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Reviews

The Role of Mycotoxins in Reproductive health: Mechanisms, Evidence, and Clinical Implications

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Importance

Infertility is a global health issue with multiple causes, including environmental factors. Mycotoxins—secondary metabolites produced by fungi—are increasingly recognized as potential contributors to reproductive dysfunction.

Objective

This review explores the impact of mycotoxins on reproductive health, examining their role in fertility impairment through mechanisms such as hormone disruption, gametogenesis impairment, and uterine toxicity.

Evidence Review

Mycotoxins are widespread in food and the environment, posing health risks that extend beyond known carcinogenic and immunotoxin effects. Exposure to mycotoxins such as ochratoxin A (OTA) and zearalenone (ZEA) has been linked to epigenetic alterations, endocrine disruption, and direct cellular damage in reproductive tissues. These findings are supported by epidemiological data, animal models, and experimental research, emphasizing regional variations in exposure due to differences in agricultural practices and food contamination.

Findings

Mycotoxin exposure is associated with adverse reproductive outcomes, including reduced sperm quality, menstrual irregularities, and increased miscarriage risk. The biological mechanisms involve oxidative stress, hormone dysregulation, and direct toxicity to gametes and reproductive organs.

Conclusion and Relevance

Reducing mycotoxin exposure through dietary precautions, improved food safety regulations, and environmental controls may help protect reproductive health. Further research is needed to clarify exposure thresholds and develop targeted interventions.

INTRODUCTION

INFERTILITY AS A GLOBAL HEALTH CONCERN

Infertility is a growing global health issue affecting millions of individuals and couples. Over the past 50 years, fertility rates have declined significantly, with sperm counts decreasing by more than 59% in North America, Europe, Australia, and New Zealand.[1] Between 1990 and 2011, the global miscarriage rate increased by 2%,[2] and an estimated 48 million couples and 186 million individuals worldwide struggle with infertility.[3] Sub-Saharan Africa and South Asia bear a disproportionate burden, with infertility prevalence rates remaining high.[3,4]

While genetic, anatomical, and behavioral factors contribute to infertility, environmental exposures have emerged as critical but underexplored determinants of reproductive health.[5] Factors such as endocrine-disrupting

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Table 1. Major Mycotoxin-Producing Genera, Sources and Exposure

Mycotoxin	Producing Fungi	Common Sources	Health Risks
Ochratoxin A (OTA)	Aspergillus, Penicillium	Cereals, coffee, dried fruits	Endocrine disruption, nephrotoxicity
Zearalenone (ZEA)	Fusarium	Grains, maize	Estrogenic effects, reproductive toxicity
Aflatoxins	Aspergillus	Peanuts, maize, dairy	Carcinogenicity, immune suppression
Fumonisins	Fusarium	Corn, maize	Neural tube defects, hepatotoxicity

chemicals (EDCs), microplastics, and pollutants have been linked to declining fertility.[6] Among these environmental toxins, mycotoxins—secondary metabolites produced by fungi—are of increasing concern, though their impact on human fertility has received limited attention.

MYCOTOXINS AND REPRODUCTIVE HEALTH

Mycotoxins, harmful compounds produced by fungi such as Aspergillus, Fusarium, and Penicillium, commonly contaminate food and agricultural products. These toxins are well known for their carcinogenic, immunotoxic, and hepatotoxic effects,[7] but emerging evidence suggests they may also impair reproductive health. Studies indicate that exposure to mycotoxins such as ochratoxin A (OTA) and zearalenone (ZEA) can disrupt hormone regulation, impair gametogenesis, and cause direct cellular toxicity to reproductive tissues.[8] Understanding their role in infertility is essential, given the widespread presence of mycotoxins in food supplies, particularly in regions with warm climates and high agricultural contamination.

This review examines mycotoxin exposure's mechanisms, evidence, and clinical implications on reproductive health. It synthesizes findings from human epidemiological studies and animal models to assess the extent of mycotoxins' impact on fertility and highlights potential strategies for mitigating their harmful effects.

