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Lead Toxicity Research: A Review of the Literature

Jingfeng[1*] Ding, Hao[1] Wang, Wei[2] He, Zhengtao[1] Xi

1. Pollution Control Engineering Technology Center of Tai Zhou City, Taizhou 318000, China
2. Zhejiang Association of Solid Waste Recycle and Soil Remediation, Hangzhou 310012, China

Abstract: Lead toxicity has always been regarded as a symbolic problem in toxicology. Lead, as a widely used industrial heavy metal, is highly persistent in the natural environment and has certain toxicity, and brings huge risks to human health. This article reviews the physical and chemical properties of lead, the sources of lead pollution, summarizes the main exposure pathways of lead, the damage of lead poisoning to the human body, and some prevention and treatment methods for lead poisoning, and discusses the strategies of controlling lead pollution. Once lead enters the human body, the existing methods are difficult to eliminate its impact on human tissues, and prevention-oriented strategies must be adopted.

Keywords: Lead Toxicity; Poisoning; Human Health;

Introduction

According to Ara' research [1], because lead has unique physical and chemical properties, it has been widely used by humans in various industries, so lead has become a common pollutant. Because lead is highly persistent in the natural environment and has certain toxicity, it poses a huge threat to the environment and human health. In the past few decades, lead toxicity has been a hallmark problem in toxicology [2]. This literature review is mainly to introduce the toxicity assessment of lead by studying on its characteristic, sources, exposure pathways, hazards to human health, approaches of preventing and treatment.

Classification

According to the International Agency for Research on Cancer (IARC), inorganic lead is classified as category 2A and may be carcinogenic to human, and organolead is classified as Group 3-Unable to classify. In addition, the US EPA classifies lead and its compounds as B2, which is a possible human carcinogen [3].

1. Characteristic of lead

2.1 Physical properties

Lead (Pb) is a natural element in the earth's crust, with an average concentration of about 15 to 20 mg / kg. It is most easily found in galena (PbS), angle iron ore (PbSO4) and copper iron ore (PbCO3). Lead is a blue-gray, dense, soft and malleable corrosion-resistant metal and it is solid at room temperature and has a low melting point [4]. Due to its low melting point and excellent corrosion resistance, lead is widely used in daily life and industrial production [5]. Lead can be used in a variety of materials, including metal alloys, batteries, ammunition, X-ray shielding materials, chemically resistant linings, and pigments. In addition, lead has historically been widely used as an additive in a variety of paints and gasoline (ATSDR 2007).

2.2 Chemical properties

The three oxidation states of lead are Pb (0) (lead metal), Pb (II) and Pb (IV) respectively. Among them, in the environment, lead primarily exists as Pb (II). The most common form of existence of lead is Pb (II)[6]. Lead Pb (0) can be found in nature, but it rarely occurs. For Pb (IV), it will only form under extreme oxidizing conditions, while inorganic Pb (IV) compounds cannot usually be found in ordinary environments. Although organic lead (II) compounds are known, in general, organic lead chemistry is mainly in the tetravalent (+4) oxidation state [7].

Lead will form thin films of lead sulfate, lead oxide and lead carbonate when it is exposed to water or air; these films can actually be regarded as a protective barrier, they can effectively slow down the corrosion process of the underlying metal. Lead also has two sides, on the one hand it can form plumb and lead acid in alkali, and it can form plumb and lead salt in acid. In theory, lead can be used as a substitute for hydrogen in acid, because its hydrogen position in the electromotive force series is slightly higher than that of hydrogen. However, due to the small potential difference, the high over voltage of hydrogen will stop this process [5].

3 Source of lead

Lead and lead compounds have been used in all aspects of our lives, such as paint, batteries, ceramics, gasoline, pipes, cosmetics, etc. Human activities, including the use of fossil fuels, leaded gasoline, certain industrial facilities, and lead paint used in the past are the main sources of lead. Lead may release to our environment from past and current usage, or it may be discharged into the environment from industrial sources and contaminated sites [8].

Although the natural lead content in the soil is very low, the lead content in the environment has increased significantly. Due to mining, smelting and refining activities, especially near mining and smelting sites, the concentration of lead in the soil has been found to be very high. Lead will also be released into the air through the pollution source, it may migrate over a long distance, and then settle to the ground, and then adhere to the soil particles. Of course, the lead in the soil may also move into the groundwater or under groundwater, which will depend on the characteristics of the soil and the type of lead compound [8].

