Pharmacology Treatment Options in Menopause Care

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Pharmacology Treatment Options in Menopause Care

Presenter is a member in good standing of the North American Menopause Society.

There is no conflict of interest or commercial support for this presentation.
Presentation Objectives

Define and identify common physiologic changes of menopause.

Define Complementary Alternative Medicine strategies.

Define Bioidentical Hormone strategies.

Identify evidence-based hormonal and non-hormonal treatment strategies and treatment side effects.

Define Osteoporosis and identify treatment strategies.

Identify evidence-based recommendations for women in midlife.
YOU CAN'T FIGHT GRAVITY...
Significance of Providing Menopause Care

- 44 million midlife women in the U.S. between 45 and 54 yrs old.
- Menopause symptoms are the more common reasons women seek care.
- Menopause symptoms can be a significant humanistic and economic burden for midlife women. (Whitely, DiBonaventura, Wagner, Alvir & Shah, 2013).
Definitions of Midlife Changes

- **MENOPAUSE** is defined as a natural, event occurring 1 year after the final last menstrual period.
- Average age is 52 years, common range of 45 – 59 years.
- Premature Menopause is < 40 years, occurs in 1% of women.

- **PERIMENOPAUSE** begins with changes in menstrual cycle.
- May last 1 – 3 years
- Intervals of amenorrhea usually > 60 days
  
  (Harlow, S. D., 2012)
ALTERING FACTORS

- ETHNICITY
  - Earlier among Hispanic women
  - Later in Japanese-American women

- GENETICS

- SMOKING HISTORY

- REPRODUCTIVE HISTORY

- OTHER; weight, activity level
Physiologic Changes; The Effects of Estrogen Loss

- Estrogen receptors are plentiful throughout the body
- Short term estrogen decline can cause:
  - Hot flashes
  - Sleep disruption
  - Menstrual cycle variations
  - Mood changes
Physiologic Changes; The Effects of Estrogen Loss

- Long term estrogen decline can cause:
  - Urogenital tract alterations
  - Bone loss
  - Cardiovascular disease
  - Joint and weight changes
  - Skin changes
Menopausal Symptoms & Signs

Classic symptoms:
- Change in menstrual cycle pattern (during perimenopause)
- Vasomotor symptoms (hot flashes & night sweats)
- Vulvovaginal symptoms, dyspareunia
- Sleep disturbances

Symptoms common with menopause:
- Cognitive concerns (memory, concentration)
- Psychological symptoms (depression, anxiety, moodiness)

(Alvis et al, 2005)
Clinically Proven Soy Isoflavones for Hot Flash Relief, Plus Boosts Energy*

Drug Free & Estrogen Free!

Estroven®
MAXIMUM STRENGTH

ENERGY

Multi-Symptom Menopause Relief:
• Helps Reduce Hot Flashes & Night Sweats
• Helps Manage Irritability & Fatigue

SAFE & EFFECTIVE
28 CAPLETS
DIETARY SUPPLEMENT

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

YOU PAY
$21.99
Replens®

LONG-LASTING
vaginal moisturizer

• Helps Replenish Vaginal Moisture
• Supplements the Body’s Natural Lubrication
• Long Lasting Formula

8 Pre-filled Disposable Applicators
NET WT .24 OZ (6.7 g) EACH

Long Lasting
Helps supplement vaginal moisture
Gentle, immediate comfort
Estrogen free
Instrucciones en Español

8 Pre-filled applicators
NET WT. 0.24 OZ (6.7 g) EACH
1.92 OZ (53.6 g) TOTAL

YOU PAY $18.99

YOU PAY $15.79
COMPLEMENTARY & ALTERNATIVE THERAPIES IN MENOPAUSE

- Up to 75% of women may trial alternative therapies.
- Evidence from RCT to show CAM therapies improve menopause symptoms, or provide same benefits as HT is poor.
- Safety of CAM therapies needs to be evaluated.
- Interactions with other Rxs is not well noted.
- Effects on women with cancer is unknown.
- Non-estrogen based rx is not as effective as estrogen for HF.
BIOLOGICALLY BASED PRACTICE
ISOFLAVONES