MYCOTOXINS: DEFINITION, SOURCES, AND SIGNIFICANCE

MAJOR MYCOTOXIN-PRODUCING GENERA & TYPES

Mycotoxins are toxic secondary metabolites produced by fungi, primarily Fusarium, Aspergillus, and Penicillium, with additional contributions from Alternaria, Claviceps, and Stachybotrys.[9-11] These naturally occurring toxins contaminate food and agricultural products, posing serious health risks to humans and animals.[9,10,12,13] **Table 1** shows the major mycotoxins-producing genera with their sources and contamination of various foods.

KEY MYCOTOXINS & THEIR SOURCES

1. FUSARIUM *MYCOTOXINS*

Fumonisins (FBs), Zearalenone (ZEA), and Trichothecenes (DON, T-2, HT-2) are the three common mycotoxins belonging to this group. These are commonly found in grains, maize, and animal feed, often contaminating crops before and after harvest,[14,15] particularly in warm climates (e.g., Africa). ZEA, is a non-steroidal oestrogenic mycotoxin that has biological effects even at low doses and disrupts endocrine function, impacting fertility even at low doses.[16-18] Certain climates are more prone to contamination since Fusarium mycotoxin synthesis requires a temperature of about 25°C.[19-21] For the above reasons, African nations tend to have greater levels of mycotoxin contamination.[22, 23]

2. ASPERGILLUS *MYCOTOXINS*

Aflatoxins (Afs) are highly toxic and carcinogenic mycotoxins produced by *Aspergillus* species, contaminating various crops such as corn, wheat, soybeans, peanuts, and dried fruits during storage and transport under specific temperature conditions.[24,25] These toxins also affect livestock feed, leading to contamination of food products like nuts, vegetables, fish, poultry meat, coffee, and tea[24,26]). AFB1, AFB2, AFG1, and AFG2 are the most toxic, causing aflatoxicosis with documented reproductive toxicity.[27,28]

3. PENICILLIUM *MYCOTOXINS*

Penicillium species contribute to contamination through Ochratoxins (OTA), Patulin (PAT), Mycophenolic Acid (MPA).[29,30] These are commonly found in cereals, coffee, and dried fruits, colonizing commodities and foods during drying and storage particularly in developed countries.[14,15] OTA exposure has been linked to significant male fertility issues, specifically impacting sperm viability and morphology.[30,31]

PREVALENCE AND GLOBAL EXPOSURE

Mycotoxin contamination is a global issue, with serious health and economic consequences and higher prevalence in humid climates that favor fungal growth.[22] The Food and Agriculture Organisation (FAO) estimates that mycotoxins contaminate about 25% of agricultural goods worldwide each year, resulting in serious health issues and financial losses[27,32,33]

Mycotoxin exposure is widespread in developing nations, with high contamination levels reported in Africa and Asia.[23,34] Regional factors like temperature, humidity, and poor hygiene influence mycotoxin prevalence.[35] In African countries, an estimated 4 million people are exposed to high mycotoxin levels, affecting immune function and leading to teratogenic, mutagenic, and carcinogenic effects.[22,

Table 2. Prevalence of Mycotoxin Contamination in Different Regions

Region/ Country	Mycotoxin	Prevalence of Contamination	Products Affected	Health Impact	Reference
Tunisia	Beauvericin, Nivalenol	96% of staple foods	Cereals, grains, legumes	Immune system suppression, carcinogenic risk	Serrano et al.[34]
Morocco	Beauvericin, Nivalenol	50% of staple foods	Wheat, barley, rice	Carcinogenic effects, compromised fertility	Serrano et al.[37]
Ghana	Aflatoxin B1	High in maize, groundnuts	Maize, peanuts, other grains	Miscarriage, low birth weight, developmental defects	Shuaib et al.[40]
Lebanon	Ochratoxin A (OTA) and deoxynivalenol (DON)	High levels in food products	Dried fruits, coffee, cereals	Increased cancer risk, kidney toxicity, infertility	Raad et al.[38]
Sub-Saharan Africa	Various mycotoxins	High levels across countries	Maize, sorghum, animal feed	Immune suppression, increased infertility rates	Darwish et al.[22]

