Postprint of: Płotka-Wasylka J., Mulkiewicz E., Lis H., Godlewska K., Kurowska-Susdorf A., Sajid M., Lambropoulou D., Jatkowska N., Endocrine disrupting compounds in the baby's world - A harmful environment to the health of babies, SCIENCE OF THE TOTAL ENVIRONMENT Vol. 881(2023), 163350, DOI: 10.1016/j.scitotenv.2023.163350

Endocrine disrupting compounds in the baby's world - a harmful environment to the health of babies

Justyna Płotka-Wasylka[1,2,*], Ewa Mulkiewicz[3], Hanna Lis[3], Klaudia Godlewska[3], Aleksandra Kurowska-Susdorf[4], Muhammad Sajid[5], Dimitra Lambropoulou[6,7], Natalia Jatkowska[1,*]

[1] *Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology, 11/12 G. Narutowicza St., 80-233 Gdańsk, Poland*

[2] *BioTechMed Center, Gdańsk University of Technology, 11/12 G. Narutowicza St., 80-233 Gdańsk, Poland*

[3] *Department of Environmental Analysis, Faculty of Chemistry, University of Gdańsk, 63 Wita Stwosza Street, 80-308 Gdańsk, Poland*

[4] *The Naval Academy, Faculty of Humanities and Social Sciences, 69 Śmidowicza Street, 81-127 Gdynia, Poland*

[5] *Applied Research Center for Environment and Marine Studies, Research Institute, King Fahd University of Petroleum and Minerals, Dhahran 31261, Saudi Arabia*

[6] *Department of Chemistry, Environmental Pollution Control Laboratory, Aristotle University of Thessaloniki*

[7] *Center for Interdisciplinary Research and Innovation (CIRI-AUTH), Balkan Center, Thessaloniki, GR-57001, Greece*

Corresponding authors:

Justyna Płotka-Wasylka: juswasyl@pg.edu.pl; plotkajustyna@gmail.com

Natalia Jatkowska: natalia.jatkowska@pg.edu.pl

Abstract

Globally, there has been a significant increase in awareness of the adverse effects of chemicals with known or suspected endocrine-acting properties on human health. Human exposure to endocrine disrupting compounds (EDCs) mainly occurs by ingestion and to some extent by inhalation and dermal uptake. Although it is difficult to assess the full impact of human exposure to EDCs, it is well known that timing of exposure is of importance and therefore infants are more vulnerable to EDCs and are at greater risk compared to adults. In this regard, infant safety and assessment of associations between prenatal exposure to EDCs and growth during infancy and childhood has been received considerable attention in the last years. Hence, the purpose of this review is to provide a current update on the evidence from biomonitoring studies on the exposure of infants to EDCs and a comprehensive view of the uptake, the mechanisms of action and biotransformation in baby/human body. Analytical methods used and concentration levels of EDCs in different biological matrices (e.g., placenta, cord plasma, amniotic fluid, breast milk, urine, and blood of pregnant women) are also discussed. Finally, key issues and recommendations were provided to avoid hazardous exposure to these chemicals, taking into account family and lifestyle factors related to this exposure.

Keywords: Endocrine disrupting compounds; Infant; Harmful environment; Biomonitoring; Education

Table of context

1. Introduction

The environment in which children grow is a very important factor influencing their development. Parents try to take care of every detail, already at the stage of fetal development of their children. However, they are not always aware of the threats that affect the development of the fetus or child. One such threats is environmental pollution, which can affect every stage of human development.

Nowadays, knowledge of the potential effects of environmental exposure on human health is alarmingly basic, which limits our ability to prevent the diseases that these exposures can cause. Undoubtedly, it is also important to raise public awareness of the impact of environmental exposure to diseases, especially among pregnant women.

Endocrine disrupting compounds (EDCs) are one of the most important groups of pollutants which are present in many areas and materials of common life. The exposure to EDCs can occur from products to personal care, from air and food, this is why fetus and children contact with this class of compounds is inevitable. EDCs are thousands of exogenous chemicals or a mixture of chemicals and they are characterized by high ability to mimic or interfere with the endocrine system and metabolism, causing side effects on health (Predieri et al., 2022). Due to the fact that EDCs mostly interpose with metabolic and endocrine pathways during very sensitive periods of human development and grow, the knowledge on several aspects connected with this group of compounds is of great importance. Nowadays, the research is going around the areas: i) pathogenic mechanisms of action of EDCs from wildlife to humans; ii) EDCs impact on health from pregnancy to adulthood; iii) methods of analysis and monitoring of EDCs in environmental, food, biological and other samples.

Three ways of EDCs uptake are known: inhalation, ingestion, and dermal contact (Ercan and Tarcin, 2022). It has been documented that some EDCs are not metabolized and remain in high levels in the environment for a long time and can be found in human and animal bodies after many years of their uptake. Other types can change into substances that are even more toxic can be detected at distances from where they were produced or released.

Many women are unaware that exposure to EDCs during pregnancy often has a significant impact on the developing fetus, which can lead to long-term postpartum pathologies. The government should

106 educate citizens that EDCs are commonly found in daily personal care products and plastic materials,
107 and compounds such as phthalates, parabens and bisphenols are continuously detected in human blood
108 at high levels (Bradman and Whyatt, 2005; Koutaki et al., 2022; Lundqvist et al., 2006; Ramadan et al.,
109 2020; Wang et al., 2019). As a result, women may be exposed to mixtures of over 50 different EDCs
110 during pregnancy. The incidence of pregnancy complications (e.g., hypertension, postpartum
111 haemorrhage) has steadily increased over the past few decades. Many scientists explain this
112 phenomenon that environmental exposure is one of the potential contributors to this problem. Organic
113 pollutants present in the human body follow the lipid status and are transferred to the fetus during
114 pregnancy and to infants through breast milk. Moreover, EDCs are often found in products intended for
115 babies and children of early stage life, such as diapers, pacifiers, bottles and toys (Arbuckle, 2010;
116 Encarnação et al., 2019; Oliveira Souzaa et al., 2022; Szczepańska et al., 2016; Turbeville and Sasser,
117 2020; Wittassek et al., 2009). The authors of guides for pregnant women should also pay attention to
118 this problem and address the issue of environmental exposure, especially in the prenatal period and early
119 childhood, and emphasize the fact that environmental exposure may be responsible for many adverse
120 changes in the body.

121 It is well known that changes that appear in the early years of life can impact on the way for disease in
122 later stages of life (Ercan and Tarcin, 2022). There is a saying that illustrates this point well, namely
123 "the fetal basis of adult disease". This term is used to depict observations of the maternal, fetal and
124 external environment and identifies an individual's propensity to develop a disorder later in life (Ercan
125 and Tarcin, 2022). Thus, the developmental age at which exhibition to an EDCs occurs is critical, and
126 the information about the uptake, mechanisms of action and biotransformation in baby/human body as
127 well as the monitoring of child environment from the initial days of life are of high importance. This
128 review summarizes these aspects. The main routes of EDCs uptake are described together with specific
129 examples, while the mechanisms of action of EDCs are depicted in very detailed way. The EDCs
130 metabolism as well as the effects of prenatal and early postnatal exposure (up to 3 years of age) on the
131 development of children are also considered. Examples of goods that are used by babies and children
132 together, which contain specific EDCs are also pointed out along with analytical methods which allow
133 to determine these compounds. As it is extremely important to conduct biomonitoring of infants and

children in early stage of life, the methods used for such purposes are also mentioned with literature examples. The Scopus database was used for the literature search with the application of following keywords: endocrine disrupting compounds, infant, biomonitoring of EDC, biological samples (urine, salivia, blood, breast milk) harmful environment, separation methods of EDC, metabolism of EDC (accessed in January 2023). The publications mainly appeared during the last two decades were considered.

As the motivation for this work was to make a complete awareness review of the dangers of EDCs exposure from an early stage of human development, this work was punctuated with advice on how to minimize the delivery of EDCs to the child's body. We believe that this review will be very useful for future readers, not only the researchers who will search for analytical methods, but also the parents who take care their infants and children.

2. EDCs: uptake, mechanisms of action and biotransformation in baby/human body

Due to widespread distribution of EDCs, humans are continuously exposed through multiple sources like polluted environment (water and air), food, consumer products, medications, and many others. However, scientific information regarding the long-term effects of chronic, low-dose exposure to complex mixtures of these chemicals is very limited. Furthermore, little is known about the quantities in which EDCs are taken up and stored in the body.

2.1. Uptake of EDCs

The main route of EDCs uptake depends on the type of chemical and its use. In turn, the fate of EDCs in the human body depends on the properties of the substance, especially its lipophilicity, and thus the susceptibility to bioaccumulation. Most EDCs are lipophilic and bioaccumulate in the adipose tissue, thus they have a very long half-life in the human body and cause a prolonged exposure to these pollutants. A particular example is DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)-ethane) and its metabolites banned for use in the 1970s and still detected in environment and humans. Some EDCs do

not bioaccumulate in the body, an example is bisphenol A (BPA) which has an estimated half-life of approximately 6 hours (Chapin et al., 2008). Nevertheless, it is very often detected in populations (in 93% of people over 6 years of age), like other plasticizers, mostly due to continuous exposure to these chemicals on a daily basis (Yilmaz et al., 2020).

Human exposure to EDCs mainly occurs by ingestion and to some extent by inhalation and dermal uptake (Yilmaz et al., 2020). Food constitutes the main source of EDCs for humans (Mantovani, 2016). Introduced into the environment, EDCs easily bioaccumulate in organisms and contaminate fish, meat, dairy products and poultry products, and from these sources they eventually get into the human body as a dietary component (Sangeetha et al., 2021; Street et al., 2018). Another source of EDCs, however not very significant, is food of plant origin (fruit and vegetable), which is contaminated by plant protection products used in agriculture, e.g. pesticides (Mantovani, 2016). Some EDCs are synthetic components of food products like food coloring additives, while others migrate into food from packaging containing metals, bisphenol A, or phthalates (Amir et al., 2021).

EDCs can be found in a variety of everyday products and goods. A release from consumer products, such as textiles, polishing and cleaning products, cosmetics, and food contact materials is another important route of exposure. In this case, EDCs can enter the human body by ingestion, inhalation, and through the skin.

Inhalation may be a very important route of exposure, especially for some volatile chemicals and semi-volatile compounds (Carpenter, 2006; Coughlin, 1998; Net et al., 2015) Indoor area is an important environment for potential exposure to air-borne chemicals and particles (Hwang et al., 2008).

As fat-soluble substances, EDCs can be transferred to human body through dermal absorption (Carpenter, 2006). Exposure to indoor organic chemicals through the dermal route accounts for only a small percentage of the total exposure, but can be significant (Coughlin, 1998). The risk of transdermal exposure to EDCs concerns also personal care products and cosmetics.

Occupational exposure to EDCs is also a significant route of contamination for people working at risky environment (Coughlin, 1998).

Of special concern is the exposure of pregnant women and infants as the risk of lifelong adverse health effects is enhanced when periods of EDC exposure coincide with the formation and differentiation of organ systems in early development (WHO, 2013).

EDCs may increase the risk of childhood diseases by disrupting hormonally mediated processes critical for growth and proper development during gestation, infancy, or childhood. For example, normal levels of thyroid hormones are of special importance in fetal development, as they condition the proper development of the brain and nervous system. During the first part of pregnancy, the fetus relies entirely on transplacental transfer of maternal thyroid hormones and thus on a normal maternal thyroid function. Thus, even minor changes in the thyroid homeostasis may affect fetal neurological development. Epidemiological studies have indicated that even a marginally low thyroxine level in a pregnant woman may give rise to reduction of cognitive functions of the offspring. Absence of thyroid hormones reduces neuronal growth and differentiation in the cerebral cortex, hippocampus, and cerebellum (Boas et al., 2012).

Development is also a particularly sensitive window of exposure due to the extensive genetic programming that occurs in this time period. Exposures during periods of development can alter the epigenome and increase susceptibility to disease later in life, after the exposure has ended. It has been suggested that exposures in utero and during early postnatal life can make a high impact, not only on development but also on the risk of disease much later in life. This might be the case for cancer, obesity, the metabolic syndrome, diabetes, cardiovascular disease, neurodegenerative disease such as Alzheimer and Parkinson, and mental retardation. Prenatal exposures might even contribute to psychoses (De Coster and Van Larebeke, 2012).

The fetus, infant, and child may have higher exposure and enhanced sensitivity to some EDCs than adults because of specific baby food they consume, behavior (hand-to-mouth activity, crawling), physiology (higher ventilation rates, intestinal absorption, surface area to volume ratios), anatomy, and toxicokinetics (Braun, 2017). In addition, breastfed infants may have higher serum concentrations of some persistent EDCs than their mothers because of lactational exposure (Grandjean and Jensen, 2004). Differences in toxicokinetics can result in higher circulating or tissue concentrations of an EDC for a

given dose. One of the important reasons may be that the fetus, compared to adults, has lower levels of several cytochrome P450 enzymes that metabolize environmental chemicals including EDCs (Cresteil, 1998; Hakkola et al., 1998).

2.2. Mechanisms of action of EDCs in baby/human body

Recent epidemiological studies suggest a link between increasing exposure to EDCs and the development of certain civilization diseases such as reproductive disorders, hormone-related cancers, metabolic disorders such as obesity and type 2 diabetes (Guarnotta et al., 2022). Therefore, understanding of molecular mechanisms underlying the physiological consequences of chronic exposure to environmentally relevant concentrations of EDCs is very important.

Endocrine signaling occurs along axes that connect the central nervous system with the target organ. In mammals, the endocrine signaling pathway usually starts at the hypothalamus by secretion of neurohormones. The release of neurohormones upon stimulation of the hypothalamus regulates secretion of the secondary hormone signal by the pituitary gland which in turn control excretion of tertiary hormones by the relevant endocrine gland followed by stimulation of gene transcription in the target organs. The endocrine system controls all the most important physiological functions of the human body. EDCs can affect this complex communication system in a wide variety of ways, disrupt the hormonal balance and cause adverse health effects.

The endocrine system is composed of glands that secrete chemical messengers (hormones) that interact with specific targets (receptors). Different nuclear hormone receptors (NRs) mediate the biological actions of estrogens, androgens, progestins, thyroid hormones, retinoids, and other lipophilic hormones and as a consequence regulate various physiological functions e.g., growth, development, reproduction, immunity, energy balance, metabolism regulation in human.

EDCs were thought to act primarily through NRs mainly steroid hormone receptors (estrogen receptors (ERs), androgen receptor (AR), progesterone receptors (PRs)) (Hall and Korach, 2021), thyroid receptors (TRs) (Brent, 2012) and peroxisome proliferator activated receptor (PPAR) (Sugden and Holness, 2008). Direct binding to hormone receptors is the most studied and best known so far

mechanism of endocrine disruption. Many EDCs have similar structures to NR ligands and can directly bind to these receptors, induce conformational changes in their tertiary structure thus can act as agonists and induce gene expression or as antagonists and inhibit the activity of the receptor (**Table 1**). It is also not uncommon for EDC to display receptor-selective actions; e.g. BPA is an agonist of ERs, but functions as an antagonist of AR (Teng et al., 2013).

Table 1. EDCs known to interact with receptors

Chemical class	**Receptor and mode of action**	**References**
Pesticides	AhR agonist/ antagonist TR agonist/ antagonist PPAR agonist	(Warner et al., 2020) (Takeuchi et al., 2006)
DDT and metabolites (DDE, DDD)	ER agonist AR antagonist	(Kuiper et al., 1998) (Kojima et al., 2004)
Phenolic compounds BPA	ER agonist AR antagonist TR agonist TR antagonist	(Kuiper et al., 1998) (Fang et al., 2003) (Kitamura et al., 2005) (Moriyama et al., 2002)
PCBs	ER agonist AR agonist/antagonist TR agonist/antagonist	(Takeuchi et al., 2011) (Takeuchi et al., 2011), (Ghassabian and Trasande, 2018), (Zoeller, 2007)
polybrominated diphenyl ethers (PBDEs)	ER agonist/antagonist AR antagonist TR	(Hamers et al., 2006) (Hamers et al., 2006) (Ghassabian and Trasande, 2018), (Zoeller, 2007)

Phthalates	ER agonist	(Harris et al., 1997)
	ER agonist/antagonist	(Takeuchi et al., 2005)
	AR antagonist	(Lee and Koo, 2007)
PFAS Perfluorooctanesulfonic acid (PFOS) Perfluorooctanoic acid (PFOA)	ER agonist PPAR agonist	(Kjeldsen and Bonefeld-Jørgensen, 2013) (Behr et al., 2020)

In addition, EDCs can affect the endocrine system by activating other signaling pathways, in particular that of aryl hydrocarbon receptor (AhR); a key regulator of the cellular response to xenobiotic exposure. AhR is strongly activated by organic compounds such as polychlorinated dibenzodioxins (referred to as dioxin), polychlorinated dibenzofurans (PCDF), polychlorinated biphenyls (PCBs) as well as polycyclic aromatic hydrocarbons (PAHs) like 3-methylcholanthrene (3-MC), benzo[a]pyrene (BaP) and benzoflavone (Swedenborg et al., 2009).

The cross-talk between the NR and AhR pathways can also lead to endocrine disruptions. There are several possible mechanisms that have been proposed for interactions between NR and AhR signaling. It has been observed that by interactions with DNA sequences close to NR binding sites AhR can modulate (inhibit or activate) transcription of respective gene. Competition between NR and AhR for common transcriptional co-activators is another mechanism by which AhR ligands may disturb steroid hormone signaling (Swedenborg et al., 2009). It has been shown that also competition between ER and AhR for ARNT is at least partly responsible for the anti-estrogenic properties of the dioxin TCDD (Rüegg et al., 2008).

Beside their interference with the genomic pathways, EDCs also exhibit non-genomic mechanisms of action through interactions with membrane-associated NRs and/or G protein-coupled estrogen receptor (GPER/GPR30) (Balaguer et al., 2019). Membrane activation of GPER was shown to rapidly promote intracellular calcium mobilization, cAMP synthesis and to induce a phosphorylation cascade in particular involving ERK1/2, PKA, and PI3K kinases. On the other hand, chromatin binding of GPER

leads to direct transcriptional activation of target genes. Moreover, GPER cross-talk with different receptors induces its downstream activities. For instance, functional interactions with (AhR) or epidermal growth factor receptor (EGFR) and subsequent activation of downstream MAPK kinase were observed (Périan and Vanacker, 2020). EDCs can also influence cell function by targeting membrane associated ion-channels to mediate rapid non-genomic responses (e.g. activation of MAPK signaling) (Warner et al., 2020). Membrane receptor signaling potentially leads to a short-term effect, since their signaling pathways exert more acute effects in target cells. Such mechanism of action was described for the plasticizer DEHP (bis-2-ethylhexyl phthalate), classified as an endocrine disruptor and also as an obesogen (Schaedlich et al., 2018). Interestingly, it has been shown that bisphenol-A exhibits a higher affinity towards GPER than towards nuclear ER receptors (Kerdivel et al., 2013).

According to the classical, ligand-dependent, molecular mechanism of action, hormones are transported through the circulatory system to reach their target intracellular receptors. The binding of a hormone to receptor triggers specific intracellular responses. Therefore, the availability of hormones determines the proper functioning of the endocrine system and all hormone-dependent processes in the body. Hormone availability to receptor is dependent on hormone biosynthesis, transport to the target tissue, levels of hormone binding proteins, and hormone catabolism. EDCs have been described to interfere with all of these processes.

Many molecules can exert endocrine disruption by affecting, positively or negatively, endogenous hormone biosynthesis or degradation. Such molecules generally exhibit structures that are different from those of hormones, since they do not compete with hormones at the receptor level. It has been shown that exposure to EDCs can negatively affect the synthesis and degradation of peptide/protein (gonadotropin-releasing hormone (GnRH), follicle stimulating hormone (FSH), luteinizing hormone (LH), and thyroid stimulating hormone (TSH)), steroid (estrogens, progesterone, and testosterone), and amino acid analogue (thyroid hormones (T4, T3)) hormones (Warner et al., 2020). Interfering with hormone quantity and availability may cause negative effects on reproductive and overall human health. Epidemiological studies of agricultural workers showed associations between pesticide exposure and levels of FSH and LH (Cremonese et al., 2017; Recio et al., 2005). Exposure to EDCs disturbs the

process of steroidogenesis (synthesis of steroid hormones) that occurs in adrenal glands, ovary, testes, placenta, and adipose tissue. Multiple chemicals have been shown to affect the synthesis of cholesterol, which is precursor for all steroid hormones, as well as enzymes involved in the synthesis and conversion of steroid hormones. Inhibition of 17β-hydroxysteroid dehydrogenase (17β-HSD; an enzyme that converts estradiol to estrone) was observed after exposure to parabens and resulted in an increase in estrogen concentrations and consequently, in an increase of the transcription of target estrogen genes (Engeli et al., 2017). EDCs often act as inhibitors of 5α-reductase, which is necessary for conversion of androgens (activation of testosterone to dihydrotestosterone (DHT)) essential for the development of the male genital tract (Ješeta et al., 2021; Sweeney et al., 2015). EDCs can also influence TH signaling at the level of gene expression and regulation of enzymatic activity of iodothyronine deiodinases (DIO). In the target tissues, three DIO (DIO1, DIO2, and DIO3) are involved in regulation of thyroid hormone (T4 (prohormone thyroxine) and T3 (triiodothyronine)) levels. DIO2 catalyzes the conversion of T4 to biologically active T3 whereas DIO1 and DIO3 metabolize both T4 (converted firstly to inactive T3 (rT3)) and T3, thereby diminishing TH signaling (Brent, 2012). Decreased gene expression of deiodinases and thyroid hormone homeostasis imbalance were reported after exposure to glyphosate-based herbicide (Sena et al., 2017). Iodine is crucial for thyroid hormone synthesis and is entrapped into thyrocytes by the sodium/iodide symporter (NIS) (Brent, 2012). Several environmental chemicals may interfere with NIS function and iodine uptake. It has been shown that DDT down-regulate the iodine-accumulation function of thyrocytes by suppressing NIS synthesis and disrupting regular thyroid function (Yaglova and Yaglov, 2015). Another mechanism by which EDCs may interfere with thyroid function, observed for BPA and also for nonylphenol, is inhibition of thyroperoxidase (TPO), enzyme which is essential for thyroid hormone synthesis (Schmutzler et al., 2004).

Moreover, some EDCs have been described to act through the induction of hepatic enzymes involved in hormone metabolism by sulphation and glucuronidation which potentially lead to a decrease in hormone levels. The decline in T4 hormone level after exposure to polybrominated diphenyl ethers (PBDEs) is believed to be an effect of glucuronidation (Boas et al., 2012). Steroid hormone catabolism is particularly affected by EDCs, since many of the xenobiotic-metabolizing enzymes induced by activated AhR (for example, the P450 enzymes CYP1A2, CYP3A4, CYP1A1, and CYP1B1) are also

involved in the catabolism of e.g., steroid hormones. Thus, induction of these enzymes upon exposure to xenobiotics can lead to reduced availability of endogenous hormones, and consequently, influence hormone signaling. Conversely, recent experiments have shown that CYP19B (aromatase), which converts testosterone to estradiol is a direct AhR target gene. Thus, activation of AhR by EDCs can lead both to increased degradation of steroid hormones as well as to higher estradiol production (Swedenborg et al., 2009).

Many hormones, especially hydrophobic ones (steroids and thyroid hormones), are transported by binding proteins in the blood. A number of EDCs directly interfere with hormone-binding transport proteins and thus affect hormone bioavailability. The chemicals exerting their effect through this mechanism exhibit some structural resemblance with the hormones, so that they can compete with them for binding with hormone-binding transport proteins. For example, numerous chemicals have been shown to interact with SHBG (steroid hormone-binding protein) (Hong et al., 2015; Sheikh et al., 2016) and thus, to interfere with steroid hormone transport and concentration in blood. The major serum TH-binding proteins are thyroxine-binding globulin (TBG) and transthyretin (TTR). EDC binding to these carrier proteins disturb even distribution and delivery of the hormone throughout the body (Boas et al., 2012).

Other EDCs affect the biosynthesis or degradation of hormone-binding transport proteins, so that both the total hormone concentration and/or its free active fraction can be affected. For example, PBDEs act through the down-regulation of the transport protein transthyretin (TTR) (Boas et al., 2012) and therefore can influence T4 concentration in the blood.

At target cells, thyroid hormones are probably actively transported across the cell surface via membrane bound transporters. Recently, MCT8/10, OATP-1c1, and System L amino acid transporters have been reported to be TH transporters that regulate T4 and T3 uptake into cells (Heuer and Visser, 2013). Interference of EDCs with these proteins may compromise the bioavailability of thyroid hormones to the nuclear thyroid hormone receptors.

The abundance of receptors can determine the magnitude of the effect produced and also the concentration of hormones in blood. EDCs can alter hormone receptor synthesis (by inducing/inhibiting

gene synthesis), distribution and degradation. Rebuli et al. (Rebuli et al., 2014) reported changes in the expression of ER gene, and receptor distribution in specific regions of the brain after exposure to BPA and suggested that subchronic, low dose BPA exposure may influence sex-specific brain development. Further, it has been shown that exposure to BPA resulted in reduced proteasome- mediated degradation of ER (Masuyama and Hiramatsu, 2004). EDCs can affect receptor abundance by inducing NR proteasome-dependent degradation with the participation of AhR. Both AhR and its heterodimerization partner (ARNT) are a part of a multi-protein complex involved in targeting proteins to the proteasome. Additionally it has been suggested that AhR ligands can interfere with hormonal signaling by targeting hormone receptors to the proteasome (Swedenborg et al., 2009).

The epigenome, which consists of all chemical and structural marks that control the accessibly of the genome, is highly sensitive to environmental conditions including chemical exposures. Recent studies have shown that EDCs can also alter the epigenome. Three mechanisms of epigenetic modification which change gene availability and expression without changing DNA sequences have been identified; acetylation and methylation of DNA and histones and expression of non- coding RNAs (particularly micro-RNAs (miRNAs) - important regulators of post-transcriptional gene expression) (Singh and Li, 2012). Methylation is generally a silencing mark, which acts by blocking access of transcription factors to genes and DNA methyltransferases (DNMTs) are responsible for DNA methylation and demethylation. It has been shown that BPA, BBP, DEHP and pesticides exert their endocrine disrupting activity by altering methylation patterns. Moreover, EDCs can also affect (induce or inhibit) expression of miRNAs, as has been seen for example for PCBs (Topper et al., 2015), BPA (Amir et al., 2021) and phthalates (Singh and Li, 2012). Changes to the epigenome can be heritable and can manifest impact on health and disease even multiple generations after the exposure occurred (Rattan and Flaws, 2019). For example, vinclozolin and methoxylchlor exposure during pregnancy have been shown to decrease fertility in male descendants for up to four generations (Anway et al., 2005). The effects of these chemicals on germ cell genomes make these outcomes heritable.

As described above, EDCs may exhibit many different molecular mechanisms of action. Some of them (such as binding to receptors or hormone transporter proteins) are related to the structural similarity of

chemical compounds to endogenous hormones. Other mechanisms of action, such as inhibition of enzymes related to the synthesis, conversion or degradation of hormones, synthesis or degradation of proteins involved in the transport of hormones or degradation of receptors, are not reserved for compounds with a specific structure. In addition, EDCs with chemical structure similar to endogenous hormones (e.g., BPA similar to estradiol) as well as all EDCs showing a mechanism of action that influence the blood levels of hormones can cause disruptive effects on the feedback regulation of the hypothalamic–pituitary–gonadal/thyroid axis. The results of studies showing that EDCs can influence the epigenome and induce changes, the effects of which can be inherited over many generations are particularly worrying.

2.3. Metabolism of EDCs in human body

The group EDCs is highly heterogeneous and comprises compounds that are very different in terms of size, chemical structure, physicochemical properties, and biotransformation susceptibility. In the human body EDCs are subjected to the two-phase detoxication mechanisms as are other foreign compounds (Reinen and Vermeulen, 2014). Phase I reactions include hydroxylation, hydrolysis, oxidation, and reduction. During these enzymatic reactions, a new functional group is introduced into the molecule, an existing group is modified, or an acceptor site for Phase II reactions is exposed to make the substrate more polar and therefore more readily excreted. The most important enzymes involved in Phase I of metabolism are Cytochromes P450 (CYPs). They are liver microsomal enzymes with monooxygenase activity and are characterized by broad substrate specificity. The multitude of reactions that CYPs can catalyze makes these enzymes highly versatile. Other Phase I biotransformation enzymes are reductases, peroxidases, monoamine oxidases, epoxide hydrolases, oxidoreductases, flavin-containing monooxygenases, xanthine oxidases, dehydrogenases, and carboxylesterases. In Phase II, the parent compound (if it has the appropriate chemical group) or the product of Phase I metabolism is conjugated with a highly water-soluble moiety (e.g. glucuronic acid) to facilitate its removal from the body, usually with bile or urine. In addition to glucuronidation Phase II biotransformation reactions include sulfonation, gluthathione and amino acid conjugation, acetylation, and methylation. Key Phase II

enzymes include UDP-dependent glucuronosyl transferases (UGTs), N-acetyl transferases (NATs), sulfotransferase SULTs, and glutathione S-transferases (GSTs), steroid sulfatase (STS) and catechol-O-methyltransferase (COMT) (Jordan and Woolf, 1987; Woolf and Jordan, 1987).

