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REVIEW

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Environmental contaminants and male infertility: a comprehensive review

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ABSTRACT

Environmental pollutants have become a topic of discussion in recent years due to their potential effects on male reproductive health. This review explores the connection between environmental pollutants and male infertility. Numerous studies have shown an alarming increase in male infertility rates across the globe and have associated environmental causes with infertility. It has been demonstrated that varied levels of male reproductive system dysfunctions are caused by pervasive pollutants, including pesticides, heavy metals, and endocrine-disrupting chemicals (EDCs). EDCs, such as bisphenol A (BPA) and phthalates, imitate or interfere with the way hormones work, altering sperm quality, sperm count, and sperm motility. Heavy metals like lead and cadmium build up in the body, impairing sperm production, while pesticides disturb hormonal balance and semen characteristics. This mini-review explores the ways through which environmental pollutants impair male fertility, identifying oxidative stress and epigenetic alterations as major factors. Strict regulations and lifestyle modifications are considered as possible tactics to lessen the effect of environmental pollutants on male infertility. In order to protect male reproductive health in a world that is becoming more contaminated, the need for additional study, public education, and legislative measures is underlined. Understanding these dynamics is essential for developing effective preventive measures and securing a healthier future for generations to come.

KEYWORDS

Male infertility; Oxidative stress; Epigenesis; Pesticides; Environmental pollutants

ARTICLE HISTORY

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Introduction

Male infertility is a serious issue for world health with far-reaching social, emotional, and financial effects. Around 15% of couples worldwide are thought to have infertility, and in roughly half of these cases, male factors play a significant role [1]. Male infertility has historically been associated with hereditary and lifestyle variables, but there is mounting evidence that environmental toxins are a major component in male reproductive health impairment [2]. Environmental pollutants are compounds that humans have discharged into the environment. They come in a variety of shapes and sizes and can be either natural or artificial, such as insecticides, heavy metals, endocrine-disrupting chemicals (EDCs), air and water pollutants, and pesticides [3]. These pollutants are present in our environment and have been linked to a number of detrimental health impacts, including a reduction in male fertility. In order to provide light on the mechanisms of action and potential mitigation techniques for environmental contaminants, this review intends to investigate the relationship between environmental pollutants and male infertility [4].

The Global Impact of Male Infertility

It is crucial to understand the bigger picture of male infertility and its worldwide implications before digging into the connection between environmental pollutants and male infertility [5].

Male infertility is described as a man's failure to have a child with a fertile female partner despite regular, unprotected sexual activity for a year. Infertility is thought to affect 7% of all men, with male factors being responsible for 20–70% of infertility cases. The prevalence of this condition has increased recently, and environmental influences are thought to be a major contributing cause [6].

Male infertility has effects that go beyond the incapacity to get pregnant. For both men and their partners, infertility frequently causes psychological discomfort, interpersonal stress, and a loss in quality of life [7]. Furthermore, infertility treatments, including in vitro fertilization (IVF) and sperm retrieval procedures, can be very expensive. Therefore, it is crucial to comprehend the variables causing male infertility, such as environmental pollutants.

Environmental Contaminants and Male Reproductive Health

Endocrine-disrupting chemicals (EDCs)

EDCs are a class of synthetic and organic substances that can disturb the normal operation of the endocrine system, including hormone production, release, and regulation. The body's hormones can be mimicked or blocked by these drugs, resulting in hormonal abnormalities that may harm a man's ability to reproduce [8]. EDC levels have been on the rise recently increasing the risk of lower sperm quality, and consequently increased male infertility [8]. For example, polybrominated diphenyl ethers (PBDE) have been increasing globally over the past 30 years; dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenylethane (DDE) use has been

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increased in Africa and other parts of the world; and multiple EDCs such as bisphenol A (BPA), alkylphenols, pentachlorophenol (PCP), and triclosan have become more prominent in the environment because of manufacturing and because of their presence in widespread consumer products such as soaps, toothpaste, and wood preservations [9-11]. The correlations between declining male fertility and rising EDC levels show that the loss in male reproductive health over the last few decades is related to both hereditary and environmental causes. Different EDCs influence sperm quality via distinct methods. Although phthalates, BPA, dioxins, and PCB have all been linked to lower sperm quality, their modes of action influence various sections of the endocrine system in connection to sperm quality and male reproduction (Figure 1).

