UW Integrative Medicine
Department of Family Medicine

University of Wisconsin
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

Supplement Sampler

Bio-Identical Hormones

Caution:

- There is limited evidence to understand the potential harm of prolonged hormone therapy.
- Therapy should be guided by unique patient need.
- Use the lowest most effective dose for the shortest amount of time necessary.

Estrogen

Type	Main Source	Effect on Breast	Increased by	Notes
E1: Estrone↴ 16-α-OH-E1 2-OH-E1 16 alpha hydroxy estrone (16-α-OH-E1) 2 hydroxy estrone (2-OH-E1)	Pre-menopause: ovaries Post-menopause: fat Estrone gets converted to estradiol. 16-α-OH converts to estriol.	Metabolites: 16-α-OH=↑ breast tissue growth/genotoxic 2-OH= ↓breast tissue growth. Goal: More 2-OH, Less 16-α-HO (high 2:16 ratio) **2:16 ratio can be ordered through some commercial labs. (?necessary?)*	↓2:16 ratio • Obesity • Animal fat • Hypothyroidism • PCBs ↑2:16 ratio • Exercise • Weight loss • Flax seed • Cruciferous Veggies • Avoid xenobiotics (PCBs, Atrazine, IGH, etc)	In patients who have had hormone positive BC, it would be to their benefit to increase the 2:16 ratio. In general, this is done through healthy lifestyle recommendations with little harm. *For more information on 'estrogen dominance'
E2: Estradiol	Ovary	Increased tissue growth. Main stimulator of hormone sensitive breast cancer	Early menarche Xenobiotics (estrogen-mimickers)	Most effective in reducing menopausal symptoms but also with most potential side effects (BC, Heart Dz)
E3: Estriol	Pregnancy	Less stimulatory	Pregnancy	The main estrogen in compounded hormones (Bi-est, Tri-est). Least potent estrogen.

***Note:** The term *"natural hormone therapy"* is misleading since many prescription hormones are "natural" or bio-identical.

Bio-Identical Hormones

Bio-identical Hormones: The use of hormones that are structurally identical to endogenous hormones. Thus when estradiol is prescribed, you are prescribing bio-identical hormones. [Non bio-identical hormones are mainly equine estrogens *(Premarin)* and medroxyprogesterone *(Provera),* which are rarely used anymore since the Women's Health Initiative study. Some use compounding pharmacies to create combinations of the above bio-identical hormones. The two most common formulations are Bi-Est and Tri-Est. These can be delivered through capsules, creams, gels, and troches.]

Bi-Est (E3,E2)= 80% Estriol, 20% Estradiol

Tri-Est (E3,E2,E1)= 80% Estriol, 10% Estradiol, 10% Estrone

Point/Counterpoint for Prescribing Estriol:

Point: Estriol dominant hormone prescribing allows lower dosing of estradiol which may reduce the risk of BC and heart disease.

Counterpoint: Estriol is much less potent than estradiol and larger doses may be needed for a similar effect negating the potential benefit.

Point: Estriol is safer than estradiol and can be used as a vaginal cream to help with dryness and atrophy associated with menopausal symptoms. Estriol helps with vaginal elasticity in preparation for birth Patients with hx of BC or strong risk who need help with vaginal atrophy/dryness when lubricants are not enough may benefit from E3 cream, 0.5 mg vaginally for two wks and then every 2-3 days.

Counterpoint: Did nature intend us to give the pregnancy estrogen this late in the lifespan? Will this stimulate nesting in our 55 year old patients? ☺ We don't know of the potential long term risks of estriol.

