

Cadmium Exposure and Health Effects

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Abstract: This article provides a comprehensive review of the sources, exposure pathways, biological effects, and toxicology of cadmium, as well as the diagnostic methods for cadmium poisoning. We delve into the release of cadmium from natural and anthropogenic sources, occupational and environmental exposure pathways, and its impact on human health, including its absorption, distribution, metabolism, and excretion processes. Additionally, the article covers specific health issues caused by cadmium, such as kidney damage and osteoporosis, along with current biomarkers used for diagnosing cadmium poisoning. By synthesizing current research findings, our aim is to offer strategies and insights for the prevention, diagnosis, and treatment of cadmium poisoning.

1. Introduction

Cadmium is a naturally occurring heavy metal and a widely prevalent environmental toxic pollutant[1], a dose of 30 milligrams of cadmium (Cd) can induce toxic reactions[2]. Long-term or high-dose exposure to cadmium is associated with a variety of health problems, raising widespread public health concerns. Even in cases where trace amounts of cadmium are detected, overexposure can occur, leading to serious health-related issues [3]. Most cadmium poisoning reactions are chronic, with acute cadmium poisoning, especially high-dose acute intoxication, being extremely rare in clinical practice. Due to its odorless and tasteless characteristics, cadmium poisoning is insidious, and hospitals can easily misdiagnose it. However, cadmium poisoning is particularly dangerous because it progresses rapidly and can lead to death within hours [2].

Given the increasingly evident hazards of cadmium, this article reviews the latest research developments regarding the sources of cadmium, its biological effects, diagnostic methods, and possible preventive measures, providing valuable information for researchers, public health experts, and policymakers.

2. Sources and Exposure Pathways of Cadmium

2.1 Natural and Anthropogenic Sources of Cadmium

Cadmium naturally exists in soil, minerals (sulfides, sulfates, carbonates, chlorides, and hydroxide salts), and water [4,5]. The metallurgical industry (zinc smelting plants or units purifying cast iron) has the highest exposure to cadmium [4,6,7]. Cadmium is primarily released into the environment

through activities such as mining and smelting. Additionally, the use of fertilizers, industrial waste discharge, and the combustion of fossil fuels are significant anthropogenic sources of cadmium [8]. Exposure to cadmium mainly occurs through oral ingestion, dermal absorption, and inhalation of contaminated dust, food, or water [9].

2.2 Occupational Exposure

Occupational exposure is one of the main pathways of cadmium exposure, especially for individuals working in the cadmium production and processing industries. This includes battery manufacturing, welding, galvanizing, and handling other cadmium-containing materials. Cadmium easily reacts with other commonly used substances in batteries and accumulators, including nickel-cadmium batteries, alloys, pigments, plastic stabilizers, dyes, and paints, as well as in glass manufacturing and the electrical industry [4,5,10-14]. Employment in the metal industry or working in cadmium-contaminated sites greatly increases the risk of exceeding safe cadmium exposure levels [15].

2.3 Environmental Exposure

Apart from specific occupational activities or smoking, diet is the main source of cadmium exposure in the general population [13,16]. Especially, the frequent consumption of large amounts of foods such as rice, potatoes, wheat, leafy salad vegetables, and other cereal crops is the most significant source of cadmium in the diet [17]. Environmental exposure primarily occurs through pathways such as drinking water and the food chain (especially through seafood and crops grown in contaminated soil) [18,19]. It is mainly caused by emissions from atmospheric pollutants, metal smelting plants, coal combustion, and the dumping of sewage sludge [18]. It has been reported that in heavy industrial areas, the levels of cadmium in the air, water, soil, and plants exceed the standard, posing a threat to public health [20,21]. Furthermore, researchers using health risk assessment models have found that cadmium in these media poses a slight carcinogenic and non-carcinogenic risk to humans [22-24].

