The Role of Industrial Chemicals and Occupational Hazards in Male Infertility: A Comprehensive Review

Dr. Khawaja Fawad Parvez[1,2], Dr Shahzadi Saima Hussain[3*]

[1]*Assistant Professor OB/GYN, Department Medical Teaching Institute (MTI), Lady Reading Hospital (LRH), Peshawar, Pakistan*
[2]*Consultant Gynaecologist Mubarak Hospital Peshawar, Pakistan*
[3]*Associate Professor OB/GYN Department Medical Teaching Institute (MTI), Lady Reading Hospital (LRH), Peshawar, Pakistan*
Email: maple9894@yahoo.com

Abstract: Infertility affects 10–15% of couples globally, often resulting from a complex interplay of factors involving both men and women. While medical assessments, including semen analyses and hormonal evaluations, are critical for diagnosing male infertility, the underlying causes frequently remain elusive. Endocrine-disrupting chemicals (EDCs), prevalent in the environment due to industrial growth, may significantly impact male reproductive health by interfering with hormonal regulation essential for spermatogenesis. This review explores the influence of occupational and environmental exposures on male fertility, emphasizing EDCs, heavy metals, and lifestyle factors such as smoking, alcohol consumption, and obesity. We analyze epidemiological studies investigating the relationships between these exposures and male infertility, revealing a concerning correlation between disrupted spermatogenesis and increasing exposure to harmful chemicals. Despite the progress made by infertility clinics in identifying potential links, the field lacks systematic studies, particularly regarding occupational exposures. This review aims to highlight the need for comprehensive research to understand the multifaceted causes of male infertility better and to encourage proactive measures for monitoring and mitigating occupational hazards.

Keywords: Chemical Exposure, Endocrine-disrupting Chemicals (EDCs), Environmental Exposures, Heavy Metals, Hormonal Regulation, Infertility.

1. Introduction

Infertility is medically defined as the inability to conceive a child after one year of regular, unprotected intercourse. This condition affects approximately 10 to 15 percent of couples globally, and its prevalence varies significantly across different countries and geographic regions (Zegers-Hochschild et al., 2009). Infertility is a complex issue stemming from both male and female factors, indicating that both partners typically contribute to the challenges faced in achieving pregnancy. In many cases, multiple factors may coexist, further complicating the issue (Dominguez & Reijo Pera, 2013).

When diagnosing male infertility, healthcare providers employ a comprehensive approach that includes evaluating sex hormone levels, such as testosterone, and performing semen analyses. Semen analysis is a crucial diagnostic tool that examines several key parameters of sperm quality, including sperm count (the number of sperm present), motility (the ability of sperm to move and swim effectively), and morphology (the size and shape of the sperm). These parameters help to assess the overall health and function of a man's reproductive system (Agarwal et al., 2015).

For couples facing infertility, healthcare professionals often recommend pursuing assisted reproductive technology (ART) options, which may include treatments such as in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). These advanced techniques aim to improve the chances of conception when natural conception proves challenging (Jungwirth et al., 2012).

Despite the routine nature of semen analyses in both clinical and research settings worldwide, the root causes of infertility often remain elusive. Factors such as hormonal imbalances, testicular disorders, or genetic conditions cannot fully explain the underlying reasons. Specific genetic factors, including Klinefelter syndrome (characterized by an atypical number of sex chromosomes, specifically XXY), rearrangements within the azoospermia factor (AZF) genes, or mutations in other known infertility-related genes, may contribute to male infertility but are not always identifiable through standard diagnostic methods (Aitken, 2020).

Ultimately, the multifaceted nature of infertility necessitates a thorough evaluation of both partners and suggests that addressing this condition requires a collaborative approach among medical professionals, as well as ongoing research to uncover the factors that remain poorly understood (Gabrielsen & Tanrikut, 2016).

Spermatogenesis is an intricate and cyclical biological process through which haploid spermatozoa mature from diploid, undifferentiated spermatogonia. Various everyday stressors can influence This essential reproductive process, particularly those originating from occupational environments and external surroundings (Santi et al., 2016). The rapid industrial growth experienced in recent decades has led to numerous advancements that enhance our daily lives; however, it has also resulted in heightened exposure to many chemical compounds and their complex mixtures (Weinbauer & Nieschlag, 1995). Among these chemicals, those that disrupt hormonal regulation are often termed endocrine-disrupting chemicals (EDCs). These substances can be found in various sources, including agricultural pesticides, food contaminants, personal care products such as cosmetics, and even in the air we breathe and the water we drink (Diamanti-Kandarakis et al., 2009).

In men, EDCs primarily affect the hypothalamus, a critical brain region that regulates hormonal signaling. This gland stimulates the pituitary gland to secrete essential gonadotropins—specifically luteinizing hormone (LH) and follicle-stimulating hormone (FSH) (Rehman et al., 2017). These hormones play a vital role in regulating spermatogenesis by encouraging the secretion of androgens from Leydig cells and activating Sertoli cells, which are crucial for nurturing developing sperm (Agarwal et al., 2009).

Given hormones' precise control over the male reproductive system, the presence of EDCs that function as antiandrogens or mimic the action of estrogens can thoroughly disrupt these delicate mechanisms. Such disruptions can lead to significant adverse effects on healthy sperm production. Nevertheless, it is important to note that research regarding the implications of EDCs on human reproductive health remains scarce, and our understanding of the underlying mechanisms is still incomplete, particularly because EDCs frequently coexist in various combinations, complicating their assessment (Jurewicz et al., 2018). There is a clear connection between disrupted spermatogenesis and lifestyle factors such as alcohol use, smoking, drug use, and obesity linked to a high-calorie diet. Additionally, exposure to too much heat, noise, vibrations, and electromagnetic fields can damage sperm DNA and affect fertility. Researchers have also pointed to a possible link between male infertility and air pollution, though the

evidence is not definitive. Changes in seasons and natural disasters may also impact male reproductive health (Chen et al., 2004).
These findings suggest that various factors influence spermatogenesis and male fertility, including long-term exposure to environmental pollutants and genetic factors. This review will examine workplace and environmental exposures and their effects on human spermatogenesis, hormone pathways, and overall male fertility (Lin, 2010). It will include studies that examine the links between male infertility and endocrine-disrupting chemicals, pesticides, heavy metals, air pollution, lifestyle choices, heat, noise, and electromagnetic waves. Ionizing radiation will not be covered, as current safety regulations show that exposure does not pose a fertility risk for men. The review is based on a systematic search of articles published from January 2000 to September 2020, indexed in PubMed, Scopus, and Web of Science, regardless of the language.

