eJBio

Electronic Journal of Biology, 2020, Vol.16(S1)144-152

Reassessing the Implications of Lead Toxicity on the Environment and its Consequences on Human Health

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Citation: Parvez Masih A, Ssr B, Rajesh G et al. Reassessing the Implications of Lead Toxicity on the Environment and its Consequences on Human Health. Electronic J Biol, 16:S1

Received: October 25, 2020; **Accepted:** November 17, 2020; **Published:** November 24, 2020

Research

Abstract

Rapid industrialization is a global trend and a cause of concern for those who care about its unwanted consequences. Industries rely heavily on chemical processes requiring heavy metal compounds which eventually lead to their efflux or emission into the surrounding environment. Heavy metals are toxic in nature to varying degrees and cause a host of diseases in man. Lead (Pd) is a greater health hazard owing to its extensive use in the products that come in our contact on a daily basis. Lead pipes are a source of lead exposure through water whereas the antiknock compounds cause its exposure through air. This review takes a closer look at the various physiological effects of lead toxicity in the light of latest studies that have added significant pieces of experimental evidence to our knowledge of mechanisms underlying toxic effects of Lead which often prove lethal and may even go undetected. The review discusses the possible sources and routes of lead exposure and elaborates on its toxic effects with special reference to nervous system, cardiovascular system, haemopoietic system, excretory system and reproductive system. It is hoped that a thorough understanding of the mechanisms of lead toxicity will lead to development of better strategies of prevention and treatment of lead toxicity.

Keywords: Heavy metals; Lead toxicity; Antiknock compounds; Environmental pollution; Toxicant exposure

Introduction

Lead, also known as Plumbum (Pb) is a natural element with a greyish blue shade. It has wide occurrence and is usually found in soil and water and being non-biodegradable in nature it stays there for an indefinitely long time posing a persistent problem for the biotic components of ecosystem. It has low melting point and is one of the heavy metals potent enough to cause not just human ailments but equipped with the capacity to threaten almost all living organisms in different ways. In fact, lead ores account for 0.002 per cent of the earth's crust. They include galena (lead sulphide), anglesite (lead sulphate), cerussite (lead carbonate) and pyromorphite (lead chlorophosphate). Human use of lead is an age-old practice. Some sources in the available literature indicate that humans have been using lead for more than 6000 years. The excavations carried out at various sites where the remains of ancient civilizations existed have shown the use of utensils made of lead such as trays and some ornamental artifacts. The most common salt of lead which causes toxic effects is lead acetate which was used in the ancient time to sweeten wine [1]. Some historical accounts available today suggest the possible use of lead in plots to kill royal individuals. Pre-industrialization literature usually addresses the cases of lead toxicity among workers, slaves or the lower strata of society [2], giving the impression that perhaps the members of the ruling class had remained unaffected by it and there exist no recommendations to limit the usage of lead in that time. Currently, the softness property of lead makes it most suitable for various domestic and industrial applications such as in making paints, dyes, glazed tiles, batteries, soldering, cable coverings for radiation sheathing and processing, weapons production, boat construction, and printing etc. [3,4]. The suitability of lead in a wide variety of domestic and industrial uses has increased the chances of its exposure. Lead is a significant pollutant to the atmosphere that impairs our organ systems through exposure via air, water or food. In addition it can enter our bodies from objects of daily use and household items such as cosmetics, beauty products, and batteries etc. In recent decades lead exposure has increased many-folds due to excessive use of chemicals and mining. The unregulated mining activities have exposed lead depots in the environment which further aggravate the threat. Mining has posed a huge problem before the locals who live in areas surrounding lead mines. As stated by Burki TK Zamfara, Nigeria has been witnessing artisanal gold mining for decades, and child mortality has increased by up to 40%. Today the population of Bagega has a lead reading of 78,000 ppm which is around 195 times higher than average [5]. The prevalent use of lead has exposed children, adults, animals and plants to lead toxicity in the majority of industrial areas. Given the severe health risks caused by lead toxicity, the U.S., the European Countries, and Can-

