The Necessity and Safety of Bioidentical Sex-Steroid Restoration in Menopause

Henry Lindner, MD
Hormonerestoration.com

This presentation is available on the CD, handout
All “HRT” is not Alike!

Menopause is a hormone-deficiency state with known deleterious consequences for quality of life and health.

Estradiol-progesterone-testosterone (EPT) replacement for menopause is medically necessary.

Estradiol replacement is safe when transdermal and accompanied by sufficient progesterone and testosterone.

Bioidential EPT therapy does not have the cardiovascular or breast cancer risks seen with PremPro®.

How to provide EPT therapy to menopausal women
Hormones are not Drugs

- **Vital parts** of our neuro-endocrine-immune system
- Proper fit in all receptors, normal metabolism-elimination
- Non-toxic, inherently safe
- No allergic or idiosyncratic reactions
- **No side effects, only effects!**
- Can monitor therapy with the usual blood tests
- The only problems that can occur with bioidentical hormones:
  - Excessive or insufficient dose
  - Lack of **balance** with other hormones
  - Unphysiological delivery: route, timing, etc.
  - Exacerbation of some underlying disease
Not Just “Sex Hormones”

Estradiol, progesterone, and testosterone are required for the growth, function and maintenance of all tissues in both sexes!

- Maintain brain function and health—vital neurosteroids
- Maintain tissue health/strength: skin, hair, bone, muscle, heart
- Improve insulin sensitivity: ↓ belly fat, ↓ risk of diabetes
- Reduce blood pressure: improve endothelial function
- Prevent atherosclerosis: reduce risk of MI, stroke

What about the loss of hormones with aging?
Adrenopause

DHEA ↔ DHEA-S

Converted into estradiol and testosterone within tissues

J Clin Endocrinol Metab. 1997 Aug;82(8):2396-402
Andropause

Testosterone in Men

Baltimore Longitudinal Study of Aging (BLSA). Harman et al., 2001
Somatopause

Growth Hormone
**Thyropause**

**Fig. 7.** Age-dependent variations in serum FT₃ concentration in healthy human subjects up to centenarians [Modified from S. Mariotti et al.: J Clin Endocrinol Metab 77:1130–1134, 1993 (147), with publisher’s permission. © The Endocrine Society.]

**Fig. 8.** Age-dependent variations in serum TSH concentration in healthy human subjects up to centenarians [Modified from S. Mariotti et al.: J Clin Endocrinol Metab 77:1130–1134, 1993 (147), with publisher’s permission. © The Endocrine Society.]

---

**HP response to low T4 (2.7-3.2 μg/dL)**

80% decline

---

Carle, Thyroid. 2007
Feb;17(2):139-44
Hormone Loss with Age

Common Assumption: Hormone loss with age is adaptive. Youthful hormone levels would cause heart attacks and cancer later in life;

But: Heart attacks, osteoporosis and sex-organ cancers occur years after hormones decline and in persons with lower hormone levels.

Fact: Aging is not adaptive: it is pre-programmed Dying—to remove individuals from the gene pool and permit evolution.

Hormone loss is caused by and contributes to aging.

The loss of hormones with age is both natural and deleterious.

Nature is Trying to Kill Us!
Menopause is
Endocrine Gland Failure

- The ovaries produce estradiol, progesterone and testosterone.
- Gradual loss of egg follicles with aging.
- The ovaries are the only endocrine glands that fail completely in all persons
- FSH remains high for life—the brain doesn’t consider menopause to be “normal” or good!
- The menopausal endocrinopathy is both natural and deleterious.
The decline in estradiol and progesterone in perimenopause along with the rise in LH and FSH.
Menopause

Male Estradiol
20-50 pg/ml

Female Estradiol
0-20

Testosterone
Progesterone
Estradiol

Young Male
Young Female
Old Male
Old Female

Estradiol
Progesterone
Testosterone
Estradiol Deficiency

- Hot flashes, night sweats
- Insomnia, depression, fatigue, achiness
- **Mental** deterioration: poor memory recall, ↑’d risk of **dementia**
- **Urogenital atrophy**: vaginal dryness, incontinence
- **Atrophy of bone, skin, and connective tissue**
- **Endothelial dysfunction**, ↑’d blood pressure
- **Atherosclerosis, heart disease**
- **Insulin resistance**—↑’d risk of **diabetes**

The **symptoms** of menopause are **warning signs** of physical and mental deterioration.
Progesterone Deficiency

- Progesterone counteracts estradiol in the breasts and uterus.