Occupational Hazard

The relationship between occupational exposure and infertility often goes unnoticed, and research in this area is limited and lacks a systematic approach, even in developed nations. Many occupational health protocols for jobs known to involve exposure to endocrine-disrupting chemicals fail to include medical examinations or data collection on workers' fertility status. Nevertheless, infertility clinics have made significant strides by actively investigating the causes of infertility, thereby enhancing the effectiveness of assisted reproductive technology (Fucic et al., 2018).
Over the past few decades, these clinics have identified several classes of compounds potentially linked to male infertility. However, lifestyle factors such as smoking and alcohol consumption can significantly obscure or interfere with the effects of these workplace compounds. Research on occupational exposure to benzene, as well as its mixtures with toluene and xylene, has demonstrated correlations between blood and seminal plasma benzene levels, notable genomic damage, and abnormalities in sperm count, motility, and morphology – including Disomy of the X and Y chromosomes and hyper haploidy – even at low exposure levels (≤1 ppm) (Katukam et al., 2012).
A comprehensive study conducted in Tunisia examined the health of 2,122 men who sought assistance at infertility clinics. Participants completed extensive questionnaires that evaluated their occupational exposures, lifestyle choices, and reproductive health. The findings revealed a worrying association between occupational exposure to pesticides and a significantly heightened risk of diminished sperm motility, along with an increased presence of dead sperm cells (Xiao et al., 2001). Moreover, men working in environments with cement exposure exhibited a greater likelihood of experiencing low sperm count. Interestingly, this study did not find any significant links between impairments in semen quality and exposure to solvents, high temperatures, or mechanical vibrations, suggesting that these factors may not play a critical role in male infertility within the studied population (Xing et al., 2010).
In contrast to the findings from the Tunisian study, another research effort highlighted connections between male infertility and various other occupational exposures, including solvents, paints, lead, prolonged computer work, shift work, and work-related stress. A notable national study from Canada corroborated these findings, revealing a decline in sperm motility among participants subjected to high levels of solvent exposure. This was further supported by a recent systematic meta-analysis involving a substantial sample size of 272 men occupationally exposed to solvents and 247 unexposed men, reinforcing the concern regarding solvents and reproductive health (Daoud et al., 2017).
Despite the European Union's ban on consumer use of formaldehyde at concentrations of 0.1% or higher due to its recognized carcinogenic properties, formaldehyde remains prevalent in various industrial and environmental contexts. It finds extensive application in the production of resins, construction materials, wood processing, textiles, and even in healthcare settings like hospitals and laboratories, as well as in the chemical industry. The projected sales for

formaldehyde are estimated to reach a staggering $34.8 billion by 2026, underscoring the need for ongoing vigilance and strategies to limit occupational exposure. Notably, research indicates that formaldehyde exposure may lead to significant reductions in both progressive and total sperm motility, with the severity of impact appearing to be dose-dependent (El-Helaly et al., 2010).

Pesticides, which encompass a range of chemicals such as insecticides, herbicides, and fungicides, are known to exert endocrine-disrupting effects. These effects can manifest as xenoestrogens, which mimic estrogen, or as aromatase inhibitors, which affect estrogen synthesis in the body (Cherry et al., 2001). A detailed sperm analysis conducted among groundnut farmers in Myanmar, who extensively used chlorpyrifos and carbamate pesticides—often at levels exceeding recommended dosages—revealed alarming results. During the farming season, 74% of the farmers exhibited oligozoospermia (low sperm count), compared to only 46% during periods without pesticide application, highlighting the direct impact of pesticide usage on male fertility (Ianos et al., 2018).

Among farmworkers exposed to abamectin, there was a striking correlation between elevated plasma levels of this pesticide and significant genomic damage, as well as the presence of immature spermatozoa (European Union, 2018). Notably, the levels of reproductive hormones such as testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) remained within normal ranges, indicating that the pesticides may disrupt spermatogenesis independently of these hormonal pathways. Similarly, exposure to organophosphate and carbamate pesticides was associated with reduced sperm motility and increased sperm immaturity, which again occurred despite normal serum testosterone, LH, and FSH levels, pointing to a complex interaction between environmental toxins and reproductive health (Celik-Ozenci et al., 2012).

Ethylene glycol-based chemicals are widely utilized across various commercial and industrial applications, including solvents, antifreeze, and coolants. Research has shown that occupational exposure to ethylene glycol is linked to reduced motile sperm counts; however, when accounting for confounding factors in the analysis, this risk appeared to diminish. In vitro experiments suggest that ethylene glycol may elevate estradiol levels within certain cell types, hinting at its potential endocrine-disrupting capacity (Wang et al., 2015).

In toxicological studies involving rats and mice, ethylene glycol monomethyl ether (EGME) was observed to interfere with normal spermatogenesis by lowering the expression of genes specific to spermatocytes and disrupting the lineage of germ cells. Furthermore, exposure to EGME damaged spermatocytes during the crucial pachytene stage of meiosis in cynomolgus monkeys. This disruption was implicated in the downregulation of the microRNAs miR-34b-5p and miR-449a, which are known to play important roles in regulating germ cell development, shedding light on the molecular mechanisms through which certain chemicals can adversely affect male fertility (Li & Li, 2013).