It has been shown that many different enzymes may be involved in the biotransformation of EDCs (Reinen and Vermeulen, 2014). This is not surprising due to the large numbers of EDCs known and their diverse chemical structure. Moreover, EDCs are characterized by different susceptibility to biotransformation. As a result unchanged mother compounds (BPA), phase I metabolites (PHAH-Ohs, monoester phthalates) as well as glucuronide and sulphate conjugates are detected in human urine (Azzouz et al., 2016; Frederiksen et al., 2007; Reinen and Vermeulen, 2014; Sangeetha et al., 2021).

Metabolism/biotransformation does not always mean detoxification; in some cases, as a result a metabolite with greater biological activity is formed. For example, CYPs can bioactivate PAHs into reactive metabolites that react with DNA. Another pathway by which PAHs can be activated is sulfonation (Reinen and Vermeulen, 2014). It has been shown that dibrominated biphenyls are activated by CYP into very potent estrogenic metabolites that similarly to hydroxylated PCB metabolites inhibit human estrogen sulfotransferase activity (Van Lipzig et al., 2005). In vitro and in vivo studies have shown that the monoester phthalate metabolites are more potent EDCs than the diester parent compounds (Sheikh et al., 2016).

2.4. Elimination of EDCs from the human body

The elimination of EDCs from the human body depends on many factors such as nature of chemical compound, the route of exposure, age, and the health condition of the body. EDCs can be eliminated from the infant and children body, depending on the nature of chemical compound, in unchanged form (as a parent compound) or as a product of metabolism The proportion of parent compound excreted from the body may depend on the route of exposure. For example it was observed that uptake of parabens through the skin resulted in more parent compound excreted in urine compared with oral uptake (Beltifa et al., 2019). Usually, EDCs like parabens, bisphenols and phthalates with half-life times of less than 24 hour considered non-persistent are quickly metabolized and completely excreted from the human body

in urine, feces and sweat (Søeborg et al., 2014). BPA-glucuronide and BPA-sulfate, parabens in native form and their two metabolites (p-hydroxybenzoic acid and p-hydroxyhippuric acid), phthalate monoesters and conjugates are frequently detected in the urine samples. Therefore urine is considered the most appropriate matrix used for biomonitoring and assessment of parabens, bisphenols and phthalates exposure (Geens et al., 2014).

Some EDCs, exemplified by PCBs, OCPs, HCBs, and dioxin, were designed for industrial purposes to have long half-lives and are known as persistent organic pollutants (POPs). The POPs are highly lipophilic and tend to accumulate in the adipose tissue. These persistent EDCs are transferred from mother to infants through breast feeding (Kabir et al., 2015).

Since metabolic and excretion systems in infants are not fully developed, they may suffer from the severe effects of EDCs (EFSA Scientific Committee, 2017).

3. Fetal and early-life exposure to EDCs and its consequence

Since EDCs are common in the environment, bearing in mind their uptake, the mechanism of action and the activity of biotransformation products, it can be expected that their presence will interact with living organisms (Nesan and Kurrasch, 2020). Among humans, the most sensitive to the effects of external factors are human fetuses, infants and children. The reason for this is the fact of their continuous dynamic development, the constant creation of new cells combined with the immaturity of the essential systems in the body. Because of this, any substance that disrupts their function can have a potentially toxic effect. The most studied EDCs with potential long-term human health effects are plastics and plasticizers (bisphenol A and phthalates). BPA is the most commonly produced substance, replaced with bisphenol F (BPF) and bisphenol S (BPS) in some consumer products (Predieri et al., 2022). As summarized in a comprehensive reviews by Ramirez et al. (Ramírez et al., 2022) and Predieri et al. (Predieri et al., 2022) epidemiological studies report that among EDCs with great impact on developmental disorders are also polybrominated flame retardants, pesticides, heavy metals, polychlorinated biphenyls, perfluoroalkyl substances (PFASs) and polycyclic aromatic hydrocarbons. According to the available literature, EDCs show effects on pregnancy and fetal development and long-term effects on the development of the

nervous system, metabolism, maturation process and functioning of the reproductive system. Examples are presented in **Figure 1.**

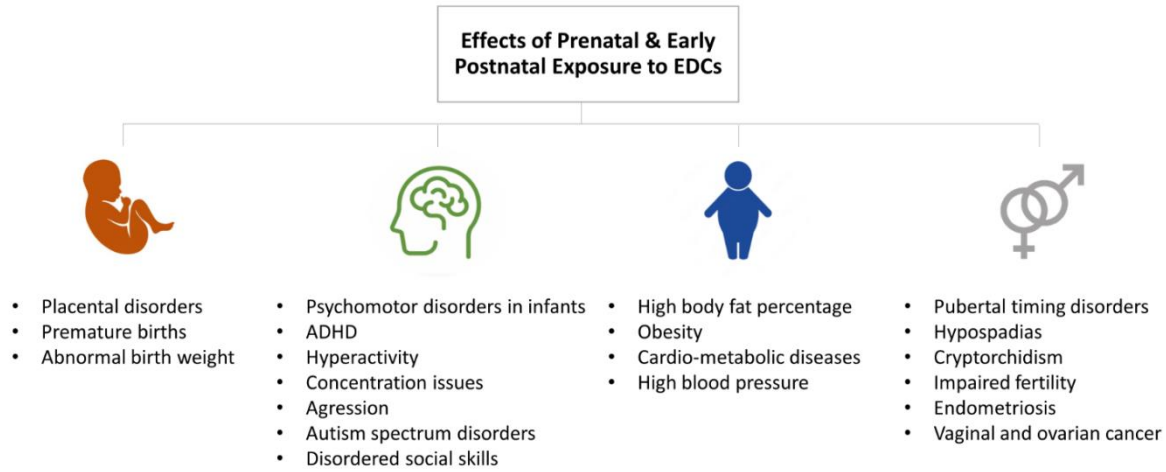


Figure 1. Effects of prenatal and early postnatal exposure (up to 3 years of age) of endocrine disrupting compounds on the development of children

3.1. Fetal growth and gestation length

Homeostasis of growth-regulating systems in the uterus can be modified by various factors, increasing the risk of pathological conditions (Gross et al., 2020; Street and Bernasconi, 2020). Maternal intake of adequate nutrients (carbohydrates, lipids, proteins, minerals, vitamins) and oxygen certainly plays a primary role in this process, as evidenced by the altered fetal growth when the intake of these substances is reduced or excessive. Also, maternal diseases (such as infections, diabetes or autoimmune diseases) and/or poor lifestyle habits of the mother (drugs, tobacco, alcohol) or the use of therapeutic drugs can derail fetal growth. Scientists have begun to look more closely at the effects that EDCs, which are widespread in the environment, can have on the health of both the mother (Varshavsky et al., 2020) and the fetus (Di Renzo et al., 2015; Street and Bernasconi, 2020). Two main issues have emerged from the studies of the effects of EDCs. The first is the issue of the EDCs producing effects at doses much lower than those used in traditional toxicology studies conducted to assess chemical risk (Mallozzi et al., 2016). These low doses can produce effects in organisms that are not predicted from effects observed at very high doses. Second, humans show high vulnerability to exposure to EDCs during critical periods

of development (e.g. gestation) (Predieri et al., 2022). According to the available literature, EDC substances affect all stages of pregnancy, from conception to delivery, as well as the health of the newborn (Predieri et al., 2022; Street and Bernasconi, 2020). Moreover, exposure to EDCs during the early life stage can cause epigenetic shifts (besides other effects) on protein content, cell number, cell size, organ size, and function. These changes can be transmitted over several generations as "non-transmissible diseases" (Rager et al., 2020).

Epidemiological studies also reported correlations between *in utero* exposure to major EDCs and birth outcomes. For example, back in 2010, data was published for Mexico showing that women who gave birth before 37 weeks gestation (i.e. classified as premature babies) had significantly more BPA and phthalates in their blood than those women who gave birth on time (Cantonwine et al., 2010; Meeker, 2012). Also, looking at more recent research results, one can see recurring relationships in terms of the effects of EDCs on fetal development and pregnancy in different countries of the world. A large-scale prospective study from 13 European cohorts suggested that exposure to one or more EDCs groups was associated with a higher risk of low birth weight (LBW) in newborns (Street et al., 2018). The risk increased with the increasing number of different EDCs suggesting a possible exposure-response relationship. Conversely, higher concentrations of persistent organic pollutants (POPs) measured in newborn dried blood spots were found to be positively associated with a slightly higher risk of larger than expected size for gestational age and higher birth weight (Bell et al., 2019). Therefore, the problem of the effect of EDCs on fetal development is complex. This is because EDCs also interact with each other, entering into competitive interactions with elements of the endocrine system. Due to this the composition of the EDCs mixture to which the pregnant woman is exposed is also important. The effect of PCBs exposure, for example, may be different from that of a mixture of PCBs and PFAS (Pearce et al., 2021). Combinations exhibiting higher levels of polybrominated diphenyl ethers and p,p'-1,1,1-trichloroo-2,2-bis(4-chlorophenyl)-ethene (p,p'-DDE) were associated with lower birth weight, while combinations with higher levels of PCBs and PFAS were associated with increased birth weight. Also, serum levels of PCBs and p,p'-DDT/DDE were measured in a German cohort of 324 pregnant women (Krönke et al., 2022). In this case neonatal birth length (the size of the baby) was negatively correlated

with elevated levels of maternal PCBs. Positive associations were observed between different levels of maternal PCBs and weight gain at birth.

As mentioned earlier, the effects of BPA and phthalates on pregnancy are also widely reported in the literature. However, there is a lack of a single coherent study on the subject, although a number of diverse papers are available. Combined exposure to BPA from dietary and non-dietary sources during pregnancy may contribute to a trend toward fetal growth restriction (Vrachnis et al., 2021). Also, high levels of BPA in maternal blood, urine or amniotic fluid have been associated with lower neonatal birth weight (Street et al., 2018). Moreover, exposure to unconjugated BPA in the 1st trimester and at the end of pregnancy was associated with a sex-dependent reduction in birth weight. In addition, early BPA exposure was shown to be negatively correlated with intrauterine linear growth. According to Predieri et al. (Predieri et al., 2022) the increase of BPA/creatinine concentration in maternal urine (tested in the 3rd trimester) may be associated with a decrease in femur length. However, in this case an increase of BPA/creatinine concentration was correlated with increased birth weight.

Phthalate exposure during pregnancy may be also associated with increased odds of prematurity. Possible mechanisms are interference with placental function and steroidogenesis (Iughetti et al., 2020). Moreover, phthalates may have trimester-specific and sex-specific effects on fetal growth and birth outcomes. It was demonstrated by Li et al. (Li et al., 2021) (in their all trimesters comprehensive study) that the 1st-trimester urinary DEHP level was negatively related to fetal growth of males, the 2nd-trimester DEHP was negatively related to their birth weight and length, and the 3rd-trimester DEHP was positively associated with birth weight of boys. Among females, the 1st-trimester DEHP was associated with increased birth length.

The pesticides may have some negative effects on fetal growth and gestation length. Pesticide exposure during the 2nd-trimester of pregnancy was negatively associated with weight, length, and head circumference at birth (Gore et al., 2015). However, prenatal exposure to pesticides, like other EDCs, can also affect birth outcomes in a variety of ways, which was confirmed by studies held in Japan and France (Béranger et al., 2020; Matsuki et al., 2020).

Fetuses exposure to PFAS may also lead to decreased birth weight, according to Predieri et al. (Predieri et al., 2022). For example, high concentrations of perfluorooctane sulfonic acid (PFOS) and perfluorohexanesulfate measured in newborn dried blood spots were demonstrated to be related to lower birth weight scores compared to those with low concentrations (Gross et al., 2020). Furthermore, increased concentration of PFOS, perfluorooctanoic acid (PFOA), perfluorononanoic acid, perfluorodecanoic acid, and perfluoroundecanoic acid levels in maternal serum during pregnancy were associated with lower birth weight and SGA at birth (Wikström et al., 2020). However, in this case the associations were significant only in girls.

Also in case of PBDEs studies reported correlations with birth weight. In case of study by Street et al. (Street et al., 2018) the differences between sexes were significant – for the males the correlation was negative, in case of females it was positive. In a study conducted by Yu Ting et al. (Yu Ting et al., 2020)19 PBDEs were detected in maternal serum samples collected during the third trimester of pregnancy and were negatively associated with placental size and birth outcomes. Concentrations of BDE-207, -208, -209 and total 19 PBDEs were higher in newborns with fetal growth restriction compared to healthy ones.

The presence of EDCs in a pregnant woman's body, and consequently her baby's body, can cause not only pregnancy-related problems, but also long-term effects on the functioning of the nervous system (**Section 3.2.),** immune and metabolic balance (**Section 3.3.**), and reproductive system (**Section 3.4.**). The consequences on the child's development are described in the following sections of this paper.

3.2. Effects of EDC on childhood neurodevelopment

Available scientific studies indicate that exposure to EDCs causes severe effects on human nervous system, due to the ability of these compounds to cross placental and blood-brain barriers (Ghassabian and Trasande, 2018; Ramírez et al., 2022). Given that pregnancy and early childhood are the most crucial stages for the proper development and function of the neuroendocrine system, both prenatal and postnatal exposure to EDCs becomes a matter of great concern. Also, puberty may be an important

period of vulnerability to the harmful effects of EDCs due to the high neuroendocrine activity that takes place during this period (Lucaccioni et al., 2020).

Exposure to low doses of neurotoxicants during these key developmental periods can lead to permanent brain damage that can affect quality of life, learning ability, memory and neurotic behavior, and increase the risk of adverse effects later in life (Grandjean and Landrigan, 2015; Ramírez et al., 2022). The neurotoxic effects of EDCs depend mainly on the type of disruptor, time of exposure, dose and duration of exposure (Gore et al., 2019; Parent et al., 2011). EDCs can exert their neurotoxic activity through multiple mechanisms. For example, interaction with nuclear hormone receptors such as estrogen receptors, androgen receptors and thyroid receptors, while hypothalamic-pituitary-thyroid (HPT) axis is known to play an essential role in perinatal brain development (Kabir et al., 2015). Therefore, early exposure to TH-disrupting EDCs is thought to be a risk factor for increased incidence of developmental disorders (Ghassabian and Trasande, 2018). Also, exposure to EDCs in general induce changes in the levels, transport and receptors of certain neurotransmitters, including dopamine, serotonin, glutamate and gamma-aminobutyric acid (Nesan and Kurrasch, 2020). Another possible mechanism of action of EDCs would be disruption of the neuroimmune system. For example, mercury species can suppress or activate immune-inflammatory pathways (Morris et al., 2018).

3.2.1. Psychomotor functions of babies

Literature data indicate that exposure of young children to POPs can cause impairments in their psychomotor development (Klocke and Lein, 2020). For example, a few available studies have evaluated the neurotoxic effects of PCB-153 (2,2′,4,4′,5,5′-hexachlorobiphenyl). With regard to cognitive deficits, exposure to PCB 153 in breast milk was found to result in impaired psychomotor development at 24 months of age (Lynch et al., 2012). Performed study assessed sensory and perceptual abilities, memory, problem solving, learning and early verbal skills. Moreover, the physical activities that require the use of both large (such as sitting and walking) and small motor skills (such as lifting small objects) were taken into consideration. The same test was applied in study by Verner (Verner et al., 2010), where infants and babies between 1 to 11 months old were observed to be more active at 11 months when

exposed to PCB-153, which indicates a differentiated mechanism of action of PCBs depending on the interacting environment and possible associated substances.

Also, pesticides have been observed to alter children's cognitive development. For example, for 3-moths-olds, where the organophosphates and pyrethroid exposure was measured for both pre- and postnatal development phase, postnatal urinary metabolites significantly impacted mental skills of the babies (Fluegge et al., 2016). For children this young, no effect on motor development has been observed. Also in paper by Kao et al. (Kao et al., 2019) it was indicated that levels of DDT and trans-CHL (trans-chlordane) are associated with lowering cognitive abilities, early language and socio-emotional skills in babies between 10 and 12 months of age. Eskenazi et al. (Eskenazi et al., 2007) performed a study, where the effect of total pesticides prenatal and postnatal exposure (to 2 years of age) on the babies neurodevelopment was measured. Prenatal exposure to organophosphates significantly increased the risk of persuasive developmental disorder at 2-year-olds (e.g. autism spectrum disorders), which is in agreement with a review article by Moosa et al. (Moosa et al., 2018). Similar results were obtained by Liu et al. (2016) and by Guo et al. (2019) (Guo et al., 2019)(for 3 year-olds), also covering problems in children's motor development. In most cases a more significant development delay was observed among boys.

Also available in the literature are studies indicating that exposure to PBDEs in the pre- and postnatal period is not without effects on the development of psychomotor functions in infants and young children. For example, higher BDE 209 levels in mother’s breast milk showed a significant association to lower mental scores in children aged from 8 to 12 months. However, exposure to BDE 196 was positively correlated with verbal development (Chao et al., 2011). Similarly, both in work by Hoffman (Hoffman et al., 2012) and Adgent (Adgent et al., 2014) it is indicated that increased level of total PBDEs in breast milk can positively influence language and motor skills in children at the age of 30-36 months. However, it was also indicated that particular BDEs can still cause severe issues with anxiety, withdrawal behaviors (BDE 99 and 28) and impulsivity (BDE 47).

3.2.2. Further neurobehavioral changes

Many of the available research findings also point to possible effects of prenatal and early postnatal EDC exposure on further children's neurobehavioral development. In the case of PCBs, some of the most extensively studied EDCs, consistent relationship was found between attention problems and hyperactivity (Verner et al., 2015). An observation in this study was performed on 2 month-olds to 5-year-olds. The same team performed study on the possible relationship between PCB-153 serum level and the development of disorders like ADHD or impulsive behavior, where both these issues were confirmed (Verner et al., 2015). This study covered 8 years from the lives of children who were exposed to PCBs from fetal life.

With regard to ADHD, a prospective Norwegian cohort study addressed postnatal exposure by determining pesticides hexachlorobenzene (HCB), beta-hexachlorocyclohexane (β-HCH), p,p'-DDT, p,p'-DDE and oxychlordane in breast milk and blood of infants collected two months after birth and during first two years of life (Lenters et al., 2019). From all tested children, 55 of them (4.6%) were diagnosed with ADHD around the age of 14 years old. Interestingly, a strong association of early exposure to β-HCH was found with an increased risk of ADHD, while DDT appeared to decrease the risk. In many of the remaining cases suspected ADHD was noted, but it is not known what diagnoses were made after the described studies were completed. At the same time, the wide pool European study made by Forns et al. (2018) shows no correlation between pre- and postnatal exposure to pesticides and a diagnosis of ADHD. Thus, the effect of pesticides on the incidence of ADHD in children is not clearly defined. According to more general influence of early pesticides exposure to long-term neurodevelopment of children, these compounds have a negative effect on verbal comprehension and working memory, which was observed among group of almost 300 tested children (Viel et al., 2015).

PBDEs pre- and postnatal exposure have also been shown to be associated with decreased ability to concentrate, but also low social skills of 4-year-olds (Gascon et al., 2011). Moreover, Vuong et al. (2019, 2018, 2017a, 2017b) conducted a study on the effects of PBDEs on the development of children of different ages (1, 2, 3, 5 and 8 years old). An increase in BDE 153 at 3 year-olds was significantly associated with increased risk of metacognition dysfunction. Further, toddlers exposure to BDE-153 was associated with decreased concentration and attention in children aged 6 years and older. In

addition, exposure to multiple PBDE congeners was associated with increased hyperactivity and aggressive behavior at age 8. Especially higher BDE 153 and 28 levels were correlated with a significant impairment in behavioral regulation, emotional and impulse control at 8 years of age. Also, differences between sexes were observed, where males showed higher functioning problems with higher BDE 153, compared to females.

There is not much information about the influence of heavy metals early exposure (prenatal and postnatal to 2nd-3rd year of live) and it long-term consequences towards the nervous system. According to a paper by Liu et al. (Liu et al., 2018) increased level of Pb in blood may negatively affect cognitive and language skills of 3-year-olds, whereas there is no correlation with Cd level.

Interesting findings were published in 2020 on the impact of children's prenatal exposure to different EDCs vs. their IQ at age 7 (Tanner et al., 2020). Early prenatal exposure to a mixture of suspected EDCs was related to lower levels of cognitive functioning, particularly among boys. Bisphenol F made the largest contribution to the mixture effect estimate, suggesting that BPA replacement analogues may not be any safer.

3.3. Obesity and metabolism diseases

Obesity is a multifactorial disease caused by a disruption of the balance between the amount of calories consumed and energy used (Casals-Casas and Desvergne, 2011; Predieri et al., 2022). It is largely influenced by genetic predisposition and environmental factors, including EDCs. Studies reported data related to the association between exposure to EDCs during pregnancy and birth weight combined with fast weight gain in early childhood, underlining the risk to develop overweight, obesity and other diseases later in life due to altered "programming" *in utero* (Iughetti et al., 2015). Moreover, metabolic diseases are among the most well-known health effects of human exposure to EDCs (Gutiérrez-Torres et al., 2018). For example, prenatal exposure to low concentrations of EDCs has implications for cardio-metabolic risk factors in preschool children. Also, "obesogens" EDCs are risk factors for type 2 diabetes and certain EDCs may directly cause defects in insulin (INS) production and secretion even without

affecting the weight. Moreover, EDCs can disrupt body glucose homeostasis by affecting both INS- and glucagon-secretory cells (Alonso-Magdalena et al., 2021; Iughetti et al., 2015; Street et al., 2018).

Regarding the impact of specific examples of EDCs on the development of obesity and related diseases, studies suggested that *in utero* exposure to p,p'-DDT, p,p'-DDE, and HCB, may increase the risk for rapid weight gain in infancy and high body mass index (BMI) later in childhood and during puberty (Warner et al., 2017). According to Guil-Oumrait et al. (Güil-Oumrait et al., 2021) HCB exposure was also associated with higher BMI, and weight-to-height ratio and a continuous increase in HCB levels were associated with higher body fat percentage and diseases like systolic and diastolic blood pressure, cardio-metabolic-risk and lipid biomarkers. Also, association between *in utero* POPs exposures and major risk factors for the adult cardio-metabolic syndrome was reported (Güil-Oumrait et al., 2021). Similar observations were made for PFAS, PCBs, propylparabens and pesticides, where prenatal exposure to these EDCs caused increased body weight of the baby in the postnatal phase (Berger et al., 2021; Lauritzen et al., 2018; Marks et al., 2021). However, there are some exceptions, like study by Guo et al. (Guo et al., 2020) where serum levels of BDE-153 and -154 in cord blood have been associated with reduced rates of obesity at seven years of age.

Obesity in children has been reported to be induced by exposure to phthalates during pregnancy. Certain phthalates and their metabolites in maternal urine were strongly associated with BMI scores, waist circumference, percent body fat in children of different ages, low-density lipoprotein cholesterol, triglyceride and glycaemia (Golestanzadeh et al., 2019; Harley et al., 2017). In a population of 12-year-olds, *in utero* levels of the metabolites diethyl phthalate, dibutyl phthalate and DEHP were positively associated with overweight or obesity (Miura et al., 2021). It is stated that differential DNA methylation may link phthalate exposure *in utero* to fetal growth, having a predictive value for child's obesity.

Also *in utero* exposure to POPs seems to determine permanent physiological changes influencing birth weight, pre-disposing to subsequent weight gain. POPs have direct effects on insulin signaling leading to insulin resistance that causes adipose tissue inflammation (Iughetti et al., 2015). Moreover, an association was found between gestational BPA levels and central obesity in early childhood (Braun et al., 2019). Maternal urinary BPA levels were associated with a higher risk of central obesity for the

children, and a positive association of dietary exposure to BPA (Mustieles et al., 2019). BPA exposure during prenatal period was also associated with increased blood pressure in girls and plasma glucose level in boys (Ouyang et al., 2020).

However, referring to the review paper by Predieri et al. (Predieri et al., 2022) it should be noted that not all data on the impact of EDCs on obesity and obesity-related diseases are conclusive. Again, as mentioned in other chapters, the mechanism of effect of EDCs on the child's body before and after birth is complex and must be considered on a case-by-case basis.

3.4. Reproductive health

Fetal and early-life exposure to EDCs may also cause severe issues in reproductive system and further pubertal development (Predieri et al., 2022). These are described in this Section.

3.4.1. Maturation

In utero exposure to some metabolites of phthalates and BPA has been linked to delayed sexual maturation in women, especially those of normal weight, and premature sexual maturation in men, especially those who are overweight/obese, emphasizing that body weight can also interfere with such associations (Berger et al., 2018). This was confirmed by Berman et al. (Berman et al., 2021), who proved that age of menarche was found to be slightly delayed in girls with higher prenatal exposure to phthalate metabolites. Depending on the sum of phthalate metabolites, the age of menarche was found to be significantly later in subjects from the middle tercile of concentrations compared to those from the lowest tercile. There is also limited evidence on the potential impact of PFAS exposure on long-term reproductive health, but gender-specific alterations of pubertal timing with different prenatal exposure to PFASs were suggested (Predieri et al., 2022). Later age of menarche with higher levels of prenatal PFOA exposure were reported, but with no particular explanation. The effects of BFRs on pubertal development were evaluated in girls exposed *in utero* to polybrominated biphenyls (PBBs) and through breastfeeding. In this case girls exposed *in utero* to high concentrations of BFRs and breastfed had menarche one year earlier than girls not exposed or exposed only *in utero* but not breastfed. Perinatal exposure was associated with early puberty in breastfed girls (Lucaccioni et al., 2020; Street and Bernasconi, 2020). These results support the hypothesis that total pubertal development may be

717 influenced by pre- and postnatal exposure to organochlorine compounds. Also, since menarche and
718 breast development are estrogen-dependent, while pubic hair development is independent of estrogen
719 levels, these data suggest that PBBs may act through different pathways. Likewise, associations between
720 prenatal and childhood exposure to PBDEs and changes in pubertal development were indicated
721 (Lucaccioni et al., 2020; Street and Bernasconi, 2020). Concentrations of four PBDEs (BDE- 47, -99, -
722 100, -153) were determined in serum taken from mothers during pregnancy, and the onset of puberty
723 was assessed in their 9-year-old children, who were followed until age 13. According to this study
724 prenatal concentrations of PBDEs were associated with delayed menarche in women.

725 *3.4.2. Male reproductive system*

726 Hypospadias and cryptorchidism were related to EDCs since the first studies led to the hypothesis of the
727 testicular dysgenesis syndrome (Predieri et al., 2022). EDCs seem to act on the tubular part of the
728 testicle, which does not develop regularly and is at subsequent risk of cancer, and the endocrine part
729 with consequent lower production of testosterone and other endocrine factors necessary to ensure the
730 normal testicular descent in the scrotum and the normal penile formation. Several examples of the effect
731 of EDCs on such conditions are available in the literature. However, a full study on this topic is still
732 lacking. The results of a research published by Fisher et al. (Fisher et al., 2021) indicate that maternal
733 serum BPA levels at 10-17 weeks of gestation were positively associated with congenital or postnatal
734 acquired cryptorchidism. Also prenatal exposure to dioxins and chlorinated pesticides can result in
735 cryptorchidism (Gore et al., 2015). In addition, high rates of hypospadias have been reported in children
736 whose mothers were exposed to phthalates and their metabolites during the first or second trimester of
737 pregnancy (Jensen et al., 2015; Ormond et al., 2009). In the case of PFAS, maternal exposure was
738 associated with decreased anogenital distance in boys, providing evidence that they may affect male
739 genital development (Tian et al., 2019).

