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Prenatal Exposure to Certain Phthalates Associated With Slightly Earlier Onset of Puberty

A study published in Environmental Research *provides new evidence on the possible effects of these endocrine-disrupting chemicals on sexual development*

Barcelona, 11 July 2022. A joint study by the Barcelona Institute for Global Health (ISGlobal), a centre supported by the "la Caixa" Foundation, and the Biosanitary Research Institute of Granada (ibs.GRANADA) has provided new evidence on the **ability of phthalates to interfere with sexual development**. The findings of this study, published in *Environmental Research*, show that prenatal exposure to certain phthalates is associated with a slightly elevated risk of children having started puberty between 7 and 10 years of age.

Phthalates are chemical compounds that are used as plasticisers and fragrance retainers in a wide range of consumer products. They are used, for example, in the manufacture of PVC and can be found in building materials, cosmetics, plastic toys and food packaging, among other products. Previous studies have found associations between these **endocrine-disrupting chemicals** and a number of **adverse reproductive health effects** such as urogenital malformations, poorer sperm quality, reduced testosterone levels, placental/umbilical dysfunction, preterm delivery, low birth weight, ovarian insufficiency and endometriosis.

In vitro and animal studies have shown that phthalates exert **anti-androgenic activity**, i.e. the ability to inhibit the effects of male sex hormones. On the basis of this hypothesis, the research team set out to assess the possible influence of these compounds on pubertal development in boys and girls. The researchers chose to study **prenatal** phthalate exposure, as it is during this stage that the adrenal and gonadal axes—which control the onset and progression of puberty—develop.

The study included **788 boys and girls** from **Gipuzkoa, Sabadell and Valencia** who were enrolled in the **INMA Project** cohort study. Prenatal exposure to phthalates was quantified by means of **maternal urine samples collected during pregnancy**. Later, when the children were between 7 and 10 years of age, **pubertal development** was assessed by means of a parental **questionnaire**. On the basis of the responses, children were classified into five developmental stages: 1) pre-puberty, 2) early puberty, 3) mid-puberty, 4) late puberty and 5) post-puberty. The children's body mass index was also taken into account, as obesity plays an important role in pubertal development.

Analyses showed that **phthalates were present in more than 99% of the urine samples** collected during pregnancy. Findings varied by compound tested, as well as by the sex and body mass index of the participants. However, it was observed that **higher prenatal exposure to certain phthalates was associated with a slightly increased risk of puberty onset**. These findings were more evident in boys with normal weight and in girls who were overweight or obese.

Specifically, **prenatal exposure to di-(2-ethylhexyl) phthalate (DEHP)**, a substance used to make plastics more flexible, was associated with **increased risk of puberty onset in both boys and girls**. Prenatal exposure to **DEHP**, di-ethyl phthalate (**DEP**) and di-n-butyl phthalate (**DnBP**) was associated with **earlier onset of puberty in normal-weight boys**. However, prenatal exposure to butyl benzyl phthalate (**BBzP**) and di-iso-nonyl-cyclohexane-1,2-dicarboxylate (**DINCH®**) was associated with **later onset of puberty only in overweight or obese boys**. As for girls, prenatal exposure to di-iso-butyl phthalate (**DiBP**), **DnBP** and **DINCH®** was associated with **slightly earlier onset of puberty in girls who were overweight or obese**.

Associations were observed for some of the phthalates studied individually, but **not for the grouping of all phthalates**.

"**We cannot affirm that phthalates are associated with precocious puberty** as a clinical pathology, as we did not assess when this process started in each participant," commented ibs.GRANADA researcher **Carmen Freire**, first author of the study. "What is clear is that the age at puberty onset has decreased in recent decades and our findings suggest that phthalates could be one of the factors involved."

"Our findings in boys are somewhat surprising," commented ISGlobal researcher **Maribel Casas**, last author of the study. "Due to the anti-androgenic activity of phthalates, we would have expected these compounds to interfere with pubertal development in the opposite direction—that is, by delaying it. However, determining the effects of these compounds is very complex, as they tend to be multifactorial and exposure never occurs in isolation, but rather in conjunction with a whole range of substances and environmental factors."

It is now considered **normal for puberty to start from the age of 8 years in girls and 9 years in boys**. Factors associated with age at puberty onset include obesity, although other factors, such as environmental exposures and stress, also play a role.

Reference

Carmen Freire, Francesca Castiello, Maria-Jose Lopez-Espinosa, Andrea Beneito, Aitana Lertxundi, Alba Jimeno-Romero, Martine Vrijheid, Maribel Casas, Association of prenatal phthalate exposure with pubertal development in Spanish boys and girls, Environmental Research, Volume 213, 2022, 113606, ISSN 0013-9351, https://doi.org/10.1016/j.envres.2022.113606

About ISGlobal

The Barcelona Institute of Global Health (ISGlobal) is the result of an innovative alliance between the "la Caixa" Foundation and academic and government institutions. The Institute was set up to contribute to the work undertaken by the international community to address global health challenges. ISGlobal has consolidated a hub of excellence in research and medical care that has its roots in work first started in the world of health care by the Hospital Clínic and the Mar Health Park and in the academic sphere by the University of Barcelona and Pompeu Fabra University. ISGlobal's work model is based on generating knowledge through its scientific programmes and research groups and translating this knowledge into practice and policy through its Education, Policy and Global Development departments. ISGlobal is accredited as a Severo Ochoa Centre of Excellence and is a member of CERCA, the Catalan Government's network of research centres.

ISGlobal Press Department

Pau Rubio
pau.rubio@isglobal.org
+34 696 91 28 41

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Una iniciativa de:

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