Chapter 6

Physical Chemical Properties of Some Heavy Metals (Arsenic, Lead And Copper) and Their Effects on Health

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Abstract

Heavy metals are associated with industrial processes, environmental pollution and natural resources and can have serious adverse effects on human health. Due to their toxic properties and their tendency to accumulate in biological systems, these metals can damage vital organs such as the nervous system, kidneys and liver. Through their chemical reactivity and by affecting biological systems, they can disrupt enzyme function, cause DNA damage and have carcinogenic properties. Due to their bioaccumulation, long-term exposure, even at low levels, can lead to serious health problems.

Arsenic causes serious health problems with long-term exposure. Chronic arsenic exposure can lead to skin lesions, cancer, circulatory system problems, nervous system damage and damage to internal organs. Arsenic from water sources can be a major health problem, especially in some areas.

Lead exposure occurs mainly through paint, water pipes, paint in old buildings, industrial waste and some foods. When it enters the body through

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inhalation or from sources such as water and soil, it is harmful to humans, especially children and fetuses. It negatively affects brain development and causes mental retardation, behavioral problems and learning difficulties. In adults, lead exposure can cause nervous system damage, high blood pressure, kidney problems and reproductive problems.

Copper is essential for the body but can be toxic in excessive amounts, causing gastrointestinal problems, liver damage, kidney problems and neurological disorders.Copper is commonly found in water pipes, some pesticides, copper containers and some foods. Uncontrolled exposure to these metals can lead to health problems, so it is important to limit or eliminate their sources and intake.

Long-term exposure to these heavy metals can cause serious health problems. Therefore, controlling heavy metals, reducing environmental contamination and minimizing exposure is critical for human health. To protect human health, drinking water sources should be controlled, food should be consumed from safe sources and appropriate measures should be taken to reduce exposure.

INTRODUCTION

Health; It is a phenomenon that has become a problem since the existence of human beings and is in constant search. Throughout our lives, it is expected to be a step towards a solution rather than a problem, which is why many developments in the field of health continue today. The negative external factors that our body is exposed to are increasing day by day. The understanding of healthy life will come to good places with the effect of scientific studies.

Heavy metals can become toxic even at low concentrations. They also have negative effects on human health. Some heavy metals (Arsenic, As; lead, Pb; copper, Cu; etc.) are sometimes necessary for us, but they can be toxic even if they are in excess in our bodies (Dağhan, 2011). Environmental pollution caused by heavy metals is a study that is in the focus of everyone. These current studies have drawn attention to the contents and reflections of heavy metals, their harm to the external environment and living health, the identification of polluted environments and the methods and possibilities of purification of these environments in order to prevent their negative effects on nature and living health. Therefore, the nature polluted by heavy metals can be purified by certain methods (chemical, physical, etc.) in order to prevent adverse effects on human health (Kocaer and Başkaya, 2003). Heavy metals can enter our body in various ways. Unfortunately, when they are in excessive amounts compared to our body density, removal from our body is not so fast, this excess has a toxic effect on our body (Pak J Bot,

2008, Biotechnol Adv, 2006). In this study, the physicochemical properties of some heavy metals such as arsenic (As), lead (Pb) and copper (Cu) and their effects on human health were investigated in detail.

1.Physical and Chemical Properties of Arsenic

Arsenic, a heavy metal with atomic number 33, melting temperature 887.15 °K, boiling temperature 1093.15 °K and mass number 74.92 g/mol, is in the VA group in the periodic table. It is a heavy metal between metal-metal in terms of structure. Since arsenic has both of these properties (metal-ametal), it is called a semi-metal in chemistry (Anal Chim Acta, 2003). Arsenic, which is not very important for humans, is a natural component of nature. It is toxic in non-organic form. Within the framework of the impact of industrialization, it is possible to find arsenic in chemical reactions of fossil fuels, in synthetic fertilizers, in the elimination of problems of unnatural wastes, almost everywhere (Proteomics, 2006). The general distribution of arsenic in nature (the earth's crust) is about 6 milligrams per kilogram, making it one of the most common elements in nature (Bissen, M., and Fritz H.F., 2003). In addition to natural arsenic in the form of yellow and gray crystals, it is common to find arsenic in nature in compounds with the elements sulfur (S), chlorine (Cl) or oxygen (O). Arsenic, which forms compounds with the elements mentioned above, appears in non-organic form. As I mentioned above, arsenic in its non-organic (inorganic) form is toxic. It is possible to find hydrogen (H) and carbon (C) elements in the bond structures of arsenic classified as organic. It is also possible to find non-organic arsenic in some rocks and soil, especially in ores containing copper (Cu) or lead (Pb) (Erdoğan, 2005). Normally, organic arsenic is encountered in drinking water; however, the organic form of arsenic is less important in terms of urgency because it is metabolized and is no longer toxic by methylation (Singh, T. S., and Pant, K.K., 2003).

1.1 Arsenic Sources

Arsenic in nature can be formed as a result of active volcanic movements, as well as natural processes, as a result of human events such as industrialization every day, as a result of pollution in the air we breathe, the soil we step on, and drinking water (Erdoğan, 2005).

1.1.1 Natural Resources

Arsenic, which is abundant in the earth's crust, is found in air, water, soil and living structures in highly variable parameters (DIP, A., 2001).

