

## **Bioidentical Hormone Risk and Benefits STUDIES-**

7 studies = not increase estrogen stim breast cell growth

13 studies progesterin = increase estrogen stim breast c growth

### **PROGESTERONE AND BREAST CANCER RISK (LOW PROGESTERONE LEVEL= MORE BREAST CANCER or HIGH = protective)**

E3N Cohort study -

#### **Fournier et al, Br CA res treat 2008: 107 (1) 103-111**

Followed 80,000 PMP women x 8 years comparing HRT with non users:

estrogen use alone, non significant increase of 1.29 x breast ca (p=.73),

synthetic progesterin + estrogen incr 1.69x risk BR CA (p=.01)

Progesterone + estrogen eliminated the increased risk and significant reduction of Br CA risk (p=0.001)

#### **Int Journal of CA 2004 Nov1:112(2); 312-8**

Prospective study 5963 premenopausal Women whose progesterone levels were measured in the luteal phase and followed for subsequent the risk of breast cancer highest progesterone levels correlated with 88% decreased risk for breast cancer

#### **Am journal epidemiology 1981 August 1 14 (2);209-17**

prospective epidemiology study 1083 women treated for infertility and followed for 13 to 33 years for risk of breast cancer

Low progesterone level 5.4 times higher risk of breast cancer you like 10 times as many different all cancers and worse breast cancer survival and growth with Lowest progesterone levels

Fer71 Steril 1995 Apr; 63(4);785--91

Chang et al double blinded placebo controlled study • 40 women given HRT or placebo prior to breast surgery • Estrogen alone increased breast cell proliferation on 62% • Bioidentical progesterone alone decreased breast cell proliferation on 66%

### **PROGESTERONE AND CV**

Speroff, Clinical Endocrinology & Infertility, 7<sup>th</sup> Edition -

**Decreases LDL, LDL oxidation, Lp(a), Homocysteine • Decreases BP • Decreases coronary atherosclerosis • Decreases platelet aggregation • Relaxes coronary arteries**

Eur J Clin Invest 1983; 13(6) 447--453 Am J Obstet Gynecol 1985; 151(6) 746--750 Maturitas 1990; 129@0 89--97

Fahraeus et al - 26 PMP => **MPA (progesterin) decreased HDL**

Ottosson et al - **P+E2 not decrease HDL, E2+MPA => decrease HDL**

Endocrinol Met 1998; 83 (2);649--659 Nat Med 1997; 3(3) 324--327 Metab 2005; 90 (6) 3706--3714

- **MPA +E2 associated with coronary vasoconstriction not E2+P**

J Am Coll Cardiol 2000; 36(7); 2154--2159

**-Progesterone Decreases Myocardial Ischemia**

Circulation 2007 Feb 20; 115(7) 840--5 -

**VTE risk reduced when bioidentical progesterone added to oral estrogen**

Singh and Su. Brain Research. June 2013 -

**Progesterone has been shown to exert protective effects in a variety of experimental models that mimic Alzheimer's disease, stroke and traumatic brain injury and spinal cord injury** ü

Progesterone induces BDNF ü Allopregnenolone, the major progesterone metabolite plays a role in the neuroprotective effects of progesterone

### **SYMPTOMS IMPROVEMENT OF PROGESTERONE**

**4 studies show fewer side effects, & improved quality of life than progestin**

Speroff. Clinical Gynecologic Endocrinology & Infertility. - **Progestin s.e. -Breast tenderness ·**

**Bloating · Increased appetite · Decreased libido · Acne · Hair loss Counteracts estrogen's positive effects on ST · Depression · Insomnia · Irritability**

**Natural Progesterone -Promotes sleep · Calming · Natural diuretic · Increase metabolic rate ·**

**Antidepressant** Smith. HRT: The Answers

### **WHY NEED ESTROGEN ? TOO MUCH PROGESTERONE WITHOUT ESTROGEN=> p.84**

Increases weight gain and fat storage · Increases total cholesterol · Decreases HDL · Increase LDL · Increase triglycerides · Elevates cortisol · Decreases growth hormone · Increases insulin resistance

### **TOO MUCH PROGESTERONE WITH enough ESTROGEN=>**

Causes depression · Causes fatigue · Decreases libido · Causes incontinence · Causes ligaments to relax and can cause backaches, leg aches, and achy hips · Suppresses the immune system ·

Increases appetite and carbohydrate cravings · Relaxes the smooth muscles of the gut (This can cause bloating, fullness, and constipation. It can also contribute to gallstones.)

## **ESTRIOL**

### **ESTRIOL AND BR CANCER PROTECTION p.84**

80 x weaker than E2, protects from BR CA, Maintains favorable GI flora · Maintains vaginal pH; prevents UTIs · No clotting issues Smith. HRT: The Answers

**Int J Cancer 1999; May 5; 81(3): 339--44**

· Risk of breast cancer among estriol users = risk of nonusers (RR 1.10 CI .95--1.29) · Risk of breast cancer among synthetic HRT users double that of nonusers

**Int J of Cancer 2004 Oct 20; 112(1): 130--4**

Bakken et al 31,451 PMP women on HRT & breast cancer incidence · Estriol was not associated with the increased risk of breast cancer seen with estrogen only or estrogen + progestin (RR 1.0; CI 0.4--2.5)

