



A review of literature concerning the impact of endocrine-disrupting substances on women's reproductive health

Przegląd literatury na temat wpływu substancji zaburzających gospodarkę hormonalną na zdrowie reprodukcyjne kobiet

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Osmala-Kurpiewska W. A review of literature concerning the impact of endocrine-disrupting substances on women's reproductive health. Med Og Nauk Zdr. 2026;32(2):87–91. doi:10.26444/monz/224391

■ Abstract

Introduction and Objective. Substances that can imitate natural hormones in the body are known as endocrine-disrupting chemicals (EDCs). Women are commonly exposed to EDCs from materials that come into contact with food and personal care products. The aim of this review is to present the current data covering the years 2020–2026 on the impact of EDCs on women's health.

Review Methods. To facilitate the literature review, the PubMed database was searched using the following search terms: «female reproductive health AND endocrine disruptors», «women's reproductive health AND EDCs», «pregnancy exposure AND endocrine disrupting chemicals», «pregnancy exposure AND EDCs», «female reproductive health AND EDCs». Articles not related to the topic were excluded during the preliminary review of summaries. A total of 17 studies published between 2016–2026 were finally analysed. in the end.

Brief description of the state of knowledge. EDC substances disrupt the binding of hormones to their respective receptors, particularly the estrogen and androgen receptors, resulting in agonistic or antagonistic effects. Consequently, EDCs may have a negative effect on reproductive functions. This includes reducing the ovarian reserve and increases the risk of infertility.

Summary. In scientific publications, the significant impact of EDC on health is emphasized, and there is therefore a need to continue research, including using advanced methods for detecting and measuring EDC mixtures.

■ Key words

reproductive health, endocrine disruptors, infertility, female, prenatal exposure

■ Streszczenie

Wprowadzenie i cel pracy. Substancje zaburzające gospodarkę hormonalną (ang. *endocrine-disrupting chemicals*, EDCs) to różnego rodzaju substancje, które mogą naśladować, w całości lub częściowo, naturalne hormony organizmu. Kobiety są powszechnie narażone na EDCs pochodzące z materiałów mających kontakt z żywnością i produktów higieny osobistej. Celem niniejszego przeglądu jest przedstawienie aktualnych danych dotyczących wpływu EDCs na zdrowie kobiet w latach 2020–2026.

Metody przeglądu. Aby przeprowadzić niniejszy przegląd literatury dotyczący wpływu EDC na zdrowie reprodukcyjne kobiet, przeszukano bazę danych PubMed, używając różnych kombinacji słów kluczowych: „female reproductive health AND endocrine disruptors”, „womens reproductive health AND EDCs”, „pregnancy exposure AND endocrine disrupting chemicals”, „regnancy exposure AND EDCs”, „female reproductive health AND EDCs”. Po wstępnym przeglądzie streszczeń wykluczono publikacje niezwiązane z tematem artykułu. Ostatecznie przeanalizowano 17 badań, opublikowanych w latach 2016–2026.

Opis stanu wiedzy. EDCs to substancje, które zakłócają wiązanie hormonów z odpowiadającymi im receptorami – w szczególności dotyczy to receptora estrogenowego i androgenowego, powodując działanie agonistyczne lub antagonistyczne. W konsekwencji EDCs mogą negatywnie wpływać na funkcje rozrodcze, m.in. obniżyć rezerwę jajnikową i zwiększać ryzyko niepłodności.

Podsumowanie. W publikacjach naukowych podkreśla się istotny wpływ EDC na zdrowie, istnieje zatem potrzeba prowadzenia dalszych badań w tym zakresie, w tym z zastosowaniem zaawansowanych metod wykrywania i pomiaru mieszanin EDC.

