Post-menopausal hormone replacement therapy

Evan Klass, MD

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Are we really still talking about this?
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- 1960-1975- estrogen prescriptions doubled. Pharma provided materials describing benefits including feeling younger and happier and prevented diseases of aging
- 1975- linkage of estrogen replacement to endometrial cancer
- By 1985- awareness that addition of progestin could prevent endometrial proliferation led to resurgence. By 1992, Premarin was the most prescribed medication in the US
- 2002- first WHI study suggested and increase in risk of breast cancer in estrogen users and use declined by 50%

So where are we now?
Endocrine Society Clinical Practice Guideline
*J Clin Endocrinol Metab* 100:3975-4011, 2015

- **Menopause:** The clinical status of a previously regularly cycling woman 12 months after last period (mean age at spontaneous menopause= 51)
- **Early menopause:** cessation of ovarian function bet. ages 40-45 in the absence of other etiologies
- **Menopause after hysterectomy w/o oophorectomy**
- **Menopausal transition (perimenopause):** variable cycle length and bleeding pattern, with sx and rising FSH
Vasomotor symptoms

• Hot flashes: ~75% of women in US; includes night sweats and sleep disruption and may be assoc. with palpitations, anxiety. May last >10 years following menopause. May be triggered by EtOH or spicy foods.

• Genitourinary syndrome of menopause: vulvar pain, vaginal dryness, dyspareunia, recurrent UTI. Changes in external genitalia.
Health Opportunities at Menopause

- Address bone health, smoking cessation, alcohol moderation, and cardiovascular and cancer risk modification
- Diet and exercise counselling
- Calcium and Vit. D intake
HRT- the good

- Consider for women < 60 or <10 years from LMP with troublesome vasomotor sx.
  - Improves vasomotor (75%) and genitourinary sx
  - May reduce future fracture risk
  - May reduce risk of diabetes, colorectal and endometrial cancer (combined treatment)
HRT- contraindications

- >10 years post menopause
- Known breast cancer
- High risk for breast cancer- 5 yr NCI risk >1.67
- High risk for CHD- >10% in 10 yrs.
- Endometrial cancer
- H/O DVT, PE or coagulation defect or family history of coagulation disorder
- Chronic liver disease
- Caution in presence of DM, hypertriglyceridemia
HRT- approaches to therapy

• Younger women with surgical menopause or premature ovarian insufficiency may need higher doses and should be treated to expected age at menopause

• Oral estradiol or conjugated estrogens- no clear evidence of benefit for one or the other

• Transdermal estradiol- may be safer in women with moderate CVD risk and may have less effect on Tg’s, SHBG, TBG, and CRP. May be preferable in metabolic syndrome...

• Vaginal estrogen- for genitourinary sx without vasomotor sx
HRT- approaches to therapy

• Progestins unnecessary in hysterectomized women but necessary in all women with a uterus irrespective of route or dose of estrogen except-

• CEE + bazedoxiphene (DuaVee)
HRT-risks

• Endometrial cancer
• Breast cancer- risk increases with duration
• CHD- best evidence suggests no increase in MI in those initiating therapy before age 60 but individual CVD assessment advised and 10 yr risk >10% represents a contraindication
• VTE- perhaps transdermal therapy has a lower risk than oral. Combined therapy may have equal risk to estrogen alone
Non-hormonal therapies

• Vaginal moisturizers and lubricants for GU sx
• For VMS consider controlling the external environment, dressing in layers, avoidance of alcohol and spicy foods and weight loss
• SSRI/SNRIs are effective
• Gabapentin/pregabalin effective but less well tolerated
• Clonidine
### Table 1. Estimated Event Rate Difference Associated With Combined Estrogen and Progestin Use vs Placebo in Postmenopausal Women

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Absolute Event Rate Difference per 10,000 Woman-Years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Harms</strong></td>
<td></td>
</tr>
<tr>
<td>Breast cancer (invasive)</td>
<td>9 (1 to 19)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>8 (0 to 18)</td>
</tr>
<tr>
<td>Dementia (probable)a</td>
<td>22 (4 to 53)</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>21 (10 to 34)</td>
</tr>
<tr>
<td>Stroke</td>
<td>9 (2 to 19)</td>
</tr>
<tr>
<td>Venous thromboembolismb</td>
<td>21 (12 to 33)</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>876 (606 to 1168)</td>
</tr>
<tr>
<td><strong>Benefits</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>−14 (−24 to −3)</td>
</tr>
<tr>
<td>All fractures</td>
<td>−44 (−71 to −13)</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>−6 (−9 to −1)</td>
</tr>
</tbody>
</table>

- Women aged 65 years and older.
- Includes deep vein thrombosis and pulmonary embolism.
**Table 2. Estimated Event Rate Difference Associated With Estrogen Use Alone vs Placebo in Postmenopausal Women**

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<tr>
<td>Dementia (probable)a</td>
<td>12 (−4 to 41)</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>30 (16 to 48)</td>
</tr>
<tr>
<td>Stroke</td>
<td>11 (2 to 23)</td>
</tr>
<tr>
<td>Venous thromboembolismb</td>
<td>11 (3 to 22)</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>1261 (880 to 1689)</td>
</tr>
<tr>
<td><strong>Benefits</strong></td>
<td></td>
</tr>
<tr>
<td>Breast cancer (invasive)</td>
<td>−7 (−14 to 0.4)</td>
</tr>
<tr>
<td>All fractures</td>
<td>−53 (−69 to −39)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>−19 (−34 to −3)</td>
</tr>
</tbody>
</table>

a  Women aged 65 years and older.
b  Includes deep vein thrombosis and pulmonary embolism.