ISOFLAVONES or PHYTOESTROGENS

- Plant derived compounds
- Estrogen-like biologic activity
- Possess estrogen-agonist & estrogen-antagonist properties

SOY

- Most widely used, derived by extracting protein from soy bean.
- Regulated in U.S. as dietary supplement.
- Mixed health effects, modestly effective.
DIETARY SUPPLEMENTS

BLACK COHOSH

- Made from rhizomes of plant (underground stems).
- Used by NA Indians for medicinal purposes.
- Many formulations.
- 1989 German Federal Inst for Drugs & Medical Devices approved supplement for menopause related s/s, PMS & dysmenorrhea.
- Recommended dose 40 – 80 mg.
  - Should have standardized 1 mg of 27-deoxyacycin tincture
- Results inconclusive, high quality product appears safe.
HERBAL SUPPLEMENTS

TOPICAL PROGESTERONE

- Many brands in without Rx in U.S., bioidentical to endogenous progesterone however “natural” is synthesized commercially by adding chemical process using soybeans & wild yam.
- Scientific evidence is lacking for improvement of menopause s/s.
- 3 RCT insufficient to support efficacy to reduce HF.
- Absorption varies among women and formulations
- Effects on endometrium are unknown.
- OTC creams are from wild yams, precursors that cannot be converted to progestin in the body.
## What Do You Need to Know?

<table>
<thead>
<tr>
<th>Medical History</th>
<th>Examination</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>GYN facts</td>
<td>Height &amp; Weight</td>
<td>Pap Test</td>
</tr>
<tr>
<td>Major medical issues (DVT/PE)</td>
<td>BP and Cardiovascular</td>
<td>Mammogram</td>
</tr>
<tr>
<td>Breast or endometrial CA</td>
<td>Pelvic exam</td>
<td>Lipids</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>Breast exam</td>
<td>FBG</td>
</tr>
<tr>
<td>CVD</td>
<td>Thyroid exam</td>
<td>TSH</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>Renal &amp; Liver function</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>Vit D</td>
</tr>
<tr>
<td>Recurrent UTIs</td>
<td></td>
<td>Dexa Scan</td>
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<tr>
<td>Liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family History (fractures)</td>
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<td></td>
</tr>
</tbody>
</table>
## What To Consider

### Perimenopause
- Health concerns & conditions
- Family History
- Lifestyle issues & counseling:
  - activity
  - diet
  - smoking
  - alcohol
  - obesity
- Contraception needs
- Menopause symptoms

### Menopause
- Health concerns & conditions
- Management of:
  - Menopause symptoms
  - vulvovaginal atrophy
  - prevention of osteoporosis
  - sexual dysfunction
- Lifestyle issues
- Life counseling

### Postmenopause
- Same as Menopause
- Management of symptoms
- Consider HT taper
- Prevention of osteoporosis
- Lifestyle issues
- Life counseling
<table>
<thead>
<tr>
<th>METHOD</th>
<th>AGE RANGE</th>
<th>ELIGIBILITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTROGEN containing OC</td>
<td>Greater than 40 y/o</td>
<td>Benefits outweigh risk</td>
</tr>
<tr>
<td>PROGESTIN only OC</td>
<td>Greater than 40 y/o</td>
<td>No Restriction</td>
</tr>
<tr>
<td>PROGESTIN Implant</td>
<td>Greater than 40 y/o</td>
<td>No Restriction</td>
</tr>
<tr>
<td></td>
<td>40 – 45 y/o</td>
<td>No Restriction</td>
</tr>
<tr>
<td></td>
<td>Greater than 45</td>
<td>Benefits outweigh risk</td>
</tr>
<tr>
<td>DMPA</td>
<td>Greater than 40 y/o</td>
<td>No Restriction</td>
</tr>
<tr>
<td>Cu-IUD</td>
<td>Greater than 40 y/o</td>
<td>No Restriction</td>
</tr>
<tr>
<td>LNG-IUS</td>
<td>Greater than 40 y/o</td>
<td>No Restriction</td>
</tr>
</tbody>
</table>
CONTRACEPTION IN
PERIMENOPAUSE

- Obtaining FSH will not give accurate results when a woman is on oral contraceptives.

