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# Effects of environmental adulterants on mammalian testis

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**Abstract**
In recent years, there has been growing concern regarding the adverse effects of various environmental contaminants on human health. High level of pesticides residue existing in the environment exerts adverse effects on reproductive health of animals leading to direct toxicity to the reproductive organs or by interference with the hormonal functions. Many of these chemicals have been shown to interfere with normal hormonal signaling and biological functions, leading to reproductive disorders or infertility, which has been a matter of concern within the recent decades. The present paper reviews adverse effects of these toxicants on mammalian testes, with emphasis on alteration of steroidgenesis, spermatogenesis, and histopathological effects. From the publications reviewed, it appears that environmental toxicants, especially heavy metals, pesticides and organic chemicals of synthetic and microbiological origins, disrupt hormone production and action in the mammalian testes. Endocrine disruption leads to disorders of testicular function. The toxicants also induce impairment of testicular cells function, testicular histology and sperm cells function directly. The release of the toxicants in the environment is still ongoing, if appropriate measures are not taken, their impact on the male reproductive function and especially on testicular function will be more serious.

**Keywords:** Hormone, Mammal, Spermatogenesis, Testis, Toxicity

## Introduction
In recent years, there has been growing concern regarding the adverse effects of various environmental contaminants on human health. With the advent of industrialization, economic development and urbanization drastic changes have occurred in the lifestyle and surroundings of humans that have resulted in the extensive production and use of beneficial substances [1]. As a result, many potentially hazardous chemicals have been released into the environment at an alarming rate and their exposure to both humans and wildlife has become inevitable. These chemicals that have been released into the environment are a leading causative factor in the high incidence of various pathological conditions, including cancers [2]. The development of modern technology and the rapid industrialization are among the foremost factors for environmental pollution. The environmental pollutants are spread through different channels, many of which finally enter into the food chain of livestock and man [3].
Pesticides, heavy metals and other agrochemicals are some of the major causes of environmental toxicity in farm animals [4]. Pesticide include all xenobiotics whose specific purpose is to kill another form of life, including insects (insecticides), small rodents (rodenticides), or even vegetation (herbicides) [5]. Globally use of synthetic pesticides has increased rapidly in the last fifty years due to intensification of farming in order to. Pesticides are responsible for several adverse effects on the human health. Several studies revealed that the risk of neurodegenerative diseases, particularly Parkinson's and Alzheimer disease, as well as the increase in endocrine, immune and neuropsychological disorders are among the harmful effects of these compounds on human health. Pesticides also possess a potential genotoxicity in occupationally exposed populations where they induced some types of cancers [6].
Punjab became the focus of many studies due to increase in the incidence of cancer mortality caused by environmental contaminants. This is particularly true for the cotton growing Malwa

region where villages Giana, Malkana and Jajjal have often been referred to as the cancer striken villages in many newspaper reports [7]. Studies conducted by various agencies have also reported a spurt in cancer cases in Bathinda region. A comprehensive study conducted by Post Graduate Institute of Medical Education and Research (PGIMER) has underlined the direct relationship between indiscriminate use of these chemicals and increased incidence of cancer in South Western regions [7].

**Pesticides and general toxicity:** Human beings are exposed to pesticides by oral ingestion, dermal absorption, and/or by inhalation. These routes of exposure vary for different pesticides depending on their properties such as volatility, water solubility, binding to fruit skin and so on. The detection of pesticides like t-HCH, heptachlor, aldrin, chlordane, t-DDT, t-endosulfan, chlorpyriphos, malathion, monocrotophos and phosphamidon in the blood samples of the residents of Malwa region indicates that they are actually being exposed to pesticides directly or indirectly. The consequences of unbridled use of these chemicals are faced mostly by the directly linked farmer's communities in the Malwa region [7, 8]. Pesticides are mainly used on cotton crops during the months of July and August. During these two months, the temperature of the region is quite high (varying from 30 $^0$C to 45 $^0$C) with high speed winds and rainfall. Due to high temperature the sprayed pesticides remain suspended in the air for a long time and due to high wind speed, they drift long distances, making the general public vulnerable to pesticide exposure. Moreover, high rainfall during the period leads to mixing of pesticides. The main adverse health effects are difficulty in breathing, headaches, neurological or psychological effects, irritation of skin and mucous membranes, skin disorders, effects on the immune system, cancer and reproductive effects [7, 9]. The manifestation of these effects depends on the type of pesticide and on level and duration of exposure.

