Female Hormones: To treat or not to treat

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Objectives

To eliminate the fear of hormone treatment in the female patient
- WHI timeline, data and consequences

Identify patients that will benefit from HRT
- LG window of opportunity and screening

Hormone options and treatment strategies
Hormones are special chemical messengers created in endocrine glands.
Estrogen: The Female Sex Hormone
Estrogen Receptors
Estrogen Metabolism
Progesterone: The Mother Hormone
Hormone Studies
Testosterone: Female Sex Hormone
WHI 2002 - “FEAR”

US National Institutes of Health – Sponsored randomized controlled trial comprised of 4 therapeutic arms

The subjects were free from symptoms

83% were 5 years past menopause

The design was to compare different therapeutic approaches to primary outcomes, such as prevention of CVD and osteoporosis

13% increased risk of comorbidities: MI, Stroke, Breast CA,

0% mortality
WHI 2002

Hastily reported data concluded young and old alike had similar risk profiles

Study design failed to account for various age groups

Risk profiles

Endothelial health

Assumed that comorbidities lead to increased mortality yet the data failed to show increased mortality

Prescription sales 2001 at 93.1 million dropped to 31.8 by 2007
Timeline

What was the course of consequences after 2002?

Media release of WHI data with misleading headlines, released by investigators for shock value

..... The adverse effects of estrogen plus progestin applied to all women, irrespective of age, ethnicity, or disease status.

WHI- reported 13% increase risk of comorbidities: MI, Stroke, and breast cancer (NO INCREASE IN MORTALITY)
Timeline

2004: Osteoporosis-related fractures increased from 9 in the year 2000-107 in the year 2004 after women stopped HRT

2006 WHI data begins to match pre-WHI data with regard to the HRT benefit in younger perimenopausal and postmenopausal women (50-59 years of age). Cardiac calcium scores were lower and total mortality was decrease in the younger age group that had been treated with HRT compared to those not treated with HRT.

2008 Osteoporosis-related hip fractures increased in women who discontinued HRT compared with those who maintained it (HR 1.55; 95% CI 1.36-1.77; P<.0001)
Timeline

2009: HRT use in women over age 40 was 4.7%; in women 50-59 it was 6.7%

2011: The “missed decade” is formally declared a disservice to the women’s community by the International Menopause Society (IMS), which states “The excessive conservatism engendered by the presentation to the media of the first results of the WHI in 2002 has disadvantaged nearly a decade of women who may have missed the therapeutic widow to reduce their future cardiovascular, fracture, and dementia risk.

Sarrel et al. estimates the number of premature deaths of women between the years 2002-2011 that can be attributed to not being treated with HRT is at least 18,601
Timeline

A maximum of 91,610 deaths might be attributable to the fear generated from the WHI trial that resulted in the precipitous drop in HRT use.

Some investigators suggest that the rising mortality rate among women in almost half the US countries could be attributable to the misinformation from the 2002 publication of the WHI trial.

By 6.5 years after the WHI trial, those who discontinued HRT were at 55% greater risk of hip fracture (HR 1.55).
Data Collection

Meta analysis in 2004 from randomized controlled trials indicate that women younger than 60 years of age benefit from a 39% reduced mortality rate.

2009- Detailed meta analysis combining both observational and experimental data also showed reduced mortality.

2008 Salpeter study incorporated 19 randomized controlled studies and 8 observational studies for a total of 16,000 women (average age 55) followed for 83,000 patient years.

Mortality reduction was 27% with HRT (bioidentical) use.
What We KNOW

“It will take time, interest, and energy for practitioners and patients who were exposed to the media hype of the premature release of WHI data to understand why the myth existed, why it has been debunked, and that the next step in the therapeutic algorithm should include HRT for the patient concerned about the quality of life and longevity”
What We KNOW

Two globally prominent societies, the NAMS and the IMS, agree that the data from the WHI shows the benefits of HRT outweigh the risks in patients under 60 years of age even, even considering the problems with non bioidentical therapy (CEE 0.625 and MPA)

IMS recognizes overall safety is closely related to the age at initiation, with the benefits largely appreciable in those patients initiating HRT within a few years of menopause

NAMS agrees on the timing, and alludes to secondary intervention with HRT in osteoporosis.

The myth of HRT as being unsafe is now debunked, similar to the myth of saturated fat causing CVD
What We KNOW

Thromboembolic risk is reduced with transdermal use

Breast cancer risk is reduced with micronized progesterone

Primary prevention is possible with CVD, osteoporosis and cognitive decline. in those treated in the LG window of opportunity

Lipid markers and other cardiovascular risk factors are stabilized with proper timing and administration

QOL has substantial improvement in those treated with appropriate therapy: sleep, sexual, mood, joint etc.

Must be clear about bioidentical hormone use and that when screened correctly HRT is not risky when bioidetical therapies are used for women with low CVD risk under age 60 years of age.
Unstable Plaque Hypothesis:

Oral estrogen increases pro-inflammatory markers, which leads to degradation of the stabilizing portion of plaque.

Instability results from degradation and will eventually increase the risk of plaque rupture and embolic events.

When ASVD is well established (in elderly women without HRT), oral estrogen therapy includes potential cardiovascular risk related to the elevation of MMP, which can cause plaque rupture: this risk is absent with treatment of estrogen therapy in the absence of significant atherosclerotic plaque.
What We KNOW

HRT for women less than 10 years from onset of menopause no later than age 60.

No history of CVD (MI), breast cancer, or severe liver disease

HRT for primary prevention of CVD, breast cancer, cognitive decline, mortality and other benefits (e.g., urogenital atrophy prevention)

HRT for a postmenopausal female if the risk benefit ratio is markedly favorable

Decision is an *individual* one, based on assessment, ability of the patient to understand, potential for risk and their degree of comfort accepting unknown factors.

Transdermal 17 beta estradiol and+/- micronized progesterone- safest profile/+ or - testosterone
Pills, Patches, Creams, and Injections
The most optimal Hormone Replacement Therapy for many
Increased energy levels
Restored interest in life
Increased sex drive
Consistency in moods
Relief from anxiety and depression
Increased mental clarity
Decreased body fat