ada have framed guidelines for the uses of lead and have put in place an efficient administration to track its unscrupulous usage. However, in developing countries like India, there is need for a strict policy on the use of lead in various industries. Rapid industrialization, over population, and unqualified employees in battery repair units are contributing factors to lead toxicity in India. In addition to the common uses of lead in paint, weapons, battery recycling and car repair, lead is also used in herbal and traditional medicines in India which is quite surprising and even hazardous in the light of what we currently know about lead toxicity. Chambial S reported a case of lead toxicity due to the use of herbal diabetes control medication prescribed by an ayurvedic practitioner [6]. Many other researchers have similar findings that pose questions about the credibility and quality control of ayurvedic drugs as per international norm [7,8]. New understanding has emerged with the availability of toxicological tests on such use of lead which was hitherto considered safe and harmless and as a consequence of this the developed nations have framed public policies to regulate the incidence of lead toxicity. This has decreased the chances of lead exposure in the occupational group, but still many developing countries such as India, need regular monitoring of lead exposure and strict implementation of policies to minimize it for betterment of workers. Many developed world countries have discouraged common use of lead, but despite this various studies indicate that lead toxicity continues to persist as a serious hazard to community health and the population groups with the greatest risk of exposure are young children and staff engaged in battery repair, construction, mining, and a few other manufacturing industries. The children when compared to adults are more likely to contribute to lead toxicity owing to the softness of their tissues, organs and bones [9]. Kalra et.al are of the view that lead poisoning occurs more in infants and children than adults due to increased absorption of lead in the guts of infants and young children than in adults [10,11]. The overexposure triggers lead poisoning, which is one of the most severe and best-recognized toxic environmental diseases in children. Lead contamination constitutes roughly 0.6 per cent of the global disease burden. Lead is a highly toxic element because it causes a variety of harmful effects at low dose levels. The Center for Disease Control and Prevention (USA, 2012) has revised the normal blood level of lead for adults and children up to 10 µg/dl and 5 µg/dl respectively, whereas previously it was same for both children and adults. In addition, there is no definite threshold value below which the exposure to lead can be considered healthy. Lead is not known to serve any biological role that is essential in our body but its presence in the body can lead to toxic effects [12]. The symptoms of lead toxicity differ considerably among individuals depending on their age, gender, nutritional intake and lead content. Poisoning and its features vary even for organic and inorganic lead. One can say, despite extensive research, there is still a debate on the toxic effects of lead, its dosage, route of exposure, degree of damage, co-factors aggregating health risk and the length of exposure. According to govt. of India notification of November 2016 regulation of Lead contents in house hold and decorative paints rule 2016, Govt of India has prohibited production, sale of decorative paints having lead or its compound more than 90ppm [13]. Breathing bad and polluted air at home or workplace, polluted dust, leaded fuel, paint water, food, soil, paint chips, and cooking utensils may cause lead exposure. Children are more likely to eat wall paint chips because of their childish habit of placing everything in their mouths and the sweet taste of lead adds to the temptation of kids. If parents are engaged in lead battery recharging industry, mining and smelters, the chances of lead exposure are higher. Ingestion, inhalation, and exposure to skin are among the most probable sources of lead toxicity. When body Lead is taken up, it is deposited in body mineral depots i.e. bone and teeth. Deliberate ingestion is the most common method among infants while inhalation and unintentional ingestion are more frequent in occupational workers. Hyperactivity, lower game activity, low IQ, slow learning cycle, poor level of test performance pattern and anorexia are usually seen in children with higher lead exposure. Lead toxicity causes defects of basophilic microcytic, hypochromic anemia in the central nervous system [14]. The chronic exposure of Lead produces reduced processing speed, fine and gross motor deficits, generally decreased cognitive functioning and fatigue [15]. Most study researchers believe that lead toxicity induces hypertension, developmental disorders, renal failure, and anemia, resulting in poor learning and memory levels in workers subject to occupational exposure of the metal [16-18]. The use of lead is inevitable in various consumer products such as paints, ceramic glazes, batteries, metal goods and in iron and steel plants. Human interaction with lead is preserved by breathing at polluted workplaces, swallowing paint chips or tainted soil. Lead compounds have been commonly used as antiknock compounds which are released from vehicles into the air and such leaded fuel has been the primary source of lead in the atmosphere. Taking lead out of gasoline has reduced exposure in many countries. However, because of its malleability, resistance to corrosion, and low melting point, lead has been widely used in industries and its levels remain high in many areas [19]. The situation in India is comparatively better following a ban on the use of leaded fuel in few metropolitan cities where the rates of its emission remain comparatively higher.There are few other sources of lead toxicity alongside leaded gasoline, such as coal and oils, lead

