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POTENTIAL TOXICOLOGICAL IMPACTS OF DIOXIN ON HUMEN- AN ENVIRONMENTAL POLLUTANT

Mr. Akash Arun Patil
Asst. Professor,
Dept. of Environment Science
Matsyodari College, Ambad

Abstract: Dioxin is super toxic chemicals, which contain chlorine. It exhibits serious health effects when it reaches as little as a few parts per trillion in body fat. And produces deleterious effects on many biologically activities like hormones, modifying genetic mechanisms of the cell, causing a wide range of effects, from cancer to reduced immunity, nervous system disorders, miscarriages and birth deformity. Various studies prove that exposure to dioxins results in multiple toxic effects on humans and experimental animals. Among the various disorders caused by dioxins are abnormalities in dentition. The effects of dioxin may last long after exposure. However, most of the mechanisms are not clear, thus several number of studies are ongoing trying to elucidate them in order to protect the public by reducing these adverse effects. In this article, we briefly focused on the impacts, of dioxin like compound on developmental, reproductive, diseases and associated molecular pathways in cells.

Keywords: *Dioxins, reproductive, contamination, molecular pathways miscarriages*

Introduction: Dioxins contain a heterocyclic 6-membered ring compound are known to exhibit toxicity. These include polychlorinated dibenzo-p-dioxins (PCDDs) known as dioxins, polychlorinated dibenzofurans (PCDFs) or furans, and polychlorinated biphenyls (PCBs). The term 'dioxin' may also refer to the basic chemical unit of more complex dioxin molecules (Pohjanvirta and Tuomisto, 1994). Generally, human exposure levels of PCB chemicals are decreasing over time in the U.S. population. This reflects the effects of legislation, industry, and changes in lifestyle or activity patterns on the population (Needham *et al.*, 2005). In addition, the effects of dioxins and DLCs at low doses were also defined in the range of human exposures or traditional toxicological studies by the National Toxicology Program (USA) (Vandenberg *et al.*, 2012).

Human can be exposed to dioxins through environmental, occupational, or accidental pollution. In the human body, most dioxins are metabolized and eliminated while the rest are stored in body fat (Marinkovic N. *et al.*, 2010). Many effects attributed to 2, 3, 7, 8-tetrachlorodibenzodioxin (TCDD), such as lethality, lymphoid and gonadal atrophy, hepatotoxicity, adult neurotoxicity, and cardio toxicity, are associated with high doses of the chemical. Exposure to dioxins also results in abroad spectrum of biological responses

including altered metabolism, disruption of normal hormone signaling pathways, reproductive and developmental effects, cancer development (Spencer *et al.*, 1999), and immune effects (Birnbaum & Tuomisto, 2000; Fracchiolla *et al.*, 2011).

Dioxins compound that share certain chemical structures and biological characteristics. Over the years about the potential health impacts of dioxins found in the environment and in food supply. According to Thornton (1997) dioxins were first discovered as the cause of severe health problems among workers who had been exposed to the byproducts of explosions in chemical plants that manufactured certain chlorine-based pesticides in the 1950s. In these accidents dioxin was formed and released into the work-place environment, causing systemic health problems among workers. Toxicological and epidemiological studies showed that dioxin was an extraordinarily potent carcinogen and caused damage to a variety of organ and system in laboratory animals Thornton, J. (1997). Hence from the above discussion it is clear that Dioxin like compound is very toxic and produces deleterious effects on living organism so in the present article we will try to focused on the few effects on the various living organism as following-

1.1 Effects of Dioxins and Dioxin-like compounds: There are several biological mechanisms that are likely to differ according to tissue and developmental period. These mechanisms may also be modulated by distinct genetic and environmental factors (Whitlock, 1987). Dioxin, an endocrine disruptor, causes reproductive and developmental toxic effects in pups following maternal exposure in a number of animal models (Koga *et al.*, 2012). Previous study has raised two important issues that the rat fetus was about 100-fold more sensitive to TCDD exposure than the adult, and fetal sensitive to TCDD appeared to exist in the hamster even through adult life (Murray *et al.*, 1979).

1.2 Data on Experimental Studies: One study showed that dioxins are accumulated in human and animal fat tissues, and their elimination depends on life expectancy and the rate of Metabolic processes Całkosiński (2005). In humans this period is about 9 years Schlatter (1991). The data on female rats decrease of dioxin concentration during lactation Korte et al., (1990). Dioxin in the human body is transported by lipids in blood serum to the liver and fat tissue where it accumulates. In the hepatocyte TCDD they bind to aryl hydrocarbon receptors, forming the complexes which are subsequently transported to the nucleus. These complexes then bind the dioxin response element (XRE) of DNA, which results in stimulation of genes for P 450 and P 448 cytochrome and consequently enhances their production. The formed cytochromes participate in the further metabolic processes of dioxins. Long-lasting accumulation of dioxins in the liver and their interaction with DNA influence metabolism of

