BPA exposure in pregnant mice changes gene expression of female offspring

June 26 2012

Prenatal exposure to bisphenol A, or BPA, a chemical found in many common plastic household items, can cause numerous genes in the uterus to respond differently to estrogen in adulthood, according to a study using a mouse model. The results will be presented Tuesday at The Endocrine Society's 94th Annual Meeting in Houston.

The study, led by Hugh Taylor, MD, professor and chief of the reproductive endocrinology section at Yale University School of Medicine, observed "major and permanent changes in gene expression" in female mice exposed to BPA as a fetus. Taylor said these differences were apparent only after estrogen exposure, either naturally at puberty or with estrogen treatment.

"Hyperresponsiveness to estrogens is a potential mechanism to explain the increased incidence of estrogen-related disorders seen after exposure to endocrine disrupters like BPA," Taylor said.

BPA has estrogen-like properties and has been linked to breast cancer and many female reproductive disorders that are sensitive to estrogen. These problems include uterine fibroids (benign tumors), endometriosis and endometrial hyperplasia, an abnormal thickening of the lining of the uterus that can lead to uterine cancer.

Taylor and his co-workers gave pregnant mice either BPA or an inactive substance for about two weeks beginning on the ninth day of pregnancy. After the mice gave birth, the scientists removed and tested the uterus of

half of the female offspring before sexual maturation, looking for changes in gene expression. The other half of the female offspring had removal of their ovaries at 6 weeks of age, followed by treatment with estradiol, an estrogen. They then underwent uterine removal and testing after puberty at 8 weeks of age.

Before sexual maturation, gene expression was "remarkably similar" among control mice—those that were not exposed to BPA in the womb—and the mice that were prenatally exposed to BPA, Taylor said. Of 45,000 genes screened, only 18 showed twofold or greater changes in expression, the authors reported.

After estrogen exposure at puberty, the gene expression profile had changed greatly in BPA-exposed offspring, with 365 genes showing altered expression, according to the study abstract. Of these genes, 208 also showed aberrations in the usual pattern of DNA methylation, a biochemical process that regulates gene expression. At least 14 of the 208 genes have known estrogen response elements, areas that indicate that they are directly regulated by estrogen through its receptor.

Among the BPA-exposed mice, another 316 genes showed altered response to estradiol at puberty. This included several genes that have not previously demonstrated an exaggerated response to estradiol treatment or genes that have not been known to be regulated by estrogen, Taylor said.

"BPA exposure in utero appears to program uterine estrogen responsiveness in adulthood," he said. "Pregnant women should minimize BPA exposure."

Provided by The Endocrine Society