smelters, tobacco smoke, and solid waste combustion. Lead gains access in drinking water due to the presence of lead in some pipes, soldering and fixtures, but use of CPVC pipe fittings has reduced the chances of lead exposure. Intake of paint flakes is one of the major routes for lead toxicity among children. Lead exposure has also to do with industries or occupations such as coal mining or smelters, and therefore coal-based thermal power plants are increasing the prevalence of lead in their surroundings. Lead gets deposited in soil or water and in due course it has a high probability of reaching the humans through the food chain.

Need of Review

Science is never static in nature as the process of scientific research and exploration is dynamic to the core. This becomes more relevant in the contemporary landscape of science when there is an explosion of knowledge and sharing of information is almost instantaneous. Heavy metal toxicity is as an area of intense research due to the pathologies associated with exposure to various heavy metals. There is a great abundance of data on routes of lead exposure, its pharmacology, and its harmful effects on man and animals. However, the exact mechanisms underlying various pathological conditions are only being discovered recently. Thus, every new study on lead toxicity expands the corpus of literature that already exists on the subject. Whereas some studies corroborate the existing hypotheses there are certain studies which add new dimensions to our knowledge and often cause paradigm shifts in it.

In case of lead, the bulk of recently emerging information mostly relates to molecular mechanisms of lead toxicity which involve interaction of lead compounds with the molecules engaged in biological pathways of cellular defense, DNA replication, protein synthesis, regulation of cell multiplication and apoptosis. At a finer level these very processes form the molecular basis of all the physiological processes encountered in lead-induced pathology. Thus, it is felt that all the available literature on various important aspects of lead toxicity needs be updated to give the readers an overview of the problem that is a global environmental concern.

One of the major aims of this review is to highlight recent advances in lead toxicity research so as to enable the planners, policy makers, environmental enthusiasts and medical practitioners in devising better strategies to minimize the industrial use of lead and cope with the unwanted lead exposure. A review of the information will also help environmental enthusiasts and medical workers in presenting reliable information before such people who run the risk of occupational lead exposure such as those working in battery factories, recycling systems, manufacturers of cosmetics, ayurvedic and conventional medical practitioners, veterinarians, researchers and others working in places where lead exposure is inevitable. This comprehensive analysis focuses on the latest lead toxicity investigations. It is a compilation of most of the harmful effects of lead discussed in one place so as to benefit researchers, policy makers, health professionals and financial planners in particular and to educate the vulnerable and susceptible people who might develop lead-based toxicity in general.

Effects of Lead on Nervous System

An enormous number of researches have demonstrated that the heavy metals such as Pb, Hg, and Cd etc have detrimental effects on our health. Lead is equipped with a high potential to jeopardize our health once we are exposed to it. Children are more vulnerable to lead exposure as their nervous system is under developing stages. Duration of the lead exposure is discussed by Davis et al., for dose interdependence. They found that lead exposure at a concentration of 10-15 µg/dl was causing abnormal nervous system performance. The extent of damage on the nervous system is determined by the dose, type of lead containing compound, exposure route and duration of exposure. Lead toxicity impairs the central nervous system which is evident in neurocognitive dysfunction and modification in nerve cell neurophysiology, triggering of hallucinations, short attention span, sluggishness, memory problems, mood changes and psychiatric disorders [21-23]. In reference to duration and dose of lead exposure, Davis has reported abnormal nervous system performance by 10-15 µg/dl or higher levels of lead exposure [24]. The dosage and length of the toxicant exposure determines whether the toxic effect is acute or chronic. Talia Sanders et al., have proposed that since calcium ions can be substituted by lead it may explain the passage of lead through the blood-brain barrier [25] which is another key site for neurotoxic effects of lead [26]. G W Goldstein observed that lead may interrupt the formation of the neural networks without any apparent pathological modifications. Many researchers have reported myelin sheath loss, neuron degeneration, disrupted neurotransmission and retarded neuronal development. Bressler J et al. have inferred a significant link between blood lead level and IQ through a test of children in the United States. They also explored how lead disrupts the function of Ca^{++} as neurotransmitter at synapse and also interferes with protein kinase C which is a key molecule in calcium-mediated signaling [27]. Many researchers have opined that it inhibits the release of neurotransmitters like glutamate which is essential for learning function. Lead is known to alter sodium ion concentration thereby impairing cell-to-cell contact, raise producing capacity for action, secretion of neurotransmitters (choline, dopamine and GABA),