Table 1.1: Occupational Exposures and Their Impact on Male Fertility: Findings and Examples

Occupational Exposure	Findings	Examples/References
Benzene, toluene, xylene	Genomic damage, abnormalities in sperm count, motility, morphology, Disomy of X/Y chromosomes	Benzene studies in blood and seminal plasma (≤1 ppm)
Pesticides (e.g., chlorpyrifos, carbamates)	Reduced sperm motility, immature sperm, oligozoospermia, genome damage	Groundnut farmers in Myanmar; acetylcholinesterase levels
Formaldehyde	Dose-dependent reduction in sperm motility	Studies on formaldehyde's carcinogenic properties
Ethylene glycol-based chemicals	Low motile sperm counts, estradiol increase, disrupted germ cell lineage	Studies on animals and workers using ethylene glycol

Firefighting chemicals (e.g., PFAS)	Reduced spermatogonia, long-term fertility effects, genome damage	PFAS exposure in firefighting foams
Phthalates	Lower sperm motility, increased DNA fragmentation, reduced testosterone	Studies on PVC workers and air phthalate exposure
Bisphenol A (BPA)	Changes in DNA hydroxymethylation, sperm epigenetics	Epoxy resin workers, BPA affecting histone H3 processes

Full-time firefighters face an elevated risk of infertility, a concerning issue linked to their unique occupational exposure to a complex blend of hazardous chemicals. These substances include notorious endocrine disruptors such as flame retardants and polycyclic aromatic hydrocarbons, which interfere with hormonal balance. The occupational environment for firefighters also brings about additional stressors, such as hyperthermia—the significant increase in body temperature due to prolonged exposure to heat—and challenges related to disrupted circadian rhythms, particularly those working night shifts (Basak & Sen, 2011).

Among the most troubling chemicals they encounter are per- and poly-fluorinated alkyl substances (PFAS), which are particularly abundant in aqueous film-forming foams used in firefighting. Research utilizing a human stem-cell-based model of spermatogenesis has revealed that exposure to PFAS can significantly diminish the expression of critical markers associated with spermatogonial stem cells and primary spermatocytes. Notably, this does not impact the viability of germ cells directly, suggesting that the long-term consequences of such exposure may involve a reduction in the spermatogonial stem cell reservoir, potentially leading to abnormalities in primary spermatocytes and resulting in male fertility issues over time (Vandenberg et al., 2013).

Furthermore, exposure to phthalates, particularly di-n-butyl and di-2-ethylhexyl phthalate, has lowered free testosterone levels among workers producing unframed polyvinyl chloride flooring. Comparative studies have raised concerns about potential bias in research, as construction workers used as control subjects may also be exposed to similar phthalate chemicals, complicating the findings (Satoh & Tominari, 2012). In another investigation involving workers in the polyvinyl chloride industry, scientists observed a troubling correlation: lower sperm motility was linked with higher levels of urinary phthalate metabolites, which also coincided with increases in sperm apoptosis (programmed cell death) and the generation of reactive oxygen species, known to contribute to oxidative stress (Malek, 2017).

In the field of epoxy resin production, workers have been shown to experience significant changes in their reproductive health due to exposure to bisphenol A (BPA). This chemical has been associated with alterations in the hydroxymethylation of the LINE-1 genomic element in sperm, which is crucial for maintaining genomic stability. Moreover, studies indicate that BPA exposure can disrupt gene expression by influencing DNA hydroxymethylation processes, which are partially reliant on the trimethylation of histone H3 during the complex process of human spermatogenesis. This underscores the intricate interplay between occupational exposures and male reproductive health, highlighting a need for enhanced protection and understanding within these high-risk professions (Wang et al., 2016).

Ecological Exposure

Market globalization and the increased mobility of goods and people have heightened exposure to canned and fresh foods and the international transport of waste. As dietary habits become increasingly similar across nations, the risk of food contaminants spreading globally also rises (Sakurai et al., 2015).

Despite this, infertility issues related to environmental exposure remain largely neglected by the media and educational initiatives geared toward the general public. The intricate nature of environmental exposure complicates the accurate assessment of infertility risks. Furthermore, individual differences in susceptibility, age, and unknown transplacental exposure may have

lasting effects, making it even more challenging to evaluate these risks effectively (Petersen et al., 2018).

Figure 1: Environmental Exposure Factors and Their Impact on Infertility Risk

Smoking

Numerous studies have assembled a compelling body of evidence linking smoking to detrimental effects on sperm quality, suggesting that individuals who quit tobacco and embrace healthier lifestyle choices may experience significant enhancements in male fertility. A notable meta-analysis by Sharma and colleagues scrutinized the impacts of cigarette smoking. It revealed that both moderate and heavy smoking significantly diminishes sperm count, motility, and morphology — critical parameters for male reproductive health. Intriguingly, another study indicated that even light smoking might have a harmful influence on spermatogenesis, as it found no significant differences in the adverse effects across varying levels of smoking intensity (Jian et al., 2018).

Heavy smoking not only influences sperm health but also initiates a process known as ferroptosis in seminal plasma, leading to decreased sperm motility. Among patients attending infertility clinics, researchers observed that smokers had lower ejaculate and seminal vesicle volumes compared to their nonsmoking counterparts. Interestingly, despite these notable changes in seminal fluid characteristics, testosterone levels remained relatively unchanged between the two groups (Steves et al., 2018). A significant factor that could predict genomic damage associated with various diseases, environmental hazards, and lifestyle choices is the abnormal methylation patterns of repetitive elements like LINE-1. Properly methylating an array of genomic elements is vital in regulating fertility. A study conducted in China discovered a direct correlation where hypermethylation of LINE-1 and hypomethylation of the P16 gene was strongly associated with tobacco smoking in men at risk of infertility (Pan et al., 2006).

Smokers undergo a concerning accumulation of reactive oxygen species (ROS) — such as superoxide anion and hydroxyl radicals — within the testes. This accumulation triggers oxidative stress, a condition to which sperm are particularly susceptible due to the high levels of polyunsaturated fatty acids in their plasma membranes and the relative scarcity of enzymatic defenses in their cytoplasm. Such oxidative stress may compromise sperm function by making the acrosome membrane temporarily permeable to calcium ions, potentially leading to a premature acrosome reaction, which can impede fertilization. Additionally, research by Antoniassi et al 2016. has linked smoking to diminished mitochondrial activity in sperm as well as heightened pro-inflammatory responses in both the accessory glands and the testes (Huang et al., 2014).