740

741 *3.4.3. Female reproductive system*

742 Compared to the effects of prenatal, perinatal and postnatal exposure to EDCs on the male reproductive
743 system, the female reproductive system is not as widely described. Most of the available literature has

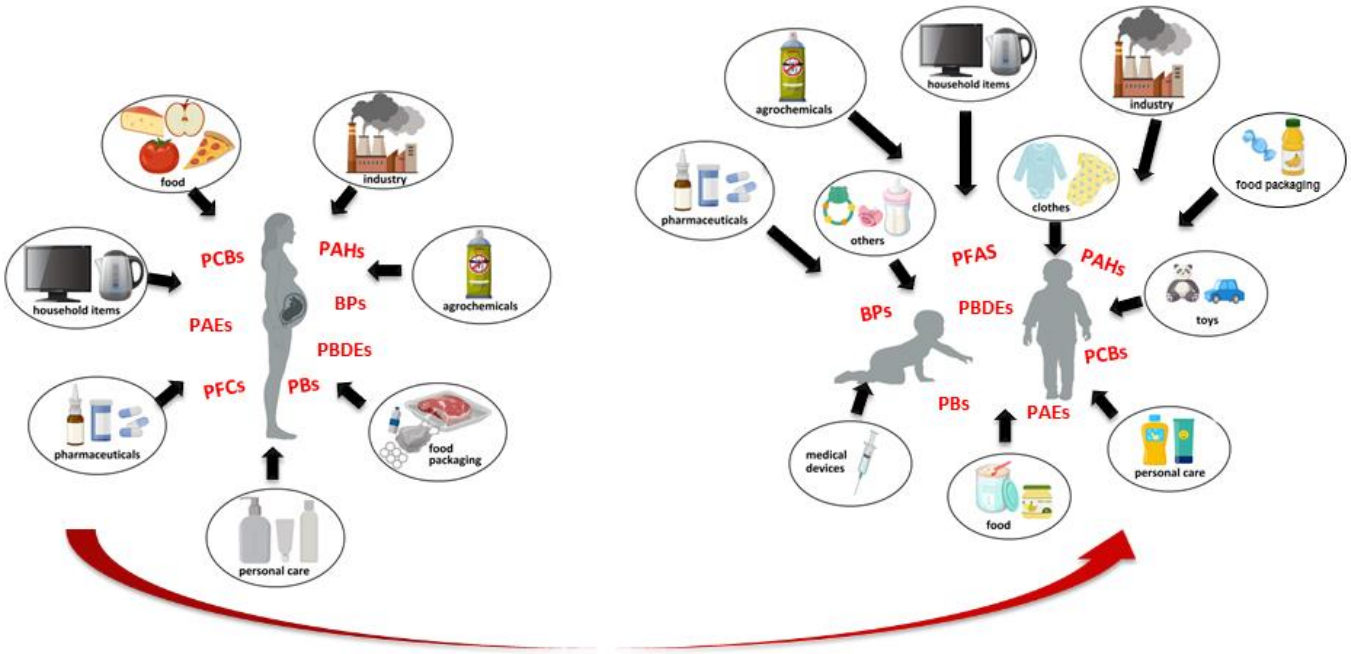
744 focused attention on delayed or early puberty, but there are few items describing possible diseases and
745 physiological dysfunctions associated with early exposure to EDCs. This is due, among other things, to
746 the great complexity of the functioning of the female reproductive system and the multitude of factors
747 affecting its proper functioning. For example, it is well known that during pregnancy the human fetal
748 adrenal glands (both male and female) are essential for the production of steroid hormones. However, it
749 is the female hypothalamic-pituitary-adrenal axis that appears to be more susceptible to programming
750 in early life than the male, and thus potentially to EDCs (Carpenter et al., 2017). Yet, it is still unclear
751 how exactly this affects the programming of the reproductive system in women.

752 What is known is that a woman's reproductive health is largely determined during embryonic and fetal
753 development, and later in adolescence (Van Duursen et al., 2020). Disorders of the female reproductive
754 system in adulthood can be attributed to disturbances in hormone levels and function during *in utero*
755 development, what was clearly demonstrated in the "DES disaster," where overt reproductive effects
756 were described in children born to women taking the synthetic estrogen diethylstilbestrol (DES) as a
757 drug during pregnancy (Patisaul, 2021). Adverse health effects included a rare form of vaginal cancer
758 in girls, an increased incidence of uterine fibroids, endometriosis, impaired fertility and an earlier age
759 of onset of menopause (Van Duursen et al., 2020). Surprisingly, reproductive effects are still seen in
760 women whose mothers were prenatally exposed to DES (Titus et al., 2019).

761 At birth, there are about 300,000 primary follicles containing eggs or oocytes per ovary, which
762 constitutes the ovarian reserve. A woman’s ovarian reserve is finite, which means that lost oocytes
763 cannot be replaced, which is a major factor limiting human reproduction. The possible actions of EDCs
764 such as BPA and DEHP on the developing oocytes and ovary have been described in a review by
765 Johansson et al. (Johansson et al., 2017). The likely influence of EDCs on the formation of ovarian
766 abnormalities, defects in the resulting oocytes and an increased risk of cancer in the reproductive system
767 have been pointed out. However, the female reproductive system is very different in the embryo, fetus,
768 newborn, young girl, teenager and adult woman. Consequently, the final effects of EDCs exposure on
769 the female reproductive system depend on the age of the woman and the exact life stage at which the
770 exposure occurred.

4. Sources of exposure

Humans are continuously exposed to a cocktail of both natural and anthropogenic chemicals with endocrine-disrupting potential through diet, inhalation, or dermal absorption. Naturally occurring compounds such as metals, metalloids, and polyaromatic hydrocarbons occur in the surrounding environment mainly as a result of metal mining and the combustion of fossil fuels. Whereas anthropogenic chemicals are commonly used in agricultural practices or are released from many different materials and products. Many EDC are currently used in a wide range of consumer goods, including personal care products, food containers and other plastic products, household items, cookware, pharmaceuticals, medical supplies, furniture, and building materials (Padmanabhan et al., 2021; Plante et al., 2022). Moreover, they are also used in the production of many products intended for infants and children (plastic bottles, teeters, toys, clothes, and food) (Kiess et al., 2021). Among the most frequently identified endocrine active compounds in such products can be distinguished: bisphenols (BPs), phthalates (PAEs), benzophenones (BPs), PCBs, polyfluorinated compounds (PFCs), parabens, and PBDEs. **Figure 2** shows different sources of EDC exposure for both adults and children. It should be borne in mind that exposure to EDC compounds begins at the stage of prenatal development and lasts until the end of life. Whereas, the uptake of EDCs varies according to age and depends on many factors, such as culture, socio-economic status, level of education, lifestyle factors, and food habits (Caspersen et al., 2016; Martina et al., 2012). Below, the different sources of exposure for both pregnant women and babies will be discussed.



793

794 **Figure 2.** Schematic representation of different sources of exposure for both pregnant women and
795 babies.

796

797 ***4.1. Prenatal exposure***

798

799 The placenta is an important selective barrier to toxicants during pregnancy, however, nowadays it
800 is known that some EDCs can be transferred to the fetus by interfering with placental transport systems.
801 Several previous studies have reported that certain endocrine active compounds can pass the placental
802 barrier (Song et al., 2020a). Thus, prenatal exposure of pregnant mothers to EDCs is directly correlated
803 with fetal exposure to these chemicals. The mechanism of crossing the placental barrier of chemicals
804 depends on many factors such as molecular size, protein binding capacity, or lipophilicity hence is not
805 fully recognized so far. However, because EDCs are mostly lipophilic, passive diffusion appears to be
806 the most likely mechanism (Kawa et al., 2021; A. Li et al., 2019; Zhang et al., 2022). Several mother-
807 infant pair studies have reported the occurrence of EDCs in cord serum and amniotic fluid indicating
808 transplacental transfer of xenobiotics from mother to fetus. In **Table 2**, there are summarized examples

of compounds detected in maternal samples as well as placenta, cord plasma, and amniotic fluid, indicating transplacental transfer.

Based on the data presented in the table, it can be concluded that, generally the xenobiotic levels detected in cord plasma is similar or lower than those reported for maternal plasma. Whereas in the case of amniotic fluid, the detected level is higher in most cases. What could be particularly unfavourable due to this fluid surrounds the unborn baby throughout the entire period of pregnancy (Shekhar et al., 2017).

Table 2. EDCs concentration levels in a placenta, cord plasma, amniotic fluid, breast milk, urine, and blood of pregnant women.

Class of EDC	Compound	Maternal urine	Maternal plasma	Maternal serum	Placenta	Cord plasma	Amniotic fluid
Bisphenols	BPA	T_1 13.04 [ng/mL] T_2 8.38 [ng/mL] (Huang et al., 2019)	5.83 [ng/mL] (Shekhar et al., 2017)	T_1 <MDL - 67.6 [ng/mL] T_3 0.71 - 11.6 [ng/mL] (Foster et al., 2019)	<LOD-43.2 [µg/L] (J. Lee et al., 2018)	1.7 [ng/mL] (Zhang et al., 2020)	5.87 [ng/mL] (Shekhar et al., 2017)
		T_1 0.06 [ng/mL] T_3 0.07 [ng/mL] (Foster et al., 2019)	0.023-0.084 [ng/mL] (Kolatorova et al., 2018)	0.5 [ng/mL] (Zhang et al., 2020)	26.0−908 [pg/g] (Pan et al., 2020)	0.049-0.30 [ng/mL] (Kolatorova et al., 2018)	0.2 [ng/mL] (Zhang et al., 2020)
		T_1 2.37±4.02 [µg/L] T_3 2.70±5.79 [µg/L] (Wang et al., 2021)	113−416 [pg/g] (Pan et al., 2020)	0.44-47.1 [µg/L] (J. Lee et al., 2018)	1.30 [ng/g w.w.] (Freire et al., 2020)	54.0−253 [pg/g] (Pan et al., 2020)	
		1.85 [ng/mL] (Chen et al., 2022)					
		0.3–61.8 [µg/L] (Casas et al., 2016)					

		T_2 35.22 [µg/L] (Martínez-Ibarra et al., 2019)				
	BPS	T_1 4.43 [ng/mL] T_3 4.60 [ng/mL] (Huang et al., 2019)	<LOD−54.7 [pg/g] (Pan et al., 2020)	0.01 [ng/mL] (Zhang et al., 2020)	<LOD−66.8 [pg/g] (Pan et al., 2020)	0.03 [ng/mL] (Zhang et al., 2020)	0.02 [ng/mL] (Zhang et al., 2020)
		T_1 0.82±2.09 [µg/L] T_3 0.73 ± 2.08 [µg/L] (Wang et al., 2021)				<LOD−31.3 [pg/g] (Pan et al., 2020)	
	BPF	T_1 2.46±6.98 [µg/L] T_3 2.29±5.25 [µg/L] (Wang et al., 2021)	<LOD−257 [pg/g] (Pan et al., 2020)		<LOD−89.2 [pg/g] (Pan et al., 2020)		
Phthalates	MEP	21.9–5115.1 [µg/L] (Casas et al., 2016)		3.11 [ng/mL] (Assens et al., 2019)			20.88 ± 31.12 [µg/mL] (Golestanzadeh et al., 2022)
		T_1 9.97 [ng/mL] T_3 13.51 [ng/mL] (Grindler et al., 2018)		<LOD-21.07 [ng/mL] (Henriksen et al., 2020)			
		T_1 11.12 [ng/mL]					

	T_3 10.32 [ng/mL] (Han et al., 2020)		
	T_1 37.6 ± 3.8 [µg/L] T_3 42.1 ± 4.5 [µg/L] (Shaffer et al., 2019)		
MnBP	3.4–402.6 [µg/L] (Casas et al., 2016)	1.27 [ng/mL] (Assens et al., 2019)	2.4-24.5 [µg/L] (Katsikantami et al., 2020)
	T_2 101.3 [µg/L] (Martínez-Ibarra et al., 2019)	<LOD-463 [ng/mL] (Henriksen et al., 2020)	20.88 ± 31.12 (Golestanzadeh et al., 2022)
	T_1 42.97 [ng/mL] T_3 55.63 [ng/mL] (Grindler et al., 2018)		
	T_1 8.3 ± 2.4 [µg/L] T_3 9.7 ± 2.7 [µg/L] (Shaffer et al., 2019)		

MEHP	T_2 12837 [µg/L] (Martínez-Ibarra et al., 2019) T_1 2.5 ± 2.5 [µg/L] T_3 2.1 ± 2.4 [µg/L] (Shaffer et al., 2019)	3.07 [ng/mL] (Assens et al., 2019) <LOD-32.2 [ng/mL] (Henriksen et al., 2020)	
MCOP	T_1 19.3±3.5 [µg/L] T_3 16.0±3.3 [µg/L] (Shaffer et al., 2019)	<LOD-7.58 [ng/mL] (Henriksen et al., 2020)	
MBzP	T_2 1.86 [µg/L] (Martínez-Ibarra et al., 2019)	<LOD-73.8 [ng/mL] (Henriksen et al., 2020)	8.89 ± 7.22 [µg/mL] (Golestanzadeh et al., 2022) 11.6-20.2 [µg/L] (Katsikantami et al., 2020)
ΣDEHP	T_1 198.2 [ng/mL] T_3 159.3 [ng/mL] (Grindler et al., 2018)	7.44 [ng/mL] (Assens et al., 2019) <LOD-16.0 [ng/mL] (Henriksen et al., 2020)	

	MeP	T_1 1.4-4770.7 [µg/L] (Bellavia et al., 2019)	8.04 [ng/mL] (Shekhar et al., 2017)	<0.01-10 [ng/mL] (Song et al., 2020b)	1.45 [ng/g w.w.] (Freire et al., 2020)	0.066-4.14 [ng/mL] (Kolatorova et al., 2018)	8.69 [ng/mL] (Shekhar et al., 2017)
		T_1 18.06 [µg/L] T_3 12.16 [µg/L] (Liu et al., 2019)	0.18-1.62 [ng/mL] (Kolatorova et al., 2018)		0.10-11.69 (Fernández et al., 2016)	<0.01-9.5 [ng/mL] (Song et al., 2020b)	<0.01-2.7 [ng/mL] (Song et al., 2020b)
		T_1 20.76 [µg/L] T_3 11.24 [µg/L] (Jiang et al., 2019)					
Parabens		132.43 [ng/mL] (Chen et al., 2022)					
		T_1 15.37 [ng/mL] T_3 9.82 [ng/mL] (J. Li et al., 2019)					
	EtP	T_1 0.66 [µg/L] T_3 0.4 [µg/L] (Liu et al., 2019)	2.27 [ng/mL] (Shekhar et al., 2017)	<0.01-6.5 [ng/mL] (Song et al., 2020b)	0.29 [ng/g w.w.] (Freire et al., 2020)	<0.01-6.4 [ng/mL] (Song et al., 2020b)	2.30 [ng/mL] (Shekhar et al., 2017)
		T_1 0.55 [µg/L] T_3 0.39 [µg/L]					<0.01-0.26 [ng/mL] (Song et al., 2020b)

	(Jiang et al., 2019) T_1 0.51 [ng/mL] T_3 0.53 [ng/mL] (J. Li et al., 2019)			0.20-5.49 (Fernández et al., 2016)		
PrP	T_1 <LOD –621 [µg/L] T_2 <LOD –2291 [µg/L] (Bellavia et al., 2019)	9.14 [ng/mL] (Shekhar et al., 2017)	<0.01-1.8 [ng/mL] (Song et al., 2020b)	0.27 [ng/g w.w.] (Freire et al., 2020)	0.046-0.78 [ng/mL] (Kolatorova et al., 2018)	10.76 [ng/mL] (Shekhar et al., 2017)
	T_1 1.10 [µg/L] T_3 0.61 [µg/L] (Liu et al., 2019)	0.031-0.24 [ng/mL] (Kolatorova et al., 2018)		0.20-4.52 (Fernández et al., 2016)	<0.01-2.6 [ng/mL] (Song et al., 2020b)	<0.01-1.1 [ng/mL] (Song et al., 2020b)
	T_1 1.02 [µg/L] T_3 0.4 [µg/L] (Jiang et al., 2019)					
	26.78 [ng/mL] (Chen et al., 2022)					
BuP	0.61 [ng/mL] (Chen et al., 2022)		<0.01-0.47 [ng/mL] (Song et al., 2020b)		<0.01-0.52 [ng/mL] (Song et al., 2020b)	2.37 [ng/mL] (Shekhar et al., 2017)

			1.96 [ng/mL] (Shekhar et al., 2017)	0.20-1.60 (Fernández et al., 2016)		<0.01-0.033 [ng/mL] (Song et al., 2020b)
Phenols	BP-1	T_1 0.34 [µg/L] T_2 0.24 [µg/L] T_3 0.20 [µg/L] (Jiang et al., 2019)		<LOD – 4.37 [ng/mL] (Krause et al., 2018)	<0.02–52.0 [ng/mL] (Song et al., 2020a)	<LOD-3.38 [ng/mL] (Krause et al., 2018)
		<LOD – 665 [ng/mL] (Krause et al., 2018)				
		T_1 0.31 [ng/mL] T_3 0.19[ng/mL] (J. Li et al., 2019)				
	BP-3	T_1 0.75 [µg/L] T_3 0.38 [µg/L] (Jiang et al., 2019)		<LOD – 71.8 [ng/mL] (Krause et al., 2018)	<0.01–56.6 [ng/mL] (Song et al., 2020a)	<LOD-11.6 [ng/mL] (Krause et al., 2018)
		<LOD – 10034 [ng/mL] (Krause et al., 2018)				
		T_1 0.52 [ng/mL]				

		T_3 0.29 [ng/mL] (J. Li et al., 2019)			
	NP		7.61 [ng/mL] (Shekhar et al., 2017)		7.79 [ng/mL] (Shekhar et al., 2017)
	OP		3.69 [ng/mL] (Shekhar et al., 2017)		3.10 [ng/mL] (Shekhar et al., 2017)
	TCS	3.1 ± 4.2 [ng/mL] (Bai et al., 2020)	7.15 [ng/mL] (Shekhar et al., 2017)	3.3 ± 9.8 [ng/mL] (Bai et al., 2020)	2.5 ± 5.3 [ng/mL] (Bai et al., 2020)	7.81 [ng/mL] (Shekhar et al., 2017)
		T_1 0.48 [ng/mL] T_3 0.32 [ng/mL] (J. Li et al., 2019)				0.56 ± 0.14 [ng/mL] (Bai et al., 2020)
Pesticides	HCB		6.3–114 [ng/g] (Caspersen et al., 2016)	T_1 103.8 [pg/mL] (Vafeiadi et al., 2017)		<LOD-0.715 [ng/mL] (Barmpas et al., 2020)

	p,p'-DDE	13.8–1375 [ng/g] (Caspersen et al., 2016)	T_1 2067.9 [pg/mL] (Vafeiadi et al., 2017)	263.3 ± 50.7 [µg/kg] (Toichuev et al., 2018)	0.65-8.81 [ng/mL] (Luo et al., 2017)	0.001-2.796 [ng/mL] (Barmpas et al., 2020)
	PCB153	<LOD-116 [ng/mL] (Müller et al., 2019) 12.8–133 (Caspersen et al., 2016)	T_1 141.6 [pg/mL] (Vafeiadi et al., 2017)			
	PCB180	6.9–142 [ng/g] (Caspersen et al., 2016)	T_1 73.8 [pg/mL] (Vafeiadi et al., 2017)			
Perfluoroalkyl substances	PFHxS	T_1 1 [µg/L] (Fisher et al., 2016)	<LOD-0.73 [ng/mL] (Fisher et al., 2016) <LOD-1.15 [ng/mL] (Gao et al., 2019)		0.05-0.83 [ng/mL] (Gao et al., 2019)	
	PFOA	T_1 1.7 [µg/L] (Fisher et al., 2016)	<LOD-1.13 [ng/mL] (Müller et al., 2019)		0.39 [µg/L] (Fisher et al., 2016)	

		0.6–8.0 [ng/g] (Mamsen et al., 2017)	<LOD-25.4 [ng/mL] (Gao et al., 2019)	0.04–0.45 [ng/g] (Mamsen et al., 2017)	0.03-10.2 [ng/mL] (Gao et al., 2019)
	PFOS	T_1 4.6 [µg/L] (Fisher et al., 2016)	<LOD-1.54 [ng/mL] (Müller et al., 2019)	0.3–3.1 [ng/g] (Mamsen et al., 2017)	0.04-8.01 [ng/mL] (Gao et al., 2019)
		2.5–16.7 [ng/g] (Mamsen et al., 2017)	0.07-22.6 [ng/mL] (Gao et al., 2019)		
	PFAS and PFAS		0.01-6.71 [ng/mL] (Cai et al., 2020)		0.04.-2.66 [ng/mL] (Cai et al., 2020)
Polybrominated substances	PBDE-28	0.04–0.5 [ng/g] (Caspersen et al., 2016)	0.015 [ng/g] (Zota et al., 2018)	0.2 [ng/g] (Matovu et al., 2020)	0.1 [ng/g] (Matovu et al., 2020)
	PBDE-47	<LOD–9.1 [ng/g] (Caspersen et al., 2016)	0.17 [ng/g] (Zota et al., 2018)	0.25 [ng/g] (Matovu et al., 2020)	0.03 [ng/g] (Matovu et al., 2020)

BPS-Bisphenol S; BPF-Bisphenol F; MeP – methylparaben; PrP-Propylparaben; MnBP - Mono-n-butyl phthalate; MEHP - Mono-(2-ethylhexyl) phthalate; MCOP- Mono-carboxy-isooctyl phthalate; MBzP- monobenzylphthalate; DEHP- Di(2-ethylhexyl)phthalate; MeP- methylparaben; EtP- Ethylparaben; PrP-Propylparaben; BuP- Butylparaben; BP-1- benzophenone-1; BP-3-benzophenone-3; NP-nonylphenol; OP-octylphenol; TCS-triclosan; HCB-hexachlorobenzene; p,p'-DDE- dichlorodiphenyldichloroethylen; PCB153- ,2,2',4',5,5'-Hexachlorobiphenyl; PCB

180-2,2′,3,4,4′,5,5′-heptachlorobiphenyl; PFHxS- perfluorohexanesulfonate; PFOA- perfluorooctanoic acid; PFOS- Perfluorooctanesulphonate; PBDE-28- 2,4,4'-tribromodiphenyl ether; PBDE-47- 2,2',4,4'-tetrabromodiphenyl ether; T_1, T_2, T_3- 1st, 2nd, 3rd trimesters

4.1.1. Mummy's style of life

As previously stated, fetal exposure is directly related to pregnant women's exposure to EDCs due to the maternal-fetal placenta transfer of contaminants. Thus, the lifestyle of the mother before and during pregnancy strictly determines the dose of pollutants to which the fetus will be exposed. Exposure via food and beverages is considered to be the major source. In the literature, one can find information that diet accounts for up to 90% of exposure to BPs, PCBs, PAEs, and OCPs (organochlorine pesticides) (Kiess et al., 2021; Padmanabhan et al., 2021). These contaminants may be present in food as contaminants from the environment, food contact materials, and food processing utensils and equipment (Padmanabhan et al., 2021). Therefore, both the food preferences and habits i.e. type and the quantity of food consumed by pregnant women can influence their dietary intake of EDCs. Bisphenols and phthalates were most often found in different kinds of products such as: milk-based products (Herrero et al., 2021), soft drinks, juices (Kumar et al., 2022; Tzatzarakis et al., 2017), canned vegetables, fruits, and meats (Lorber et al., 2015; Szczepańska et al., 2020). The high concentrations of BPA and its analogues are also noted in seafood and fish (Gardener et al., 2022). Several studies have found significant correlations between urinary and blood BPA concentrations and consumption of canned food and food stored in plastic containers (Hartle et al., 2016; Peng et al., 2019; Snoj Tratnik et al., 2019). Moreover, consumption of food re-heated in plastic containers was also associated with a higher urinary BPA level (Haq et al., 2020; Snoj Tratnik et al., 2019). What is more, in several studies, the dependence between increased BPA (Ami R. Zota, Cassandra A. Phillips, 2016) and phthalates (Smith et al., 2022; Varshavsky et al., 2018) exposure was also connected with increased consumption of fast foods and ultra-processed foods (Buckley et al., 2019). One study reported, 20% higher BPA urinary level of pregnant women who reported eating hamburgers three times per week or more compared to women who reported not consuming any hamburgers (Quirós-Alcalá et al., 2013). Numerous epidemiological studies have shown that consuming high-fat foods, such as fish, dairy products, red meat, and eggs, is a main source of exposure to PCBs and OCPs (Harmouche-Karaki et al., 2019; Witczak and Abdel-Gawad, 2014). A few findings also demonstrated the role of fruits and vegetable consumption in influencing serum levels of PCBs and OCPs (Arrebola et al., 2018; Helou et al., 2021; H. A. Lee et al., 2018). Similarly, the eating of grilled or charred foods such as meats is indicated as the main source of

exposure to PAHs, which are other known EDCs (Alomirah et al., 2011). It should be noted that throughout pregnancy, the mother's body goes through physiologic changes, increasing the need for energy and the amount of food and water consumed (Plante et al., 2022). As a result, during pregnancy, exposure to EDCs may increase. Another important source of women's exposure to EDCs is the use of personal care products. The main endocrine active compounds occurred in cosmetics are parabens, benzophenone-UV filters and phthalates. Over the past years, these synthetic compounds have been commonly found in body lotions, skin care products, shampoos, deodorants, and lipsticks. These compounds applied to the skin along with the cosmetic are easily absorbed and thus enter the body (Martín-Pozo et al., 2021). The use of personal care products corresponded positively to the detection of phthalate metabolites and paraben metabolites (Martín-Pozo et al., 2021; Pagoni et al., 2022) in urine samples. Some EDC can also be emitted into the indoor environment. Some reports showed that PAEs, PBDEs, PFAAs, PCBs, and PAHs can be released from vinyl floor (Benning et al., 2013), carpets (Lucattini et al., 2018; Vojta et al., 2017), upholstery (Harris et al., 2021; Lucattini et al., 2018), nonstick cookware (Sajid and Ilyas, 2017), electronics devices (Yang et al., 2020) , paints and other widely used materials in buildings (Hou et al., 2018; Teil et al., 2016).

4.2. Infant and early-life children exposure

Early life exposure to EDCs and related chemicals have been associated with many diseases. As per some reports, 99–100% of pregnant women tested positive for the presence of several chemical classes, including PCBs, organochlorine pesticides, PFASs, PBDEs, phthalates, and PAHs (Woodruff et al., 2011). Given that numerous of these substances have been found in amniotic fluid and cord blood, it is obvious that the placenta does not shield the fetus from exposure (De Cock et al., 2017). Newborn TSH levels are impacted by early exposure to PCB-153 and p,p′-DDE. Higher exposure levels were linked to TSH levels that were 12–15% lower (De Cock et al., 2017).

4.2.1. Medical devices

Medical supplies are substantial source of exposure to numerous types of EDCs, such as phthalates, bisphenol A, parabens, perfluoroalkyl compounds, and triclosan. Some of the EDCs were detected in syringes, microcapillary blood tubes and venous catheters. Evidence of release into parenterally given solutions, including many parabens, phthalates, and other suspected EDCs, may be of much greater concern. The release of phthalates from medical use polymers is not surprising as they make 30-40% of such polymers and generally non-covalently bonded. Although the countries like France restricted the use of phthalates in medical goods, still the hospital exposure occurred through extracorporeal membrane oxygenators, blood transfusion sets, and intravenous extension lines. Because of their all-encompassing antibacterial action, parabens are frequently employed in medical products. For methylparaben, their concentrations in intravenous solutions might reach 0.72%. Additionally, parabens are used in ultrasonic gels because of their bacteriostatic properties. To avoid bloodstream infections brought on by catheters, several hospitals additionally include parabens into their heparin lock solutions. The release of BPA has also been linked to medical supplies (Genco et al., 2020).

The population of Neonatal Extensive Care Units (NICU) is at significant risk as a result of the frequent and intensive medical interventions, neonates' reduced capacity to eliminate toxic pollutants, and their increased vulnerability to endocrine disruptors. Recently, a study was conducted to measure the exposure of NICU patients to PVC medical device plasticizers and it was compared with those discharged from the hospital. DEHP and TEHTM metabolites urinary concentrations were lower at discharge compared to NICU. The primary sources of exposure were medical devices used for respiratory support, infusion treatment, enteral nutrition, and transfusion. The babies' exposure was considerably elevated by smaller gestational age and body weight (Bernard et al., 2023).

Similarly, research was designed to find the exposure of BPA through nutritional intake and medical devices. Mother and the premature infants who were in NICU for last 3 days were registered for this study. One sample of nutritional intake (breast milk or formula) was collected from 43 mothers and two samples of urine (before and after nutritional intake) were collected from the infants. The median urinary total BPA concentration among infants who needed the use of 4 or more medical devices in the past 3 days was significantly higher (36.6 µg/L) than among infants who required 0 to 3 devices (13.9 µg/L).

Exposure to BPA was positively correlated with the quantity of medical equipment used during the previous three days but not with dietary consumption (Duty et al., 2013).