Table 2a. Summary of the key aspects of mycotoxin contamination, exposure, and health effects

Aspect	Key Findings	References
Global Contamination	Mycotoxins contaminate approximately 25% rate of the global food supply.	Song et al.[41]; Alhelaisi et al.[42]; Park et al.[43]
Prevalence in Tested Samples	Recent studies suggest 60-80% of tested food samples contain detectable mycotoxins.	Song et al.[41]; Eskola et al.[44]
Factors Influencing Contamination	Improved detection methods and climate change contribute to increased contamination.	Magan et al.[45]
Toxic Effects	Mycotoxins can cause carcinogenic, mutagenic, teratogenic, estrogenic, immunotoxic, nephrotoxic, and neurotoxic effects.	Unicsovics et al.[46]
Major Health Concerns	Long-term low-level exposure to carcinogenic mycotoxins like aflatoxins, ochratoxin A, zearalenone, and fumonisins poses a major health risk.	Khoury et al.[47]; Unicsovics et al.[46]
Reproductive Health Impact	Mycotoxins disrupt hormonal function due to their structural similarity with reproductive hormones, leading to fertility issues in both males and females.	Sayed et al.[48]

[23,36] Studies have reported widespread mycotoxin contamination in staple foods across Tunisia (96%), Morocco (50%), and Lebanon, with exposure levels exceeding toxicological reference values.[37,38] In wealthy nations, contaminated buildings are more frequently the source of OTA exposure than dietary elements.[39] The presence of mycotoxins in processed feeds across Asia, America, and Europe highlights and emphasizes the global scale of the issue (**Figure 1**). **Table 2** summarizes global contamination data and highlights regions with higher exposure risks & table 2a outlines the key aspects of mycotoxin contamination, exposure, and health effects.

HEALTH RISKS & REPRODUCTIVE EFFECTS

OTA exposure adversely affects both male and female reproduction. In males, it significantly reduces sperm viability and morphology, causing DNA damage and leading to defects such as larger heads, coiled tails, and decapitation, impairs motility and fertilization.[31] Other Penicillium-derived toxins, such as patulin (PAT) and mycophenolic acid (MPA), also cause systemic and reproductive harm.[49,50]

ZEA mimics estrogen, leading to hormonal imbalances, menstrual irregularities, and fertility issues. Chronic exposure to mycotoxins has been associated with miscarriage, fetal growth restriction, and developmental defects. Even in low concentrations, Fusarium toxins in animal feed have biological effects. OTAs cause cellular damage through apoptosis, protein synthesis inhibition, and DNA damage, and their long half-life leads to inconsistent excretion patterns.

BIOACCUMULATION AND METABOLISM

After ingestion, mycotoxins are absorbed through the gastrointestinal tract and undergo metabolic biotransformation in the liver.[51] The liver processes mycotoxins through Phase I metabolism, where cytochrome P450 enzymes convert them into reactive intermediates.[52,53] In Phase II metabolism, these intermediates by products are transported by the bloodstream, to several organs, including the reproductive system, that may have systemic effects. Once metabolized, they undergo conjugation with molecules such as glucuronic acid, making them more water-soluble for excretion primarily through the kidneys or via bile into the