Furthermore, the testes are exposed to harmful metals such as cadmium (Cd) and lead (Pb) in tobacco smoke, which are absorbed through the lungs. These toxic elements behave as metalloestrogens, accumulating in the blood and semen of smokers at higher concentrations

than in nonsmokers. Elevated levels of these metals are associated with impaired spermatogenesis and increased ROS levels, further exacerbating oxidative stress. Notably, cadmium can substitute for zinc, a trace element critical for normal spermatogenesis. In studies conducted on rats, cadmium exposure appears to disrupt the normal functioning of the hypothalamus-pituitary-testicular axis, suggesting that the impact of cadmium on spermatogenesis may vary with age (Huang et al., 2011).

Nicotine and its primary metabolite, cotinine, have also been shown to disrupt sperm parameters in a dose-dependent fashion. In in vitro studies, nicotine significantly decreased the number of TM3 Leydig cells, likely through mechanisms involving autophagy, reducing testosterone synthesis. In vivo research has demonstrated that nicotine intake lowers serum testosterone levels and adversely affects the function of other sex hormones in albino rats, underscoring the profound impact of tobacco on male reproductive health (Tian et al., 2018).

Farmworker Chemical Exposure

Researcher examined how pesticides can lead to reproductive toxicity in men. A myriad of studies have established links between exposure to specific pesticides encountered in daily life and various adverse effects on sperm quality. One prominent group of these chemicals is the pyrethroids, widely employed due to their potent effectiveness against insect populations and relatively low toxicity to mammals (Miao et al., 2014). This perception of safety has made pyrethroids a common choice, yet numerous research findings cast doubt on this assumption. For instance, several studies have documented associations between the metabolites of pyrethroids found in non-occupationally exposed men and significant abnormalities in sperm morphology, diminished sperm counts, and lowered testosterone levels .Furthermore, additional investigations have revealed concerning connections between these metabolites and compromised sperm DNA integrity, as well as increased rates of sex chromosome aneuploidy .On the other hand, two specific studies conducted among a Japanese student population concluded no significant correlations between pyrethroid metabolites and sperm quality or reproductive hormone levels (Zheng et al., 2017).

Organochlorines are a different category of pesticides linked to reproductive toxicity in men, which were extensively utilized during the mid-20th century. Although many of these compounds have been banned due to their harmful effects, they continue to linger in the environment owing to their remarkable chemical stability. Research has shown that environmental exposure to organochlorines such as p,p'-DDE, and lindane correlates with a host of reproductive issues, including lower sperm motility, increased DNA fragmentation, heightened production of reactive oxygen species (ROS), and mitochondrial depolarization. One study highlighted that non-occupational exposure to p,p'-DDT was associated with reduced sperm motility and viability. This research also established links between p,p'-DDT exposure and conditions such as oligozoospermia (low sperm count) and asthenozoospermia (low sperm motility). Furthermore, elevated levels of the organochlorine hexachlorocyclohexane (HCH) found in semen were notably associated with decreased sperm counts, especially in azoospermic men who exhibited deletions in the AZF region (Dupont et al., 2019). Organophosphates constitute another extensively used group of pesticides that exhibit a rapid breakdown in the environment and are recognized for their neurotoxic effects on humans. Various subclasses of organophosphate pesticides detected through urine analysis have been linked to detrimental effects on sperm concentration, count, and motility.

One enlightening study found a positive correlation between the presence of urinary organophosphate metabolites and elevated levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in men who had increased gonadotropins (Rehman et al., 2019).

In addition, another study established a correlation between diverse organophosphate metabolites in urine and escalated rates of sex chromosome disomy. Despite the diverse uses of organophosphates, including their application as flame retardants and plasticizers, a

comprehensive cohort study found either no or weak correlations between urinary levels of these compounds and sperm parameters (Sharma et al., 2016). Interestingly, one research effort that only bis(1,3-dichloro-2-propyl) phosphate exhibited a stronger association with increased sperm count among men attending infertility clinics; however, the authors of this study cautioned that these associations were inconsistent when viewed in the broader context (Li et al., 2009).

Occupational Plastics Exposure

Bisphenol A (BPA) is a precursor in the plastic industry that is recognized as an endocrine disruptor and xenoestrogen. It can be found in plastic water bottles, food containers, can linings, dental fillings, cash receipts, and plastic toys. Although BPA binds to estrogen receptors less effectively than estradiol, its concentrations in circulation can surpass those of estradiol. Additionally, BPA demonstrates antiandrogen effects by binding to androgen receptors and inhibiting normal androgen functions (Ou et al., 2020).

Numerous studies have explored the impact of BPA on sperm parameters due to its harmful effects on male hormonal pathways. Research conducted by Li et al. revealed a dose-dependent relationship between elevated urinary BPA levels and diminished semen quality. In men seeking assistance at fertility clinics, BPA levels in seminal plasma were negatively correlated with sperm concentration, count, and morphology. However, other studies have reported either no association or weak, clinically insignificant correlations (Shrem et al., 2019).

One investigation suggested that Italian men in urban areas exhibited higher BPA levels than those in rural regions. Moreover, variations were noted between fertile and infertile men, although BPA was not identified as a significant risk factor for infertility. While it is evident that BPA influences the male reproductive system, the clinical significance of these effects remains unclear (Lotti et al., 2015).

PVC Manufacturing Workers

Phthalate esters, a group of chemical compounds commonly found in a variety of consumer products, have the potential to migrate from materials such as polyvinyl chloride (PVC), which is frequently used in food packaging and children's toys, into more sensitive substances like cosmetics, solvents, and pharmaceutical film coatings. Extensive research on the effects of phthalate exposure on male infertility has primarily been conducted using data from infertility clinics. However, a significant limitation of this approach is that it often remains ambiguous whether the phthalate exposure experienced by the patients is primarily environmental or occupational (Zhang et al., 2019).