Some of the minerals are rich in arsenic and as a result of the weathering of minerals, arsenic in the soil passes into the water in the soil (Fujimoto, M., 2001). In some areas of heated water, arsenic, which is a heavy metal, is observed in high amounts (DIP, A., 2001). While arsenic concentration in salty waters is at low levels, it is at much higher levels in waters such as hot springs compared to salty waters. A certain part of the natural arsenic is mixed with atmospheric gases, and the remaining part can be formed due to the evaporation of high temperatures as a result of the movements of volcanic mountains. It is also possible to come across the synthesis of arsenic as a result of evaporation in the oceans and seas. Some fires, especially forest fires, can mix with nature. If we need to talk about more important sources, the most important of these is coal from fossil fuels. Depending on the types of coal, it is also possible to find different amounts of arsenic in its content (Erdoğan, 2005).

1.1.2 Non-natural Resources

The contamination of water, air and soil with arsenic as a result of human activities is a well-known phenomenon. These human behaviors can be classified as the discharge of unnatural wastes, the smelting of arsenic-rich minerals, the burning of some fossil fuels such as coal, and the use of arsenic in some industries (Leist, M., Casey, R.J., and Caridi, D., 2000). The unconscious release of arsenic-containing industrial wastes into nature is effective in the pollution of water and air as a result of natural events. As a result of these behaviors, people actually expose themselves to toxic effects with their own hands. Therefore, these unnatural sources will pollute the nature with more arsenic (Chakravarty, S., Dureja, V., Bhattacharya, G., Maity, S., and Bhattacharjee, S., 2002). Arsenic is released from the smelting of some minerals (copper, lead, nickel, zinc, etc.). Therefore, it is assumed that a large amount of arsenic is formed annually. Arsenic has also been found in abundant amounts in the soil in the light of mining studies in some geographical regions of the world (Smedley, P.L., Kinniburgh, D.G., 2002).

As a result of the burning of some fossil fuels in factories and households, arsenic oxide (As O46) enters the air and arsenic emission occurs. The mixing of ash waste resulting from the combustion of fossil fuels into the soil is also an activity that contributes to soil pollution. The burning of waste oil is an activity that causes less emissions compared to the burning of coal. Oil, which is a fossil fuel, contains a small amount of arsenic (0.134 mg/kg). Currently, arsenic compounds are used to produce glass in organized industries. This contributes to a certain degree of sensitivity of the resistive strength of the material and better wear conditions. In addition, it is known

that arsenic is used in the production of instruments that absorb toxic gases and give clean air to nature and in industries such as light technology (Fujimoto, M., 2001, Leist, M., Casey, R.J., and Caridi, D., 2000).

Some arsenic-containing chemicals (insecticides, herbicides) used in the agricultural sector have caused arsenic contamination of the soil. Since these chemicals contain high levels of non-organic arsenic compounds such as calcium arsenate, sodium arsenate and zinc arsenite, they have led to excessive arsenic residues. When we look at the agricultural sector, these practices are used by many countries to protect plants in forestry activities, although these practices remain in history. In a country like the United States, a high proportion of arsenic consumption is used for conservation purposes, as in the forestry sector (Leist, M., Casey, R.J., and Caridi, D., 2000).

2.Toxicity

Many formations containing arsenic in their structure are toxic. The most toxic of these formations is known as AsH3 (Arsin gas). If we consider the exposure time to this gas, it can be fatal (250 mg/m3) in a short time like 30 minutes. If we look at some other formations; NaAsO2 (sodium arsenate) between 14 and 18 mg/kg, NaNO3 (sodium arsenite) 4.5 mg/kg, MMA (mono methyl arsenic acid) 1800 mg/kg, DMA (dimethyl arsenic acid) 1200 mg/kg, As O23 (arsenic trioxide) average lethal dose is 34.5 mg/kg (Bissen, M., and Fritz H.F., 2003). As a result, it has been observed that non-organic forms of arsenic are more toxic than organic ones (Ng J.C., Wang J., and Shraim, A., 2003).

3. Harmful Effects of Arsenic on Human Health

Arsenic, which has toxic properties, is absorbed in our body as a result of activities such as feeding and breathing. Although the absorption rate of non-organic arsenic in the stomach and intestine is very high, the most absorption occurs in the Intestinum tenue (small intestine). Most of the arsenic taken into our body through breathing (80%) results in absorption. Inorganic arsenic is converted into compounds that are less reactive in our body than organic arsenic. The volume of methylation in adults is approximately 400 μg/day to 500 μg/day (Bissen, M., and Fritz H.F., 2003). Mono methyl arsenic acid (MMA) and dimethyl arsenic acid (DMA) are simply excreted from the body through the excretory system. However, when the methylation rate is low, toxic effects are possible (Ng J.C., Wang J., and Shraim, A., 2003). The estimated half-life of arsenic in the human body is four days (Erdoğan, 2005).

While the kidneys and liver are the organs that are most severely affected by rapid arsenic ingestion, our brain, which we thought would not be affected, is badly affected. Arsenic taken orally unexpectedly causes many side effects in our body. The resistance of our body exposed to toxic effects decreases. Some of these symptoms include burning in the mouth, vomiting, severe abdominal pain, nausea, leg cramps and burning in the throat. As a result of these events, death occurs within a few hours as a result of heart failure and circulation. Such high doses of toxic exposure can be easily recognized by the physical appearance of the poisoned person. In daily intake, arsenic accumulates in our skin, nails and hair, which are rich in keratin. In addition, high amounts accumulate in our lungs. Studies conducted with appropriate methods for diseases have revealed that the presence of excess arsenic in the water we drink increases the risk of kidney, spleen, lung, etc. cancer. In addition, scientific experiments have shown that arsenic entering our body destroys our hormonal system (Lenoble, V., Bouras, O., Deluchat, V., Serpaud, B., and Bollinger, J.C., 2002). The presence of arsenic in drinking water above a certain dose (50μg/l) can increase our body's cancer risk up to 1 percent (Morales, K.H., Ryan, L., Kuo, T.L., Wu, M.M., and Chen, C.J., 2000).