- Estrogen dominance → heavy menses, breast tenderness, fluid retention, moodiness.

- Overstimulation of breast and uterine epithelia ↑’d risk of breast and uterine cancers.

- Progesterone production declines as early as age 30 → luteal phase insufficiency = estrogen dominance.

- Perimenopause — anovulation; little-to-no progesterone production for years.

- The treatment for perimenopausal estrogen dominance is progesterone, not hysterectomy.
Testosterone Deficiency

- Female testosterone levels are 1/20th those of men.
- Female testosterone drops 50% between age 20 and 40. (Zumoff B, J Clin Endocrinol Metab. 1995 Apr;80(4):1429-30)
- 50% of serum testosterone in females comes from DHEAS.
- Oral estradiol HRT → ↓total testosterone 42%, ↓DHEAS 23% (Casson PR, Obstet Gynecol.1997 Dec;90(6):995-8)
Testosterone Restoration

- Improves energy, mood, well-being  

- Reduces fearfulness, anxiety

- Improves sexual desire and sensation

- Improves muscle strength and recovery

- Improves insulin sensitivity  
  Miller KK, J Clin Endocrinol Metab. 2007 Jul;92(7):2474-9

- With estradiol, increases in bone density  
  Davis SR, Maturitas 1995; 21:227-236 

- Improves flow-mediated arterial dilation

- May decrease risk of heart attack  
  Rako S, J Womens Health. 1998 Sep;7(7):825-9
  Kaczmarek A, Int J Cardiol. 2003 Jan;87(1):53-7

- Anti-proliferative effect in breast; reduces risk of breast cancer
Breast cancer, cardiovascular disease (CVD), and osteoporosis are all rare before menopause.

All three diseases are related to aging and to sex-steroid deficiencies or imbalances.

The youthful estradiol-progesterone-testosterone hormonal milieu protects women from these diseases.
Reproduction and Sex-Organ Cancers

The complex female endocrine system is an evolutionary compromise; to produce and feed babies.

Reproduction has costs: poses threats to female health and quality of life.

Breast, uterine and ovarian tissues undergo a monthly cycle of proliferation, differentiation, and breakdown.

Defects in this cycle can lead to cancers in female organs and to many medical disorders.
Menstrual Cycle

- Ripening of follicles
- Ovulation
- Ripening of the corpus luteum

Graph showing the levels of LH (luteinizing hormone), FSH (follicle-stimulating hormone), Estrogen, and Progesterone over the course of the menstrual cycle:

- **Start of the cycle**: Day 1
- **Day 7**: Initial rise in Estrogen
- **Day 14**: Ovulation peak, followed by decline in Estrogen, then rise in Progesterone
- **Day 21**: Peak Progesterone, followed by decline
- **Day 28**: Menstruation

From: http://www.multi-gyn.com/
Historical Perspective

Throughout history, women were usually pregnant or breast feeding; both protective against breast cancer.

They had only 4 years of cycling on average.

Today, women may experience 35 years of cycling →

↑’d risk of breast, ovarian and uterine cancers and other diseases and disorders (PCOS, PMS, endometriosis, ovarian cysts, etc.).
Estradiol and Cancer

- Cancers are caused by genetic mutations; not sex hormones
- Estradiol stimulates cellular proliferation in the breasts and uterus.
- Progesterone and testosterone oppose estradiol’s stimulatory effects in the breasts.
- Unopposed estradiol and some progestins facilitate cancer growth, thereby increasing tumor detection in short-term studies.
Estradiol-Progesterone Complementarity

- Estradiol promotes proliferation in uterus and breasts.

- Progesterone stops proliferation and promotes maturation and differentiation in the uterus and breasts.

- Progesterone withdrawal → sloughing and necrosis of uterine lining and breast duct epithelium.
  