- Continue OC use until the woman is statistically postmenopausal.
  - Nonsmoking Women; mid 50's

- Can transition to HT if menopausal symptoms

- Can transition directly from OC to hormone therapy
Current Consensus On The Use of Hormone Therapy

- Most effective treatment for vasomotor symptoms associated with menopause at any age.
- Benefits outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause.”

Endorsement by: American Society for Reproductive Medicine, the Asia Pacific Menopause Federation, the Endocrine Society, the European Menopause and Andropause Society, the International Menopause Society, the International Osteoporosis Foundation and the North American Menopause Society.
HORMONE THERAPY

- One of the most prescribed drugs worldwide.
- HRT was approved by FDA 60+ yrs ago but best practice prescribing is STILL confusing!
- 1966 Dr. Robt Wilson published “Feminine Forever”, menopause was curable!
- 2001; 67 million were on Premarin or Prempro.
- 2002; WHI study was published.
HORMONE THERAPY

- For mod-severe menopausal symptoms
- Safe for the majority of women
  - Exceptions; Br ca, CHD, VTE, stroke or > risk for same.
- RCTs were done on Cont Conjugated Estrogen (CCE).625mg and MPA.
- Prescribe lowest effective dose for shortest time.
- Need progestin if intact uterus
- Recommend Rx for no > 5 yrs
  - Change route to transdermal if intractable
  - Consider other potential causes if no effect
  - Can stop x 2 wk then restart if intractable
TERMONOLOGY

- ESTROGEN THERAPY (ET)
  Unopposed estrogen to treat women without a uterus
  Low doses for woman with vaginal symptoms

- ESTROGEN-PROGESTOGEN THERAPY (EPT)
  To protect women with a uterus

- BAZEDOXIFENE (BZA)-CONJUGATED ESTROGEN (CE)
  Estrogen agonist/antagonist (BZA) + CE
  Treat vasomotor symptoms
  Prevent osteoporosis
ESTROGEN

3 Basic Types:

HUMAN ESTROGENS:
- E1 estrone, wks form most abundant PM.
- E2 estradiol, primary and most potent before meno.
- E3 estriol, primary estrogen of pregnancy.

NONHUMAN ESTROGENS: conjugated estrogens (CE), mixture of estrogens from natural sources.

SYNTHETIC ESTROGENS: esterified estrogens a mixture of sodium salts, primarily from estrone derived from Yams.
FORMS OF ESTROGEN

ESTROGEN OPTIONS:

- **ORAL**: Bolus of estrogen metabolized by liver known as “First Pass Effect”, stimulating biochemical factors such as elev CRP.

- **TRANSDERMAL**: Therapeutic effects at lower dose, serum levels remain constant, rapid cessation after removal.

- **VAGINAL**: Local effect, little systemic concerns, can be used for long term tx.
FORMS OF ESTROGEN

ESTROGEN OPTIONS:
- SPRAY
- GEL

**PROS** | **CONS**
--- | ---
Easy of application | Unintended application
No first pass effect | Cost
ORAL ESTROGEN PROS AND CONS

**PROS**
- EASY ADMINISTRATION
- BENEFITS HDL-C, LDL-C and TCHOL.
- LARGE AMT OF DATA
- RELATIVELY LOW COST

**CONS**
- RISK OF THROMBOSIS, STROKE
- INCREASES TG, C-Reactive Protein, Hepatic Proteins
- REDUCES LIBIDO Thru Sex hormone-binding globulin impact
TRANSDERMAL ESTROGEN

**PROS**
- Avoids hepatic 1st pass
- < inc of TG than oral E
- < effect on C-reactive P
- < risk of reducing libido
- Fewer GI s/e
- Perhaps < risk of VTE

