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Endocrine disrupting chemicals and their impact on reproductive functions

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Abstract

Background. Compounds that disrupt the functioning of the endocrine system (*EDC - endocrine disrupting chemicals*) are widespread in the environment. Their ubiquitous presence and increasingly common use in many industries and economies prompt numerous attempts to characterize their biological effects. From the point of view of public health, the impact of EDCs on the functioning of the reproductive system - both in childhood and adulthood - is considered one of the most important.

Purpose of the study. The aim of the study was to collect and analyze publications focusing on the impact of endocrine-disrupting compounds on reproductive functions - with particular emphasis on the process of sexual maturation, fertility and reproduction.

Material and methods. A review of the literature available on PubMed was performed using various combinations of keywords: 'EDC/endocrine disrupting chemicals' + 'puberty', 'EDC/endocrine disrupting chemicals + 'fertilily', 'EDC' + 'pregnancy', 'EDC/endocrine disrupting chemicals' + 'reproduction' and others.

Results. The analysis of the collected publications allows to conclude that EDCs have a multidirectional biological effect on the human body, affecting all stages of hormonal action - synthesis, metabolism, the process of binding to the receptor and many others. The role of EDCs has been confirmed in the pathogenesis of many autoimmune, metabolic and structural disorders.

Conclusions. EDCs, as widely distributed compounds that disrupt the functioning of the endocrine system, are a promising direction for research on processes and disorders important from the point of view of public health, for which reproductive health is one of the most important areas of interest.

Keywords: endocrine-disrupting chemicals (EDCs), bisphenol A (BPA), phthalates, atrazine, reproductive health, puberty, infertility, hypothalamic-pituitary-gonadal axis, epigenetics

1. Introduction

Endocrine-disrupting chemicals are defined as exogenous chemicals or mixtures of chemical substances that have the ability to have a multidirectional effect on the endocrine system [1]. By influencing the synthesis of hormones, the process of connecting them to the receptors and metabolism, they lead to endocrine dysregulation and, as a result, developmental, neurological, sexual and reproductive disorders [2], [3], [4].

Research conducted in recent years has contributed to the characterization of many substances that disrupt the functioning of the endocrine system. These include both natural and synthetic compounds: dioxins, dioxin and dioxin-like compounds, polychlorinated biphenyls, DDT and other pesticides, and components of plastics such as bisphenol A (BPA) and phthalates [5]. Exposure to EDCs occurs mainly through dietary intake and, to some extent, through inhalation or cutaneous routes [1]. EDCs are found in many everyday products-including plastic bottles, metal food cans, detergents, flame retardants, food additives, toys, cosmetics, and pesticides [5]. The above-mentioned substances enter the ecosystem both directly during spraying of gardens and agricultural fields (herbicides, fungicides, pesticides) and indirectly through inappropriate management of production waste [6]. Another example of an important source of compounds that disrupt the functioning of the endocrine system is landfills, where, as a result of degradation processes, numerous substances are released into the soil (e.g. alkylphenols from cleaning products or bisphenols in plastics). One of the important sources of EDC is also industrial sewage, which contains, among others, halogenated aromatic hydrocarbons and household sewage, often contaminated with pharmaceuticals, drugs or hormones [7]. An occupational environment that favors exposure to industrial chemicals (e.g. PFAS) and metals that have properties that disrupt the functioning of the endocrine system (mercury, lead) is also important. In addition to the localized sources mentioned above, runoff from agriculture, roads and roofs should also be mentioned, e.g. steroids administered to farm animals and phthalates in road runoff. They are a more spatially dispersed source, but equally common and important from the point of view of environmental protection and biological effects on the human body [8].

It should be emphasized that once these substances enter the terrestrial or aquatic environment, they may persist for decades. Compounds that disrupt the functioning of the

endocrine system may also be 'pseudo-persistent' in the environment, which means that despite degradation, their continuous release leads to their permanent presence in the environment [8]. It is also worth emphasizing the ability of some EDCs to bioaccumulate (as a result of which the concentration of these compounds in plant and animal tissues is higher than in the surrounding environment) and biomagnification, during which the concentration of a toxic compound gradually increases at subsequent links in the food chain [9].

In 2009, the Endocrine Society published a statement recognizing EDC as a "significant concern for public health" [10]. For this reason, many attempts have been made to characterize the mechanism of action of EDCs and their impact on the pathogenesis of various disorders more precisely - especially those of a civilization-related nature.

2. Mechanisms of action

The mechanism of action of EDCs is based on their structural similarity to endogenous steroid hormones such as androgens and estrogens. This applies especially to naturally occurring EDCs, which, by binding to steroid receptors, influence the action and metabolism of sex hormones [11].

Initial studies suggested that the action of EDCs is mainly related to the above-mentioned action at the receptor level: nuclear hormone receptors - estrogen receptors ER (bisphenol A, dioxins), progesterone receptors PR, thyroid receptors TR (BPA, dioxins, perchlorates, furans) and retinoid receptors (organotins, BPA) [12] . However, the latest reports indicate that the profile of EDCs action is much broader and multidirectional. They also affect non-steroidal receptors, transcription coactivators, enzymatic pathways involved in the synthesis and metabolism of steroids, as well as the signaling pathway related to nitric oxide [2], [13] . Direct effects on DNA are also emphasized - changes in the level of DNA methylation, histone modification and destabilization of the genetic material by affecting the mitotic spindle [14]. Moreover, EDCs act as inducers of endoplasmic reticulum stress, which contributes to their pro-apoptotic effect on certain cell types [15].