■ Słowa kluczowe

zdrowie reprodukcyjne, zaburzaczce układu hormonalnego, niepłodność kobiet, ekspozycja prenatalna

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INTRODUCTION

Anthropogenic activity has caused the introduction of organic and inorganic chemical substances into the environment on a global scale. These substances have the potential to disrupt the hormonal balance in the human body [1]. Endocrine-disrupting chemicals (EDCs) are substances that can affect the endocrine system, which is a network of cells and glands that produce and release hormones into the bloodstream. As the blood circulates, hormones reach every tissue and organ in the body. The endocrine system, for instance, regulates appetite, the manner in which the body metabolises nutrients, the duration of sleep, physical development and sexual maturity, the secretion of sex hormones that regulate the menstrual cycle, and the production of insulin, which maintains blood glucose levels [2]. The United States Environmental Protection Agency (USEPA) defines it as 'an exogenous factor that disrupts the synthesis, secretion, transportation, metabolism, binding or elimination of natural blood-borne hormones in the body, which are responsible for disrupting homeostasis, reproduction and developmental processes' [1].

In the late 1990s, a theory emerged proposing that certain exogenous chemicals disrupt endocrine hormonal axes, exerting influence over diverse regions. The presence of EDCs in the environment is varied and can include different groups [2, 3]. Some examples of EDCs include industrial chemicals such as dioxins and polychlorinated biphenyls (PCBs), and agricultural chemicals, such as pesticides, herbicides, fungicides and insecticides. Other examples include phthalates, bisphenol A (BPA), perfluorinated compounds (PFCs), currently referred to as per- and polyfluoroalkyl substances (PFAS), certain medications (e.g., cardiovascular drugs), heavy metals, and parabens [3, 4]. EDC may be able to copy natural hormones in the body, either completely or in part, and can act as agonists or antagonists [3]. The presence and durability of EDCs in the environment may have an impact on living organisms. The main cause of threats to the environment is the incorrect methods used in the production and recycling of synthetic materials, including adhesives and paints. The significant exposure at EDC is due to the use of a wide range of chemicals and pollutants that can contaminate the food chain. EDC builds up mainly in the soil and water, which causes it to contaminate food and beverages [2].

Women are more likely to be exposed to harmful chemicals that disrupt hormonal activity (EDCs), which can originate from materials that have contact with food and personal hygiene products [5]. Problems with the endocrine system and reproductive health in women can also be caused by the presence of these substances in food, housing, and the environment [6, 7]. The main groups of EDCs, their sources and routes of exposure in women are presented in Table 1.

Understanding the relationship between exposure to EDCs and women's health is an important area of research. Therefore, the aim of this review is to present the current data on the impact of EDCs on women's health in the years 2020–2026.

MATERIALS AND METHOD

To facilitate the current literature review on the impact of EDCs on female reproductive health, the PubMed database was searched using the following search terms: 'female reproductive health AND endocrine disruptors', 'women's reproductive health AND EDCs', 'pregnancy exposure AND endocrine disrupting chemicals', 'pregnancy exposure AND EDCs', 'female reproductive health AND EDCs'. Articles not related to the topic of the review were excluded during the preliminary review of summaries. Finally, a total of 17 studies published between 2016–2026 were analysed.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Mechanism of action. EDCs interfere with the binding of hormones to their receptors, especially the estrogen and androgen receptors. This results in agonistic or antagonistic actions, which can disrupt physiological signal transduction pathways, leading to further changes in gene expression and cellular function [8]. Depending on the duration of exposure and the type of EDC, they may have a different effect on hormonal signalling [9]. They have the capacity to activate a variety of hormonal receptors, including the androgen receptor (AR), estrogen receptor (ER), estrogen-related receptor (ERR), aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR), and pregnane X receptor (PXR). EDCs can also act in an antagonistic manner by binding to various receptors without activating them,

Table 1. Substances that disrupt the endocrine system (EDCs) – primary sources, exposure pathways and health implications