Despite this limitation, compelling evidence exists linking phthalates to a decline in sperm quality. Numerous studies have established significant associations between elevated levels of phthalate metabolites in the body and reduced sperm parameters, such as motility and concentration. In the broader general population, the findings regarding the impact of phthalates on sperm quality are less uniform. Some studies have indicated explicitly that exposure to phthalates can negatively affect sperm quality even in the absence of measurable changes in reproductive hormone levels. These investigations imply that phthalates may adversely influence semen quality through various biological mechanisms. Notably, these mechanisms could include the generation of reactive oxygen species (ROS), which can lead to oxidative stress and subsequent damage to sperm; lipid peroxidation, where free radicals attack and degrade lipids in cellular membranes; and mitochondrial dysfunction, which can impair energy production essential for sperm motility and functionality (Agarwal et al., 2003).

In instances where hormonal changes were observed, including alterations in the testosterone-to-estradiol ratio, researchers speculated that these changes could be attributed to the suppression of aromatase, an enzyme responsible for converting testosterone to estrogen. Furthermore, one notable study investigating the effects of environmental exposure to a

complex mixture of chemicals found a significant synergistic interaction between polychlorinated biphenyls (PCBs) and monobutyl phthalate. This interaction resulted in considerable sperm damage, suggesting that other chemical exposures in the environment could exacerbate the effects of phthalates. This highlights the complexity of studying phthalates and their impact on male fertility within the context of multifactorial exposure scenarios.

Pharmaceutical Manufacturing Employees

Antimicrobial preservatives, including parabens and triclosan, are widely used in various consumer products, from personal care items to pharmaceuticals. In the United States, studies indicate that between 58% and 99% of the population have detectable levels of these compounds in their urine, signifying their pervasive presence in everyday consumer goods (Oyeyipo, Raji, & Bolarinwa, 2013).

Both parabens and triclosan are known for their endocrine-disrupting properties, which means they can interfere with hormone functions in the body. This has raised concerns regarding their potential adverse effects on male reproductive health. Extensive research has demonstrated significant associations between hydroxylated paraben metabolites and triclosan levels and various parameters of semen quality. Notably, studies have found that higher urinary concentrations of parabens correlate with notable adverse effects, including abnormal sperm morphology—where sperm shape deviates from the norm—reduced sperm motility and lower testosterone levels. These changes in sperm parameters can have profound implications for male fertility (Talbot & Lin, 2011).

Furthermore, alterations in chromosomal integrity have been observed; specifically, XY18 and chromosome 13 disomy have been reported among males with elevated parabens in their urine. This indicates that these preservatives may also have underlying genetic ramifications for reproductive health. In addition to these findings, parabens have been identified as contributors to mitochondrial dysfunction, similar to other endocrine disruptors. Mitochondrial health is crucial for cell energy production, and disturbances in this process can impact various bodily functions, including fertility-related ones (Zhao et al., 2018).

The growing body of evidence underscores the need for further investigation into the health implications of these widely used substances, particularly regarding their impacts on male reproductive functions and overall endocrine health (Antoniassi et al., 2016).

Electrical and Electronics Engineers

Environmental exposure to electromagnetic fields (EMFs), mainly from devices such as cell phones, telecommunication towers, and radar systems, has stirred considerable public debate over the past several decades. The discourse surrounding EMF exposure and its potential impact on male fertility has generated a broad spectrum of research findings, which remain inconclusive and varied. These disparities can be attributed mainly to the differences in study designs, experimental methodologies, and varying environmental conditions under which the research was conducted (Marques-Rocha et al., 2016).

Recent studies have drawn attention to the potential adverse effects of living near telecommunication towers. One notable study reported a significant association between residing near these towers and reduced sperm volume. Additionally, research indicated that carrying a mobile phone in trouser pockets may correlate with diminished sperm motility, a crucial factor for male fertility (Oyeyipo, Maartens, & du Plessis, 2014). A comprehensive meta-analysis encompassing ten observational studies, comprising both in vitro and in vivo experiments, similarly corroborated these findings, highlighting a trend that suggests a detrimental impact on sperm quality due to EMF exposure (Jurasović, Cvitković, Pizent, Colak, & Telisman, 2004).

Furthermore, another study emphasized a relationship between the duration of mobile phone usage and a decline in sperm count and concentration. This finding raises concerns, especially

given the increasing reliance on mobile technology in daily life among men of reproductive age. Some scientific investigations suggest that the adverse effects on sperm quality may be linked to disruptions in mitochondrial function caused by exposure to extremely low-frequency electromagnetic fields. This alteration can lead to enhanced production of reactive oxygen species (ROS), which are harmful and can result in oxidative stress, affecting sperm health. The implications of these findings are particularly worrisome for adolescents, a demographic increasingly engaging with mobile devices for extended periods—often exceeding 10 hours per day (Kiziler et al., 2007).

However, the situation becomes more complicated with the rapid advancements in technology and the diverse applications of cell phones that differ significantly in their EMF emissions. These variations add complexity to the ability to perform comparable studies examining the effects of EMF exposure on fertility (Lafuente, Márquez, Pérez-Lorenzo, Pazo, & Esquifino, 2000). Additionally, the impact of other electronic devices that individuals are exposed to from a young age further complicates the assessment. Variability in biological effects related to sex, age, and individual susceptibility creates a multifaceted exposure scenario. This scenario resembles the complexities associated with exposure to various chemical mixtures, making it particularly challenging to firmly establish causality between specific types of EMF exposure and their biological consequences on male fertility (Ranganathan, Rao, Sudan, & Balasundaram, 2018).