Some of the symptoms of high doses of arsenic poisoning can be listed as hyperpigmentation (skin discoloration), diarrhea, paralysis, hyperkeratosis (flaking of the skin), weakness, cancer, some nervous system diseases, anemia, high blood pressure, some circulatory system diseases, diabetes, wear and tear of blood tissue. Among these symptoms, skin diseases are the most prominent. The cancer effect occurs in certain doses in our body after a long period of time such as ten years. Kidney, bladder, lung and liver organs are the places where cancer is found (Fujimoto, M., 2001). Our body, which is exposed to arsenic for many years, is unable to eliminate even the deformation of DNA (Morales, K.H., Ryan, L., Kuo, T.L., Wu, M.M., and Chen, C.J., 2000).

4. Physical and Chemical Properties of Lead

The element lead, with atomic number 82, atomic weight 207.19 g/mol, specific gravity 11.34 g/cm3 and symbol Pb, is a bright, dense element that conducts heat and electricity like other metals. Lead is a non-reactive transition element compared to other elements. Unlike most metals, lead is widely used industrially due to its low melting point, ease of forming, ideal alloying properties and softness. Today, lead is used in construction and sanitary materials production, architectural paints, cable production, insulation and solder production, primer paints against moisture, pesticides,

hair dyes and cosmetics, rubber industry, glass industry, automotive industry, etc. (Dündar and Aslan R, 2005).

Due to the widespread use of lead in industry, human exposure to lead has become a widespread health problem and a major problem in both developed and developing countries (Özbolat, 2016).

Lead metal is resistant to sulfuric and phosphoric acids, but not to hydrochloric or nitric acids. Organic acids such as acetic acid dissolve lead in the presence of oxygen (Boldyrev, 2018). Lead is not a very reactive element, but it dissolves slowly in water under certain conditions. Therefore, lead is more susceptible to oxidation in humid environments. Lead reacts with carbon dioxide in the atmosphere to form bird carbonate. The most common lead compounds in nature are sulfur-containing galena (PbS), carbonate-containing cerussite (PbCO3) and sulfate-containing anglesite (PbSO). Lead carbonate forms a protective layer for lead. The widespread use of lead in industry and its partial solubility also increase exposure to this heavy metal. It is becoming a major problem in both developed and developing countries. The organic form of lead to which we are most exposed is tetraethyl lead (PbC2 H5).

4.1 Possible Sources of Lead Exposure

4.1.1 Smoking and Food

For non-smokers, the biggest source of daily lead intake is food and dust. As for food, cereals and legumes can contain high levels of lead, and spices may also be contaminated with lead. The use of lead-containing foods, especially acidic foods and beverages, stored or sold in metal cans can significantly increase the lead content in food and beverages. Eating fish raised in lead-contaminated water makes it easier for people to become infected. Since alcoholic beverages are acidic and lead dissolves faster in acidic environments, the storage and handling of alcohol and alcoholic beverages in metal cans can easily leach lead to consumers. Leaded pottery and ceramics transferred from tableware to food is also a source of exposure, and smoking greatly increases lead absorption. During breastfeeding, even small amounts of lead can pass into breast milk, exposing the baby to lead (Dursun et al. 2016).

4.1.2 Lead-based paints

Direct or indirect human exposure to lead in paints is common. Toys, furniture and park playgrounds painted with lead-based paint are common sources of lead pollution.

4.1.3 Lead in soil

Lead does not normally occur in soil. However, houses painted with lead-based paint or dust from home renovations, lead-contaminated soil and soil contaminated with batteries or battery waste are all sources of lead.

4.1.4 Lead in air and dust

Lead added to gasoline to prevent engine explosions is the main source of airborne lead, and lead pollution increases with traffic density. Most airborne lead is in the form of fine particles with an average mass equivalent diameter of less than 1 μm. This indicates that some of the lead in the air is transported over long distances. Lead is removed from the atmosphere by dry or wet precipitation. The residence time of lead-containing particles in the atmosphere depends on many factors, including particle size, wind flow, precipitation and emission levels. Chipping, peeling or crumbling of lead-based paint in older homes contributes to children's exposure, especially if some young children put pieces in their mouths or lick their dusty fingers. For various reasons, lead in residential paint can also produce lead dust, which can accumulate on floors, carpets, toys and other objects, leading to human exposure. Lead-containing dust can also settle on the clothing of industrial workers, leading to exposure.

4.1.5 Lead in Water

Years ago, lead was present in tap water that was piped into the city through lead pipes. According to WHO, the lead content in tap water should not exceed 0.01 mg/l (WHO, 2000). Lead is also found in metal alloys used in the joints of copper alloy pipes, which replaced the abandoned lead pipes in the 1960s. Lead in tap water rarely comes from dissolution from natural sources, but mainly from lead pipes or household plumbing systems with lead-lined pipes and fittings. So lead pollution persists. Concentrations are higher in water that is in contact with lead for long periods of time (e.g. overnight) (Dündar and Aslan, 2005). Lead concentrations can therefore vary throughout the day, making flushing faucets before use a control mechanism. If you suspect that the pipes in your home are damaged, you should flush them every time you use hot or cold water, or by running the tap for a few minutes in the morning. Lead is most soluble in soft acidic water.

