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Toxicity of Cadmium and Lead in Mammal: A Brief Review

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Abstract: Some substances are very toxic and can have adverse effects on vital organ of organisms and, in some cases, even may be lethal. Heavy metals occur naturally in the environment in various forms and affect the various biological systems of an organism including human and provoke morphological and physiological effects and other health impairments. The heavy metals can directly enter the animal's body through the contaminated drinking water and/or direct contact with them. The general toxicity of metal ions to mammalian physiology and histology is due to the chemical reaction of the ions with the cellular structure of enzymes, proteins, and cell membrane, which directly affects the liver, kidney, brain, and other body parts like the gonads (testes and ovaries). Today we are also concerned with the carcinogenicity of metal substances. Heavy metals are Cadmium, Lead, Mercury, Arsenic, Chromium, and Magnesium etc. which may cause widespread problems in mammalian reproductive physiology and histology, such as irregular menstruation cycles, theca cells, and granulosa cells in females and decreased sperm counts and hormonal regulation in males. Heavy metals affect gametogenesis, germ cell loss, sperm dysfunction, sperm motility, viability, and impairment of both testicular stroma, testicular necrosis, testicular edema, and seminiferous tubules in males, and pregnancy and foetus development in females. Heavy metals also cause infertility problems and alter the structure and function of testes and ovaries in male and female mammals. Heavy metals have also been linked to breast cancer, endometriosis, and endometrial cancer in humans. It has also been reported that the toxicity of heavy metals causes spontaneous abortions, placenta growth as well as pre-term delivery and atrophy. This review focused on the many diverse and adverse effects of heavy metals on mammals particularly reproductive physiology.

Keywords: Heavy metals, Lead, Cadmium, Reproductive physiology, Testes, Ovary, Liver, Kidney

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Introduction

Heavy metals are described as metallic element which possess high density in comparison to water. Heavy metals are also taken into

consideration as trace elements due to their presence in trace concentrations (in the ppb range to much less than 10 ppm) in numerous

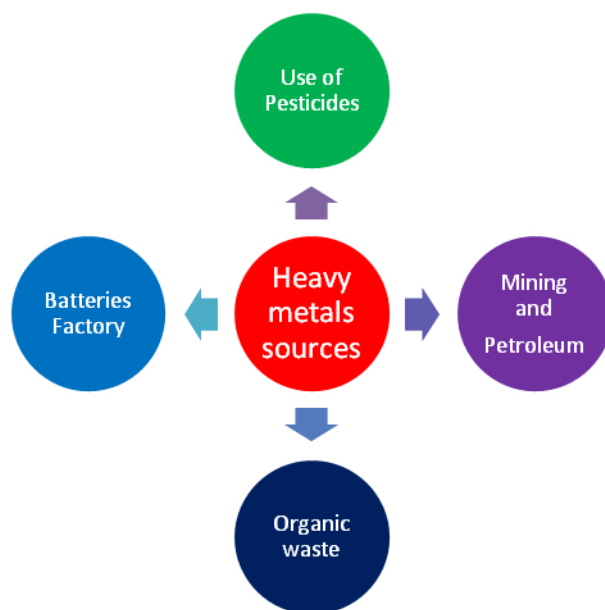


Fig. 1: Different source of heavy metals.



Fig. 2: Occurrence of different types of heavy metals in the environment.

environmental matrices (Tchounwou *et al.*, 2012). Despite the fact that heavy metals are naturally occurring factors that can be found throughout the earth's crust, most environmental contamination and human exposures result from anthropogenic activities, including mining and smelting operations, business production and use, and agricultural and domestic use of metals and steel-containing compounds (Tchounwou *et al.*, 2012).

