HRT UPDATE: THE ESTROGEN WINDOW

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By 2025, the number of postmenopausal women is expected to rise to 1.1 billion worldwide.
CARMEN DELL 85

World oldest working Supermodel. Still graces magazine covers & actively modeling. She attributes her enduring youthfullness to plenty of movement & Estrogen Therapy.
When is Medical Intervention Required?

Symptoms and Disorders in Relation to Age and Menopause

Menopause

40 yrs  ↓  50 yrs  →  60 yrs

Vasomotor Symptoms
Sleep Disorders
Mood Changes

Vaginal Atrophy
Dyspareunia
Skin Atrophy

Menstrual Disorders

Osteoporosis
Atherosclerosis
Coronary Heart Disease
Cerebrovascular Disease

Health outcome of 10,700 women on Estrogen Therapy followed for over 11 years:

- **23% reduction in breast cancer risk**
- **30% reduction in mortality rate**
  - mostly because of decreased heart disease, although there was also a lower risk of cancer & other causes of death
- **30-40% reduction in osteoporotic fractures**

HEART DISEASE

• Most major cause of death after menopause

• Women are 10 times more likely to die from heart disease than of breast cancer

• More women die from CVD than from all other causes of death combined
• The benefits of estrogen initiated within the first few years of menopause far outweigh any potential side-effects.

• A delay of 10 years or more before beginning MHT allows time for adverse changes such as artherosclerosis to develop.

• ET begun during the estrogen window reduces heart attacks & stroke.
OSTEOPOROSIS – Silent Killer

• Preventable & Treatable

• MHT protects women against post-menopausal osteoporosis & fractures

• 30% of women above 65 who do not take MHT will suffer from an osteoporotic fracture

• 20% die within 1 year of hip fracture

• Mortality is greater for hip fracture than breast cancer in elderly women

• Any therapy, particularly MHT, which reduces the risk of osteoporosis will result in a lessening of premature death among post-menopausal women
HIP FRACTURES INCREASED AFTER WHI because many women stopped MHT

• After WHI, many women stopped MHT & 10 years later, research confirmed what was feared may happen had happened.

• The Kaiser Permanente Health Organization in Southern California carried out a longitudinal study of 80,955 post-menopausal women.

• During a mean of 6.5 years of follow up after the release of the WHI findings it was found that hip fractures increased by 55% among those who ceased MHT compared to those who continued on their estrogen therapy.

ESTROGEN PREVENTS BONE LOSS

- When estrogen was replaced immediately after surgical menopause, there was no bone loss over the next 12 years.
- Delay of 3 years before starting estrogen, women already lost 10% of their bone density - but if given estrogen at that time, the bones were able to regain the lost density.
- Delay of 6 years before starting estrogen - unable to regain lost bone - but no further bone loss.

ALZHEIMER’S DEMENTIA

• New epidemic, 1 in 3 die with dementia
• Begin 10-15 years after menopause.
• Based on evidence to date, it is likely that estrogen reduces toxic damage to all body cells, but in particular it helps protect brain cells.
• Estrogen therapy if begun in the peri-menopause & during the estrogen window, helps to control the release of enzymes that may result in a reduction in Alzheimer’s dementia by 30%.
• Estrogen therapy started 10 or more years after the menopause may actually increase the incidence of dementia.

THE UNNECESSARY FEAR OF BREAST CANCER

• The worry about breast cancer is the major reason why women say NO to estrogen.

• WHI: less than 1 additional case of breast cancer diagnosed per 1,000 women who had formerly used EPT (rare)

• EPT does not increase the risk of dying from breast cancer.
BREAST CANCER

• The etiology is **multifactorial** & is likely to involve more than just 1 factor when it does occur.

• It develops in about **12% of women who live to 90**.

• The large majority are **sporadic** in nature.

• **Over 80% of breast cancers in postmenopausal women occur in women who have never taken hormone therapy.**

Nick Panay, Paula Briggs, Gab Kovacs, Managing the Menopause. 21st Century Solutions 2015
WHAT CAUSES BREAST CANCER

• Caused by an accumulation of up to 200 abnormal mutation of genes within the cell & the majority of these mutations probably occur prior to menopause.

• 25% are diagnosed in pre-menopausal women.

• Estrogen does not cause mutations but may accelerate the growth of a cell that has already accumulated some of the mutations if the cell contains a receptor for estrogen.

• After 50, risk doubles every 10 years regardless of whether on estrogen therapy or not.
RISK FACTORS FOR DEVELOPING BREAST CANCER

• Family history 3-5x
• Age
• Dense tissue in breasts 2x
• **Smoking** 10/> cigarettes daily 2x
• 2/> **alcoholic** drinks daily 2x
• **Obesity** 1.5x
• **Sedentary** lifestyle 1.5x
• EPT 1.3x (ET no increase risk)

• Never pregnant 1.2x
• Early menarche +/- or late menopause 1.2x.
BREAST CANCER

• The risk of breast cancer in women over 50 years associated with HRT is a complex issue.
• The increase risk of breast cancer is primarily associated with the addition of a synthetic progestogen to estrogen therapy & the duration of use.
• The risk may be lower with micronized progesterone or dydrogesterone than with other progestogen.

