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Review

Environmental Chemicals and Female Reproductive Health: Unraveling Mechanisms and Societal Impacts — A Narrative Review

Yidong Xie[1,2], Ruoti Peng[3], Li Xiao[1,2,*]

[1]Department of Reproductive Medicine, West China Second University Hospital, Sichuan University, 610041 Chengdu, Sichuan, China
[2]Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, 610041 Chengdu, Sichuan, China
[3]West China School of Medicine, Sichuan University, 610041 Chengdu, Sichuan, China
*Correspondence: xiaoli2006929@126.com (Li Xiao)

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Abstract

Objectives: To examine the impacts of environmental chemicals on female reproductive health, identify key mechanisms of reproductive toxicity, and discuss potential strategies to mitigate these effects. **Mechanism**: Environmental chemicals such as per- and polyfluoroalkyl substances, heavy metals, pesticides, microplastics, quaternary ammonium compounds, and other pollutants, disrupt the hypothalamic-pituitary-gonadal axis (HPG), impair ovarian function, and contribute to reproductive dysfunction through mechanisms such as oxidative stress, hormonal disruption, and epigenetic modifications. **Findings in Brief**: These chemicals contribute to menstrual irregularities, infertility, and pregnancy complications. They also increase the risk of reproductive system disorders, including endometriosis, polycystic ovary syndrome (PCOS), and ovarian cancer. Additionally, transgenerational effects mediated by epigenetic modifications, germ cell damage, and placental transfer may adversely affect offspring health, increasing the risk of reproductive dysfunction, neurodevelopmental disorders, metabolic diseases, and cancer. **Conclusions**: Despite growing evidence, significant knowledge gaps remain in understanding the mechanisms of reproductive toxicity, identifying biomarkers for early detection, and assessing the long-term effects of low-dose, chronic exposure. Addressing these challenges requires stricter regulations, the development of safer chemical alternatives, public awareness campaigns, and continued research to safeguard reproductive health for current and future generations.

Keywords: environment pollution; reproductive health; toxicity; hormone disruption; maternal exposure; female infertility

1. Introduction

Environmental pollution has emerged as a critical global health concern in recent decades, with significant implications for human reproductive health. The escalating presence of synthetic chemicals in our environment—from industrial processes, agricultural practices, and consumer products—represents an unprecedented challenge to public health systems worldwide. Female reproductive health is vital to well-being, family planning, and overall societal stability. It is closely linked to general health through hormonal balance, immune regulation, and the proper functioning of the hypothalamic-pituitary-gonadal (HPG) axis. Across life stages from puberty to menopause, reproductive health is not only essential for fertility but also for maintaining hormonal and metabolic stability. Environmental chemicals, commonly present in consumer products, industrial applications, and agricultural activities, enter the body through diet, inhalation, and skin exposure. Once inside, they can disturb hormone regulation, impair reproductive processes, and contribute to long-term health outcomes [1,2].

Current scientific literature has established strong associations between various environmental chemicals and adverse reproductive outcomes. Numerous epidemiological and experimental studies have linked endocrine-disrupting chemicals (EDCs) and other pollutants with adverse reproductive effects, including hormonal imbalances, reduced fertility, and pregnancy complications. For example, phthalates and bisphenol A (BPA), widely used in plastics, are linked to diminished ovarian reserves and menstrual disturbances. Similarly, pesticides and per- and polyfluoroalkyl substances (PFAS) are known to decrease fertility and cause developmental abnormalities. Heavy metals such as lead, cadmium, and mercury further disrupt the HPG axis, aggravating hormonal imbalances and reproductive dysfunction [3].

Despite significant progress in identifying these risks, important knowledge gaps remain in our understanding of reproductive toxicity caused by environmental chemicals. Real-world exposure typically involves long-term, low-level exposure to complex mixtures, yet most research focuses on the high-dose effects of individual chemicals. Additionally, the transgenerational effects of chemical exposure, particularly how maternal exposure may influence health and fertility in subsequent generations, are still not fully understood. Current evidence suggests that epigenetic changes, such as DNA methylation and histone modifications, play a role, but further investigation is needed [4].

In this review, we present an updated summary of current evidence regarding how environmental chemicals af-

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fect female reproductive health. We draw on findings from epidemiological, experimental, and mechanistic studies to provide a thorough perspective on this significant public health concern. The review explores the ways in which various classes of environmental pollutants influence distinct parts of the female reproductive system, discusses the molecular mechanisms involved, and considers the potential for transgenerational effects. By integrating these aspects, our aim is to guide future research priorities, improve methods for detecting and assessing exposures, and support the development of effective prevention and policy measures that protect reproductive health for present and future generations.

2. Sources and Hazards of Environmental Chemicals

2.1 Plasticizers

Plasticizers, such as phthalates, BPA, and bisphenol S (BPS), are synthetic chemicals widely used to improve the flexibility, durability, and functionality of plastics [5]. As a prominent class of EDCs, plasticizers interfere with hormonal systems and are commonly present in everyday items, including vinyl flooring, medical devices, cosmetics, cleaning agents, and food packaging. BPA and BPS are particularly used in the manufacturing of polycarbonate plastics and epoxy resins, found in products like water bottles, food cans, and thermal paper [6].