EDC substance	Main sources of exposure	Main exhibition route	Main health effects on women	Selected literature
Bisphenols (BPA, BPS)	Plastic packaging (e.g. polycarbonate containers, food and drink cans)	Ingestion	Hormonal disorders, PCOS, reduced number and quality of oocytes	19, 20, 33
Phthalates (DEHP, MEHP)	Packaging for food and drink, cosmetics	Ingestion, dermal	PCOS, uterine fibroids, estrogen-dependent diseases	35, 36
PFAS (PFOA, PFOS)	Containers for food, kitchen utensils, textiles and fire extinguishers	Ingestion, respiratory, dermal	Metabolic disorders, adiposity, risk of pregnancy complications	26, 29, 34
POPs (PCB, DDE)	Industrial solvents, lubricants, pesticides (formerly)	Ingestion, respiratory, dermal	Hormonal disorders, increased progesterone secretion in granulosa HGrC1	21
Parabens	Cosmetics, personal care products, food and drinks (preservatives)	Dermal, ingestion	Potential impact on the risk of infertility	24

Source: [19–21], [24, 26, 29], [33–36].

BPA – Bisphenol A; **BPS** – Bisphenol S; **DEHP** – di(2-ethylhexyl) phthalate; **MEHP** – Mono-2-ethylhexyl phthalate; **PFAS** – Per- and Polyfluoroalkyl Substances; **PFOA** – Perfluorooctanoic acid; **PFOS** – Perfluorooctanesulfonic acid; **POPs** – Persistent Organic Pollutants; **PCB** – Polychlorinated biphenyls; **DDE** – dichlorodiphenyldichloroethylene.

and can influence hormone levels, synthesis, metabolism, transport, or elimination [10–12]. Some EDCs, such as non-ylphenol (NP), BPA, and zearalenone (ZEN), exhibit a high binding affinity for the G protein-coupled receptor 30 (GPR30), also known as the G protein-coupled estrogen receptor (GPER) [13–15]. Activation of this signalling pathway is mediated by GPER and initiated by estrogenic hormones. A key mechanism disrupting estrogenic signalling involves indirect activation through GPER [16]. In turn, EDCs, such as PCBs and dioxins, have relatively high affinity for AhR, which regulates the transcription of a large group of dioxin-reactive genes and causes a decrease in estrogen levels in the cytosol [17, 18]. Disruption to the synthesis and signalling of hormones in reproductive tissues and throughout the hypothalamic-pituitary-gonadal axis, thyroid and other tissues influencing reproductive function, may have significant consequences for sexual maturation and reproductive function [10–12].

Bisphenols, including BPA and its analogues, such as bisphenol S (BPS) and bisphenol F (BPF), are widely described as EDCs. These chemicals can interact with estrogen and, to a lesser extent, androgen receptors. This interaction alters hormonal signalling pathways. They are also reported to influence steroidogenesis, which can lead to changes in sex hormone synthesis and endocrine regulation disruption. These mechanisms are commonly observed in experimental studies (*in vitro* and *in vivo*) and are key to understanding the biological effects of EDC exposure on reproductive systems [6, 18].

REVIEW OF RESEARCH ON THE IMPACT OF EDC ON FEMALE REPRODUCTIVE HEALTH

Reproductive health. Women's fertility declines with age, but their lifestyle and environmental factors (e.g. exposure to chemicals) can influence the likelihood of having a healthy baby. It is estimated that about one-in-four infertile couples is affected by ovulatory disorders, among which polycystic ovary syndrome (PCOS) and primary ovarian insufficiency (POI) are the most common causes of ovulatory disorders. Problems with hormone levels, for example due to exposure to BPA, can cause irregular menstrual cycles and affect the number and quality of available oocytes. They can also play a significant role in the development of PCOS [19, 20]. The presence of EDCs in the follicular fluid may have negative health consequences. These chemicals may disrupt the function of oocytes, which are the primary cells in the ovary, which can have a detrimental effect on a woman's reproductive health [21]. Research shows that exposure to various EDCs is linked to poorer early reproductive outcomes in women undergoing assisted reproduction.