3. The Biological Effects and Toxicology of Cadmium

3.1 Human Absorption and Accumulation of Cadmium

Cadmium is primarily absorbed through the respiratory system (approximately 13-19% of cadmium comes from the air), but it can also enter through the digestive system (approximately 10-44%), after which it is distributed throughout the body [25]. Cadmium has a long half-life in the human body. Once absorbed, it accumulates irreversibly, especially in the liver and kidneys [26]. The biological half-life of cadmium in the human body averages between 16 to 30 years [25]. This element most commonly accumulates in the lungs, liver, kidneys, pancreas, testes, muscles, adipose tissue, and skin, where it inhibits the activity of sulfur-containing enzymes [4,14,27-29]. Cadmium is expelled from the human body at a slow pace, predominantly through urine, feces, saliva, or perspiration, presenting significant health hazards.

3.2 The mechanisms of cadmium's impact on human health

Cadmium can interfere with various cellular and molecular pathways, leading to oxidative stress, DNA damage, and apoptosis. These mechanisms are the foundation of the various health problems caused by cadmium exposure. Cadmium exposure in cell lines can lead to chromosomal anomalies,

increased sister chromatid exchanges, breaks in DNA strands, and DNA-protein crosslinking. It has the potential to induce mutations and chromosomal deletions[30,31]. Cadmium toxicity results from the reduction of glutathione levels, binding to protein's sulfhydryl groups, and the increased generation of reactive oxygen species (ROS) including superoxide ions, hydrogen peroxide, and hydroxyl radicals. Additionally, cadmium suppresses the function of antioxidant enzymes, namely catalase, manganese-superoxide dismutase, and copper/zinc-superoxide dismutase[32]. Animal studies have shown that cadmium accumulation in the liver significantly increases the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase, and alkaline phosphatase. Various liver tissue pathological changes, including parenchymal damage and inflammatory cell infiltration, as well as the activation of Kupffer cells, were observed[33]. Currently, the molecular mechanisms of cadmium-induced liver toxicity primarily involve thiol group inactivation, oxidative stress, mitochondrial dysfunction, and apoptosis[34]. The molecular mechanisms of cadmium-induced renal toxicity primarily include oxidative stress, mitochondrial stress, endoplasmic reticulum stress, apoptosis, autophagy, DNA methylation, and calcium ion dysregulation[35]. Cadmium disrupts the metabolism of essential minerals like calcium, magnesium, iron, zinc, and copper within cells, leading to bone demineralization, osteomalacia, and osteoporosis. It also interferes with the regulatory functions these ions are involved in[14].

3.3 Specific Health Problems Caused by Cadmium

Cadmium can cause a range of health issues, including liver damage [36], kidney damage [37], lung injury [14], bone damage [14], reproductive system issues[10][12]and cardiovascular diseases [38]. The liver and kidneys are the primary organs involved in the elimination of cadmium and are particularly sensitive to its toxic effects [39,40]. Research indicates that there is a 10% rise in the occurrence of renal tubular proteinuria when the concentration of cadmium (Cd) in urine reaches 1.0 nmol/mmol of creatinine[37]. Some chronic lung diseases, such as emphysema, asthma, and bronchitis, as well as hypertension, are believed to be associated with low-dose, slow cadmium poisoning[6,23,41,42]. Long-term exposure to cadmium (Cd) particles through inhalation is linked to abnormalities in lung function and chest X-rays that show signs consistent with emphysema [14]. One of the most extensively documented diseases caused by cadmium exposure is Itai-Itai disease [25]. It is manifested by pain in the bones and joints, a specific waddling gait due to bone distortion, and susceptibility to complex fractures in the joints . Cadmium can cross the placenta and barriers to reach the fetus, causing teratogenic effects [10,27]. Previous studies have found that cadmium has the potential to affect the reproduction and development of several mammalian species, and recent research has confirmed these findings [43]. Compared to animal studies, it's reported that cadmium exposure can reduce sperm density, volume, and count, and increase the proportion of immature sperm forms [44]. Following these issues are defects in sperm production, sperm quality, and the secretory function of the accessory glands. Additionally, cadmium exposure can reduce fertility and serum testosterone levels [45]. In the female reproductive system, the function of the ovaries and the development of oocytes may be suppressed. Under the toxic effects of Cd, steroidogenesis decreases, and ovarian bleeding and necrosis can occur simultaneously [43]. It has been reported that the rate of spontaneous miscarriage and the time to pregnancy increase, while the live birth rate decreases [44]. Research indicates that cadmium is associated with endothelial dysfunction and the thickness of the intima-media in the carotid artery (IMT). Furthermore, the formation of atherosclerotic plaques is promoted in the body [46]. Following cadmium poisoning, there may occur early endothelial dysfunction associated with cardiovascular diseases (CVD), loss of endothelial cell structure leading to cell death, and events of thrombus formation [47].