Pesticides such as organophosphate (OP) exposure are a major public health issue in terms of death, morbidity, health care and general safety from toxicity [10]. Organophosphates (OPs) are nonetheless highly toxic to humans and are responsible for tens of thousands of poisonings in developing countries [11] and thousands of poisonings in the U S each year [12]. Many OPs are limited in the extent to which their effects discriminate between target and non-target organisms including humans [13]. Insecticides of the class known as organochlorines (OC), cause a variety of neurological symptoms that may lead to convulsion, stupor and coma as well as damage to organs and endocrine and immune systems [14]. The National Pesticides Policy (NPP) class also includes the carbamates and pyrethroids, both of which are neurotoxins and have similar effects on human health as the OPs. Pyrethroids, which are chemicals synthesized to mimic a naturally occurring plant pesticide are also neurotoxins but are generally considered less harmful than OPs, OCs, or environmental [5]. In various environmental samples, pesticides have been detected in groundwater, surface water, ambient air and soil samples. In living systems, the pesticides have been reported in human blood, milk, animal blood, animal milk, tissues of animals and also in crops, vegetables and plants. The study conducted by Singh and Kaur (2014) indicates the presence of organophosphate chlorpyrifos in the range of 0.80 to 0.91 ppm in the blood of rats collected from Bathinda district of Punjab [16]. High level of pesticide residue existing in the environment exerts adverse effects on reproductive health of 14 animals and humans population evidenced by serious health implications in human domestic and wild life species [17].

**Exposure pathways of Pesticides**

Pesticides are used in 85% of homes in the US but they or their residues can be found even on surfaces that have never been directly or peripherally treated [18]. Persistent organic pollutants (POPs) introduced into the environment years ago are still around today, transported by human activity and through the food chain. Despite being banned in the US (and many other countries) some 30 years ago, traces of these insecticides are still found in the homes and bodies of individuals in the US who were not even alive when these products were used [15,19]. Chlorpyrifos (a nonpersistent OP) has also been found to accumulate on newly introduced surfaces, such as pillows, carpet and soft toys, when brought into a treated area up to two weeks after application, even if applied according to manufacturer's instructions [20].

**Male Reproductive Toxicity**

A combination of genetic, environmental and lifestyle factors contributes to adverse effects on the reproductive health in men. As per various reports from Kheti Virasat Mission, Faridkot (Punjab), the number of childless couples and young males with infertility was alarmingly high in more than 100 villages of the Malwa region [21]. In the Jajjal village of Bathinda, 12.7% of boys (age 13–23 years) failed to show puberty (i.e., voice change and moustaches) 3.4% of boys failed for enlargement of external genitalia, and 5.8% of girls (age 13–20 years) had not started menstruation before age 15 years and there were 0.012% cases of infertility [2]2]. Similar effects of pesticides on the reproductive system have also been reported by Whorton et al (1990), Fig`a-Talamanca et al (2001), and Bretveld *et al*. (2006) [23-25]. Various reproductive problems have been recorded in male formulator's engagedin production of dust and liquid formulations of various pesticides such as malathion, methyl parathion, DDT, and lindane [26]. Luccio-Camelo and Prins (2011) reported that DDT, DDE, methoxychlor, lindane, and dieldrin/aldrin interfere with the biosynthesis, metabolism, or action of endogenous androgens, resulting in a deflection from normal male developmental programming and reproductive tract growth and function [27]. Khan et al (2010) reported that the increased HCH levels cause a significant decrease in semen quality as well as sperm count [28]. The cause of infertility among males is Y chromosome micro-deletion and alteration in sperm quality after organochlorine exposure, which affects the seminal and prostatic functions [29]. The effect of pesticide on reproduction may include menstrual abnormalities, male or female infertility or hormonal disturbances [1, 17]. Several research studies have indicated that sperm counts have been in decline for decades and scientists say modern lifestyles and contacts with chemicals are a contributing factor. Exposure to pesticides is just one of the reasons for this decline. Pesticides have the potential to interfere with androgen action and affect the development and maturation of the reproductive tract in males and cause declination in semen quality (30). Miscarriages in the spouses of farmers have shown direct connection to pesticide exposure. The miscarriage rate varies with the pesticide used [31-33] investigated the possible association of organochlorine pesticides in the pathogenesis of recurrent miscarriages. The increase in insecticide levels in

the blood of vertebrates has been repo..rted to cause reproductive dysfunction [34].

