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A Study on Lead Intoxication

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ABSTRACT

Exposure to lead is a silent threat to the environment and human life. Lead (Pb) pollution has been considered a major threat to human health. It has the potential to harm almost every organ system of our body. The most significant source of ingestion-related lead exposure in humans and animals is the consumption of fish. Long-term exposure to lead compounds from different sources (e.g., water, food, soil, and air) can lead to toxic effects on skin, cardiovascular, hematopoietic system, renal effects, reproductive health effects, and neurological systems. Lead toxicity is found to pose more significant health hazards to certain occupational groups (e.g., gold miners and dental personnel). Because continuous exposure to lead can be dangerous, it is desirable to re-evaluate the current reference (risk-free) values. The purpose of this review is to provide brief information concerning the effects of lead exposure on various organ systems. According to this study, lead (Pb) may initiate a cascade of direct and indirect biochemical reactions which may cause an imbalance in homeostatic physiology.

1.1 INTRODUCTION:[1, 2, 3, 4, 5, 6, 7, 8]

Lead (Pb) is a non-essential heavy metal and an environmental pollutant, which is universally present in the ecosystem. Men have used led due to its unique properties (Somervaille et al. 1988; Gulson, 2000). Lead exposure usually occurs in humans by inhalation and oral ingestion, whereas its excretion occurs through urine and bile, some bind to red blood, while few are known to accumulate in bone (Mason LH, Harp JP, Han DY; 2014). The main target of lead-induced toxicity in the hippocampus part and for so, children's are also much sensitive for lead intoxication (Nava-Ruiz C, Méndez-Armenta M, Ríos C; 2012 and Mushak, 1992).

Lead exposure usually occurs through food sources, drinking water supplied through old pipes(Kazantzis, 1989). Occupational exposure frequently occurs in those workers working in smelting, painting, plumbing, and printing industries. Lead (Pb) is a bluish-gray heavy metal (atomic weight 207.2), that occurs naturally in various mineral forms in the earth's crust. Lead can exist in three forms: metallic, inorganic, and organic. (Patrick, 2006).The respiratory route is the most usual routes of lead exposure since 30–40 percent of inhaled lead is known to remain in with erythrocytes for approximately 30-35days. (Barbosa F.Jr., Tanus-Santos J.E., Gerlach R.F., Parsons P.J.; 2005).

1.2 Toxicity of Lead[9, 10, 11, 12, 13]

Lead (Pb) toxicity is known to affect a number of organ systems. It causes neurodegeneration in infants which may result in behavioral abnormality (P. A. Meyer, M. J. Brown; 2008) and (A. C. Callan, A. L. Hinwood; 2011). Respiratory and gastrointestinal (GI) tracts are the main route of exposure to lead. Tetraethyl lead (leaded gasoline) is capable to pass through the skin. In respiratory exposure, 35–40% of inhaled lead particles get deposited in the lungs,37% of lead particles (≤1 μm)get deposited in alveolar region and 50% of the gets absorbed and enters the systemic circulation. Adult lead toxicity result from short-term, high dose lead absorption. Symptoms of lead exposure generally include normocytic anemia, abdominal pain, constipation, arthralgia, myalgia and other CNS disorders (like a headache, mood disorder, and encephalopathy) and may occur within weeks of the onset of sufficient exposure (Levin SM, Goldberg M; 2000). Low-dose lead exposure can result in adverse effects in multiple organ systems, including effects in neurologic, cardiovascular, reproductive, and renal function (MJ Kosnett, RP Wedeen, SJ Rothenberg et.al.2007). Even

in the low range of 10±20mg/dl in blood, lead (Pb) is known to affect the normal intellectual quality of children (Needleman, Bellinger; 2001).

1.3 Mechanism of Lead Toxicity [14, 15,16,17,18]

1.3.1 Lead (Pb) induced neurotoxicity occurs due to the ability of Lead (Pb^{2+}) cation to replace other divalent cations like calcium (Ca^{2+}) and zinc (Zn^{2+}) in the cellular machinery of the living organism(Godwin, 2001). These interactions expose lead to its affect different vital processes like regulation of metal transport, cellular respiration, apoptosis, ionic conduction across the cell membrane, cellular adhesion, molecular signaling at intra and extracellular levels, enzyme kinetics, structural rearrangement of proteins and alternation in genetic makeup (Markowitz, 2000).

1.3.2 The mechanisms underlying the neurotoxic effects of lead have been linked to exciting toxicity, alteration of neurotransmitter storage and release, induction of brain cell apoptosis, inflammation and oxidative stress (J Sirivarasai, 2013).Particularly, lead-exposure associated increase in inflammatory mediators has been reported in human population studies, experimental animal models and cell culture systems (DA Ghareeb, HM Hussien; 2009).For instance, Ghareeb et al. have reported that lead exposure in rats caused increase in inflammatory markers, NO and TNFα, coupled with a significant decrease of glutathione (GSH) levels and impairment of antioxidant activities of superoxide dismutase (SOD) and catalase (CAT) (JR Vane, YS Bakhle, RM Botting; 1998).

