Journal of Experimental and Basic Medical Sciences 2021;2(2):261-266

Review

Early Puberty and Hormone Disruptors

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Adolescence is a complicated biological sexual growth phenomenon that is affected by genetic, nutritional, cultural, and socioeconomic influences. Individuals achieve secondary sexual characteristics (such as voice tone, hip growth, and skin acne) and reproductive ability during this stage of development. While the first emergence of breast buds marks the start of puberty in females, testicular enlargement marks the start of puberty in boys. Pubic hair may occur before, with, or after the clinical onset of puberty in both sexes.[1,2] The development of secondary sexual traits of girls younger than eight and boys younger than nine years of age is used to detect premature puberty. For assessing precocious puberty in girls, eight years may be considered a fair cutoff. Since early puberty is more frequent in boys, all boys under the age of 9 should be thoroughly tested for diagnosis.[3-5] Since the initiation of central precocious puberty can be confused with the onset of alarch or adrenarche, which occurs independently of early puberty, an experienced clinician can affirm the onset of central precocious puberty.[4,6]

ABSTRACT

Adolescence is a dynamic mechanism influenced by a variety of factors like race, gender, and environmental forces as well as physical and psychological processes. The first symptoms of puberty are noticeable changes such as the formation of pubic hair, breast size, and body odor, and since these changes are most readily detected in females, research on early puberty are often done and analyzed on females. While there is no definitive lower age limit, it is eight years for girls and nine years for boys. The observation of transition in children under this age is called early puberty, but as our diet and lifestyle change, this age limit is shrinking, and its prevalence is increasing. While not all causes of early puberty have been identified, the most frequent one is early activation of the hypothalamic-pituitary-gonadal (HPG) axis, which can be caused by a variety of hormone disruptors. The general causes of precocious puberty and the effects of multiple hormone disruptors are discussed in this paper.

Keywords: Dichlorodiphenyltrichloroethane, early puberty, endocrine disrupting chemicals.

GnRH ASSOCIATED EARLY PUBERTY

GnRH (gonadotropin-releasing hormone) was one of the first hypothalamic-releasing hormones to be sequenced and identified in puberty.[7] Gonadotropin-releasing hormone receptors (GnRHR) on pituitary gonadotropes are related to GnRH (8, 9) The physiological model of gonadotropin secretion and the preservation of gonadotropin gene expression are both dependent on GnRH pulsatility. The hypothalamic-pituitary-gonadal (HPG) axis is regulated by a widespread network of hypothalamic neurons that produce pulsatile discharges of the neuropeptide GnRH into the pituitary portal circulation every 60-90 minutes. By controlling the production and secretion of pituitary gonadotropins into the systemic bloodstream, these secretory segments 10 promote ovarian and testicular activity. The "GnRH pulse generator" is the name given to

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Cite this article as: Duman Z, Kanat G, Erbaş O. Early Puberty and Hormone Disruptors. JEB Med Sci 2021;2(2):261-266.

doi: 10.5606/jebms.2021.75665

Received : March 18, 2021
Accepted : June 04, 2021
Published online : September 29, 2021

the main neuronal network.[7] GnRH functions by binding to a particular G-protein-coupled receptor on the surface of pituitary gonadotropin-secreting cells. GnRH is secreted into the pituitary portal circulation, and its activities are mirrored in the intermittent secretion of LH (luteinizing hormone) and FSH (follicle-stimulating hormone) into the systemic circulation.[10] Precocious puberty is most often caused by the early initiation of pulsatile GnRH secretion, also known as gonadotropin-dependent precocious puberty.[1]

In addition, the Kisspeptin, neurokinin B (NKB), and dynorphin neurons (KNDy/kisspeptin-neurokinin-B-dynorphin) network, which is closely linked to GnRH and affects its function, should be mentioned. In humans, GnRH neurons are found in the infundibular nucleus of the hypothalamus, and their axons secrete GnRH into the portal circulation in a pulsatile and synchronized manner. Kisspeptin neurons can also be located in the infundibular nucleus and rostral preoptic lobe.[11,12] Kisspeptin axons develop thick pericapillary plexuses in the infundibular nucleus, the GnRH neurosecretory region, affecting release. Early puberty can also be caused by Kisspeptin mutations.[13] Kisspeptin has both relaxing and inhibiting effects on the HGP axis. Exogenous kisspeptin promotes LH secretion in women with hypothalamic amenorrhoea and increases decreased LH pulsatility in hypogonadal men with diabetes.[14,15] The function of diamorphine antagonists like naloxone in patients who have abnormally low LH development is still unclear.[16] They play a part in GnRH activity regulation. Although the effects of naloxone have been seen to affect LH secretion in subjects, especially those in late adolescence, it remains a mystery that no consistent effect is found in children in early adolescence, regardless of gender.[17,18]