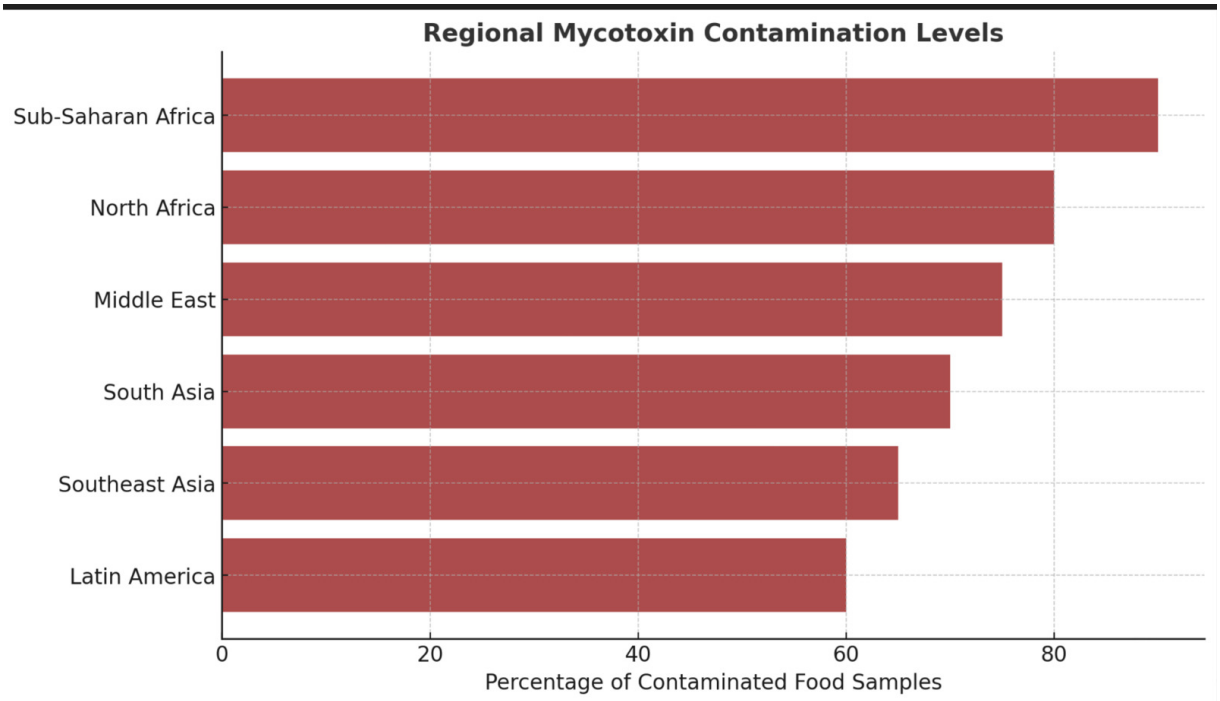

Figure 1. Regional Mycotoxin Contamination Levels

This bar chart illustrates the estimated mycotoxin contamination levels across different global regions. The data are derived from studies reporting staple food contamination and associated health risks. Sub-Saharan Africa exhibits the highest contamination levels (90%), predominantly due to aflatoxin and fumonisin presence in maize and groundnuts. North Africa follows with 80%, where wheat, barley, and rice are frequently contaminated. The Middle East (75%) faces high ochratoxin A and deoxynivalenol exposure, while South Asia (70%) has significant risks linked to maternal health. Southeast Asia (65%) and Latin America (60%) report contamination in livestock feed, maize, and coffee, with implications for reproductive toxicity and cancer risks.

Table 3. Summary of Mycotoxin Metabolism in Humans

Mycotoxin	Absorption	Metabolism (Phase I & II)	Excretion	Impact on Reproductive Organs	Study
Zearalenone (ZEA)	Absorbed through the GI tract	Metabolized in the liver, converted to conjugates	Excreted through urine and feces	Mimics estrogen, affects ovarian and testicular function	Zheng et al.[54]
Ochratoxin A (OTA)	Absorbed via gastrointestinal system	Phase I metabolism by cytochrome P450 enzymes	Excreted in urine, long half-life	Reduces sperm viability, alters ovarian steroidogenesis	Chakraborty et al.[31]
Aflatoxin B1	Absorbed through GI tract	Phase I oxidation, Phase II conjugation	Excreted in bile and urine	Impairs testicular function, reduces sperm motility	Ibeh et al.[55]
Deoxynivalenol (DON)	Absorbed via gastrointestinal tract	Liver metabolism to less toxic metabolites	Excreted via urine	Alters ovarian function, disrupts steroid hormone production	Guerrero-Netro et al.[56]

intestines, where they may be further broken down by gut microbiota and eliminated in faeces.[52,53]

Some mycotoxins bioaccumulate in reproductive tissues, where they disrupt hormone balance, impair gametogenesis, and cause cellular damage. For example, zearalenone (ZEA) mimics estrogen, binding to estrogen receptors in the ovaries and testes, leading to hormonal imbalances and infertility.[8] Table 3 summarizes the absorption, metabolism, and excretion processes of mycotoxins and their impact on reproductive organs.