- A high persistent progesterone/estradiol ratio suppresses proliferation and prevents uterine and breast cancers.
Progesterone’s Anti-Estrogenic Actions in Uterus and Breast

- **Decreases** synthesis of estradiol receptors
- **Increases** conversion of estradiol to inactive estrone by inducing $17\beta$-hydroxysteroid dehydrogenase 2
- **Reduces** conversion of inactive estrone to estradiol by inhibiting $17\beta$-hydroxysteroid dehydrogenase 1
- **Increases** sulfation (inactivation) of estrogens
- **Inhibits** binding of estradiol to receptors
- **Inhibits** production of estradiol by aromatization
Progesterone Deficiency/Resistance → Breast Cancer

- Premenopausal women with low progesterone levels have 5x risk of early breast cancer
  

- Many breast cancer victims have progesterone resistance.
  

- BRCA1 and 2 carriers have progesterone resistance.
  

- Progesterone reduces estradiol-induced growth of ER+/PR+ breast cancer tumors.
  

- Progesterone receptor positivity predicts better long-term survival with breast cancer
  
High Luteal Progesterone Prevents Breast Cancer

6,000 women
5 yr. F/U

Progesterone vs. Breast Cancer

- **Progesterone** cream applied to the breasts reduces proliferation.  

- Breast cells proliferate with E2 treatment, but become quiescent when P is added.  

- Estradiol promotes cancers in breast cell cultures unless progesterone is present.  

- Estradiol upregulates cancer-promoter gene bcl-2, progesterone downregulates it.  

- Progesterone decreases proliferation and induces apoptosis in breast cancer cell lines.  
  Ansquer Y, Anticancer Res. 2005 Jan-Feb;25(1A):243-8  
EP Studies: No ↑ in Breast Cancer

TD-E2=transdermal estradiol; progesterone=100mg oral capsule


The Europeans Get It

“The balance of the in vivo evidence is that progesterone does not have a cancer-promoting effect on breast tissue.”


“The hypothesis of progesterone...decreasing the proliferative effect of estradiol in the postmenopausal breast remains highly plausible and (progesterone) should be...the first choice for symptomatic postmenopausal women.”

Breast Cancer Rate vs. Age

Loss of progesterone → higher risk of breast cancer

Menopause

Progesterone

Reduced surveillance

No progesterone

The Key: Intramammary Steroids

Breasts produce estradiol locally from adrenal androgens (DHEA, androstenedione)

Compared to the premenopausal breast, postmenopausal breast nipple aspirate fluid has:

- Same estradiol concentration (~youthful serum conc.)
- Much lower progesterone concentration

Chatterton RT Clin Endocrinol Metab. 2005 Mar;90(3):1686-91

Breasts get progesterone from the blood, concentrate it by 3-4x.


No progesterone → intramammary estrogen dominance → breast cancer.
Testosterone Prevents Breast Cancer in Estradiol-Replete Women

Testosterone **opposes** estradiol-induced breast stimulation.

Testosterone and DHT inhibit *in vitro* growth of breast cancer cells.
Ortmann J, Gynecol Endocrinol 2002; 16: 113-120

Addition of testosterone to estrogen/progestin therapy reduces breast cancer incidence to baseline.
Dimitrakakis C, Menopause. 2004 Sep-Oct;11(5):531-5 (508 women; 8 yrs.)

Testosterone in F→M transsexuals →involution of breast tissue
Slagter MH,J Histochem Cytochem. 2006 Aug;54(8):905-10

Testosterone is an effective treatment for breast cancer.
Confusion about Androgens in Women

Some studies show increased breast cancer and cardiovascular disease in premenopausal women with higher testosterone levels.

Confounder—PCOS: Higher premenopausal testosterone levels are caused by polycystic ovarian syndrome with high insulin and low progesterone levels.

Postmenopause: DHEA and testosterone can be converted into estradiol within the breasts, at some levels may increase risk of breast cancer in the absence of progesterone.
Don’t estrogen and progesterone cause heart attacks?
Coronary Heart Disease vs. Age

CAD and Female Hormones

After menopause, women’s rate of CAD rises faster than men’s! Higher risk than men after 65, and higher mortality after 70!