The endoplasmic reticulum is a cellular organelle which function is to synthesize membrane proteins and proteins secreted outside the cell. The initially formed proteins are unfolded - their folding process takes place with the participation of chaperones. Only proteins that are correctly folded are capable of performing their function. Proteins that are incorrectly folded are retained within the endoplasmic reticulum and subjected to degradation [16] . Endoplasmic reticulum stress occurs when the protein-folding capacity of the endoplasmic reticulum is saturated and exceeded. Endoplasmic stress disorders may be

caused by a decreased ability of the cell to fold membrane or secretory proteins, a decreased ability to recognize and respond to misfolded proteins, and an increased load of misfolded proteins. Recent scientific reports highlight the important role of endoplasmic stress in the pathogenesis of many endocrine disorders, including diabetes, central diabetes insipidus, Wolfram syndrome and isolated type II growth hormone receptor deficiency [16], [17], [18], [19].

Among the postulated mechanisms of action, the immunomodulatory and immunotoxic potential of EDCs also seems to be important. Their multidirectional influence on the immune system is exerted at the cellular level mainly through the receptors - aryl hydrocarbon receptor (AHR), the estrogen receptor (ER), and the peroxisome proliferator-activated receptor (PPAR). EDCs mainly affect processes involving T lymphocytes (especially Th17 and Treg subpopulations), B lymphocytes and dendritic cells, and thus play an important role, among others, in the pathogenesis of autoimmune diseases [20].

As in the case of classic hormonal effects, EDCs have the potential to act at low doses, which are considered safe from a toxicological point of view. In addition to their tissue-specific effects, they also have the potential to exert a dose-independent effect due to the high dynamics in terms of the number and saturation of receptors. For this reason, small doses may, for example, have a greater effect than large doses, and what is more, the effect may be completely different [21].

Age at the time of exposure is also an important factor influencing the final effect of EDC. Exposure to compounds that disrupt endocrine balance in childhood has a different effect than exposure to that compound in adulthood. Adults require higher concentrations of EDCs to cause toxic effects than an organism in the development stage, and this effect persists only in the presence of a given compound. In the case of the developmental stage, the toxicity of the compound is revealed at lower concentrations, and the effect persists long after the EDC is excreted from the body [22]. The above-mentioned relationship is related to the theory of the fetal basis of adult diseases, which describes the interactions between the developing organism and the environment that influence the probability of developing specific disorders in the future [23].

In recent years, attention has also been drawn to the fact that EDCs may not only affect an individual directly influenced by them, but also subsequent generations. This transmission takes place mainly with the participation of epigenetic mechanisms related to germ cells, which include changes in the level of DNA methylation or histone acetylation [24].

3. Brief characteristics of selected EDCs

3.1 Bisphenol A

Bisphenol A is a well-known synthetic chemical globally used to manufacture epoxy resins, polycarbonates and other polymer materials. The continuous increase in demand for polymers ,which production requires bisphenol A, is primarily related to their increasingly wide use [25]. Since the first synthesis of bisphenol A in 1891, polymers have been used to produce, among others, plastic cups, bottles, food containers, components used in microwave ovens, toys, and in recent years also electronic and optical equipment [26]. BPA derivatives are also used as stabilizers and antioxidants in the printing of tickets and newspapers, in the production of dental sealants, and even in the textile industry in the production of baby socks. Epoxy resins, in turn, are used as lining in metal products (cans), in the paints and inks, compact discs, digital video discs and thermal paper industries. Polycarbonate plastics produced using BPA are characterized by favorable physicochemical properties - including high hardness, strength, thermal stability and resistance to oils and acids [27]. In food-contact materials, BPA may leach into the food or drink when exposed to high temperatures, physical manipulation, or repeated use [28]. The estrogenic properties of BPA have been known since 1936. This fact, combined with numerous subsequent reports on the multidirectional adverse biological effects of BPA, led to numerous attempts to develop methods to limit exposure to BPA. However, its ubiquitous presence in everyday life has made the elimination of contamination difficult, even during carefully controlled quantitative procedures. Measurements of free or bioactive BPA in serum are also controversial. However, it is assumed that according to the US Environmental Protection Agency (EPA) the safety level of BPA is set at 50 μg/kg/d, whereas the European Food Safety Authority's temporary tolerable daily intake was recently lowered to 4 μg/kg/d [29].

