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Endogenous sex hormones and subsequent breast cancer in premenopausal women.
Micheli A1, Muti P, Secreto G, Krogh V, Meneghini E, Venturelli E, Sieri S, Pala V, Berrino F.
Abstract
Because of large intra-individual variation in hormone levels, few studies have investigated the relation of serum sex hormones to breast cancer (BC) in premenopausal women. We prospectively studied this relation, adjusting for timing of blood sampling within menstrual cycle. Premenopausal women (5,963), recruited to the Hormones and Diet in the Etiology of Breast Tumors (ORDET) cohort study, provided a blood sample in the 20-24th day of their menstrual cycle. After 5.2 years of follow-up, 65 histologically confirmed BC cases were identified and matched individually to 4 randomly selected controls. Sera, stored at -80 degrees C, were assayed blindly for dehydroepiandrosterone sulfate, total and free testosterone (FT), androstenedione, androstanediol-glucoronide, progesterone, 17-OH-progesterone, sex hormone-binding globulin, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Fifty-five cases had information for multivariate analyses. Compared to controls, BC cases had shorter cycles and intervals between blood sampling and bleeding, and lower LH and FSH. FT was significantly associated with BC risk: relative risk (RR; adjusted for age, body mass index and ovarian cycle variables) of highest vs. lowest tertile was 2.85 [95% confidence interval (CI) = 1.11-7.33, p for trend = 0.030]. Progesterone was inversely associated with adjusted RR for highest vs. lowest tertile of 0.40 (95% CI = 0.15-1.08, p for trend = 0.077), significantly so in women with regular menses, where adjusted RR was 0.12 (95% CI = 0.03-0.52, p for trend = 0.005). These findings support the hypothesis that ovarian hyperandrogenism associated with luteal insufficiency increases the risk of BC in premenopausal women.