and the regulation of absorption and retention of Ca^{++} by synaptosomes. Both the central nervous system and the peripheral cells are affected by the exposure to lead. Few other researchers are of the opinion that peripheral malfunctioning of the nervous system in adults under the influence of lead is greater than that of the central nervous system [28]. Children are more susceptible to lead toxicity and experience neurological and behavioral changes such as low learning activity, low class concentration, poor study performance and low IQ [29]. C Parikh asserts that in almost every case of lead poisoning encephalopathy is identified. Striking characteristics include lack of sleep, heavy heading, head ache, vomiting, stupor, loss of control and coma [30].

Sanders et al. reported that lead primarily affects the central nervous system, producing a severe impact on the growing nervous system of children, which makes them more vulnerable. Lead passes through the blood brain barrier and causes neurotoxic effects by distorting the structure of cerebral cortex, hippocampus, and cerebellum. They also mention significance of biomarkers for lead toxicity [31]. Jain NB et al. have established an interrelation between low dose lead exposure and anemia among Indian children. They also considered the association of lead toxicity with various other factors such as children's age, total period of breast feeding, parents' literacy status, maternal heath, father's occupation, family living status and total number of children in a target family [32].

Effects of lead on cardiovascular system and blood

Lead is expected to alter blood vessel permeability and synthesis of collagens. Reza et al., reported that low-level exposure to lead acetate can cause hypertension in both humans and laboratory animals, changes in heart beat rate and contractility [33].

Many workers noticed contractile shifts, elevating the systolic blood pressure of rats exposed to lead. A study released in The Lancet Public Health Review, USA, reports that 2,56,000 premature deaths from cardiovascular disorders in the USA could be associated with past middle-aged lead exposure in older adults aged 44 years or older [34]. Ana Acien Navas et al., stressed the causal association between lead exposure and hypertension in her report, but did not conclude with firmness on the role of lead in other cardiac disorders [35]. Anemia is the most serious form of toxicity caused by lead. A reduction in the lifespan of red blood corpuscles and impaired heam biosynthesis is a predictor and tell tale sign of lead toxicity. The low chronic lead exposure has been found to be associated with blood pressure elevation [36,37]. Developed nations such as the US grant labour holidays to employees if lead levels in their blood are equal to or above 60 µg/dl and they are not permitted to rejoin work until blood lead levels drop to <40µg/dl [38,39]. During measurement of blood lead levels among children and adults, multiple studies point out paint flakes to be a major reason causing lead exposure in the babies.