4.2.2. Food

Food contaminated with chemicals poses a serious risk to human health and is a major global food safety problem. Both manmade and naturally existing environmental variables can contaminate food. Food items have been shown to include several chemical groups concurrently, including those from metal(oids), polycyclic aromatic hydrocarbons, persistent organic pollutants, perfluorinated compounds, radioactivity, plastics, and nanoparticles. Additionally, when consumed in significant doses, several ingredients used in food processing, such as emulsifiers and artificial sweeteners, may be damaging to consumers' health. Eating contaminated food is the main exposure pathway for the majority of human and animal populations (Calatayud Arroyo et al., 2021).

Phytoestrogens, phthalates, POPs, pesticides, bisphenol A and many other EDCs are found in the food items. The contaminated foods may include eggs, breast milk and drinking water. The infants can be exposed to EDCs through the breast milk as well as infant formula, as the presence of such chemicals have been reported in both of them. The mammary gland of nursing mothers is concentrated with highly lipid-soluble compounds. So, breast milk with a high lipid content in particular carries a greater risk. Additionally, the number of births, length of breastfeeding, and mother age all have an impact on the level of exposure. The contaminated drinking water can be another source (Ercan and Tarcin, 2022).

Depending on physicochemical conditions like temperature, UV light, pH, microwave, and mechanical stress, EDCs can migrate as residual monomers, additives used in polymeric material of food containers (Bang et al., 2012). Phthalates can be the common EDCs coming from the food packaging (Meeker, 2012).

OCPs and some metals were found in infant formula and baby foods in Turkey (Kilic et al., 2018). 4-Nonylphenols (NPs) were analyzed in 60 commercial foods in Germany. Regardless of the food's fat content, the concentrations of NPs on a fresh weight basis ranged between 0.1 and 19.4 μg/kg (Guenther et al., 2002). A study was designed to study the presence of bisphenol analogues (BPA, BPAF, BPC,

BPE, BPFL, BPS, and BPZ) in powdered baby formula from several Indian brands and to calculate the dietary exposure to these substances for infants aged 0 to 12 months. BPA (mean = 5.46 ng/g) had the highest concentration, followed by BPZ and BPS. There was no evidence of BPAF, BPFL, BPC, or BPE detection in any of the samples (Karsauliya et al., 2021). In another study, infants who were solely breastfed had lower total BPA metabolite concentrations than those who were exclusively formula-fed or breastfed with supplements (Fisher et al., 2019). There are many reports on migration of BPA from canned bottles to the foods (A. Goodson, 2002; Biles et al., 1997).

4.2.3. Personal care products and cosmetics

Cosmetics and personal care products (PCPs) are essential items in our everyday lives. Since they are so widely used, some toxins that people ordinarily wouldn't be exposed to might potentially be exposed through them. UV filters, parabens, phthalates, synthetic musks, and other antimicrobial compounds are commonly used in cosmetics and PCPs. Like benzophenones in sunscreens or parabens used as preservatives and antimicrobials, the majority of EDCs are purposefully included in PCP formulations. Additionally, several of these substances have the potential to passively migrate into the PCP over time if they are not chemically bonded to the polymer matrix. When the component can be extracted under severe circumstances, typically by laboratory manipulation, they are referred to be leachable and extractable in this context (Martín-Pozo et al., 2021).

One study investigated the relationship between phthalate metabolite concentrations in infant urine and maternal reported use of infant skin care products. This study measured the concentrations of 9 phthalate metabolites in 163 infants born in 2000-2005. In 81% of the infants, the concentrations of 7 phthalate metabolites were above the LOD. Increased urinary concentrations of monoethyl phthalate, monomethyl phthalate, and monoisobutyl phthalate were found in infants exposed to lotion, powder, and shampoo, and these connections become stronger the more items were used. Young newborns may be particularly susceptible to the developmental and reproductive toxicity of phthalates due to their underdeveloped metabolic systems and greater dose per unit body surface area. This link was highest in this population (Sathyanarayana et al., 2008). In another study investigated 11 PAEs in 198 PCPs collected from the

market of Shanghai and it was found DEP was the most detected compounds (29.8%) and other PAEs were also detected (Bao et al., 2015). The phthalate metabolite concentrations in infant urine were higher when baby lotion or baby powder had been applied to them within the preceding 24 hours (Fisher et al., 2019).

4.2.4. Toys

Due to physiological differences (e.g., lower metabolic capacity compared to adults) and unique exposure patterns, such as hand-to-mouth behavior, young children, especially those under the age of 36 months, are thought to be more sensitive to chemical substance exposure. Additionally, windows of vulnerability to substances with endocrine action are associated with developmental phases. This may account for the rising prevalence of some conditions, including those that affect the reproductive system or neurodevelopmental problems. Children put a wide variety of things in their mouths, including toys, according to several studies based on observations of children's mouthing behavior between the ages of 0 and 36 months. To produce plastic toys, complicated combinations of one or more polymers are frequently used, along with several additives including plasticizers, flame retardants, and antioxidants. Plastics have been demonstrated to leak compounds like phthalates or UV filters, which are recognized endocrine disruptors, since some of these ingredients are not covalently bonded to the polymers (Kirchnawy et al., 2020). A Directive that governs toys in the European Union forbids the use of carcinogenic, mutagenic, and reprotoxic (CMR) compounds in categories 1A, 1B, or 2 in toys or structurally independent pieces, unless the ingredient is inaccessible or present in amounts below a certain level. In a recent study, migration experiments of toys were conducted in saliva simulants. Nine out of the 18 toys that were evaluated had discernible estrogenic action. By identifying the well-known endocrine active chemical BPA in two samples, the discovered estrogenic activity could be well explained. Analysis of 41 known or suspected endocrine active substances in plastic failed to explain the origin of the estrogen activity in seven out of nine estrogen-active samples, indicating that the estrogen activities were caused by endocrine active substances that are currently unknown or that are not currently suspected in toys (Kirchnawy et al., 2020).

This is also fact that infants and toddlers are constantly exposed to toys at childcare. A study evaluated leaching of BPA and phthalates from the toys used at several day care facilities in Philadelphia and found an average leaching of 13–280 ng/cm^2 of BPA and phthalates (Andaluri et al., 2018). In another study, DEHP was the highest detected phthalate in toy sample (Praveena et al., 2021).

4.2.5. Clothes

Industrial textile production uses about 1900 chemicals, many of which (around 165) are deemed potentially harmful to humans and/or the environment. These chemicals include pesticides, plasticizers, dyes, antioxidants, and flame retardants, and others to achieve various effects in the cloths (Freire et al., 2019; K. Lacasse, 2012; Swedish Chemicals Agency, 2013). Human exposure to environmental toxins is greatly influenced by clothing. On the one hand, limiting exposure to environmental toxins can protect humans. On the other side, clothes can also be a source of chemical exposure. Wearers of the cloths, especially children, can be exposed to these chemicals either directly or indirectly. Some of these chemicals may stay in the finished textile product, either purposefully or accidently. Previous research has demonstrated that semi-volatile organic compounds (SVOCs) partition between clothes and air (Li and Kannan, 2018).

To give materials fire and heat resistance as well as wrinkle-free qualities, melamine-based resins are widely utilized in textiles. However, nothing is understood about the presence of melamine and its compounds in textiles. The levels of melamine, ammeline, ammelide, and cyanuric acid in 77 textile samples and infant clothes bought in Albany, New York, USA, were examined. All textile samples contained one or more target analytes. Melamine accounted for 52% of the total concentrations of the four analytes, making it the most prevalent component (Zhu and Kannan, 2020).

BPA and parabens were found in infants and children's socks in Spain. BPA was detected in 91% of socks at concentrations ranging from <0.70 to 3736 ng/g. Ethyl-paraben was detected in 100% of socks, followed by methyl- and propyl-paraben. 41% of socks extracts were estrogenic and 19% were anti-androgenic (Freire et al., 2019). Socks were shown to be the main source of cutaneous exposure to benzotriazoles and benzothiazoles in a study that examined multiple newborn apparel items (Liu et al.,

2017). One study found up to a few percent total amounts of 23 EDCs in pantyhose gathered from six different nations (Li and Kannan, 2018). Infant exposure to phthalates from cotton clothes was shown to be a major route for dermal absorption (H. L. Li et al., 2019). Printed graphics over the cloths are also thought to be the contributor of exposure to several chemicals (Liu et al., 2017).

4.2.6. Others

Water and milk bottles can also contribute to exposure of infants and early-life children to EDCs. BPA can release from the baby bottles under the normal use conditions (Li et al., 2010). Even at low dosages, infants are unquestionably the group most at risk from BPA exposure. BPA may have an impact on how the brain, prostate glands, and behavior of fetuses, neonates, and early children develop. The primary sources of BPA exposure for infants are the migration of BPA from the can liner into infant formula and from polycarbonate baby bottles. As a result, Canada and Europe have banned the use of BPA in baby bottles. The Tolerable Daily Intake (TDI) of BPA has been set by the European Food Safety Authority (EFSA) at 4 μg/kg body weight/day due to the risk that BPA presents to human health. The European standards defined the specific migration limits (SML) of BPA from plastics in contact with food at 600 μg/kg in 2011. New legislation decreased the SML threshold to a more restrictive amount of 50 μg/kg. However, BPA migration from varnishes or coatings applied to materials and goods especially intended for newborns and young children (under 3 years old) is not allowed (Karsauliya et al., 2021).

One research found that serum BPA levels of bottle-fed infants (n=30) were significantly higher than those of breast-fed infants (n=30) and it was concluded that bottle feeding seems to enhance the risk of BPA exposure to infants (Rhie et al., 2014). The migration of BPAAs was examined in baby bottles (20 brands) and sippy cups (13 brands) in Canada. BPS, BPA, BPF, BPAF, BPM, and BPTMC had detection frequencies (DF) of more than 50%, making them the most frequently found analytes in baby bottles. The only substances often detected in sippy cups were BPA, BPS, and BPF. The average BPA content in infant bottle leachate was 31.5 ng/L in the water simulant but was 1.4 times higher in

the 50% EtOH simulant (Siddique et al., 2021). Plastic water containers can also release BPA and phthalates to water (Notardonato et al., 2019).

5. Biological samples coming from infant and children of early stage life – a need for public awareness, analysis and biomonitoring

It is extremely important to conduct biomonitoring of infants and children of early stage life and to develop sensitive and reliable analytical procedures. The methods should make it possible to estimate the exposure to EDCs and to assess the short- and long-term impact of these exposures on human health (Becker et al., 2009; Eskenazi et al., 2007; Hoffman et al., 2018). In the case of the biomonitoring of some chemical compounds (e.g. phthalates), special care should be taken with regard to the sampling materials used in order to reduce the potential contamination of the sample (Arbuckle, 2010). Generally, determination of EDCs in biological samples is performed using accurate and sensitive analytical instruments. The most common methods for this purpose are high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS) or gas chromatography coupled with tandem mass spectrometry (GC-MS/MS) (**Table 3**).

5.1. Breast milk monitoring

Mother's milk is the first and basic food of newborns, which provides not only the necessary nutrients (lipids, proteins, vitamins, minerals and saccharides) but also antibodies. Thanks to this, breastfeeding strengthens the immune system and protects the baby from the first infections and diseases. The World Health Organization (WHO) and others recommend exclusive breastfeeding for infants up to 6 months, followed by partial breastfeeding for at least 2 years. Unfortunately, although breastfeeding is very beneficial, breast milk, in addition to essential and valuable ingredients, also contains harmful xenobiotics, including EDCs. Therefore, breast milk appears to be a critical body fluid for biomonitoring, as it simultaneously provides information on the exposure of both the mother and the breast-fed infant (Bernasconi et al., 2022; Macheka-Tendenguwo et al., 2018).

Naturally, EDCs are present in breast milk in trace amounts and the milk itself is a very complex matrix, hence the use of sensitive and selective analytical methods in human milk biomonitoring is required. However, in addition to the need to use sensitive analytical methods, great care must also be taken in selecting the appropriate sample preparation technique. The sample pre-treatment step is critical when biomonitoring EDCs in complex matrices such as breast milk due to the presence of lipids and proteins that make the determination of target compounds difficult. Moreover, the analytes themselves do not make the task easier, because the ubiquity of EDCs (mainly bisphenols, phthalates and parabens) increases the risk of sample contamination during sampling, pre-treatment and analysis of these compounds. For example, it has been proven that the use of containers and breast pumps during sampling breast milk and the use of laboratory equipment with plastic parts can be a source of BPA contamination (Dualde et al., 2019). One of the popular sample preparation techniques for EDCs biomonitoring in breast milk is the QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) method based on liquid-liquid partitioning with acetonitrile, followed by salting out of the aqueous layer and then a purification step by dispersive solid-phase extraction (Czarczyńska-Goślińska et al., 2021; Dualde et al., 2019; Tuzimski et al., 2020). For example, Czarczyńska-Goślińska et al. (Czarczyńska-Goślińska et al., 2021)used the QuEChERS method in the biomonitoring of bisphenols and parabens in human milk to assess the nutritional risk of breast-fed infants. The highest average concentrations of parabens in the tested samples were found for methylparaben (MeP), which is not surprising because MeP is the most commonly used paraben in cosmetics. Interestingly, the milk samples taken from the woman who declared avoiding the use of cosmetics during pregnancy and breastfeeding contained the lowest concentration of parabens. In the case of bisphenols, the highest average concentration was found for BPA, which was close to the average MeP concentration. However, the authors emphasize that the estrogenic activity of MeP is as much as 2.5-3 million times lower than that of estradiol, while the estrogenic activity of BPA is only 1-10 thousand times lower than that of estradiol. Therefore, the detection of BPA in breast milk, which may have a more significant effect on infants, is of much greater concern. This has been proven by determining the hazard quotient (the ratio of the potential exposure to a substance and the level at which no adverse effects are expected), which for BPA (0.0723-0.1266) are much higher than for MP (0.00063-0.00182). Nevertheless, the authors reassure that the margin of safety

is still high because the hazard index (sum of hazard quotient for BPA and parabens) is much lower than one.

Witczak et al. (Witczak et al., 2021) examined the concentration of selected OCPs in breast milk during lactation. OCPs were detected in most samples in the range of 0 to 7.5 ng/g lipids. It was shown that the concentration of OCPs decreased throughout the duration of lactation. Redundancy analysis showed that the diet of pregnant women has a significant impact on the concentration of pesticides in their milk. Therefore, the authors emphasize that avoiding excessive consumption of meat, fish, eggs and dairy products can reduce the content of OCPs in breast milk. However, the determined hazard quotients for OCPs were very low.

In conclusion, despite many reports in the literature regarding contaminants in breast milk, breastfeeding is still recommended and fully supported. Nevertheless, some studies indicate negative consequences in infants fed breast milk containing EDCs, such as reduced weight and/or length gain associated with exposure to BPA or PFAS (Braun, 2017; Vela-Soria et al., 2020). Therefore, there is a need for further monitoring of EDCs in human milk and risk assessment of infants.

5.1. Blood monitoring

The problems of the biomonitoring of infants and toddlers appear at the first stage of the research, i.e., taking a sample from a small patient. Sampling urine or saliva is a non-invasive procedure, while taking a child's blood samples multiple times is associated with both physical and mental discomfort for the patient and his parents. Hence, such research are most often based on samples of the mother's milk and blood taken from infants at one time in order to characterize postnatal exposure to a target chemical compounds (Walkowiak et al., 2001). Obviously, infant toxicokinetic is a complex issue, and studies based on a one-time measurement provide only a partial view of the infant's exposure profile. To overcome these limitations and simultaneously follow ethic, many scientists believe that modelling the concentration of chemicals in a patient's blood after birth is the most correct approach to creating an infant exposure profile. In the literature, we can distinguish the lactation exposure model (LEM) (Pan et al., 2009) and a physiologically based pharmacokinetic model (PBPK) (Verner et al., 2009). The LEM

model is a single measurement of the analytes concentration and multiplies it by the duration of the breastfeeding. This approach is based on a large simplification assuming either constant postpartum exposure or an exposure that increases with lactation and then remains constant after the end of the breastfeeding (Pan et al., 2009). In contrast, the PBPK model, to put it simply, is a mathematical representation of the physiological processes that govern the absorption, distribution, metabolism, and excretion of chemicals in the body. On the one hand, the PBPK model gives slight measurement errors, but on the other hand, it is complicated and can only be described with a computer code. Therefore, PBPK model is difficult to use, and it is more demanding to assess the influence of each factor included in the model. Taking the above into account, Stigum et al., (2015) proposed a two-compartment (mother and child lipid) pharmacokinetic model described by three easy equations, offering researchers a model that is simpler to apply and understand than PBPK model. The model equations use a number of the parameters, including measured concentration of analytes in mother's milk, baby and mother weight at birth and in subsequent months of life, extrapolated fat weight of baby and mother, duration of the breastfeeding, and the approximate amount of the mother's milk consumed. Stigum et al., (2015) used the proposed model to investigate the effect of hexachlorobenzene on the growth of infants in the first two years of life. Studies have shown that the concentration of HCB in babies after birth was low (median of 11.2 ng/g lipids). However, during the lactation period, the median concentration increased and reached a maximum (36.5 ng/g lipids) after 15 months. Following the end of the breastfeeding period, the median gradually decreased. Children exposed to HCB through breast milk reached levels 1-5 times higher than their mothers. The obtained results proved that the two-compartment pharmacokinetic model is more accurate than the LEM model and, simultaneously easier to implement than the PBPK model. Lenters et al., (2019) also used this model to determine the concentrations of PBDEs, PFAS, PCBs and OCPs in the blood of infants from birth to 24 months of age. The studies showed a positive relationship between the concentration of β-HCH (median 4.37 ng/L in breast milk, median 4.14-12.02 ng/g in toddlers under 2 years of age) and PFOS (median 117 ng/L in breast milk) in breast milk and ADHD, with a suggestion that PFOS only affects the female sex (**Table 3**).

By contrast, Verner et al., (2010) used the PBPK model to simulate the levels of PCBs in the blood during the prenatal and postnatal periods and to assess the relationship of these levels to infant

behaviour. The authors showed that exposure to PCBs in early stage life induced behavioural changes in attention and activity levels. The median concentration of PCBs in the blood was 103 ng/g lipids, and the maximum analytes concentration was reached immediately after birth for bottle-fed infants and at the end of the lactation period for breast-fed infants (**Table 3**). However, the authors emphasize that the risks to the baby, even with relatively high levels of PCBs exposure, are unlikely to outweigh the benefits of breastfeeding.

5.2. Urine biomonitoring

As already mentioned, biomonitoring of the babies by sampling their urine is more acceptable for parents and children, less invasive and relatively easy to perform compared to the blood matrix. In the case of toddlers who have a diaper, it is possible to use paediatric urine bags for sampling (Fluegge et al., 2016). Unfortunately, the younger the child, the more difficult it is to conduct biomonitoring studies using urine samples. From birth to 12 months of age, the volume of urine available for sampling from toddlers per evacuation is usually less than 10 ml per sample and is slightly higher in children from 2 to 3 years of age. As children reach the age of 4-11 years, urine sampling becomes somewhat easier as the urine volume is approximately from 30 to 50 ml per evacuation (Barr et al., 2005). Although toddlers urinate more often, older children can control the timing of urination, which is quite an important convenience in the biomonitoring process. Another problem is that urine is an unregulated body fluid which composition and volume can vary between evacuations. In order to overcome this difficulty, the most common practice is a creatinine adjustment of the urinary metabolites to calculate the urine dilution (Bradman and Whyatt, 2005). Collection of all urine samples excreted by a young patient during the day is generally uncomfortable and problematic (e.g., greater possibility of sample contamination). An easier approach is a spot urine sampling. However, it should be remembered that the spot urine sample is not as representative as the round-the-clock urine samples (Kissel et al., 2005). Hence, it is recommended to collect first-morning urine because it is more concentrated, shows a longer accumulation time (approximately 8 hours) and is more representative (Barr et al., 2005; Fenske et al., 2005; Kissel et al., 2005).

Gys et. al. (Gys et al., 2020) examined the concentration of bisphenols in samples of the morning urine sampled from 7-year-old children (**Table 3**). Since BPA is an unstable pollutant that is rapidly and largely excreted in the urine, this matrix has been found to be an appropriate for assessing exposure to bisphenols in children. In the selected group, all tested bisphenols (7) were detected, with BPA, BPF and BPS showing a detection frequency of> 50%, which indicates widespread exposure. Gys et. al. (Gys et al., 2020)also assessed the trends in the concentration of bisphenols in 2012-2017. They proved that BPA concentration dropped significantly from 2012 to 2017, which is not surprising given the increasingly rigorous regulations on the use of BPA around the world. The BPF concentration remained constant over time. On the other hand, the frequency of BPB (bisphenol B) and BPS detection increased by about 10% in the studied years. The obtained results are probably related to the fact that the legal regulations cause manufacturers to move away from BPA in favour of BPA analogues. It has been shown that lower family income was associated with higher levels of BPF, and BPA measured in the urine of children. The presence of children in the smoking environment was also associated with the determination of higher BPA concentrations.

Lehmler et al., (2018) also tested the concentration of bisphenols (BPA, BPF and BPS) in urine samples collected from three study groups: adults (>20 years), teenagers (12-19 years) and children (6-11 years). All target contaminants were detected in the urine of the studied populations: BPA in 95.7%, BPS in 89.4% and BPF in 66.5% of the samples, which is consistent with the above-described results of Gys et al. (Gys et al., 2020). It was determined that the median concentration of bisphenols in children was 1.34 ng/mL for BPA, 0.27 ng/mL for BPS and 0.27 ng/mL for BPF. On the other hand, the median concentration of bisphenols in teenagers was 1.14 ng/mL for BPA, 0.30 ng/mL for BPS and 0.37 ng/mL for BPF. Children had statistically significantly higher median BPA concentrations in urine compared to adolescents. In contrast, urinary BPS and BPF levels did not differ significantly between these age groups. Lehmler et al. (Lehmler et al., 2018) also found that children from high-income families had lower levels of BPA in their urine compared to children from low-income families.

Whereas, Frederiksen et al. (Frederiksen et al., 2022)measured the concentrations of the metabolites of 15 phthalates and their two substitutes in urine from infants and their parents to

investigate possible patterns of exposure (**Table 3**). In addition, urinary analyte concentrations were considered in two separate groups: during exclusively breastfeeding and later in infancy after diet expansion, to investigate whether dietary changes altered chemicals exposure. The metabolites of 11 phthalates and both substitutes were present in 59–100% of all tested urine samples collected from infants (median concentrations in the range 0.10-5.64 ng/mL) and their parents (median concentrations in the range 0.06-18.1 ng/mL and 0.07-25.6 ng/mL for mothers and fathers, respectively). However, 9 metabolites out of 15 phthalates and both substitutes were present in >74% of all tested biological samples. The determined concentrations of phthalates and their substitutes in urine were independent of gender. Moreover, it was shown that, regardless of the type of the infant diet, exposures to most of these substances were generally of the same order of magnitude. The results of the research are quite surprising and worrying, as the use of several of the phthalates found has been legally regulated and even banned in the European Union (Frederiksen et al., 2022).

5.3. Saliva biomonitoring

In the case of the saliva biomonitoring of the chemicals, care should be taken to ensure that the sampling tools do not interfere with the analytes. Also, contamination from food or drink is a problem and attention should be paid to eliminate food and drink approximately one hour prior to saliva sampling which can sometimes be quite troublesome. Unfortunately, the common methods of saliva collection are very often unsuitable for use in very young children. For example, frequently used cotton sponges, absorbent pads, or absorbent chewing plugs may pose a choking hazard and the moment of the saliva sampling may cause discomfort to children. Literature reports indicate that the level of the contaminants in saliva may be significantly lower than the concentration of the labile chemicals in the blood, depending on the degree of the protein binding that may occur. Hence, a very sensitive analytical technique is required (Bradman and Whyatt, 2005; Morgan et al., 2011). Accordingly, Stefan-van Staden et al. (Stefan-van Staden et al., 2014) proposed three types of microsensors: stochastic microsensors, amperometric microsensors and multimode microsensors based on the stochastic and differential pulse voltammetry modes for the determination of BPA in children's saliva (**Table 3**). All the microsensors used were highly sensitive and reliable, and the results obtained were well correlated and compared with

the results obtained by the standard method (enzyme-linked immunosorbent assay, ELISA). More importantly, the authors proved that the standard method did not cover all the time the concentration ranges in which BPA is present in saliva samples, and therefore cannot be reliable for its analysis in children's saliva.

5.4. Biomonitoring of perinatal matrices

Due to the fact that exposures occurring during pregnancy are particularly worrying, as their effects on the developing fetus lead to long-term postpartum pathologies, EDCs are also determined in alternative matrices such as amniotic fluid (Shekhar et al., 2017; Wittassek et al., 2009), cord blood (Chen et al., 2017; Eick et al., 2021; Sunman et al., 2019), and placenta (Chen et al., 2017; Ruis et al., 2019). However, the sampling of these biological matrices is costly and complicated. Since the time of the delivery is not exactly predicted (apart from the scheduled caesarean section), researchers must be constantly on the phone. Also, the atmosphere in the delivery room can be hectic and tense, so there is a possibility of missing a sample. Wittassek et al. (Wittassek et al., 2009)collected amniotic fluid samples and appropriate maternal urine samples during caesarean delivery for phthalate metabolites analysis. They proved that several of the tested phthalates or their metabolites can cross the placental barrier and reach the human fetus (**Table 3**). It was observed that the concentrations of the phthalate metabolites were higher in the maternal urine samples than in the amniotic fluids. Moreover, no significant correlation was found between the concentrations of analytes in the amniotic fluid/maternal urine pairs. However, the authors admit that, due to the constant changes in the amniotic fluid, the measured levels of pollutants are not very accurate. Sunman et al. (Sunman et al., 2019)analysed cord blood samples to determine BPA, di-2-ethylhexyl phthalate and mono-2-ethylhexyl phthalate concentrations (**Table 3**). The analytes were detectable in approximately 99% of the samples (n = 100). It has been shown that exposure to the target chemical compounds in the fetal period has an adverse effect on the reproductive development of male newborns.

The abundance of hormone receptors in the placenta makes it particularly susceptible to endocrine disorders. It is also widely accepted that the placenta is a persistent organic pollutant absorber (Gingrich et al., 2020). Hence Ruis et al. (Ruis et al., 2019) quantified PBDEs in human placenta samples

from pregnant women who underwent caesarean section. The measured concentrations of the analytes in the fetal and maternal layers are presented as the ratio of the two concentrations (**Table 3**). Despite the lack of the differences in the amount of the lipids between the two tissue layers, the levels of the target compounds were higher in the fetal layers as compared to the maternal layers (2-5 times higher). The determined concentration ratios ranged from 1.2 to 5.5. The obtained results suggest that PBDEs are actively transported across the placental barrier between the mother and the fetus. If this is true, nutrients and hormones can compete for transport across the placental barrier, with potentially serious consequences for the developing fetus. Whereas, Chen et al. (Chen et al., 2017) determined the concentrations of the chlorinated polyfluoroalkyl ether sulfonic acids (Cl-PFESAs) and PFOS in maternal serum, cord serum and placenta (**Table 3**). PFOS concentrations were higher in all tested matrices than Cl-PFESAs concentrations. It was also shown that the concentrations of the analytes decreased in the tested matrices in the following order: maternal serum > cord serum > placenta. The detection of the target chemical compounds in placenta and cord sera indicates that these analytes may be effective in transport through the placenta into the cord blood. Moreover, higher concentrations of Cl-PFESAs and PFOS in the cord serum than in the placenta suggest that these analytes can largely accumulate in the fetal cord blood.

1265 **Table 3.** Biomonitoring and analysis of endocrine disrupting compounds in biological samples coming from infant and children of early stage life.