Exposure to a mixture of EDCs, including phthalates found in follicular fluid, was found to be inversely correlated with the number of mature and fertilised oocytes, and with the number of high-quality embryos [22]. Research findings suggest that EDCs may have an impact on the reproductive health of women, but it is important to note that this effect can vary depending on the population and existing health issues [22]. A case-control study showed that the presence of mixtures of substances disrupting hormonal function in the follicular fluid was associated with a higher risk of diminished ovarian reserve in women. The effect of these

mixtures was stronger than that of the individual substances. This highlights the importance of exposure to mixtures of EDCs on women's reproductive health [23]. In another case-control study, it was found that exposure to EDC mixtures, which include parabens, bisphenols, benzophenones and phthalate metabolites, was higher in women experiencing infertility than in fertile women, and analysis suggested a link between these substances and infertility [24]. BPA, BPS and BPF have been linked to changes in female reproductive outcomes, such as altered follicular development and oocyte maturation. Some studies have reported associations with reduced oocyte quality, ovulatory dysfunction, and menstrual cycle irregularities. Evidence from assisted reproduction settings suggests a potential relationship between exposure to mixtures of endocrine-disrupting chemicals and poorer oocyte and embryo quality. However, findings are inconsistent, and causality has not been established [2, 6, 12, 18].

Pregnancy. There are periods during pregnancy when the foetus is particularly sensitive to external factors due to the growth and development of organs and systems. A European meta-analysis has shown that exposure to professional chemicals during pregnancy is linked to a higher risk of low birth weight in newborns. This risk increases with the number of EDCs to which the pregnant woman is exposed [25]. A meta-analysis of the results showed that exposure of mothers to PFOS may be associated with preterm birth, but further research is needed because the impact of PFAS on human health is complex [26]. Another study has shown that exposure to heavy metals – lead, cadmium, chromium, copper and manganese, as well as phthalates, is linked to an increased risk of preterm birth in mothers [27]. Furthermore, exposure to chloroorganic compounds and PFAS during pregnancy has been linked to a lower level of total thyroxine (TT4) in newborns [28]. A systematic review and meta-analysis of data from over 100 studies showed that exposure to various endocrine-disrupting substances, including PFAS, phthalates and bisphenols, was associated with an increased risk of adverse pregnancy outcomes, such as preterm birth, low birth weight and miscarriage [29]. A thorough review and meta-analysis of almost 26,000 mother-child pairs revealed a link between exposure to endocrine-disrupting chemicals, including metals, phthalates and PFAS, during pregnancy and developmental delays in neurobehavioural functions, particularly in the areas of cognitive, motor and language skills in early childhood [30]. It was also revealed by the cohort studies that there is an increased risk of miscarriage in cases of early pregnancy and exposure to EDCs (including bisphenols, parabens and anti-inflammatory agents) at the same time. Some EDCs, such as bisphenol B (BPB), have been associated with an increased risk of miscarriage, possibly mediated by reduced progesterone (P4) levels. Exposure to bisphenols and other EDCs during pregnancy has been linked to potential impacts on early developmental processes, such as implantation and embryonic development.

While some studies have suggested possible links to adverse pregnancy outcomes, the evidence is inconsistent and largely based on observational and experimental data. In assisted reproduction, exposure to EDCs has been linked to differences in embryo development and treatment outcomes. However, findings vary, and causality has not been established [2, 5, 12]. The impact of EDCs also varies with

women's age, suggesting the need for particular attention in high-risk groups [31].

Disorders of metabolism and hormones in women. In recent years, many studies have highlighted a link between exposure to EDCs and metabolic and hormonal disorders in women. The risk of developing metabolic syndrome (MetS) may be increased by exposure to EDCs. MetS is characterised by at least four of the following: high blood pressure, high blood glucose levels, high triglyceride levels, increased waist-to-hip ratio, and low levels of high-density lipoprotein (HDL) cholesterol [32]. A study of a multi-ethnic cohort was used to evaluate the relationship between concentrations of substances that disrupt hormonal function — such as bisphenol A, triclosan, parabens and metabolites of phthalates — and the presence of metabolic syndrome in women. Although no significant positive associations were identified between EDC and the overall metabolic profile, differences in the associations with such factors as body mass index and ethnicity, were observed. In addition, an inverse correlation with parabens was identified, indicating the complexity of the impact of EDC on the metabolic state of women [32].