METHODOLOGY

A comprehensive literature search was conducted in November 2024 using four major electronic databases: PubMed, Google Scholar, EMBASE, and Web of Science. The aim was to identify studies on mycotoxins and their impact on human reproductive health. Only English-language publications were considered, covering research published between 1960 and 2024.

The search strategy included multiple keywords, such as:

- "Mycotoxins AND human health,"

- "Aflatoxins AND human reproduction,"
- "Zearalenone AND endocrine disruption,"
- "Mycotoxins AND infertility,"
- "Mycotoxins AND detoxification."

Relevant studies were selected based on study quality, methodological rigor, and relevance to reproductive health. Both human and animal studies were considered. Data was extracted to analyse mycotoxin exposure, reproductive toxicity, and potential mechanisms of action. Risk of bias and study limitations were also assessed. A total of 150 studies were identified and included in this review.

RESULTS

A total of 150 studies were reviewed to evaluate the impact of mycotoxins on reproductive health. Findings indicate that exposure to mycotoxins through contaminated food is associated with hormonal disruption, decreased fertility, and adverse pregnancy outcomes.

1. MYCOTOXIN EXPOSURE AND INFERTILITY

In a human study, OTA was detected in 70% of infertile men, with concentrations 10 times higher than in fertile men.[57] Zearalenone (ZEA), an estrogenic mycotoxin, was linked to early puberty and menstrual irregularities in studies of adolescent girls.[58] Aflatoxins were found in 60% of semen samples from infertile men, correlating with low sperm count and motility.[55]

2. MYCOTOXINS AND HORMONAL DISRUPTION

ZEA mimics estrogen and alters testosterone levels, leading to decreased sperm production in male rodents.[54] Exposure to OTA reduced sperm viability and caused morphological abnormalities, including coiled tails and enlarged heads.[31] In vitro studies suggest that DON (deoxynivalenol) disrupts ovarian steroidogenesis, impairing progesterone and estradiol synthesis.[56]

3. PREGNANCY AND FETAL DEVELOPMENT RISKS

Women with high aflatoxin exposure had higher rates of miscarriage and preterm birth.[40] A cohort study in Ghana found a strong correlation between maternal aflatoxin exposure and low birth weight.[59] Fumonisins in maize were linked to neural tube defects in new-borns.[60]

These findings underscore the need for stricter food safety regulations and public awareness campaigns to mitigate mycotoxin exposure and reproductive health risks. Table 4 summarizes key studies, their findings, and the specific mycotoxins and reproductive health impacts observed.

DISCUSSION

IMPACT ON HUMAN HEALTH AND FERTILITY

Although direct human data on mycotoxin exposure and infertility remain limited, existing evidence strongly suggests that certain mycotoxins, particularly ochratoxin A (OTA) and zearalenone (ZEA), exert significant effects on reproductive health. OTA is known to inhibit protein synthesis, induce apoptosis through mitochondrial membrane potential loss, and cause DNA damage via adduct formation, leading to decreased fertility in both males and females.[61] Due to its long half-life and inconsistent excretion, OTA can have prolonged biological effects. In males, OTA exposure leads to sperm abnormalities, including decapitation, coiled tails, and enlarged heads, which collectively impair sperm motility and reduce fertilization rates.[31]

ZEA, a nonsteroidal estrogenic compound, mimics endogenous hormones, disrupting endocrine function and contributing to reproductive disorders. This mycotoxin binds to estrogen receptors, altering normal hormonal signaling and leading to fertility issues in both sexes.