Analytes	**Type of samples**	**Age of children**	**Country**	**Analysis method**	**Concentration range**	**Literature**
Bisphenols	Breast milk	2 weeks	Spain	LC-MS/MS	0.13-1.62 ng/mL	(Dualde et al., 2019)
Parabens					0.13-7.00 ng/mL	
Bisphenols	Breast milk	/	Poland	LC-MS/MS	2.12 to 116.22 ng/mL	(Tuzimski et al., 2020)
Bisphenols and parabens	Breast milk	2-7 weeks	Poland	LC-MS/MS	Median = 0.05-1.48 ng/mL	(Czarczyńska-Goślińska et al., 2021)
		3-4 months			Median = 0.03-0.37 ng/mL	
Perfluoroalkyl substances	Breast milk	/	Spain	HPLC-MS/MS	22-52 pg/mL	(Vela-Soria et al., 2020)
Organochlorine Pesticides	Breast milk	>7 days - >1 year	Poland	GC-MS	0-7.5 ng/g lipids	(Witczak et al., 2021)
Bisphenols	Urine	7 years	Japan	GC-MS/MS	Median = 0.07-0.89 ng/mL	(Gys et al., 2020)

Bisphenols	Urine	6-11 years 12-19 years >20 years	U.S.A.	HPLC-MS/MS	Median = 0.12-2.72 ng/mL Median = 0.13-2.30 ng/mL Median = 0.14-2.49 ng/mL	(Lehmler et al., 2018)
Organophosphate esters, phenols, parabens, phthalates	Urine	3-6 years	U.S.A.	HPLC-MS/MS	Median = 0.46-57 ng/mL	(Hoffman et al., 2018)
Phthalate metabolites Bisphenol A	Urine	3-5 years	Germany	LC/LC-MS/MS GC-MS/MS	Median = 4.6-100 ng/mL Median = 3.53 ng/mL	(Becker et al., 2009)
Bisphenol A	Urine	2-5 years	U.S.A.	GC-MS	Median = 5.2 ng/mL	(Morgan et al., 2011)
Organophosphate pesticides	Urine	6 months 12 months 24 months	U.S.A.	GC-MS	GM = 45.5 nmol/L GM = 59.5 nmol/L GM = 70.9 nmol/L	(Eskenazi et al., 2007)
Organophosphate and synthetic pyrethroid insecticides	Urine	3 months	U.S.A.	GC-MS	Median = 5.6-13.9 ng/kg/day	(Fluegge et al., 2016)

Phthalate and substitute metabolite	Urine	7-342 days	Denmark	LC-MS/MS	Median = 0.10-5.64 ng/mL	(Frederiksen et al., 2022)
Polychlorinated biphenyls	Blood	0-11 months	Canada	HRGC	Median = 25-2142 ng/g lipids	(Verner et al., 2010)
Polychlorinated biphenyls	Serum	42 months	Germany	HRGC	Median = 1.22 ng/mL	(Walkowiak et al., 2001)
Polybrominated diphenyl ethers, poly- and perfluoroalkyl substances, poly-chlorinated biphenyls and organochlorine pesticides	Blood	0 months (birth)	Norway	/	Median = 0.03-45.13 ng/g	(Lenters et al., 2019)
		3 months			Median = 0.05-83.50 ng/g	
		6 months			Median = 0.06-108.72 ng/g	
		12 months			Median = 0.07-134.06 ng/g	
		18 months			Median = 0.07-128.47 ng/g	
		24 months			Median = 0.07-122.25 ng/g	
Bisphenol A	Saliva	4-10 years	Romania	Differential pulse voltammetry and	10-880 ng/mL	(Stefan-van Staden et al., 2014)

				stochastic measurements		
Phthalate metabolites	Amniotic fluid	0 months	Germany	LC-MS/MS	Median = 0.53-7.8 ng/mL	(Wittassek et al., 2009)
Phenols	Amniotic fluid	0 months	India	GC-MS	Median = 0.94-21.41 ng/mL	(Shekhar et al., 2017)
Bisphenol A	Cord blood	0 months	Turkey	HPLC	Median = 4.77 ng/mL	(Sunman et al., 2019)
Phthalates					Median = 0.13-0.29 ng/mL	
Poly- and perfluoroalkyl substances	Cord blood	0 months	U.S.A.	LC-MS/MS	GM = 0.1-2.0 ng/mL	(Eick et al., 2021)
Polybrominated diphenyl ethers				GC-HRMS	GM = 2.2-10.7 ng/mL	
Polybrominated diphenyl ethers	Placenta	0 months	U.S.A.	GC-MS	Ratio of analytes in fetal vs maternal placentas = 1.2-5.5	(Ruis et al., 2019)

Chlorinated polyfluoroalkyl ether sulfonic acids	Cord serum	0 months	China	UPLC-MS/MS	Median = 0.01-0.60 ng/mL	(Chen et al., 2017)
Perfluorooctane sulfonate					Median = 3.64 ng/mL	
Chlorinated polyfluoroalkyl ether sulfonic acids	Placenta				Median = 0-0.34 ng/mL	
Perfluorooctane sulfonate					Median = 0.35 ng/mL	

GC-MS - gas chromatography coupled with mass spectrometry, GC-MS/MS - gas chromatography coupled with tandem mass spectrometry, HPLC-MS/MS - high performance liquid chromatography coupled with tandem mass spectrometry, UPLC-MS/MS – ultra high performance liquid chromatography coupled with tandem mass spectrometry LC-MS/MS - liquid chromatography coupled with tandem mass spectrometry, LC/LC-MS/MS - multidimensional liquid chromatography coupled with tandem mass spectrometry, HRGC - high resolution gas chromatography, HPLC - high performance liquid chromatography, GC-HRMS - gas chromatography coupled with high resolution mass spectrometry, GM – geometric mean, U.S.A. - United States of America

6. Avoiding harmful chemicals in baby products: advices

Every parent instinctively cares about the welfare of the child. Sometimes, however, a lack of knowledge and awareness can cause them to make the wrong choices. Chemicals are all around us, found in everyday products. Babies and young children are exposed to chemicals through various routes including inhalation, ingestion or absorption through the skin.

Children in order to develop properly need to explore the surrounding world with all the senses. They play with different surfaces by touching it or putting an item in the mouth, therefore, all objects that are accessible to the youngest in everyday life need to be safe, free of harmful chemicals.

Babies and children can be exposed to harmful chemicals in products in widespread use, such as food, and food packaging, cosmetics, toys, clothes, baby bottles and all the items used in a baby room such as furniture, paint, mattresses or cribs, not to mention products not designed for kids but in their closest vicinity. Children are particularly vulnerable as they are still developing, thus parents need to be aware of the steps that need be taken to reduce baby's risk of exposure to harmful chemicals, including endocrine disruptors.

There are three basic principles (Time, Product, Alternative) that are important to remember when making decisions about how to organise the daily lives of children.

1.Giving a time: the baby's space, shopping, preparing meals should be planning Good, conscious decisions take time.

2. Reading the composition of products: looking for products intended exclusively for children and bearing the EU label; looking for products with an Ecolabel which certifies products with a guaranteed, independently-verified low environmental impact. Remembering which chemicals to avoid!

3. Looking for alternatives: the possibility of using greener substitutes, made of natural, non-toxic materials should be checked. The less intense the smell and colours, the better.

Table 4 summarizes some bullet points summarising the most basic tips for parents.

Table 4. Information on some bullet points summarising the most basic tips for parents

Aspect	Advices	Alternatives
Home	Steps that you can take to limit the exposure to harmful chemicals, including endocrine disruptors, while preparing your home for your baby: • renovate at least 3 months before the due date, ventilate your home well afterwards; • choose water-based, solvent-free and low-emission products; • use non-toxic mattresses and cribs with the EU Ecolabel (these are not treated with the most toxic flame retardants); • air any new mattresses thoroughly before sleeping on them; • consider an alternative flooring such as solid wood, cork, tile or natural linoleum as carpets may contain hazardous chemicals.	
Food	You can reduce your and your child's risk of exposure to EDCs in foods by: • reducing your consumption of meat and dairy products, opting for organic food, and avoiding fast food; • choosing fish lower down the food chain, such as sardines or anchovies as larger fish higher up the food chain eat smaller fish (bioaccumulation); • limiting intake of certain species of fish (long-lived and higher up the food chain species – such as shark,	Try to choose: • baby bottles that are free from all bisphenols. Choose BPA-free • stainless steel water bottles and food containers (for example for

	swordfish, pike, tuna, hake, tilefish and king mackerel (“Avoiding harmful chemicals in baby products: advice for parents,” n.d.).	children’s school lunches) • fruit and vegetables loose • food in glass jars • take-aways reduction.(“Avoiding harmful chemicals in baby products: advice for parents,” n.d.)
Food preparation process	To limit the risk of exposure to harmful chemicals: • choose a stainless steel or glass reusable cup; • don’t microwave food in plastic packaging; • avoid black plastic cooking utensils; • avoid non-stick pans.	
Food packaging	Avoid: • plastic bottles; • plastic food wrap; • packaging with greaseproof lining; • canned foods; • take-away and fast-food containers; • packaging labelled with recycling codes 3 and 7.	
Personal care products	Try to: • choose non-toxic baby care products such as shampoos, moisturisers, creams, soaps or nappies by reading a label, if possible pick those with an ecolabel; • avoid parabens, triclosan and chemicals with ‘fluoro’ in the name or ‘PTFE’; • look for paraben-free baby shampoo and soap; • select fragrance-free, organic cotton and reusable nappies with an ecolabel.	

Toys	Toys are regulated under the Toy Safety Directive in the EU. Try to: • reduce the risk of the toys containing harmful chemicals; • buy toys from trustworthy shops and online stores; • avoid toys that smell strongly of chemicals or are heavily scented; • avoid soft plastic toys, as they may contain endocrine disruptors like phthalates; • choose free from lead, and non-toxic if it is painted, and make sure it is meant for children.	
Clothes	To avoid exposure to endocrine disruptors: • read a label to avoid PFAS (or an old name PFC); • buy garments labelled PFAS-free or PFC-free; • use alternatives.	Some yarns used in homemade baby clothes, in order to be more durable or washable, may contain plastic as they are mixed with acrylic or nylon fibres. Wool could be a natural alternative as it do not contain plastics. Moreover, untreated wool has more advantages, it is naturally flame retardant and water repellent.

.296

.297 **7. Summary**

The fetus, infant, and child are widely exposed to chemicals with known or suspected endocrine disrupting effects and given increasing evidence of links to adverse effects in their life, research on EDCs is urgently needed. In the present article, a comprehensive literature survey was performed in order to provide an overview on the exposure of infants to EDCs and insights on the uptake, the mechanisms of action and biotransformation in baby/human body. In addition, detection and chemical identification methods were discussed in view of the relevant literature.

Based on the published data it is evident that EDCs have been routinely detected in trace amounts in different biological samples creating global concern over their potential adverse effects. Despite biomonitoring studies documenting that infants are exposed to dozens of potential EDCs across the lifespan and that some EDC exposures are correlated with each other, most of the studies are focused on the effects on single compounds and there is a lack of research on health effects of EDC mixtures. There is also much less information on the risks of chronic, low dose exposure of these compounds to infants. Based on this, monitoring in biological samples is almost certain to continue, in the ongoing studies of EDCs occurrence and toxicity.

Existing regulatory frameworks actions are not sufficient to address EDCs concerns on infants. This is due partly to the huge number of compounds that can be classed as EDCs. Hence, as research continues, anxious parents can take preventive measures to diminish infants' exposure to EDCs.

Considering all of the information mentioned in this publication, it is essential to bear in mind what is already known about EDCs and to deepen our knowledge to establish rules of conduct aimed at limiting exposure to EDCs' negative effects. We need to be aware that there is plenty of evidence showing that exposure to EDCs may adversely impact the health of adults and children through altered endocrine function—suggesting their link to endocrinopathies. In addition, we also need to remember about the environment. As the ECDs are release to the environment from various products and some of ECDs are slow to break-down in the environment, we should be aware how important is to choose the proper goods which are in use in our daily life. This is the reason why gaining knowledge about EDCs and their impact on human health as well as environment is of high importance.

Acknowledgements

Financial support of this study from Gdańsk University of Technology by the 32/WCh-BR/2021 grant under the Iconic Scholars-'Excellence Initiative-Research University' program is gratefully acknowledged by J.P.-W.

Declaration of interest: none.

CRediT authorship contribution statement: Conceptualization – J. Płotka-Wasylka, N. Jatkowska **Bibliographic research** – J. Płotka-Wasylka, E. Mulkiewicz, H. Lis, K. Godlewska, A. Kurowska-Susdorf, M. Sajid, D. Lambropoulou, N. Jatkowska. **Writing – Original Draft** – J. Płotka-Wasylka, E. Mulkiewicz, H. Lis, K. Godlewska, A. Kurowska-Susdorf, M. Sajid, D. Lambropoulou, N. Jatkowska. **Writing – Review & Editing** – J. Płotka-Wasylka, D. Lambropoulou. **Supervision** – J. Płotka – Wasylka, N. Jatkowska.

References

A. Goodson, W.S. and I.C., 2002. Survey of bisphenol A and bisphenol F in canned foods. Food Addit. Contam. 19, 796–802. https://doi.org/10.1080/0265203021014683

Adgent, M.A., Hoffman, K., Goldman, B.D., Sjödin, A., Daniels, J.L., 2014. Brominated flame retardants in breast milk and behavioural and cognitive development at 36 months. Paediatr. Perinat. Epidemiol. 28, 48–57. https://doi.org/10.1111/ppe.12078

Alejandra Martínez-Ibarra, Luis Daniel Martínez-Razo, Edgar Ricardo Vázquez-Martínez, Nayeli Martínez-Cruz, Rogelio Flores-Ramírez, ElizabethGarcía-Gómez, M.L.-L., Carlos Ortega-González, Ignacio Camacho-Arroyo, M.C., 2019. Unhealthy Levels of Phthalates and Bisphenol A in Mexican Pregnant Women with Gestational Diabetes and Its Association to Altered Expression of miRNAs Involved with Metabolic Disease. Int. J. Mol. Sci. 20, 3343. https://doi.org/10.3390/ijms20133343

Alomirah, H., Al-Zenki, S., Al-Hooti, S., Zaghloul, S., Sawaya, W., Ahmed, N., Kannan, K., 2011. Concentrations and dietary exposure to polycyclic aromatic hydrocarbons (PAHs) from grilled

and smoked foods. Food Control 22, 2028–2035. https://doi.org/10.1016/j.foodcont.2011.05.024

Alonso-Magdalena, P., Quesada, I., Nadal, A., 2021. Endocrine disruptors in the etiology of type 2 diabetes mellitus. Nat. Rev. Endocrinol. 7, 346–353. https://doi.org/10.1038/nrendo.2011.56

Ami R. Zota, Cassandra A. Phillips, S.D.M., 2016. Recent Fast Food Consumption and Bisphenol A and Phthalates Exposures among the U.S. Population in NHANES, 2003–2010. Environ. Health Perspect. 124, 1521. https://doi.org/10.1289/ehp.1510803

Amir, S., Shah, S.T.A., Mamoulakis, C., Docea, A.O., Kalantzi, O.I., Zachariou, A., Calina, D., Carvalho, F., Sofikitis, N., Makrigiannakis, A., Tsatsakis, A., 2021. Endocrine disruptors acting on estrogen and androgen pathways cause reproductive disorders through multiple mechanisms: A review. Int. J. Environ. Res. Public Health 18, 1–20. https://doi.org/10.3390/ijerph18041464

Andaluri, G., Manickavachagam, M., Suri, R., 2018. Plastic toys as a source of exposure to bisphenol-A and phthalates at childcare facilities. Env. Monit Assess 190, 65. https://doi.org/10.1007/s10661-017-6438-9

Arbuckle, T.E., 2010. Maternal-infant biomonitoring of environmental chemicals: the epidemiologic challenges. Birth Defects Res. A. Clin. Mol. Teratol. 88, 931–937. https://doi.org/10.1002/bdra.20694

Arrebola, J.P., Castaño, A., Esteban, M., Bartolomé, M., Pérez-Gómez, B., Ramos, J.J., 2018. Differential contribution of animal and vegetable food items on persistent organic pollutant serum concentrations in Spanish adults. Data from BIOAMBIENT.ES project. Sci. Total Environ. 634, 235–242. https://doi.org/10.1016/j.scitotenv.2018.03.283

Assens, M., Frederiksen, H., Petersen, J.H., Larsen, T., Skakkebæk, N.E., Juul, A., Andersson, A.M., Main, K.M., 2019. Variations in repeated serum concentrations of UV filters, phthalates, phenols and parabens during pregnancy. Environ. Int. 123, 318–324. https://doi.org/10.1016/j.envint.2018.11.047

Avoiding harmful chemicals in baby products: advice for parents [WWW Document], n.d. URL https://chemtrust.org/advice-for-parents/ (accessed 12.22.22).

Azzouz, A., Rascón, A.J., Ballesteros, E., 2016. Determination of free and conjugated forms of

endocrine-disrupting chemicals in human biological fluids by GC-MS. Bioanalysis 8, 1145–1158. https://doi.org/10.4155/bio-2015-0008

Bai, X., Zhang, B., He, Y., Hong, D., Song, S., Huang, Y., Zhang, T., 2020. Triclosan and triclocarbon in maternal-fetal serum, urine, and amniotic fluid samples and their implication for prenatal exposure. Environ. Pollut. 266, 115117. https://doi.org/10.1016/j.envpol.2020.115117

Balaguer, P., Delfosse, V., Bourguet, W., 2019. Mechanisms of endocrine disruption through nuclear receptors and related pathways. Curr. Opin. Endocr. Metab. Res. 7, 1–8. https://doi.org/10.1016/j.coemr.2019.04.008

Bang, D.Y., Kyung, M., Kim, M.J., Jung, B.Y., Cho, M.C., Choi, S.M., Kim, Y.W., Lim, S.K., Lim, D.S., Won, A.J., Kwack, S.J., Lee, Y., Kim, H.S., Lee, B.M., 2012. Human Risk Assessment of Endocrine-Disrupting Chemicals Derived from Plastic Food Containers. Compr. Rev. Food Sci. Food Saf. 11, 453–470. https://doi.org/10.1111/j.1541-4337.2012.00197.x

Bao, J., Wang, M., Ning, X., Zhou, Y., He, Y., Yang, J., Gao, X., Li, S., Ding, Z., Chen, B., 2015. Phthalate concentrations in personal care products and the cumulative exposure to female adults and infants in Shanghai. J. Toxicol. Environ. Health. A 78, 325–341. https://doi.org/10.1080/15287394.2014.968696

Barmpas, M., Vakonaki, E., Tzatzarakis, M., Sifakis, S., Alegakis, A., Grigoriadis, T., Sodré, D.B., Daskalakis, G., Antsaklis, A., Tsatsakis, A., 2020. Organochlorine pollutants' levels in hair, amniotic fluid and serum samples of pregnant women in Greece. A cohort study. Environ. Toxicol. Pharmacol. 73, 103279. https://doi.org/10.1016/j.etap.2019.103279

Barr, D.B., Wang, R.Y., Needham, L.L., 2005. Biologic monitoring of exposure to environmental chemicals throughout the life stages: Requirements and issues for consideration for the National Children's Study. Environ. Health Perspect. 113, 1083–1091. https://doi.org/10.1289/ehp.7617

Becker, K., Göen, T., Seiwert, M., Conrad, A., Pick-Fuß, H., Müller, J., Wittassek, M., Schulz, C., Kolossa-Gehring, M., 2009. GerES IV: Phthalate metabolites and bisphenol A in urine of German children. Int. J. Hyg. Environ. Health 212, 685–692. https://doi.org/10.1016/j.ijheh.2009.08.002

Behr, A.C., Plinsch, C., Braeuning, A., Buhrke, T., 2020. Activation of human nuclear receptors by perfluoroalkylated substances (PFAS). Toxicol. Vitr. 62, 104700. https://doi.org/10.1016/j.tiv.2019.104700

Bell, G.A., Perkins, N., Buck Louis, G.M., Kannan, K., Bell, E.M., Gao, C., Yeung, E.H., 2019. Exposure to Persistent Organic Pollutants and Birth Characteristics: The Upstate KIDS Study. Epidemiology 30, 94–100. https://doi.org/10.1097/EDE.0000000000001095

Bellavia, A., Chiu, Y.H., Brown, F.M., Mínguez-Alarcón, L., Ford, J.B., Keller, M., Petrozza, J., Williams, P.L., Ye, X., Calafat, A.M., Hauser, R., James-Todd, T., 2019. Urinary concentrations of parabens mixture and pregnancy glucose levels among women from a fertility clinic. Environ. Res. 168, 389–396. https://doi.org/10.1016/j.envres.2018.10.009

Beltifa, A., Machreki, M., Ghorbel, A., Belaid, A., Smaoui, E., Akrout, F.M., Di Bella, G., Khdary, N.H., Reyns, T., Mansour, H. Ben, Van Loco, J., 2019. Human urine contamination with environmental pollutants: Simultaneous determination using UPLC-MS/MS. J. Water Health 17, 371–379. https://doi.org/10.2166/wh.2019.264

Benning, J., Liu, Z., Tiwari, A., Little, J., Marr, L.C., 2013. Characterizing gas-particle interactions of phthalate plasticizer emitted from vinyl flooring. Environ. Sci. Technol. 1, 2696–2703.

Béranger, R., Hardy, E.M., Binter, A.C., Charles, M.A., Zaros, C., Appenzeller, B.M.R., Chevrier, C., 2020. Multiple pesticides in mothers' hair samples and children's measurements at birth: Results from the French national birth cohort (ELFE). Int. J. Hyg. Environ. Health 223, 22–33. https://doi.org/10.1016/j.ijheh.2019.10.010

Berger, K., Eskenazi, B., Kogut, K., Parra, K., Lustig, R.H., Greenspan, L.C., Holland, N., Calafat, A.M., Ye, X., Harley, K.G., 2018. Association of prenatal urinary concentrations of phthalates and bisphenol a and pubertal timing in boys and girls. Environ. Health Perspect. 126, 1–9. https://doi.org/10.1289/EHP3424

Berger, K., Hyland, C., Ames, J.L., Mora, A.M., Huen, K., Eskenazi, B., Holland, N., Harley, K.G., 2021. Prenatal exposure to mixtures of phthalates, parabens, and other phenols and obesity in five-year-olds in the chamacos cohort. Int. J. Environ. Res. Public Health 18, 1–18.

https://doi.org/10.3390/ijerph18041796

Berman, Y.E., Doherty, D.A., Main, K.M., Frederiksen, H., Hickey, M., Keelan, J.A., Newnham, J.P., Hart, R.J., 2021. Associations between prenatal exposure to phthalates and timing of menarche and growth and adiposity into adulthood: A twenty-years birth cohort study. Int. J. Environ. Res. Public Health 18. https://doi.org/10.3390/ijerph18094725

Bernard, L., Masse, M., Boeuf, B., Chennell, P., Decaudin, B., Durand, N., Genay, S., Lambert, C., Le Basle, Y., Moreau, E., Pinguet, J., Ponsonnaille, V., Richard, D., Saturnin, N., Storme, L., Sautou, V., 2023. Medical devices used in NICU: The main source of plasticisers' exposure of newborns. Sci. Total Environ. 858, 159994. https://doi.org/10.1016/J.SCITOTENV.2022.159994

Bernasconi, S., Street, M.E., Iughetti, L., Predieri, B., 2022. Chemical contaminants in breast milk: a brief critical overview. Glob. Pediatr. 2, 100017. https://doi.org/10.1016/j.gpeds.2022.100017

Biles, J.E., McNeal, T.P., Begley, T.H., 1997. Determination of Bisphenol a Migrating from Epoxy Can Coatings to Infant Formula Liquid Concentrates. J. Agric. Food Chem. 45, 4697–4700. https://doi.org/10.1021/jf970518v

Boas, M., Feldt-Rasmussen, U., Main, K.M., 2012. Thyroid effects of endocrine disrupting chemicals. Mol. Cell. Endocrinol. 355, 240–248. https://doi.org/10.1016/j.mce.2011.09.005

Bradman, A., Whyatt, R.M., 2005. Characterizing exposures to nonpersistent pesticides during pregnancy and early childhood in the National Children's Study: A review of monitoring and measurement methodologies. Environ. Health Perspect. 113, 1092–1099. https://doi.org/10.1289/ehp.7769

Braun, J.M., 2017. Early-life exposure to EDCs: Role in childhood obesity and neurodevelopment. Nat. Rev. Endocrinol. 13, 161–173. https://doi.org/10.1038/nrendo.2016.186

Braun, J.M., Li, N., Arbuckle, T.E., Dodds, L., Massarelli, I., Fraser, W.D., Lanphear, B.P., Muckle, G., 2019. Association between gestational urinary bisphenol a concentrations and adiposity in young children: The MIREC study. Environ. Res. 172, 454–461. https://doi.org/10.1016/j.envres.2019.02.038

Brent, G.A., 2012. Mechanisms of thyroid hormone action. J. Clin. Invest. 122, 3035.

https://doi.org/10.1172/JCI60047

Buckley, J.P., Kim, H., Wong, E., Rebholz, C.M., 2019. Ultra-processed food consumption and exposure to phthalates and bisphenols in the US National Health and Nutrition Examination Survey, 2013–2014. Environ. Int. 131, 105057. https://doi.org/10.1016/j.envint.2019.105057

Cai, D., Li, Q.Q., Chu, C., Wang, S.Z., Tang, Y.T., Appleton, A.A., Qiu, R.L., Yang, B.Y., Hu, L.W., Dong, G.H., Zeng, X.W., 2020. High trans-placental transfer of perfluoroalkyl substances alternatives in the matched maternal-cord blood serum: Evidence from a birth cohort study. Sci. Total Environ. 705, 135885. https://doi.org/10.1016/j.scitotenv.2019.135885

Calatayud Arroyo, M., García Barrera, T., Callejón Leblic, B., Arias Borrego, A., Collado, M.C., 2021. A review of the impact of xenobiotics from dietary sources on infant health: Early life exposures and the role of the microbiota. Environ. Pollut. 269, 115994. https://doi.org/10.1016/j.envpol.2020.115994

Cantonwine, D., Meeker, J.D., Hu, H., Sánchez, B.N., Lamadrid-Figueroa, H., Mercado-García, A., Fortenberry, G.Z., Calafat, A.M., Téllez-Rojo, M.M., 2010. Bisphenol a exposure in Mexico City and risk of prematurity: A pilot nested case control study. Environ. Heal. A Glob. Access Sci. Source 9, 1–7. https://doi.org/10.1186/1476-069X-9-62

Carpenter, D.O., 2006. Polychlorinated biphenyls (PCBs): Routes of exposure and effects on human health. Rev. Environ. Health 21, 1–23. https://doi.org/10.1515/reveh.2006.21.1.1

Carpenter, T., Grecian, S.M., Reynolds, R.M., 2017. Sex differences in early-life programming of the hypothalamic-pituitary-adrenal axis in humans suggest increased vulnerability in females: A systematic review. J. Dev. Orig. Health Dis. 8, 244–255. https://doi.org/10.1017/S204017441600074X

Casals-Casas, C., Desvergne, B., 2011. Endocrine disruptors: From endocrine to metabolic disruption. Annu. Rev. Physiol. 73, 135–162. https://doi.org/10.1146/annurev-physiol-012110-142200

Casas, M., Valvi, D., Ballesteros-Gomez, A., Gascon, M., Fernández, M.F., Garcia-Esteban, R., Iñiguez, C., Martínez, D., Murcia, M., Monfort, N., Luque, N., Rubio, S., Ventura, R., Sunyer, J., Vrijheid, M., 2016. Exposure to bisphenol a and phthalates during pregnancy and ultrasound

measures of fetal growth in the INMA-sabadell cohort. Environ. Health Perspect. 124, 521–528. https://doi.org/10.1289/ehp.1409190

Caspersen, I.H., Kvalem, H.E., Haugen, M., Brantsæter, A.L., Meltzer, H.M., Alexander, J., Thomsen, C., Frøshaug, M., Bremnes, N.M.B., Broadwell, S.L., Granum, B., Kogevinas, M., Knutsen, H.K., 2016. Determinants of plasma PCB, brominated flame retardants, and organochlorine pesticides in pregnant women and 3 year old children in The Norwegian Mother and Child Cohort Study. Environ. Res. 146, 136–144. https://doi.org/10.1016/j.envres.2015.12.020

Chao, H.R., Tsou, T.C., Huang, H.L., Chang-Chien, G.P., 2011. Levels of breast milk PBDEs from southern taiwan and their potential impact on neurodevelopment. Pediatr. Res. 70, 596–600. https://doi.org/10.1203/PDR.0b013e3182320b9b

Chapin, R.E., Adams, J., Boekelheide, K., Gray, L.E., Hayward, S.W., Lees, P.S.J., McIntyre, B.S., Portier, K.M., Schnorr, T.M., Selevan, S.G., Vandenbergh, J.G., Woskie, S.R., Shelby, M.D., 2008. NTP-CERHR expert panel report on the reproductive and developmental toxicity of bisphenol A. Birth Defects Res. Part B - Dev. Reprod. Toxicol. 83, 157–395. https://doi.org/10.1002/bdrb.20147

Chen, F., Yin, S., Kelly, B.C., Liu, W., 2017. Chlorinated Polyfluoroalkyl Ether Sulfonic Acids in Matched Maternal, Cord and Placenta Samples: a Study of Transplacental Transfer. Environ. Sci. Technol. 51, 6387–6394. https://doi.org/doi.org/10.1021/acs.est.6b06049

Chen, W.J., Robledo, C., Davis, E.M., Goodman, J.R., Xu, C., Hwang, J., Janitz, A.E., Garwe, T., Calafat, A.M., Peck, J.D., 2022. Assessing urinary phenol and paraben mixtures in pregnant women with and without gestational diabetes mellitus: A case-control study. Environ. Res. 214, 113897. https://doi.org/10.1016/j.envres.2022.113897