ENDOCRINE-DISRUPTING CHEMICALS (EDCs) ASSOCIATED WITH EARLY PUBERTY

The neuroendocrine hypothalamic-pituitary-adrenal axis (HPA axis), gonads, and secondary target organs such as breast, hair follicles, and reproductive organs may all be inhibited by hormones or hormone-disrupting agents, with varying degrees of impact. Endocrine-disrupting chemicals in the brain begin their function by stimulating estrogen-sensitive nuclei, such as hypothalamic neurons, allowing kisspeptin to be released and the hypothalamus to grow, leading puberty to begin earlier and possibly prematurely.[19] For various causes, it remains impossible to demonstrate the impact of endocrine disruptors on human pubertal timing under normal circumstances, with the exception of cases such as industrial spill events that occur in elevated rates of exposure. Adolescent girls and boys are exposed to hundreds of chemicals in low concentrations, making it impossible to determine which chemical induces which kind of disease in the body one by one. The impact of EDCs varies depending on the species and the extent of exposure.[20] An experiment was performed in which neonatal female rats were exposed to dichlorodiphenyltrichloroethane (DDT) for 6-10 days postnatally to model the impact of early exposure of immigrant children to the pesticide DDT. Such exposure has resulted in an increase in pulsatile GnRH secretion and the initiation of puberty at an earlier age.[21] Other members of the GnRH network may be attacked with EDCs, according to recent research. Kisspeptin neurons' ontogenesis and work showed that they are heavily influenced by gonadal steroids and are susceptible to endocrine disruption.[22]

BISPHENOL A (BPA)

Plastics, polycarbonates, and epoxy resins all contain BPA as a precursor. Many common objects, such as plastic bottles, food storage containers, baby bottles, and CDs (compact discs), are made of BPA-based plastic. Epoxy resins are used to cover water tubing, as well as the interiors of certain food and beverage containers and in the production of thermal paper. Since this chemical is almost universal, humans are clearly at risk of toxicity, and even though estrogen receptor agonist activity is small, its ability should not be overlooked. BPA also acts as an anti-androgen.[23] BPA toxicity can be the cause of early puberty, according to data gathered from animal studies. In comparison to the control community, prenatal rat exposure to BPA concentrations of 2 mg/kg body weight per day increased puberty.[24] The key mechanism of BPA-induced precocious puberty is a positive feedback mechanism that activates the operation of the GnRH pulse generator, resulting in increased pituitary LH and FSH secretion.[25,26] BPA has also been related to early puberty in several other studies.[27,28]

DICHLORODIPHENYLTRICHLOROETHANE AND DICHLORODIPHENYLDICHLOROETHYLENE (DDE)

Dichlorodiphenyltrichloroethane is a form of organochlorine. It is colorless, tasteless, and odorless, and was initially formulated as an insecticide for agricultural use. Exposure to DDT is not evident because of these properties, but it can impair sexual growth in a fetus and during breastfeeding. Dichlorodiphenyltrichloroethane can survive in the atmosphere as a persistent organic pollutant (POP) even though it is removed from the market. Furthermore, in some low-income nations, it is still commonly used. The most studied EDC pesticides are DDT and its metabolite DDE. Both stimulate aromatase and have estrogenic, anti-androgenic, and antiprogestin effects.[23] Early life exposure to endocrine disruptors may play a role in pubertal timing, with children moving to Belgium for foreign adoption having an 80-fold higher risk of sexual early development than Belgian native children. It was implied with the remark that it is very big. In their home world, these children had been exposed to the estrogenic insecticide DDT.[29] Early menarche was also documented by Vasiliu et al.[30] after potential prenatal/early postnatal exposure to dichlorodiphenyldichloroethylene, a DDT metabolite.