REDUCED RISK OF BREAST CANCER MORTALITY IN WOMEN USING MHT

- 489,105 women on MHT were followed-up for 15 years (1994-2009)
- Breast cancer mortality was reduced in all MHT users with exposure for 5, 10 and >10 years
- A significant larger risk reduction was detected in the 50-59 years age group
- The death risk reductions in ET users are better than EPT users - in all age groups.
- In the Finnish unselected population, breast cancer is fatal in 1 of 10 patients, but in MHT user the mortality risk is reduced by 50% (1 in 20)

2016 IMS (International Menopause Society) RECOMMENDATIONS on WOMEN’S MIDLIFE HEALTH & MENOPAUSE HORMONE THERAPY
The 2017 Hormone Therapy position statement of The North American Menopause Society (NAMS)

Vol.24, No. 7, pp. 728-753 (June 2017)

Endorsed by The International Menopause Society (IMS)
Governing principles on MHT

1. MHT remains the most effective therapy for vasomotor symptoms & urogenital atrophy.

2. Other menopause-related complaints, such as joint & muscle pains, mood swings, sleep disturbances & sexual dysfunction (including reduced libido) may improve during MHT.

3. Quality of life & sexual function may also improve.
PREMATURE MENOPAUSE

- Women experiencing spontaneous or iatrogenic menopause before 45 & particularly before 40 are at higher risk for CVD & osteoporosis & may be at increased risk of dementia.

- MHT may reduce symptoms & preserve bone density & is advised *at least until the average age of menopause*.
FDA-APPROVED INDICATIONS FOR MHT

1. Vasomotor symptoms

2. Prevention of osteoporosis

3. Premature menopause

4. Genitourinary syndrome of menopause (GSM)

CONTRAINDICATIONS to MHT

• Known past or suspected breast/endometrial cancer
• Progesterone-dependant meningioma
• Undiagnosed genital bleeding
• Previous/current venous thromboembolism
• Known thrombophilic disorders
• Active or recent heart attacks/angina
• Acute/history of liver disease
• Known hypersensitivity
Governing principles on MHT

• The dosage should be titrated to the lowest effective dose.

• Lower doses of MHT than previously used may reduce symptoms sufficiently & maintain quality of life for many women.
CHOICE OF PROGESTOGEN

• The choice of the progestogen component in combined MHT is of importance.

• Regarding breast cancer risk, it could be preferable to use micronized progesterone or dydrogesterone.”¹,²

FEMOSTON CONTI 0.5MG/2.5MG

• Efficacy in relieving estrogen-deficiency symptoms was established in 3 studies.

• 1 long-term double-blind controlled study showed it was effective in alleviating vasomotor symptoms & improving QOL, high amenorrhoea rate & a good tolerability profile.

• The study showed that the reduction of moderate to severe hot flushes was statistically significant versus the placebo from 4th week onwards.

• The number of moderate to severe hot flushes decreased further until the end of the Rx period in week 13.

• Lower incidences of side-effects than the standard dose.
• A French study on 80,377 postmenopausal women: the use of oestradiol-dydrogesterone therapy was associated with a lower risk of breast cancer compared with therapies combining estrogen with other synthetic progestogens.

• A Finnish Study also reported no increased risk of breast cancer after 5 years of therapy in 50,210 postmenopausal women.

FEMOSTON MINIMISE VTE RISK

A multicentre study concluded that dydrogesterone in Femoston could benefit women in “minimising the VTE risk among women who require hormone therapy” to manage their menopausal symptoms. This is not the case with other types of progestogens.

NEW EVIDENCE FOR CARDIAC BENEFIT OF MHT

• New data accumulated in the USA & in Europe indicate that the use of estradiol-based MHT regimens does not endanger the heart, but rather, it significantly reduces the incidence of CAD events & mortality.

• To get maximal cardioprotective efficacy of MHT, a woman should initiate MHT as soon as symptoms occur, & preferably within the first 10 postmenopausal years.
NO GENERAL RULE FOR STOPPING AT 65

• HT doesn’t need to be routinely discontinued in women above 60 or 65

• Can be considered for continuation beyond 65 for persistent VMS, QOL issues, or prevention of osteoporosis after appropriate evaluation & counselling of benefits & risks.
CONCLUSION

• The most important medical decision for women is whether to take MHT or not.

• Whether taking MHT or not will affect almost every part of her body.

• Her choice will affect the quality of her work & sex life, mood, memory, skin, weight control etc.

• The decision will change her risk of major health conditions like osteoporosis, heart disease & dementia.

• MHT is safe for the majority of women when started during the estrogen window.
ANGELINA JOLIE

• BRCA1 gene mutation (risk of developing Breast Ca 60% & Ovarian Ca 39%)
• Strong family history of Ca
• Prophylactic Mastectomy (37) & BSO (39)
• Surgical menopause
• Is she on MHT?
Nola Ochs
World oldest college graduate at 95. Masters Degree in Liberal Studies at 98.

• I don’t dwell on my age.
• It might limit what I can do.
• As long as I have my mind & health, age is just a number.
Meiko Nagaoka, 103-year-old Japanese woman
1st centenarian to complete a 1500m swim record

Started swimming at 82.
Now training for her next swim race.

THANK YOU
ERNESTINE SHEPHERD 80, the oldest competitive female body-builder in the world.

Started working out in her 50s, and then decided to pick it up in her 70s.
Irene O’Shea 101, oldest person in the world to skydive & jump out of a plane from 14,000 feet.