Early surgical menopause → ↑mortality, ↑atherosclerosis, 2-7x risk of heart attacks; earlier age = greater risk


Bulk of Evidence: The youthful estradiol-progesterone-testosterone milieu is protective against CAD.
Estradiol vs. Cardiovascular Disease

- Prevents the oxidation of LDL
- Improves lipid profile
- Reduces plaque formation
- Reduces lipoprotein (a)
- Improves endothelial function
- Dilates arteries, reduces blood pressure
- Improves insulin sensitivity
Transdermal Estradiol Prevents Heart Attacks

Differences in heart attack risk in Danish hormone users compared with non-users:

- Estrogen pills: -2%
- Estrogen patch: -38%
- Continuous estrogen plus progestin pills: 35%
- Cyclic estrogen plus progestin pills: -8%
- Estrogen plus progestin patch: -5%
- Vaginal gel: -44%

1 – Not considered statistically significant.
Source: European Heart Journal
By Frank Pompa, USA TODAY

Oral ERT Prevents Atherosclerosis

- Long-term Premarin® shown to reduce risk of heart disease in 40 observational and case-control studies
- Angiographic studies: atherosclerosis ↓’d 50-80%
- Estrogen reduces plaque size and progression with age.
  Christian RC, J Clin Endocrinol Metab. 2002 Mar;87(3):1062-7
- EPAT trial showed less increase in carotid intimal thickness with oral estradiol vs. placebo.
- Confounder: There’s a problem with oral estrogens....
Changes in Women's Bone Mass with Age

Bone mass (grams of calcium)

Fracture threshold
Vertebral fractures
Hip fractures

Age (in years)

Speroff L, Fritz M Clinical Gynecologic Endocrinology and Fertility, 7th Ed.
Osteoporosis—Impact

Bone loss occurs in menstruating women with lower estradiol and testosterone levels.
Steinberg KK, J Clin Endocrinol Metab 1989 Sep;69(3):533-9

Menopause: 5% bone loss/year for first 5 years = 25% — due to loss of estradiol!

20 yrs. post menopause—50% reduction in trabecular bone, 30% reduction in cortical bone

50% of women >65 yrs. old have spinal compression fractures

30% lifetime risk of hip fracture for 80 yr. old woman
Speroff L, Fritz M Clinical Gynecologic Endocrinology and Fertility, 7th Ed.
Osteoporosis

- A hormone deficiency disease—the proper prevention and treatment is hormone restoration.

- Estradiol prevents resorption of old bone while testosterone and progesterone build new bone. (Raisz LG, J Clin Endo Metab. 1996; 81:37-43)
  Barrett-Connor E, J Reprod Med. 1999 Dec;44(12):1012-20

- EPT therapy increases both bone mineral density and collagen content, maintains normal bone remodeling

- Bisphosphonate drugs poison osteoclasts, suppress bone turnover → “rotting jaw”, poor diaphyseal fracture healing and non-traumatic femur/pelvic fractures after 8 years

- Vits. D3 (a hormone) and K₂ preserve bone mass
  Iwamoto J, Keio J Med. 2003 Sep;52(3):147-50
Estrogen Replacement Prevents Alzheimer’s Disease


RR 0.65 Paganini-Hill A, Arch Intern Med 1996;156:2213-2217

RR 0.4, Tang M-X, Lancet 1996;348:429-432

72% used Premarin® only
Bioidentical Hormone Restoration is the Best Medical Practice

- **Youthful-Optimal** hormone levels and balance improve health and quality of life

- **Logical**: If a hormone is **missing**, replace it! If **insufficient**, optimize it!

- Use bioidentical molecules = **correct chemical structure**; if not bioidentical, not a human hormone!

- Bioidentical HRT is the **Best Medical Practice**: insulin, levothyroxine, growth hormone, cortisol (hydrocortisone), etc.

- Also optimize **vitanutrients**: Multivitamin/Mineral, Vit.D: 40-60ng/ml, ferritin: 80-100pg/ml, magnesium, Vit C., Omega-3 fatty acids, etc.
Q: Why does everyone think that HRT for menopause is dangerous?