Atrazine treatment provoked a decrease in sperm number and motility in epididymis of rats [35]. Histological analysis of testicular tissue from treated rats showed the cell disorganization and cell clusters together with spermatocytes. Electron microscopy presented 16 differently vacuolated cytoplasm, collagen fibre was reduced, Leydig cells were of irregular shape with unequal form and cisternae of rough endoplasmic reticulum were accentuated and softly widened. In Sertoli cell cytoplasm, atrazine treatment provoked degenerative changes. Atrazine reduced the semen quality in atrazine exposed workers [35]. Choudhary *et al*. (2003) investigated the effects of malathion on the male reproductive system of Wistar rats. There was a reduction in the weight of testes, epididymis, seminal vesicle and ventral prostate. Testicular and epididymal sperm density were decreased in the animals treated with malathion. Pre and post fertility test showed 80% negative results after treatment. Malathion also suppressed the level of testosterone. The rats given malathion alone or in combination with vitamins also had lower plasma FSH, LH and testosterone levels than the control rats [36].

Studies of males exposed to DDT have found decrements in serum bioavailable testosterone levels [37] and reduced semen volume on ejaculation and reduced sperm counts [38]. Ben et al (2001) evaluated the reproductive toxicity of DDT in adult male rats exposed to 50 and 100 mg/kg body weight (b.wt) day- 1 for ten successive days. Administration of DDT led to reduction of testicular weight and the number as well as the percentage of motile spermatozoa in the epididymis. Testicular histological observations revealed also a marked loss of gametes in the lumen of seminiferous tubules. In DDT-treated rats, the seminal vesicles weights dropped, resulting from a decrease of testosterone production by testes, whereas serum LH and FSH increased after pesticide exposure [38]. Yao and Wang (2008) observed a new type of pesticides and because of their high performance and low toxicity, pyrethroid insecticides are widely used in place of organochlorine insecticides both in agriculture and in the home [39]. In the recent years, more and more evidence indicates that pyrethroid insecticides can reduce sperm count and motility cause deformity of the sperm head, increase the count of abnormal sperm, damage sperm DNA and induce its aneuploidy rate, as well as affect sex hormone levels and produce 17 reproductive toxicity. Cadmium is one of environmental pollutants arising from electroplating, fertilizers, pigment and plastic manufactures. Therefore it easily contaminates the soil, plants, air and water [40].

**Heavy Metals**

Heavy metals like lead, Cadmium, Mercury, Chromium and Arsenic have great impact on male reproductive system. These metals caused alteration in sperm morphology, count, morphology and disruption of enzymes and harmones. The effect of heavy metals increased day by day due to industrialization and overgrowing urbanisation [41].

Lead widely used in fuel combustion industry, printing press, acid battery plant refinery, smelter where tetraethyl lead acts as anti knocking agent. When lead gets deposited in testis, epidydmis, seminal vesicle, vas deferens and seminal ejaculate the toxicity is menifested in male reproductive system. It decreased sperm count and retard the activity of motile sperm [42, 43]. The decreased motility and increased incidence of teratospermia at higher dose of lead exposure (0 – 50%) were noted [44, 45]. Study with male CF-1 mice indicated decrease in epididymal sperm count at low dose of lead exposure (0 – 25% via drinking water) [44].

It is released from battery crushing unit, smelter and tannery. Cadmium specially acts on spermatogenic stage. After exposure of different doses of cadmium testicular tissues degenerate and which cause rupture of blood vessels. Rapid testicular edema, haemorrhage and necrosis caused by high dose of cadmium chloride [46]. Electronic microscope observation revealed that DNA fragmentation in mouse testicular tissues showed positive effects after cadmium exposure. Zinc required the maintained structure of Superoxide dismutase (SOD), which scavanges free radicals and maintained appropriate spermatozoon milieu [47, 48]. Zinc replaced by Cadmium which distorts the enzyme structure by which the SOD reduced. Spermatozoa viability also reduced the Cadmium exposed groups. Cadmium targets GSHB – Px which catalyse the destruction of H2O2 and lipid hydroperoxides by reduced glutathione (GSH) and protect the lipid membrane from peroxidative damage in highly oxidative stress condition. Ultimate result is membrane degenration of spermatozoa leading to abnormal and dead sperm in semen [47, 48].

**Conclusion**

Significantly reduced body weight, testicular and epididymal weights, sperm concentration, sperm motility and testosterone in the males indicates the effect of environmental contaminants especially pesticides that may be responsible for alteration in biochemical and physiological processes from the normal range.

**Conflict of Interest**

Authors declare no conflict of interest.

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