Perinatal exposure to mixtures of anti-androgenic chemicals causes proliferative lesions in rat prostate - DTU Orbit (13/04/2019)

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BACKGROUND:
Elevated levels of endogenous or exogenous estrogens during fetal life can induce permanent disturbances in prostate growth and predispose to precancerous lesions. Recent studies have indicated that also early anti-androgen exposure may affect prostate cancer risk.

METHODS:
We examined the influence of perinatal exposure to mixtures of anti-androgenic and estrogenic chemicals on prostate development. Wistar rats were exposed from gestation day 7 to postnatal day 22 to a mixture of 8 anti-androgenic compounds (AAMix), a mixture of four estrogenic compounds (EMix), or paracetamol or a mixture of all 13 compounds (TotalMix) in mixture ratios reflecting human exposure levels.

RESULTS:
Ventral prostate weights were reduced by the TotalMix and AAMix in pre-pubertal rats. Histological changes in prostate appeared with increasing age and indicated a shift from the normal age-dependent epithelial atrophy towards hyperplasia. These lesions showed similarities to pre-cancerous lesions in humans. Increased proliferation was observed already in pre-puberty and it was hypothesized that this could be associated with reduced ERβ signaling, but no clear conclusions could be made from gene expression studies on ERβ-related pathways. The influences of the estrogenic chemicals and paracetamol on prostate morphology were minor, but in young adulthood the estrogen mixture reduced ventral prostate mRNA levels of Igf1 and paracetamol reduced the mRNA level of Pbps3.

CONCLUSIONS:
Mixtures of endocrine disrupters relevant for human exposure was found to elicit persistent effects on the rat prostate following perinatal exposure, suggesting that human perinatal exposure to environmental chemicals may increase the risk of prostate cancer later in life.

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