Heavy metals are also released from powered vehicles, automobiles, diesel cars, and aircraft (Sharma and Agrawal, 2005). Some sources of heavy metals which contaminants environment is shown in Figure 1. Heavy metals (Fig. 2) include lead (Pb), cadmium (Cd) cobalt (Co), copper (Cu), chromium (Cr), Iron (Fe), magnesium (Mg), manganese (Mn), arsenic (As), molybdenum (Mo), nickel (Ni), Selenium (Se), and zinc (Zn) which are

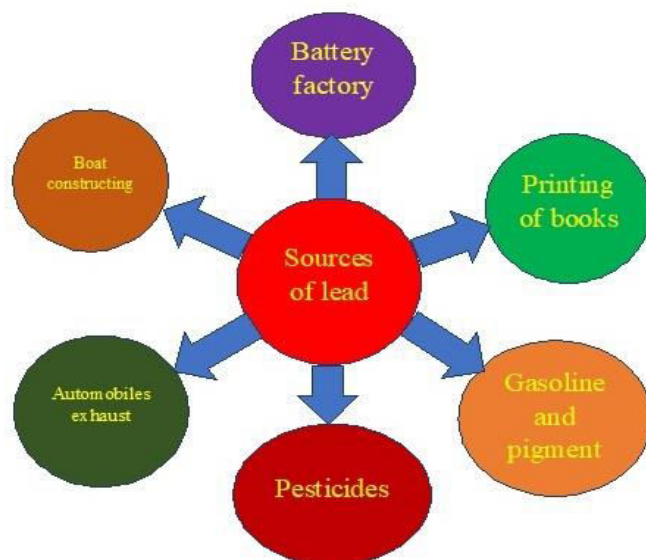


Fig. 3: Sources of lead.

constitutive nutrients which might be required for several physiological and biochemical functions (Tchounwou *et al.*, 2012; Mishra *et al.*, 2023). Heavy metals enter in organism's body via inhalation, ingestion, or absorption (direct contacts), as well as eating and grazing on contaminated food and drinking contaminated water. Heavy metals reach plant tissues via irrigation with contaminated water and soil. Heavy metals are dangerous to health because they cause bioaccumulation, i.e., an accumulation of chemicals in a biological organism over a period of time. These chemicals cause mutagenicity, carcinogenicity, embryotoxicity, renal toxicity, and hepatotoxicity. Heavy metals are typically found in aquatic and soil ecosystems rather than the atmosphere (Verma *et al.*, 2018).

Toxicity of Lead:

Lead is the most critical toxic heavy element in the ecosystem. Its use can be traced back to historical times due to its essential physio-chemical properties. Globally, it is an abundantly allotted, essential, but dangerous environmental chemical (Wani *et al.*, 2015). Human exposure to lead and its compounds occurs more often than not in lead-related occupations with numerous resources like leaded fuel, industrial techniques that include smelting of lead and its combustion, pottery, boat

construction, lead-based painting, lead-containing pipes, battery recycling, grids, the arm industry, pigments, and the printing of books (Fig. 3).

Lead is a highly toxic metal that affects nearly every organ in the body. Many years of exposure to Pb have been reported to cause high blood pressure, anaemia, reduce fertility in males and females, and also damage the kidney and brain in adults as well as children (Wani *et al.*, 2015). Pb exposure on the central nervous system causes irritability, loss of memory, dullness, headaches, and poor attention span. Lead poisoning is now the most common Paediatric health problem in the United States (Tchounwou *et al.*, 2012). Lead gets accumulated in the kidney, brain, liver, and bones (Verma *et al.*, 2018). Lead affects most of the organs and also causes physical and mental impairments in the human body in adults as well as children (Juberg *et al.*, 1997). Lead also affects the synthesis of heme and alters the metabolism of erythrocytes (Charkiewicz and Jeffrey, 2020). It also caused paralysis and chronic abdominal pain (Jonasson *et al.*, 2018) and inhibits the formation of neurons in young children and increases blood pressure in adults (Lockitch *et al.*, 1993).

Lead accumulates in the epididymis, vas deferens, seminal vesicle, and testes of males. Lead causes male reproductive physiology defects

