



MEDPAGE TODAY®

Pediatrics > General Pediatrics **CME/CE**

Exposure to Endocrine-Disrupting Chemicals Associated with Early Puberty in Girls

— Relationship with the ubiquitous parabens, phthalates, and phenols and early puberty not seen among boys

CME DISCLOSURE

Vicki Brower, CME Writer, MedPage Today; Henry A Solomon, MD, FACP, FACC, Clinical Associate Professor, Weill Cornell Medical College, Reviewer; and Dorothy Caputo, MA, BSN, RN, Nurse Planner have disclosed that they have no relevant financial relationships or conflicts of interest with commercial interests related directly or indirectly to this educational activity. The staff of Projects In Knowledge®, Inc. and the staff of MedPage Today have no relevant financial relationships or conflicts of interest with commercial interests related directly or indirectly to this educational activity.

by Vicki Brower, CME Writer, MedPage Today

December 05, 2018

CME Author: Vicki Brower

Study Authors: Kim G. Harley, Brenda Eskenazi, et al.

Target Audience and Goal Statement:

Endocrinologists, internists, obstetricians, and environmental health experts.

The goal is to determine whether there are any associations between prenatal and peripubertal exposure to phthalates, parabens, and phenols, and early pubertal development in boys and girls.

Questions Addressed by this Study:

Is exposure in utero and peripubertally to phthalates, parabens, and other phenols, which are considered to be endocrine disruptors and are found in personal care and household

cleaning products, associated with early timing of puberty in girls and boys?

Study Synopsis and Perspective:

While there are animal studies with the three classes of endocrine disruptors, human studies that have examined associations between these chemicals and onset of puberty are scarce. Researchers note that the prenatal and prepubertal time periods are "critical windows" in reproductive development that may be particularly sensitive to endocrine disruption. Importantly, these chemicals or their metabolites are ubiquitous, found in the urine of 75% to more than 90% of individuals in studies conducted over the past decade. However, associations between these chemicals and early onset of puberty have been inconsistent.

During 1999 and 2000, in a longitudinal study of 338 pregnant Hispanic mothers from the Salinas Valley in California, researchers took urine samples and analyzed them for three phthalate metabolites, methyl paraben, and propyl paraben, as well as four phenols, to determine whether the endocrine disruptors might be associated with premature puberty in the children. At age 9, peripubertal urine samples were collected from the children to assess phenol and paraben levels; phthalate levels were not assessed due to budget constraints and a limitation of the findings.

The children were followed up every 9 months between the ages of 9 and 13 using clinical Tanner staging.

After examining urinary biomarker concentrations of several phthalates, parabens, and other chemicals used in consumer personal care products, Kim Harley, PhD, of the University of California, Berkeley, and colleagues found an association between the chemicals biomarkers in prenatal urine and early puberty in girls, but not in boys.

As reported in the study online in [Human Reproduction](#), the researchers found a statistically significant twofold increase in mothers' urine biomarker concentrations for certain chemicals during pregnancy, which was associated with a significantly earlier average onset of pubarche (first appearance of pubic hair) and menarche (first menstruation) in girls, although not with thelarche (first onset of breast development).

Elevated exposure to propyl paraben at age 9 was the only biomarker tied with a significantly early onset of gonadarche in boys (average 1.0 month earlier, 95% CI -1.8 to -0.1 months). None of the other environmental chemicals showed an association with earlier gonadarche or pubarche in boys.

Harley noted that these chemicals are widely used in everyday products, with phthalates commonly used in fragrances, and triclosan frequently found in soaps and toothpaste due

to the antibacterial properties.

The researchers also found that exposure to these chemicals outside the womb was associated with early puberty in girls -- specifically, a twofold increase in urine concentrations for propyl paraben and 2,5-dichlorophenol at age nine was associated with an 0.8-month (95% CI -1.6 to -0.1) and 1-month (95% CI 0.1-1.9) earlier onset of pubarche.

Source Reference:

Human Reproduction, December 4, 2018. doi: 10.1093/humanrep/dey337

Study Highlights: Explanation of Findings

The investigators observed an association between prenatal urinary biomarkers and "earlier pubertal milestones," with higher concentrations of monoethyl phthalate (MEP), triclosan, and 2,4-dichlorophenol (2,4-di). Each doubling of prenatal MEP concentration was associated with a shift in timing of pubarche by -1.3 months (95% CI -2.5 to -0.1), and each doubling of concentrations of prenatal triclosan and 2,-4 di (a degradation product of triclosan) was associated with a shift in menarche of -0.7 months (95% CI -1.2 to -0.2) and -0.8 months (95% CI -1.6 to 0.0), respectively.