4.Exposure pathways

Inhalation, ingestion and dermal absorption are the main exposure pathways of lead. The most common ways of human exposure to lead primarily happens by ingestion or inhalation.

4.1 Ingestion

In the general population, lead exposure occurs mainly through ingestion, such as swallowing lead-containing foreign bodies and accidentally ingesting lead-containing soil. Among the ingested lead, 20% to 70% will be absorbed by the body, and the proportion of lead absorbed by children is usually higher than that of adults [6].

4.2 Inhalation

Inhalation is another major route of lead exposure. In general, the particle size of inhaled lead, the amount of respiration, deposition amount and the mucous cilia clearance rate determine the amount of lead absorbed by the respiratory system. The inhaled lead can be absorbed by the body, and children have a higher absorption rate than adults due to the higher breathing rate [4].

4.3 Dermal

Dermal exposure is common exposure to organic lead among related industrial workers [6]. However, in the general population, it is not a significant pathway.

5.Hazard assessment

Exposure to lead can cause damage to the human's nervous system, reproductive system, kidney system, hematopoietic system and cardiovascular. The resulting health risks include neurotoxin, reproductive damage, developmental delay, damage to hemoglobin synthesis and so on. Among them, the nervous system, kidneys and blood are the most sensitive aims for lead toxicity. However, since the pathophysiology of lead toxicity is very complicated and there are many ways of lead acting in biological systems, any system or organ in the human body may be affected [9]. Blood lead content is considered an important indicator for evaluating lead exposure [3]. The research of Suljević [2] seems to confirm this. They exposed Japanese quail to lead (II) chloride ($PbCl_2$) through water ingestion, and found that $PbCl_2$ triggered a series of complex events in the biological system of Japanese quails, but these events were first observed in the blood and serum parameters and then occurred into the hematopoietic centers [2].

5.1 Nervous system

The nervous system is considered to be the most sensitive target for lead poisoning compared to other organ systems [10]. Exposure to lead can cause gradual degradation of certain parts of the brain, causing irritability, inattention, memory loss, headaches, and sluggishness. It can even cause convulsions, paralysis, and coma at very high exposures [11]. Lead exposure can affect the central nervous system and the peripheral nervous system. In adults, the impact on the peripheral nervous system is more pronounced, while the impact on children's central nervous system is more prominent. Children are the group most susceptible to lead toxicity on the nervous system because the developing nervous system has a higher rate of lead absorption than adults. Low-lead exposure may cause children to lose concentration, hyperactivity and irritability, while high-lead exposure may cause decline in intelligence, memory and hearing, developmental delay, and more severe cases may cause permanent brain damage or even death[10].

5.2 Reproductive system

Lead can cause a lot of damage to the human reproductive system and its functions (both male and female). Common symptoms of women include infertility, miscarriage, premature delivery, pregnancy-induced hypertension and so on. The adverse effects on men include decreased libido, decreased sperm motility and reduced numbers, chromosomal damage, and abnormal prostate function [12].

Humans are usually more likely to cause renal impairment at high levels of lead exposure (> 60 μg / dL) [13]. Abnormal renal function can generally be divided into acute kidney disease and chronic kidney disease. Acute kidney disease is characterized by impaired renal tubular transport mechanisms. Although it does not cause protein excretion with urine, abnormal excretion of glucose, phosphate and amino acids can be found. Chronic kidney disease may be more severe than acute kidney disease. It may lead to irreversible damage to renal function, such as changes in the glomeruli and tubules, which will lead to renal failure, hypertension, and hyperuricemia [14].

5.3 Hematopoietic system

Lead inhibits the synthesis of hemoglobin, which is accomplished by inhibiting the relevant key enzymes in the heme synthesis pathway, including delta-aminolevulinic acid dehydratase (ALAD), aminolevulinic acid synthetase (ALAS) and the mitochondrial enzyme ferrochelatase. The hematopoietic system will be affected to a certain extent. Lead inhibits the above three important enzymes in this pathway, but its effect on ALAD is more obvious, and its inhibitory effect has been used clinically to assess the degree of lead poisoning. Lead will also make the cell membrane brittle, which will shorten the life of circulating red blood cells. The combined effects of the two processes will lead to anemia [10].

