Reviews: Transdermal estradiol and progesterone restoration does not carry the same risks as CEE-MPA (PremPro®)


...Natural, 'body-identical' progesterone...appears to be the optimal progestogen in terms of cardiovascular effects, blood pressure, VTE, probably stroke and even breast cancer...


...The combination of oral oestrogen and thrombogenic mutations or obesity further enhanced the risk of venous thromboembolism, whereas transdermal oestrogen did not seem to confer additional risk in women at high risk of venous thromboembolism.


...The combination of transdermal estradiol+micronized progesterone appears to be effective and relatively safe if elementary precautions are taken, and seems to be presently the best choice for HRT in most postmenopausal women.

Holtorf K. The bioidentical hormone debate: are bioidentical hormones (estradiol, estriol, and progesterone) safer or more efficacious than commonly used synthetic versions in hormone replacement therapy? Postgrad Med. 2009 Jan;121(1):73-85.

...Physiological data and clinical outcomes demonstrate that bioidentical hormones are associated with lower risks, including the risk of breast cancer and cardiovascular disease, and are more efficacious than their synthetic and animal-derived counterparts.


...Unlike oral estrogens, transdermal estradiol has been shown not to increase the risk of VTE, or stroke (doses ≤ 50 μg), and to confer a significantly lower risk for gallbladder disease. Unlike some progestogens, progesterone is also not associated with an increased risk of VTE, or with an increased risk of breast cancer.

Ribot C, Tremollieres F. [Hormone replacement therapy in postmenopausal women: all the treatments are not the same.] Gynecol Obstet Fertil. 2007 May;35(5):388-397.

...the bio-identicals hormones, estradiol 17beta and progesterone, have intrinsic properties which can lead to tangible differences in therapeutic results...cardiovascular and breast cancer risks might be lower with bio-identical hormones than with other therapeutic schemes.


...unlike oral estrogens, transdermal estradiol does not increase the risk of venous thromboembolism...and does not increase the risk of stroke. It is cardioprotective, significantly reducing the risk of myocardial infarction...Micronized progesterone has also been shown not to increase the risk of venous thromboembolism.
Studies: Transdermal estradiol and progesterone do not increase thrombotic risk (DVT’s, heart attacks or strokes)


...odds ratios (ORs) for VTE in current users of oral and transdermal estrogen compared with nonusers were 4.2 and 0.9, respectively. There was no significant association of VTE with micronized progesterone (OR: 0.7).


...Oral but not transdermal estrogen is associated with an increased VTE risk...micronized progesterone and pregnane derivatives appear safe with respect to thrombotic risk.


...participants receiving an estradiol transdermal system have a significantly lower incidence of venous thromboembolism than do participants receiving oral estrogen-only hormone therapy.


...Significantly lower risk (of MI) was found with dermal route (transdermal estradiol - RR 0.6) compared to no HRT (RR 1.0) or oral unopposed oestrogen therapy (RR 1.0)... (Transdermal estradiol reduced MI risk by 40%.)


...oral estrogen/progesterone replacement therapy may result in coagulation activation...whereas opposed transdermal estrogen appears without any substantial effects on hemostasis.


...oral estradiol was associated with lower hazard ratios (HRs) for stroke than oral conjugated equine estrogens (HR, 0.64)... transdermal estradiol was associated with a lower risk of CHD compared with oral CEE (HR, 0.63)


...risk was significantly greater for oral estrogen-progestin than oral estrogen-only therapy (RR=2.07 versus 1.42), with no increased risk with transdermal estrogen-only therapy (RR=0.82).


...Oral HRT use was associated with increased plasma levels of Factor IX, activated protein C (APC) resistance, and CRP...The foregoing associations were not observed in users of transdermal HRT;...
Studies and Reviews: Estradiol-progesterone restoration does not increase proliferation in the breast or breast cancer incidence.


...progesterone does not have a detrimental effect on breast tissue...medroxyprogesterone acetate and 19-Nortestosterone-derivatives are endowed with some non-progesterone-like effects, which can potentiate the proliferative action of estrogens.


...Among users of EP therapy containing a synthetic progestin, the odds ratio for breast cancer was 1.57 for progesterone-derived and 3.35 (1.07-10.4) for testosterone-derived progestagens. No increased risk was apparent among EP therapy users treated with natural micronized progesterone.


...Breast cancer incidence in the exposed group...estradiol alone 0.28%; estradiol + progesterone 0.40%; estradiol + synthetic progestin 0.94%.


...the relative risk was 1.00 for estrogen-progesterone,...and 1.69 for estrogen with other progestagens.


...However, all progestogens are not equivalent in their effects on the breast and breast cancer risk. Micronized progesterone does not increase cell proliferation in breast tissue in postmenopausal women compared with synthetic medroxyprogesterone acetate (MPA).


...estradiol (E2) gel 1.5 mg and oral micronized progesterone (P) 200 mg/day...did not significantly increase breast epithelial proliferation...oral conjugated equine estrogens (CEE) 0.625 mg and oral medroxyprogesterone acetate (MPA)...significantly increased proliferation at both the cell level and at the mRNA level, and significantly enhanced mammographic breast density,...CEE/MPA affected around 2,500 genes compared with just 600 affected by E2/P.


...The hypothesis of progesterone and some progesterone-like progestins decreasing the proliferative effect of estradiol in the postmenopausal breast remains highly plausible...
Studies and Reviews: Testosterone restoration in women does not increase cardiovascular or breast cancer risks.


...Except for hirsutism and acne, the therapeutic administration of T in physiologic doses is safe for up to several years.


...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.


... the addition of testosterone to conventional hormone therapy for postmenopausal women does not increase and may indeed reduce the hormone therapy-associated breast cancer risk...


...Results showed safety of the extended androgen therapy regarding cardio-vascular system, carbohydrate metabolism and impact on hepatic function.


...Based on such simulations, inclusion of testosterone in postmenopausal estrogen-progesterin regimens has the potential to ameliorate the stimulating effects of combined estrogen-progesterin on the breast.


...Available data indicate the inclusion of testosterone in estrogen-progesterin regimens has the potential to ameliorate the stimulating effects of hormones on the breast.


...No significant serious adverse effects were reported in FMTs treated with pharmacological doses of T...


...Short-term testosterone administration over a wide range of doses for 24 weeks in women with low T levels was not associated with worsening of cardiovascular risk markers.


...Thus, the preponderance of data suggests that testosterone use in females is not associated with an increased risk of breast carcinoma.