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# Effect of Heavy Metals on Reproductive Health of Women: Health Alarm!

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**Abstract—***Clean environment plays a major role in promoting good health in living beings. However during the last few decades, exponential growth of human population, industrialization and haphazard urbanization has modified our environment increasing the burden of environmentally mediated diseases. Heavy metals like Cu, Pb, As, Zn, Cd, Cr, Hg are a major group of pollutants that are disposed through industrial effluents, untreated wastewater, vehicular emission and sewage water. Vegetables, which form an essential part of our diet, become contaminated with heavy metals when grown in this polluted environment. Toxic heavy metals enter the food chain through consumption of these vegetables resulting in biomagnification and bioaccumulation. Since there is no effective method of excretion, these heavy metals accumulate in different organs causing health hazards. The metals- Pb, Ni, Cr, Cd, Hg over the past few years have become a major concern as they interfere with reproduction in women, reducing fecundity. They alter the development, maturation or endocrine function of female reproductive functions. Extensive studies have shown the relation of Pb, Hg and Cd with increasing causes of infertility in women. Cd is a metalloestrogen, which cause endometriosis, endometrial cancer and spontaneous abortions. Increased levels of Pb can cause spontaneous abortion and also have teratogenic effect. Toxic levels of Hg effect the menstrual cycle and indirectly cause infertility. The environment in which women reside should be evaluated and there should be general awareness among women of the harmful effects of these metals. Steps should be taken to check the cause at its root and prevent pollution of our environment.*

## 1. INTRODUCTION

According to WHO environment plays a major role in the influencing our health through exposures to physical, chemical and biological factors and altering our behavior in response to these factors. Intensive studies show that greater than 80% of the diseases of children reported by WHO, are due to modified environment resulting in nearly one quarter of all deaths. The burden of 'environmentally mediated' diseases is higher in developing countries than in developed countries (WHO, 2006). Implementing policies to create a cleaner environment can be a step towards prevention of a wide range of disorders and diseases. Geometric growth of human population has however created an environmental burden. Industrialization and unplanned urbanization to cater to the increasing population, has resulted in modifying our natural resources-air, water and soil thus increasing environmental contamination. One of the major pollutants modifying our environment are the heavy metals. They are defined as metallic elements with density greater than water [8]. These elements are present in the environment at ultratrace levels. However unchecked anthropogenic activities have disturbed their geochemical cycle, resulting in significant increase of their level in the environment [28]. Some of these elements include microelements – Copper (Cu), Zinc (Zn), Chromium (Cr III), Nickel (Ni), that are essential for various metabolic regulations. Inadequate supply of these elements can result in deficiency syndromes (WHO, 1997). Other heavy metals-Lead (Pb), Cadmium (Cd), Arsenic (As) and Mercury (Hg) have no metabolic role and are toxic at even low concentrations. The main source of heavy metal contamination includes industrial effluents, poor waste-water management, mining, smelting, vehicular emission, combustion of fossil fuels, dumping sites of waste and indiscrete use of fertilizers. These heavy metals are non-biodegradable with a long biological half-life and therefore persist in nature. They enter the food chain resulting in bioaccumulation, geoaccumulation and biomagnification in the environment [28]. One of the ways of exposure to heavy metal toxicity is by consumption of the contaminated vegetables, which are grown in polluted environment. There is no effective method of their excretion thus resulting in accumulation of these metals at toxic levels in our body [11]. As, Cd, Cr act as carcinogens [8, 43] and Pb and Hg [12, 30] are associated with developmental abnormalities in children. Gold mining in Zamfara, Nigeria, lead to the death of 400 children due to Pb poisoning. Pb are found in problemetic concentrations in these gold bearing

deposits [21]. Reproduction is an important aspect of life. To ensure a healthy population, it is important that women should be in good reproductive health. These toxic heavy metals have a detrimental effect on the female reproductive system in turn affecting the developing embryo, which are most susceptible to them. The placenta functions to support the embryo by providing it with nutrients and removing waste materials produced. A pregnant woman under the influence of toxic heavy metals will have a few metals crossing the placenta barrier. Cd crosses the placenta during the early stages of gestation and retards the foetal growth causing morphological changes in experimental [7]. As enters the placenta easily. Pb too enters the placenta less readily than methylmercury but more than Cd. Adverse effect of Pb includes prevention of implantation. Pb, Cd, Hg and Cr cause prenatal death either before or after implantation [25]. The fertility of a woman is the result of the integrated function of hypothalamus, pituitary, ovary and uterus. Sexual maturity is mediated by hypothalamus [31]. Pb, Cd, Hg and Ni have an adverse effect on hypothalamic-pituitory function altering the sexual maturity and the uterine function [25]. Pb and Cd have a toxic effect on the growing and pre-ovulatory follicles of ovary. There is now awareness in the society of the toxic effects of heavy metals on female reproductive health.