3.2 Phthalates

Phthalates and phthalate esters are a large group of compounds used since the 1920s, mainly as liquid plasticizers added to polyvinyl chloride (PVC) plastics to obtain a softening effect [30]. Phthalates with short chains and low molecular weight (e.g. dimethyl phthalate) are used in the production of personal hygiene products (e.g. hair care products), pharmaceuticals and medical devices (e.g. medical tubes) [31]. The use of phthalates in the food industry is highly controversial. One of the most famous examples was the situation in Taiwan. It was found that food companies in Taiwan intentionally used phthalates (mainly

di(2-ethylhexyl) phthalate (DEHP) and diisononyl phthalate (DiNP)) in very high concentrations as food emulsifiers. The detection of irregularities resulted in the issuance of a government warning in 2011 on the contamination of certain types of food products (sports drinks, tea and fruit drinks, jams, jellies, supplements in the form of powders or tablets) [32]. 965 products were found to be contaminated, of which 206 were exported to 22 countries. However, later studies showed that contamination was even more widespread and also included ice cream, frozen foods and ready-made cake mixes. Research conducted by Justin Yang et al. showed that consuming even one serving of contaminated beverages and certain powders would lead to daily DHEP intake significantly exceeding established safety standards [33]. The global plastics industry absorbs over 3 million tons of phthalates annually, which - assuming their versatile use - makes the exposure of the human body to phthalates seem inevitable [30]. This fact, especially considering the negative long-term biological effects of exposure, prompts governments to look for effective ways to manage the plastics industry.

3.3 Atrazine

ATZ (2-chloro-4-ethylamino-6-isopropylamino-s-triazine), since its introduction to the herbicide market in 1958, has become the most frequently used herbicide used in the form of sprays, liquids, concentrates or granules for agricultural crops, especially corn, sorghum, sugar cane, pineapples and, to a lesser extent, landscape plants (golf courses, Christmas tree farms, parks) [34]. Chemically, this compound has a ring structure - it consists of a triazine ring connected to a chlorine atom and five nitrogen atoms. ATZ's long activity, favorable price and broad spectrum of herbicidal activity make ATZ very commonly detected in many places - especially those related to water accumulation (ponds, wells, groundwater) [34], [35]. Atrazine and its metabolites are the most frequently detected pesticides in surface waters in the USA, and therefore also in drinking water. For this reason, the EPA (Enviromental Protection Agency) has recognized ATZ and related chlorothiazines as a significant threat, especially to aquatic organisms - not only due to their potential to disrupt the functioning of the endocrine system, but also due to their possible carcinogenic effects [35], [36], [37].

4. The effect on EDC on puberty

The process of puberty is regulated by a network of neurotransmitters, neuropeptides and genetic and epigenetic factors that allow for its precise coordination. The key moment is the initiation of gonadal-independent pulsatile secretion of gonadotropin-secreting hormone (GnRH) by the hypothalamus [38]. The preparation and organization of this process begins in utero. Therefore, exposure to substances that disrupt the functioning of the endocrine system

during critical periods of development may affect the process of sexual maturation and cause long-term reproductive effects, which will be discussed later in this study. Despite the fact that most studies point to the gonads and peripheral organs as the key target for EDCs, recent animal studies also indicate an effect on the developing brain and hypothalamus, and thus also on hypothalamic control of maturation [39].

Most GnRH-secreting neurons in humans are located in the medial basal hypothalamus, the infundibulum and the periventricular regions. These neurons are initially located on the olfactory placode, from which they migrate during development to the above-mentioned areas [40]. The surrounding glial cells regulate the functioning of GnRH-secreting neurons by acting at the level of cell bodies and nerve endings. By constituting an important component of the blood-brain barrier, they also integrate circulating metabolic signals such as sitrulin, AMPK and others. The GnRH neurosecretory system is regulated directly by kisspeptin neurons. The central inhibition of GnRH secretion that occurs in childhood occurs with the participation of the main inhibitory transmitter - GABA - and macorin 3, which serves as an inhibitory signal for kisspeptin [40], [41].

What is worth emphasizing - GnRH is released not only during actual sexual maturation, but also during the fetal period and in the first months of life during the so-called "mini-puberty" [42] . This phenomenon is described as a transient activation of the hypothalamic-pituitary-gonadal axis in the first six months of life for boys and in the first two years of life for girls. This activation leads to an increase in the concentrations of LH, FSH, estradiol and testosterone. The causes of this phenomenon and its role are still the subject of intensive research. It is suggested that this activation plays an important role in the process of gonad development and has a multidirectional impact on metabolism - affecting body composition, growth speed and BMI. It is also worth emphasizing its participation in the development of cognitive functions - especially language functions. The importance of the pre-puberty period has been demonstrated especially in boys. A particularly important aspect of the process in this context seems to be the influence on the cellular composition of the testes, which manifests itself in the increase in the number of Sertoli cells, whose role is crucial in the subsequent process of spermatogenesis. The importance of the mini-puberty process in girls is less clear. Unlike boys, in girls the oocyte pool is established at birth. However, it cannot be ruled out that gonadotropin stimulation during the mini-puberty period is also important in the process of maturation and atresia of ovarian follicles [41], [42], [43].