**CONS**
- Patch sensitivity
- Patch is < private
- Usually higher cost
VAGINAL ESTROGEN

**PROS**
- Vaginal benefit at < cost
- Low-dose therapy avoids adverse systemic effects.

**CONS**
- Increase in vaginal d/c
- Maybe < convenient
- Lack of long term uterine safety data
ESTROGEN PRODUCTS

CONJUGATED ESTROGENS (CE)
Most clinical trials used CE
Premarin has been on the market for 65 yrs, no generic!
Standard dose; 0.625 mg
Studies show benefit at lower doses; 0.45 mg – 0.3 mg

SYNTHETIC CONJUGATED ESTROGENS (SCE)
2 types available as oral tablet
- SCE-A; 9 estrogens (CENESTIN)
- SCE-B; 10 estrogens (ENJUVIA)
Not considered generic equivalents to PREMARIN
ESTROGEN PRODUCTS

ESTRADIOL

Most biologically active
Micronized for oral product (ESTRACE)
Oral generics are available
EPT formulation; ACTIVELLA
Transderm systems; DIVIGEL, ESTROGEL, ELESTRIN
Transderm spray; EVAMIST
Topical emulsion; ESTRASORB
Transderm EPT; COMBIPATCH, CLIMARA PRO
Vaginal forms; ESTRACE cream, ESTRING, VAGIFEM, FEMRING
# APPROXIMATE EQUIVALENT ESTROGEN DOSES

<table>
<thead>
<tr>
<th>ORAL</th>
<th>EQUIVALENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogens</td>
<td>0.625 mg</td>
</tr>
<tr>
<td>Synthetic conjugated estrogens</td>
<td>0.625 mg</td>
</tr>
<tr>
<td>Esterified estrogens</td>
<td>0.625 mg</td>
</tr>
<tr>
<td>Estropipate (0.75 mg)</td>
<td>0.625 mg</td>
</tr>
<tr>
<td>Ethinyl estradiol</td>
<td>0.005 mg – 0.015 mg</td>
</tr>
<tr>
<td>17 B-estradiol</td>
<td>1.0 mg</td>
</tr>
</tbody>
</table>
BIOIDENTICAL HORMONES

- Derivatives of plant extracts chemically modified to be structurally indistinguishable from human hormones. (E2 or 17-B estradiol, E1 or estrone and E3 estriol).

- “Natural” compounded formulations are from E1 and E2. Hence are no < natural than conventional HRT.

- Prometrium is only bioidentical progestogen.
Government-Approved Natural Hormone Therapy Products

**ESTRADIOL**

*Systemic doses of estradiol for treatment of hot flashes*

**Oral tablet:** Estrace, generics

**Skin patch:** Alora, Climara, Esclim, Menostar, Vivelle (Dot), Estraderm,

**Skin gel/cream:** EstroGEl, Elestrin, Divigel, Estrasorb

**Skin spray:** Evamist

**Vaginal ring:** Femring
Government-Approved Natural Hormone Therapy Products

**ESTRADIOL**
Vaginal estradiol for dryness and dyspareunia

*Vaginal cream:* Estrace vaginal cream  
*Vaginal ring:* Estring  
*Vaginal tablet:* Vagifem

**PROGESTERONE**

*Oral tablet:* Prometrium
### Menopausal Hormonal Treatment

<table>
<thead>
<tr>
<th>Uterus Intact</th>
<th>Post Hysterectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Combined transdermal (E + P) patch</td>
<td>- Transdermal E patch or gel</td>
</tr>
<tr>
<td>- Transderm E patch or gel plus LNG-IUD</td>
<td>- Oral E</td>
</tr>
<tr>
<td>- Oral E plus oral P or LNG-IUD</td>
<td>- Vaginal tablet</td>
</tr>
<tr>
<td>- E plus SERM</td>
<td>- E spray</td>
</tr>
<tr>
<td>- Vaginal tablet plus oral P or IUD</td>
<td></td>
</tr>
</tbody>
</table>
EPT REGIMENS

