Accumulation of Toxic Elements Disrupts Metabolic Processes in the Human: Review

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Abstract

Background Toxic elements are inorganic substances that do not have a physiological or functional role within the human body. Most metabolic processes are disrupted due to their accumulation through prolonged exposure to them from the environment. Toxic elements make up an extensive and very toxicologically dangerous group of substances. Usually, four elements are considered: Hg (mercury), Pb (lead), Cd (cadmium), and As (arsenic).

Results Exposure to methylmercury has been associated with widespread neurological injury and diffuse encephalopathy. However, selectivity has been noted. The substance is toxic to some groups of nerve cells over others. Clinical signs of acute mercury exposure include Headache, nausea, and tremors. After chronic exposure, the onset of peripheral neuropathies has been described.

Conclusion The accumulation of toxic heavy elements in general and cadmium, mercury, and lead (Pb) in particular leads to an imbalance in the metabolic processes and results in fat accumulation in the body. Thus, it causes obesity.

Keywords: Obesity; Mercury; Lead; Cadmium.

1 Introduction

Toxic elements are inorganic substances that do not have a physiological or functional role within the human body. Most metabolic processes are disrupted due to their accumulation through prolonged exposure to them from the environment. Toxic elements make up an extensive and very toxicologically dangerous group of substances. Usually, four elements are considered: Hg (mercury), Pb (lead), Cd (cadmium), and As (arsenic).

Not all toxic elements are poisonous, some of them are necessary for the normal life of humans and animals. Therefore, it is often difficult to draw a clear line between substances that are biologically necessary and harmful to human health. In most cases, the realization of one effect or another depends on the concentration. With an increase in the optimal physiological concentration of an element in the body, intoxication can occur, and a deficiency of many elements in food and water can lead to quite severe and difficult-to-recognize deficiency phenomena.

As described, toxic elements in the environment and food can trigger various poisonings causing irreparable damage to human and animal health, as serious as teratogenic effects, cancer, and even death. It is essential to consider that high concentrations of these metals in the organism of living beings alter biochemical and physiological processes, causing various pathologies [1].

The three hazardous heavy elements are mercury, cadmium, lead (Pb), and As (arsenic), which are even
deadly. Toxic elements can affect a range of species permanently by preventing biological processes, including enzymatic inactivation by the creation of links between the element and sulfhydryl groups (-SH) such as (Hg-SH) and other functional groups of proteins and enzymes [2]. They can indeed change the active conformation of biological molecules or remove other metal ions.

Most physiological processes typically carried out are disrupted by lead (Pb), which also influences the peripheral nervous system and changes gene expression, and also causes deficiencies in vision and hearing [3]. The main route through which lead enters the human body is through the respiratory system and the most dangerous lead (Pb) molecules are those that are soluble [4]. Once inside the body, it interacts with proteins’ -SH groups to change the way they function or interact with other necessary elements for their active sites. Lead (Pb) interacts with several calcium-dependent functions because it shares chemical similarities with calcium [5].

Lead (Pb) can also affect a person’s lipid profile over time, including activating lipid synthesis, altering polyunsaturated fatty acid metabolism, causing peroxidation, causing mutations in artery cells, and inhibiting antioxidant enzymes [6]. It may also stimulate lipid synthesis in various organs, primarily the liver.

In particular, the -SH in proteins like albumin, metallothionein, and others is where cadmium (Cd²⁺) interacts with anionic groups [7]. Similar to how Ca²⁺ and Zn²⁺ are handled by other crucial metal cations, cadmium (Cd²⁺) sequesters those systems as a cation [8]. The primary cells that protect the body from oxidative damage can be sequestered and weakened by cadmium, which also appears to interfere with the mitochondrial respiratory chain. Nonetheless, interference with redox homeostasis is probably a component of several stages of Cd-induced carcinogenesis [9]. For instance, endonucleases, which are used in DNA repair, activated by redox processes, and inhibited by Cd, are involved in DNA repair. Cd is harmful to a variety of human tissue and organs, with the kidneys, bones, liver, and lungs being the main target organs [10].