## 2. HEAVY METAL TOXICITY BY CONSUMPTION OF CONTAMINATED VEGETABLES

Food is important for our survival and is a major source of our nourishment. Vegetables form an essential part of our diet and are consumed both in raw and cooked form. They are the main source of nutrients, fibres, and antioxidant, which are important for our good health. Vegetables also buffer the acid produced during digestion [22] and supply microelements such as Zn, Mn, Mo, Se, Cr (III) and Cu. These are essential parts of various biochemical reactions in our metabolism for eg:- Mn is the cofactor for many enzymes in our body [40]. The vegetables are grown in peri-urban areas to avoid the hustle and disturbance of the cities. In last fifty years industrial revolution and unplanned urbanization has polluted our environment resulting in infiltration of toxic levels of heavy metals in the sub-urban areas where vegetables are commonly grown. Accumulation of heavy metals and metalloids in agricultural soil is of great concern as it affects our food quality and safety. Vegetables take up heavy metals and accumulate them in their edible or non-edible parts at concentrations, which are toxic for both man and animals. Thus vegetables are the major intake source of toxic metals and soil to plant transfer is the major pathway to human exposure through food chain [18]. Accumulation of these metals beyond maximum permissible level (MPL) leads to neurological impairment, functional damage of liver and kidney and bone diseases (WHO 1992) [17, 43]. Pd, Hg, Cd and Cr also affect the female reproductive health resulting in miscarriage and low birth weights in pregnant women [23]. Heavy metal contamination in vegetables is not the woe of developing countries only but is a global phenomenon. Assessment of heavy metal contamination in vegetables from market site has been carried out both in developed and developing countries (Sharma *et al*., 2009). Vegetable samples from the markets in New York City and Buffolo were found to have Pb concentrations above MPL [26]. In a study carried out by Radwan and Salama in 2006, vegetables sold in Egyptian markets were found to have high levels of Cd. Heavy metal accumulation in vegetables has also been reported from local markets of Riyadh, Saudi Arabia [1], Varanasi [38] and New Delhi [24] India. A study carried out by Lacatusu *et al*., in 1996 showed that Pb and Cd around non-ferrous smelters in Copsa Mica and Baia Mare, Romania have significantly decreased the human life expectancy by 9-10 years within affected area.

The transfer factors (TF) value from soil to vegetables varies greatly between plant species and locations. TF of different locations maybe related to the soil nutrient management and soil properties [18]. There is also a variation in distribution of the toxic metals in different vegetables [28]. Toxicity of vegetables is dependent on the rate of uptake of soil metals by the vegetable crops and whether metal accumulation occurs in the edible or non-edible part of the vegetables. Studies show a high concentration of heavy metals in green leafy vegetables [37] whereas herbaceous plants concentrate these metals in their stem and root [53]. Root vegetables accumulate a higher concentration of soil Cd in comparison to other metals [47]. National and international bodies of food regulation have revised the MPL of metals in food, lowering their allowed concentrations because of increased awareness of their toxicity.

## 3. TOXIC EFFECT OF HEAVY METALS ON FEMALE REPRODUCTIVE SYSTEM

Reproduction is a continuous phenomenon in women beginning from prenatal development of reproductive organs to sexual maturation and finally ending with reproductive senescence. Environmental contamination with heavy metals may interfere with their reproductive ability. There have been reports of interference of these metals with development, maturation or function of female reproductive functions [25]. Studies have detected the presence of few of the heavy metals in follicular fluid [3]. Exposure to toxic levels of heavy metals can have an impact on hormonal profiles, fertility and thus reduce fecundity. Clinical infertility is the inability to become pregnant after 12 months of unprotected sex. Infertility has become a common problem. According to CDC, approximately 6% of married women between the ages of 15–44 years in the United States of America are unable to get pregnant and 12% of women between the age of 15–44 years have difficulty getting pregnant or carrying a pregnancy to full term, regardless of marital status (impaired fecundity) (CDC and Prevention). Of lately 15-30% of couples are diagnosed

with unexplained infertility [32]. Declining fertility is not a problem of couple wanting to start a family but is an indicator of the toxic burden on the environment.

Significant studies have been done to find the effect of different heavy metals on hypothalamic-pituitory-ovarian axis, resulting in impaired estradiol and progesterone production and in turn effecting the normal oocytic development and chromosomal damage [35]. These heavy metals have been reported to cause aneuploidy in chromosomes, which may result in spontaneous abortions and teratogenesis [25]. One of these highly toxic elements is Pb, which freely crosses the blood-placenta barrier. The accumulating Pb is not only harmful to the woman but also to the developing foetus [42]. Studies in rodents have shown that high concentrations of Pb prevents implantation which is due to decreased responsiveness to sex steroids estradiol 17 and progesterone [48]. Development of embryos is also slightly delayed if exposed to Pb during early gestational period, which is decisive in the process of implantation [16]. The other toxic elements causing impairment in female reproductive system are Cd and Hg. This review discusses the effects of these heavy metals on female reproductive system in details.