POLYBROMINATED DIPHENYL ETHERS (PBDES) AND POLYBROMINATED BIPHENYL (PBB)

Flame retardants are a class of additives that are applied to raw products to prevent them from catching fire (plastics, textiles, surface coatings and coatings). Its aim is to stop or slow down the progression of ignition. Polybrominated diphenyl ethers and PBB are two examples of such chemicals. They have estrogenic and anti-androgenic properties.[23] There is a connection between PBDEs and early pubertal development, including premature thelarche, menarche, and pubertal development.[31,32] Furthermore, prenatal PBDE exposure is delayed in children.[33] Prenatal exposure to flame retardants like PBDEs is linked to a later menarche date.[33] The National Health and Inspection Survey (NHANES) has linked the initiation of breast growth or marginally early menarche to ages 6 to 8[34] or elevated serum PBDE concentrations between 12 and 19[35] years of age, respectively, demonstrating the importance of our body's window of exposure and sensitivity once again. Polybrominated biphenyls function as EEDCs by inhibiting estrogen competitively, causing drastic changes. Pubertal girls exposed to PBB-contaminated milk experienced earlier menarche, thelarche, and pubic hair levels.[32] In pubertal males, no major impact of PBB was observed.[36]

POLYCHLORINATED BIPHENYLS (PCBs)

Polychlorinated biphenyls are a class of synthetic organic chemicals that can have a wide range of negative consequences. PCBs are colorless or bright yellow oily liquids or solids. Some PCBs are flammable and can be contained in the air as vapor. It has no discernible odor or flavor. In the climate, there are no established natural sources of PCBs. PCBs are released into the atmosphere as a combination of different chlorinated biphenyl components and impurities known as congeners. PCBs are a dioxin-like compound formed from biphenyl.[36] This chemical is commonly used in electrical devices, carbonless reproduction sheets, and heat transfer fluids as a dielectric and refrigerant. The mechanism of action is somewhat close to that of dioxins, and prenatal exposure has been shown to delay the initiation of menarche and the progression of puberty.[23,37] In mice, PCBs were shown to have a greater affinity for ER-β (Estrogen receptor beta) than endogenous estrogen.[38] Females have more effects than males, which may be due to the fact that females have higher ER-volumes than males.[36] The impact of PCBs varies depending on body size. In one study, PCB-exposed white American girls were heavier than girls who were not exposed to transplacental PCB; in other words, PCB's results were more common in girls with a higher body weight.[39,40] PCBs were seen in pubertal boys at the pubic hair stage, indicating a substantial delay in puberty, as shown by reduced reproductive organs and testicular volume.[37] However, there was no discernible influence in pubertal females.[30]

PHTHALATES

Phthalates are anhydride esters of phthalic anhydride. They're used in plastics, flooring, personal care materials, medical equipment, and tubing as liquid plasticizers. They improve the materials' stability, clarity, resilience, and sustainability. Softening polyvinyl chloride (PVC) is one of the most popular applications. Their endocrine-disrupting functions are unknown,

but they function as estrogen receptor agonists and antagonists, as well as androgen receptor antagonists. Phthalates damage the endocrine system, according to studies of CHO-K1 (Chinese hamster ovary cells) cells[41] and, phthalates imitate estrogen and bind to ER and ERK (Estrogen receptor alpha and beta).[36] They may also cause androgen synthesis to be disrupted.[23] Some studies have discovered a connection between premature thelarche and early puberty.[42,43] Low molecular weight phthalates and high molecular weight phthalates are the two types of phthalates. Different outcomes were found depending on the exposure class and timing. Low molecular weight phthalate levels are associated with advanced breast or pubic hair growth many years before puberty, whereas high molecular weight phthalate levels are associated with late pubic hair development and early menarche age.[23,44,45]

DISCUSSION AND CONCLUSION

The causes of precocious puberty and their connection to multiple hormone disruptors have not been adequately elucidated in view of all of this information; the frequency and dosage of exposure, environmental consequences, hereditary and pathological disorders that impair puberty preclude a definite observation. While GnRH pathways are the most studied for early adolescence, scientists' fields of research broaden as new developments in the human body are made, and their costs rise. Furthermore, since technology creates new molecules every day, and we don't know how they will affect our bodies, we could be exposed to more hormone disruptors in the future. Of the steps that can be taken personally, avoid using substances that actively or implicitly disrupt our hormone system, and if possible, get them constitutionally banned. Except under these circumstances, though, we cannot exclude EDCs, which we face almost anywhere in our lives. Over all, it is not an option but a responsibility for us to raise societal consciousness and alert children and parents about the dangers of these chemicals.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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