Table 1.2: Biochemical, Cytological, Genetic, and Epigenetic Disorders in Male Infertility Due to Occupational and Environmental Exposures

Disorder	Occupational Exposure	Environmental Exposure
Hormonal	Testosterone ↓	Testosterone ↓, Oestradiol ↓, Aromatase ↓, Gonadotropins ↑
		Aromatase ↑, Leptin ↑
Sperm	Sperm motility ↓, Apoptosis ↑, Reactive Oxygen Species (ROS) production	Sperm count ↓, Reduced motility ↓, Abnormal sperm morphology ↑, Oligozoospermia
	Sperm count ↓, Asthenozoospermia, Necrozoospermia, Oligozoospermia, Sperm immaturity ↑	Asthenozoospermia, Azoospermia, Apoptosis ↑
Mitochondrial	-	Disrupted mitochondrial function
DNA	DNA fragmentation, Genomic damage, Increased Disomy of X and Y chromosomes, Excess haploidy	XY18 disomy, Chromosome 13 disomy, Damaged DNA integrity, Sex chromosome aneuploidy, AZF region deletions, Sex chromosome disomy, DNA damage, DNA fragmentation
DNA Methylation	Sperm LINE-1 hydroxymethylation, DNA hydroxymethylation (influenced by trimethylation of H3 in spermatogenesis)	Hypermethylation of LINE1 and hypomethylation of P16 gene

2. Conclusion

This review underscores the multifaceted nature of male infertility, highlighting the interplay between environmental and occupational exposures, lifestyle factors, and hormonal regulation in spermatogenesis. The significant impact of endocrine-disrupting chemicals (EDCs), heavy metals, and adverse lifestyle choices on male reproductive health is evident, yet the complexity of these interactions warrants further investigation. Despite emerging evidence linking these factors to impaired fertility, gaps remain in our understanding, particularly concerning the mechanisms of action of EDCs and other contaminants.

Given the increasing prevalence of infertility and the potential contribution of environmental factors, there is a pressing need for comprehensive research that systematically explores the associations between occupational exposures and male fertility outcomes. Policymakers,

healthcare providers, and researchers must collaborate to develop proactive measures to minimize exposure to harmful substances in the workplace and broader environment.
Ultimately, advancing our knowledge in this field is crucial for informing targeted interventions and promoting better reproductive health among men. By addressing these critical factors, we can work towards enhancing male fertility outcomes and supporting couples facing infertility challenges.

References

1. Agarwal, A., Desai, N. R., Makker, K., Varghese, A., Mouradi, R., Sabanegh, E., & Sharma, R. (2009). Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: An in vitro pilot study. Fertility and Sterility, 92(4), 1318-1325. https://doi.org/10.1016/j.fertnstert.2008.08.022
2. Agarwal, A., Mulgund, A., Hamada, A., & Chyatte, M. R. (2015). A unique view on male infertility around the globe. Reproductive Biology and Endocrinology, 13, 37. https://doi.org/10.1186/s12958-015-0032-1
3. Agarwal, A., Saleh, R. A., & Bedaiwy, M. A. (2003). Role of reactive oxygen species in the pathophysiology of human reproduction. Fertility and Sterility, 79(5), 829-843. https://doi.org/10.1016/s0015-0282(02)04948-8
4. Aitken, R. J. (2020). The male is significantly implicated as the cause of unexplained infertility. Seminars in Reproductive Medicine, 38(1), 3-20. https://doi.org/10.1055/s-0040-1718941
5. Basak, A. M., & Sen, A. (2011). Male infertility in relation to pesticide exposure in agricultural workers. Journal of Environmental Biology, 32(4), 443-446.
6. Celik-Ozenci, C., Tasatargil, A., Tekcan, M., Sati, L., Gungor-Ordueri, N., Isbir, M., Usta, F., Akar, M., Erler, F. (2012). Effect of abamectin exposure on semen parameters indicative of reduced sperm maturity: A study on farmworkers in Antalya (Turkey). Andrologia, 44(6), 388-395. https://doi.org/10.1111/j.1439-0272.2012.01297.x
7. Chen, Z., Godfrey-Bailey, L., Schiff, I., & Hauser, R. (2004). Impact of seasonal variation, age, and smoking status on human semen parameters: The Massachusetts General Hospital experience. Journal of Experimental and Clinical Assisted Reproduction, 1, 2. https://doi.org/10.1186/1743-1050-1-2
8. Cherry, N., Labrèche, F., Collins, J., & Tulandi, T. (2001). Occupational exposure to solvents and male infertility. Occupational and Environmental Medicine, 58(10), 635-640. https://doi.org/10.1136/oem.58.10.635
9. Daoud, S., Sellami, A., Bouassida, M., Kebaili, S., Ammar Keskes, L., Rebai, T., & Chakorun Feki, N. (2017). Routine assessment of occupational exposure and its relation to semen quality in infertile men: A cross-sectional study. Turkish Journal of Medical Sciences, 47(4), 902-907. https://doi.org/10.3906/sag-1605-47
10. Diamanti-Kandarakis, E., Bourguignon, J.-P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M., Zoeller, R. T., & Gore, A. C. (2009). Endocrine-disrupting chemicals: An Endocrine Society scientific statement. Endocrine Reviews, 30(3), 293-342. https://doi.org/10.1210/er.2009-0002
11. Dominguez, A. A., & Reijo Pera, R. A. (2013). Infertility. In S. Maloy & K. Hughes (Eds.), Brenner's encyclopedia of genetics (2nd ed., pp. 71-74). Academic Press.
12. Dupont, C., Faure, C., Daoud, F., Gautier, B., Czernichow, S., & Levy, R.; ALIFERT Collaborative Group. (2019). Metabolic syndrome and smoking are independent risk factors of male idiopathic infertility. Basic and Clinical Andrology, 29, 9. https://doi.org/10.1186/s12610-019-0090-x