"We already suspect that certain chemicals that are widely used in personal care products -- like phthalates, parabens, and triclosan -- are endocrine disruptors," said Harley in a statement, explaining that these chemicals "mimic, block, or otherwise interfere with natural hormones in our bodies, such as estrogen."

"In laboratory studies, these chemicals have been shown to cause earlier puberty in rats, but there are very few studies in humans," she continued. "Additionally, we know that endocrine disrupting effects are particularly important during specific critical windows of development, such as in the womb or during puberty. This study is important because it is one of the first studies to look at human exposure in the womb and because it gives us a chance to examine exposures both in the womb and at puberty."

As for methyl paraben exposure in childhood, this was linked to a significantly earlier onset of thelarche, pubarche, and menarche in girls:

- 1.1 month earlier thelarche (95% CI -2.1 to 0.0)
- 1.5 month earlier pubarche (95% CI -2.5 to -0.4)
- 0.9 month earlier menarche (95% CI -1.6 to -0.1)

"This is important because we know that the age at which puberty starts in girls has been getting earlier in the last few decades," Harley said. "One hypothesis is that chemicals in the environment might be playing a role, and our findings support this idea. Earlier puberty in girls increases their risk of mental health problems and risk-taking behavior as teenagers and increases their risk of breast and ovarian cancer over the long-term, so this is an important issue to address."

No association between prenatal biomarkers and prepubertal timing in boys was seen. With peripubertal concentrations, the researchers saw an association of earlier gonadarche with each doubling of propyl paraben (mean shift of -1.0 months, 95% CI: -1.8, -0.1).

"This is still an active area of research and more studies are needed," Harley noted. "However, we are concerned about evidence that some widely used chemical in the products that we put on our bodies every day may be having an impact on hormonal and reproductive development. Future studies should examine multiple concurrent exposures of these chemicals."

The research team noted the following limitations for the analysis: The women in the study were almost all Latino, with 73% of mothers having lived in the U.S. for less than 11 years at the time of pregnancy. Participants lived in agricultural settings; most of the mothers had not completed high school; 69% of the children at age 9 were living below the federal poverty threshold; and 55% were overweight or obese, as were 65% of the mothers before pregnancy. In addition, reverse causality was a possibility, since children who experience early puberty may be more likely to use personal care products.

Harley and co-authors noted that in a previous study, called [ELEMENT](#), which was conducted by another group, a longitudinal birth cohort from Mexico City was observed to look for possible associations of prenatal exposure to low molecular weight phthalates with puberty timing. ELEMENT found that prenatal concentrations of MEP were associated with earlier menarche in girls. "While we found prenatal MEP concentrations to be associated with earlier pubarche, these findings are not necessarily consistent, since menarche is regularly governed by the hypothalamic-pituitary-gonadal axis while pubarche is governed by adrenal mechanisms," wrote those researchers, led by Deborah Watkins, PhD, of the University of Michigan.

But like Harley's group, the ELEMENT team found no associations of any of the low molecular weight phthalates with pubertal timing in boys. There may be no other research to date that examined prenatal exposure to parabens and phenols in relation to pubertal time, Harley and co-authors wrote.

Harley noted that additional studies have examined peripubertal exposure in girls, with one finding peripubertal MEP concentrations associated with earlier menarche in overweight/obese girls in Peru, and a U.S. study reporting peripubertal concentrations of triclosan associated with earlier breast development. Only one other study looked at prenatal and peripubertal exposure to these chemicals, she added.

Original story on MedPage Today by Kristen Monaco

Reviewed by [Henry A. Solomon, MD, FACP, FACC](#)
*Clinical Associate Professor, Weill Cornell Medical
College and Dorothy Caputo, MA, BSN, RN, Nurse
Planner*

Primary Source

Human Reproduction

Source Reference: [Harley K, et al "Association of phthalates, parabens and phenols found in personal care products with pubertal timing in girls and boys" Human Reproduction 2018; DOI:10.1093/humrep/dey337.](#)