The health impacts of plasticizer exposure are widespread, and have been associated with conditions such as immunosuppression, oxidative stress, and neurotoxicity [7]. These effects contribute to metabolic disorders, developmental abnormalities, and a greater risk of chronic diseases. In particular, plasticizers disrupt the HPG axis, causing hormonal imbalances that impair ovarian function, decrease oocyte quality, and accelerate ovarian aging [8]. Long-term exposure has been linked to higher risks of reproductive diseases, including polycystic ovary syndrome (PCOS), endometriosis, uterine leiomyoma, and hormone-dependent cancers such as breast and ovarian cancer [9–11]. These findings highlight the significant reproductive health risks posed by plasticizers, emphasizing the urgent need for stricter regulations and safer alternatives to reduce human exposure.

2.2 Per- and Polyfluoroalkyl Substances

PFAS are synthetic chemicals with unique physicochemical properties that make them highly effective as water and oil repellents [12]. Often referred to as “forever chemicals” due to their extreme resistance to degradation, PFAS persist in the environment and gradually accumulate over time. Humans are exposed to PFAS through contaminated drinking water, food, household dust, and air [13–15]. These chemicals have high solubility and mobility, allowing them to infiltrate water systems and contaminate drinking water sources on a large scale [16]. Millions of people worldwide are exposed to PFAS-contaminated water, particularly in areas near industrial or military sites.

Emerging research in both animals and humans links PFAS exposure to numerous adverse health outcomes. Maternal PFAS exposure has been associated with adverse pregnancy outcomes including hypertensive disorders [17, 18], miscarriage [19], fetal growth restriction [20], low birth weight [21], premature birth [22,23]. Such exposure can disrupt hormone signaling pathways by mimicking or blocking natural hormones, leading to impaired follicular development, reduced oocyte quality, and disrupted ovulation [4]. This hormonal imbalance may result in irregular menstrual cycles, amenorrhea [24], and overall decreased fertility [25,26].

Overall, PFAS pose significant risks to reproductive health, underscoring the need for stricter regulations and further research to mitigate their impact.

2.3 Heavy Metals

Heavy metals are persistent environmental pollutants that pose significant threats to human health, particularly to the reproductive system. Their widespread presence is primarily linked to industrial activities, agricultural practices, and inadequate waste management. Common heavy metals, including cadmium, lead, mercury, and arsenic [27], are released into the environment through processes such as smelting, battery production, and coal combustion [28,29].

Heavy metals are associated with systemic toxicity, affecting multiple organs and biological systems. By generating reactive oxygen species (ROS), they induce oxidative stress, damage lipids, proteins, and DNA, and contribute to chronic illnesses such as cardiovascular disease, neurodegenerative disorders, and cancer [30,31]. In terms of reproductive health, heavy metals impair ovarian and testicular function, disrupt follicular development, and diminish sperm quality. Cadmium, for example, mimics estrogen by binding to estrogen receptors, acting as a “metalloestrogen”, and causing hormonal imbalances that contribute to conditions like PCOS and endometriosis [32,33]. Prenatal exposure to heavy metals such as lead and mercury can cross the placental barrier, leading to adverse pregnancy outcomes, including low birth weight, preterm labor, and developmental delays [28]. Given these profound impacts on both systemic and reproductive health, heavy metal pollution highlights the urgent need for stricter environmental regulations and preventive measures to minimize human exposure.

2.4 Pesticides

Pesticides are extensively used in agriculture and other industries to control pests (a variety of insects, fungi, and weeds). More than a thousand different pesticides are in use, and these can be classified into categories such as insecticides, fungicides, herbicides, and plant growth regulators. However, their persistence in the environment and

bioaccumulation in the food chain pose significant risks to human health, particularly reproductive health [34]. Neonicotinoid pesticides are a class of neuroactive compounds structurally related to nicotine. They target nicotinic acetylcholine receptors in the insect central nervous system and peripheral nerves [35].

Many pesticides induce oxidative stress, thereby generating ROS that damage reproductive tissues [36,37]. This exposure has been shown to impair ovarian and testicular function, disrupt oocyte maturation, and reduce sperm quality. Organophosphates can cause imbalances in sex hormone levels, resulting in reduced libido, altered menstrual cycles, ovarian dysfunction, and impaired spermatogenesis, ultimately decreasing fertility in both men and women [38]. Other pesticides, such as glyphosate and organochlorines, are linked to DNA strand breaks, chromosomal abnormalities, and micronucleus formation in reproductive cells [39]. Pesticides primarily affect human reproduction by functioning as endocrine disruptors, by either enhancing or inhibiting the effects of natural hormones. Additionally, they can induce oxidative stress, leading to cellular damage, metabolic disturbances, and cell death [40]. Exposure to pesticides by women primarily leads to reduced fertility, increased risk of miscarriages, babies born prematurely or with low birth weight, developmental issues, ovarian dysfunction, and disruption of hormonal regulatory pathways [41,42]. Additionally, pesticide toxicity can further disrupt placental function, contributing to adverse pregnancy outcomes [43]. The pervasive use of pesticides highlights the urgent need for stricter regulations and research into safer alternatives to minimize their impact on human health.

