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BODY-IDENTICAL HORMONE THERAPY - THE WAY FORWARD

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The adverse outcomes seen in WHI were mainly to an over-dosage of hormones in a relatively elderly population. However, differences exist between conjugated equine estrogens and 17 beta estradiol and between medroxyprogesterone acetate and natural progesterone. It is likely that these differences also contributed to the adverse outcomes in WHI, which were contrary to the cardiovascular benefits seen in previous observational trials. Recent studies of cardiovascular risk markers in younger women have been designed using predominantly estradiol and natural progesterone as the primary interventions.

Synthetic progestogens bind to the glucocorticoid, mineralocorticoid and androgen receptors. This can lead to unwanted side effects such as unfavourable glucose metabolism, fluid retention, acne, weight gain. Natural progesterone binds weakly to the mineralocorticoid receptor, but here there is an antagonistic effect which gives it mild diuretic properties. Menopause societies are now advising that natural progesterone may have more favourable metabolic and breast effects effects compared to synthetic progestogens. Natural progesterone appears to have a beneficial cardiovascular effect; it does not attenuate the beneficial effects of estradiol in reducing insulin resistance and may have additional benefits on blood pressure.

There appear to be differential effects of progesterone and progestogens on the the breast. Natural progesterone has a pro apoptotic effect on breast epithelial cells whereas androgenic progestogens such as medroxyprogesterone acetate appear to have a proliferative effect, possibly through non specific effects on the glucocorticoid receptors and gene expression. This might explain the small increase risk in breast cancer promotion when synthetic progestogens are combined with estrogen. Observational data such as the E3N cohort from the EPIC cohort suggest that women using natural progesterone are not at increased risk of breast cancer within the first 5 years of use; ideally these data would be confirmed by long term randomised prospective studies.

Thus, replication of the physiological hormonal environment with transdermal estradiol and natural progesterone can maximise the benefits and minimise the side effects and risks of hormone therapy. It is time we moved away from the notion, often propagated by epidemiologists and the media, that HT

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products have a single class effect.