A: Pharmaceutical Hormone Substitution
Human Steroid Hormones

- Testosterone
- Estradiol
- Progesterone
- DHEA
- Cortisol
Pharmaceutical “Hormone Replacement”

- Pregnant mare’s urine (Premarin®) approved in 1942
- Progesterone: first steroid synthesized from a plant molecule in 1940. Poorly absorbed orally
- Orally-effective progestins were produced—norethindrone in 1952, medroxyprogesterone acetate (Provera®) in 1956.
- For 70 years “HRT” has meant the use of non-human steroid molecules with hormone-like effects.
- Human hormones cannot be patented, limited profitability
“HRT” has been “HST”
Hormone Substitution Therapy

**Progesterone substitutes:** medroxyprogesterone acetate (MPA-Provera®) and 30+ other “progestins”

**Estradiol substitutes:** CEE-Premarin®, ethinyl estradiol

**Testosterone substitute:** methyltestosterone in Estratest® (metabolizes to super-potent estrogen, ↑’d breast cancer)

**Widespread confusion** due to careless nomenclature: “HRT”, “hormone”, “estrogen”, “progesterone” and “testosterone” often used for hormone substitutes.

**Substitutes** are **Drugs**—not hormones; but all problems caused by substitutes are attributed to hormones as “drug class effects”.

Estradiol

Ethynyl Estradiol

Oral Contraceptives

EE is much more thrombogenic than oral estradiol.
EE cannot be inactivated by normal oxidation.
EE does not interact with estrogen receptor β.
EE is 12,000-60,000 times more potent by weight.
Premarin®
Conjugated Equine Estrogens

CEE contains at least 10 estrogens, only 3 are human; also contains horse androgens and progestins.

2002 WHI Study—Premarin® Arm

- **Adverse CV effects** in the first year (strokes, blood clots)

- **Long-term reduction in CHD** (anti-atherosclerotic effect).

- **Reduced CHD and mortality** when started in 50-59yr. olds, but **increased** when started in 70-79yr olds (with atherosclerosis).

- Hip fractures **reduced** by 39%
Oral Estrogens Promote Thrombosis

- First-pass effect on the liver $\rightarrow \uparrow$ clotting factors $\rightarrow$ blood clots, strokes, heart attacks especially in the first year, especially in persons with coagulation disorders.

- Transdermal estradiol does not promote thrombosis!

> “Oral but not transdermal estrogen is associated with an increased VTE risk.”


- Transdermal estradiol improves insulin sensitivity more than oral estrogens.

- Transdermal estradiol delivery mimics natural secretion.
CV Risk Factors: Oral ≠ Transdermal E

Table 7 Effects of oral and transdermal estrogen replacement therapy on the cardiovascular system and various surrogate parameters. The effects may vary according to the type and dose of the estrogens, and may be modulated by the addition of progestogens.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oral estrogens</th>
<th>Transdermal estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of thrombosis</td>
<td>increase</td>
<td>possibly smaller increase</td>
</tr>
<tr>
<td>Hemostasis</td>
<td>procoagulatory effect</td>
<td>minor effect</td>
</tr>
<tr>
<td>APC resistance</td>
<td>increase</td>
<td>minor increase</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>prevention</td>
<td>prevention</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>increase</td>
<td>minor decrease</td>
</tr>
<tr>
<td>HDL cholesterol, triglycerides, Apo A</td>
<td>increase</td>
<td>minor increase</td>
</tr>
<tr>
<td>LDL cholesterol, remnants, Apo B</td>
<td>reduction</td>
<td>minor reduction</td>
</tr>
<tr>
<td>Size of LDL particles</td>
<td>decrease</td>
<td>increase</td>
</tr>
<tr>
<td>Activity of metalloproteinases</td>
<td>increase</td>
<td>no effect</td>
</tr>
<tr>
<td>Vasodilation</td>
<td>increase</td>
<td>increase</td>
</tr>
<tr>
<td>Release of NO, prostacyclin</td>
<td>increase</td>
<td>increase</td>
</tr>
<tr>
<td>Release of endothelin-1</td>
<td>reduction</td>
<td>reduction</td>
</tr>
<tr>
<td>Angiotensinogen</td>
<td>increase</td>
<td>no effect</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>increase</td>
<td>no effect</td>
</tr>
<tr>
<td>Adhesion molecules</td>
<td>decrease</td>
<td>decrease</td>
</tr>
<tr>
<td>Cytokines (IL-1, IL-6, TNF-α)</td>
<td>no effect</td>
<td>no effect</td>
</tr>
<tr>
<td>PAI-1</td>
<td>decrease</td>
<td>no effect</td>
</tr>
<tr>
<td>IGF-1, IGFBP-3</td>
<td>decrease</td>
<td>no effect</td>
</tr>
<tr>
<td>IGFBP-1, GH, GHBP</td>
<td>increase</td>
<td>no effect</td>
</tr>
</tbody>
</table>