2.5 Organophosphate Flame Retardants

Organophosphate flame retardants (OPFRs) are increasingly used in place of polybrominated diphenyl ethers (PBDEs) in many consumer products and materials, following regulatory restrictions on PBDEs [44]. Human exposure to OPFRs has been recognized for over two decades, primarily occurring through inhalation of air and dust, ingestion of food, and skin contact [45]. OPFRs exposure was widespread among women of childbearing age [46]. While some OPFRs are persistent and bioaccumulative, others are rapidly metabolized but contribute to ongoing exposure due to their widespread environmental presence.

Although OPFRs are effective for fire safety, growing evidence indicates OPFRs can induce oxidative stress by generating reactive oxygen species, damaging cellular components [47]. OPFRs have shown carcinogenicity, neurotoxicity, liver toxicity, and reproductive and developmental toxicity [48]. Environmental exposure to OPFRs is positively associated with gestational diabetes mellitus (GDM) and reduced ovarian reserve [46,49]. OPFRs disrupt ovarian function by altering steroid hormone production and cholesterol biosynthesis in granulosa cells [50]. As a major class of environmental contaminants, OPFRs pose significant risks to female reproductive health and pregnancy outcomes, highlighting the urgent need for safer alternatives, stricter regulations, improved exposure assessment methods, and further investigation of their complex toxicological mechanisms and long-term health effects.

2.6 Polychlorinated Biphenyls

Polychlorinated biphenyls (PCBs) are a class of typical EDCs consisting of 209 highly toxic congeners, widely present in the environment and recognized as persistent organic pollutants (POPs) [51]. Humans can be continuously exposed to low levels of PCBs through inhalation, diet, and skin contact [52]. PCBs are lipophilic and are bioaccumulated in food chains. Their stability and resistance to degradation allow them to persist in the environment and human body [53]. Once absorbed, PCBs are metabolized into hydroxylated or methylsulfonyl derivatives, which can interfere with several cellular functions. PCBs have been detected in human plasma, serum, saliva, umbilical-cord blood, placental tissue, adipose tissue, and even breast milk [54].

PCBs adversely affect animal reproduction by disrupting endocrine processes, macromolecular organelle function, DNA methyltransferase expression, and germ-cell-cytoskeleton assembly, potentially leading to epigenetic modifications in offspring [55]. PCBs are shown to harm the endocrine, nervous, immune, and reproductive systems, leading to chronic diseases, cancer, deformities, and mutations. PCB exposure has been demonstrated to have a significant effect on female fertility and also on fetal development, leading to spontaneous abortion, congenital abnormalities, and long-term effects on offspring [56]. Chronic exposure to PCBs has been associated with a variety of adverse health outcomes, including neurodevelopmental disorders, immune suppression, liver toxicity, and cancer [57], but reproductive effects are particularly concerning, with PCBs linked to decreased fertility, disrupted ovarian function, and premature ovarian failure. For example, PCB exposure has been found to impair follicular development and interfere with hormone-regulated pathways, contributing to conditions such as PCOS, endometriosis, primary ovarian insufficiency, and other fertility-related issues [58–60]. Additionally, PCBs may act as antiestrogens or antiandrogens, further exacerbating hormonal imbalances and reproductive toxicity.

2.7 Volatile Organic Compounds

Volatile organic compounds (VOCs) are ubiquitous environmental pollutants that are primarily released through industrial activities like chemical manufacturing and petroleum refining, indoor air pollution from household products such as paints, cleaning agents, and building materials, and vehicle emissions [61]. Poor ventilation exacerbates indoor VOC concentrations, and vehicle emissions

further increase exposure, particularly in urban areas [62]. VOCs, including toluene and xylene, were detected in menstrual products [63].

Exposure to VOCs, such as benzene, toluene, and xylene, generates ROS, thereby disrupting mitochondrial function and impairing energy production [64]. Oxidative stress and inflammation caused by VOCs contribute to cellular apoptosis and DNA-strand breaks, leading to mutations and increased risks of various health hazards [65–69]. VOCs harm reproduction in both sexes by disrupting the HPG axis and causing hormonal imbalances [70]. Exposure to 2,5-dimethylfuran and benzene may contribute to endocrine abnormalities related to female sex hormones, particularly in non-overweight women [71]. VOC exposure also causes menstrual irregularities and raises the risk of spontaneous abortion due to oxidative stress and inflammation [70].

