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HRT optimization, using transdermal estradiol plus micronized progesterone, a safer HRT.

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Abstract

Hormone replacement therapy (HRT) remains the gold standard for treatment of climacteric symptoms in menopausal women; it is relatively safe in healthy subjects for at least 5 years, provided it had been initiated before the age of 60 years and/or within 10 years from menopause. **Estrogen probably adds some cardioprotection, that can, however, be obscured by progestogens, especially medroxyprogesterone acetate (MPA)**. Oral HRT is associated with an increased risk of venous thromboembolism (VTE), gallbladder disease and possibly stroke. The increased occurrence of all these events can be prevented by the use of the transdermal route of estradiol administration; this route seems also advantageous for women with diabetes, hypertension and other cardiovascular risk factors, and also especially with advancing age. **Endometrial protection by any progestogen is insufficient in the mid to long term when cyclical, sequential regimens are used; full protection can be secured only by continuous combined estrogen + progestogen**. Natural, 'body-identical' progesterone, devoid of any androgenic as well as glucocorticoid activities but being slightly hypotensive due to its antimineralocorticoid activity, appears to be the optimal progestogen in terms of cardiovascular effects, blood pressure, VTE, probably stroke and even breast cancer (contrary to synthetic progestogens and particularly MPA, which appear to be mitogenic on breast cells, in synergism with estrogen). **HRT optimization can thus be achieved by combining low doses of estrogen given transdermally with micronized oral progesterone; such optimized HRT will allow us to treat symptomatic women for as long as required. Asymptomatic women at risk of (osteoporotic) fractures can also be treated with this optimized HRT as long as their individual risk/benefit ratio remains favorable (thanks to the absence of increased risks of VTE, stroke and breast cancer).**