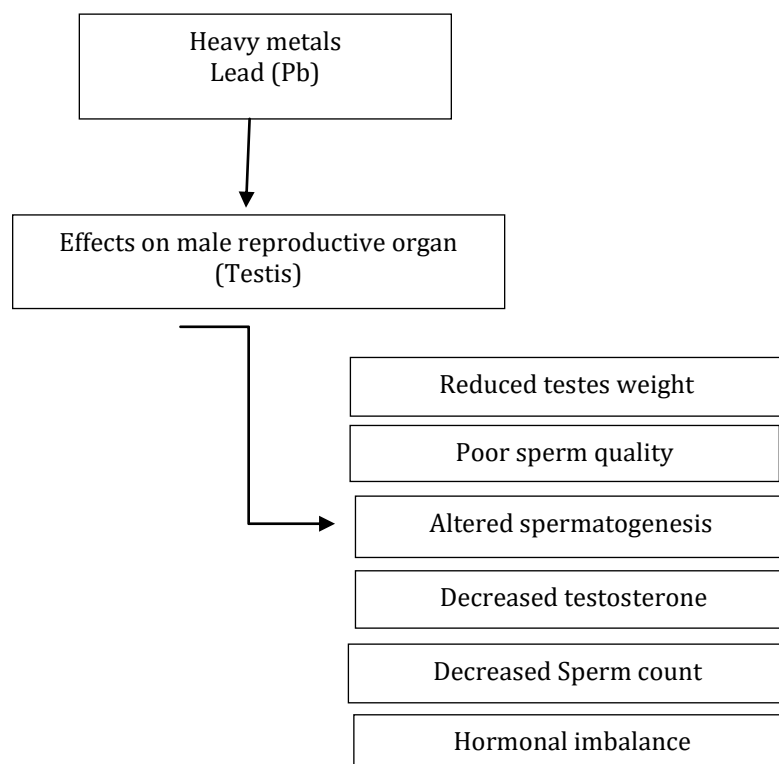


Fig. 4: Effects of lead on male reproductive system.

(Massanyi *et al.*, 2020). Male fertility reduces with age via decreasing spermatozoa quality (Apostoli *et al.*, 1998). High concentrations of lead present in the blood affect male reproductive activity (Fig. 4) like decreasing spermatozoa volume, count, and density, as well as changing the morphology and motility of spermatozoa (Massanyi *et al.*, 2020). The people working in battery-producing factories possess high concentrations of lead, which caused male infertility such as low sperm count and less motility, as well as an increase in the number of immature germinal cells (De Celis *et al.*, 1996). The effect of lead on the germinal cell layer detaching from the basal membrane of the testes altered the activity of steroidogenesis and spermatogenesis, as well as causing Leydig cell atrophy (Verma *et al.*, 2018). Lead exposure alters the quality of semen and production of sperm as well as the values of LH, FSH, and testosterone due to the disruption of the hypothalamic-pituitary axis (Anyanwu and Orisakwe, 2020). A blood lead level >40 mg/dl has been linked to impaired male reproductive function, possibly by reducing

spermatozoa count, volume, density, morphology, and motility of sperm. Lead acetate exposure in rats via drinking water for 45 days results in a significant decrease in testicular weight, sperm count, testosterone level, and antioxidant enzyme level (Massayni *et al.*, 2020). Increased blood lead levels also affect LH and FSH levels, sperm count and motility, and the number of immatures in germ cells (De Celis *et al.*, 1996). Lead can also affect testicular size, sperm quality, prostate secretion function, seminal vesicles, and cause prostate cancer (Pizent *et al.*, 2012). Human male reproductive impairments were caused by exposure of low levels of lead, including sperm density, sperm count, poor sperm quality, motility, altered sperm morphology, and a decrease in the number of motile sperm (Wirth *et al.*, 2010). The direct effect of lead exposure on the testicular cell alters hormonal balance, which causes disturbances in spermatogenesis, reduces fertility, decreases testosterone, and increases luteinizing hormone but does not affect the hypothalamus (Figa-Talamanca *et al.*, 2000).