2.8 Micro(nano)plastics

Micro(nano)plastics (MNPs) are plastic particles smaller than 5 mm, originating from the fragmentation of larger plastics or intentionally manufactured for products like cosmetics and industrial applications [72]. MNPs are found in various forms, including fibers, microbeads, fragments, nurdles, and Styrofoam particles [73]. MNPs have been detected in various human biological samples and organs, including blood, urine, sputum, feces, breast milk, lungs, colon, and spleen [74]. Humans are exposed to MNPs through ingestion (contaminated food and water), inhalation (airborne particles), and dermal contact (cosmetics) [75].

MNPs may impair reproductive function through a combination of oxidative stress, inflammation, genotoxicity, endocrine disruption, and direct cellular toxicity. Their ability to cross biological barriers further increases the risk of adverse reproductive and developmental outcomes in mammals [76–78]. This oxidative damage triggers chronic inflammation, which is linked to, and involved in, the disruption of immune function, and leads to neurotoxicity [75]. Several chemicals known to leach from plastics are well known to induce a variety of adverse health conditions in humans, including in developing fetuses exposed *in utero* [79]. MNPs impair oocyte quality, disrupt mitochondrial function, and accumulate in embryos, leading to abnormal development and reduced viability. They also cause pregnancy complications, and some of the involved fetuses suffer from intrauterine growth restriction [80]. MNPs are pervasive pollutants with systemic and reproductive health risks. Their toxicity mechanisms, including oxidative stress, inflammation, and endocrine disruption, highlight the urgent need for stricter plastic regulations, improved waste management, and further research into their long-term effects.

2.9 Quaternary Ammonium Compounds

Quaternary ammonium compounds (QACs) are antimicrobial agents widely used in disinfectants, sanitizers, and personal care products [81]. Found in hair conditioners, fabric softeners, antiseptic wipes, and industrial processes like water treatment, human exposure to QACs arises through inhalation, dermal contact, and ingestion. They persist in the environment, accumulating in water, soil, and sediments; wastewater treatment plants only partially remove them. QACs are linked to bioaccumulation in human tissues, including blood and breastmilk, with potential health effects such as inflammation, mitochondrial dysfunction, and developmental toxicity [82].

QACs may impact reproductive function through mitochondrial injury, endocrine and lipid metabolism disruption, induction of oxidative stress and inflammation, direct germ cell toxicity, and microbiome alterations [83]. Effects on females consist of a longer interval between estrus cycles (nonhumans), lower rates of ovulation and implantation, as well as higher post-implantation losses. Effects on males includes reduced sperm concentration and decreased sperm motility [84]. However, due to the pervasiveness of QACs in daily-use products, humans are constantly exposed. However, little is known about the health effects of everyday QAC exposure, particularly its specific effects on human reproduction and development.

2.10 Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs), widely recognized as persistent environmental pollutants, are a class of organic compounds composed of multiple aromatic rings [85]. Major sources of PAHs include industrial emissions, vehicle exhaust, residential heating, and grilled or smoked foods [86]. These compounds are highly stable in the environment, accumulating in air, soil, and water, and can enter the human body through inhalation, ingestion, and dermal contact [87]. Once inside the body, PAHs are metabolized into reactive intermediates that can bind to DNA and proteins, leading to cellular damage. PAHs exert their toxic effects through mechanisms such as oxidative stress, endocrine disruption, and direct genotoxicity, making them a significant concern for both environmental and human health [87].

Chronic exposure to PAHs has been linked to a wide range of adverse health effects. PAHs can function as antiestrogens or antiandrogens by directly interacting with either the estrogen receptor or the androgen receptor. For instance, compounds such as benz(a)anthracene, fluoranthene, benzo(a)pyrene, and chrysene have been found to suppress androgenic activity, leading to hormonal imbalances that can impair fertility [88]. The adverse reproductive outcomes due to PAH exposure mainly concern PCOS and premature ovarian failure [89]. Overall, PAHs pose significant risks to systemic and reproductive health, em-

phasizing the need for strategies to reduce exposure, such as minimizing emissions and limiting the consumption of grilled or smoked foods.

3. Comprehensive Impact of Chemical Substances on the Female Reproductive System

Environmental chemicals exert multiple effects on the female reproductive system, having an impact on the ovaries, uterus, fallopian tubes, and hormonal regulation, which is showing in Table 1 (Ref. [6,8,17–23,41,42,46,49,50,58,60,84,90–143]). These disruptions contribute to a range of reproductive dysfunctions, including infertility, menstrual irregularities, and pregnancy complications, as well as the development of diseases such as endometriosis and cancers.