The process of proper maturation begins between the ages of 8 and 13 for girls and between 9 and 14 for boys [44] . Pulsatile GnRH secretion leads to a number of systemic

changes, including several stages. In girls, the puberty process begins with the development of breasts (thelarche). An increase in estrogen concentration leads to the development of the lactoferous duct system, while an increase in progesterone concentration results in an increase in the number of lobular alveoli at the ends of the lactoferous ducts. Approximately six months after thelarche, pubic hair growth (pubarche) begins. The next, final stage is the appearance of menarche - the first menstrual period [45]. The first ovulation usually occurs six to nine months after the onset of menstruation due to immature positive feedback mechanisms [46]. In boys, the first sign of puberty is an increase in testicular volume. Increased LH concentration causes the production of testosterone by Leydig cells, while an increase in FSH concentration affects the process of spermatogenesis with the participation of Sertoli cells. The increase in testicular volume causes thickening and darkening of the scrotal skin. About a year after testicular growth begins, the first ejaculation usually occurs. However, its occurrence does not mean full reproductive readiness - it is usually achieved one year after the first ejaculation. In boys, the growth of pubic hair usually occurs simultaneously with the development of the testicles. After the completion of testicular growth, the penis grows - initially in length, then in width [45].

The favorable changes in the quality of health care and the improvement of socioeconomic conditions taking place in recent years mean that environmental factors, including exposure to substances that modify the functioning of the endocrine system, are becoming the predominant factors in determining the time of puberty [47].

Several studies have demonstrated a correlation between early (prenatal or childhood) exposure to EDCs and the concentration of circulating sex hormones and the clinical time of onset of puberty. Intrauterine exposure to atrazine, for example, is associated with earlier onset of menstruation in girls, while exposure to organophosphate pesticides resulted in delayed puberty in both girls and boys. It should be emphasized that many pesticides also caused an earlier onset of puberty. The mechanisms of this action are multidirectional. EDCs directly influence genetic material and epigenetic processes, thus influencing genes related to the process of sexual maturation. Many substances considered to be endocrine disrupting chemicals act at the level of estrogen or androgen receptors, imitating the action of endogenous hormones. In some cases, the combination of a chemical compound with a receptor within the cell results in the blocking of endocrine functions [47], [48], [49]. In the context of sexual maturation, an indirect effect also seems to be important, which is exerted by influencing metabolic programming in the prenatal period and early childhood, especially through obesogenic compounds [50].

5. The effect of EDC on other reproductive system

According to the latest research, EDCs have a multidirectional impact on the functioning of the reproductive system in both men and women. Their involvement in the pathogenesis of infertility, polycystic ovary syndrome, premature ovarian insufficiency (POI), premature menopause, endometriosis and uterine fibroids is known [51], [52], [53]. Moreover, their impact on reducing the regularity of menstrual cycles and increasing the frequency of miscarriages is postulated [54].

In recent years, the hypotheses that some of the disorders affecting the reproductive health of adult women may have a common origin and may be the result of early changes in the structure and function of the ovaries resulting from exposure to EDCs in utero have gained increasing interest. This relationship applies, among others, to PCOS, POI, endometriosis and reproductive organ cancers [55], [56], [57] . BPA (bisphenol A) affects the ovarian reserve, which is a basic determinant of reproductive potential. Higher levels of BPA in the urine of the studied women were associated with a smaller number of antral follicles (AFC) and a lower number of properly fertilized oocytes in the in-vitro fertilization process during medically assisted reproduction. Moreover, higher concentrations of BPA in the mother's blood were associated with an increased risk of miscarriages - both euploid and aneuploid. Higher levels of BPA were also found in the blood of women diagnosed with PCOS [58].

In addition to bisphenol derivatives, many studies also focus on phthalene compounds and their impact on reproduction. Also in relation to phthalenes, their negative impact on the number and quality of oocytes and the quality of embryos in medically assisted reproductive techniques has been demonstrated [59], [60] . Furthermore, increased levels of monoethyl phthalate in pregnant women were associated with subsequent reductions in AMH levels in their adolescent daughters [61] . A positive correlation is also indicated between the concentrations of phthalate esters in plasma and their metabolites in urine and endometriosis [62] . Research suggests that the effects of both BPA and phthalenes are based on their estrogenic effects.

At this point, it is also necessary to mention the compound most widely characterized in terms of its activity that disrupts the functioning of the endocrine system - DES (diethylstilbestrol). This compound - a synthetic estrogen derivative - has been recommended since the 1940s - initially to supplement estrogen deficiencies (vaginitis, menopausal

symptoms), and then to prevent obstetric complications such as miscarriages or premature births. Research results published in 1953 clearly suggested that this compound did not prevent complications, but this did not result in the cessation of its use. The scale of exposure is difficult to estimate, but it is suggested that approximately 10 million people around the world have been exposed to it [62]. The results of study conducted by Hoover and his team in 2011 showed that exposure to DES increases the risk of reproductive system cancers (cervical cancer, vaginal cancer, breast cancer) [63]. Apart from the direct impact of DES, its indirect role is emphasized, which mainly involves inducing a state of hypersensitivity and excessive responsiveness of uterine myometrium to sex hormones, which increases the risk of developing uterine fibroids and endometrial cancer in later life. Numerous reports also indicate the association of exposure to DES with the risk of premature menopause, infertility, miscarriages, ectopic pregnancies, preeclampsia, premature delivery and intrauterine fetal death [64].