Colborn, T., 2004. Neurodevelopment and endocrine disruption. Environ. Health Perspect. 112, 944–949. https://doi.org/10.1289/ehp.6601

Coughlin, J.R., 1998. Sources of human exposure. Biol. Trace Elem. Res. 66, 87–100. https://doi.org/10.1007/bf02783129

Cremonese, C., Piccoli, C., Pasqualotto, F., Clapauch, R., Koifman, R.J., Koifman, S., Freire, C.,

2017. Occupational exposure to pesticides, reproductive hormone levels and sperm quality in young Brazilian men. Reprod. Toxicol. 67, 174–185. https://doi.org/10.1016/j.reprotox.2017.01.001

Cresteil, T., 1998. Onset of xenobiotic metabolism in children: Toxicological implications. Food Addit. Contam. 15, 45–51. https://doi.org/10.1080/02652039809374614

Czarczyńska-Goślińska, B., Grześkowiak, T., Frankowski, R., Lulek, J., Pieczak, J., Zgoła-Grześkowiak, A., 2021. Determination of bisphenols and parabens in breast milk and dietary risk assessment for Polish breastfed infants. J. Food Compos. Anal. 98, 103839. https://doi.org/10.1016/j.jfca.2021.103839

De Cock, M., De Boer, M.R., Govarts, E., Iszatt, N., Palkovicova, L., Lamoree, M.H., Schoeters, G., Eggesbø, M., Trnovec, T., Legler, J., Van De Bor, M., 2017. Thyroid-stimulating hormone levels in newborns and early life exposure to endocrine-disrupting chemicals: Analysis of three European mother-child cohorts. Pediatr. Res. 82, 429–437. https://doi.org/10.1038/pr.2017.50

De Coster, S., Van Larebeke, N., 2012. Endocrine-disrupting chemicals: Associated disorders and mechanisms of action. J. Environ. Public Health 2012. https://doi.org/10.1155/2012/713696

Di Renzo, G.C., Conry, J.A., Blake, J., Defrancesco, M.S., Denicola, N., Martin, J.N., McCue, K.A., Richmond, D., Shah, A., Sutton, P., Woodruff, T.J., Van Der Poel, S.Z., Giudice, L.C., 2015. International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals. Int. J. Gynecol. Obstet. 131, 219–225. https://doi.org/10.1016/j.ijgo.2015.09.002

Dualde, P., Pardo, O., F. Fernández, S., Pastor, A., Yusà, V., 2019. Determination of four parabens and bisphenols A, F and S in human breast milk using QuEChERS and liquid chromatography coupled to mass spectrometry. J. Chromatogr. B 1114–1115, 154–166. https://doi.org/10.1016/J.JCHROMB.2019.03.004

Duty, S.M., Mendonca, K., Hauser, R., Calafat, A.M., Ye, X., Meeker, J.D., Ackerman, R., Cullinane, J., Faller, J., Ringer, S., 2013. Potential Sources of Bisphenol A in the Neonatal Intensive Care Unit. Pediatrics 131, 483–489. https://doi.org/10.1542/PEDS.2012-1380

EFSA Scientific Committee, 2017. Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age. EFSA J. 15. https://doi.org/10.2903/j.efsa.2017.4849

Eick, S.M., Goin, D.E., Cushing, L., DeMicco, E., Park, J.S., Wang, Y., Smith, S., Padula, A.M., Woodruff, T.J., Morello-Frosch, R., 2021. Mixture effects of prenatal exposure to per- and polyfluoroalkyl substances and polybrominated diphenyl ethers on maternal and newborn telomere length. Environ. Heal. A Glob. Access Sci. Source 20, 1–11. https://doi.org/10.1186/s12940-021-00765-4

Encarnação, T., Pais, A.A.C.C., Campos, M.G., Burrows, H.D., 2019. Endocrine disrupting chemicals: Impact on human health, wildlife and the environment. Sci. Prog. 102, 3–42. https://doi.org/10.1177/0036850419826802

Engeli, R.T., Rohrer, S.R., Vuorinen, A., Herdlinger, S., Kaserer, T., Leugger, S., Schuster, D., Odermatt, A., 2017. Interference of paraben compounds with estrogen metabolism by inhibition of 17β-hydroxysteroid dehydrogenases. Int. J. Mol. Sci. 18. https://doi.org/10.3390/ijms18092007

Ercan, O., Tarcin, G., 2022. Overview on Endocrine disruptors in food and their effects on infant's health. Glob. Pediatr. 2, 100019. https://doi.org/10.1016/j.gpeds.2022.100019

Eskenazi, B., Marks, A.R., Bradman, A., Harley, K., Barr, D.B., Johnson, C., Morga, N., Jewell, N.P., 2007. Organophosphate pesticide exposure and neurodevelopment in young Mexican-American children. Environ. Health Perspect. 115, 792–798. https://doi.org/10.1289/ehp.9828

Fang, H., Tong, W., Branham, W.S., Moland, C.L., Dial, S.L., Hong, H., Xie, Q., Perkins, R., Owens, W., Sheehan, D.M., 2003. Study of 202 Natural, Synthetic, and Environmental Chemicals for Binding to the Androgen Receptor. Chem. Res. Toxicol. 16, 1338–1358. https://doi.org/10.1021/tx030011g

Fenske, R.A., Bradman, A., Whyatt, R.M., Wolff, M.S., Barr, D.B., 2005. Lessons learned for the assessment of children's pesticide exposure: Critical sampling and analytical issues for future studies. Environ. Health Perspect. 113, 1455–1462. https://doi.org/10.1289/ehp.7674

Fernández, M.F., Arrebola, J.P., Jiménez-Díaz, I., Sáenz, J.M., Molina-Molina, J.M., Ballesteros, O.,

1567 Kortenkamp, A., Olea, N., 2016. Bisphenol A and other phenols in human placenta from children
1568 with cryptorchidism or hypospadias. Reprod. Toxicol. 59, 89–95.
1569 https://doi.org/10.1016/j.reprotox.2015.11.002
1570 Fisher, B.G., Thankamony, A., Mendiola, J., Petry, C.J., Frederiksen, H., Andersson, A.M., Juul, A.,
1571 Ong, K.K., Dunger, D.B., Hughes, I.A., Acerini, C.L., 2021. Maternal serum concentrations of
1572 bisphenol A and propyl paraben in early pregnancy are associated with male infant genital
1573 development. Hum. Reprod. 35, 913–928. https://doi.org/10.1093/humrep/deaa045
1574 Fisher, M., Arbuckle, T.E., Liang, C.L., Leblanc, A., Gaudreau, E., Foster, W.G., Haines, D., Davis,
1575 K., Fraser, W.D., 2016. Concentrations of persistent organic pollutants in maternal and cord
1576 blood from the maternal-infant research on environmental chemicals (MIREC) cohort study.
1577 Environ. Heal. A Glob. Access Sci. Source 15, 1–14. https://doi.org/10.1186/s12940-016-0143-y
1578 Fisher, M., Arbuckle, T.E., MacPherson, S., Braun, J.M., Feeley, M., Gaudreau, É., 2019. Phthalate
1579 and BPA Exposure in Women and Newborns through Personal Care Product Use and Food
1580 Packaging. Environ. Sci. Technol. 53, 10813–10826. https://doi.org/10.1021/acs.est.9b02372
1581 Fluegge, K.R., Nishioka, M., Wilkins Ill, J.R., 2016. Effects of simultaneous prenatal exposures to
1582 organophosphate and synthetic pyrethroid insecticides on infant neurodevelopment at three
1583 months of age. J Env. Toxicol Public Heal. 60–73. https://doi.org/10.5281/zenodo.218417
1584 Forns, J., Stigum, H., Høyer, B.B., Sioen, I., Sovcikova, E., Nowack, N., Lopez-Espinosa, M.J.,
1585 Guxens, M., Ibarluzea, J., Torrent, M., Wittsiepe, J., Govarts, E., Trnovec, T., Chevrier, C., Toft,
1586 G., Vrijheid, M., Iszatt, N., Eggesbø, M., 2018. Prenatal and postnatal exposure to persistent
1587 organic pollutants and attention-deficit and hyperactivity disorder: A pooled analysis of seven
1588 European birth cohort studies. Int. J. Epidemiol. 47, 1082–1097.
1589 https://doi.org/10.1093/ije/dyy052
.590 Foster, W.G., Kubwabo, C., Kosarac, I., Gregorovich, S., Aryal, G., Coleman, K., 2019. Free
.591 bisphenol A (BPA), BPA-Glucuronide (BPA-G), and total BPA concentrations in maternal
.592 serum and urine during pregnancy and umbilical cord blood at delivery. Emerg. Contam. 5, 279–
.593 287. https://doi.org/10.1016/j.emcon.2019.08.002

1594 Frederiksen, H., Skakkebæk, N.E., Andersson, A.M., 2007. Metabolism of phthalates in humans. Mol.
1595 Nutr. Food Res. 51, 899–911. https://doi.org/10.1002/mnfr.200600243
1596 Frederiksen, H., Upners, E.N., Ljubicic, M.L., Fischer, M.B., Busch, A.S., Hagen, C.P., Juul, A.,
1597 Andersson, A.M., 2022. Exposure to 15 phthalates and two substitutes (DEHTP and DINCH)
1598 assessed in trios of infants and their parents as well as longitudinally in infants exclusively
1599 breastfed and after the introduction of a mixed diet. Environ. Int. 161.
1600 https://doi.org/10.1016/j.envint.2022.107107
1601 Freire, C., Molina-Molina, J.M., Iribarne-Durán, L.M., Jiménez-Díaz, I., Vela-Soria, F., Mustieles, V.,
1602 Arrebola, J.P., Fernández, M.F., Artacho-Cordón, F., Olea, N., 2019. Concentrations of
1603 bisphenol A and parabens in socks for infants and young children in Spain and their hormone-
1604 like activities. Environ. Int. 127, 592–600. https://doi.org/10.1016/j.envint.2019.04.013
1605 Freire, C., Vela-Soria, F., Beneito, A., Lopez-Espinosa, M.J., Ibarluzea, J., Barreto, F.B., Casas, M.,
1606 Vrijheid, M., Fernandez-Tardon, G., Riaño-Galan, I., Fernandez, M.F., 2020. Association of
1607 placental concentrations of phenolic endocrine disrupting chemicals with cognitive functioning
1608 in preschool children from the Environment and Childhood (INMA) Project. Int. J. Hyg.
1609 Environ. Health 230. https://doi.org/10.1016/j.ijheh.2020.113597
1610 Gao, K., Zhuang, T., Liu, X., Fu, Jianjie, Zhang, J., Fu, Jie, Wang, L., Zhang, A., Liang, Y., Song, M.,
1611 Jiang, G., 2019. Prenatal Exposure to Per- and Polyfluoroalkyl Substances (PFASs) and
1612 Association between the Placental Transfer Efficiencies and Dissociation Constant of Serum
1613 Proteins-PFAS Complexes. Environ. Sci. Technol. 53, 6529–6538.
1614 https://doi.org/10.1021/acs.est.9b00715
1615 Gardener, H., Nguyen, V., Hoepner, L.A., 2022. Phthalate and bisphenol a exposures during
1616 pregnancy: Findings from the National Children's Study. Environ. Res. 214, 114122.
.617 https://doi.org/10.1016/j.envres.2022.114122
.618 Gascon, M., Vrijheid, M., Martínez, D., Forns, J., Grimalt, J.O., Torrent, M., Sunyer, J., 2011. Effects
.619 of pre and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment
.620 and thyroid hormone levels at 4years of age. Environ. Int. 37, 605–611.

https://doi.org/10.1016/j.envint.2010.12.005

Geens, T., Bruckers, L., Covaci, A., Schoeters, G., Fierens, T., Sioen, I., Vanermen, G., Baeyens, W., Morrens, B., Loots, I., Nelen, V., de Bellevaux, B.N., Larebeke, N. Van, Hond, E. Den, 2014. Determinants of bisphenol A and phthalate metabolites in urine of Flemish adolescents. Environ. Res. 134, 110–117. https://doi.org/10.1016/j.envres.2014.07.020

Genco, M., Anderson-Shaw, L., Sargis, R.M., 2020. Unwitting accomplices: endocrine disruptors confounding clinical care. J. Clin. Endocrinol. Metab. 105, 1–6. https://doi.org/10.1210/clinem/dgaa358

Ghassabian, A., Trasande, L., 2018. Disruption in thyroid signaling pathway: A mechanism for the effect of endocrine-disrupting chemicals on child neurodevelopment. Front. Endocrinol. (Lausanne). 9, 1–8. https://doi.org/10.3389/fendo.2018.00204

Gingrich, J., Ticiani, E., Veiga-Lopez, A., 2020. Placenta Disrupted: Endocrine Disrupting Chemicals and Pregnancy. Trends Endocrinol. Metab. 31, 508–524. https://doi.org/10.1016/j.tem.2020.03.003

Golestanzadeh, M., Goodarzi-Khoigani, M., Shahrbanoo Daniali, S., Ebrahimpour, K., Zarean, E., Yazdi, M., Basirat, Z., Kelishadi, R., 2022. Association between phthalate metabolites in human amniotic fluid and offspring birth size: a sub-study of the PERSIAN birth cohort. Environ. Sci. Pollut. Res. https://doi.org/10.1007/s11356-022-20839-1

Golestanzadeh, M., Riahi, R., Kelishadi, R., 2019. Association of exposure to phthalates with cardiometabolic risk factors in children and adolescents: a systematic review and meta-analysis. Environ. Sci. Pollut. Res. 26, 35670–35686. https://doi.org/10.1007/s11356-019-06589-7

Gore, A.C., Chappell, V.A., Fenton, S.E., Flaws, J.A., Nadal, A., Prins, G.S., Toppari, J., Zoeller, R.T., 2015. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocr. Rev. 36, 1–150. https://doi.org/10.1210/er.2015-1010

Gore, A.C., Krishnan, K., Reilly, M.P., 2019. Endocrine-disrupting chemicals: Effects on neuroendocrine systems and the neurobiology of social behavior. Horm. Behav. 111, 7–22. https://doi.org/10.1016/j.yhbeh.2018.11.006

1648 Grandjean, P., Jensen, A.A., 2004. Breastfeeding and the Weanling'S Dilemma. Am. J. Public Health
1649 94, 1075–1075. https://doi.org/10.2105/ajph.94.7.1075
1650 Grandjean, P., Landrigan, P.J., 2015. Neurobehavioural effects of developmental toxicity. Lancet
1651 Neurol. 13, 330–338. https://doi.org/10.1016/S1474-4422(13)70278-3.Neurobehavioural
1652 Grindler, N.M., Vanderlinden, L., Karthikraj, R., Kannan, K., Teal, S., Polotsky, A.J., Powell, T.L.,
1653 Yang, I. V., Jansson, T., 2018. Exposure to Phthalate, an Endocrine Disrupting Chemical, Alters
1654 the First Trimester Placental Methylome and Transcriptome in Women. Sci. Rep. 8, 1–9.
1655 https://doi.org/10.1038/s41598-018-24505-w
1656 Gross, R.S., Ghassabian, A., Vandyousefi, S., Messito, M.J., Gao, C., Kannan, K., Trasande, L., 2020.
1657 Persistent organic pollutants exposure in newborn dried blood spots and infant weight status: A
1658 case-control study of low-income Hispanic mother-infant pairs. Environ. Pollut. 267.
1659 https://doi.org/10.1016/j.envpol.2020.115427
1660 Guarnotta, V., Amodei, R., Frasca, F., Aversa, A., Giordano, C., 2022. Impact of Chemical Endocrine
1661 Disruptors and Hormone Modulators on the Endocrine System. Int. J. Mol. Sci. 23.
1662 https://doi.org/10.3390/ijms23105710
1663 Guenther, K., Heinke, V., Thiele, B., Kleist, E., Prast, H., Raecker, T., 2002. Endocrine disrupting
1664 nonylphenols are ubiquitous in food. Environ. Sci. Technol. 36, 1676–1680.
1665 https://doi.org/10.1021/es010199v
1666 Güil-Oumrait, N., Valvi, D., Garcia-Esteban, R., Guxens, M., Sunyer, J., Torrent, M., Casas, M.,
1667 Vrijheid, M., 2021. Prenatal exposure to persistent organic pollutants and markers of obesity and
1668 cardiometabolic risk in Spanish adolescents. Environ. Int. 151, 106469.
1669 https://doi.org/10.1016/j.envint.2021.106469
1670 Guo, J., Miao, W., Wu, C., Zhang, J., Qi, X., Yu, H., Chang, X., Zhang, Y., Zhou, Z., 2020. Umbilical
.671 cord serum PBDE concentrations and child adiposity measures at 7 years. Ecotoxicol. Environ.
.672 Saf. 203, 111009. https://doi.org/10.1016/j.ecoenv.2020.111009
.673 Guo, J., Zhang, J., Wu, C., Lv, S., Lu, D., Qi, X., Jiang, S., Feng, C., Yu, H., Liang, W., Chang, X.,
.674 Zhang, Y., Xu, H., Cao, Y., Wang, G., Zhou, Z., 2019. Associations of prenatal and childhood

chlorpyrifos exposure with Neurodevelopment of 3-year-old children. Environ. Pollut. 251, 538–546. https://doi.org/10.1016/j.envpol.2019.05.040

Gutiérrez-Torres, D.S., Barraza-Villarreal, A., Hernandez-Cadena, L., Escamilla-Nuñez, C., Romieu, I., 2018. Prenatal exposure to endocrine disruptors and cardiometabolic risk in preschoolers: A systematic review based on cohort studies. Ann. Glob. Heal. 84, 239–249. https://doi.org/10.29024/aogh.911

Gys, C., Ait Bamai, Y., Araki, A., Bastiaensen, M., Caballero-Casero, N., Kishi, R., Covaci, A., 2020. Biomonitoring and temporal trends of bisphenols exposure in Japanese school children. Environ. Res. 191, 110172. https://doi.org/10.1016/j.envres.2020.110172

Hakkola, J., Tanaka, E., Pelkonen, O., 1998. Developmental expression of cytochrome P450 enzymes in human liver. Pharmacol. Toxicol. 82, 209–217. https://doi.org/10.1111/j.1600-0773.1998.tb01427.x

Hall, J.M., Korach, K.S., 2021. Endocrine disrupting chemicals (EDCs) and sex steroid receptors, 1st ed, Advances in Pharmacology. Elsevier Inc. https://doi.org/10.1016/bs.apha.2021.04.001

Hamers, T., Kamstra, J.H., Sonneveld, E., Murk, A.J., Kester, M.H.A., Andersson, P.L., Legler, J., Brouwer, A., 2006. In vitro profiling of the endocrine-disrupting potency of brominated flame retardants. Toxicol. Sci. 92, 157–173. https://doi.org/10.1093/toxsci/kfj187

Han, X., Li, J., Wang, Y., Xu, S., Li, Y., Liu, H., Zhou, Y., Zhao, H., Fang, J., Cai, Z., Xia, W., 2020. Association between phthalate exposure and blood pressure during pregnancy. Ecotoxicol. Environ. Saf. 189, 109944. https://doi.org/10.1016/j.ecoenv.2019.109944

Haq, M.E.U., Akash, M.S.H., Sabir, S., Mahmood, M.H., Rehman, K., 2020. Human exposure to bisphenol A through dietary sources and development of diabetes mellitus: a cross-sectional study in Pakistani population. Environ. Sci. Pollut. Res. 27, 26262–26275. https://doi.org/10.1007/s11356-020-09044-0

Harley, K.G., Berger, K., Rauch, S., Kogut, K., Claus Henn, B., Calafat, A.M., Huen, K., Eskenazi, B., Holland, N., 2017. Association of prenatal urinary phthalate metabolite concentrations and childhood BMI and obesity. Pediatr. Res. 82, 405–415. https://doi.org/10.1038/pr.2017.112

1702 Harmouche-Karaki, M., Mahfouz, Y., Salameh, P., Matta, J., Helou, K., Narbonne, J.F., 2019. Patterns
1703 of PCBs and OCPs exposure in a sample of Lebanese adults: The role of diet and physical
1704 activity. Environ. Res. 179, 108789. https://doi.org/10.1016/j.envres.2019.108789
1705 Harris, C.A., Henttu, P., Parker, M.G., Sumpter, J.P., 1997. The estrogenic activity of phthalate esters
1706 in vitro. Environ. Health Perspect. 105, 802–811. https://doi.org/10.1289/ehp.97105802
1707 Harris, D., Davis, A., Ryan, P.B., Cohen, J., Gandhi, P., Dubiel, D., Black, M., 2021. Chemical
1708 exposure and flammability risks of upholstered furniture. Fire Mater. 45, 167–180.
1709 https://doi.org/10.1002/fam.2907
1710 Hartle, J.C., Navas-Acien, A., Lawrence, R.S., 2016. The consumption of canned food and beverages
1711 and urinary Bisphenol A concentrations in NHANES 2003–2008. Environ. Res. 150, 375–382.
1712 https://doi.org/10.1016/j.envres.2016.06.008
1713 Helou, K., Matta, J., Harmouche-Karaki, M., Sayegh, N., Younes, H., Mahfouz, Y., Mahfouz, M.,
1714 Karake, S., Finan, R., Abi-Tayeh, G., Narbonne, J.F., 2021. Maternal and cord serum levels of
1715 polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) among Lebanese
1716 pregnant women and predictors of exposure. Chemosphere 266, 129211.
1717 https://doi.org/10.1016/J.CHEMOSPHERE.2020.129211
1718 Henriksen, L.S., Mathiesen, B.K., Assens, M., Krause, M., Skakkebæk, N.E., Juul, A., Andersson,
1719 A.M., Hart, R.J., Newnham, J.P., Keelan, J.A., Pennell, C., Main, K.M., Frederiksen, H., 2020.
1720 Use of stored serum in the study of time trends and geographical differences in exposure of
1721 pregnant women to phthalates. Environ. Res. 184, 109231.
1722 https://doi.org/10.1016/j.envres.2020.109231
1723 Herrero, L., Quintanilla-López, J.E., Fernández, M.A., Gómara, B., 2021. Plasticisers and
1724 preservatives in commercial milk products: A comprehensive study on packages used in the
.725 Spanish market. Food Chem. 338, 128031. https://doi.org/10.1016/j.foodchem.2020.128031
.726 Heuer, H., Visser, T.J., 2013. The pathophysiological consequences of thyroid hormone transporter
.727 deficiencies: Insights from mouse models. Biochim. Biophys. Acta - Gen. Subj. 1830, 3974–
.728 3978. https://doi.org/10.1016/j.bbagen.2012.04.009

1729 Hoffman, K., Adgent, M., Goldman, B.D., Sjödin, A., Daniels, J.L., 2012. Lactational exposure to
1730 polybrominated diphenyl ethers and its relation to social and emotional development among
1731 toddlers. Environ. Health Perspect. 120, 1438–1442. https://doi.org/10.1289/ehp.1205100
1732 Hoffman, K., Hammel, S.C., Phillips, A.L., Lorenzo, A.M., Chen, A., Calafat, A.M., Ye, X., Webster,
1733 T.F., Stapleton, H.M., 2018. Biomarkers of exposure to SVOCs in children and their
1734 demographic associations: The TESIE Study. Environ. Int. 119, 26–36.
1735 https://doi.org/10.1016/j.envint.2018.06.007
1736 Hong, H., Branham, W.S., Ng, H.W., Moland, C.L., Dial, S.L., Fang, H., Perkins, R., Sheehan, D.,
1737 Tong, W., 2015. Human sex hormone-binding globulin binding affinities of 125 structurally
1738 diverse chemicals and comparison with their binding to androgen receptor, estrogen receptor, and
1739 α-Fetoprotein. Toxicol. Sci. 143, 333–348. https://doi.org/10.1093/toxsci/kfu231
1740 Hou, M., Wang, Y., Zhao, H., Zhang, Q., Xie, Q., Zhang, X., Chen, R., Chen, J., 2018. Halogenated
1741 flame retardants in building and decoration materials in China: Implications for human exposure
1742 via inhalation and dust ingestion. Chemosphere 203, 291–299.
1743 https://doi.org/10.1016/j.chemosphere.2018.03.182
1744 Huang, S., Li, J., Xu, S., Zhao, H., Li, Y., Zhou, Y., Fang, J., Liao, J., Cai, Z., Xia, W., 2019.
1745 Bisphenol A and bisphenol S exposures during pregnancy and gestational age – A longitudinal
1746 study in China. Chemosphere 237, 124426. https://doi.org/10.1016/j.chemosphere.2019.124426
1747 Hwang, H.M., Park, E.K., Young, T.M., Hammock, B.D., 2008. Occurrence of endocrine-disrupting
1748 chemicals in indoor dust. Sci. Total Environ. 404, 26–35.
1749 https://doi.org/10.1016/j.scitotenv.2008.05.031
1750 Iughetti, L., Lucaccioni, L., Predieri, B., 2015. Childhood obesity and environmental pollutants: A
1751 dual relationship. Acta Biomed. 86, 5–16.
.752 Iughetti, L., Lucaccioni, L., Street, M.E., Bernasconi, S., 2020. Clinical expression of endocrine
.753 disruptors in children. Curr. Opin. Pediatr. 32, 554–559.
.754 https://doi.org/10.1097/MOP.0000000000000926
.755 Jensen, M.S., Anand-Ivell, R., Nørgaard-Pedersen, B., Jönsson, B.A.G., Bonde, J.P., Hougaard, D.M.,

1756 Cohen, A., Lindh, C.H., Ivell, R., Toft, G., 2015. Amniotic fluid phthalate levels and male fetal
1757 gonad function. Epidemiology 26, 91–99. https://doi.org/10.1097/EDE.0000000000000198
1758 Ješeta, M., Navrátilová, J., Franzová, K., Fialková, S., Kempisty, B., Ventruba, P., Žáková, J., Crha, I.,
1759 2021. Overview of the Mechanisms of Action of Selected Bisphenols and Perfluoroalkyl
1760 Chemicals on the Male Reproductive Axes. Front. Genet. 12, 1–13.
1761 https://doi.org/10.3389/fgene.2021.692897
1762 Jiang, Y., Zhao, H., Xia, W., Li, Y., Liu, H., Hao, K., Chen, J., Sun, X., Liu, W., Li, J., Peng, Y., Hu,
1763 C., Li, C., Zhang, B., Lu, S., Cai, Z., Xu, S., 2019. Prenatal exposure to benzophenones, parabens
1764 and triclosan and neurocognitive development at 2 years. Environ. Int. 126, 413–421.
1765 https://doi.org/10.1016/j.envint.2019.01.023
1766 Johansson, H.K.L., Svingen, T., Fowler, P.A., Vinggaard, A.M., Boberg, J., 2017. Environmental
1767 influences on ovarian dysgenesis-developmental windows sensitive to chemical exposures. Nat.
1768 Rev. Endocrinol. 13, 400–414. https://doi.org/10.1038/nrendo.2017.36
1769 Jordan, R.A., Woolf, T.F., 1987. Basic Concepts in Drug Metabolism: Part II. J. Clin. Pharmacol. 27,
1770 87–90. https://doi.org/10.1002/j.1552-4604.1987.tb02166.x
1771 K. Lacasse, W.B., 2012. Textile Chemicals: Environmental Data and Facts. Springer Science &
1772 Business Media. https://doi.org/https://doi.org/10.1007/978-3-642-18898-5
1773 Kabir, E.R., Rahman, M.S., Rahman, I., 2015. A review on endocrine disruptors and their possible
1774 impacts on human health. Environ. Toxicol. Pharmacol. 40, 241–258.
1775 https://doi.org/10.1016/j.etap.2015.06.009
1776 Kao, C.C., Que, D.E., Bongo, S.J., Tayo, L.L., Lin, Y.H., Lin, C.W., Lin, S.L., Gou, Y.Y., Hsu, W.L.,
1777 Shy, C.G., Huang, K.L., Tsai, M.H., Chao, H.R., 2019. Residue levels of organochlorine
1778 pesticides in breast milk and its associations with cord blood thyroid hormones and the
.779 offspring's neurodevelopment. Int. J. Environ. Res. Public Health 16.
.780 https://doi.org/10.3390/ijerph16081438
.781 Karsauliya, K., Bhateria, M., Sonker, A., Singh, S.P., 2021. Determination of Bisphenol Analogues in
.782 Infant Formula Products from India and Evaluating the Health Risk in Infants Asssociated with

Their Exposure. J. Agric. Food Chem. 69, 3932–3941. https://doi.org/10.1021/acs.jafc.1c00129

Katsikantami, I., Tzatzarakis, M.N., Alegakis, A.K., Karzi, V., Hatzidaki, E., Stavroulaki, A., Vakonaki, E., Xezonaki, P., Sifakis, S., Rizos, A.K., Tsatsakis, A.M., 2020. Phthalate metabolites concentrations in amniotic fluid and maternal urine: Cumulative exposure and risk assessment. Toxicol. Reports 7, 529–538. https://doi.org/10.1016/j.toxrep.2020.04.008