Effects of Lead on Haemopoietic System

Lead has significant effects on heam synthesis. US health agency and Indian health advisory consider 10 µg/dl blood lead level (BLL) as safe but studies suggest that even 5 µg/dl blood level of lead may also cause negative health effects in a few cases depending on age, gender, genetic makeup and nutritional status of the subjects and these aspects need detailed study. Continuous exposure to lead causes inhibition of certain cytoplasmic and mitochondrial enzymes and can adversely affect the synthesis of heam in the body [40]. Lead inhibits three main enzymes: Delta Amino dehydratase of levulinic acid, Delta Amino synthetase of levulinic acid, and Ferro chelatase [41]. The metabolic reactions controlled by these enzymes affect and increase the urinary levels of random ALA, coproporphyrin, erythrocyte protoporphyrin and zinc protoporphyrin [42]. The US Health authority recommends that 10 µg/dl lead in the blood is safe but several researches indicate that the inhibition of ALA dehydratase begins at 5 µg/dl BLL which further increases complicated metabolic disorders, and finally, ALA rises in plasma and is excreted in urine [41,43]. Michael Kirberger found that lead displaces metal ions in proteins which is physiologically important. He studied possible interactions between lead protein complexes and toxicity, and found that Pb^{++} had substituted Ca^{++} in 5-aminolevulinic acid dehydratase (ALAD) and Zn^{++} in calmodulin (CAM). He also mentions Pb adoption ability to structurally diverse binding and it plays an active role in molecular Pb toxicity [44]. K Mahaffey observed during the study of lead toxicity on rats that deficiency affects the retention of lead in the kidneys, liver and increased urinary excretion of lead [45]. Hemoglobin synthesis is curbed by the loss of essential enzymes involved in haem synthesis. R Lilis et al., have found that Delta amino levulinic acid dehydrogenase is highly sensitive to lead, its inhibition may increase ALA in the blood, and it may be observed in urine and plasma at low level of lead exposure. A number of researches have shown retarded haem synthesis due to inhibition of several essential enzymes involved in its biosynthetic pathway. To put it precisely, it appears that the biochemical implications of lead toxicity on the blood involve disturbed heam synthesis, impaired functioning of mitochondrial enzymes e.g, ferrochelatase, and effects on delta amino levulinic acid and amino levulinic acid synthetase. Lead toxicity disturbs the functioning of various key enzymes to retard anemia and results in heam synthesis. In

their research, Amit Kumar et al., found that the presence of lead in pregnant women reduces delta amino levulinic acid dehydrogenase levels [46]. Imran Khan Mohammad et al., have evaluated the antioxidant status of 35 painters aged 20 to 50 years from Lucknow, who had blood lead levels ≤ 400 µg. It was found that even on mild exposure the levels of blood lead in painters were about seven times higher than in controls. It was also accompanied by low antioxidant activity in the subjects exposed to lead. The levels of the delta aminolevulinic acid dehydratase were also substantially decreased and zinc protoporphyrin increased among the exposed painters when compared with the control group [47].

Effects of Lead on Kidneys and Liver

Lead is toxic to multiple organs and hence the kidney and liver which are central to the overall metabolism also show detrimental effects under lead exposure. Given this effect of even mild lead exposure, many developed countries have framed guidelines which raise health concerns. Saeed Al Waleed observed that when mice are exposed to sub lethal doses [0.4,0.8 and 1.2 mg/kg body weight] of lead acetate for 12 weeks a meaningful escalation in functions of the key liver enzymes such as alanine aminotransferase, aspartate aminotransferase, gamma–glutamyl transferase, alkaline phosphatase and lactate dehydrogenase was found, which was suggestive of an underlying liver abnormality [48]. Blood lead level is contained in bones at over 90 per cent [48]. Generally, lead is excreted from the body very slowly. Several researchers have stated unequivocally that lead impairs the functional capacities of the kidneys. MA Loghman found that acute lead poisoning causes disruption of proximal tubular architecture along with functional disturbances including amino aciduria, glycosuria, and phosphaturia in human and animal models [49]. Many workers have reported findings about the interrelationship between renal failure, hypertension, hyperuricemia and gout. Nolan CV et al. have stressed the irreversibility of chronic lead nephropathy which is typically accompanied by interstitial fibrosis [50].

Many researchers and civil agency reports have demonstrated that lead toxicity induces histopathological changes in the proximal tubular epithelium, and interstitial, nephritis causes alteration there. Chronic lead toxicity has an effect on the hematopoietic, gastrointestinal, excretory, and reproductive and nervous systems [51]. High level exposure to lead [>60 µg/dL] can cause dysfunction in the renal system. Even lower levels of lead exposure (~10 µg/dL) can also pose the same problem [52]. Tubulointerstitial and glomerular changes describe kidney failure resulting in hyperuricemia, hypertension and renal breakdown [52]. In his study Carmignani et al. stated that under the influence of the oxidative stress it induces, the pathological effect of lead exposure on the renal systems of both people and animals tends to result in renal toxicity. Nevertheless, an earlier study suggested that clinically significant damage to kidneys occurs only in chronic exposure but not in acute exposure [53, 54].