- Goal to provide uterine protection, maintain estrogen benefits and minimize side effects.
- Careful endometrial monitoring for quarterly or every 6 month progestin regimen.
- BTB in 40% of women during first 3 months of cont/combined tx.
- Recently menopausal women exp > BTB.
- Tx with testosterone derived P or with prometrium, have < BTB during first months.
<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>PROGESTOGEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTINUOUS-CYCLIC</td>
<td>12 – 14 D/mo with QD Estrogen</td>
</tr>
<tr>
<td>(sequential)</td>
<td></td>
</tr>
<tr>
<td>CONTINUOUS-CYCLIC LONG CYCLE</td>
<td>14 D EVERY 2 – 6 mos with QD E</td>
</tr>
<tr>
<td>(sequential)</td>
<td></td>
</tr>
<tr>
<td>CONTINUOUS-COMBINED</td>
<td>Daily with QD Estrogen</td>
</tr>
</tbody>
</table>
### MINIMUM PROGESTOGEN DOSING FOR ENDOMETRIAL PROTECTION

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>CYCLIC EPT (12-14 D/MO)</th>
<th>DAILY EPT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORAL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>5 mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Norethindrone</td>
<td>0.35 mg – 0.7 mg</td>
<td>0.35 mg</td>
</tr>
<tr>
<td>Norethidrone acetate</td>
<td>2.5 mg</td>
<td>0.5 mg – 1 mg</td>
</tr>
<tr>
<td>Micronized progesterone</td>
<td>200 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td><strong>IUS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgesterol</td>
<td></td>
<td>20 mu g/d or 6 mu g/d</td>
</tr>
<tr>
<td><strong>VAGINAL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progesterone gel</td>
<td>45 mg</td>
<td>45 mg</td>
</tr>
</tbody>
</table>
PROGESTOGENS

- Reduces risk of endometrial cancer in women on HRT who have an intact uterus.
- Hyperplasia or cancer can occur in 6 months otherwise.
- Progestins are synthetic products that have progesterone like activity.
- Structurally related to progesterone; (MPA, megestrol); or testosterone; (norethindrone, levonorgestrel, norgestrel desogestrel gestodene, norgestimate, drospirenone).
- Bioidentical progestin is prometrium.
PROGESTERONE OPTIONS

- **PROMETRIUM** is the only FDA approved bioidentical progestogen. * It is in p-nut oil.

- Synthetic oral progestin (Norethindrone, MPA)

- **IUD**: Mirena that has a 5 yr use (levonorgestrel). Not FDA approved for HRT.

- **Vaginal gel**: Thru custom compounding. May not exert sufficient activity to protect endometrium.
**PROGESTOGENS**

**PROS**
- Reduce adverse effect on endometrium.
- Some progestogens reduce adverse effect on TG.
- Progesterone dosed at HS can dec insomnia, improve sleep.

**CONS**
- Some can inc risk Breast cancer.
- Some dec beneficial effect of HDL-C.
- Bloating.
- Dysphoria for some women.
POTENTIAL SIDE EFFECTS OF HORMONE THERAPY

- Uterine bleeding
- Breast tenderness
- Nausea
- Abdominal bloating
- Fluid retention
- Changes in cornea
- H/a, dizziness
- Mood changes
DEALING WITH SIDE EFFECTS OF HORMONE THERAPY

- Restrict salt, increase water, exercise, mild diuretic
- Change to E patch; decrease P or change formulation
- Lower E dose, change formulation, reduce caffeine and ethanol.
- Investigate preexisting depression
- Take meds with meals or at HS.
DURATION OF USE

- Use of HT for 5 years or less is considered safe for most women.
- Employ lowest dose effective to reduce symptoms.
- Extending EPT use is acceptable for:
  - Women who request it and are aware of its risks
  - Prevention of osteoporosis for women at high risk of osteoporotic fracture when alternate therapies are not appropriate
CESSATION OF HT