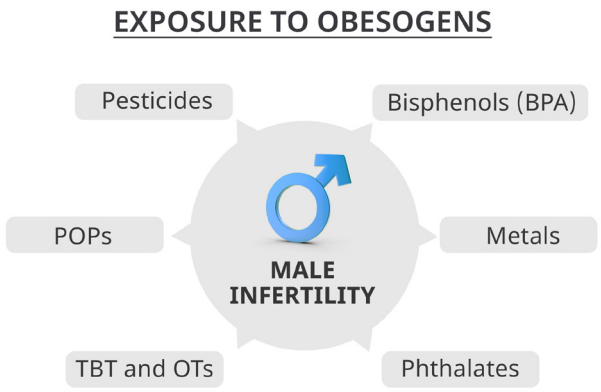

Figure 1. Impact of EDCs on Male Infertility.

Bisphenol A (BPA)

A well-known EDC called Bisphenol A (BPA) can be found in canned foods, food packaging, and plastics. According to research, BPA exposure can harm the male reproductive system by preventing testosterone production, a crucial hormone for sperm formation (Figure 2).

BPA exposure has also been linked to decreased sperm quality and motility [12]. Biomonitoring investigations in the general population demonstrated widespread and continuous BPA exposure in humans, with more than 80% of subjects having measurable levels in the urine [13]. The reproductive system is one of the targets of BPA toxicity. This drug causes metabolic disorders, spermatogenesis abnormalities, and/or infertility in men by mimicking the impact of oestrogen, changing DNA methylation, and modulating enzyme activity [14]. Male reproductive function can be negatively impacted during embryonic, pubertal, and/or adulthood [14].

BPA's disruptive endocrine effects on male reproductive health have generated concerns in recent decades. According to studies, exposure to this compound is linked to lower sperm count, decreased sperm motility and speed, decreased epididymis weight, poor insulin signaling and glucose homeostasis, and lower serum testicle steroids, follicle-stimulating hormone (FSH), and testosterone (T). These findings, however, are based on animal models and in vitro investigations [15-19]. There have been few researches on the effects of BPA on the human male reproductive system, and the underlying molecular pathways are unknown.

Phthalates

A class of compounds known as phthalates is frequently found in plastics, personal care items, and medical equipment. Exposure to phthalates has been associated in several studies with male infertility. These substances may cause the endocrine system to malfunction, which would affect testicular development, sperm motility, and count [20]. Phthalates can enter the human body through the skin, food, or inhalation, and substances or their metabolites have been found in sperm [21,22]. Phthalates have been shown to have a detrimental impact on sperm parameters [23]. The exact mechanism by which phthalates affect fertility is unknown, although they are thought to alter the endocrine system by mimicking endogenous hormones, binding or blocking endogenous hormone receptors, and interfering with receptor metabolism [21,24].