APC, activated protein C; HDL, high density lipoprotein; LDL, low density lipoprotein; Apo, apolipoprotein; NO, nitric oxide; IL, interleukin; TNF, tumor necrosis factor; PAI-1, plasminogen activator inhibitor-1; IGF, insulin-like growth factor; IGFBP, insulin-like growth factor-binding protein; GH, growth hormone; GHBP, growth hormone-binding protein.
WHI Study—Prempro® Arm

- Adding Provera® to Premarin® caused additional heart attacks, strokes, breast cancer, and dementia (prob. vascular).

- Thousands of lawsuits pending—drug companies running legal-protection propaganda campaign

- Women are told, “All HRT is dangerous!”

- Negative results of WHI have never been documented with transdermal estradiol with progesterone
Progesterone vs. Provera

Progesterone

Medroxyprogesterone acetate

Prempro® increases cellular proliferation and breast density and affects 2500 genes; estradiol plus progesterone does not increase proliferation or density and affects only 600 genes.

Scientific studies show that:

**Provera® ≠ Progesterone**

- Birth defects
- Depression
- Insomnia, irritability
- Reduces neuroprotection
- Fluid retention
- Glucocorticoid-like effects
- Raises blood sugar
- Vasoconstriction
- Smooth muscle proliferation
- Increases blood clotting
- Worsens lipid profile
- Causes heart attacks
- Increases MMP activity
- Increases estrogenic stimulation of breasts
- **Promotes breast cancer**

- Hormone of Pregnancy
- Improves mood
- Improves sleep
- Neuroprotective
- Diuretic
- Anti-glucocorticoid
- Lowers blood sugar
- Coronary vasodilation
- Decreases SM proliferation
- No increase in clotting
- Improves lipid profile
- No evidence of ↑ CVD
- Reduces MMP activity
- Reduces estrogenic stimulation of breasts
- **Prevents breast cancer**
Progestins ≠ Progesterone

Drospirenone (Yasmin®)  
Norethisterone  
Levonorgestrel

Most progestins increase breast cancer risk (RR~1.4 to 2.0)  
Each progestin has a different spectrum of androgenic, estrogenic, glucocorticoid, and progestational effects.
Atherosclerosis and Clotting

“In both peripheral and cerebral vasculature (of live animals), synthetic progestins caused endothelial disruption, accumulation of monocytes in the vessel wall, platelet activation and clot formation, which are early events in atherosclerosis, inflammation and thrombosis. Natural progesterone or estrogens did not show such toxicity.”

Thomas T, Progestins initiate adverse events of menopausal estrogen therapy. Climacteric. 2003 Dec;6(4):293-301

“In addition, our data suggest that norpregnane derivatives (progestins) may be thrombogenic, whereas micronized progesterone and pregnane derivatives appear safe with respect to thrombotic risk.”

Any Questions about EPT benefits and safety or dangers of pharmaceutical HST?

Next: How to do bioidentical EPT restoration
Principles of Bioidentical EPT Therapy

**Clinical Endocrinology:** Adjust doses by **symptoms** first, serum levels second.

**Eliminate** symptoms/signs of **deficiency** while **producing no** symptoms/signs of **excess**

**No side effects:** all problems that occur are due to **dosing, balance, route** or other hormonal or medical issues.

For peace of mind: Have patient sign a **consent form**.

Provide **written instructions** for using hormones, preventing transfer, adjusting doses (see handouts).
Serum Testing for Menopause

🌟 Good to get **baseline** levels even in menopause—show patient.