Mercury (Hg) that binds by protein changes the production and activity of proteins and the cell cycle may be disturbed due to Genetic damage; therefore mercury has been connected to autism and several cancers [11]. One significant reason for this element’s biological action is Mercury’s strong selectivity (Hg²⁺) for the -SH groups of proteins. Hg changes the permeability of cell membranes by causing the creation of mercaptides and inactivating several enzymes, structural proteins, or transport mechanisms in addition to the thiol group of cysteine can bind to mercury (Hg²⁺), creating a complex where the Hg atom is joined by valence bonds to the nearby Fe atom [12].

Mercury can increase lipid peroxidation, oxidative stress, mitochondrial malfunction, and changes in heme metabolism by modifying the status of intracellular -SH groups.

2 Cadmium (Cd)

Cadmium is a toxic element widely distributed in the environment [13]. Cadmium is a toxic metal with no physiological function and is commonly considered harmful [14]. For many non-smoking people, diet is the most cause of external exposure to cadmium. For smokers, tobacco is the primary cause of exposure to cadmium toxicity. The amount of cadmium absorbed by the digestive system is about 5%, while the lung absorbs about 60% of tobacco smoke [15,16]. When comparing two people at the age of 50 years, one of whom smokes for life and the other is a non-smoker, the concentration of cadmium in the blood is 30 mg, while the other is 15 mg. It is known that cadmium levels are five times higher than those of non-smokers [17–20]. By inhalation, the cadmium cysteine complex enters the circulatory system [21]. Cadmium binds to albumin and metallothionein when it enters the bloodstream and reaches the liver. When it comes the liver, cadmium releases metallothionein, and programmed cell death occurs [22]. In the hepato-intestinal cycle, cadmium enters the bile ducts as conjugates of cadmium and glutathione [22]. Some studies on human childbirth revealed that cadmium was associated with poor fetal growth before birth due to exposure to large amounts of cadmium, as well as low birth weight and delivery at a young age compared to the gestational age [23,24].

The clinical manifestations of cadmium exposure can be classified into acute and chronic symptoms and those resulting from inhalation and ingestion, according to the time and method of disclosure. Usually, Contamination, like food, is often chronic; however, it is common in the population Professionals find acute and chronic poisonings very distinct. Symptoms of poisoning depend on the dose, duration, and type of exposure, the presence of other chemicals, and the variable properties of cadmium. Their effects on health are similar to those of any hazardous substance and depend on the person’s habits [25].

Inhalation of large amounts of cadmium can produce a symptomatic picture that is not well defined at first but is later characterized by fever, gastrointestinal disturbances, chest pain, shortness of breath, and acute pulmonary edema that can cause death from respiratory failure [26]. Another effect that often occurs after exposure to cadmium is skin and eye irritation;
symptoms take several hours to appear after exposure and usually last from one to two days.

Workers exposed to cadmium for an extended period may develop a condition that includes pulmonary emphysema and proteinuric renal tubulopathy. In these situations, additional consequences have also been noted, including anemia, liver problems, and modifications in mineral metabolism [27]. There is typically bone loss; even relatively moderate levels of prolonged exposure can result in irreparable damage to the renal tubules, causing glomerular disease and renal failure. Those occupationally exposed to air pollution usually experience pulmonary consequences, including lung cancer. However, other dangers may manifest months or years after cadmium exposure, such as the risk of cancer and reproductive issues [28]. The body’s cadmium fates include: According to previously mentioned, cadmium can enter the bloodstream by being absorbed in the stomach or intestines after ingesting food or drink and absorbed in the lungs after inhalation [28]. In the first stage, the mucosal cells absorb the cadmium in the intestinal lumen [29]. In the second stage, a portion of the cadmium passes the lateral membrane of the enterocytes to enter the circulation [30].