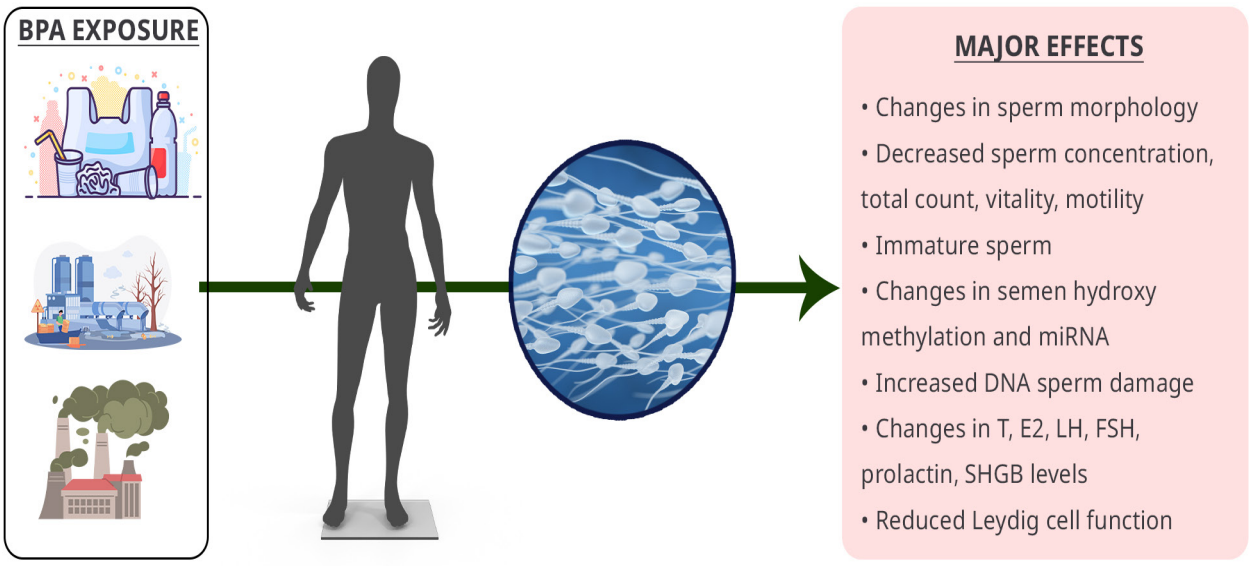

Figure 2. BPA exposure and its effects on male fertility.

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Other hypothesized modes of action include decreased Leydig cell testosterone synthesis, expression of steroidogenic proteins or growth factors, and induction of germ cell death [25-28]. Cai and colleagues conducted a meta-analysis in 2015 to consolidate data supporting relationships between phthalate exposure and human sperm quality [29]. Their meta-analysis comprised 14 researches that investigated phthalates and their metabolite levels in urine and blood, as well as the link to human sperm quality. They discovered that urinary monobutyl phthalate (MBP) and monobenzyl phthalate (MBzP) were linked to lower sperm concentrations, MBP and MEHP were linked to lower motility and motion semen parameters, and MBzP and MEP were linked to higher sperm DNA damage.

Heavy metals

Heavy metals are poisonous compounds that can build up in the environment and enter the body through a variety of pathways, including food, water, and air. Examples include lead, cadmium, and mercury. Male reproductive health may suffer as a result of exposure to these metals [30]. Heavy metal exposure has been linked to decreased male sperm production and fertility [31-33]. The mechanisms that modify reproductive processes, on the other hand, are complex. Toxic effects can be induced directly by acting on reproductive organs or indirectly by disrupting hormonal control [34]. Furthermore, many biological matrices are employed to assess male reproductive risks. Blood, serum, sperm, seminal plasma, urine, and hair are the most common biological matrices studied. Heavy metal concentrations are higher in blood or urine. A recent study from the EcoFoodFertility program indicated that semen might be used as an early indicator of environmental exposure to Zn, Cr, and Cu because higher quantities of these elements were found in men living in high-impact areas [35].

Lead

Numerous harmful health effects, including reproductive toxicity, are linked to lead exposure. It may affect sperm function and production, lessen sperm motility, and raise the possibility of sperm cell DNA damage. Male infertility is recognized to be at increased risk due to occupational lead exposure [36].

Cadmium

The effects of cadmium (Cd) exposure on sperm quality and function have been linked to testicular injury. This heavy metal can build up in the testes, which can damage sperm cells' DNA and cause oxidative stress. Cadmium exposure from smoking is frequent, and men who smoke may have an increased risk of infertility [37]. Cd is a frequent contaminant in many industrial operations as well as smoking [38]. Cd is a byproduct of other metal production, such as zinc, lead, or copper, and is mostly utilized in batteries, pigments, coatings and electroplating, plastic stabilizers, and other uses [38]. After contamination, Cd penetrates the food chain [39]. Cd is ingested by humans through contaminants in the air, water, and food [38]. Another source of Cd is smoking [40]. Smokers' Cd concentration is 4-5 times higher than nonsmokers' after smoking [41]. Humans consume 1.06 g/kg body weight per day on average [42]. Despite the lower Cd intake, Cd has a longer elimination half-life (20-40 years in humans) and can accumulate in the body [42]. Furthermore, the testis is a tissue where Cd can accumulate in significant numbers [43]. After 14 days of therapy, Cd levels in the testes were 100 times greater than in the blood [44]. Numerous studies have demonstrated that mammalian testes are Cd-sensitive organs [41,45,46]. Cd has been linked to male reproductive toxicity, including testicular damage [42].