3.1 Effects on Oocytes and Ovarian Function

3.1.1 Follicular-development Disruption

The female reproductive system is tightly regulated by hormones that are essential for follicle growth and maturation. However, environmental pollutants can disrupt these processes, causing significant damage to granulosa cells and oocytes, which are critical for ovarian follicular development. The pollutants, including heavy metals, cigarette smoke, and agrochemicals, impair oocyte multiplication, growth, and maturation through mechanisms such as oxidative stress, endocrine disruption, and DNA damage [90]. The endocrine-disrupting effects of pesticides can influence both germ cells and somatic cells in the ovary, interfering with the processes of folliculogenesis and steroidogenesis [91,92]. BPA and phthalates interfere with meiotic progression, compromise spindle integrity, and induce DNA damage in oocytes, ultimately reducing their quality and fertility [93,94]. Similarly, heavy metals such as cadmium and lead inhibit cumulus expansion, decrease the number of oocytes reaching metaphase II, and increase oocyte degeneration, collectively impairing follicular development [95]. Pesticides further exacerbate these issues by inducing oxidative stress and DNA damage in ovarian tissues, leading to cellular dysfunction and apoptosis [96]. *In vitro* exposure of bovine oocytes to neonicotinoids results in excessive ROS generation and a reduction in mitochondrial membrane potential, leading to oxidative stress and DNA damage, and ultimately causing apoptosis and necrosis [97]. PCB exposure differentially affects follicular dynamics, with intrauterine noncoplanar PCB exposure reducing preantral and antral follicles and increasing atretic follicles [98]. Ultimately, these mechanisms collectively impair the intricate hormonal regulation and cellular processes required for proper oocyte development and follicular growth, posing significant risks to female reproductive health.

3.1.2 Decline in Ovarian Reserve

Environmental pollutants such as BPA, PFAS, and pesticides contribute to a decline in ovarian reserve by accelerating ovarian aging and promoting follicular atresia. A recent study on human epithelial ovarian cells exposed to BPA identified hundreds of differentially expressed genes linked to pathways such as oocyte meiosis, cellular senescence, and transcriptional misregulation. BPA also disrupted pathways critical for oocyte maturation, highlighting its potential to impair ovarian function [93]. Those findings emphasize the need for further research using advanced models to better understand the impact of BPA on ovarian health [144]. Phthalates disrupt folliculogenesis and reduce fertility by altering gene expression involved in follicle development. Urinary phthalate metabolites were significantly associated with increased antral follicle count, likely due to accelerated primordial follicle recruitment, with stronger effects in older women and potential inverse effects in younger women [99]. PFAS exposure reduces ovarian reserve and disrupts menstrual cycles by interfering with hormone synthesis. Pesticides worsen this by causing oxidative stress, inflammation, endoplasmic-reticulum stress and impaired mitochondrial function [100]. Exposure to MNPs weakens the function of ovaries and causes a decrease in ovarian reserve capacity. Also, continuous exposure to MNPs leads to increased levels of ROS, induction of oxidative stress, inflammatory responses, apoptosis of granulosa cells, and reduction of the number of ovarian follicles [101].

3.2 Potential Risks to Uterine Health

The uterus, essential for pregnancy and childbirth, is highly vulnerable to chemical exposure, which can disrupt its structural and functional integrity. Pesticides like organochlorines alter estrogen signaling and gene expression critical for endometrial receptivity, causing hyperplasia and impaired implantation in animal models [102]. BPA exhibits dose-dependent effects on uterine leiomyoma cells, in which low concentrations (10^{-6}–10 μM) stimulate hormonally driven proliferation, whereas higher doses (100–200 μM) inhibit growth [103]. The insecticide fipronil reduces cellular viability in porcine trophectoderm and endometrial cells, impairing implantation potential during early pregnancy [104]. Similarly, benzo(a)pyrene (BaP), a known endocrine-disrupting pollutant, disrupts molecular pathways critical for implantation and decidualization. BaP exposure reduces homeobox A10 (HOXA10) and bone morphogenetic protein 2 (BMP2) expression, markers essential for endometrial receptivity, while activating the WNT5A/β-catenin pathway, which inhibits stromal cell apoptosis, thereby disrupting endometrial homeostasis [105]. Other chemicals, such as PFAS, harm uterine immunity, increasing the risk of endometrial disorders like endometriosis and uterine leiomyoma [106,107]. Mercury, through increased ROS production, damages endometrial

Table 1. Environmental chemicals and their impact on female reproductive health.