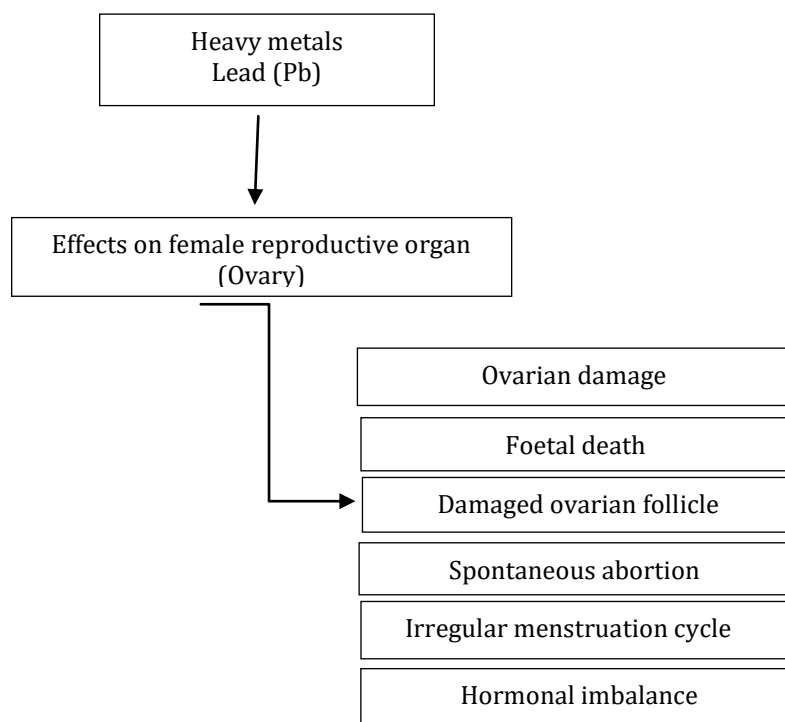


Fig. 5: Effects of lead on female reproductive system.

Lead exposure alters female reproductive physiology (Fig. 5), primarily reducing fertility, causing irregular menstruation cycles, altering hormone production, and decreasing pregnancy rates (Massanyi *et al.*, 2020). Sengupta *et al.* (2015) have also reported infertility, spontaneous abortion, neonatal, and foetal deaths. Treatment of lead to rabbits and sheep caused foetal anomalies, decreases the number of ovarian follicles and spontaneous abortions in females (Verma *et al.*, 2018). Lead exposure caused delayed opening of the vagina, delayed oestrogen secretion from the ovary, enzyme dysfunction, and impairment in the endometrial wall due to decreased secretion of progesterone from the ovarian cells which also decreased the FSH level (Mattison *et al.*, 1989). High levels of lead exposure caused pre-term birth, abortion, and a decrease in female fertility (Dumitrescu *et al.*, 2015). Lead exposure caused deleterious effects on the development of gonads and altered the ovulation and maturation of the ovarian follicles, secondary sexual characteristics, and also caused infant mortality as well as pre-mature delivery (Ibtisam, 2017). The exposure to

high levels of lead caused damage to mice's ovaries as well as a change in the histology of granulosa cells and altered granulosa cell activity (Sharma *et al.*, 2013). Lead can cross through the placenta and can be deposited in the foetus' tissue during pregnancy (Handle *et al.*, 2016).

Lead can also be deposited in the liver and kidney, altering histological structure of these organs. Lead exposure caused changes in the volume and number of renal glomeruli as well as damage to the tissue of both the kidney and liver. Lead can also damage the stomach, lung, brain, and immune cells (Nakhaee *et al.*, 2019).

Toxicity of Cadmium:

Cadmium (Cd) is released into the environment from industrial wastes and agricultural processes and is a very toxic substance for organisms (Massanyi *et al.*, 2020). The characteristics of cadmium include its long environmental existence and non-biodegradable nature (Anyanwu and Orisakwe, 2020). Cadmium enters the body through inhalation, food intake, and contaminated drinking water, and it can be deposited in the

