Balancing All Hormones Can Reduce Cancer Risk From Estrogen!

Dimitrakakis C, Zhou J et al. ***A physiologic role for testosterone in limiting estrogenic stimulation of the breast.*** Menopause. 2003 Jul-Aug; 10(4): 292-8.

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OBJECTIVE: The normal ovary produces abundant testosterone in addition to estradiol (E(2)) and progesterone, but usually only the latter two hormones are "replaced" in the treatment of ovarian failure and menopause. Some clinical and genetic evidence suggests, however, that endogenous androgens normally inhibit estrogen-induced mammary epithelial proliferation (MEP) and thereby may protect against breast cancer.

DESIGN: To investigate the role of endogenous androgen in regulating mammary epithelial proliferation, normal-cycling rhesus monkeys were treated with flutamide, an androgen receptor antagonist. To evaluate the effect of physiological testosterone (T) supplementation of estrogen replacement therapy, ovariectomized monkeys were treated with E(2), E(2) plus progesterone, E(2) plus T, or vehicle.

RESULTS: We show that androgen receptor blockade in normal female monkeys results in a more than twofold increase in MEP, indicating that endogenous androgens normally inhibit MEP. Moreover, we show that addition of a small, physiological dose of T to standard estrogen therapy almost completely attenuates estrogen-induced increases in MEP in the ovariectomized monkey, suggesting that the increased breast cancer risk associated with estrogen treatment could be reduced by T supplementation. Testosterone reduces mammary epithelial estrogen receptor (ER) alpha and increases ERbeta expression, resulting in a marked reversal of the ERalpha/beta ratio found in the estrogen-treated monkey. Moreover, T treatment is associated with a significant reduction in mammary epithelial MYC expression, suggesting that T's antiestrogenic effects at the mammary gland involve alterations in ER signaling to MYC.

CONCLUSIONS: These findings suggest that treatment with a balanced formulation including all ovarian hormones may prevent or reduce estrogenic cancer risk in the treatment of girls and women with ovarian failure.