Reproductive System Part	Type of Impact	Involved Environmental Chemicals	Citations
Hypothalamic-Pituitary-Gonadal (HPG) Axis	Disruption of hormonal regulation and steroidogenesis	BPA, phthalates, PFAS, POPs, parabens, pesticides, heavy metals, PCBs, PAHs	[8,60,109–115]
	Altered gonadotrophin release	BPA, organophosphates, PCBs	[109,115]
	Exacerbation of hyperandrogenism	BPA	[8,110]
Ovaries	Follicular development disruption	BPA, phthalates, heavy metals (cadmium, lead), pesticides, PCBs, neonicotinoids	[90–98]
	Diminished ovarian reserve	BPA, PFAS, phthalates, pesticides, MNPs	[93,99–101]
	Oxidative stress and DNA damage	Heavy metals, pesticides, MNPs	[95–97,101]
	Impaired steroidogenesis	BPA, phthalates, PCBs	[8,50,115]
	Accelerated ovarian aging	BPA, phthalates, MNPs	[8,99,101]
Uterus	Altered endometrial receptivity	Pesticides (organochlorines), BaP	[102,105]
	Impaired implantation	BPA, pesticides (fipronil), BaP	[102–105]
	Endometrial hyperplasia	Organochlorines	[102]
	Increased risk of endometriosis and uterine leiomyoma	BPA, phthalates, PFAS, PCBs	[58,106,107,116,117]
	Damage to endometrial stromal cells	Heavy metals (mercury)	[108]
Fallopian Tubes	Disrupted ciliary movement	BPA	[119,120]
	Altered oviduct motility and contractility	PCBs	[121,122]
	Compromised structural integrity	BPA, heavy metals	[118,119]
	Increased risk of ectopic pregnancy	BPA, heavy metals (zinc, copper imbalance)	[118,120]
	Epithelial cell degeneration	PCBs and other organohalogens	[121]
Embryonic Development & Pregnancy	Implantation failure	PFAS, microplastics	[123,124]
	Increased risk of miscarriage	PFAS, pesticides	[19,41,42]
	Pregnancy complications (hypertensive disorders, GDM)	PFAS, OPFRs	[17,18,46,49]
	Fetal growth restriction and low birth weight	PFAS, PBDEs	[20,21,132]
	Premature birth	PFAS	[22,23]
	Embryonic developmental disorders	QACs	[84]
Transgenerational Effects	Reproductive dysfunction in offspring	Phthalates, BPA, PBDEs, QACs	[127,128,130–133]
	Epigenetic modifications	BPA, heavy metals, POPs, phthalates	[6,93,125–127]
	Neurodevelopmental disorders in offspring	BPA, PFAS, pesticides, heavy metals	[134–139]
	Increased cancer risk in offspring	PFAS, DDT, PCB, benzene, pesticides	[129,140–143]

BPA, bisphenol A; PFAS, polyfluoroalkyl substances; POPs, persistent organic pollutants; PCBs, polychlorinated biphenyls; PAHs, polycyclic aromatic hydrocarbons; MNPs, micro(nano)plastics; BaP, benzo(a)pyrene; OPFRs, organophosphate flame retardants; DDT, dichlorodiphenyltrichloroethane; PBDEs, polybrominated diphenyl ethers; QACs, quaternary ammonium compounds; GDM, gestational diabetes mellitus.

stromal cells, impairing fertility and *in vitro* fertilization (IVF) success [108]. These findings underscore the complex interplay between chemical pollutants and uterine health, highlighting the urgent need for stricter environmental regulations to mitigate these risks.

3.3 Disruption of the Reproductive Endocrine Axis

The HPG axis is essential for regulating reproductive functions, including follicular growth, ovulation, spermatogenesis, and hormone production. However, this system is highly vulnerable to disruption by EDCs [145]. EDCs, in particular, have been extensively studied for their ability to interfere with the HPG axis. EDCs mimic sex hormones and disrupt HPG axis homeostasis by affecting gonadotrophin releasing hormone (GnRH) and subsequent gonadotrophin release, leading to impaired folliculogenesis, ovulation, conception, spermatogenesis, and fertility. EDCs that affect the HPG axis include BPA, phthalates, POPs, parabens, pesticides, and heavy metals [109]. Nearly 48.28% of PCOS patients were found to have detectable BPA in their urine. BPA disrupts the HPG axis, altering ovarian steroidogenesis, exacerbating hyperandrogenism, impairing oocyte development and folliculogenesis, and aggravating metabolic parameters [8,110]. PFOA, a type of PFAS, has been linked to menstrual irregularities and elevated serum levels in women with PCOS [111]. Flame retardants (FRs) were found to be associated with significant changes in reproductive and steroid hormone levels in peripubertal girls [112]. PAH exposure can interfere with the proper functioning of the HPG axis, which regulates the production and release of sex hormones [113,114]. PCBs impair steroidogenesis by forming non-polar, π-stacking, and halogen bonds with key residues in *StAR* and *CYP11A1*. This induces conformational changes that prevent cholesterol binding and transport, thereby inhibiting cholesterol conversion to pregnenolone through a "block-cluster" mechanism that may predict similar endocrine-disrupting effects of other environmental pollutants [115]. Women with PCOS had significantly higher serum PCB levels; increased PCB levels were linked to a higher risk of PCOS, indicating that PCB exposure may play a role in the onset and progression of the condition [60]. Additionally, exposure to BPA and phthalates has been associated with impaired estrogen secretion and a higher risk of developing endometriosis [116,117].

In summary, understanding and mitigating the impact of EDCs on the HPG axis is essential to addressing their profound effects on reproductive health and preventing the development of related endocrine disorders.

3.4 Effects on Fallopian Tube Function

The fallopian tube serves as a vital "life channel" in the conception process, ensuring the proper transport of oocytes and embryos. However, exposure to various chemicals can significantly impair its function, affecting fertility and increasing the risk of pregnancy-related complications.