### 3.1 Lead

Environmental Pb toxicity is an old concern as a public health issue, with children being more affected by lead poisoning than adults [2]. It is also a matter of concern in pregnant women as it affects the implantation and development of embryo. Pb is toxic at low concentrations and has an easy passage through placenta; therefore if there are increased levels of Pb in maternal blood, there will be a high concentration of Pb in foetal circulation. Pb also has teratogenic effects, which include prenatal toxicity (embryotoxicity and foetotoxicity) and behavioral teratogenicity (behavioral alterations or functional deficits) [46]. The teratogenic effects of Pb have been reported in rodents and birds. Studies showed that when the pregnant hamsters were fed with variable dosage of Pb salts, the embryo developed congenital malformations, which were largely restricted to the tail region [10]. Studies on Swiss female mice generated data that reactive oxygen species generated by Pb is responsible for the ovarian dysfunction affecting the female reproduction, increased incidences of reduced fertility and low birth weight [41]. Pb is also known to produce direct ovarian toxicity. Junaid *et al*. in 1997 carried out studies on mice, which showed follicular development anomalies when exposed to high concentrations of Pb. Uterine function is also altered by high concentrations of Pb. It affects the estrogen receptors resulting in a hostile endometrial environment for pre-implantation embryo [48]. Although animals may have different responses in comparison to human yet documented responses of toxic effects of Pb on animals to some extent maybe extrapolated to human thus generating awareness.

### 3.2 Cadmium

Cd is another heavy metal having a detrimental effect female reproductive health. It gets rapidly distributed in the tissues, accumulating at maximum concentration in vascular system, liver and kidney [51]. Chiquone (1965) showed the abortive effects of Cd on pregnant Swiss Albino female mice. It is an endocrine disruptor, which enhances or lowers the production of progesterone a sex hormone primarily required for periodicity of menstrual cycle and to maintain pregnancy. It may interfere by either replacement of $Zn^{2+}$ with $Cd^{2+}$ in DNA binding zinc fingers or by acting as endocrine disrupting chemical and mimic or inhibit the action of estrogen [14]. Monsefi and Fereydouni in 2013 carried out studies on Wistar female mice to evaluate the effect of Cd on estrogen and progesterone thus altering their estrous cycle. To study the toxic effects of dietary consumption of Cd, experiments were carried out in hyline white hens. The experimental group showed extensive damage in ovarian tissue due to altered antioxidant defense enzyme systems, lipid peroxidation, apoptosis and endocrine disturbance [52]. The effect of Cd is species specific and also seen to accumulate in human ovary. Cd gets incorporated in the chromatin of the developing gamete effecting the oocyte development and resulting in failure of ovulation. It has also been linked to decreased birth weights and premature birth during pregnancy [13].

### 3.3 Mercury

Spanish history speaks about harmful affects of Hg, where about 200 years ago, the slaves working in mercury mines got sick and died. Instances of organic mercury poisoning from consumption of grain treated with organomercurial fungicides have also occurred in Iraq and Guatemala. In Iraq, children exposed to Hg during foetal development had severe neurological impairment. Recent reports of Faraoe Island have shown that low doses of exposure to pregnant mothers have a negative impact on the brain development in embryo (How does mercury effect our Health?). Hg is abundant in most of our daily use articles - fungicide, thermometer, traditional blood pressure, switches, mirrors and dental amalgam fillings. Release of processed Hg in the environment results in its entry in the food chain and bioaccumulation in the environment Major route of Hg poisoning is via consumption of contaminated food. Hg in its vaporized form is lipid soluble and accumulates in the renal cortex, liver, and especially the brain. Studies have shown that it is most toxic to female reproductive system in this vapor state. It prolongs the estrous cycle in animals [13] and causes reproductive dysfunction in both laboratory animals and women [36]. The menstrual cycle is disturbed in women, resulting in abnormalities including irregular and painful menstruation, which causes decreased fertility [34]. Several studies on female laboratory animals show the disruptive effects of Hg on their reproductive health. Accumulation of Hg was found in the anterior pituitary of vervet monkeys implanted with amalgam fillings thus interfering with the hormonal function [54]). This toxic

element also affects the placental function. Reports on *in-vitro* studies on full term placenta show inhibition in amino acid transport in placenta either causing impaired organogenesis during early pregnancy or abnormal development of foetus during the last trimester [45].

## 4. CONCLUSION

Unchecked anthropogenic activity has created immense environmental burden. In order to achieve the short-term goals offered by technology and advancement, there has been rapid industrialization and unplanned urbanization disturbing the balance of nature. Our surroundings have become rapidly polluted with industrial effluents, untreated wastewater and vehicular effluents. Pollution by heavy metal deposition has become a matter of great concern. They enter the food chain mainly by consumption of vegetables grown in contaminated environment. Due to absence of their excretion process these metals accumulate in different tissues and have detrimental effect on the health of both animals as well as human. Heavy metals like Pb, Cd and Hg have toxic effect on the function of female reproductive system, even at low concentrations. There are increased incidences of abnormal foetal development, spontaneous abortion and high rates of infertility due to heavy metal toxicity. This is a matter of great concern as it results in decreased fertility and fecundity of the population. The need of the hour is for the authorities to spread awareness of the toxic effects of these metals and formulate policies to combat the increasing concentration of heavy metals in our vegetables and environment. We also require more competent physicians who can evaluate the affects of heavy metal toxicity and treat them at the early stages and prevent their harmful effect on the female reproductive system.

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