1.4 Effect of lead in the human body in different organs

1.4.1 Effect on the Nervous System [19, 20, 21, 22, 23]

CNS is the most sensitive to lead toxicity (Cory-Slechta, 1996). Lead toxicity frequently affects the CNS of children whereas, the peripheral nervous system is more susceptible in adults(Brent, 2006; Bellinger, 2004). Lead is known to cause neurodegeneration in specific regions of the brain like prefrontal cerebral cortex, hippocampus, and cerebellum, which may result in nerve damage responsible for mental and behavioral abnormality, and may precipitate diseases like Alzheimer's disease, Parkinson's disease, and schizophrenia.Lead toxicity leads to encephalopathy with progressive degeneration of certain brain regions, the major symptoms include dullness, loss of memory, vision, cognitive problems, behavioral problems, mental retardation, hallucinations, headache, poor attention span, and irritability,

while high-level lead exposure may cause delirium, convulsion, and coma (Flora et al. 2006). Lead toxicity is the CNS may exacerbate apoptosis (programmed cell death) and excitotoxicity, which affects the storage and release of neurotransmitters, may alter the normal physiology of neurotransmitter receptors, mitochondria, secondary messengers, cerebrovascular endothelial cells, and both astroglia and oligodendroglia (Hwang L., 2007).

1.4.2 Effect on the Hematopoietic System [24, 25, 26, 27]

Lead restricts the synthesis of hemoglobin by inhibiting various key enzymes inhibiting enzymes involved in the involved in the heme synthesis pathway. Lead destabilizes the cell membrane of circulating erythrocytes, thus decreasing their lifespan. The collective outcome of such processes leads to anemia (Guidotti et al., 2008; Cornelis, 2005).The anemia induced by lead, primarily occurs due to impairment of the heme biosynthesis, but an increased rate of erythrocyte destruction may also occur Acute high-level lead exposure is known to cause hemolytic anemia, whereas frank anemia is caused only when the blood lead level remains elevated for long time periods (Vij, 2009, Schwartz et al., 1990).

1.4.3 Renal Effects [28, 29, 30, 31, 32, 33]

The higher level of lead may cause acute renal failure and then due to insufficient renal blood flow, the level of the nitrogenous compound in blood will increase (Coyle et al.2005; Wedeen et al.1979). Lead causes renal dysfunction that high-dose (>60 µg/dL) and low dose (~10 µg/dL) of lead exposure (Grant, 2008). Acute nephropathy is characterized by an impaired tubular transport mechanism, morphologically shows the emergence of degenerative changes in the tubular epithelium and includes the presence of nuclear inclusion bodies with lead protein complexes. Chronic lead exposure causes irreversible alternations in the renal physiology which may result in, hypertension and hyperuricemia (Rastogi, 2008). Toxic nephropathy occurs in only is 1% of all cases of the end-stage renal disease, which require dialysis or transplantation (Wing A. J. et al, 1978).Acute administration of lead results in its excretion via glomerular filtration and tubular secretion. Lead enters into renal tubular cells across the luminal and basolateral membranes. In rat renal cortical slices, lead enters the cell as a free ion, probably by an active transport process (Vander A.J. et al., 1977).

1.4.4 Reproductive Health Effects [34, 35, 36, 37, 38]

Lead affects the reproductive system of both men and women. In men reduced libido, reduced motility and number of sperm, chromosomal damage,abnormal prostatic function and changes in serum testosterone are observed, whereas women are vulnerable to prolonged and abnormal menstruations, infertility, miscarriage, stillbirth, premature membrane rupture, premature delivery, menstrual irregularities, preterm deliveries and stillbirths (Flora et al., 2011; WHO, 1986). Lead exposure affects the development of a fetus and also causes hypertension (Saleh et al., 2009). The blood lead levels remain same in both mother and infant since lead is present in the mother's blood, which passes through the breast milk and also through the placenta (Dart et al. 2004).Lead damages the germinal epithelium and spermatocytes, thus it causes sterility in males (Goldfrank et al., 1986).

1.4.5 Cardiovascular Effects [39, 40, 41, 42, 43, 44, 45, 46, 47]

The chronic exposure of lead or the existence of lead nephropathy may develop cardiovascular disorders like hypertension, ischemic coronary heart disease, cerebrovascular disease and peripheral vascular disease (Navas-Acien et al., 2007; ATSDR, 2005). Even low blood lead (Pb) levels are known to cause cardiovascular mortality in the general population, which makes it a major public health-related problem (Menk et al., 2006). However, insufficient information is available to prove the existence of any causal relationship between lead exposure and clinical cardiovascular outcomes (Navas-Acien et al., 2007). Cardiovascular disease is one of the major causes of mortality in the worldwide human population. The existence of environmental toxicants like lead and other metals in a particular region may explain the trend of population variation suffering from cardiovascular disease rates (Bhatnagar, 2006; Weinhold, 2004). Natural blood lead level is 0.016 µg/dl, which is about 600 times lower than the standard set for children by the United States Department of Health and Human Services Centers for Disease Control and Prevention (CDC) (Flegal& Smith, 1992). Studies have shown that heart rhythm disorders were more frequent in groups of men occupationally exposed to lead. Occupational exposure of lead is well known to produce symptoms like decreased heart rate variability (Poręba et al., 2011), more frequent incidence of tachycardia, and irregular heart rate (Gajek et al., 2004; Poręba et al., 2010a).

Pica in pregnancy **(48, 49, 50, 51)**

Pica is a psychological disorder in which pregnant women crave to eat soil, ceramic fragments or other nonfood materials. In some instances, these materials may contain high levels of lead. As a result, high blood lead levels may occur in these pregnant women. Lead can cause serious prenatal brain damage in the fetus since it can cross freely from the material to the fetal circulation through the placenta in pregnancy (Shannon, 2003; Erdem et al., 2004). Pregnant women with higher blood lead levels are often exposed to preterm labor, miscarriage, spontaneous abortion or stillbirth, low birth weight (Baghurst PA, McMichael AJ et al., 1987).

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