Pesticide chemicals

Pesticide chemicals are employed in agriculture to manage weeds and pests. Some of these substances can harm the health of male reproductive organs and disturb the endocrine system [47]. Natural and inorganic pesticides, such as lead arsenate, were the sole insecticides used until the late 1940s when they were replaced by new and strong synthetic organic compounds [48]. Organochlorine pesticides (OCPs) were the first to be introduced, followed by organophosphates (OPs), carbamates, pyrethroids, phenylpyrazoles, and, more recently, neonicotinoids. Pesticides, in particular, can harm the male reproductive system in several ways: (i) reproductive toxicity with direct cell structure damage; (ii) changes in DNA structure, resulting in gene mutations that can cause birth defects or inability to conceive; and (iii) epigenetic effects caused by changing the way genes are expressed (Figure 3). Indeed, there is evidence that environmental influences are related to changes in the genome. Disorders may be passed from father to child by epigenetic cell components such as DNA methylation, histone modification, and non-coding RNAs [49]. Pesticides can also harm the male reproductive system by functioning as EDCs. Indeed, EDCs account for the great majority of pesticides [50]. Furthermore, as previously stated, pesticides can serve as obesogens, with 30 to 40% of all cases of male infertility strongly connected with obesity [51,52].

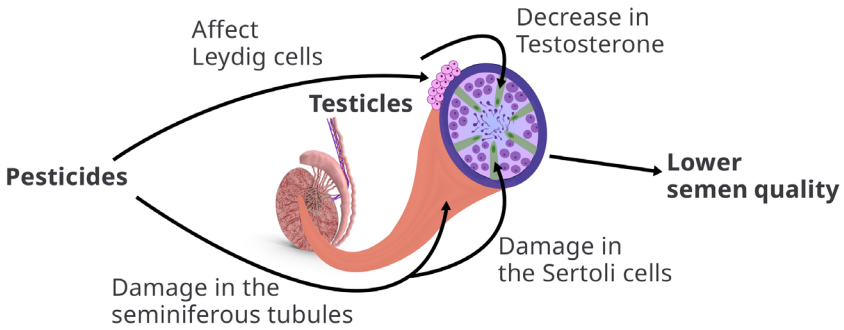

Figure 3. Pesticides exposure affecting sperm quality.

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Atrazine

A common herbicide called atrazine has been linked to lower sperm quality and changed hormone levels in males. Atrazine exposure has been associated with a higher risk of sperm abnormalities and reduced fertility [53]. ATZ has been shown in studies to disrupt the reproductive system in both humans and animals [54-57]. ATZ damages the sperm cell membrane, which could be another explanation for the decrease in sperm motility and motility duration. A robust sperm membrane in fish sperm is critical for generating depolarization and initiating movement to reach the oocyte's micropyle and fertilize it [58]. Furthermore, a broken membrane may impair sperm motility by interfering with the exchange of nutrients between the cell and its surroundings [59].

Organophosphates

Organophosphate pesticides are utilized in agriculture and as insecticides. These substances have been associated with hormonal imbalances, poor sperm quality, and a higher risk of infertility in those who are exposed to them [60]. Organophosphate exposure has been linked to aberrant sperm parameters such as decreased sperm counts, motility, viability, and density, as well as increased DNA damage and abnormal morphology [61]. Furthermore, organophosphates have been linked to macroscopic testicular alterations such as decreased testicular volume [61]. Numerous other research shows that organophosphates change blood reproductive hormones and may be linked to lower total testosterone levels. Organophosphates may affect fertility by directly affecting spermatogenesis through decreased antioxidant capacity, impairing testicular testosterone production, altering testosterone metabolism systemically, or affecting gonadotropin production centrally [62]. Pesticides containing organophosphates are the most frequent organophosphates.