4.1.6 Occupational Exposure

Occupational lead exposure is the leading cause of lead poisoning in adults. Lead workers who manufacture and use radiation protection equipment are

constantly exposed to lead. Such workers are at high risk of lead poisoning. People working in lead-containing areas, auto mechanics, painters, potters and construction workers are generally more likely to be exposed to lead (Wani, et al., 2015).

4.1.7 Lead in household items

Some kitchen utensils, such as old pottery and ceramic pots, may contain lead. Acidic substances in these items can move with the glaze and increase the release of lead. Therefore, it is more dangerous to store acidic foods such as tomato sauce, orange, tomato and other fruit juices and vinegar in glass containers (Tchounwou et al., 2012). 1.8. Clothing and Metal Jewelry: Metal-based jewelry and various clothing accessories also contribute to lead exposure. Various metals used in clothing accessories are often used without being tested for lead. Candle wicks, costume jewelry and children's backpacks have been found to contain toxic levels of lead (Sanborn et al., 2002).

4.1.8 Clothing and Jewelry

Metal-based jewelry and various clothing accessories also contribute to lead exposure. Various metals used in clothing accessories are often used without being tested for lead. Candle wicks, costume jewelry and children's backpacks have been found to contain toxic levels of lead (Sanborn et al., 2002). 1.9. Toys and School Supplies: Some children's toys and school supplies are made from lead-containing materials (e.g. some plastics and paints) or paint materials may contain lead (Şimşek and Önal, 2019). 1.10. Folk remedies and cosmetics: Some cosmetics, especially those from the Middle East, India and Asia, may contain high levels of lead. For example, certain types of cabbage (kajal, surma, sindoor) have been reported to contain high levels of lead. Some traditional medicines and cosmetics (such as cabbage) contain lead. Moisturizers, hair dyes and some cosmetics (such as eye shadow, eyeliner and lipstick) may contain lead. Consumers therefore need to be careful to buy and use only regulated products. Various cosmetic products such as kohl, kohl (alcohol), kajal, tiro and tozali also contain large amounts of lead. Using cabbage results in repeated ingestion of particles from your hands into your eyes and mouth. Toxic levels of lead have also been reported in spices produced in some Far Eastern countries (Debnath et al., 2019).

5. Effects of Lead on Human Health

Exposure to lead causes a variety of harmful effects in humans. These effects can range from mild clinical symptoms to acute or chronic very

severe poisoning. Human exposure to lead occurs primarily through the gastrointestinal and respiratory tracts. The circumstances of the effect depend on factors such as the degree of exposure, the physiological and psychological characteristics of the person or the general condition of the tissues, organs or systems exposed to lead (Boskabady et al., 2018). The clinical manifestations and progression of lead exposure differ between adults and children. This is because organs and systems are affected differently. In addition, some people are sensitive to lead toxicity.

In addition, the diet and psychological structure of the person also affect the clinic (Çaylak and Halifeoğlu, 2010). Lead exposure is associated with many health effects in adults. Most adults with elevated blood lead levels have been exposed to lead at work. Mining, blacksmithing or welding, construction including building renovation and remodeling, metals, food and canning containers, glazed porcelain and ceramic materials, glassware, automotive, lead-acid batteries, smelting, shooting ranges, automotive battery manufacturing and disposal, car radiator repair, pottery and stained glass work are important areas of lead exposure (Özbolat and Tuli, 2016). The main routes of lead exposure are the respiratory and gastrointestinal tracts. Tetraethyl lead (Pb(C2H5)4) used in Benzin 124 is also easily absorbed through the skin. About 35-40% of inhaled lead accumulates in the lungs. 37% of lead particles smaller than 1 μm are found in the alveolar region and 50% of the lead accumulated in the respiratory tract is absorbed and enters the systemic circulation (Levin and Goldberg, 2000). Of the lead ingested through food, 5-15% is absorbed from the gastrointestinal mucosa and the rest is excreted in the feces. The intake depends on the age of the individual, pregnancy status, the availability of elements such as iron, zinc, phosphate, magnesium, etc., and thus dietary characteristics.

It is estimated that healthy people ingest up to 200 mg of lead every day through their diet. In our country, adults are reported to ingest about 70 μg of lead per day through food (Fişek and Piyal, 1991).

Lead is widely distributed in the body after exposure and disrupts various biochemical processes by binding to sulfhydryl groups and other nucleophilic functional groups and contributing to oxidative stress (Kasten-Jolly et al., 2010). If you want to assess your lead exposure, you can rank it as follows: Blood lead levels above 15 mcg/dL are associated with reproductive problems, including cardiovascular disease, neurological disorders, reduced kidney function and adverse effects on sperm and semen. Delayed pregnancy, low sperm count and motility. Blood lead levels below 10 μg/dL are associated

with decreased kidney function, increased blood pressure, hypertension and the development of essential tremor, a degenerative disease of the central nervous system. The most prominent symptom of poisoning is involuntary tremor of the arms and hands while eating or writing. There is also evidence that adults with blood lead levels below 5 μg/dl may have reduced kidney function (WHO, 2010). More research is needed to fully understand the varying health effects of lead from person to person.