According to several studies, obesity and cadmium are related [31,32]. A survey conducted by Skulnaya et al. (2014) on young women over 22 demonstrated the association of cadmium content in hair with body mass index [33]. According to research by Akinloye et al. (2010), there is a correlation between total body mass index and cadmium content in diabetes patients [34]. Over the past years, there has been a growing concern about the health effects that the human body can be exposed to in an environment due to the accumulation of the toxic element cadmium, especially in children and pregnant women. There are significant hypotheses about environmental exposure at an early stage that affects the structure of tissues and the functions of organs, which ultimately leads to causing many future diseases [18].

3 Mercury (Hg)

Mercury is a toxic heavy metal without any physiological function in the human body [35]. In regards to the environment, mercury is widespread, present in many natural products, and a large part of daily life [36]. Mercury is founds in different forms: elemental mercury (Hg), inorganic (IHg), and organic mercury (like Methylmercury) [37,38]. Inorganic mercury is an allergen and produces digestive problems [39]. They are water-soluble and have a 7% to 15% bioavailability after consumption [40]. Scientists have not yet found how much mercury the human body requires. Contrarily, it is highly poisonous and builds up in the brain, where it may damage the neurological system [41]. Therefore, it is advised to avoid mercury because it is fast disappearing and should not be handled, carried in hand, or touched. Mercury has a half-life of more than a year (possibly many years) in the human brain [42].

Methylmercury (MeHg) that is ingested concentrates mainly in the kidneys and causes renal damage [43]. On the other hand, humans are primarily exposed to elemental mercury (Hg) by breathing mercury-contaminated air, which is then quickly absorbed and distributed throughout all organs [4,44]. The absorption of elemental mercury after intake is low—less than 0.01%. The brain and kidney are the main organs that elemental mercury affects [40]. The element mercury is distinguished by its solubility in fats. Elemental mercury (Hg) crosses the blood-brain barrier, while inorganic mercury compounds do not cross the blood-brain border because it is insoluble in fats compared to elemental mercury [40].

Henriksson and Tjälve suggested that mercury in dental amalgam fillings enters the brain and settles in its tissues via the smelling pathway in the nasal cavity, as on the transfer of manganese particles [45–47]. The mercury level in food, like other minerals and salts, is measured in parts per million [48]. The risk level for a girl weighing 60 kilograms is six micrograms of mercury daily. If the mercury level in canned light white tuna is 0.35 parts per million (micrograms per gram of fish), she can eat about 17 grams of tuna per day (without any other fish) or a weekly meal of 120 grams. Smaller than mercury because it dissolves in water and not in fat. The processes underlying mercury toxicity are still poorly understood. However, it is generally recognized that this element may bind with other molecules, deplete sulfhydryl groups, disrupt cell cycle progression, and cause apoptosis.

Exposure to methylmercury has been associated with widespread neurological injury and diffuse encephalopathy [49]. However, selectivity has been noted. The substance is toxic to some groups of nerve cells over others. Clinical signs of acute mercury exposure include Headache, nausea, and tremors. After chronic exposure, the onset of peripheral neuropathies has been described [50].

Numerous sad occurrences recorded in the literature made it feasible to establish a direct association between poisoning by methylmercury and its deadly effects on embryonic brain development. When methylmercury exposure was severe, it was found that pregnant women had minimal or no symptoms. Conversely, prolonged inhalation of mercury vapor has been associated with tremors, personality changes, and unconsciousness [51].
4 Lead (Pb)

Lead (Pb) is the most potentially toxic element. Additionally, it exists in the environment constantly [52]. It is a significant worldwide ecological danger, an ecologically determined part, and one of the causes of many diseases for many people [53,54]. Lead accumulation affects the bones, kidneys, heart, and all body systems [55]. When lead (Pb) accumulates in the body, frequently over months or years, it causes toxicity and death [56]. Lead (Pb) has significant health risks, even at small doses. Lead poisoning, which hurts mental and physical development, is particularly dangerous for children under six. When lead poisoning is severe, it can be fatal.