Effect of Lead on Reproductive System

Although lead toxicity affects the reproductive organs in both the sexes yet the deleterious effects of lead on female reproductive organs are relatively more pronounced than in males. A variety of studies have shown that the occupational exposure of lead causes inferior semen quality and libido disruption. Lu wang found decreased sperm concentration and poor semen quality on lead exposure and similar findings are reported for test weight in rats in many studies [55]. Many researchers have reported that lead has adverse effects on testicular tissues, reduces diameter of seminiferous tubules, and decreases sperm yield in experimental animals. Many studies clearly indicate that the effect of lead toxicity on the reproductive system is influenced by the route of exposure, as inhalation produces weaker effects than oral administration of lead on experimental animals. Yousuf et al., have found that lead acetate exposure to female rabbits for 8 weeks (5 days a week) causes degenerative changes in growing and mature follicles, and degeneration of endometrial epithelial lining [56] SE Chia et al., have performed a study on 35 male patients having depressed sperm profile without any known medical reason. The aim was to find a correlation between blood concentrations of lead, cadmium, mercury and copper with different seminal characteristics viz volume, sperm count, sperm viability, sperm morphology and its movement. All patients had normal mean concentrations of lead, mercury, copper and zinc except cadmium concentration. Although the asthenozoospermic group had a significantly higher mean PbB level (7.2 pg/Dl) than the normozoospermic group (5.1 pg/dL), yet the researchers concluded that higher blood cadmium has an adverse effect on spermatogenesis, semen volume etc and patients have more immature spermatozoa than others [57]. Saxena DK et al., found that male weaned albino rats co-exposed to lead and cadmium for 120 days show decreased sperm count than rats exposed to either lead and cadmium alone. They further asserted that the changes in sperm count and sperm morphology are more due to Cadmium than Lead [58]. Beata M Pace et al., reported that the BALB/c mice were exposed from Postnatal Day (PND)1 to PND 42 to 0.1 ppm lead acetate, which was delivered during the first 21 days with mother's milk and thereafter with drinking water. After PND42 test for fertility, sperm DNA and the macrophage number in lead-exposed males was

done, which yielded normal result. On their mating with non exposed females a clear downfall in fertility is reported. The authors concluded that 0.1 ppm lead acetate exposure at neonatal stage is enough to produce adverse effects in adult male mice. An increased number of testicular apoptotic cells (<1n of DNA) can be diagnosed with defective sperm function [59]. Cuiling Li et al., found that male adult mice show low sperm count, agility, higher sperm proportions with compromised sperm morphology and notional sperm DNA integrity when exposed to lead acetate for six weeks in drinking water [60]. Lancranjan et al. reported that high level of lead is associated with a reduction in libido and an increase in semen abnormality in the exposed workers [61]. Udayraj Premdas Nakade et al. observed the effects of exposure of various doses (30, 100 and 300 ppm) of lead acetate for 28 days and compared the response with untreated control. Histopathological examination of the uterus showed histological changes, endometrial thickening, uterine lumen restriction, and endometrial gland defilements [62]. A noticeable damage in follicular growth and decreased follicular size were reported during the identification of the protective role of vitamin E in exposure to lead acetate by Durgesh Nandini Sharma et al., [63]. Eugenia Dumetriscu et al. demonstrated structural changes in ovaries, uterus, follicular growth and fallopian tubes and found a correlation of these changes with the dose of lead acetate exposure to Wistar female rats. These changes are indicators of poor fertility in female rats [64]. Andrei N et al., reported the consequences of prenatal lead subjection on various parameters of estrogen triggering in the uterus of the pre-pubertal rats. In prenatally and perinatally exposed rats, estrogen-induced responses like endometrial stroma edema, and movement of eosinophils towards the endometrium and related effects were found. The overall effects resulted in a decrease of fertility in rats [65]. J Xuezhi et al., wrote an article on a series of studies in China from 1978 to 1991, which discusses a possible link between low-level lead exposure to reproductive systems and its harmful effects. Its effects on menstrual status and the result of pregnancy were most noticeable in the predominance of menstrual disease, accidental abortion and threatened abortion among exposed women. Increased levels of lead were observed in the mother's milk and blood of infants which suggests transplacental crossing of lead [66].