In ectopic pregnancy, in which the embryo implants outside the uterus, serum zinc levels decrease and copper levels increase, leading to a higher Cu/Zn ratio, which is associated with oxidative stress. This imbalance not only has diagnostic value, with sensitivity and specificity rates of 73.3% and 80% [118], but also disrupts oocyte and embryo transport, contributing to infertility. BPA exposure further aggravates these issues by causing proliferative lesions and compromising the structural integrity of the oviduct, resulting in long-term reproductive complications [119]. Additionally, BPA interferes with ciliary movement and alters the expression of genes critical for tubal function, significantly increasing the risk of ectopic pregnancy—a severe condition with serious health implications [120]. Environmental mixtures of PCBs and other organohalogens exacerbate these effects, inducing degeneration of mouse oviduct epithelial cells [121]. PCB exposure disrupts oviduct motility by reducing the contractility of longitudinal and circular muscles and increasing leukemia inhibitory factor expression, further impairing oviduct function [122]. These combined impacts highlight the profound threat that environmental chemical exposure poses to fallopian tube function. Addressing this issue requires stricter regulation of toxic substances and further research into preventative strategies to safeguard reproductive health.

3.5 Impacts on Embryonic Development and Pregnancy

Environmental chemical exposure profoundly affects embryonic development and pregnancy outcomes. Substances like PFAS and microplastics are closely associated with implantation failure. PFAS disrupt estrogen and progesterone signaling, trigger chronic inflammation, and reduce endometrial receptivity, thereby impairing implantation rates [123,124]. QACs directly damage reproductive cells and interfere with embryonic development. Results of a 2021 study indicated that QAC exposure induces apoptosis in reproductive cells and disrupts embryonic processes, increasing the risk of birth defects and genetic disorders [84]. Those findings underscore the urgent need to minimize environmental chemical exposure to protect reproductive health and support healthy pregnancy outcomes.

4. Transgenerational Effects of Environmental Chemicals

Environmental chemicals affect not only exposed individuals but also future generations through mechanisms such as epigenetic modifications, germ-cell damage, and placental transfer. Pollutants like PFAS, heavy metals, pesticides, microplastics, and QACs have been linked to adverse effects on offspring, including impaired reproductive, neurological, metabolic, and immune health, as well as increased cancer risk. Understanding these mechanisms is essential for reducing the long-term health risks to future generations.

4.1 Mechanisms of Transgenerational Effects

Environmental chemicals can induce epigenetic changes, including DNA methylation, histone modifications, and non-coding RNA regulation, which alter gene expression without changing the DNA sequence. These heritable alterations can persist across generations, affecting offspring health and development. For example, BPA exposure disrupts endocrine and reproductive systems through epigenetic mechanisms, such as DNA methylation patterns, histone remodeling, and non-coding RNA signaling [6,94]. Studies have reported DNA methylation changes in oocytes exposed to bisphenols both *in vitro* and *in vivo*, including alterations in imprinted genes and histone methylation. These epigenetic modifications have also been observed in F1 offspring exposed to bisphenols during fetal development [125,126].

BPA further disrupts oogenesis and folliculogenesis, leading to oocyte aneuploidy and multi-oocyte follicle formation. Heavy metals and POPs directly damage DNA in oocytes and sperm, causing mutations or chromosomal abnormalities that are passed to offspring. Phthalate exposure alters ovarian gene expression related to the cell cycle, steroidogenesis, and miRNA in F1 and F2 female rats, impairing folliculogenesis, oocyte maturation, and steroid production [127].

4.2 Health Impact of Transgenerational Effects

Environmental chemicals exert transgenerational effects on offspring health, influencing reproductive, neurological, metabolic, immune, and cancer-related outcomes. These effects are driven by mechanisms such as epigenetic modifications, germ-cell damage, and placental transfer. Below is a detailed integration of specific chemicals and their transgenerational effects on offspring.

4.2.1 Reproductive Health of Offspring

Transgenerational exposure to environmental chemicals significantly impairs offspring reproductive health, including reduced ovarian reserve, disrupted follicular development, altered oviduct morphology and function, and poor sperm quality [128,129,146]. Phthalates are particularly concerning, as maternal exposure disrupts folliculogenesis, steroidogenesis, and ovarian gene and miRNA expression, leading to reduced oocyte quality, premature ovarian aging, and diminished fertility across generations [127,130]. Prenatal exposure to PBDEs is associated with elevated risk of the incidence of fetal growth restriction and reproductive damage [131,132]. BPA exposure during gestation alters the cell composition and decreases the expression of key proteins in the fetal oviduct, affecting its structure and function later in life [128]. Similarly, maternal exposure to cetylpyridinium chloride, a widely used QAC, induces mitochondrial dysfunction in neonatal ovaries, causing long-term fertility issues in female offspring [133]. In summary, these findings highlight the profound and lasting effects of maternal chemical exposures on the reproductive health of future generations, underscoring the need to mitigate exposure risks to safeguard fertility outcomes.

