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Dietary Cadmium Exposure and the Risk of Hormone-Related Cancers

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ABSTRACT

The toxic metal cadmium has been widely dispersed into the environment mainly through anthropogenic activities. Even in industrially non-polluted areas, farmland and consequently foods are, to a varying degree, contaminated. Food is the main source of exposure besides tobacco smoking. Cadmium accumulates in the body, particularly in the kidney where it may cause renal tubular damage. Recently, cadmium was discovered to possess endocrine disrupting properties, mainly mimicking the in vivo-effects of estrogen. The metal is classified as a human carcinogen by the International Agency for Research on Cancer based on lung cancer studies of occupational inhalation. It is, however, not clear whether cadmium exposure via the diet may cause cancer. Possible health consequences related to estrogenic effects such as increased risk of hormone-related cancers are virtually unexplored.

The aims of this thesis were to: 1) estimate the dietary exposure to cadmium, 2) estimate cadmium's toxicokinetic variability using a population model and to establish the link between urinary cadmium concentrations (a biomarker of accumulated kidney cadmium) and the corresponding long-term dietary exposure to cadmium in the population, 3) evaluate the comparability between food frequency questionnaire (FFQ)-based estimates of dietary cadmium exposure and urinary cadmium concentrations and 4) prospectively assess the association between dietary cadmium exposure and incidence of hormone-related cancers (endometrial, breast, ovarian and prostate cancers) in two population-based cohorts consisting of around 60 000 Swedish women and 40 000 men.

The main sources of dietary cadmium exposure (~80%) in both women and men were bread and other cereals, potatoes, root vegetables, and other vegetables. A one-compartment toxicokinetic model provided similar predictions of individual urinary cadmium concentrations as a more complex toxicokinetic model. We estimated the cadmium half-life to be about 11.6 years with 25% between-person variability in the population. The Pearson correlation between FFQ-based estimates of dietary cadmium exposure and urinary cadmium concentration was 0.2 and the observed sensitivity and specificity was 58% and 51%, respectively. Estimated dietary cadmium exposure was associated with a statistically significant increased risk of cancer of the endometrium, breast, and prostate (39%, 21% and 13% respectively) – but not with ovarian cancer – comparing the highest tertile of cadmium with the lowest. The risk estimates were higher in lean and normal weight women and men: we observed statistically significant increased risks of 52%, 27% and 49% for endometrial cancer, overall breast cancer and localized prostate cancer, respectively. Never-smoking women with lower endogenous (normal body mass index) and exogenous estrogens (no postmenopausal hormone use) and with a consistently high dietary exposure to cadmium assessed twice, 10 years apart, had a 2.9-fold increased risk of endometrial cancer, which may indicate an estrogenic effect. The highest risk of breast cancer (60% increase) was observed for diets high in cadmium and low in whole grain and vegetables, as compared to diets low in cadmium and high in whole grain and vegetables. Taken together these results indicate that dietary cadmium exposure may play a role in the development of hormone-related cancers.

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