13. El-Helaly, M., Awadalla, N., Mansour, M., & El-Biomy, Y. (2010). Workplace exposures and male infertility: A case-control study. International Journal of Occupational Medicine and Environmental Health, 23(4), 331-338. https://doi.org/10.2478/v10001-010-0039-y
14. European Union. (2018). Commission Regulation (EU) 2018/675 of 2 May 2018 amending the Appendices to Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards CMR substances. Official Journal of the European Union. Retrieved from http://data.europa.eu/eli/reg/2018/675/oj
15. Fucic, A., Galea, K. S., Duca, R. C., El Yamani, M., Frery, N., Godderis, L., Halldorsson, T. I., Iavicoli, I., Ndaw, S., Ribeiro, E., Viegas, S., Moshammer, H. (2018). Potential health risk of endocrine disruptors in construction sector and plastics industry: A new paradigm in occupational health. International Journal of Environmental Research and Public Health, 15(6), 1229. https://doi.org/10.3390/ijerph15061229
16. Gabrielsen, J. S., & Tanrikut, C. (2016). Chronic exposures and male fertility: The impacts of environment, diet, and drug use on spermatogenesis. Andrology, 4(5), 648-661. https://doi.org/10.1111/andr.12198
17. Huang, L.-P., Lee, C.-C., Fan, J.-P., Kuo, P.-H., Shih, T.-S., & Hsu, P.-C. (2014). Urinary metabolites of di(2-ethylhexyl) phthalate relation to sperm motility, reactive oxygen species generation, and apoptosis in polyvinyl chloride workers. International Archives of Occupational and Environmental Health, 87(6), 635-646. https://doi.org/10.1007/s00420-013-0905-6
18. Huang, L.-P., Lee, C.-C., Hsu, P.-C., & Shih, T.-S. (2011). The association between semen quality in workers and the concentration of di(2-ethylhexyl) phthalate in polyvinyl chloride pellet plant air. Fertility and Sterility, 96(1), 90-94. https://doi.org/10.1016/j.fertnstert.2011.04.093
19. Ianos, O., Sari-Minodier, I., Villes, V., Lehucher-Michel, M. P., Loundou, A., Perrin, J. (2018). Meta-analysis reveals the association between male occupational exposure to solvents and impairment of semen parameters. Journal of Occupational and Environmental Medicine, 60, e533-e542. https://doi.org/10.1097/jom.0000000000001422
20. Jian, J.-M., Chen, D., Han, F.-J., Guo, Y., Zeng, L., Lu, X., & Wang, F. (2018). A short review on human exposure to and tissue distribution of per- and polyfluoroalkyl substances (PFASs). Science of The Total Environment, 636, 1058-1069. https://doi.org/10.1016/j.scitotenv.2018.04.380
21. Jungwirth, A., Giwercman, A., Tournaye, H., Diemer, T., Kopa, Z., Dohle, G., Krausz, C., & European Association of Urology Working Group on Male Infertility. (2012). European Association of Urology guidelines on male infertility: The 2012 update. European Urology, 62(2), 324-332. https://doi.org/10.1016/j.eururo.2012.04.048
22. Jurewicz, J., Dziewirska, E., Radwan, M., & Hanke, W. (2018). Air pollution from natural and anthropic sources and male fertility. Reproductive Biology and Endocrinology, 16, 109. https://doi.org/10.1186/s12958-018-0430-2
23. Katukam, V., Kulakarni, M., Syed, R., Alharbi, K., & Naik, J. (2012). Effect of benzene exposure on fertility of male workers employed in bulk drug industries. Genetic Testing and Molecular Biomarkers, 16(6), 592-597. https://doi.org/10.1089/gtmb.2011.0241
24. Li, Q., & Li, X. (2013). Occupational exposure to pesticides and the risk of male infertility. Environmental Toxicology and Pharmacology, 36(3), 879-885. https://doi.org/10.1016/j.etap.2013.09.015
25. Li, Y., Lin, H., Ma, M., Li, L., Cai, M., Zhou, N., Han, X., Bao, H., Huang, L., Zhu, C., Li, C., Yang, H., Rao, Z., Xiang, Y., Cui, Z., Ao, L., Zhou, Z., Xiong, H., & Cao, J.

(2009). Semen quality of 1346 healthy men, results from the Chongqing area of southwest China. Human Reproduction, 24(2), 459-469. https://doi.org/10.1093/humrep/den399
26. Lin, C.-Y. C. (2010). Instability, investment, disasters, and demography: Natural disasters and fertility in Italy (1820-1962) and Japan (1671-1965). Population and Environment, 31(3), 255-281. https://doi.org/10.1007/s11111-010-0103-3
27. Lotti, F., Corona, G., Vitale, P., Maseroli, E., Rossi, M., Fino, M. G., & Maggi, M. (2015). Current smoking is associated with lower seminal vesicles and ejaculate volume, despite higher testosterone levels, in male subjects of infertile couples. Human Reproduction, 30(3), 590-602. https://doi.org/10.1093/humrep/deu347
28. Malek, A. (2017). Impact of occupational exposure to heavy metals on fertility: A review. Environmental Toxicology and Pharmacology, 54, 134-142. https://doi.org/10.1016/j.etap.2017.06.009
29. Miao, M., Zhou, X., Li, Y., Zhang, O., Zhou, Z., Li, T., Yuan, W., Li, R., & Li, D.-K. (2014). LINE-1 hypomethylation in spermatozoa is associated with Bisphenol A exposure. Andrology, 2(1), 138-144. https://doi.org/10.1111/j.2047-2927.2013.00166.x
30. Ou, Z., Wen, Q., Deng, Y., Yu, Y., Chen, Z., & Sun, L. (2020). Cigarette smoking is associated with high level of ferroptosis in seminal plasma and affects semen quality. Reproductive Biology and Endocrinology, 18, 55. https://doi.org/10.1186/s12958-020-00615-x
31. Pan, G., Hanaoka, T., Yoshimura, M., Zhang, S., Wang, P., Tsukino, H., Inoue, K., Nakazawa, H., Tsugane, S., & Takahashi, K. (2006). Decreased serum free testosterone in workers exposed to high levels of di-n-butyl phthalate (DBP) and di-2-ethylhexyl phthalate (DEHP): A cross-sectional study in China. Environmental Health Perspectives, 114(11), 1643-1648. https://doi.org/10.1289/ehp.9016
32. Petersen, K. U., Hansen, J., Ebbehoej, N. E., & Bonde, J. P. (2018). Infertility in a cohort of male Danish firefighters: A register-based study. American Journal of Epidemiology, 188(2), 339-346. https://doi.org/10.1093/aje/kwy235
33. Rehman, I., Ahmad, G., & Alshahrani, S. (2017). Lifestyle, environment, and male reproductive health: A lesson to learn. In S. Sikka & W. Hellstrom (Eds.), Bioenvironmental issues affecting men's reproductive and sexual health (pp. 157-171). Academic Press.
34. Rehman, R., Zahid, N., Amjad, S., Baig, M., & Gazzaz, Z. J. (2019). Relationship between smoking habit and sperm parameters among patients attending an infertility clinic. Frontiers in Physiology, 10, 1356. https://doi.org/10.3389/fphys.2019.01356
35. Sakurai, K., Mikamoto, K., Shirai, M., Iguchi, T., Ito, K., Takasaki, W., & Mori, K. (2015). MicroRNA profiling in ethylene glycol monomethyl ether-induced monkey testicular toxicity model. Journal of Toxicological Sciences, 40(4), 375-382. https://doi.org/10.2131/jts.40.375
36. Santi, D., Vezzani, S., Granata, A. R., Roli, L., De Santis, M. C., Ongaro, C., Donati, F., Baraldi, E., Trenti, T., Setti, M., & Simoni, M. (2016). Sperm quality and environment: A retrospective, cohort study in a Northern province of Italy. Environmental Research, 150, 144-153. https://doi.org/10.1016/j.envres.2016.05.053
37. Satoh, H., & Tominari, T. (2012). Endocrine-disrupting chemicals and male infertility: Mechanisms and effects. Environmental Toxicology, 27(3), 188-197. https://doi.org/10.1002/tox.20656
38. Sharma, R., Harlev, A., Agarwal, A., & Esteves, S. C. (2016). Cigarette smoking and semen quality: A new meta-analysis examining the effect of the 2010 World Health Organization laboratory methods for the examination of human semen. European Urology, 70(4), 635-645. https://doi.org/10.1016/j.eururo.2016.04.010
39. Shrem, G., Brudner, Y., Atzmon, Y., Michaeli, M., Ellenbogen, A., & Shalom-Paz, E. (2019). The influence of obesity, smoking, and serum follicular stimulating hormone in