- Abrupt withdrawal may result in return of HF.
- 55% of women will have some recurrence.
- 40 – 50% of HF will stop in 1 yr.
- 65 – 75% of HF will cease in 2 yrs.
- Taper oral dosing to 1 less pill per wk or transition to transdermal.
- Risks outweigh benefits after 5 yrs.
- Consider non-estrogen alternative.
OSPEMIFENE

OSPEMIFENE (Osphena)

SERM

- Estrogen receptor modulator; selectively binds to estrogen receptors in vagina.
- Changes vaginal epithelium and decreases vaginal PH.
- Indicated for mod-severe menopausal dyspareunia
- Dose 60 mg every day
DUAVEE

SERM

- Estrogen receptor modulator combination of CCE and bazedoxifene referred to as the tissue-specific estrogen complex.
- In trials, relieves vasomotor s/s, preserves BD, maintains endometrial protection with low BTB and shows efficacy for vulvovaginal atrophy.
- Dosing BZA 20 mg/CCE.45mg
- Concerns about stroke risk.
HT formulation, route of administration, and timing of initiation produce different effects

Individual benefit-risk profiles are essential

Absolute risks in healthy women ages 50-59 are low

Long-term use or HT initiation in older women, however, has greater risks

Breast cancer risk increases with EPT beyond 3-5 years

ET can be considered for longer duration of use due to its more favorable safety profile
## NONHORMONAL OPTIONS

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine</td>
<td>7.5 – 20 mg/d</td>
<td>Headache, nausea, dry mouth (Takes 4 wk – 6 mo for effect)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20 – 30 mg/d</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 – 150 mg/d</td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>20 – 30 mg/d</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100-800 mg TID, 300 mg HS</td>
<td>Dizziness, unsteadiness, fatigue (12 wks for effect)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>PO: 0.025-0.075 mg BID Transderm: 0.1 mg wkly</td>
<td>Dry mouth, drowsiness, dizzy (4-8 wks for effect)</td>
</tr>
</tbody>
</table>
## NONHORMONAL OPTIONS

<table>
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<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISOFLAVONES</td>
<td>40 – 164 mg/d (Takes 6 – 12 wks)</td>
<td>GI Effects; constipation, diarrhea,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Itching or rash</td>
</tr>
<tr>
<td>SOY</td>
<td>40 – 160 mg/d (Takes 3 – 12 months)</td>
<td>GI upset</td>
</tr>
<tr>
<td>RED CLOVER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BLACK COHOSH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Qualitative data lacking</td>
<td></td>
</tr>
<tr>
<td>Ginseng</td>
<td>Level of Evidence C</td>
<td></td>
</tr>
<tr>
<td>Primrose oil</td>
<td></td>
<td></td>
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<tr>
<td>Acupuncture, yoga</td>
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</tr>
</tbody>
</table>
Data regarding HT in women over age 50 should not be extrapolated to younger postmenopausal women.

Likely that risks attributable to HT are smaller and benefits greater in these younger women.

Use of HT or oral contraceptives until median age of menopause is recommended, at which time decision can be reevaluated.
Vaginal Estrogen Use in Women With a History of E-Dependent Breast Cancer

American College of Obstetricians and Gynecologists Committee Opinion in March 2016:

- Non-hormonal approaches are first line options
- In women with urogenital symptoms and history of breast CA, vaginal estrogen should be reserved for those unresponsive to non-hormonal remedies.
- Decision to use vaginal estrogen maybe made with oncologist.
- Preceded by informed decision-making consent process.
- Data do NOT show increased risk of cancer reoccurrence.
NAMS POSITION ON BR CA RISK ASSOC WITH HT:

- Br CA risk increases with EPT if used beyond 3 – 5 yrs.
- Progestogen seems to contribute substantially.
- EPT increases mammographic density.
- EPT may impede dx interpretation of mammograms.
Data on HT and risk of ovarian cancer are conflicting.

There were increases of ovarian cancer in those using EPT in the WHI but the numbers did not reach statistical significance.
YOU LOOK SO MUCH THINNER!