A systematic meta-analysis has shown that women with PCOS have significantly higher levels of BPA in their blood compared to women without PCOS, suggesting that this EDC may play a role in the development of PCOS by affecting insulin resistance and the androgenic profile [33]. Prospective studies have shown that higher concentrations of PFAS, considered EDCs, were associated with subsequent weight gain and increased hip circumference in adults, including women, and a beneficial dietary intervention could significantly modify this effect [34]. In turn, it was shown by a meta-analysis of 22 studies that an increased risk of estrogen-dependent diseases in women, such as PCOS and endometriosis, as well as the risk of endometrial cancer, was associated with exposure to plastic-related EDCs, including BPA and phthalate metabolites [35]. Zhang et al. demonstrated that higher concentrations of di(2-ethylhexyl) phthalate (DEHP) metabolite and exposure to phthalate mixtures were associated with increased risk of endometriosis in adult women. This suggests a potential role for these compounds in the development of estrogen-dependent diseases [36]. The sources, routes, and effects of EDCs on women's health are presented in Figure 1.

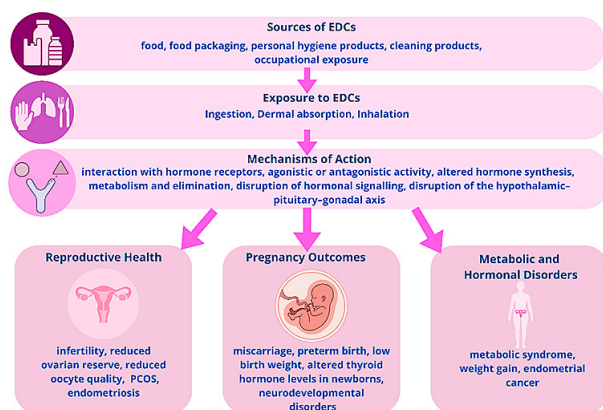


Figure 1. Overview of sources, routes and effects of EDCs on women's health

CONCLUSIONS

The presence of chemicals in the food we eat, on our skin, or in the air we breathe, may be a contributing factor to hormonal imbalances. Endogenous hormones play an important role in cell proliferation and differentiation, tissue development, and maintaining cell function in organs. Many EDCs have been found to interact with hormone receptors in the body, either by blocking their signals or causing problems in different organs (including reproductive issues, metabolic issues, endocrine problems and cancer). EDCs include a wide range of substances found in many consumer products (e.g. food, food packaging, personal hygiene products and cleaning products) [37]. In many scientific publications, the significant impact of EDC on health is highlighted, emphasizing the need for further research, including the use of advanced methods for detection, and studies on larger groups of patients. Furthermore, most of the available studies are observational, which limits the ability to draw conclusions about the relationship between exposure and adverse effects on health, as well as between exposure and adverse effects on health and disorders [33]. Much of the research still focuses on exposure to individual substances (e.g. BPA and phthalates), while exposure to multiple mixtures is realistic, thereby overlooking possible synergistic effects resulting from exposure to multiple EDCs [33, 36]. Should evidence of the adverse effect of exposure to EDC emerge, it will continue to be based on epidemiological evidence derived from exposure to individual substances. It goes without saying that the EDC mechanisms in place require further research, especially since the current state of knowledge is largely based on *in vitro* and animal studies [35]. The need to intensify research in this area also arises from the fact that women are exposed to new or lesser-known substances that are classified as EDCs. BPA analogues, BPS and BPF, should not be mentioned here. Some reports, however, have indicated that BPA analogues also have a negative effect on the endocrine system of humans and animals [38].

More research is also needed on dimer acid of hexafluoropropylene oxide (HFPO-DA, GenX), which belongs to the group of PFAS. Exposure to HFPO-DA may have similar effects to those previously observed in PFAS toxicity assessments [39].

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