Increased breast cancer mortality in women who survived the siege of Leningrad (1941–1944)

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Aims: It has been hypothesized that caloric restriction may reduce the risk of breast cancer. Surprisingly, the risk of breast cancer was, in a dose response manner, increased in women who were exposed to a short but severe caloric restriction as children during the 1944–1945 Dutch famine. The population of Leningrad suffered from severe starvation, cold and psychological stress during the siege in 1941–1944. We investigated long-term effects of the siege on cancer mortality in surviving men and women.

Study design: Participants in the US–USSR Lipid Research Clinics program who were examined in 1975–1982, were followed till end 2005.

Subjects: 3905 men and 1015 women born 1916–1935, resident in St Petersburg (formerly Leningrad) between 1975 and 1982, of whom a third experienced the siege as children, adolescents or young adults.

Outcome measures: Effects of siege exposure on risk of death from cancer was studied in multivariate Cox-regression stratified by gender and period of birth, adjusted for age, smoking, alcohol and social characteristics.

Results: Women who were 10–18 years-old at the peak of starvation were taller as adults (age adjusted difference 1.8 cm, 95% CI 0.5–3.0) and had substantially higher risk of dying from breast cancer compared to unexposed women born during the same period (age-adjusted HR 9.9, 95% CI 1.1–86.5). Mortality from prostate cancer was non-significantly higher in exposed men.

Conclusions: The experience of severe stress and starvation during childhood and adolescence may have long-term effects on cancer in surviving men and women.

Cord estrogens, androgens, IGF-I and IGFBP-3 in Chinese and U.S. Caucasian neonates

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Aims: Markedly lower breast cancer rates in Asians than Caucasians are not explained by established adult risk factors. The involvement of in utero hormonal exposure is hypothesized.

Study design: Concentrations of steroid hormones and IGFs were measured in umbilical cord sera. Pregnancy characteristics were ascertained by interview and medical records.

Subjects: Subjects were 121 neonates born in Shanghai, China and 111 neonates born in Boston, MA, USA.

Outcomes measures: Means and percent differences in hormone concentrations by race/ethnicity (Chinese vs. U.S.) and 95% CI were estimated from linear regression models.

Results: Percent differences in cord concentrations of androstenedione (91.9%), testosterone (257%), estradiol (48.6%) and IGFBP-3 (21.1%) were significantly higher in the Chinese than U.S. samples, and cord prolactin was lower (–14.9%). Cord estradiol and IGF-I concentrations did not differ by race/ethnicity. With adjustment for gestational length, maternal age, pre-pregnancy weight and pregnancy weight gain, androstenedione (60.5%), testosterone (185%) and IGFBP-3 (40.4%) remained significantly higher in the Chinese, whereas the higher estriol and lower prolactin concentrations were attenuated. In addition, estradiol levels became lower in the Chinese (–29.8%) but did not reach statistical significance. Results were generally similar when restricted to first full-term pregnancies with the adjusted, reduced concentrations in estradiol in the Chinese reaching statistical significance.

Conclusions: These data are consistent with the hypothesis that elevated prenatal androgen exposure could mediate reductions in breast cancer risk. The interpretation of the change in findings for estrogens after control for pregnancy factors is unclear with regard to explaining international breast cancer differences.

Growth and white blood cell telomere length at age 50: the Newcastle Thousand Families Study

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Aims: Telomere length is emerging as a potential factor in the pathogenesis of cardiovascular disease. We investigated whether birth weight, infant growth and adult height were associated with white blood cell telomere length at age 50.

Study design: Prospective cohort study.

Subjects: 318 members of the Newcastle Thousand Families Study, which includes all individuals born in Newcastle, England in May and June 1947, who attended for clinical examination at age 50 and had telomere length successfully measured.

Outcome measures: Telomere length in peripheral blood mononucleocytes, measured using real-time PCR analyses of DNA extracted from blood donated at age 50. This was related to birth weight, childhood measures of height and adult height measured at age 50.

Results: There was a highly significant positive association between adult height and telomere length at age 50 (r = 24.9 base pairs per cm, 95% CI 0.1 to 39.7, p = 0.001). However, this was not independent of adjusting for sex (p = 0.3) (a previous report of these data noted that telomere length was longer in men than in women in this cohort). The associations for men and women were not significantly different (p = 0.7). Telomere length was not associated with birth weight (p = 0.7), birth weight standardised for gestational age (p = 0.8) or height at 9 (p = 0.3) or 13 years (p = 0.8).

Conclusions: While our unadjusted results suggest that taller individuals have longer telomeres, this is possibly a consequence of men being taller than women. Further research is required to assess this potential association, including studies powered to assess potential growth–sex interactions.

Neonatal Exendin-4 administration normalizes epigenetic modifications of the proximal promoter of Pdx-1

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An abnormal intrauterine environment affects the development of the fetus by permanently modifying gene expression and function of susceptible cells, like the β-cell. Pdx-1, a homeobox