

Alterations in mammary gland function and reproductive capacity in CD-1 mice exposed perinatally to bisphenol-A

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Bisphenol A (BPA) is used in the manufacture of polycarbonate plastics and epoxy resins; thus, exposure to BPA occurs through the use of many consumer products, dental and medical materials. Pups born to mothers exposed to BPA during gestation present a plethora of health effects that appear long after exposure has ended. Our studies showed that female mice perinatally exposed to low doses of BPA have altered mammary gland (MG) development at all ages. We also observed alterations in reproductive tract, hypothalamus, gonadotropin levels and estrous cyclicity in the exposed offspring. We hypothesize that the first generation (F1) of female mice perinatally exposed to BPA (*BPA daughters*) will develop abnormal MGs during pregnancy and lactation, and their reproductive success will be compromised.

Pregnant CD-1 mice were exposed to 50% DMSO (vehicle-control), 25ng, 250ng or 25 $\mu$ g BPA/kg body weight/day via an osmotic pump. The *BPA daughters* were exposed from the end of embryonic day 8 until postnatal day (PND) 16. At two months of age all F1 mice were mated. MGs were collected 1) on the day of delivery, or 2) on lactation day 15. In a cross-fostering experiment, pups born to unexposed dams and nursed by *BPA daughters* gained more weight than pups of *BPA daughters* nursed by unexposed dams. Similar results were observed when the *BPA daughters* were mated at 6 months of age and allowed to nurse their own pups. The MGs of all *BPA daughters* were studied and subtle changes in their development were observed which suggests the *BPA daughters'* MG development and function is altered during pregnancy and lactation.

Additionally, *BPA daughters* were housed with fertile males for a period of 8 months. *BPA daughters* exposed perinatally to 25ng or 25 $\mu$ g BPA, and DES (positive controls), had significantly lower cumulative number of pups compared to unexposed control. *BPA daughters* exposed to 25ug BPA also had significantly fewer pregnancies compared to controls. Furthermore, 40% of *BPA daughters* exposed to 25 $\mu$ g BPA delivered less than 4 times, and 65% had less than 6 deliveries. These preliminary results indicate that the reproductive outcome may be altered in mice exposed perinatally to BPA.