5.1 Lead Metabolism

Lead is absorbed into the body primarily through inhalation, then through the mouth with food and to a lesser extent through the skin. The particle size of lead is important for inhalation absorption. Those larger than 1 μm in diameter enter the digestive tract via the mucociliary pathway of the respiratory tract. Those between 0.5 and 1 μm in diameter enter the blood via the alveoli. Of the daily intake of lead, 40% comes from cooking utensils, 16% from food and the rest from airborne dust particles (Bellinger, 2004). The World Health Organization (WHO) reports that the permissible amount of lead in drinking water is 10 μg/L. A lack of the minerals phosphorus and calcium in the foods you consume will accelerate the absorption of lead from your intestines. When sufficient calcium is present in foods, lead absorption is reduced 10-fold (Campbell and Osterhoudt, 2000). Therefore, calcium supplementation and consumption of milk and dairy products are important for people who have been or may be exposed to lead. Adults absorb an average of 10-15% of their food intake, but this can be as high as 50% in infants, young children and pregnant women. In children, intestinal absorption is the most common route and absorption is increased when dietary levels of iron, calcium, phosphorus or zinc are low.

Lead accumulates in calcified tissues due to its low phosphate solubility (Vijayamar et al., 2012). No matter how lead enters the body, it first binds to hemoglobin in red blood cells. Once bound to red blood cells, lead circulates in the body through the blood and is stored in organs and tissues. Approximately 93% of the RBCs in the bloodstream are bound to red blood cells, the remaining 6% are bound to serum albumin, and the remaining small amount is in free ionized form in plasma. The concentration of lead in plasma is more important than in whole blood for its distribution to target organs such as the brain, lungs, spleen, renal cortex, aorta, teeth and bones. Bones are the main target organ of lead toxicity. 94% of the lead consumed by adults and 73% of the lead consumed by children is deposited and stored in the bones. The movement of lead from the blood into soft tissues is slow

and takes about 4 to 6 weeks. This is not the case in the brain, where lead crosses the blood-brain barrier slowly and has a half-life of more than 12 months. The placenta does not prevent the passage of lead and the fetus is exposed to lead through the mother (Şanlı et al. 2005). The estimated half-life of lead in blood is 35 days, 40 days in soft tissues and 20-30 years in bones (Papanikolaou et al., 2005).

The bone metabolic cycle is higher in children than in adults. Older people tend to accumulate lead. It inhibits the production of osteoblasts, the bone-forming cells. It also reduces active vitamin D 1,25(OH)2D3 by inhibiting renal hydroxylase enzyme activity, which is essential for vitamin D production (Needleman et al. 2004; Piomelli et al. 2002). In other words, exposure to pathological levels of lead can cause serious health problems such as orthoporosis, bone tumors and rickets in both adults and children (Figure 3). Lead is excreted in the urine and the rest in the intestines. Breast milk has also been shown to contain very low levels of lead (Rebelo, 2016).

5.2 Acute lead poisoning

Acute lead poisoning is a rare disease. Many records show that acute poisoning can exacerbate chronic lead poisoning if large amounts of lead are suddenly released from the bones into the bloodstream. Acute poisoning occurs in the form of gastrointestinal toxicity, but Encephalopathy can also occur in children. Acute encephalopathy occurs at blood lead concentrations between 80 and 100 μg/dl (Şanlı et al. 2005). Symptoms of acute lead poisoning usually include loss of appetite, dysphagia, abdominal pain, metallic taste, constipation or diarrhea (lead sulfide can turn stools black), vomiting, hyperactivity or lethargy, ataxia, behavioral changes, convulsions, coma (Papanicolaou, 2005).

5.3 Chronic lead poisoning

In adults, there is mild gastrointestinal and central nervous system disturbance, sometimes with flaccidity of the wrists, rarely with colic. In children, poisoning is manifested by weight loss, weakness and anemia. Early symptoms in children may be mild neuropsychological impairments that adversely affect behavior and social interactions in the classroom. Chronic lead poisoning is divided into three stages: mild, moderate and severe.

5.3.1 Mild poisoning

Blood lead concentration: 40-60μg/100ml: Muscle pain, tingling numbness, fatigue, irritability, abdominal pain.

5.3.2 Moderate poisoning

Blood lead concentration: 60-100μg/100ml: Joint pain (especially at night), muscle fatigue, chills, headache, diffuse abdominal pain, loss of appetite, metallic taste, vomiting, constipation, weight loss, high blood pressure.

5.3.3 Severe poisoning

Blood lead concentration higher than 100 μg/100 ml: lead paralysis, dropping of the wrists or feet, blue-black lead streaks (Burton's streaks) with spasms of the gums and tenderness around the navel. Colic - Severe, intermittent abdominal pain. There may be tenderness around the umbilicus (Vijayakumar et al., 2012).

5.4 Effects of lead on some important organs

5.4.1 Lead and the nervous system

Lead is a neurotoxic substance. In the early years of development of the nervous system, it can cause permanent damage, particularly in areas associated with learning pathways and memory consolidation processes. Chronic exposure to lead in childhood can therefore continue to have harmful consequences into adulthood. Chronic lead exposure in the first few years of life can cause various cognitive impairments in children and may also affect neurological development and intelligence (Souza et al., 2018).

5.4.2 Lead and the Cardiovascular System

Several epidemiological and clinical studies have revealed an association between chronic lead exposure and hypertension. The study examined 543 men aged 40 to 59 years and found a significant association between lead in the blood and systolic and diastolic blood pressure. Vaziri et al. reported that chronic lead exposure in young adult rats promotes autonomic dysfunction with increased chemoreceptor sensitization, leading to marked impairment of autonomic function in the cardiovascular and respiratory systems (Vaziri et al., 2008).