🌟 Pre-treatment: order **total** an **free estradiol**, **total** and **free testosterone**; progesterone always low.

🌟 **Free** hormone level best represents bioavailable hormone

🌟 **Cannot use saliva testing** to monitor **EPT** therapy—overeacts to transdermal steroid hormones → spuriously high results

🌟 **To monitor replacement**: have blood drawn ~12 hrs after daily dose for best estimate of 24hr average. Typically: AM test after bedtime application of hormones.
FDA-Approved Bioidenticals

- Estradiol patch (Climara®, Vivelle®, etc.)
- Estradiol gel (Estrogel®, Divigel®, etc.)
- Estradiol vaginal ring (Femring®)
- Progesterone capsules (Prometrium®, generic)
- Progesterone vaginal gel (Crinone®)
- **No FDA-approved testosterone product for women**

Problems: weak, inconvenient, fixed doses, and/or expensive
Problems with FDA-Approved E&P

- **Estradiol** patches: Adhesion/allergy problems, otherwise very good. Estradiol level should be checked mid-way between patch changes.

- **Estradiol** gels: very expensive ($200/mo)

- **Oral progesterone-in-oil** capsules are inefficient: immunoassay progesterone levels are 80% metabolites, quite sedating.

- 200mg oral Prometrium® yields same 24hr whole blood LC/MS/MS progesterone levels as 80mg progesterone in transdermal cream.
  
  Hermann AC et al., J Clin Pharmacol 2005;45:614-619

- **Oral progesterone** caps best take vaginally (100mgs) or punctured to apply oil to skin (200mgs).
Compounded Bioidentical Hormones

- **Locally made** from USP-certified micronized hormone powders
- Standardized compounding practices with PCCA (Professional Compounding Centers of America) and other organizations.
- **Completely customizable** delivery systems and concentrations
- Can make **testosterone** cream, **progesterone** cream, **EPT** combo creams, sublingual **progesterone** (**No** FDA-approved equivalents)
- **Inexpensive**—Often less than co-pays for FDA-approved bios.
- **Physician-monitored**: adjust dose by clinical effects and serum levels
Estradiol Restoration

- 3mg/0.5ml cream, 0.1ml (1 line) applied to face or neck at bedtime, ↑ as needed to 0.3ml. Adjust strength of cream if needed.

- Good for facial skin tone: E2 increases skin collagen.

- Clinical Dosing: eliminate hot flashes, vaginal dryness, insomnia; avoid breast fullness-tenderness, vaginal bleeding, fluid retention

- 12 hr. serum estradiol is usually 30-125pg/ml (similar to follicular phase). Free estradiol usually 0.5 to 1.5pg/ml (More accurate measure—same as male free estradiol range).

- No need for estriol (E3), a weak metabolite of E2.

- Avoid transfer to other persons or pets (See handout)
**Progesterone Restoration**

- **100mg sublingual tablet** at bedtime, better absorbed than cream

- **Pulse therapy**: levels very high at 3-6 hrs., low-luteal at 12 hrs.

- **100 mg in cream**, serum levels (2-4 ng/dL) **underestimate** effect.

- Sufficient **progesterone prevents** breast tenderness, bleeding

For unusual bleeding tendency use **vaginal tabs/cream/caps**.

- **Progesterone** is **SAFE at any dose**. Too much → sedation, heartburn, constipation

- For premenopausal menorrhagia or early breakthrough bleeding try **twice-daily sublingual P** or **vaginal P** in luteal phase or continuously
Testosterone Restoration

- **2mg/0.2ml Versabase cream**, apply 0.1ml (1 line) to inner labia or 0.2ml to back of knees.

- Best absorbed **genitally**, improves libido and vaginal moisture, no clitoromegaly reported.

- If not tolerated labially, use higher strength/amount to inner thighs or back of knees (no local hair growth)

- **Lower T dose for excess** acne or facial hair—but a few pimples, more body hair are **natural effects** of youthful **testosterone** levels!

- Good dose: 12 hr. serum total **testosterone** usually **high**, but bioavailable **testosterone** above mid-range (range 1 to 8.5pg/ml).