6. Conclusion

Endocrine-disrupting chemicals are an important and increasingly well-recognized factor affecting human health, particularly in the context of reproductive function and development. As discussed in this review, these compounds are widely present in the environment and everyday products, which makes human exposure common and, in many cases, unavoidable. Their biological effects are complex and involve not only interactions with hormone receptors, but also epigenetic modifications, disturbances in intracellular homeostasis, and alterations in immune function.

Particular attention should be given to exposure during critical periods of development, such as prenatal life, early childhood and mini-puberty, when the endocrine system is especially sensitive to external influences. Disruptions occurring at these stages may lead to long-term consequences, including altered timing of puberty and an increased risk of reproductive disorders such as PCOS, endometriosis, premature ovarian insufficiency and infertility. The example of diethylstilbestrol clearly demonstrates that the effects of EDC exposure may persist across the lifespan and even affect subsequent generations.

Considering both the ubiquity of EDCs and the growing body of evidence linking them to adverse health outcomes, further research is needed to better understand their mechanisms of action and long-term effects, especially in the context of combined exposure. At the same

time, limiting exposure, particularly in vulnerable populations, remains an important element of preventive strategies in public health and clinical practice.

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References

[1] B. Yilmaz, H. Terekeci, S. Sandal, and F. Kelestimur, "Endocrine disrupting chemicals: exposure, effects on human health, mechanism of action, models for testing and strategies for prevention," *Rev. Endocr. Metab. Disord.*, vol. 21, no. 1, pp. 127–147, Mar. 2020, doi: 10.1007/S11154-019-09521-Z.

[2] S. De Coster and N. Van Larebeke, "Endocrine-disrupting chemicals: associated disorders and mechanisms of action," *J. Environ. Public Health*, vol. 2012, 2012, doi: 10.1155/2012/713696.

[3] F. Özel and J. Rüegg, "Exposure to endocrine-disrupting chemicals and implications for neurodevelopment," *Dev. Med. Child Neurol.*, vol. 65, no. 8, pp. 1005–1011, Aug. 2023, doi: 10.1111/DMCN.15551.

[4] H. B. Patisaul, "Endocrine Disruption and Reproductive Disorders: Impacts on Sexually Dimorphic Neuroendocrine Pathways," *Reproduction*, vol. 162, no. 5, p. F111, Nov. 2021, doi: 10.1530/REP-20-0596.

[5] T. T. Schug, A. Janesick, B. Blumberg, and J. J. Heindel, "Endocrine disrupting chemicals and disease susceptibility," *Journal of Steroid Biochemistry and Molecular Biology*, vol. 127, no. 3–5, pp. 204–215, Nov. 2011, doi: 10.1016/j.jsbmb.2011.08.007.

[6] C. Ahn and E. B. Jeung, "Endocrine-Disrupting Chemicals and Disease Endpoints," *Int. J. Mol. Sci.*, vol. 24, no. 6, Mar. 2023, doi: 10.3390/IJMS24065342.

[7] T. Wintgens, M. Gallenkemper, and T. Melin, “Occurrence and removal of endocrine disrupters in landfill leachate treatment plants,” *Water Science and Technology*, vol. 48, no. 3, pp. 127–134, Aug. 2003, doi: 10.2166/WST.2003.0180.

[8] M. G. Bertram, A. C. Gore, C. R. Tyler, and T. Brodin, “Endocrine-disrupting chemicals,” *Current Biology*, vol. 32, no. 13, pp. R727–R730, Jul. 2022, doi: 10.1016/j.cub.2022.05.063.

[9] T. Encarnação, A. A. C. C. Pais, M. G. Campos, and H. D. Burrows, “Endocrine disrupting chemicals: Impact on human health, wildlife and the environment,” *Sci. Prog.*, vol. 102, no. 1, pp. 3–42, Mar. 2019, doi: 10.1177/0036850419826802.

[10] E. Diamanti-Kandarakis *et al.*, “Endocrine-disrupting chemicals: an Endocrine Society scientific statement,” *Endocr. Rev.*, vol. 30, no. 4, pp. 293–342, Jun. 2009, doi: 10.1210/ER.2009-0002.

[11] H. Tan *et al.*, “Structures of Endocrine-Disrupting Chemicals Determine Binding to and Activation of the Estrogen Receptor α and Androgen Receptor,” *Environ. Sci. Technol.*, vol. 54, no. 18, pp. 11424–11433, Sep. 2020, doi: 10.1021/ACS.EST.0C02639.

[12] M. A. La Merrill *et al.*, “Consensus on the key characteristics of endocrine-disrupting chemicals as a basis for hazard identification,” *Nat. Rev. Endocrinol.*, vol. 16, no. 1, pp. 45–57, Jan. 2020, doi: 10.1038/S41574-019-0273-8.

[13] M. M. Tabb and B. Blumberg, “New modes of action for endocrine-disrupting chemicals,” *Mol. Endocrinol.*, vol. 20, no. 3, pp. 475–482, Mar. 2006, doi: 10.1210/ME.2004-0513.