5.4.3 Lead and the Urinary System

The kidneys are usually responsible for excreting toxic substances through the urine. This is one of the most important areas affected by lead accumulation. Exposure to low levels of lead at a young age has been shown to cause glomerular hypertrophy, which is characterized by

an increase in glomerular capillary volume. Lead exposure can impair glomerular development and ultimately lead to kidney failure later in life (Orr and Bridges, 2017). Lead is one of several toxic substances associated with chronic kidney disease. Lead exposure is associated with nephropathy, renal adenocarcinoma and metabolic bone defects. Chronic lead exposure causes leukocyte infiltration. 130 It causes progressive tubulointerstitial nephritis characterized by interstitial fibrosis and tubular atrophy. Lead causes oxidative stress and calcium deposition in kidney cells. We know that there are changes in distribution. Lead also binds to the renal tubules, which also has an effect. Acute exposure impairs the transport of soluble acids and amino acids within the renal tubules. A common defect of Fanconi syndrome (Hashi, 2017).

6. Physical and Chemical Properties of Copper

The element copper is found in many parts of the world and its name is derived from the Latin word for Cyprus (aes cyprium, Cyprium ore, Cyprium, later Cuprum), where it was first discovered. The heavy metal has an atomic number of 29 and a toxic weight of 63.57 g/mol. Copper has a specific gravity of 11.34 g/cm3, a melting point of 1083 °C and a boiling point of 2300 °C. (Raven, J.A., et al, 1999.) Copper is one of the essential micronutrients abundant in various rocks and minerals. It is required for various metabolic processes in both prokaryotes and eukaryotes. At least 30 copper-containing enzymes are known that function as oxygen transporters (hemocyanins) or redox catalysts (cytochrome oxidase, nitrate reductase). Copper, Cu, is a transition metal with three oxidation states: Cu+1 and Cu+2. It is classified as a heavy metal because its density exceeds 5 g/cm3.

Its colors are yellow, dark red and brown. Copper is a soft metal. Because it is a soft metal, it is easy to shape. Copper was one of the first metals used in human history. It was used to make jewelry, weapons and other necessities in everyday life. Currently, more than 13 million tons of copper are consumed. This usage makes it the second most used metal in the world. Copper is used in its pure form as well as in its compounds.

6.1 Uses of Copper Compounds and Sources of Copper Exposure

Today, more than 400 copper alloys are used. Brass and bronze alloys are widely used, especially in jewelry. Brass, bronze, nickel and aluminum alloys are also used in coin making. Among these are very high electrical conductivity, wear and corrosion resistance, and the ability to be drawn and forged from structures and materials. Copper is therefore a component of many alloys. It reacts with acidic substances such as hydrochloric acid,

nitric acid and sulfuric acid. When copper is oxidized, it forms various compounds; sulfates, nitrates and chlorides. When these compounds enter food, poisoning known as "copper theft" occurs. For this reason, copper pots are coated with tin. Copper also has antiseptic properties. Because of this property, medicines used to treat some skin conditions contain copper.

Copper compounds, especially copper sulphate (eye stone), are used in agriculture to kill microorganisms. Recently, oxidized copper chloride has been used for this purpose instead of copper sulfate. Copper compounds are also widely used in the production of rayon threads, in the ceramic, glaze and glass industries, in pharmaceuticals and coatings. Copper's chemical resistance and appearance make it a popular material for many building and decorative materials, as well as for painting ship hulls and building exteriors. Copper's properties also allow it to be used in many plaques, vases, flower pots and other materials. Due to its high melting point, copper is widely used in cookware such as teapots and pots, as well as in industrial distillation, heating and cooling systems and plumbing equipment. Another important use of copper is in transportation vehicles, where large quantities of copper and copper materials are used (Dameron, C. et al, 1999). It is used in distilled spirits, beer vinegar, petroleum and sugar industries.

6.1.1 Some Applications of Compounds

Copper acetate is used as a fungicide, textile dye and as a catalyst in some organic reactions.

Copper arsenate; insecticides, wood preservatives.

Copper carbonate; Used as paint, varnish, ceramic products, pigments.

Copper chloride is used as a catalyst for photography, deodorants, organic chemicals and petroleum products.

Copper oxide is used as a catalyst in viscose, ceramics, colored glass and chemicals.

Copper sulphate is used in insecticides, viscose, anthelmintics, dyes, leather and wood products.

6.1.2 Uses of Copper

Electrical industry; Motors, generators, dynamos, control panels, conductive materials, lighting, communications and all household appliances.

Construction industry; Construction, decorative materials and alloys.

Means of transportation; All land and sea transportation vehicles.

Industrial machinery; ventilation, heating, agricultural machinery.

7. Effects of Copper on Human Health

In addition to its use in various environmental areas, copper is also found in trace amounts in living organisms, thus playing important roles in various biological processes (Chemosphere et al, 2021). Copper (Cu) is found in almost all tissues and is involved in various metabolic reactions. It is absorbed by living organisms through inhalation of air, drinking water, digestion of food or skin contact with copper-containing compounds (Alkış, M., 2011). Copper is important for the functioning of the body, but it is also the main component of hair, soft parts of the skin, bones and some internal proportions. Copper, which averages between 50-120 mg in adults, is an essential element for the metabolic reactions of amino acids, fatty acids and vitamins under normal conditions. Copper is involved in the structure of metalloenzymes and has many functions as a biocatalyst in human metabolism.