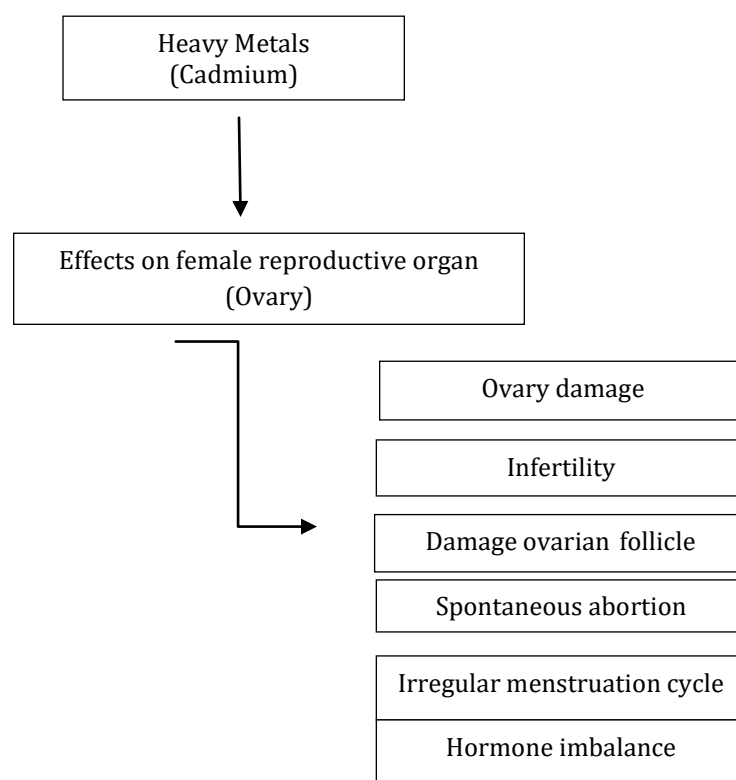


Fig. 6: Effects of Cd on the female reproductive system.

liver and kidney Cadmium has been reported to damage different body organs like the gonads, liver, kidney, and brain. Cadmium can break the DNA strand chain, alter the DNA repair function, and also induce apoptosis in various kinds of cells (Maretta *et al.*, 2022). Cadmium affects both male and female reproduction in mammals, alters hormone synthesis and regulation, and reduces pregnancy rates (Kumar and Sharma, 2019).

Cadmium causes necrosis in mammalian testicular cells in males (Verma *et al.*, 2018). In males the toxicity of Cd provoked damage to the testes, changes in the Sertoli cells, and a loss of sperm quality and count (Massayni *et al.*, 2020). Cadmium can harm the morphology of the testes, reduce sperm motility and viability, and cause altered spermatogenesis. It can also alter male fertility and decrease testosterone levels in plasma and testes (Anyanwu and Orisakwe, 2020). Cadmium can alter the shape of testes and is able

to break the blood-testes barrier and decrease the motility of sperm and testosterone concentration (Wirth *et al.*, 2010). According to Wang *et al.* (2017), cadmium treatment causes damage to the testes and inhibits sperm motility and fertilisation ability in the male reproductive organ. Oral administration of Cd to rats for 14 days altered spermatogenesis and caused testicular necrosis (Thompson and John, 2008).

In female rats, repeated Cd treatment resulted in decreased shape of the ovary and uterus, as well as morphological changes and inhibition of ovulation from the ovary (Mattison *et al.*, 1989). In women, long-term cadmium exposure caused endometriosis, implantation failure, infertility, spontaneous abortion, and pre-mature delivery (Rzymiski *et al.*, 2015). Low concentrations of cadmium decreased the production of progesterone in female rats (Sengupta *et al.*, 2015). High concentrations of Cd can cause

premature birth and suppress progesterone production and placental activity, as well as act as an oestrogen mimic (Verma *et al.*, 2018). Treatment with Cadmium leads to reduced ovulation, ovarian necrosis, and serum progesterone levels (Thompson and John, 2008). The toxicity of Cd affects the female reproductive system (Fig. 6), including impairment of steroidogenesis, infertility, hormonal imbalance, delayed menarche and puberty timing, irregularity of the menstrual cycle, and spontaneous abortion (Olaolu *et al.*, 2018). Cadmium is always recognised as a reproductive toxicant that deposits in and damages granulosa cells of the ovary and inhibits the steroidogenic enzyme function of ovarian cells (Monsefi *et al.*, 2013). Mareta *et al.* (2022) have also reported the effect of Cd on the reproductive physiology of mammals. Cd can accumulate in ovarian and uterine cells and can block the function and growth of the ovary and cause damage to the ovarian follicles, including the formation of follicles as well as structural changes in granulosa cells.

Conclusion

Now a days, anthropogenic activities increased the level of heavy metals, in the environment which is responsible for global health issue in the world. Mainly, the heavy metals act on the kidney, liver, gonads, brain, and nervous system. The heavy metal toxicity caused various reproductive disturbances in the mammal. Heavy metals act as a reproductive toxin and produce adverse effects on the ovary and testes. In ovaries, different changes can be seen after the treatment of heavy metals, including ovarian necrosis, a decrease in follicular cells, hormonal imbalance, pre-mature delivery and foetal death. Heavy metals affect the male reproductive system causing low testicular weight, decreased spermatogenesis, and poor sperm motility. Heavy metals due to this mimicking behaviour cause physiological and structural dysfunction related to reproductive physiology.

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