



# Comprehensive Plus Panel

The expanded Comprehensive Plus Panel builds on the Labrix comprehensive panel by including estrone (E1) and estriol (E3) plus an Estrogen Quotient calculation. The Estrogen Quotient is calculated by dividing E3 by E1 + E2 and was developed by Dr. H.M. Lemon in the 1980's. The EQ is especially pertinent for women who need to focus on minimizing breast cancer risk. When assessing for estrogen dominance you can now use both the Progesterone/Estradiol (Pg/E2) ratio and the Estrogen Quotient (EQ) for risk-preventative assessment in your patients.

## Estrogen interaction

Estrogen exists in the human body in at least three forms. Estrone, estradiol and estriol. Estradiol (E2) is the most potent estrogen in terms of its ability to relieve hot flashes and other menopausal symptoms. Unfortunately, however, estradiol and estrone are also the forms of estrogen that promote cancer growth and play a role in various pathologies including BPH and PCOS. E1 and E2 can be converted back and forth, from one to the other, and various physiologic states determine this cascade. Estriol (E3) is considered the 'weak' estrogen, and cannot be converted by the body into estradiol or estrone. It is sometimes referred to as the 'anti-estrogen' since, when it is present, it blocks further uptake at the tissue receptor sites by E2 and E1. Both E1 and E2 can be converted into E3, and once the hormone is converted to the E3 form it will not be converted back to E1 or E2. So despite estriol having the weakest activity of the estrogens - it is the only protective estrogen. Measuring these three estrogens through saliva testing is a critical assessment tool for determining when some of your patients have a higher risk for developing certain types of cancer. For women, an optimal EQ is also associated with lower incidence of autoimmune diseases like multiple sclerosis.

## Estrone

Research has shown that elevated estrone is associated with increased risk of cardiovascular disease, endometrial cancer, PCOS, and breast cancer in women. Estrone can also be viewed as a marker for prostate health and cardiovascular disease risk in men.

### In women:

- In post-menopausal women, CRP is higher when estrone and testosterone levels are higher.<sup>i</sup>
- In endometrial cancer cases, circulating levels of E1 and E2 were significantly higher compared with unaffected controls.<sup>ii</sup>
- The combination of elevated estrone and free testosterone appears to discriminate with high sensitivity and specificity between women with and without PCOS.<sup>iii</sup>
- Overweight and obese women with breast cancer have poorer survival compared with thinner women. Obese women had 35% higher concentrations of estrone and 130% higher concentrations of estradiol compared with lighter weight women.<sup>iv</sup>
- In premenopausal women, estrone levels generally parallel those of estradiol. After menopause, estrone levels increase, possibly due to increased conversion of androstenedione to estrone.

### In men:

- Higher estrone is strongly related to an increase in benign prostatic hypertrophy (BPH) and prostate cancer.<sup>v</sup>
- Higher estrone levels may be associated with a poorer prognosis in men with prostate cancer.<sup>vi</sup>
- Men with coronary artery disease had lower testosterone levels and higher levels of estrone.<sup>vii</sup>

## Estriol

The only time there is a dramatic increase in endogenous estriol is during pregnancy. However, it should also be noted that some women have higher endogenous E3 levels than others, which may protect some from developing breast cancer. Research has shown that supplemental estriol can help to increase bone mineral density, can be an effective treatment for multiple sclerosis and other autoimmune diseases, and decrease the risk of developing breast cancer.

- Oral estriol therapy has been shown to increase bone mineral density without increasing triglycerides (commonly seen with CEE) and causes less endometrial proliferation and uterine bleeding.<sup>viii</sup>
- Multiple sclerosis patients who become pregnant

experience a significant decrease in relapses. Animal models of MS have shown that the pregnancy hormone estriol can ameliorate disease.<sup>ix</sup>

- Estriol pellets implanted in rats exposed to carcinogenic substances decreased the risk of their developing breast cancer.<sup>x</sup>

## Estrogen Quotient   $\text{EQ}=\text{E3}/(\text{E1}+\text{E2})$

Because of the anticancer effects of estriol in animals, Dr. Lemon investigated whether estriol had any relationship to breast cancer in humans. He developed a mathematical formula, which he called the *estrogen quotient (EQ)*. The EQ is a ratio of the E3 (anti-estrogen) divided by the sum of E1 plus E2 (cancer promoting estrogens) and helps predict breast cancer risk. If a woman's EQ is low (<1.0), her risk of breast cancer is higher. When the EQ is >1, it is associated with lower cancer risk. The optimal ratio that is considered most protective to the breast is an **EQ >1.5**.

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## End Notes

- i. "Association of endogenous hormones with C-reactive protein, fibrinogen, and white blood cell count in post-menopausal women." Eur J Epidemiol. 2005;20(12):1015-22.
- ii. "Circulating Estrogens in Endometrial Cancer Cases and Their Relationship with Tissular Expression of Key Estrogen Biosynthesis and Metabolic Pathways." J Clin Endocrinol Metab. 2010 Apr 6.
- iii. "Are there any sensitive and specific sex steroid markers for polycystic ovary syndrome?" J Clin Endocrinol Metab. 2010 Feb; 95(2):810-9.
- iv. "Adiposity and sex hormones in postmenopausal breast cancer survivors." J Clin Oncol. 2003 May 15;21(10):1961-6.
- v. "Sex Hormones and the Risk of Incident Prostate Cancer." Urology. 2010 May 6.
- vi. "Estrone sulfate (E1S), a prognosis marker for tumor aggressiveness in prostate cancer (PCa)." J Steroid Biochem Mol Biol. 2008 Mar; 109(1-2):158-67.
- vii. "Evaluation of sex hormone levels and some metabolic factors in men with coronary atherosclerosis." Aging Male. 2004 Sept;7(3):197-204.
- viii. "Beneficial Aspect of Oral Estriol as Hormone Replacement Therapy: Consideration on Bone and Lipid Metabolism." Tokai J Exp Clin Med., Vol.34, No. 3, pp. 92-98, 2009.
- ix. "Treatment of Multiple Sclerosis with the Pregnancy Hormone Estriol" Ann Neurol 2002;52:421-428.
- x. Lemon, Henry M.D. "Estriol Prevention of Mammary Carcinoma Induced by 7,12-Dimethylbenzanthracene and Procarbazine." Cancer Research 35, 1341-1353, May 1975.