Kawa, I.A., Akbar masood, Fatima, Q., Mir, S.A., Jeelani, H., Manzoor, S., Rashid, F., 2021. Endocrine disrupting chemical Bisphenol A and its potential effects on female health. Diabetes Metab. Syndr. Clin. Res. Rev. 15, 803–811. https://doi.org/10.1016/J.DSX.2021.03.031

Kerdivel, G., Habauzit, D., Pakdel, F., 2013. Assessment and molecular actions of endocrine-disrupting chemicals that interfere with estrogen receptor pathways. Int. J. Endocrinol. 2013. https://doi.org/10.1155/2013/501851

Kiess, W., Häussler, G., Vogel, M., 2021. Endocrine-disrupting chemicals and child health. Best Pract. Res. Clin. Endocrinol. Metab. 35, 101516. https://doi.org/10.1016/j.beem.2021.101516

Kilic, S., Tongur, T., Kilic, M., Erkaymaz, T., 2018. Determination of Some Endocrine-Disrupting Metals and Organochlorinated Pesticide Residues in Baby Food and Infant Formula in Turkish Markets. Food Anal. Methods 11, 3352–3361. https://doi.org/10.1007/s12161-018-1299-6

Kirchnawy, C., Hager, F., Piniella, V.O., Jeschko, M., Washüttl, M., Mertl, J., Mathieu-Huart, A., Rousselle, C., 2020. Potential endocrine disrupting properties of toys for babies and infants. PLoS One 15, 1–22. https://doi.org/10.1371/journal.pone.0231171

Kissel, J.C., Curl, C.L., Kedan, G., Lu, C., Griffith, W., Barr, D.B., Needham, L.L., Fenske, R.A., 2005. Comparison of organophosphorus pesticide metabolite levels in single and multiple daily urine samples collected from preschool children in Washington State. J. Expo. Anal. Environ. Epidemiol. 15, 164–171. https://doi.org/10.1038/sj.jea.7500384

Kitamura, S., Suzuki, T., Sanoh, S., Kohta, R., Jinno, N., Sugihara, K., Yoshihara, S., Fujimoto, N., Watanabe, H., Ohta, S., 2005. Comparative study of the endocrine-disrupting activity of bisphenol A and 19 related compounds. Toxicol. Sci. 84, 249–259. https://doi.org/10.1093/toxsci/kfi074

1810 Kjeldsen, L.S., Bonefeld-Jørgensen, E.C., 2013. Perfluorinated compounds affect the function of sex
1811 hormone receptors. Environ. Sci. Pollut. Res. 20, 8031–8044. https://doi.org/10.1007/s11356-
1812 013-1753-3
1813 Klocke, C., Lein, P.J., 2020. Evidence implicating non-dioxin-like congeners as the key mediators of
1814 polychlorinated biphenyl (Pcb) developmental neurotoxicity. Int. J. Mol. Sci. 21.
1815 https://doi.org/10.3390/ijms21031013
1816 Kojima, H., Katsura, E., Takeuchi, S., Niiyama, K., Kobayashi, K., 2004. Screening for estrogen and
1817 androgen receptor activities in 200 pesticides by in vitro reporter gene assays using Chinese
1818 hamster ovary cells. Environ. Health Perspect. 112, 524–531. https://doi.org/10.1289/ehp.6649
1819 Kolatorova, L., Vitku, J., Hampl, R., Adamcova, K., Skodova, T., Simkova, M., Parizek, A., Starka,
1820 L., Duskova, M., 2018. Exposure to bisphenols and parabens during pregnancy and relations to
1821 steroid changes. Environ. Res. 163, 115–122. https://doi.org/10.1016/j.envres.2018.01.031
1822 Koutaki, D., Paltoglou, G., Vourdoumpa, A., Charmandari, E., 2022. The impact of bisphenol a on
1823 thyroid function in neonates and children: A systematic review of the literature. Nutrients 14, 1–
1824 15. https://doi.org/10.3390/nu14010168
1825 Krause, M., Frederiksen, H., Sundberg, K., Jørgensen, F.S., Jensen, L.N., Nørgaard, P., Jørgensen, C.,
1826 Ertberg, P., Juul, A., Drzewiecki, K.T., Skakkebaek, N.E., Andersson, A.M., 2018. Presence of
1827 benzophenones commonly used as UV filters and absorbers in paired maternal and fetal samples.
1828 Environ. Int. 110, 51–60. https://doi.org/10.1016/j.envint.2017.10.005
1829 Krönke, A.A., Jurkutat, A., Schlingmann, M., Poulain, T., Nüchter, M., Hilbert, A., Kiviranta, H.,
1830 Körner, A., Vogel, M., Söder, O., Bornehag, C.G., Kiess, W., 2022. Persistent organic pollutants
1831 in pregnant women potentially affect child development and thyroid hormone status. Pediatr.
1832 Res. 91, 690–698. https://doi.org/10.1038/s41390-021-01488-5
.833 Kuiper, G.G.J.M., Lemmen, J.G., Carlsson, B., Corton, J.C., Safe, S.H., Van Der Saag, P.T., Van Der
.834 Burg, B., Gustafsson, J.Å., 1998. Interaction of estrogenic chemicals and phytoestrogens with
.835 estrogen receptor β. Endocrinology 139, 4252–4263. https://doi.org/10.1210/endo.139.10.6216
.836 Kumar, A., Singh, D., Bhandari, R., Malik, A., Kaur, S., Singh, B., 2022. Bisphenol a in Canned Soft

1837 Drinks, Plastic-Bottled Water, and Household Water Tank from Punjab, India. SSRN Electron. J.
1838 9, 100205. https://doi.org/10.2139/ssrn.4160295
1839 Lauritzen, H.B., Larose, T.L., Øien, T., Sandanger, T.M., Odland, J.O., Van De Bor, M., Jacobsen,
1840 G.W., 2018. Prenatal exposure to persistent organic pollutants and child overweight/obesity at 5-
1841 year follow-up: A prospective cohort study. Environ. Heal. A Glob. Access Sci. Source 17, 1–12.
1842 https://doi.org/10.1186/s12940-017-0338-x
1843 Lee, B.M., Koo, H.J., 2007. Hershberger assay for antiandrogenic effects of phthalates. J. Toxicol.
1844 Environ. Heal. - Part A Curr. Issues 70, 1365–1370. https://doi.org/10.1080/15287390701432285
1845 Lee, H.A., Hwang, H.J., Oh, S.Y., Ha, E.H., Park, H., 2018. Dietary patterns related to exposure to
1846 persistent organic pollutants based on the Ewha Birth and Growth Cohort. Environ. Pollut. 243,
1847 189–196. https://doi.org/10.1016/J.ENVPOL.2018.08.072
1848 Lee, J., Choi, K., Park, J., Moon, H.B., Choi, G., Lee, J.J., Suh, E., Kim, H.J., Eun, S.H., Kim, G.H.,
1849 Cho, G.J., Kim, S.K., Kim, Sungjoo, Kim, S.Y., Kim, Seunghyo, Eom, S., Choi, S., Kim, Y.D.,
1850 Kim, Sungkyoon, 2018. Bisphenol A distribution in serum, urine, placenta, breast milk, and
1851 umbilical cord serum in a birth panel of mother–neonate pairs. Sci. Total Environ. 626, 1494–
1852 1501. https://doi.org/10.1016/j.scitotenv.2017.10.042
1853 Lehmler, H.J., Liu, B., Gadogbe, M., Bao, W., 2018. Exposure to Bisphenol A, Bisphenol F, and
1854 Bisphenol S in U.S. Adults and Children: The National Health and Nutrition Examination Survey
1855 2013-2014. ACS Omega 3, 6523–6532. https://doi.org/10.1021/acsomega.8b00824
1856 Lenters, V., Iszatt, N., Forns, J., Čechová, E., Kočan, A., Legler, J., Leonards, P., Stigum, H.,
1857 Eggesbø, M., 2019. Early-life exposure to persistent organic pollutants (OCPs, PBDEs, PCBs,
1858 PFASs) and attention-deficit/hyperactivity disorder: A multi-pollutant analysis of a Norwegian
1859 birth cohort. Environ. Int. 125, 33–42. https://doi.org/10.1016/j.envint.2019.01.020
.860 Li, A., Zhuang, T., Shi, J., Liang, Y., Song, M., 2019. Heavy metals in maternal and cord blood in
.861 Beijing and their efficiency of placental transfer. J. Environ. Sci. (China) 80, 99–106.
.862 https://doi.org/10.1016/j.jes.2018.11.004
.863 Li, A.J., Kannan, K., 2018. Elevated Concentrations of Bisphenols, Benzophenones, and

1864 Antimicrobials in Pantyhose Collected from Six Countries. Environ. Sci. Technol. 52, 10812–
1865 10819. https://doi.org/10.1021/acs.est.8b03129
1866 Li, H.L., Ma, W.L., Liu, L.Y., Zhang, Z., Sverko, E., Zhang, Z.F., Song, W.W., Sun, Y., Li, Y.F.,
1867 2019. Phthalates in infant cotton clothing: Occurrence and implications for human exposure. Sci.
1868 Total Environ. 683, 109–115. https://doi.org/10.1016/J.SCITOTENV.2019.05.132
1869 Li, J., Liu, W., Xia, W., Zhao, H., Zhou, Y., Li, Y., Wu, C., Liu, H., Zhang, B., Zhu, Y., Hu, J., Wang,
1870 X., Ye, D., Xu, S., Cai, Z., 2019. Variations, Determinants, and Coexposure Patterns of Personal
1871 Care Product Chemicals among Chinese Pregnant Women: A Longitudinal Study. Environ. Sci.
1872 Technol. 53, 6546–6555. https://doi.org/10.1021/acs.est.9b01562
1873 Li, J., Qian, X., Zhou, Y., Li, Y., Xu, S., Xia, W., Cai, Z., 2021. Trimester-specific and sex-specific
1874 effects of prenatal exposure to di(2-ethylhexyl) phthalate on fetal growth, birth size, and early-
1875 childhood growth: A longitudinal prospective cohort study. Sci. Total Environ. 777, 146146.
1876 https://doi.org/10.1016/j.scitotenv.2021.146146
1877 Li, X., Ying, G.G., Su, H.C., Yang, X.B., Wang, L., 2010. Simultaneous determination and assessment
1878 of 4-nonylphenol, bisphenol A and triclosan in tap water, bottled water and baby bottles.
1879 Environ. Int. 36, 557–562. https://doi.org/10.1016/J.ENVINT.2010.04.009
1880 Liu, H., Li, J., Xia, W., Zhang, B., Peng, Y., Li, Y., Zhou, Y., Fang, J., Zhao, H., Jiang, Y., Liu, W.,
1881 Sun, X., Hu, C., Cai, Z., Xu, S., 2019. Blood pressure changes during pregnancy in relation to
1882 urinary paraben, triclosan and benzophenone concentrations: A repeated measures study.
1883 Environ. Int. 122, 185–192. https://doi.org/10.1016/j.envint.2018.11.003
1884 Liu, L., Zhang, B., Lin, K., Zhang, Y., Xu, X., Huo, X., 2018. Thyroid disruption and reduced mental
1885 development in children from an informal e-waste recycling area: A mediation analysis.
1886 Chemosphere 193, 498–505. https://doi.org/10.1016/j.chemosphere.2017.11.059
.887 Liu, W., Xue, J., Kannan, K., 2017. Occurrence of and exposure to benzothiazoles and benzotriazoles
.888 from textiles and infant clothing. Sci. Total Environ. 592, 91–96.
.889 https://doi.org/10.1016/J.SCITOTENV.2017.03.090
.890 Lorber, M., Schecter, A., Paepke, O., Shropshire, W., Christensen, K., Birnbaum, L., 2015. Exposure

1891 assessment of adult intake of bisphenol A (BPA) with emphasis on canned food dietary
1892 exposures. Environ. Int. 77, 55–62. https://doi.org/10.1016/j.envint.2015.01.008
1893 Lucaccioni, L., Trevisani, V., Marrozzini, L., Bertoncelli, N., Predieri, B., Lugli, L., Berardi, A.,
1894 Iughetti, L., 2020. Endocrine-disrupting chemicals and their effects during female puberty: A
1895 review of current evidence. Int. J. Mol. Sci. 21. https://doi.org/10.3390/ijms21062078
1896 Lucattini, L., Poma, G., Covaci, A., de Boer, J., Lamoree, M.H., Leonards, P.E.G., 2018. A review of
1897 semi-volatile organic compounds (SVOCs) in the indoor environment: occurrence in consumer
1898 products, indoor air and dust. Chemosphere 201, 466–482.
1899 https://doi.org/10.1016/j.chemosphere.2018.02.161
1900 Lundqvist, C., Zuurbier, M., Leijs, M., Johansson, C., Ceccatelli, S., Saunders, M., Schoeters, G., Ten
1901 Tusscher, G., Koppe, J.G., 2006. The effects of PCBs and dioxins on child health. Acta Paediatr.
1902 Int. J. Paediatr. 95, 55–64. https://doi.org/10.1080/08035320600886257
1903 Luo, D., Pu, Y., Tian, H., Wu, W., Sun, X., Zhou, T., Tao, Y., Yuan, J., Shen, X., Feng, Y., Mei, S.,
1904 2017. Association of in utero exposure to organochlorine pesticides with thyroid hormone levels
1905 in cord blood of newborns. Environ. Pollut. 231, 78–86.
1906 https://doi.org/10.1016/j.envpol.2017.07.091
1907 Lynch, C.D., Jackson, L.W., Kostyniak, P.J., McGuinness, B.M., Buck Louis, G.M., 2012. The effect
1908 of prenatal and postnatal exposure to polychlorinated biphenyls and child neurodevelopment at
1909 age twenty four months. Reprod. Toxicol. 34, 451–456.
1910 https://doi.org/10.1016/j.reprotox.2012.04.013
1911 M.A. Verner, J.E. Hart, S.K. Sagiv, D.C. Bellinger, L.M. Altshul, S.A.K., 2015. Measured Prenatal
1912 and Estimated Postnatal Levels of Polychlorinated. Environ. Health Perspect. 888, 888–894.
1913 Macheka-Tendenguwo, L.R., Olowoyo, J.O., Mugivhisa, L.L., Abafe, O.A., 2018. Per- and
.914 polyfluoroalkyl substances in human breast milk and current analytical methods. Environ. Sci.
.915 Pollut. Res. Int. 25, 36064–36086. https://doi.org/10.1007/S11356-018-3483-Z
.916 Mallozzi, M., Bordi, G., Garo, C., Caserta, D., 2016. The effect of maternal exposure to endocrine
.917 disrupting chemicals on fetal and neonatal development: A review on the major concerns. Birth

1918 Defects Res. Part C - Embryo Today Rev. 108, 224–242. https://doi.org/10.1002/bdrc.21137
1919 Mamsen, L.S., Jönsson, B.A.G., Lindh, C.H., Olesen, R.H., Larsen, A., Ernst, E., Kelsey, T.W.,
1920 Andersen, C.Y., 2017. Concentration of perfluorinated compounds and cotinine in human foetal
1921 organs, placenta, and maternal plasma. Sci. Total Environ. 596–597, 97–105.
1922 https://doi.org/10.1016/j.scitotenv.2017.04.058
1923 Mantovani, A., 2016. Endocrine disrupters and the safety of food chains. Horm. Res. Paediatr. 86,
1924 279–288. https://doi.org/10.1159/000441496
1925 Marks, K.J., Howards, P.P., Smarr, M.M., Flanders, W.D., Northstone, K., Daniel, J.H., Sjödin, A.,
1926 Calafat, A.M., Hartman, T.J., 2021. Prenatal exposure to mixtures of persistent endocrine
1927 disrupting chemicals and postnatal body size in British girls. Early Hum. Dev. 161.
1928 https://doi.org/10.1016/j.earlhumdev.2021.105450
1929 Martín-Pozo, L., Gómez-Regalado, M.D.C., Moscoso-Ruiz, I., Zafra-Gómez, A., 2021. Analytical
1930 methods for the determination of endocrine disrupting chemicals in cosmetics and personal care
1931 products: A review. Talanta 234, 122642. https://doi.org/10.1016/j.talanta.2021.122642
1932 Martina, C.A., Weiss, B., Swan, S.H., 2012. Lifestyle behaviors associated with exposures to
1933 endocrine disruptors. Neurotoxicology 33, 1427–1433.
1934 https://doi.org/10.1016/j.neuro.2012.05.016
1935 Masuyama, H., Hiramatsu, Y., 2004. Involvement of Suppressor for Gal 1 in the
1936 Ubiquitin/Proteasome-mediated Degradation of Estrogen Receptors. J. Biol. Chem. 279, 12020–
1937 12026. https://doi.org/10.1074/jbc.M312762200
1938 Matovu, H., Ssebugere, P., Sillanpää, M., 2020. Prenatal exposure levels of polybrominated diphenyl
1939 ethers in mother-infant pairs and their transplacental transfer characteristics in Uganda (East
1940 Africa). Environ. Pollut. 258. https://doi.org/10.1016/j.envpol.2019.113723
.941 Matsuki, T., Ebara, T., Tamada, H., Ito, Y., Yamada, Y., Kano, H., Kurihara, T., Sato, H., Kato, S.,
.942 Saitoh, S., Sugiura-Ogasawara, M., Kamijima, M., 2020. Association between prenatal exposure
.943 to household pesticides and neonatal weight and length growth in the japan environment and
.944 children's study. Int. J. Environ. Res. Public Health 17, 1–19.

https://doi.org/10.3390/ijerph17124608

Meeker, J.D., 2012. Exposure to environmental endocrine disruptors and child development. Arch. Pediatr. Adolesc. Med. 166, 952–958. https://doi.org/10.1001/archpediatrics.2012.241

Miura, R., Ikeda-Araki, A., Ishihara, T., Miyake, K., Miyashita, C., Nakajima, T., Kobayashi, S., Ishizuka, M., Kubota, T., Kishi, R., 2021. Effect of prenatal exposure to phthalates on epigenome-wide DNA methylations in cord blood and implications for fetal growth: The Hokkaido Study on Environment and Children's Health. Sci. Total Environ. 783, 147035. https://doi.org/10.1016/j.scitotenv.2021.147035

Moosa, A., Shu, H., Sarachana, T., Hu, V.W., 2018. Are endocrine disrupting compounds environmental risk factors for autism spectrum disorder? Horm. Behav. 101, 13–21. https://doi.org/10.1016/j.yhbeh.2017.10.003

Morgan, M.K., Jones, P.A., Calafat, A.M., Ye, X., Croghan, C.W., Chuang, J.C., Wilson, N.K., Clifton, M.S., Figueroa, Z., Sheldon, L.S., 2011. Assessing the quantitative relationships between preschool children's exposures to bisphenol a by route and urinary biomonitoring. Environ. Sci. Technol. 45, 5309–5316. https://doi.org/10.1021/es200537u

Moriyama, K., Tagami, T., Akamizu, T., Usui, T., Saijo, M., Kanamoto, N., Hataya, Y., Shimatsu, A., Kuzuya, H., Nakao, K., 2002. Thyroid hormone action is disrupted by bisphenol A as an antagonist. J. Clin. Endocrinol. Metab. 87, 5185–5190. https://doi.org/10.1210/jc.2002-020209

Morris, G., Puri, B.K., Frye, R.E., Maes, M., 2018. The Putative Role of Environmental Mercury in the Pathogenesis and Pathophysiology of Autism Spectrum Disorders and Subtypes. Mol. Neurobiol. 55, 4834–4856. https://doi.org/10.1007/s12035-017-0692-2

Müller, M.H.B., Polder, A., Brynildsrud, O.B., Grønnestad, R., Karimi, M., Lie, E., Manyilizu, W.B., Mdegela, R.H., Mokiti, F., Murtadha, M., Nonga, H.E., Skaare, J.U., Solhaug, A., Lyche, J.L., 2019. Prenatal exposure to persistent organic pollutants in Northern Tanzania and their distribution between breast milk, maternal blood, placenta and cord blood. Environ. Res. 170, 433–442. https://doi.org/10.1016/j.envres.2018.12.026

Mustieles, V., Casas, M., Ferrando-Marco, P., Ocón-Hernández, O., Reina-Pérez, I., Rodríguez-

1972 Carrillo, A., Vela-Soria, F., Pérez-Lobato, R., Navarrete-Muñoz, E.M., Freire, C., Olea, N.,
1973 Fernández, M.F., 2019. Bisphenol A and adiposity measures in peripubertal boys from the
1974 INMA-Granada cohort. Environ. Res. 173, 443–451.
1975 https://doi.org/10.1016/j.envres.2019.03.045
1976 Nesan, D., Kurrasch, D.M., 2020. Gestational Exposure to Common Endocrine Disrupting Chemicals
1977 and Their Impact on Neurodevelopment and Behavior. Annu. Rev. Physiol. 82, 177–202.
1978 https://doi.org/10.1146/annurev-physiol-021119-034555
1979 Net, S., Sempéré, R., Delmont, A., Paluselli, A., Ouddane, B., 2015. Occurrence, fate, behavior and
1980 ecotoxicological state of phthalates in different environmental matrices. Environ. Sci. Technol.
1981 49, 4019–4035. https://doi.org/10.1021/es505233b
1982 Notardonato, I., Protano, C., Vitali, M., Bhattacharya, B., Avino, P., 2019. A Method Validation for
1983 Simultaneous Determination of Phthalates and Bisphenol A Released from Plastic Water
1984 Containers. Appl. Sci 9, 2945. https://doi.org/10.3390/app9142945
1985 Oliveira Souzaa, J.M., Oliveira Souzaa, M.C., Rocha, B.A., Nadal, M., Domingo, J.L., Barbosa Jr, F.,
1986 2022. Levels of phthalates and bisphenol in toys from Brazilian markets: Migration rate into
1987 children's saliva and daily exposure. Sci. Total Environ. 828.
1988 https://doi.org/10.1016/j.scitotenv.2022.154486
1989 Ormond, G., Nieuwenhuijsen, M.J., Nelson, P., Toledano, M.B., Iszatt, N., Geneletti, S., Elliott, P.,
1990 2009. Endocrine disruptors in the workplace, hair spray, folate supplementation, and risk of
1991 hypospadias: Case-control study. Environ. Health Perspect. 117, 303–307.
1992 https://doi.org/10.1289/ehp.11933
1993 Ouyang, F., Zhang, G.H., Du, K., Shen, L., Ma, R., Wang, Xia, Wang, Xiaobin, Zhang, J., 2020.
1994 Maternal prenatal urinary bisphenol A level and child cardio-metabolic risk factors: A
.995 prospective cohort study. Environ. Pollut. 265, 115008.
.996 https://doi.org/10.1016/j.envpol.2020.115008
.997 Padmanabhan, V., Song, W., Puttabyatappa, M., 2021. Praegnatio perturbatio—impact of endocrine-
.998 disrupting chemicals, Endocrine Reviews. https://doi.org/10.1210/endrev/bnaa035

1999 Pagoni, A., Arvaniti, O.S., Kalantzi, O.I., 2022. Exposure to phthalates from personal care products:
2000 Urinary levels and predictors of exposure. Environ. Res. 212, 113194.
2001 https://doi.org/10.1016/j.envres.2022.113194
2002 Pan, I.J., Daniels, J.L., Goldman, B.D., Herring, A.H., Siega-Riz, A.M., Rogan, W.J., 2009.
2003 Lactational exposure to polychlorinated biphenyls, dichlorodiphenyltrichloroethane, and
2004 dichlorodiphenyldichloroethylene and infant neurodevelopment: An analysis of the pregnancy,
2005 infection, and nutrition babies study. Environ. Health Perspect. 117, 488–494.
2006 https://doi.org/10.1289/ehp.0800063
2007 Pan, Y., Deng, M., Li, J., Du, B., Lan, S., Liang, X., Zeng, L., 2020. Occurrence and Maternal
2008 Transfer of Multiple Bisphenols, including an Emerging Derivative with Unexpectedly High
2009 Concentrations, in the Human Maternal-Fetal-Placental Unit. Environ. Sci. Technol. 54, 3476–
2010 3486. https://doi.org/10.1021/acs.est.0c00206
2011 Parent, A.S., Naveau, E., Gerard, A., Bourguignon, J.P., Westbrook, G.L., 2011. Early developmental
2012 actions of endocrine disruptors on the hypothalamus, hippocampus, and cerebral cortex. J.
2013 Toxicol. Environ. Heal. - Part B Crit. Rev. 14, 328–345.
2014 https://doi.org/10.1080/10937404.2011.578556
2015 Patisaul, H.B., 2021. Reproductive toxicology : Endocrine disruption and reproductive disorders :
2016 Impacts on sexually dimorphic neuroendocrine pathways. Reproduction 162, F111–F130.
2017 https://doi.org/10.1530/REP-20-0596
2018 Pearce, J.L., Neelon, B., Bloom, M.S., Buckley, J.P., Ananth, C. V., Perera, F., Vena, J., Hunt, K.,
2019 2021. Exploring associations between prenatal exposure to multiple endocrine disruptors and
2020 birth weight with exposure continuum mapping. Environ. Res. 200.
2021 https://doi.org/10.1016/j.envres.2021.111386
2022 Peng, C.Y., Tsai, E.M., Kao, T.H., Lai, T.C., Liang, S.S., Chiu, C.C., Wang, T.N., 2019. Canned food
2023 intake and urinary bisphenol a concentrations: a randomized crossover intervention study.
2024 Environ. Sci. Pollut. Res. 26, 27999–28009. https://doi.org/10.1007/s11356-019-05534-y
2025 Périan, S., Vanacker, J.M., 2020. GPER as a Receptor for Endocrine-Disrupting Chemicals (EDCs).

Front. Endocrinol. (Lausanne). 11, 1–7. https://doi.org/10.3389/fendo.2020.00545

Ping, L., Wu, C., Chang, X., Qi, X., Minglam, Z., Zhou, Z., 2016. Children's Health Adverse Associations of both Prenatal and Postnatal Exposure to Organophosphorous Pesticides with Infant Neurodevelopment. Environ. Health Perspect. 124, 1637–1643.

