AU
Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ
SO
J Clin Endocrinol Metab. 2015;100(11):3975.

Midwinter, A. (1976). Contraindications to estrogen therapy and management of the menopausal syndrome in these cases. In: Campbell, S. (eds) The Management of the Menopause & Post-Menopausal Years.

56

Relative Contraindications

- History of breast cancer
  - E2 only
  - Remote s/p mastectomy (?)
- History of endometrial cancer
- Enlarging uterine fibroids
- Uncontrolled HTN
- History of heart disease / valve replacement / pacemaker
- Atrial fibrillation on anticoagulant therapy
- CAD with 7-10% risk
- Untreated sleep apnea
- Smokers
- Estrogen-dependent migraine
- Severe Psychiatric disorders
- Self assessed “Sensitivities to Hormones”

Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline.
AU
Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ
SO
J Clin Endocrinol Metab. 2015;100(11):3975.

Midwinter, A. (1976). Contraindications to estrogen therapy and management of the menopausal syndrome in these cases. In: Campbell, S. (eds) The Management of the Menopause & Post-Menopausal Years.

Contact

info@hormonalhealthinstitute.com
www.drhotflash.com
www.hormonalhealthinstitute.com


50%
50%