### **ESTRIOL NOT CAUSE UTERINE CA**

**Lancet 1999 May 29; 353(9167):1824--8 Eur J Obstet Gynecol Reprod Biol. 1995**

**Sept;62(1):101--6**

Review of 12 studies determined intravaginal estriol did not cause endometrial proliferation · Topical estriol not associated with increased risk of uterine cancer

### **ESTRIOL improve CV HEALTH**

**Hum Reprod. 2000 May;15(5):1028--36 Life Sci 2002 May 24;71(1):31--42**  
estriol decreased BP, TC, TG, & increased HDL

### **ESTRIOL IMPROVE MENOPAUSAL SX**

**JAMA 1978 Apr 21;239(16):1638--42 Hum Reprod. 2000 May;15(5):1028--36 Horm Met Res 1987 Nov;19(11):579--84**

52 women given oral estriol in varying doses for 6 months with resolution of vasomotor symptoms & without mammogram changes or endometrial hyperplasia · 53 women with surgical menopause given oral estriol for 12 months with symptom resolution & no mammogram changes or endometrial hyperplasia · 5 yr study 71% of menopausal symptoms completely eliminated w/ estriol

### **ESTRIOL IMPROVE BONE DENSITY**

**J Obstet Gynaecol Res. 1996 Jun;22(3):259--65 J Bone Miner Metab. 1998; 16:21--6**

2 Japanese studies women given oral estriol + calcium increased bone density · 1.66% increase in bone density w/ estriol + calcium X 1 yr · 5% increase in bone density w/ estriol + calcium X 10 mths; 3% decrease in calcium only group

### **ESTRIOL IMPROVE URINARY SX/ INCONTINENCE AND UTI**

**Menopause. 2004 Jan;11(1):49--56 N Engl J Med. 1993 Sep 9;329(11):753--6**

Randomized placebo--controlled study women given vaginal estriol had 68% improvement of incontinence symptoms · Randomized double--blinded placebo controlled trial estriol reduced the incidence of recurrent UTIs by 91%

### **ESTRIOL IMPROVE ATROPHIC VAGINITIS**

**Eur J Obstet Gynecol Reprod Biol. 1993 Sept;51(1):29--33 Orv Heti. 1995 Feb 12;136(7):343--5 Maturitas. 2001 Sep 28;39(3):253--7**

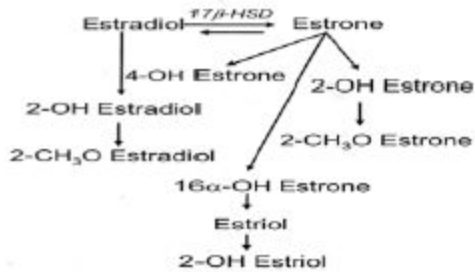
· At least 3 studies demonstrate both oral & vaginal estriol improve symptoms of atrophic vaginitis w/o side effects

## **ESTRODIOL**

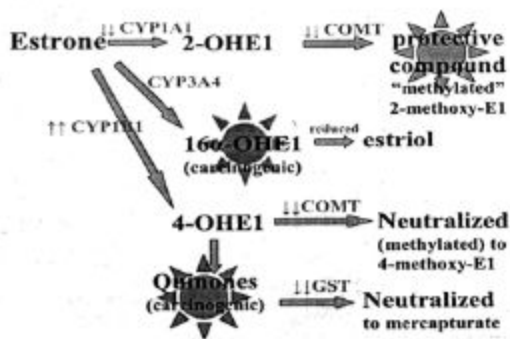
**Climacteric 2012 Apr;15 Suppl 1:11--7**

Estradiol controls 400 functions in the female body Estradiol protects the brain – evidence supports its role in neuronal survival against beta amyloid · Estradiol protects bones – many studies have shown that E2 prevents advancement of osteoporosis · Vaginal estradiol treats dyspareunia, dryness and incontinence · Estradiol is cardioprotective · Estradiol reduces the risk of new--onset diabetes

**Estrogen metabolism - 2 competing pathways 2OH estrone, 16 OH estrone, 1 minor -4 OH estrone**



## Estrone Metabolism



## 2--OH Estrone/Methylation p86

Good estrogen. It does not stimulate the cell growth. • Blocks action of stronger estrogen products that may be carcinogenic.

• 2--OH estrone is protective against cancer when methylated by catechol--O--methyltransferase (COMT) into 2--methoxy--estrone.

Urine 2-- methoxyestrone to 2--hydroxyestrone gauge of the body's ability to methylate.  
measure methylation ability by check homocysteine

Low ratios of 2/16 hydroxy estrogen are also associated with an increased rate of developing lupus.

## HOW TO Support Methylation

SAME • Methionine • B2, B6, B12 • Folic acid (also as folinic acid, 5--formyl THF, or 5--methyltetrahydrofolate---MTHF) • TMG (betaine) • Reducing catecholamine production by decreasing stress

## HOW TO increase 2-OH Estrone

Moderate exercise

• Cruciferous vegetables

• Flax •

Soy •

Kudzu •

Broccoli derivatives: indole--3--carbinol taken as a supplement. Daily dose is 200 to 300 mg.

Other derivatives of broccoli that have been shown to be effective are DIM (diindolymethane, a breakdown product of I-3-C) and sulforaphane glucosinolate • High protein diet

Omega-3 fatty acids •

B6, B12, and folate • MTHF •

TMG •

Rosemary

Tumeric •

Weight loss

Updated 2/2017