azoospermic patients on testicular sperm extraction-intra cytoplasmic sperm injection outcomes: A retrospective cohort study. Medicine (Baltimore), 98(4), e14048. https://doi.org/10.1097/MD.0000000000014048

40. Steves, A. N., Turry, A., Gill, B., Clarkson-Townsend, D., Bradner, J. M., Bachli, I., Caudle, W. M., Miller, G. W., Chan, A. W. S., & Easley IV, C. A. (2018). Per- and polyfluoroalkyl substances impact human spermatogenesis in a stem-cell-derived model. Systems Biology in Reproductive Medicine, 64(3), 225-239. https://doi.org/10.1080/19396368.2018.1481465
41. Tian, Y., Zhou, X., Miao, M., Li, D.-K., Wang, Z., Li, R., Liang, H., & Yuan, W. (2018). Association of bisphenol A exposure with LINE-1 hydroxymethylation in human semen. International Journal of Environmental Research and Public Health, 15(8), 1770. https://doi.org/10.3390/ijerph15081770
42. Vandenberg, L. N., Colborn, T., Hayes, T., Heindel, J. J., Jacobs, D. R., Lee, D. H., Shioda, T., & Soto, A. M. (2013). Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocrine Reviews, 34(3), 243-274. https://doi.org/10.1210/er.2012-1053
43. Wang, H.-X., Li, H.-C., Lv, M.-Q., Zhou, D.-X., Bai, L.-Z., Du, L.-Z., Xue, X., Lin, P., & Qiu, S.-D. (2015). Associations between occupational exposure to formaldehyde and semen quality, a primary study. Scientific Reports, 5, 15874. https://doi.org/10.1038/srep15874
44. Wang, Z., Li, J., Cao, D., Liu, X., & Zhu, D. (2016). Generation and application of male mice with specific expression of green fluorescent protein in germ cells. Molecular Imaging and Biology, 18(5), 659-666. https://doi.org/10.1007/s11307-016-0947-8
45. Weinbauer, G. F., & Nieschlag, E. (1995). Gonadotropin control of testicular germ cell development. Advances in Experimental Medicine and Biology, 377, 55-65. https://doi.org/10.1007/978-1-4899-0952-7_4
46. Xiao, G., Pan, C., Cai, Y., Lin, H., & Fu, Z. (2001). Effect of benzene, toluene, xylene on the semen quality and the function of accessory gonads of exposed workers. Industrial Health, 39(2), 206-210. https://doi.org/10.2486/indhealth.39.206
47. Xing, C., Marchetti, F., Li, G., Weldon, R. H., Kurtovich, E., Young, S., Schmid, T. E., Zhang, L., Rappaport, S., Waidyanatha, S., Wyrobek, A. J., & Eskenazi, B. (2010). Benzene exposure near the U.S. permissible limit is associated with sperm aneuploidy. Environmental Health Perspectives, 118(6), 833-839. https://doi.org/10.1289/ehp.0901531
48. Zegers-Hochschild, F., Adamson, G. D., de Mouzon, J., Ishihara, O., Mansour, R., Nygren, K., Sullivan, E., & Vanderpoel, S. (2009). International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. Fertility and Sterility, 92(5), 1520-1524. https://doi.org/10.1016/j.fertnstert.2009.09.009
49. Zhang, W., Li, M., Sun, F., Xu, X., Zhang, Z., Liu, J., Sun, X., Zhang, A., Shen, Y., Xu, J., Miao, M., Wu, B., Yuan, Y., Huang, X., Shi, H., & Du, J. (2019). Association of sperm methylation at LINE-1, four candidate genes, and nicotine/alcohol exposure with the risk of infertility. Frontiers in Genetics, 10, 1001. https://doi.org/10.3389/fgene.2019.01001
50. Zheng, H., Zhou, X., Li, D.-K., Yang, F., Pan, H., Li, T., Miao, M., Li, R., & Yuan, W. (2017). Genome-wide alteration in DNA hydroxymethylation in the sperm from bisphenol A-exposed men. PLoS One, 12(6), e0178535. https://doi.org/10.1371/journal.pone.0178535