

## ***In utero* exposure to Bisphenol A alters mammary gland development in mice**

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**Background:** Developmental exposure to estrogenic chemicals induces morphological, functional and behavioral anomalies associated with reproduction. Humans are exposed to bisphenol-A (BPA), an estrogenic compound that leaches from dental materials and plastic food and beverage containers.

**Objective:** To determine the effects of perinatal exposure to low, environmentally relevant doses of BPA on the peripubertal development of the mammary gland.

**Methods:** Osmotic pumps delivering vehicle (DMSO) or BPA [25 or 250ng /kg body weight (bw)/day] were implanted in CD-1 pregnant mice from day 9 of pregnancy until postnatal day 4. The female offspring were studied.

**Results:** BPA exposure enhanced the mammary glands' sensitivity to estradiol in ovariectomized CD-1 mice. In their intact 30-day-old littermates, the area and number of terminal end buds (TEB) relative to the gland ductal area increased while their apoptotic activity decreased. The slope of the correlation between ductal length and age at first proestrus was reduced as the BPA dose increased, suggesting that BPA slows down ductal invasion of the stroma. There was also a significant increase of progesterone receptor-positive ductal epithelial cells that were localized in clusters, suggesting future branching points. Indeed, lateral branching was significantly enhanced at 4 months of age in mice exposed to 25 ng BPA /kg bw/day.

**Conclusions:** Perinatal exposure to environmentally relevant BPA doses results in persistent alterations in mammary gland morphogenesis. Of special concern is the increased TEB density at puberty as well as the increased number of terminal ends reported previously in adult animals, since these two structures are the sites where cancer arises in humans and rodents.