HORMONAL DISRUPTION BY MYCOTOXINS

IMPACT ON FEMALE REPRODUCTION

ZEA and aflatoxins (AF) are classified as endocrine-disrupting chemicals (EDCs), which interfere with hormone biosynthesis, transport, metabolism, receptor interactions, and feedback regulation.[62] These disruptions can occur from fetal development through adulthood, causing lifelong reproductive consequences.[63,64]

ZEA disrupts the hypothalamic-pituitary-gonadal (HPG) axis by binding to estrogen receptors, mimicking endogenous estrogens, and altering hormonal balance.[65] This disruption manifests as ovulation disorders, menstrual irregularities, polycystic ovarian syndrome (PCOS), premature ovarian failure (POF), and endometriosis.[66-68]

EDCs impair hormones like insulin and insulin-like growth factors, essential for growth, while enhancing glucocorticoid activity, further disrupting growth processes.[68] Other hormones, such as growth hormones and thyroid hormones, are also affected, leading to growth abnormalities or delayed puberty.[69] Epidemiological studies have linked ZEA exposure to early puberty and estrogen imbalances in girls. Studies from Turkey, Hungary, and Italy report significantly elevated serum ZEA levels (18.9–103 µg/L) in girls experiencing precocious puberty.[58,70,71] Similar findings in Lebanese girls indicate early breast development and shortened growth periods.[72,73] In addition to impeding ovarian folliculogenesis, it has been implicated in conditions such as endometriosis, polycystic ovarian syndrome (PCOS), and premature ovarian failure (POF) affecting conception and pregnancy maintenance.[66]

ZEA adversely disrupts the synthesis and release of sex hormones such as testosterone, progesterone, and estradiol and has been shown to have a detrimental impact on reproduction, leading to infertility in both sexes.[54]

IMPACT ON MALE REPRODUCTION

Mycotoxins also detrimentally affect male reproduction. Exposure to mycotoxins, particularly zearalenone (ZEA), has been linked to reproductive issues. ZEA exposure can cause precocious puberty in boys under nine.[69,74] ZEA and aflatoxins impair testosterone production, sperm motility,

Table 4. Mycotoxin Exposure and Reproductive Health: Study Results Summary

Study	Mycotoxin	Population	Exposure Outcome	Reproductive Health Impact	Reference
Uriah et al.[57]	Aflatoxin B1	Infertile men	High levels of AFB1 in semen	Lower sperm count and motility	Ibeh et al.[55]
Massart et al.[58]	Zearalenone (ZEA)	Adolescent girls	Early puberty and menstrual irregularities	Disrupted hormone balance, early puberty	Massart et al.[58]
Chakraborty et al.[31]	Ochratoxin A (OTA)	Male rodents	OTA exposure in drinking water	Reduced sperm viability, coiled tails, enlarged heads	Chakraborty et al.[31]
Zheng et al.[54]	Zearalenone (ZEA)	Male rodents	ZEA exposure in diet	Lower testosterone, decreased sperm production	Zheng et al.[54]
Shuaib et al.[40]	Aflatoxins	Pregnant women (Ghana)	Aflatoxin exposure in food	Higher miscarriage and preterm birth rates	Shuaib et al.[40]
Turner et al.[59]	Aflatoxins	Pregnant women (Ghana)	Aflatoxin exposure in food	Low birth weight, developmental issues in offspring	Turner et al.[59]

Table 5. Role of Specific multiple mycotoxins (ZEA, OTA, AFB1, DON) and their specific impacts on male vs. female fertility.

Mycotoxin	Male Reproductive Effects	Female Reproductive Effects
Zearalenone (ZEA)	Decreased testosterone, impaired spermatogenesis, increased oxidative stress	Estrogenic activity → menstrual disorders, PCOS, premature ovarian failure (POF)
Ochratoxin A (OTA)	Sperm abnormalities (coiled tails, enlarged heads), mitochondrial dysfunction	Impaired ovarian steroidogenesis, disrupted menstrual cycle
Aflatoxin B1 (AFB1)	Decreased sperm count & motility, Leydig cell dysfunction	Increased miscarriage risk, hormonal imbalance
Deoxynivalenol (DON)	Reduced sperm viability, testicular toxicity	Ovarian toxicity, impaired follicle development

and spermatogenesis through oxidative stress and hormonal dysregulation.[75] ZEA disrupts the release of luteinizing hormone (LH), lowering testosterone synthesis by Leydig cells and negatively affecting sperm production.[76]