4.2.2 Neurodevelopmental Disorders in Offspring

Environmental chemical exposure disrupts brain development in offspring through mechanisms like epigenetic changes and oxidative stress, contributing to neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD), and autism spectrum disorder (ASD) [134,135]. Human studies reveal chemical-specific effects: BPA and PFAS exposure is linked to increased ADHD risk [135,136], whereas exposure to pesticides within 2 km of residences during early pregnancy correlates with increased ASD diagnoses after adjusting for agricultural confounders [134]. Heavy metal mixtures exhibit distinct neurotoxic profiles, with maternal urinary concentrations inversely correlating with offspring's cognitive/motor performance, through disrupted biogenic-amine metabolism and neural-circuit signaling [137]. Maternal BPA exposure severely impaired spatial learning and exploratory behaviors in males [138]. Moreover, exposure to chemical mixtures during pregnancy has been shown to affect neurodevelopment, particularly affecting fine motor functions without affecting cognitive abilities [139].

This evidence underscores the importance of reducing environmental chemical exposure during critical periods of neurodevelopment to protect offspring health.

4.2.3 Cancer Risk in Offspring

Transgenerational exposure to environmental chemicals has been linked to an increased risk of hormone-related cancers, such as breast and testicular cancer, in offspring. For example, maternal exposure to dichlorodiphenyltrichloroethane (DDT) has been associated with a higher risk of breast cancer in descendants [129]. Mechanisms driving these impacts include epigenetic modifications, germ cell damage, and placental transfer. Notable chemicals contributing to these transgenerational effects include EDCs like BPA, PFAS, benzene, PCB, and various pesticides. For instance, maternal exposure to PFAS has been implicated in an elevated risk of childhood acute lymphoblastic leukemia (ALL) and chromosomal abnormalities [140,141]. Similarly, maternal exposure to EDCs—such as PCB, pesticides, benzene, and DDT—during fetal development is consistently associated with a higher risk of testicular cancer, particularly nonseminomas, in male offspring [142]. Additionally, occupational exposure to benzene during pregnancy has been linked to an increased risk of ALL in children [143]. However, evidence on these associations varies in quality, and few studies have examined the cumulative effects of multipollutant mixtures. Addressing this pressing public health issue requires stricter regulation of harmful chemicals, enhanced public awareness, and intensified research efforts to better understand the underly-

ing mechanisms and long-term consequences of exposure. Taking proactive measures now is critical for ensuring the health and well-being of future generations.

5. Limitations and Strengths of the Current Review

This review has several limitations. Due to the vast variety and complexity of environmental chemicals, comprehensive coverage is challenging, and some emerging contaminants were beyond our scope. The included studies use heterogeneous designs and exposure assessments, limiting direct comparison and consensus. In addition, most rely on single-point biospecimen measurements, which may not reflect long-term exposure. Establishing causality remains difficult given ethical constraints and confounding factors, while differences in susceptibility further complicate generalization. Moreover, much of the existing evidence is derived from high-dose or acute exposure studies, whereas real-world scenarios more commonly entail chronic, low-level, and mixed exposures; this may distort risk assessment and limits our understanding of the true epidemiological and dose-response relationships. Given current data limitations and the scope of this narrative review, detailed discussion of dose thresholds and reference values could not be comprehensively included. Establishing causality remains difficult given ethical constraints and confounding factors, while differences in susceptibility further complicate generalization.

Nevertheless, this review provides a broad overview of major chemical classes impacting female reproductive health, integrating recent epidemiological and experimental findings. By addressing multi-organ effects and underlying mechanisms, we offer a holistic perspective and highlight research gaps, vulnerable populations, and potential intervention targets. This synthesis supports future efforts for risk assessment and early prevention.

6. Future Perspective on the Environmental Effects of Female Reproductive Health

Environmental chemicals like phthalates, PFAS, heavy metals, and pesticides pose significant risks to reproductive health, particularly female reproductive health, causing hormonal disruption, reduced gamete quality, infertility, miscarriage, and developmental issues in offspring. These substances, widely present in daily products and the environment, remain a major public health concern. However, the effects of long-term, low-dose exposure, particularly on reproduction, are still poorly understood, as most studies focus on high-dose exposures that do not reflect real-world conditions. This is especially worrisome as many environmental chemicals are suspected endocrine disruptors, with the potential to interfere with hormonal balance and disrupt reproductive health. To address these risks, more research is needed to understand how long-term, low-dose exposure to these chemicals affects female reproduction.

There is a critical need for developing safer alternatives, identifying reliable biomarkers for early detection, and taking preventive actions are critical steps to mitigate harm. Collaboration among researchers, policymakers, industries, and communities is vital to reducing exposure, protecting reproductive health, and ensuring a healthier environment for future generations.

Author Contributions

YX, RP, and LX validated the results and conducted the investigation. RP and LX carried out the formal analysis. YX curated the data. YX and LX drafted the original manuscript. LX reviewed and edited the manuscript, supervised the project, and secured funding. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGpt in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

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