Mechanisms of Action

Creating solutions to lessen the effect of environmental exposures on male reproductive health requires an understanding of how environmental pollutants affect human health. A number of theories have been put forth to explain how these pollutants affect male fertility.

Hormonal disruption

Numerous environmental pollutants, particularly EDCs, have the ability to mimic or otherwise affect hormones like testosterone and estrogen. This hormonal imbalance can cause the endocrine system to become unbalanced, which can impact sperm production and function as well as the growth of the male reproductive system [63]. Hormones have a wide range of effects on male reproductive potential, including sperm DNA integrity and parameters. The most difficult problem in infertility clinics, oligoasthenoteratospermias, is connected with an aberrant spermatogenic process that could be induced by hormonal imbalance [64]. Gonadotropin and testosterone concentrations are important in maintaining proper spermatogenesis. Furthermore, any change in their serum levels could result in an aberrant sperm profile, sperm DFI, and, ultimately, reproductive issues [65]. Excess PRL, like TSH, has been shown to have reversible effects on male reproduction. In males, early detection of hyperprolactinemia can prevent irreparable infertility and unnecessarily invasive operations for establishing pregnancy [66]. Sertoli cells produce AMH, which may indicate its importance in normal testicular function and spermatogenesis [67].

Oxidative stress

An imbalance between free radicals and antioxidants in the body leads to oxidative stress. Heavy metals and pesticides in the environment can cause oxidative stress in the testes, which can damage sperm DNA and impair sperm motility [68]. Oxidative stress impairs sperm function by altering DNA integrity as a result of concomitant damage to proteins and lipids in the sperm cell plasma membrane, reducing cell membrane fluidity and permeability [69] (Figure 4). The first observation of oxidative-stress-induced defective sperm function dates back to 1943 when Dr. John MacLeod reported that human spermatozoa lose motility when incubated in conditions of high oxygen tension via a mechanism that could be inhibited by the presence of catalase — an enzyme that catalyzes the decomposition of H2O2 [70]. ROS are produced by spermatozoa, as well as by leukocytes in seminal plasma [71,72]. Mild oxidative stress is required for tyrosine phosphorylation, which is required for sperm cell capacitation and supports telomere length preservation [73]. Severe oxidative stress, caused by seminal ROS levels greater than 35 relative light units (RLU)/s per million sperm cells, results in accelerated telomere shortening, whereas mild oxidative stress, caused by seminal ROS levels between 21.3 and 35 RLU/s per million sperm cells, promotes telomere length maintenance [74]. Spermatozoa's functional capability is determined not only by their ability to fertilize oocytes but also by their ability to transfer the entire paternal genome [75].

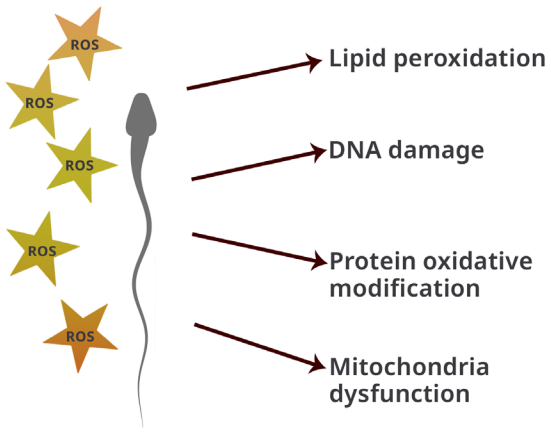

Figure 4. Oxidative stress and male infertility.