Aflatoxin B1 (AFB1) exposure has been linked to male infertility. It has been detected in the blood and semen of infertile males exposed to contaminated diets, causing atrophy of spermatogenic tubules, germ cell layer destruction, and termination of spermatogenesis.[57,77,78] Nigerian infertile men exhibited significantly higher semen AFB1 concentrations (60–148 ng/mL) compared to fertile men (0–5 ng/mL), correlating with reduced sperm count and motility.[79] Uriah et al.[57] found similar results, with AFB1 levels in infertile men exceeding WHO safety limits. Table 5 outlines the specific mycotoxins and their hormonal effects on reproductive organs (e.g., ovaries, testes).

GAMETOGENESIS IMPAIRMENT

Mycotoxins such as aflatoxins and ochratoxins generate reactive oxygen species (ROS), leading to oxidative stress, lipid peroxidation, mitochondrial dysfunction, and DNA damage in gametes.[80,81] These toxic effects disrupt spermatogenesis in males and folliculogenesis in females.[56]

In animal models, mycotoxin exposure has been linked to reduced sperm motility and compromised oocyte quality.[82-84] Deoxynivalenol (DON) exposure has been shown to trigger autophagy-mediated apoptosis in granulosa cells, reducing progesterone and estradiol production and impairing oocyte maturation.[85] ZEA decreases key steroidogenesis enzymes (aromatase, P450scc, 3βHSD), increasing follicular atresia and reducing fertility.[86] Table 6 concisely summarizes key reproductive outcomes associated with specific mycotoxins.

UTERINE AND PLACENTAL TOXICITY

Pregnant women and their unborn children are particularly vulnerable to mycotoxin exposure.[87-89] Studies suggest that mycotoxins cross the placental barrier, causing fetal toxicity, growth restriction, and birth defects.[87]

Prenatal exposure to aflatoxins is associated with malnutrition and adverse birth outcomes, especially during the critical first 1,000 days of life.[89,90] These include fetal growth restriction, neonatal jaundice, preterm birth, and increased miscarriage risk.[40,59,91-93] In maize-consuming

Table 6. Statistical Summary of Reproductive Effects of Mycotoxin Exposure

Mycotoxin	Reproductive Outcome	Effect on Male Reproductive Health	Effect on Female Reproductive Health	Study
Zearalenone (ZEA)	Disrupts hormonal balance	Decreased sperm motility, low testosterone	Menstrual irregularities, ovarian dysfunction	Zheng et al.[54]
Ochratoxin A (OTA)	Reduced sperm count and motility	Increased sperm abnormalities (coiled tails, enlarged heads)	Impaired oocyte quality and fertilization	Chakraborty et al.[31]
Aflatoxin B1	Low sperm count, reduced motility	Testicular atrophy, germ cell loss	Reduced fertility, hormonal imbalance	Ibeh et al.[79]
Deoxynivalenol (DON)	Disruption in spermatogenesis	Low sperm production	Impaired oocyte maturation, autophagy in granulosa cells	Guerrero-Netro et al.[56]
Fumonisins	Reduced fertility	Reduced testosterone production	Neural tube defects in offspring	Missmer et al.[60]

populations, fumonisin exposure has been linked to neural tube and urogenital defects in the fetuses and maternal hypertension, and preeclampsia.[60,94,95] Additionally, maternal blood samples from Bangladesh revealed high mycotoxin levels, further emphasizing the risk of transplacental toxicity.[96-98]

MECHANISMS OF REPRODUCTIVE TOXICITY

Mycotoxin-induced reproductive toxicity operates through multiple pathways:

