# Girls may start puberty early due to chemical exposure, research suggests

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Girls exposed to certain endocrine-disrupting chemicals (EDCs) may be more likely to start puberty early, according to a paper titled "Identification of Environmental Compounds that May Trigger Early

Female Puberty by Activating the Human GnRHR and KISS1R," and published in *Endocrinology*. EDCs mimic, block or interfere with hormones in the body's endocrine system.

There has been an alarming trend toward early puberty in girls, suggesting the influence of chemicals in our environment. Early puberty is associated with an increased risk of psychosocial problems, obesity, diabetes, cardiovascular disease, and breast cancer.

"We conducted a comprehensive screen of 10,000 environmental compounds with extensive follow-up studies using human brain cells that control the reproductive axis, and our team identified several substances that may contribute to early puberty in girls," said study author Natalie Shaw, M.D., M.M.Sc., of the National Institutes of Health's (NIH) National Institute of Environmental Health Sciences (NIEHS) in Durham, N.C.

Those substances include musk ambrette, which is a fragrance used in some detergents, perfumes, and personal care products, and a group of medications called cholinergic agonists.

"More research is needed to confirm our findings," noted Shaw. "But the ability of these compounds to stimulate key receptors in the hypothalamus—the gonadotropin-releasing hormone receptor [GnRHR] and the kisspeptin receptor [KISS1R]—raises the possibility that exposure may prematurely activate the reproductive axis in children."

According to the research team, musk ambrette is potentially concerning because it can be found in personal care products, and some rat studies have suggested it can cross the blood-brain barrier. Children are less likely to encounter cholinergic agonists in their daily lives.

Canadian and European regulations restrict musk ambrette use because

of its potential toxicity, and the U.S. Food and Drug Administration removed the fragrance from its "generally recognized as safe" list. Yet it is still available on the market in some personal care products.

"This study suggests that, out of an abundance of caution, it is important for parents to only use personal care products for their children that are federally regulated," Shaw said.

As part of the study, the research team screened a Tox21 10,000-compound library of licensed pharmaceuticals, environmental chemicals and dietary supplements against a human cell line overexpressing GnRHR or KISS1R. They conducted follow-up analysis using human hypothalamic neurons and zebrafish, finding that musk ambrette increased the number of GnRH neurons and GnRH expression.

"Using human hypothalamic neurons and zebrafish provides an effective model for identifying environmental substances that stimulate the KISS1R and GnRHR," said co-author Menghang Xia, Ph.D., from the National Center for Advancing Translational Sciences (NCATS) in Bethesda, Md., which is part of NIH.

"This study was a multidisciplinary team effort, and it showed that we can efficiently reduce the time and cost of assessing environmental chemicals for their potential effects on human health."

**More information:** Identification of Environmental Compounds that May Trigger Early Female Puberty by Activating the Human GnRHR and KISS1R, *Endocrinology* (2024)

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