Cytochrome c oxidase, dopamine β-hydroxylase, urate oxidase, superoxide dismutase, tyrosinase, amine oxidase and ascorbate oxidase are the main known copper metalloenzymes. It is also essential for the regular utilization of iron in the body. Without copper, iron cannot bind to hemoglobin Copper is present in all organs and tissues of the human body. Concentrations range from a few ppm to 100 ppm. It is found in high concentrations in the liver. It is also found in large quantities in various parts of the brain, heart, stomach and intestines. Copper, an essential nutrient and toxic substance, is absorbed from the small intestine. Absorbed copper is loosely bound to serum albumin and amino acids and distributed throughout the body. Copper enters the liver as copper-albumin-copper-histidine complexes and is used in the synthesis of ceruloplasmin in parenchymal cells. Approximately 90% of the copper in mammalian plasma is in the form of copper metalloproteins and ceruloplasmin. (Shorrocks, 1984) Copper is a metal that accumulates in mammalian tissues and can cause toxic effects when tissue concentrations reach critical levels. Exposure to this metal has been reported to cause pathological changes in many tissues, especially in the liver and kidneys (Alkış M, 2011). (Alkış M, 2011) The most serious copper-related poisoning occurs by mouth (Yang, J. et al, 2016).

Acute poisoning is rare. The LD50 (lethal dose) for acute poisoning by oral ingestion in humans is 100 mg/kg, but treatment up to 600 mg/kg is possible. “Menkes syndrome” occurs when the absorption of copper from

the intestines is blocked. In this disease, plasma copper and copper oxidase levels are low. Growth slows down, body temperature drops, hair turns gray and brain degeneration occurs. Copper deficiency reduces the risk of heart disease. "Wilson's disease" occurs when copper absorption from the intestines increases. Copper accumulates in the brain and liver. It is normally excreted in the feces and to a lesser extent in the urine (Zucchini IC and others). The use of copper-containing utensils when preparing or serving food can cause copper poisoning. Nausea, vomiting, heartburn and diarrhea are symptoms of copper poisoning. Copper; A normal adult contains up to 100-150 mg of copper. About 90% of this is stored in muscles, bones and liver. Copper deficiency may occur in people with severe malnutrition and impaired intestinal absorption. In this case, anemia, skin and bone defects, mental development disorders are observed. Excess copper is poisonous. Ingestion of more than 15 mg of elemental copper causes symptoms such as nausea, vomiting, diarrhea, abdominal pain and widespread muscle pain. High intake during pregnancy can cause miscarriage. Depression, coma and death can also occur (Stern, B., 2007).

CONCLUSION

Although some activities that benefit some people, such as industrialization, bring great benefits to humanity, they also bring serious public health problems such as exposure to heavy metals such as lead (Pb), arsenic (As) and copper (Cu). In Turkey, research on the health effects of heavy metals such as lead (Pb), arsenic (As) and copper (Cu) and how to avoid exposure is scarce and insufficient. It is necessary to increase tests for lead (Pb), arsenic (As) and copper (Cu) heavy metal levels in adults who are at higher risk of exposure and to take precautions against possible negative effects. Especially people who frequently come into contact with heavy metals at workplaces should be more conscious and scientific research on this subject should be increased. In this study, we have compiled and presented the physicochemical properties of some heavy metal elements such as lead (Pb), arsenic (As), copper (Cu) and their effects on human health in detail. The positive and negative effects of these heavy metals on human health as a result of their interactions were discussed in detail.

REFERENCE

Daghan, H., 2011. Effects of heavy metal pollution in natural resources on human health. *Mustafa Kemal University Journal of Faculty of Agriculture*, 16(2): 15-25.

Kocaer, F.O., Başkaya, H.S., 2003. Technologies applied in the cleanup of metal contaminated soils. *Journal of Uludag University Faculty of Engineering and Architecture*, 8(1): 121-131.

Farooq M, Anwar F, Rashid U, Appraisal of heavy metal contents in different vegetables grown in the vicinity of an industrial area. Pak J Bot. 2008; 40:2099-106.

Jianlong W, Can C. Biosorption of heavy metals by saccharomyces cerevisiae. Biotechnol Adv. 2006; 24:427-51.

Maciel CJD, Miranda GM de Oliveira DP de Siqueira MEPB, Silveira JN, Leite EMN et al. Determination of cadmium in human urine by electrothermal atomic absorption spectrometry, Anal Chim Acta. 2003; 491:231-7.

Requejo R, Tena M. Maize response to arsenic toxicity as revealed by proteome analysis of plant shoots. Proteomics. 2006; 6:156-162.

Bissen, M., and Fritz H.F., 2003. Arsenic-a review part I: occurrence, toxicity, speciation, mobility, *Acta Hydrochim. Hydrobiol.*, 31, 9-18.

Erdogan Y.A. 2005. Arsenic removal from wastewater with various adsorbents. *Master's Thesis,* I.T.Ü Institute of Science and Technology, Istanbul. 2(1), 3.

Singh, T. S., and Pant, K.K., 2003. Equilibrium, Kinetics and Thermodynamic Studies for Adsorption of As (III) on Activated Alumina, *Separation and Purification Technology*, 36, 139-147.

DIP A. 2001. Free radicals and antidote studies in arsenic toxicity. *Master's Thesis* A.Ü Institute of Health Sciences, Ankara. 2(2), 6.

Fujimoto, M. 2001. The removal of arsenic from drinking water by carbon adsorption. Michigan State University, MSc. Thesis.

Leist, M. Casey, R.J. Caridi, D. 2000. The management of arsenic wastes: Problems and prospects. J Caspian Mater., 125-138.