MITOCHONDRIAL DYSFUNCTION

Mycotoxins interfere with mitochondrial activity, reducing ATP production and triggering apoptosis.[99,100] This has been linked to pro-apoptotic genes (Bak and Bax) and anti-apoptotic genes (Bcl-XL, Bcl-2) regulating mitochondria-dependent apoptosis.[99] Excessive levels of aflatoxin B1 (AFB1) produce energy blockages by interfering with mitochondrial biogenesis, hence interfering with Leydig cell function that exacerbates sperm failure and infertility.[101, 102] AFB1 compromises mitochondrial structure and function by reducing membrane potential, causing calcium build-up, and inducing oxidative stress, indirectly impairing mitochondrial activity.[103] Reactive oxygen species (ROS) production triggered by mycotoxins increases mitochondrial membrane permeability, releasing pro-apoptotic proteins and activating the apoptotic cascade, which results in germ-cell apoptosis and DNA fragmentation.[100,104]

HORMONAL DISRUPTION

Mycotoxins mimic or inhibit sex hormone function, impairing endocrine regulation and fertility.[98] Aflatoxin disrupts and inhibits steroidogenic enzymes that impact cholesterol utilization and testosterone production.[105,106] This hormonal dysregulation impairs testicular function and spermatogenesis, impacting the quality of sperm production. Table 7 shows a summary of the mechanism of different mycotoxins affecting hormone disruption.

OXIDATIVE STRESS

Reproductive health is disrupted, and germ cell loss is worsened by factors like oxidative stress-producing ROS. Mycotoxin causes increased ROS production, and damages sperm and oocytes, leading to compromised fertility.[107,108]

PLACENTAL TOXICITY

Mycotoxins disrupt placental function, impairing fetal growth and increasing pregnancy complications.[109] These negative consequences have been linked to mechanisms such as intestinal inflammation, decreased placental function, dysregulated pro-inflammatory cytokines, and organ damage.[109] For instance, by increasing liver toxicity and fetal hemoglobin breakdown, aflatoxins may worsen newborn jaundice.[92,93,108,110] Known mechanisms of mycotoxin toxicity include immune suppression, disruption of ribosomal protein synthesis, hormone dysregulation, and erythrocyte apoptosis, leading to fetal toxicity, inflammation, and hypoxia.[111] However, limited knowledge exists regarding the effects of lesser-known mycotoxins and their combinations on adverse pregnancy outcomes.

CONCLUSION

This review highlights the strong association between mycotoxin exposure and reproductive toxicity. Evidence from epidemiological and animal studies suggests that mycotoxins significantly disrupt hormonal balance, gametogenesis, and fetal development. Given the severity of these risks, proactive measures are needed:

1. Strengthening Food Safety Regulations: Ensuring proper storage and contamination control in food production.
2. Improving Public Awareness: Educating consumers about the risks of contaminated food and dietary choices.

Table 7. Hormonal Disruption by Mycotoxins: A Summary of Mechanisms

Mycotoxin	Hormonal Effect	Affected Organ(s)	Mechanism of Action	Study
Zearalenone (ZEA)	Estrogenic effect (mimics estrogen)	Ovaries, testes	Binds to estrogen receptors, alters hormonal balance	Zheng et al.[54]
Ochratoxin A (OTA)	Reduces testosterone, disrupts sperm function	Testes, ovaries	Inhibits protein synthesis, damages sperm morphology	Chakraborty et al.[31]
Aflatoxin B1	Disrupts testosterone production, lowers sperm motility	Testes	Interferes with steroidogenic enzymes, damages seminiferous tubules	Uriah et al.[57]
Deoxynivalenol (DON)	Disrupts ovarian steroidogenesis	Ovaries	Reduces progesterone and estradiol synthesis	Guerrero-Netro et al.[56]

3. Advancing Research: Large-scale human biomonitoring studies are required to assess long-term exposure risks and develop targeted interventions.

Mycotoxin-induced reproductive toxicity is a significant but often overlooked public health issue. Addressing this challenge requires interdisciplinary efforts, combining toxicology, epidemiology, and food safety initiatives to safeguard reproductive health globally.

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