[14] A. Alavian-Ghavanini and J. Rüegg, “Understanding Epigenetic Effects of Endocrine Disrupting Chemicals: From Mechanisms to Novel Test Methods,” *Basic Clin. Pharmacol. Toxicol.*, vol. 122, no. 1, pp. 38–45, Jan. 2018, doi: 10.1111/BCPT.12878.

[15] K. Kim, J. S. Kwon, C. Ahn, and E. B. Jeung, “Endocrine-Disrupting Chemicals and Their Adverse Effects on the Endoplasmic Reticulum,” *Int. J. Mol. Sci.*, vol. 23, no. 3, Feb. 2022, doi: 10.3390/IJMS23031581.

[16] D. S. Schwarz and M. D. Blower, “The endoplasmic reticulum: structure, function and response to cellular signaling,” *Cell. Mol. Life Sci.*, vol. 73, no. 1, pp. 79–94, Jan. 2016, doi: 10.1007/S00018-015-2052-6.

[17] M. F. Zhou *et al.*, “Endoplasmic reticulum stress induces apoptosis of arginine vasopressin neurons in central diabetes insipidus via PI3K/Akt pathway,” *CNS Neurosci. Ther.*, vol. 25, no. 5, pp. 562–574, May 2019, doi: 10.1111/CNS.13089.

[18] S. Morikawa and F. Urano, “The Role of ER Stress in Diabetes: Exploring Pathological Mechanisms Using Wolfram Syndrome,” *Int. J. Mol. Sci.*, vol. 24, no. 1, Jan. 2022, doi: 10.3390/IJMS24010230.

[19] L. Ozcan and I. Tabas, “Role of endoplasmic reticulum stress in metabolic disease and other disorders,” *Annu. Rev. Med.*, vol. 63, pp. 317–328, 2012, doi: 10.1146/ANNUREV-MED-043010-144749.

[20] O. Sabuz Vidal, D. Deepika, M. Schuhmacher, and V. Kumar, “EDC-induced mechanisms of immunotoxicity: a systematic review,” *Crit. Rev. Toxicol.*, vol. 51, no. 7, pp. 634–652, 2021, doi: 10.1080/10408444.2021.2009438.

[21] L. R. Rhomberg and J. E. Goodman, “Low-dose effects and nonmonotonic dose-responses of endocrine disrupting chemicals: Has the case been made?,” *Regulatory Toxicology and Pharmacology*, vol. 64, no. 1, pp. 130–133, Oct. 2012, doi: 10.1016/j.yrtph.2012.06.015.

[22] G. Di Pietro, F. Forcucci, and F. Chiarelli, “Endocrine Disruptor Chemicals and Children’s Health,” *International Journal of Molecular Sciences 2023, Vol. 24, Page 2671*, vol. 24, no. 3, p. 2671, Jan. 2023, doi: 10.3390/IJMS24032671.

[23] R. R. Newbold, “Developmental exposure to endocrine-disrupting chemicals programs for reproductive tract alterations and obesity later in life,” *American Journal of Clinical Nutrition*, vol. 94, no. 6, Dec. 2011, doi: 10.3945/ajcn.110.001057.

[24] F. Xin, M. Susiarjo, and M. S. Bartolomei, “Multigenerational and transgenerational effects of endocrine disrupting chemicals: A role for altered epigenetic regulation?,” *Semin. Cell Dev. Biol.*, vol. 43, p. 66, Jul. 2015, doi: 10.1016/J.SEMCDB.2015.05.008.

[25] A. C. Gore *et al.*, “EDC-2: The Endocrine Society’s Second Scientific Statement on Endocrine-Disrupting Chemicals,” *Endocr. Rev.*, vol. 36, no. 6, pp. 1–150, 2015, doi: 10.1210/ER.2015-1010.

[26] Y. Ma *et al.*, “The adverse health effects of bisphenol A and related toxicity mechanisms,” *Environ. Res.*, vol. 176, Sep. 2019, doi: 10.1016/j.envres.2019.108575.

[27] M. F. Manzoor *et al.*, “An insight into bisphenol A, food exposure and its adverse effects on health: A review,” *Front. Nutr.*, vol. 9, Nov. 2022, doi: 10.3389/FNUT.2022.1047827.

[28] E. Khalili Sadrabad, S. A. Hashemi, A. Nadjarzadeh, E. Askari, F. Akrami Mohajeri, and F. Ramroudi, “Bisphenol A release from food and beverage containers - A review,” *Food Sci. Nutr.*, vol. 11, no. 7, pp. 3718–3728, Jul. 2023, doi: 10.1002/FSN3.3398.

[29] V. Ramírez, S. Merkel, T. Tietz, and A. Rivas, “Risk assessment of food contact materials,” *EFSA J.*, vol. 21, no. Suppl 1, Nov. 2023, doi: 10.2903/J.EFSA.2023.E211015.

[30] Y. Wang and H. Qian, “Phthalates and Their Impacts on Human Health,” *Healthcare 2021, Vol. 9, Page 603*, vol. 9, no. 5, p. 603, May 2021, doi: 10.3390/HEALTHCARE9050603.