Plante, I., Winn, L.M., Vaillancourt, C., Grigorova, P., Parent, L., 2022. Killing two birds with one stone: Pregnancy is a sensitive window for endocrine effects on both the mother and the fetus. Environ. Res. 205, 112435. https://doi.org/10.1016/j.envres.2021.112435

Praveena, S.M., Siok Fong, C., Amaruddin, A.F., 2021. Phthalates in children toys available in Malaysian market: Quantification and potential human health risk. J. Steroid Biochem. Mol. Biol. 213, 105955. https://doi.org/10.1016/j.jsbmb.2021.105955

Predieri, B., Alves, A.D., Iughetti, L., 2022. New insights on the effects of endocrine-disrupting chemicals on children. J. Pediatr. 98, 73–85. https://doi.org/10.1016/j.jped.2021.11.003

Quirós-Alcalá, L., Eskenazi, B., Bradman, A., Ye, X., Calafat, A.M., Harley, K., 2013. Determinants of urinary bisphenol A concentrations in Mexican/Mexican-American pregnant women. Environ. Int. 59, 152–160. https://doi.org/10.1016/j.envint.2013.05.016

Rager, J.E., Bangma, J., Carberry, C., Chao, A., Grossman, J., Lu, K., Manuck, T.A., Sobus, J.R., Szilagyi, J., Fry, R.C., 2020. Review of the environmental prenatal exposome and its relationship to maternal and fetal health. Reprod. Toxicol. 98, 1–12. https://doi.org/10.1016/j.reprotox.2020.02.004

Ramadan, M., Cooper, B., Posnack, N.G., 2020. Bisphenols and phthalates: Plastic chemical exposures can contribute to adverse cardiovascular health outcomes. Birth Defects Res. 112, 1362–1385. https://doi.org/10.1002/bdr2.1752

Ramírez, V., Gálvez-Ontiveros, Y., González-Domenech, P.J., Baca, M.Á., Rodrigo, L., Rivas, A., 2022. Role of endocrine disrupting chemicals in children's neurodevelopment. Environ. Res. 203. https://doi.org/10.1016/j.envres.2021.111890

Rattan, S., Flaws, J.A., 2019. The epigenetic impacts of endocrine disruptors on female reproduction across generations. Biol. Reprod. 101, 635–644. https://doi.org/10.1093/biolre/ioz081

Rebuli, M.E., Cao, J., Sluzas, E., Barry Delclos, K., Camacho, L., Lewis, S.M., Vanlandingham, M.M., Patisaul, H.B., 2014. Investigation of the effects of subchronic low dose oral exposure to bisphenol a (BPA) and ethinyl estradiol (EE) on estrogen receptor expression in the juvenile and adult female rat hypothalamus. Toxicol. Sci. 140, 190–203. https://doi.org/10.1093/toxsci/kfu074

Recio, R., Ocampo-Gómez, G., Morán-Martínez, J., Borja-Aburto, V., López-Cervantes, M., Uribe, M., Torres-Sánchez, L., Cebrián, M.E., 2005. Pesticide exposure alters follicle-stimulating hormone levels in Mexican agricultural workers. Environ. Health Perspect. 113, 1160–1163. https://doi.org/10.1289/ehp.7374

Reinen, J., Vermeulen, N.P.E., 2014. Biotransformation of Endocrine Disrupting Compounds by Selected Phase I and Phase II Enzymes – Formation of Estrogenic and Chemically Reactive Metabolites by Cytochromes P450 and Sulfotransferases. Curr. Med. Chem. 22, 500–527. https://doi.org/10.2174/0929867321666140916123022

Rüegg, J., Swedenborg, E., Wahlström, D., Escande, A., Balaguer, P., Pettersson, K., Pongratz, I., 2008. The transcription factor aryl hydrocarbon receptor nuclear translocator functions as an estrogen receptor β-selective coactivator, and its recruitment to alternative pathways mediates antiestrogenic effects of dioxin. Mol. Endocrinol. 22, 304–316. https://doi.org/10.1210/me.2007-0128

Ruis, M.T., Rock, K.D., Hall, S.M., Horman, B., Patisaul, H.B., Stapleton, H.M., 2019. PBDEs Concentrate in the Fetal Portion of the Placenta: Implications for Thyroid Hormone Dysregulation. Endocrinol. (United States) 160, 2748–2758. https://doi.org/10.1210/en.2019-00463

Sajid, M., Ilyas, M., 2017. PTFE-coated non-stick cookware and toxicity concerns: a perspective. Environ. Sci. Pollut. Res. 24, 23436–23440. https://doi.org/10.1007/s11356-017-0095-y

Sangeetha, S., Vimalkumar, K., Loganathan, B.G., 2021. Environmental Contamination and Human Exposure to Select Endocrine-Disrupting Chemicals: A Review. Sustain. Chem. 2, 343–380. https://doi.org/10.3390/suschem2020020

Sathyanarayana, S., Karr, C.J., Lozano, P., Brown, E., Calafat, A.M., Liu, F., Swan, S.H., 2008. Baby

care products: possible sources of infant phthalate exposure. Pediatrics 121. https://doi.org/10.1542/PEDS.2006-3766

Schaedlich, K., Gebauer, S., Hunger, L., Beier, L.S., Koch, H.M., Wabitsch, M., Fischer, B., Ernst, J., 2018. DEHP deregulates adipokine levels and impairs fatty acid storage in human SGBS-adipocytes. Sci. Rep. 8, 1–14. https://doi.org/10.1038/s41598-018-21800-4

Schmutzler, C., Hamann, I., Hofmann, P.J., Kovacs, G., Stemmler, L., Mentrup, B., Schomburg, L., Ambrugger, P., Grüters, A., Seidlova-Wuttke, D., Jarry, H., Wuttke, W., Köhrle, J., 2004. Endocrine active compounds affect thyrotropin and thyroid hormone levels in serum as well as endpoints of thyroid hormone action in liver, heart and kidney. Toxicology 205, 95–102. https://doi.org/10.1016/j.tox.2004.06.041

Sena, J., Souza, D., Kizys, L., Rodrigues, R., Glebocki, G., Marino, R., Ortiga-carvalho, T.M., Giannocco, G., Dale, I., Guerreiro, C., Regios, M., Aurélio, M., Izabel, M., 2017. Perinatal exposure to glyphosate-based herbicide alters the thyrotrophic axis and causes thyroid hormone homeostasis imbalance in male rats. Toxicology 377, 25–37. https://doi.org/10.1016/j.tox.2016.11.005

Shaffer, R.M., Ferguson, K.K., Sheppard, L., James-Todd, T., Butts, S., Chandrasekaran, S., Swan, S.H., Barrett, E.S., Nguyen, R., Bush, N., McElrath, T.F., Sathyanarayana, S., 2019. Maternal urinary phthalate metabolites in relation to gestational diabetes and glucose intolerance during pregnancy. Environ. Int. 123, 588–596. https://doi.org/10.1016/j.envint.2018.12.021

Sheikh, I.A., Turki, R.F., Abuzenadah, A.M., Damanhouri, G.A., Beg, M.A., 2016. Endocrine disruption: Computational perspectives on human sex hormone-binding globulin and phthalate plasticizers. PLoS One 11, 1–13. https://doi.org/10.1371/journal.pone.0151444

Shekhar, S., Sood, S., Showkat, S., Lite, C., Chandrasekhar, A., Vairamani, M., Barathi, S., Santosh, W., 2017. Detection of phenolic endocrine disrupting chemicals (EDCs) from maternal blood plasma and amniotic fluid in Indian population. Gen. Comp. Endocrinol. 241, 100–107. https://doi.org/10.1016/j.ygcen.2016.05.025

Siddique, S., Zhang, G., Coleman, K., Kubwabo, C., 2021. Investigation of the migration of

bisphenols from baby bottles and sippy cups. Curr. Res. Food Sci. 4, 619–626. https://doi.org/10.1016/j.crfs.2021.08.006

Singh, S., Li, S.S.L., 2012. Epigenetic effects of environmental chemicals bisphenol A and phthalates. Int. J. Mol. Sci. 13, 10143–10153. https://doi.org/10.3390/ijms130810143

Smith, A.R., Kogut, K.R., Parra, K., Bradman, A., Holland, N., Harley, K.G., 2022. Dietary intake and household exposures as predictors of urinary concentrations of high molecular weight phthalates and bisphenol A in a cohort of adolescents. J. Expo. Sci. Environ. Epidemiol. 32, 37–47. https://doi.org/10.1038/s41370-021-00305-9

Snoj Tratnik, J., Kosjek, T., Heath, E., Mazej, D., Ćehić, S., Karakitsios, S.P., Sarigiannis, D.A., Horvat, M., 2019. Urinary bisphenol A in children, mothers and fathers from Slovenia: Overall results and determinants of exposure. Environ. Res. 168, 32–40. https://doi.org/10.1016/j.envres.2018.09.004

Søeborg, T., Frederiksen, H., Andersson, A.M., 2014. Considerations for estimating daily intake values of nonpersistent environmental endocrine disruptors based on urinary biomonitoring data. Reproduction 147, 455–463. https://doi.org/10.1530/REP-13-0458

Song, S., He, Y., Huang, Y., Huang, X., Guo, Y., Zhu, H., Kannan, K., Zhang, T., 2020a. Occurrence and transfer of benzophenone-type ultraviolet filters from the pregnant women to fetuses. Sci. Total Environ. 726, 138503. https://doi.org/10.1016/j.scitotenv.2020.138503

Song, S., He, Y., Zhang, T., Zhu, H., Huang, X., Bai, X., Zhang, B., Kannan, K., 2020b. Profiles of parabens and their metabolites in paired maternal-fetal serum, urine and amniotic fluid and their implications for placental transfer. Ecotoxicol. Environ. Saf. 191, 110235. https://doi.org/10.1016/j.ecoenv.2020.110235

Stefan-van Staden, R.I., Gugoaşă, L.A., Calenic, B., van Staden, J.F., Legler, J., 2014. Screening of children saliva samples for bisphenol A using stochastic, amperometric and multimode microsensors. Anal. Chem. Res. 1, 1–7. https://doi.org/10.1016/j.ancr.2014.06.001

Stigum, H., Iszatt, N., Polder, A., Mandal, S., Eggesbø, M., 2015. A novel model to characterize postnatal exposure to lipophilic environmental toxicants and application in the study of

2134 hexachlorobenzene and infant growth. Environ. Int. 85, 156–162.
2135 https://doi.org/10.1016/j.envint.2015.08.011
2136 Street, M.E., Angelini, S., Bernasconi, S., Burgio, E., Cassio, A., Catellani, C., Cirillo, F., Deodati, A.,
2137 Fabbrizi, E., Fanos, V., Gargano, G., Grossi, E., Iughetti, L., Lazzeroni, P., Mantovani, A.,
2138 Migliore, L., Palanza, P., Panzica, G., Papini, A.M., Parmigiani, S., Predieri, B., Sartori, C.,
2139 Tridenti, G., Amarri, S., 2018. Current knowledge on endocrine disrupting chemicals (EDCs)
2140 from animal biology to humans, from pregnancy to adulthood: Highlights from a national italian
2141 meeting. Int. J. Mol. Sci. 19, 1–44. https://doi.org/10.3390/ijms19061647
2142 Street, M.E., Bernasconi, S., 2020. Endocrine-disrupting chemicals in human fetal growth. Int. J. Mol.
2143 Sci. 21. https://doi.org/10.3390/ijms21041430
2144 Sugden, M.C., Holness, M.J., 2008. Role of nuclear receptors in the modulation of insulin secretion in
2145 lipid-induced insulin resistance. Biochem. Soc. Trans. 36, 891–900.
2146 https://doi.org/10.1042/BST0360891
2147 Sunman, B., Yurdakök, K., Kocer-Gumusel, B., Özyüncü, Ö., Akbıyık, F., Balcı, A., Özkemahlı, G.,
2148 Erkekoğlu, P., Yurdakök, M., 2019. Prenatal bisphenol a and phthalate exposure are risk factors
2149 for male reproductive system development and cord blood sex hormone levels. Reprod. Toxicol.
2150 87, 146–155. https://doi.org/10.1016/j.reprotox.2019.05.065
2151 Swedenborg, E., Rüegg, J., Mäkelä, S., Pongratz, I., 2009. Endocrine disruptive chemicals:
2152 Mechanisms of action and involvement in metabolic disorders. J. Mol. Endocrinol. 43, 1–10.
2153 https://doi.org/10.1677/JME-08-0132
2154 Swedish Chemicals Agency, 2013. Report 3/13: Hazardous chemicals in textiles.
2155 Kemikalieinspektionen.
2156 Sweeney, M.F., Hasan, N., Soto, A.M., Sonnenschein, C., 2015. Environmental endocrine disruptors:
!157 Effects on the human male reproductive system. Rev. Endocr. Metab. Disord. 16, 341–357.
!158 https://doi.org/10.1007/s11154-016-9337-4
!159 Szczepańska, N., Kubica, P., Płotka-Wasylka, J., Kudłak, B., Namieśnik, J., 2020. Ultrasound assisted
!160 solvent extraction of porous membrane-packed samples followed by liquid chromatography-

tandem mass spectrometry for determination of BADGE, BFDGE and their derivatives in packed vegetables. Sci. Total Environ. 708. https://doi.org/10.1016/j.scitotenv.2019.135178

Szczepańska, N., Namieśnik, J., Kudłak, B., 2016. Assessment of toxic and endocrine potential of substances migrating from selected toys and baby products. Environ. Sci. Pollut. Res. 23, 24890–24900. https://doi.org/10.1007/s11356-016-7616-y

Takeuchi, S., Iida, M., Kobayashi, S., Jin, K., Matsuda, T., Kojima, H., 2005. Differential effects of phthalate esters on transcriptional activities via human estrogen receptors α and β, and androgen receptor. Toxicology 210, 223–233. https://doi.org/10.1016/j.tox.2005.02.002

Takeuchi, S., Matsuda, T., Kobayashi, S., Takahashi, T., Kojima, H., 2006. In vitro screening of 200 pesticides for agonistic activity via mouse peroxisome proliferator-activated receptor (PPAR)α and PPARγ and quantitative analysis of in vivo induction pathway. Toxicol. Appl. Pharmacol. 217, 235–244. https://doi.org/10.1016/j.taap.2006.08.011

Takeuchi, S., Shiraishi, F., Kitamura, S., Kuroki, H., Jin, K., Kojima, H., 2011. Characterization of steroid hormone receptor activities in 100 hydroxylated polychlorinated biphenyls, including congeners identified in humans. Toxicology 289, 112–121. https://doi.org/10.1016/j.tox.2011.08.001

Tanner, E.M., Hallerbäck, M.U., Wikström, S., Lindh, C., Kiviranta, H., Gennings, C., Bornehag, C.G., 2020. Early prenatal exposure to suspected endocrine disruptor mixtures is associated with lower IQ at age seven. Environ. Int. 134, 105185. https://doi.org/10.1016/j.envint.2019.105185

Teil, M.J., Moreau-Guigon, E., Blanchard, M., Alliot, F., Gasperi, J., Cladière, M., Mandin, C., Moukhtar, S., Chevreuil, M., 2016. Endocrine disrupting compounds in gaseous and particulate outdoor air phases according to environmental factors. Chemosphere 146, 94–104. https://doi.org/10.1016/j.chemosphere.2015.12.015

Teng, C., Goodwin, B., Shockley, K., Xia, M., Huang, R., Norris, J., Merrick, B.A., Jetten, A.M., Austin, C.P., Tice, R.R., 2013. Bisphenol A affects androgen receptor function via multiple mechanisms. Chem. Biol. Interact. 203, 556–564. https://doi.org/10.1016/j.cbi.2013.03.013

Tian, Y., Liang, H., Miao, M., Yang, F., Ji, H., Cao, W., Liu, X., Zhang, X., Chen, A., Xiao, H., Hu,

H., Yuan, W., 2019. Maternal plasma concentrations of perfluoroalkyl and polyfluoroalkyl substances during pregnancy and anogenital distance in male infants. Hum. Reprod. 34, 1356–1368. https://doi.org/10.1093/humrep/dez058

Titus, L., Hatch, E.E., Drake, K.M., Parker, S.E., Hyer, M., Palmer, J.R., Strohsnitter, W.C., Adam, E., Herbst, A.L., Huo, D., Hoover, R.N., Troisi, R., 2019. Reproductive and hormone-related outcomes in women whose mothers were exposed in utero to diethylstilbestrol (DES): A report from the US National Cancer Institute DES Third Generation Study. Reprod. Toxicol. 84, 32–38. https://doi.org/10.1016/j.reprotox.2018.12.008

Toichuev, R.M., Zhilova, L.V., Paizildaev, T.R., Khametova, M.S., Rakhmatillaev, A., Sakibaev, K.S., Madykova, Z.A., Toichueva, A.U., Schlumpf, M., Weber, R., Lichtensteiger, W., 2018. Organochlorine pesticides in placenta in Kyrgyzstan and the effect on pregnancy, childbirth, and newborn health. Environ. Sci. Pollut. Res. 25, 31885–31894. https://doi.org/10.1007/s11356-017-0962-6

Topper, V.Y., Walker, D.M., Gore, A.C., 2015. Sexually dimorphic effects of gestational endocrine-disrupting chemicals on microRNA expression in the developing rat hypothalamus. Mol. Cell. Endocrinol. 414, 42–52. https://doi.org/10.1016/j.mce.2015.07.013

Turbeville, H.R., Sasser, J.M., 2020. Preeclampsia beyond pregnancy: Long-term consequences for mother and child. Am. J. Physiol. - Ren. Physiol. 318, F1315–F1326. https://doi.org/10.1152/ajprenal.00071.2020

Tuzimski, T., Szubartowski, S., Gadzała-Kopciuch, R., Miturski, A., Wójtowicz-Marzec, M., Kwasniewski, W., Buszewski, B., 2020. Comparison of DAD and FLD detection for identification of selected bisphenols in human breast milk samples and their quantitative analysis by LC-MS/MS. J. AOAC Int. 103, 1029–1042. https://doi.org/10.1093/JAOACINT/QSAA027

Tzatzarakis, M.N., Karzi, V., Vakonaki, E., Goumenou, M., Kavvalakis, M., Stivaktakis, P., Tsitsimpikou, C., Tsakiris, I., Rizos, A.K., Tsatsakis, A.M., 2017. Bisphenol A in soft drinks and canned foods and data evaluation. Food Addit. Contam. Part B Surveill. 10, 85–90. https://doi.org/10.1080/19393210.2016.1266522

Vafeiadi, M., Roumeliotaki, T., Chalkiadaki, G., Rantakokko, P., Kiviranta, H., Fthenou, E., Kyrtopoulos, S.A., Kogevinas, M., Chatzi, L., 2017. Persistent organic pollutants in early pregnancy and risk of gestational diabetes mellitus. Environ. Int. 98, 89–95. https://doi.org/10.1016/j.envint.2016.10.005

Van Duursen, M.B.M., Boberg, J., Christiansen, S., Connolly, L., Damdimopoulou, P., Filis, P., Fowler, P.A., Gadella, B.M., Holte, J., Jääger, K., Johansson, H.K.L., Li, T., Mazaud-Guittot, S., Parent, A.S., Salumets, A., Soto, A.M., Svingen, T., Velthut-Meikas, A., Wedebye, E.B., Xie, Y., van den Berg, M., 2020. Safeguarding female reproductive health against endocrine disrupting chemicals—The FREIA project. Int. J. Mol. Sci. 21. https://doi.org/10.3390/ijms21093215

Van Lipzig, M.M.H., Commandeur, J.N., De Kanter, F.J.J., Damsten, M.C., Vermeulen, N.P.E., Maat, E., Groot, E.J., Brouwer, A., Kester, M.H.A., Visser, T.J., Meerman, J.H.N., 2005. Bioactivation of dibrominated biphenyls by cytochrome P450 activity to metabolites with estrogenic activity and estrogen sulfotransferase inhibition capacity. Chem. Res. Toxicol. 18, 1691–1700. https://doi.org/10.1021/tx0501233

Varshavsky, J., Smith, A., Wang, A., Hom, E., Izano, M., Huang, H., Padula, A., Woodruff, T.J., 2020. Heightened susceptibility: A review of how pregnancy and chemical exposures influence maternal health. Reprod. Toxicol. 92, 14–56. https://doi.org/10.1016/j.reprotox.2019.04.004

Varshavsky, J.R., Morello-Frosch, R., Woodruff, T.J., Zota, A.R., 2018. Dietary sources of cumulative phthalates exposure among the U.S. general population in NHANES 2005-2014. Environ. Int. 115, 417–429. https://doi.org/10.1016/j.envint.2018.02.029

Vela-Soria, F., Serrano-López, L., García-Villanova, J., de Haro, T., Olea, N., Freire, C., 2020. HPLC-MS/MS method for the determination of perfluoroalkyl substances in breast milk by combining salt-assisted and dispersive liquid-liquid microextraction. Anal. Bioanal. Chem. 412, 7913–7923. https://doi.org/10.1007/S00216-020-02924-X/TABLES/5

Verner, M.A., Ayotte, P., Muckle, G., Charbonneau, M., Haddad, S., 2009. A physiologically based pharmacokinetic model for the assessment of infant exposure to persistent organic pollutants in epidemiologic studies. Environ. Health Perspect. 117, 481–487.

https://doi.org/10.1289/ehp.0800047

Verner, M.A., Plusquellec, P., Desjardins, J.L., Cartier, C., Haddad, S., Ayotte, P., Dewailly, É., Muckle, G., 2015. Prenatal and early-life polychlorinated biphenyl (PCB) levels and behavior in Inuit preschoolers. Environ. Int. 78, 90–94. https://doi.org/10.1016/j.envint.2015.02.004

Verner, M.A., Plusquellec, P., Muckle, G., Ayotte, P., Dewailly, T., Jacobson, S.W., Jacobson, J.L., Charbonneau, M., Haddad, S., 2010. Alteration of infant attention and activity by polychlorinated biphenyls: Unravelling critical windows of susceptibility using physiologically based pharmacokinetic modeling. Neurotoxicology 31, 424–431. https://doi.org/10.1016/j.neuro.2010.05.011

Viel, J.F., Warembourg, C., Le Maner-Idrissi, G., Lacroix, A., Limon, G., Rouget, F., Monfort, C., Durand, G., Cordier, S., Chevrier, C., 2015. Pyrethroid insecticide exposure and cognitive developmental disabilities in children: The PELAGIE mother-child cohort. Environ. Int. 82, 69–75. https://doi.org/10.1016/j.envint.2015.05.009

Vojta, Š., Melymuk, L., Klánová, J., 2017. Changes in Flame Retardant and Legacy Contaminant Concentrations in Indoor Air during Building Construction, Furnishing, and Use. Environ. Sci. Technol. 51, 11891–11899. https://doi.org/10.1021/acs.est.7b03245

Vrachnis, N., Loukas, N., Vrachnis, D., Antonakopoulos, N., Zygouris, D., Kolialexi, A., Pergaliotis, V., Iavazzo, C., Mastorakos, G., Iliodromiti, Z., 2021. A systematic review of bisphenol a from dietary and non-dietary sources during pregnancy and its possible connection with fetal growth restriction: Investigating its potential effects and the window of fetal vulnerability. Nutrients 13, 1–20. https://doi.org/10.3390/nu13072426

Vuong, A.M., Yolton, K., Dietrich, K.N., Braun, J.M., Lanphear, B.P., Chen, A., 2018. Exposure to polybrominated diphenyl ethers (PBDEs) and child behavior: Current findings and future directions. Horm. Behav. 101, 94–104. https://doi.org/10.1016/j.yhbeh.2017.11.008

Vuong, A.M., Yolton, K., Poston, K.L., Xie, C., Webster, G.M., Sjödin, A., Braun, J.M., Dietrich, K.N., Lanphear, B.P., Chen, A., 2017a. Prenatal and postnatal polybrominated diphenyl ether (PBDE) exposure and measures of inattention and impulsivity in children. Neurotoxicol. Teratol.

64, 20–28. https://doi.org/10.1016/j.ntt.2017.09.001

Vuong, A.M., Yolton, K., Xie, C., Dietrich, K.N., Braun, J.M., Webster, G.M., Calafat, A.M., Lanphear, B.P., Chen, A., 2019. Prenatal and childhood exposure to poly- and perfluoroalkyl substances (PFAS) and cognitive development in children at age 8 years. Environ. Res. 172, 242–248. https://doi.org/10.1016/j.envres.2019.02.025

Vuong, A.M., Yolton, K., Xie, C., Webster, G.M., Sjödin, A., Braun, J.M., Dietrich, K.N., Lanphear, B.P., Chen, A., 2017b. Childhood polybrominated diphenyl ether (PBDE) exposure and neurobehavior in children at 8 years. Environ. Res. 158, 677–684. https://doi.org/10.1016/j.envres.2017.07.028

Walkowiak, J., Wiener, J.A., Fastabend, A., Heinzow, B., Krämer, U., Schmidt, E., Steingrüber, H.J., Wundram, S., Winneke, G., 2001. Environmental exposure to polychlorinated biphenyls and quality of the home environment: Effects on psychodevelopment in early childhood. Lancet 358, 1602–1607. https://doi.org/10.1016/S0140-6736(01)06654-5

Wang, J., Mei, H., Zhou, A.F., Huang, L.L., Cao, Z.Q., Hong, A.B., Yang, M., Xie, Q.T., Chen, D., Yang, S.P., Xiao, H., Yang, P., 2021. The associations of birth outcome differences in twins with prenatal exposure to bisphenol A and its alternatives. Environ. Res. 200, 111459. https://doi.org/10.1016/j.envres.2021.111459

Wang, Y., Zhu, H., Kannan, K., 2019. A review of biomonitoring of phthalate exposures. Toxics 7, 1–28. https://doi.org/10.3390/TOXICS7020021

Warner, G.R., Mourikes, V.E., Neff, A.M., Brehm, E., Flaws, J.A., 2020. Mechanisms of action of agrochemicals acting as endocrine disrupting chemicals. Mol. Cell. Endocrinol. 502, 110680. https://doi.org/10.1016/j.mce.2019.110680

Warner, M., Ye, M., Harley, K., Kogut, K., Bradman, A., Eskenazi, B., 2017. Prenatal DDT exposure and child adiposity at age 12: The CHAMACOS study. Environ. Res. 159, 606–612. https://doi.org/10.1016/j.envres.2017.08.050

WHO, 2013. State of the Science of Endocrine Disrupting Chemicals 2012 Summary for Decision-Makers INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF

2296 CHEMICALS, World Health Organization.
2297 Wikström, S., Lin, P.I., Lindh, C.H., Shu, H., Bornehag, C.G., 2020. Maternal serum levels of
2298 perfluoroalkyl substances in early pregnancy and offspring birth weight. Pediatr. Res. 87, 1093–
2299 1099. https://doi.org/10.1038/s41390-019-0720-1
2300 Witczak, A., Abdel-Gawad, H., 2014. Assessment of health risk from organochlorine pesticides
2301 residues in high-fat spreadable foods produced in Poland. J. Environ. Sci. Heal. - Part B Pestic.
2302 Food Contam. Agric. Wastes 49, 917–928. https://doi.org/10.1080/03601234.2014.951574
2303 Witczak, A., Pohoryło, A., Abdel-Gawad, H., 2021. Endocrine-Disrupting Organochlorine Pesticides
2304 in Human Breast Milk: Changes during Lactation. Nutr. 2021, Vol. 13, Page 229 13, 229.
2305 https://doi.org/10.3390/NU13010229
2306 Wittassek, M., Angerer, J., Kolossa-Gehring, M., Schäfer, S.D., Klockenbusch, W., Dobler, L.,
2307 Günsel, A.K., Müller, A., Wiesmüller, G.A., 2009. Fetal exposure to phthalates - a pilot study.
2308 Int. J. Hyg. Environ. Health 212, 492–498. https://doi.org/10.1016/j.ijheh.2009.04.001
2309 Woodruff, T.J., Zota, A.R., Schwartz, J.M., 2011. Environmental chemicals in pregnant women in the
2310 united states: NHANES 2003- 2004. Environ. Health Perspect. 119, 878–885.
2311 https://doi.org/10.1289/EHP.1002727
2312 Woolf, T.F., Jordan, R.A., 1987. Basic Concepts in Drug Metabolism: Part I. J. Clin. Pharmacol. 27,
2313 15–17. https://doi.org/10.1177/009127008702700102
2314 Yaglova, N. V., Yaglov, V. V., 2015. Mechanisms of Disruptive Action of
2315 Dichlorodiphenyltrichloroethane (DDT) on the Function of Thyroid Follicular Epitheliocytes.
2316 Bull. Exp. Biol. Med. 160, 231–233. https://doi.org/10.1007/s10517-015-3136-x
2317 Yang, C., Harris, S.A., Jantunen, L.M., Kvasnicka, J., Nguyen, L. V., Diamond, M.L., 2020.
2318 Phthalates: Relationships between Air, Dust, Electronic Devices, and Hands with Implications
2319 for Exposure. Environ. Sci. Technol. 54, 8186–8197. https://doi.org/10.1021/acs.est.0c00229
2320 Yilmaz, B., Terekeci, H., Sandal, S., Kelestimur, F., 2020. Endocrine disrupting chemicals: exposure,
2321 effects on human health, mechanism of action, models for testing and strategies for prevention.
2322 Rev. Endocr. Metab. Disord. 21, 127–147. https://doi.org/10.1007/s11154-019-09521-z

Yu Ting, J.I.N., Deng, X.K., Zhoa, Y.Y., Li, J.L., Song, Q., Zhang, Y.H., Yang, Q., Chen, S.Q., 2020. Concentrations of Polybrominated Diphenyl Ethers in Maternal Blood, Placental Size, and Risk for Fetal Growth Restriction: A Nested Case-control Study. Biomed. Environ. Sci. 33, 821–828. https://doi.org/10.3967/bes2020.112

Zhang, B., He, Y., Zhu, H., Huang, X., Bai, X., Kannan, K., Zhang, T., 2020. Concentrations of bisphenol A and its alternatives in paired maternal–fetal urine, serum and amniotic fluid from an e-waste dismantling area in China. Environ. Int. 136, 105407. https://doi.org/10.1016/j.envint.2019.105407

Zhang, B., Zhang, H., Bai, X., Zhang, T., Xue, J., Lu, S., Kannan, K., 2022. Placental transfer of bisphenol diglycidyl ethers (BDGEs) and its association with maternal health in a population in South of China. Eco-Environment Heal. 1, 244–250. https://doi.org/10.1016/j.eehl.2022.11.004

Zhu, H., Kannan, K., 2020. Determination of melamine and its derivatives in textiles and infant clothing purchased in the United States. Sci. Total Environ. 710, 136396. https://doi.org/10.1016/J.SCITOTENV.2019.136396

Zoeller, R.T., 2007. Environmental chemicals impacting the thyroid: Targets and consequences. Thyroid 17, 811–817. https://doi.org/10.1089/thy.2007.0107

Zota, A.R., Mitro, S.D., Robinson, J.F., Hamilton, E.G., Park, J.S., Parry, E., Zoeller, R.T., Woodruff, T.J., 2018. Polybrominated diphenyl ethers (PBDEs) and hydroxylated PBDE metabolites (OH-PBDEs) in maternal and fetal tissues, and associations with fetal cytochrome P450 gene expression. Environ. Int. 112, 269–278. https://doi.org/10.1016/j.envint.2017.12.030