Effect of Lead among Pregnant Women

There are extensive studies of lead toxicity among children, and the same applies to pregnant women among adults. Sir Thomas Oliver said the chances of miscarriage among the girls engaged in pottery workshop before marriage increase two-fold and the pregnant women who continued to work in pottery workshop have risk of unsuccessful pregnancy three times more frequently than those who had worked in ordinary homes after their marriages [67]. Ong CN et al., in their research discussed the possibility of lead crossing placenta and getting access to the breast milk. They collected mother's blood sample, umbilical cord blood and breast milk from 114 women who were occupationally unexposed to lead. Their work suggested crossing of the placenta by lead and also increased the chances of lead contamination of milk [68,69]. Some studies have mentioned that the British ceramic industry in the 19th century was aware of lead toxicity. Lead toxicity causes adverse effects on the uterus, changes in endometrium, serious impairment of the reproductive capacity, increased chances of spontaneous abortion, impaired fetal growth and even fetal loss in various animal and human models. Lead absorbed by the pregnant mother is transferred to the developing fetus quite readily [70]. RA Goyer mentioned that in the absence of placental fetal barrier, lead reaches the fetus which produces adverse effects on the nervous system at very initial stage and has been reported even in 3 months old foetus [71]. Marie Lynn Miranda et al., have shown that blood lead among pregnant women may impair cognitive development even at small levels [72]. Important studies concerning human and animal exposure to lead are recorded on irregular endocrine secretions during pregnancy. Shally Awasthi et al., in a study on pregnant women of slums reported that pregnant women living in the slums of Lucknow having relatively higher BLL (30µg/dL) were found to have lesser chances of low birth weight babies [73]. Women living in Ecuader's Andean communities and engaged in the production and application of Lead based glazes have very high concentration of lead in their breast milk and low levels of blood lead. Dumitrescu et al. observed degenerative changes in the ovary and uterus in female rats during gestational exposure to lead acetate [73].

Conclusion

The literature reviewed here presents an overview of lead toxicity as it is understood today. The widespread use of lead and its compounds in various forms has been prevalent over centuries of evolution of human civilization largely because the harmful effects of lead on human health were completely under dark. Toxicity of lead and the mechanisms underlying its adverse effects on physiology came to light only recently and the regulatory steps undertaken since then have led to emergence of appropriate substitutes of lead compounds. However, the threat of lead toxicity still persists because certain sectors of industry continue to rely heavily on lead products.

The exploration of lead-related health hazards reveals a wide spectrum of serious implications for various

systems and processes of the body such as nervous system, digestive system, haemopoietic system, excretory system and reproductive system. This information is vital in creating lead-free environment and in developing proper antidotes against toxic exposure of lead. Periodic assessment of statistics related to lead toxicity and review of the whole problem is an important prerequisite for minimizing the cases of lead poisoning and also for developing suitable therapeutic remedy against it

Acknowledgement

Authors are grateful to management committee, Shia Post Graduate College, Lucknow for their kind support. We are highly indebt to Prof Abbas Ali Mahdi, Former Vice Chancellor, Lucknow Eras Medical University, Lucknow and Presently, Head, Department of Biochemistry, King George Medical University, Lucknow. He is renounced research worker of lead toxicity and has hundreds of research articles and academic talks on lead toxicity. His valuable advices have played pivotal role in writing this review article.

Author Contributions

Masih, A Parvez and Baqri S S R wrote the manuscript. Gupta Rajesh, Bajpai K Gaurav and Abbas S Sadiq edited the manuscript.

Funding

Authors have not received financial assistance from any agency or funding body.

Conflict of Interest

The authors declare that the review article is written in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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