protein in liver and also in the hematopoietic system Całkosiński (2005). Exposure of monkeys to just 5 parts per-trillion of 2, 3, 7, 8 – TCDD concentrations caused impaired neurological development and endometriosis Belazzi and Pexa (2001). Pregnant rats receiving a single dose of 2, 3, 7, 8 – TCDD on day is of pregnancy had male off springs which appear normal at birth, but at puberty were demasculinized with altered reproductive anatomy, reduced sperm count, feminized sexual behaviour Enan et al., (1992). The recent finding that the genome of the HIV – 1 virus contains regulatory sequences that bind the dioxin receptor complex and active transcription of viral genes is a cause for concern that dioxin-like chemicals may also play a role in the expression of infectious disease Enan et al., (1992).

Dioxins clearly cause cancer. All 18 studies on the carcinogenicity of 2, 3, 7, 8 – TCDD have been positive demonstrating that dioxin is a multi-site carcinogen in both sexes in the rat, mouse, and hamster by all routes of exposure EPA (1994b). EPA has estimated that current background exposures pose cancer risks as high as one-in-one thousand, a level that exceeds 'acceptable' risk standards by up to a thousand times and, if accurate, could correspond to as many as 3,500 U.S cancer deaths per year due to dioxin exposure EPA (1994a).

1.3 Effects on Thyroid-function: Recent studies demonstrated that thyroid diseases are increasing and neurodevelopmental damage due to thyroid-disrupting chemicals has also been observed (Langer, 2008; Radikova *et al.*, 2008; Patrick, 2009). There is significant evidence that PCBs, dioxins, and furans cause hypothyroidism in animals and disrupt human thyroid homeostasis; even small changes in thyroid homeostasis may adversely affect human health (Crofton *et al.*, 2005; Suzuki *et al.*, 2007; Boas *et al.*, 2009). A previous study also uncovered possible effects of exposure to dioxin-like chemicals in maternal milk including reduced vitamin K levels, increased thyroxin concentrations, and mild liver enzyme changes in children (Pohl & Hibbs, 1996).

1.4 Immune System: Immune system development is very sensitive to Immunotoxic reagents. TCDD, a well-known immuno toxicant, has been shown to produce adverse effects in rodents and humans, and is considered a prototypical developmental immuno toxicant (Van Loveren *et al.*, 2003). A recent investigation has expanded the physiological role of dioxin molecular pathways to include modulation of hematopoietic progenitor production and immune regulation (Smith *et al.*, 2011).

1.5 Cancer and Cardiovascular Disease: Laboratory research has utilized a variety of vertebrate models to elucidate potential mechanisms that mediate this cardio teratogenicity and measure the sensitivity of different species for predicting potential risk to environmental and human health (Tuomisto & Tuomisto 2012). It is notable that in all models, dioxin-associated

cardio teratogenicity is associated with increased cardiovascular apoptosis and decreased cardiocyte proliferation (Kopf & Walker, 2009). In addition, research in animal has confirmed the human epidemiological finding that dioxin exposure during adulthood is associated with hypertension and cardiovascular disease (Kopf & Walker, 2009). Dioxins and DCLs contamination in fish are associated with increased risk of cardiovascular disease (Bushkin-Bedient & Carpenter, 2010). Exposures to TCDD in utero and through breast milk in C57BL/6 mice alter cardiac gene expression as well as cardiac and renal morphology in adults, thus increasing the susceptibility to cardiovascular dysfunction (Aragon *et al.*, 2008).

The (IARC) has classified dioxins as a human carcinogen although they are not associated with the development of specific tumors (Donato & Zani, 2010). Recently, dioxin was shown to be a developmental toxicant in the mammary gland as well as a sensitivity chemical to potential carcinogens in rodents (Birnbaum *et al.*, 2003). TCDD also induce changes in estrogen metabolism and may alter the growth of hormone-dependent tumor cells, thus producing a potential carcinogenic effect (Gierthy *et al.*, 1993). Furthermore, *in vitro* dioxin exposure leads to accelerated cell differentiation, increased cell proliferation, and decreased senescence in differentiation processes (Ahn *et al.*, 2005; Kumar, 2011). These changes are accompanied by decreased levels of several regulatory proteins (p53), indicating that dioxins may exert cancer-promoting effects through this mechanism (Ray and Swanson, 2003).

Conclusion: Based on various studies that environmental exposure, dioxins may result in multiorgan functional and morphological disorders, including multiple teeth disorders, especially if the exposure takes place in developmental stage of life. The effects of exposure can also manifest themselves over a long period of time. As a result of the health risk posed by dioxin, there is an urgent need for a control and monitoring assessment especially in the developing countries. There is low awareness about the health consequences and environmental impacts of dioxins. The adverse effects of this compound on human health cannot be over emphasized.

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