- More androgen effect than **testosterone** levels suggest because DHT is higher with transdermal, especially genital application.
Troubleshooting

- Recurrent bleeding/spotting may occur due to submucosal fibroid, polyp, or adenomyosis; try lower estradiol dose, higher progesterone dose or vaginal progesterone.

- Postmenopausal cancer-surveillance guidelines do not apply: Endometrial evaluation only if bleeding persists in spite of dose changes and off EP therapy.

- If hot flashes worsen with estradiol, lower dose then increase very slowly, try AM dosing

- Inability to tolerate estradiol or progesterone may be due to hypocortisolism (a.k.a. adrenal insufficiency).

- Hair loss: ↑estradiol, ↓testosterone (some women have androgen-sensitive alopecia)
Almost all studies of estrogen/progestin (pro-proliferative) therapy in women with breast cancer show no increase in recurrence rates.

One human and two rat studies indicate that bioidentical estradiol-progesterone therapy is an effective preventative and treatment for breast cancer.

Estradiol-deprivation therapies (tamoxifen, aromatase inhibitors) only reduce 5-to-10 year recurrence rates, they do not cure cancer; and have a high cost in quality of life and health.

Estradiol-progesterone-testosterone replacement is not contraindicated and may reduce recurrence rates due to the anti-proliferative effects of progesterone.

EPT therapy can be combined with aromatase inhibitor—as the latter will reduce intra-mammary estradiol production while EPT maintains systemic health.
For More Information

- See presentation, handouts, practice forms on CD
- www.hormonerestoration.com
- Essays on Hormone Restoration
- Thousands of abstracts under The Evidence
- Contact me: henry@hormonerestoration.com
Q: Why don’t physicians and the public know about the benefits and safety of bioidentical HRT?

A: Pharmaceutical Corporation Clout
HRT Information Warfare

After WHI report, lawsuits piled up and women switched from Prempro® to pharmacy-compounded bioidentical hormones.

US professional associations proclaimed “All HRT is alike”; FDA-approved and compounded bioidentical hormones had the same risks as all other FDA-approved “hormone products”.

The North American Menopause Society (NAMS) published an anti-bioidentical article — confounding bioidentical HRT with questions surrounding compounding and saliva testing.


“Bioidentical” ridiculed as a “marketing term”, “fad”, “snake oil”.

Muddying the waters: NAMS advised that progesterone and progestins now be called “progestogens”!

NAMS tells women and their doctors: “Use any FDA-approved progestogen, but don’t use compounded progesterone”.
ACOG Helps Big Pharma

October 31, 2005, ACOG NEWS RELEASE “There is no scientific evidence to support claims of increased efficacy or safety for individualized estrogen or progesterone regimens prepared by compounding pharmacies, ... ...ACOG recommends that they should be considered to have the same safety issues as those hormone products that are approved by the FDA and may also have additional risks unique to the compounding process.” ...Furthermore, hormone therapy does not belong to a class of drugs with an indication for individualized dosing (!?!)

ALL LIES!

ACOG, NAMS and The Endocrine Society are funded by Pharmaceutical Corporations.

Conflict of Interest: professional associations and policy makers should have zero (0) industry funding.

Rothman DJ et al, Professional medical associations and their relationships with industry: a proposal for controlling conflict of interest. JAMA. 2009 Apr 1;301(13):1367-72.
Wyeth Jumps In

October 2005: Wyeth (maker of Prempro®) files “citizen petition” asking FDA to impose restrictions on physicians’ ability to prescribe and pharmacists’ ability to make compounded bioidentical hormones!

Demands that compounding pharmacies cease promoting bioidentical hormones as more natural or safer than its dangerous hormone substitutes!

Demands the same warnings for compounded bioidentical hormone preparations as for its dangerous hormone substitutes

Motives: Legal protection (Prempro® lawsuits) and market share (Prempro® is still being prescribed!)
HRT Wars: Conclusions

Women have been victimized by propaganda from pharmaceutical corporations and the “professional” associations that they fund.

Things are changing: Recent guidelines from International Menopause Society, NAMS and The Endocrine Society contain statements about the greater safety of transdermal estradiol and progesterone. (“may not have the same risks…”)

Estradiol (transdermal), progesterone and testosterone restoration will soon be standard medical practice.