[31] A. Giuliani, M. Zuccarini, A. Cichelli, H. Khan, and M. Reale, “Critical Review on the Presence of Phthalates in Food and Evidence of Their Biological Impact,” *Int. J. Environ. Res. Public Health*, vol. 17, no. 16, pp. 1–43, Aug. 2020, doi: 10.3390/IJERPH17165655.

[32] H. J. Wen *et al.*, “Phthalate exposure and reproductive hormones and sex-hormone binding globulin before puberty – Phthalate contaminated-foodstuff episode in Taiwan,” *PLoS One*, vol. 12, no. 4, p. e0175536, Apr. 2017, doi: 10.1371/JOURNAL.PONE.0175536.

[33] J. Yang, R. Hauser, and R. H. Goldman, “Taiwan food scandal: The illegal use of phthalates as a clouding agent and their contribution to maternal exposure,” *Food and Chemical Toxicology*, vol. 58, pp. 362–368, Aug. 2013, doi: 10.1016/j.fct.2013.05.010.

[34] S. Das *et al.*, “Atrazine Toxicity: The Possible Role of Natural Products for Effective Treatment,” *Plants 2023, Vol. 12, Page 2278*, vol. 12, no. 12, p. 2278, Jun. 2023, doi: 10.3390/PLANTS12122278.

[35] T. B. Hayes *et al.*, “Atrazine induces complete feminization and chemical castration in male African clawed frogs (Xenopus laevis),” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 107, no. 10, pp. 4612–4617, Mar. 2010, doi: 10.1073/PNAS.0909519107.

[36] H. Yang, Y. Jiang, K. Lu, H. Xiong, Y. Zhang, and W. Wei, “Herbicide atrazine exposure induce oxidative stress, immune dysfunction and WSSV proliferation in red swamp crayfish Procambarus clarkii,” *Chemosphere*, vol. 283, p. 131227, Nov. 2021, doi: 10.1016/J.CHEMOSPHERE.2021.131227.

[37] L. Jowa and R. Howd, “Should Atrazine and Related Chlorotriazines Be Considered Carcinogenic for Human Health Risk Assessment?,” *Journal of Environmental Science and Health, Part C*, vol. 29, no. 2, pp. 91–144, Apr. 2011, doi: 10.1080/10590501.2011.577681.

[38] M. Spaziani *et al.*, “Hypothalamo-Pituitary axis and puberty,” *Mol. Cell. Endocrinol.*, vol. 520, Jan. 2021, doi: 10.1016/J.MCE.2020.111094.

[39] D. Lopez-Rodriguez, D. Franssen, S. Heger, and A. S. Parent, “Endocrine-disrupting chemicals and their effects on puberty,” *Best Pract. Res. Clin. Endocrinol. Metab.*, vol. 35, no. 5, Sep. 2021, doi: 10.1016/J.BEEM.2021.101579.

[40] R. P. Millar and J. A. Tello, “Gonadotropin-Releasing Hormones,” *Endocrinology: Adult and Pediatric*, vol. 2–2, pp. 2003-2022.e7, Jan. 2015, doi: 10.1016/B978-0-323-18907-1.00115-3.

[41] M. Becker and V. Hesse, “Minipuberty: Why Does it Happen?,” *Horm. Res. Paediatr.*, vol. 93, no. 2, pp. 76–84, Aug. 2020, doi: 10.1159/000508329.

[42] J. Rohayem, E. C. Alexander, S. Heger, A. Nordenström, and S. R. Howard, “Mini-Puberty, Physiological and Disordered: Consequences, and Potential for Therapeutic Replacement,” *Endocr. Rev.*, vol. 45, no. 4, pp. 460–492, Aug. 2024, doi: 10.1210/ENDREV/BNAE003.

[43] C. H. Renault, L. Aksglaede, D. Wojdemann, A. B. Hansen, R. B. Jensen, and A. Juul, “Minipuberty of human infancy – A window of opportunity to evaluate hypogonadism and differences of sex development?,” *Ann. Pediatr. Endocrinol. Metab.*, vol. 25, no. 2, p. 84, Jun. 2020, doi: 10.6065/APEM.2040094.047.

[44] N. Brix *et al.*, “Timing of puberty in boys and girls: A population-based study,” *Paediatr. Perinat. Epidemiol.*, vol. 33, no. 1, pp. 70–78, Jan. 2019, doi: 10.1111/PPE.12507.

[45] L. Breehl and O. Caban, “Physiology, Puberty,” *StatPearls*, Mar. 2023, Accessed: May 25, 2026. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK534827/

[46] K. Zhang *et al.*, “Onset of Ovulation after Menarche in Girls: A Longitudinal Study,” *J. Clin. Endocrinol. Metab.*, vol. 93, no. 4, p. 1186, 2008, doi: 10.1210/JC.2007-1846.

[47] C. S. Uldbjerg *et al.*, “Prenatal and postnatal exposures to endocrine disrupting chemicals and timing of pubertal onset in girls and boys: a systematic review and meta-analysis,” *Hum. Reprod. Update*, vol. 28, no. 5, pp. 687–716, Sep. 2022, doi: 10.1093/HUMUPD/DMAC013.