THANKS! I HAD MY APPENDIX REMOVED...
Obesity in Peri and Menopausal Women

- In U.S. > 65% of women 45 – 55 are overweight (BMI > 25).
- PMW are < likely to lose visceral adipose tissue.
- Neither Menopause nor Hormone Therapy cause added weight.
- Women who slept 5 hrs or less gained 2.5# per yr than those sleeping 7 hrs a night.
- Physical activity AND caloric intake are required to lose weight.
Osteoporosis
NORMAL BONE LOSS

- Peak bone mass achieved by 3\textsuperscript{rd} decade
- Loss accelerates after menopause
- 80 y/o Ave woman loses 30% of bone

- Low bone density does not equal bone loss.
- Women who do not achieve peak mass, may have LBD without substantial bone loss in aging.
Definition of osteoporosis

A disease characterized by low bone mass and micro architectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk.

Normal Bone

Osteoporosis

PREVALENCE OF OSTEOPOOROSIS

- 4% of women age 50 – 59 yrs
- 52% of women age 80 + yrs
- Hip fx is most common fx in 80 y/o
- 25% increase in mortality in 1 yr

- Varies with ethnicity
  - African American women > BMD
  - Asian American women < BMD
WORLD HEALTH ORGANIZATION
RISK FACTORS FOR FX

- AGE (50 – 90)
- SEX (f)
- WEIGHT (< 127 # OR BMI < 21 KG/M2)
- HEIGHT (loss > 1.5”)
- LOW FEM NECK BMD
- PRIOR FRAGILITY FX
- PARENTAL H/O HIP FX
- CURRENT TOBACCO SMOKING
- LG TERM USE OF GLUCOCORTICODS
- RA
- ETOH > 2 UNITS DAY
- OTHER CAUSES OF SECONDARY OSTEOPOROSIS
BONE DENSITY DEFINITIONS

- **NORMAL**  T SCORE >  -1.0
- **OSTEOPENIA**  T SCORE  - 1.0 to – 2.5
- **OSTEOPOROSIS**  T SCORE <  - 2.5

- LOWEST OF 3 SCORES OF WHAT IS MEASURED
  - HIP; TL HIP, FEM NECK
  - SPINE; 2 VERTEBRAL BODIES
  - RADIUS; 1/3 OF RADIUS SITE
WORLD HEALTH ORGANIZATION
DEFINITION OF OSTEOPOROSIS

- BMD T SCORE < -2.5 at TOTAL HIP, FEM NECK OR LUMBAR SPINE.

OR

- PRESENCE OF FRAGILITY FRACTURE EVEN WITH NORMAL T OR Z SCORE.
STANDARD VALUES OF BMD

- **T SCORE**: BMD in post menopause calculated by comparing measured BMD to mean peak BMD of normal young white women.

- **Z SCORE**: BMD of premenopausal women.

Measures differences b/t BMD and mean BMD of reference pop of same age and ethnicity.
WHEN IS DRUG THERAPY NEEDED?

- History of vertebral, hip, fragility, or low-trauma fracture

- BMD values consistent with osteoporosis (T score $\leq -2.5$)

- 10-year FRAX risk of major osteoporotic fracture of at least 20% or hip fracture of at least 3%
SELECTING A SPECIFIC THERAPY

- No clinical evidence one tx is better than another
- No head-to-head trials
- Base decision on individual and tolerable side effects
- Adherence to therapy is poor
- Risks have been reported with long term use
- Generally after 5 years a respite in treatment can be had
ANTIRESORPTIVE AGENTS

BISPHOSPHATES

- (FOSAMAX, BONIVA, ACTONEL, ETC)
- INHIBIT ACTIVITY OF OSTEOCLASTS
- SHORTENS OSTEOCLAST LIFESPAN REDUCING BONE REABSORPTION.
- ORAL IS POORLY ABSORBED
- CK SERUM CALCIUM, CREATININE BEFORE TX

S/E: Esophageal, gastric irritation, ulcer, hypocalcemia and renal impairment,
ANTIRESORPTIVE AGENTS
POTENTIAL SIDE EFFECTS

- OSTEONECROSIS OF JAW AFTER DENTAL EXTRACTION OCCURS AFTER IV DOSES IN PT WITH CANCER RELATED DISEASES.