Progesterone

Type	Main Source	Effect on Breast	Notes
Micronized PGE *(Prometrium, Utrogestan, Minagest, Microgest)*	Cholesterol→Pregnenolone→PGE Often made from yeast and micronized to enhance oral absorption.	Neutral-reduced risk? In pregnancy, PGE inhibits lactation. The fall in PGE post pregnancy is associated with breast/milk tissue growth.	PGE reduces breast cell proliferation and stimulates apoptosis. Can be formulated in sublingual tablets, oil caps and transdermal creams.
Trans-dermal PGE (OTC) *Many formulations* Also available by Rx as vaginal gel *(Prochieve, Endometrin, Crinone)*	Mexican wild yam, soybeans (These have to be converted to PGE in the lab. If the label says "wild yam" without mentioning PGE content, it will have none and be ineffective.)	Neutral-reduced risk?	Label should state that it has progesterone at a dose of 400 mg per oz. 1/4 tsp is rubbed into thin skin on abdomen, inner thigh or inner forearm daily.

*Medroxyprogersterone (MPA, *Provera*) may increase the risk of BC (1.4 RR) compared to oral micronized progesterone (0.9 RR) (Fournier et al. Int J Cancer. 2005;114)

*Another source of PGE is milk. Most cows are milked when pregnant which increases the PGE content. But non-organic milk has other hormones (IGH) that may be harmful.

A Sample Protocol

A practical non-controlled study of 189 menopausal women were treated with bio-identical estrogen and progesterone, with or without DHEA and testosterone and followed for 12 mths in a clinic in Minneapolis, MN. Ninety-eight percent had symptom control, 90% improved mental clarity and 60% who complained of weight gain with menopause lost an average of 14.8 lbs (This was a surprise finding; no other weight loss recommendations were given). The protocol they used is described below. (Mahmud, K. Natural hormone therapy in menopause. *Gynecological Endocrinology*. 2010;26(2):81-85.) Limitations: An observational study in a clinic with a pro-hormone bias. No control group with short-term follow-up.

Hormone	Dose	Lab Level Goal	Notes
Bi-Est (E2, E3) in a transdermal cream *Those who did not respond were changed to sublingual form.	Estradiol 1 mg + Estriol 4 mg per gram. 1/2 gm of cream twice daily. Dose titrated by 1/2 gram up (hot flashes) or down (breast tenderness) as needed.	50 pg/mL	Transdermal route was chosen due to less risk of hypercoaguability and rise of CRP compared to oral dosing.
Progesterone in sublingual triturate form	50-100 mg sublingual before bed	4 ng/mL	Dosed in the evening due to sedation to help sleep. Could also use Rx micronized PGE *(eg. prometrium)* 100 mg orally at bedtime.
Testosterone in a "vanishing peri-vaginal cream" applied nightly	2-10 mg cream daily Used in those with ↓ libido with ↓serum levels	Titrate total testosterone level near 25 ng/dL	Long term risk leaning towards harm
Dehydroepiandrosterone (DHEA) OTC	25 mg orally daily if serum DHEA found to be ↓	Titrate near 120 ug/dL	Can be low due to chronic lifestyle stress; (↓DHEA,↑Cortisol) Better to help reduce stress than to prescribe DHEA.

*__Note:__ Many clinicians don't order lab levels for estrogen and progesterone due to variability and added cost. An option is to dose hormones based on symptoms starting low and increasing as needed. If testosterone or DHEA are considered, serum levels should be ordered and found to be low prior to prescribing.

Prescribing:
Except for estriol and estrone, most of the above hormones can be prescribed traditionally (estradiol, micronized progesterone, testosterone) or found over the counter (DHEA, PGE cream). Compounding pharmacies mainly help by placing the hormones in various delivery forms such as creams, sublingual tablets, suppositories, troches, etc. The hormones are generic and relatively inexpensive.

There are many compounding pharmacies in the U.S. One of the largest in the nation is in Madison, Wisconsin. **Women's International Pharmacy:** (608) 221-7800 or 1-800-279-5708 (option 1 to speak directly to pharmacist). http://www.womensinternational.com/bioidentical_hormone_therapies.html

Brought to you by your colleagues in the UW Dept. of Family Medicine Integrative Medicine Program.

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