Most lead (Pb) absorption happens in the digestive and respiratory systems [57]. By breathing in lead-contaminated air, more than 30% of lead (Pb) is absorbed into the bloodstream [58,59]. After the process of absorbing lead (Pb) from the digestive system, lead (Pb) remains in the bloodstream for about a month at a rate of 99% of its concentration, and then it is distributed to tissues [60]. Lead (Pb) reduces and inhibits the levels of glutathione and aminolevulinic acid dehydrogenase. At the same time, it stimulates lipid peroxidation by direct binding to phosphatidylcholine, which eventually leads to changes in the biological properties of the cell membrane [61–63]. A study by Olusegun I. Alatise and Gerhard N. Schrauze stated that the concentration of lead (Pb) for breast cancer patients was very high in their samples taken from blood and hair and that the increase in lead level was correlated with the increase in tumor growth [64]. So lead (Pb) is a very toxic and carcinogenic factor.

Protoporphyrin ferrochelatase is an enzyme that encodes the ferrochelatase gene in the human body [65]. Protoporphyrin ferrochelatase activates the enzyme ferrochelatase by converting protoporphyrin 9 to heme B, where a chelation reaction occurs with iron (II) ions [65,66]. Protoporphyrin and ferrous form a complex called heme. Hemes include important proteins, such as hemoglobin and myoglobin [67]. Other complexes can also be formed with zinc (zinc- protoporphyrin ) [68]. Measuring the level of complexes zink protoporphyrin and the level of Lead (Pb) in the blood is evidence of the person’s lead poisoning. The stories of zink protoporphyrin accumulate inside the red blood cells due to the inhibition process in the production of heme. The levels of free protoporphyrin reach very high levels when exposed to lead poisoning and remain elevated for several months. A ferrochelatase deficiency may result in unreliable analytical results [19]. The story of lead the body absorbs, and the harmful effects of measuring lead in tissues are unpredictable and are only helpful in estimating doses. Therefore, it is necessary to determine an appropriate preventive approach. Cyclic adenosine monophosphate is a critical essential intermediate in several biochemical functions. After several studies, many scientists proved that exposure to lead leads to the stimulation of cyclic adenosine monophosphate after the stimulation of calmodulin [69]. The release of reactive oxygen and nitrogen species is one of the effects of lead exposure and the depletion of antioxidants [70].

Finding the preclinical impacts of lead exposure is essential for early planning since the detrimental effects of lead (Pb) are sometimes only seen once the condition has progressed. Any tasks involving the extraction, processing, preparation, and use of lead, its metals, alloys, and compositions, and all products containing information are considered occupational activities with a high risk of lead exposure. Examples include using lead in plumbing, printing, ceramics, pottery, and soldering and tinning. In this instance, exposure can also occur through the skin, the gastrointestinal tract, or inhalation. Lead paint, pesticides used in gardening, lead, solder pipes that carry drinking water, and lead-sealed cans are a few non-occupational forms of lead exposure.

Table 1: Clinical Aspects of Chronic Toxicities of Cadmium, lead, and Mercury [26].

<table>
<thead>
<tr>
<th>Metal</th>
<th>Target Organs</th>
<th>Primary Sources</th>
<th>Clinical effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadmium</td>
<td>Renal, Pulmonary Skeletal</td>
<td>Industrial Dust and Fumes and Polluted Water and Food</td>
<td>Proteinuria, Glucosuria, Osteomalacia, Aminoaciduria, Emphysema</td>
</tr>
<tr>
<td>Lead</td>
<td>Nervous System, Hematopoietic System, Renal</td>
<td>Industrial Dust and Fumes and Polluted Food</td>
<td>Encephalopathy, Peripheral Neuropathy, Central Nervous Disorders, Anemia.</td>
</tr>
<tr>
<td>Mercury</td>
<td>Nervous System, Renal</td>
<td>Industrial Dust and Fumes and Polluted Water and Food</td>
<td>Proteinuria</td>
</tr>
</tbody>
</table>
5 Conclusion

We can say that the accumulation of toxic heavy metals in general and cadmium, mercury, and lead (Pb) in particular leads to an imbalance in the metabolic processes and results in fat accumulation in the body. Thus, it causes obesity.

Conflict of Interest: No conflicts of interest exist between the authors and the publication of this work.

Ethical consideration: The ethical committee approved the study at University of Grodno, Belarus.

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