- NO DATA TO SUGGEST DENTAL SURGERY IS CONTRAINDIATED IN PTS ON BISPHOSPHATES.

- NEW LABEL FOR 5 YR LIMIT ON USE

- NEW FDA WARNING FOR RARE-TYPE FEM FX
OTHER TX OPTIONS

- Estrogen only formulations
- Estrogen/Progestin formulations
- SERMS
- Calcitonin
- Parathyroid Hormone
- RANK Ligand Inhibitor
HORMONE THERAPY TREATMENT FOR OSTEOPOROSIS

- HT reduced fracture risk in postmenopausal women in the WHI who were not selected on basis of osteoporosis.
- Many systemic HT products approved for preventing postmenopausal osteoporosis; no HT product approved for treating osteoporosis.
- Extended use of HT is option for women at high risk of osteoporotic fracture when alternate therapies are not appropriate.
- Risks of long-term HT use should be considered.
- Benefits of HT on bone mass dissipate quickly after discontinuation of HT.
TESTING AND FOLLOW UP

- Measurements in other sites may predict FX risk but not osteoporosis.
- First DEXA based on risk and rec of screening at age 65.
- Repeat testing in untreated women in 2–5 yrs.
- Women receiving therapy repeat testing in 1–2 yrs, however recent retrospective analysis suggests 10 yrs may be sufficient.
LIFESTYLE MODIFICATIONS

- Maintain a healthy weight
- Eat a balanced diet
- Obtain adequate calcium and vitamin D
  - For calcium: 1,000 - 1,200 mg/d from food (preferably) and/or supplement
  - Vitamin D: 800 iu – 1,000 iu D3 for women > 50 years
  - Participate in appropriate exercise
- Avoid excessive alcohol consumption
- Do not smoke
- Institute measures to prevent falls
A TIME FOR HEALTHY CHANGES!

FOCUS ON LIFE STYLE!

- WEIGHT BEARING EXERCISE
- OPTIMAL WEIGHT
- BETTER NUTRITION
- CALCIUM INTAKE
- VITAMIN D3
- HEALTHFUL STRESS REDUCTION
- SMOKING CESSATION
- ETOH REDUCTION
PAP TESTING

- Cervical CA in US decreased by 50% in past 30 yrs.
- HPV 16 causes 55 – 60% of all cx cancers
- HPV 18 causes 10 – 15%
- Severe dysplasia may take 3-7 yrs to progress
- New guidelines support HPV genotyping women aged 25-65.
- Cytology alone every 3 years is acceptable
- Age 30-65 years:
  - Screening can be discontinued after 3 neg PAP or 2 neg PAP and HPV tests within 10 years, provided most recent test was in 5 years.
  - H/o CIN 2, or adenoca in situ, continue routine screening for age at least 20 years.
MAMMOGRAM SCREENING

- FALSE NEG RATE IS 10 – 15%

- ACS  Begin screening age 40

- NATL CA INST  Q 1 – 2 yrs b/t 40 -50, then Q 1 yr.

- NAMS  Q yr beg at age 40 and before HRT.

- US PREV TASK F  Screening Q 2 yrs, 50 – 74

  - Rec not teaching SBE

- WHO  Q 2 yrs at ages 50 – 69.

  - CBE, SBE not rec
LIFESTYLE COUNSELING

- RELATIONSHIP HEALTH
- SLEEPING
- WORK HEALTH
- SUBSTANCE USE
- PRESCRIPTION USE
- DIET AND EXERCISE
- INJURY PREVENTION
- SEXUAL BEHAVIOR
- DENTAL HEALTH
- IMMUNIZATIONS; TDap, FLU, PNEUMONIA, PREVNAR, SHINGLES


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www.menopause.org

www.shef.ac.uk/FRAX (fracture risk assessment tool)

www.ahrq.gov/ppip/women50.htm (USDHHS)
BIBLIOGRAPHY AND RESOURCES