Epigenetic modifications

During the differentiation process to produce a mature spermatozoon, sperm cells undergo substantial epigenetic changes. Epigenetic alterations, including DNA methylation, histone modifications, and chromatin remodeling, play important roles in spermatogenesis. Epigenetic changes involve histone proteins, which are involved in DNA packing, as well as a variety of DNA modifications. DNA encircles histone proteins and is the primary structural unit of chromatin, known as the nucleosome. It affects gene expression under changing temporal and environmental situations by regulating DNA methylation and histone and chromatin modifications [76,77].

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Inflammation

Environmental factors such as food and hazardous materials, genetic abnormalities, infection and inflammation, and so on are all issues to consider [78-82]. Infection is still the most common cause of infertility in Africa, especially in Sub-Saharan Africa [83,84]. When the reproductive tract is infected, one important function of the innate immune system is to recruit more phagocytic cells and effector molecules to the infection site through the release of a battery of cytokines and other inflammatory mediators that have profound effects on subsequent events. Inflammation in the male reproductive tract can be caused by a number of factors. These are some examples:

1. Ejaculatory duct obstruction: This is a common cause of male infertility, with infections found in at least 20-50% of these men [85].
2. Epididymitis: This is an inflammation of the epididymis, which connects the testes with the vas deferens in the male reproductive system.
3. Inflammation is caused by sexually transmitted infections such as gonorrhoea, Chlamydia, and E. coli. Although E. coli is the most common cause of epididymitis in older men, other bacteria, such as mycobacteria and ureaplasma, can also cause this condition.
4. Urethritis: A bladder or urethral infection that spreads to the epididymis is also possible. Mumps and other viral infections in children can cause epididymitis.
5. Testicular torsion is a common fertility issue caused by a supporting tissue defect that permits the testes to twist inside the scrotum, resulting in severe edema. Torsion induces testicular injury by pinching the blood arteries that feed the testes tight.
6. Varicocoele: A varicocoele is an expansion of the internal spermatic veins that drain blood from the testicle to the belly (and back to the heart). When the one-way valves in the spermatic veins are broken, an aberrant backflow of blood from the belly into the scrotum occurs, providing a hostile environment for sperm growth. (vii) Other causes include male urogenital blockage, chronic prostatitis, testicular inflammation (orchitis), and medication therapy.

Strategies for Mitigation

In order to address the effect of environmental toxins on male infertility, a multi-pronged strategy encompassing governmental policy, regulatory frameworks, and individual initiatives is necessary.

Regulation and monitoring

The use of environmental toxins, particularly EDCs, and pesticides, should be subject to tight regulations from governments and regulatory organizations. Monitoring programs can assist in determining the environmental concentrations of the toxins and the potential health concerns they pose [86].

Consumer awareness

It is crucial to inform the public of the dangers posed by environmental toxins. By avoiding items that are known to contain EDCs or choosing foods that are organic and pesticide-free, consumers can make educated decisions.

Occupational safety

Environmental pollutant exposure at work is a major problem. Employers should take precautions to safeguard workers from dangerous material exposure, provide the necessary protective equipment, and enforce workplace safety regulations [87].

Lifestyle Changes

By leading a healthier lifestyle, people can lessen their exposure to environmental toxins. This entails giving up smoking, eating organic and locally sourced food, and avoiding plastic objects made with EDCs [88-90].

Conclusions

The complicated and multidimensional problem of male infertility impacts millions of couples worldwide. Environmental toxins may have a substantial impact on male infertility, even though genetic and lifestyle variables have long been known as causes. EDCs, heavy metals, and pesticides are examples of substances that can alter hormonal balance, cause oxidative stress, cause epigenetic changes, and eventually harm male reproductive health. It is crucial to comprehend the mechanisms through which environmental pollutants affect male fertility in order to create methods that effectively reduce their effects. Regulation and oversight, consumer education, workplace safety precautions, dietary adjustments, and ongoing research and innovation should all be part of these programs. It is important not only for people's personal and public health but also for society and the economy to address the issue of environmental pollutants and male infertility. By adopting proactive measures to lessen exposure to these toxins and encouraging research into their effects, we may move toward a future in which male infertility is less common, and couples have a better chance of achieving their desire for parenthood.

Disclosure statement

No potential conflict of interest was reported by the author.

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