5.4 Cardiovascular

Both acute and chronic lead poisoning can cause heart and blood vessel damage, leading to many cardiovascular diseases, including hypertension, ischemic coronary heart disease, cerebrovascular accidents and peripheral vascular diseases,

and more serious may lead to death [7].

6 Treatment and prevention

6.1 Treatment for lead poisoning

There are many methods for treating lead poisoning, including:

6.1.1 Succimer

In general, treatment with succimer as chelation therapy is believed to reduce blood lead levels, thereby protecting the development of children's nervous system and improving their mental health [15].

6.1.2 Metal chelating agents

Metal chelating agents such as chelating salt disodium calcium edentate (the calcium chelate of the disodium salt of ethylene-diamine-tetracetic acid) is always considered effective in the lead poisoning treatment. The principle is that those chelating agents always have a nice affinity to the removing agent. Taking the chelating salt disodium calcium disodium salt as an example, the chelating agent of lead has a greater affinity for calcium than lead, so calcium chelates can be exchanged with lead to form lead chelates, which are then excreted through urine, leaving only harmless calcium [15].

6.1.3 Antioxidants

Many antioxidants can be used to combat the toxicity of lead and its compounds. A new technique, nanoencapsulation of antioxidants, is thought to improve the biodistribution and bioavailability of poorly soluble drugs through solubilization [10].

6.1.4 Beta-carotene

Some studies have shown that β-carotene has been observed to have antioxidant effects, not related to chelation, but it does play an effective role in lead poisoning [14].

6.1.5 N-acetylcysteine (NAC)

A study on workers exposed to lead found that N-acetylcysteine (NAC) can effectively reduce blood lead levels of workers. Studies have shown that all workers receiving NAC treatment have significantly increased glutamate dehydrogenase activity. Therefore, NAC is considered that it could be as a great option for chronic lead poisoning treatment in humans [16].

6.2 Prevention for lead poisoning

Once lead enters the human body, it is almost difficult to remove it or eliminate its damage to human body tissues. Based on this fact, and considering the toxic effects of lead, preventive measures play a more important role than therapeutic measures [10]. The initial methods to prevent lead poisoning mainly include personal intervention, preventive medicine strategy and public health strategy [17].

For individuals, nutrition is very important in preventing lead poisoning. Researches have shown that some nutrients include certain minerals, mineral elements, flavonoids and vitamins are significant in restoring the imbalanced oxidant ratio that arises due to oxidative stress. The intake of these nutrients can provide some protection for the human body, thereby reducing the damage of lead to human body systems, organs, and tissues [10].

The goal of preventive medicine is to screen blood lead levels in children at high risk of lead exposure. If the lead content in their blood is detected to exceed the standard, they will be treated accordingly to control the harm of lead poisoning to the human body and further prevent the accumulation of lead [17].

Compared with preventive medicine strategies, public health strategies have a greater impact. Its strategy is to reduce and control the risk of lead exposure in habitable areas. Without controlling lead pollution and lead poisoning, many preventive measures have been put forward by the public health service, including prohibiting the establishment of the lead industry

around habitable areas and prohibiting the use of lead if there are relevant alternatives.

7 Bioavailability

Lead has very low bioavailability [18], which makes lead in soil difficult to be absorbed by plants. Therefore, it can be said that, of all the toxic heavy metals, the content of lead in plants is the least. Generally speaking, soil characteristics affect the potential absorption and transport of heavy metals by plants, but in most soils, water-soluble and exchangeable lead easily absorbed by plants accounts for only 0.1% of the total lead [18].

Conclusion

Due to its unique physical and chemical properties, lead has now become one of the most widely used industrial heavy metals. The main sources of lead are fossil fuels, industrial production and mining-related human activities. Among them, inhalation, ingestion, and skin absorption are the main exposure routes of lead, and the most common route of human exposure is ingestion or inhalation. Children are considered to be the most sensitive group exposed to lead. Lead will cause huge harm to human nervous system, reproductive system, renal system, hematopoietic system and cardiovascular. Exposure to high levels of lead may even lead to death, bringing a huge risk for human health. In order to deal with the damage caused by lead to human health, a strategy of prevention should be prioritized. Succimer, metal chelating agents, etc. can be used to treat lead poisoning. However, once lead enters the human body, it is almost difficult to remove or eliminate its damage to human tissues with existing methods. Controlling the release of lead from the source and cutting off the possibility of lead entering the human body may be the most effective strategy for controlling lead pollution.

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