Long-term exposure to Cd can lead to a variety of diseases, such as cancer, leukemia, and

genotoxicity [12-14]. However, many studies have confirmed that exposure to heavy metals, even at low levels, can cause serious damage to human organs. Acute ingestion can cause abdominal pain, burning sensation, nausea, vomiting, drooling, muscle cramps, dizziness, shock, coma, and even convulsions within 15-30 minutes [48,49].

4. Diagnostic methods for cadmium poisoning

Blood and urinary cadmium concentrations are common biomarkers for assessing cadmium exposure and poisoning. The extended half-life of cadmium, reaching up to 30 years, can be attributed to its prolonged retention in the body. However, the relatively brief half-life of cadmium in blood, spanning three to four months, suggests it may be indicative of recent exposure. The detection threshold for cadmium concentration in blood is established at 0.3 µg/L[50]. Elevated levels of cadmium in the blood are linked to heightened mortality risks from all causes, cardiovascular diseases, and Alzheimer's disease among hypertensive patients. The impact of blood cadmium levels on mortality related to cardiovascular issues may be especially significant in hypertensive patients who have never smoked [51].

Beta-2 microglobulin in urine can serve as an early indicator of kidney damage, this study utilized metabolomics to analyze urine samples from OCCP patients and healthy controls, identifying significant differences in metabolite profiles. It found elevated levels of specific metabolites like creatine, glutamic acid, quinolinic acid, and nicotinic acid in OCCP patients, suggesting these as potential biomarkers. Creatine, in particular, showed promise as a sensitive marker for diagnosing and monitoring OCCP, highlighting its potential utility in the absence of effective treatments and reliable biomarkers for this condition[52].

Although diagnosing cadmium poisoning presents challenges, it can be effectively assessed and identified through the detection of biomarkers in blood and urine, supplemented with imaging studies, to evaluate cadmium exposure and its health impacts. This requires medical professionals to possess a high level of vigilance and a deep understanding of these diagnostic tools.

5. Conclusion

The close association between cadmium exposure and human health has been extensively proven, posing significant risks to both individual and public health. This review thoroughly examines the main sources and exposure pathways of cadmium, including its natural occurrence and anthropogenic activities, occupational and environmental exposure, as well as potential contacts in daily life. By deeply analyzing the absorption, distribution, and toxicological effects of cadmium in the human body, we reveal how cadmium can lead to a range of health issues, including but not limited to kidney damage, osteoporosis, cardiovascular diseases, and the occurrence of cancer. In the face of the health threats posed by cadmium, multifaceted preventive and management measures need to be taken. This includes strengthening industrial and environmental regulation, reducing cadmium emissions, raising public awareness of the risks of cadmium exposure, and implementing strict safety and health monitoring programs among groups at high risk of occupational exposure. Future research should aim to gain a deeper understanding of the toxicological impacts of cadmium, develop new diagnostic methods, and explore effective treatment strategies to mitigate the health effects of cadmium. In summary, the issue of cadmium exposure requires attention and comprehensive strategies from the entire society. Through ongoing research, education, and policy reforms, we can better prevent and manage health problems caused by cadmium, thereby protecting human health and environmental safety.

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