Urinary androgens and breast cancer risk: results from a long-term prospective study based in Guernsey

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Between 1961 and 1967 a cohort of over 5000 women volunteered for a prospective study to determine the relationship between the urinary androgen metabolites, androsterone (A) and aetiocholanolone (E), and risk of breast cancer. During the first 10 years of the study the concentration of urinary A and E was determined in 1887 of the urine specimens. In 1971 we reported that subnormal amounts of urinary A and E were associated with a significantly increased risk of breast cancer. The cohort has been followed regularly during the 37 years since inception of the study and, by May 1998, 248 women had been diagnosed with breast cancer. Urinary androgen metabolites had been measured in 116 of these cases. Analysis of these data confirmed that women diagnosed in the first decade of the study were more likely to have low levels of urinary androgen metabolites. In the following decades, however, those who developed breast cancer were more likely to have manifested an increased A and E excretion. The reversal in the relationship between androgen metabolite excretion and risk suggests that age, or probably more importantly, menopausal status at diagnosis is an important modifying factor. Dichotomizing at age 50 it was found that in the younger age group (predominantly premenopausal) the rate ratios in the lowest tertile of A or E excretion were two- to threefold greater than for those in the highest tertile \( \chi^2(1) = 3.57; p = 0.06; \chi^2(1) = 4.70; p = 0.03 \) for A and E respectively. In contrast, in the older age group comprising predominantly post-menopausal women, the rate ratios associated with the lowest tertile of A or E were half that of those in the highest tertile \( \chi^2(1) = 4.10; p = 0.04; \chi^2(1) = 8.72; p = 0.003 \) for A and E respectively. This suggests that there may be different endocrine promotional factors for pre- and post-menopausal breast cancer. Hormonal risk factors may vary during the lifetime of an individual woman and this may have profound consequences for prevention strategies.

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Postmenopausal hormone therapy increases risk for venous thromboembolic disease. The Heart and Estrogen/progestin Replacement Study

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Background Oral contraceptive use increases risk for venous thromboembolism, but data on the effect of postmenopausal hormone therapy are limited. Objective To determine the effect of therapy with estrogen plus progestin on risk for venous thromboembolic events in postmenopausal women. Design Randomized, double-blind, placebo-controlled trial. Setting 20 clinical centers in the United States. Participants 2763 postmenopausal women younger than 80 years of age (mean age, 67 years) who had coronary heart disease but no previous venous thromboembolism and had not had a hysterectomy. Intervention Conjugated equine estrogens, 0.625 mg, plus medroxyprogesterone acetate, 2.5 mg, in one tablet \( n = 1380 \) or placebo that was identical in appearance \( n = 1383 \). Measurements Documented deep venous thrombosis or pulmonary embolism. Results During an average of 4.1 years of follow-up, 34 women in the hormone therapy group and 13 in the placebo group experienced venous thromboembolic events (relative hazard, 2.7 [95% CI, 1.4 to 5.0]; \( p = 0.003 \); excess risk, 3.9 per 1000 woman-years [CI, 1.4 to 6.4 per 1000 woman-years]; number needed to treat for harm, 256 [CI, 157 to 692]). In multivariate analysis, the risk for venous thromboembolism was increased among women who had lower-extremity fractures (relative hazard, 18.1 [CI, 5.4 to 60.4]) or cancer (relative hazard, 3.9 [CI, 1.6 to 9.4]) and for 90 days after inpatient surgery.