Prenatal Exposure to the Xenoestrogens Bisphenol A (BPA) and N-Butyl Benzyl Phthalate (BBP) Alter the Pattern of Rat Mammary Gland Development.

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Bisphenol A (BPA) and n-butyl benzyl phthalate (BBP) are environmental estrogens (xenoestrogens) that mimic estrogenic actions by binding to the estrogen receptor, thus affecting both human and wildlife health. BPA is used in food packaging, dental sealants and polycarbonate plastic products, which range from CDs and eyeglass lenses to tableware and food and beverage containers, including baby bottles. BBP is widely used in the production of vinyl tiles and polyvinyl chloride (PVC). In order to determine whether prenatal and prepubertal exposure to BPA and BBP affect the development of the rat mammary gland we designed the following studies: A) prenatal (transplacental) study, in which pregnant Sprague Dawley female rats that were maintained in a phytoestrogen-free diet were administered a low and a high dose of BPA (25 and 250 µg/kg body weight, respectively), or BBP (120 and 500 mg/kg body weight, respectively) during the length of pregnancy, and B) neonatal/prepubertal study, in which after delivery lactating mothers were gavaged with 250 µg BPA/kg body weight, 500 mg BBP/kg body weight, or an equivalent volume of sesame oil (control rats) from day 1 to 21. Mammary glands of 10 female offspring from each group were collected at 21, 35, 50 and 100 days of age for whole mount analysis. The mammary gland architecture was evaluated by quantitation of epithelial terminal ductal structures, i.e., terminal end buds (TEBs), alveolar buds (ABs), terminal ducts (TDs), and lobules type 1 (Lob 1).

The mammary glands of rats prenatally exposed to high dose of BPA had a significantly higher ($p<0.05$) number of TEBs at 21 days; TDs at 21 and 100 days of age, and Lob 1 at 35 days of age, whereas low dose of BPA did not produce significant morphological changes. Prenatal exposure of rats to high dose of BBP increased significantly ($p<0.05$) the number of TDs at 21 days of age and the number of ABs at 35 days of age. The low dose of BBP significantly increased ($p<0.05$) the number of ABs at 100 days of age only. Neonatal and prepubertal exposure to BPA and BBP, on the other hand, did not induce any statistically significant alterations in the number of epithelial terminal ductal structures. Our data support the concept that prenatal exposure to both BPA and BBP induce alterations in the pattern of mammary gland development. The effect of neonatal/prepubertal exposure is less evident. The relevance of these data on cancer susceptibility is under investigation.

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