[48] A. M. Binder *et al.*, “Prepubertal and Pubertal Endocrine-Disrupting Chemical Exposure and Breast Density among Chilean Adolescents,” *Cancer Epidemiol. Biomarkers Prev.*, vol. 27, no. 12, p. 1491, Dec. 2018, doi: 10.1158/1055-9965.EPI-17-0813.

[49] V. N. Brito *et al.*, “The Congenital and Acquired Mechanisms Implicated in the Etiology of Central Precocious Puberty,” *Endocr. Rev.*, vol. 44, no. 2, pp. 193–221, Apr. 2023, doi: 10.1210/ENDREV/BNAC020.

[50] J. E. Lee, H. W. Jung, Y. J. Lee, and Y. A. Lee, “Early-life exposure to endocrine-disrupting chemicals and pubertal development in girls,” *Ann. Pediatr. Endocrinol. Metab.*, vol. 24, no. 2, p. 78, Jun. 2019, doi: 10.6065/APEM.2019.24.2.78.

[51] B. Vessa, B. Perlman, P. G. McGovern, and S. S. Morelli, “Endocrine disruptors and female fertility: a review of pesticide and plasticizer effects,” *F and S Reports*, vol. 3, no. 2, pp. 86–90, Jun. 2022, doi: 10.1016/j.xfre.2022.04.003.

[52] S. Siddiqui, S. Mateen, R. Ahmad, and S. Moin, “A brief insight into the etiology, genetics, and immunology of polycystic ovarian syndrome (PCOS),” *J. Assist. Reprod. Genet.*, vol. 39, no. 11, p. 2439, Nov. 2022, doi: 10.1007/S10815-022-02625-7.

[53] A. Santoro *et al.*, “Neuro-toxic and Reproductive Effects of BPA,” *Curr. Neuropharmacol.*, vol. 17, no. 12, pp. 1109–1132, Jul. 2019, doi: 10.2174/1570159X17666190726112101.

[54] S. A. Krieg, L. K. Shahine, and R. B. Lathi, “Environmental exposure to endocrine-disrupting chemicals and miscarriage,” *Fertil. Steril.*, vol. 106, no. 4, pp. 941–947, Sep. 2016, doi: 10.1016/j.fertnstert.2016.06.043.

[55] M. Hewlett, E. Chow, A. Aschengrau, and S. Mahalingaiah, “Prenatal Exposure to Endocrine Disruptors: A Developmental Etiology for Polycystic Ovary Syndrome,” *Reprod. Sci.*, vol. 24, no. 1, pp. 19–27, Jan. 2017, doi: 10.1177/1933719116654992.

[56] S. PG *et al.*, “Endocrine disruptors in utero cause ovarian damages linked to endometriosis,” *Front. Biosci. (Elite Ed).*, vol. 4, no. 5, p. 1724, 2012, doi: 10.2741/493.

[57] M. E. Street and S. Bernasconi, “Endocrine-Disrupting Chemicals in Human Fetal Growth,” *International Journal of Molecular Sciences 2020, Vol. 21, Page 1430*, vol. 21, no. 4, p. 1430, Feb. 2020, doi: 10.3390/IJMS21041430.

[58] A. Rutkowska and D. Rachoń, “Bisphenol A (BPA) and its potential role in the pathogenesis of the polycystic ovary syndrome (PCOS),” *Gynecol. Endocrinol.*, vol. 30, no. 4, pp. 260–265, 2014, doi: 10.3109/09513590.2013.871517.

[59] K. L. Land, F. G. Miller, A. C. Fugate, and P. R. Hannon, “The effects of endocrine-disrupting chemicals on ovarian- and ovulation-related fertility outcomes,” *Mol. Reprod. Dev.*, vol. 89, no. 12, pp. 608–631, Dec. 2022, doi: 10.1002/MRD.23652.

[60] E. M. Panagiotou, V. Ojasalo, and P. Damdimopoulou, “Phthalates, ovarian function and fertility in adulthood,” *Best Pract. Res. Clin. Endocrinol. Metab.*, vol. 35, no. 5, Sep. 2021, doi: 10.1016/j.beem.2021.101552.

[61] J. H. Kim and S. H. Kim, “Exposure to Phthalate Esters and the Risk of Endometriosis,” *Dev. Reprod.*, vol. 24, no. 2, p. 71, Jun. 2020, doi: 10.12717/DR.2020.24.2.71.

[62] K. L. Noller and C. R. Fish, “Diethylstilbestrol usage: its interesting past, important present, and questionable future,” *Medical Clinics of North America*, vol. 58, no. 4, pp. 793–810, 1974, doi: 10.1016/S0025-7125(16)32122-8.

[63] R. N. Hoover *et al.*, “Adverse health outcomes in women exposed in utero to diethylstilbestrol,” *N. Engl. J. Med.*, vol. 365, no. 14, pp. 1304–1314, Oct. 2011, doi: 10.1056/NEJMOA1013961.

[64] J. M. Goldberg and T. Falcone, “Effect of diethylstilbestrol on reproductive function,” *Fertil. Steril.*, vol. 72, no. 1, pp. 1–7, 1999, doi: 10.1016/S0015-0282(99)00153-3.