Chakravarty, S., Dureja, V., Bhattacharya, G., Maity, S., and Bhattacharjee, S., 2002. Removal of Arsenic from Groundwater Using Low Cost Ferruginous Manganese Ore, *Water Research*, 36, 625-632.

Smedley, P.L., Kinniburgh, D.G., 2002. A Review of the Source Behaviour and Distribution of Arsenic in Natural Waters, *Applied Geochemistry*, 17, 517-568.

Ng, J.C., Wang J., and Shraim, A., 2003. A Global Health Problem Caused by Arsenic fron Natural Sources, *Chemosphere*, 52, 1353-1359.

Lenoble, V., Bouras, O., Deluchat, V., Serpaud, B., and Bollinger, J.C., 2002. Arsenic Adsorption onto Pillared Clays and Iron Oxides, *Journal of Colloid and Interface Science*, 255, 52-58.

Morales, K.H., Ryan, L., Kuo, T.L., Wu, M.M., and Chen, C.J., 2000. Risk of Internal Cancers from Arsenic in Drinking Water, *Environmental Health Perspectives*, 108, 103-111.

Dündar Y, Aslan R. The effects of heavy metal lead surrounding life. The Medical Journal of Kocatepe. 2005; 6:1-5.

Ozbolat. G. 2016. Effects of Heavy Metal Toxicity on Human Health. *Journal of Archival Resource Scanning,* 2(2), 6-7.

Paithankar, J.G., et al., Heavy metal associated health hazards: An interplay of oxidative stress and signal transduction. Chemosphere, 2021. 262: p. 128350.

Barbosa F, Tanus-Santos JE, Gerlach RF, Parsons PJ. A critical review of biomarkers used for monitoring human exposure to lead: advantages, limitations, and future needs. Environ Health Perspect. 2005; 113:1669-74.

Parsons PJ. C40-A: Analytical Procedures for the Determination of Lead in Blood and Urine: Approved Guideline. Wayne, PA, National Committee for Clinical Laboratory Standards,2001.

Kiaune L, Singhasemanon N. Pesticidal copper (I) oxide: environmental fate and acoustic toxicity. Rev Environ Contam Toxicol. 2011; 213:1-26.

Favier A. Is zinc a cellular mediator in the regulation of apoptosis. Met Ions Biol Med. 1998; 5:164- 7.

Alkış M. Determination of heavy metals in Turkish wines (Master's thesis) Ankara, Ankara University, 2011.

Shorrocks VM. Copper and Human Health. USA, Copper Development Association Press,1984.

Ranjan R, Naresh R, Patra RC, Swarup D. Erythrocyte lipid peroxides and blood zinc and copper concentrations in acute undifferentiated diarrhoea in calves. Vet Res Commun.2006;30:249-54.

Kabak YB, Gülbahar MY. Determination of apoptosis in liver and kidney tissues in experimental copper poisoning in rats. Vet Fak Derg. 2013; 60:39-45.

Soylak M, Elçi L, Doğan M. Determination of trace amounts of cobalt in natural water samples as 4-(2-thiazolylazo)recorcinol complex after adsorptive preconcentration. Anal Lett. 1997; 30:623- 31.

Uyanık F. The main functions of some trace elements in the organism and their effects on immunity. Health Science Journal. 2000; 9:49-58.

Stern B, Solioz D, Krewski P, Aggett TC, Baker S, Crump K et al. Copper and human health: biochemistry, genetics, and strategies for modeling do-

se-response relationships. J Toxicol Environ Health B Crit Rev. 2007; 10:157-222.

Kara H, Colakoglu N, Kükner A, Ozan E. Structural changes induced by cadmium chloride in rat kidney tissue and the effects of metallothionein on these changes: a light microscopic study. Turkiye Klinikleri J Med Sci.2004;24:592-7

Kraume, E.: KUPFER- Die Metallischen Rohstoffe, 4th Band, Ferdinand Enke Verlag, Stuttgart, 1964. Metallgeselschaft A.G.: Sonderheft Kupfer, No. II, 1968

Keller, H.- Eickhoff, K.: Copper and Copper Alloys, Trans: Şefik Güleç, Î.T.Ü. Turkish Technical Communication Center, İskender Matbaası, İstanbul 1969. Othmer, Kirk: Encyclopedia of Chemical Technology.

GDMB: Erzmetall, 1972, p. 416. 6 - Mineral Facts and Problems 1970 Edition ubstances. 1-303. 1991.

Vural H. 1993. Contamination of Foods by Heavy Metal Ions. Journal of Environment 1993; 8: 3-8.

Okcu M, Tozlu E, Kumlay AM, Pehluvan M. Effects of Heavy Metals on Plants. Alteri Journal of Agricultural Sciences. 2009; 17(2): 14-26.

Raven JA, Evans MCW, Korb RE. The role of trace metals in photosynthetic electron transport in O2-evolving organisms Pho. Res. 1999; 60:111-149

Dunand VF, Epron D, Sossé AB, Badot PM. Effects of copper on growth and on photosynthesis of mature and expanding leaves in cucumber plants. Plant Science. 2002; 163:53-58.

Lee J, Peña M, Nose Y, Thiele D. 2002. Biochemical characterization of the human copper transporter Ctr1. J Biol Chemistry277: 4380-4387.

Knöpfel M, Solioz M. 2002. Characterization of cytochrome b (558) ferric/cupric reductase from rabbit duodenal brush border membranes. Biochemistry Biophys Res Society291: 220-225.

Ohgami R, Campagna D, McDonald A, Fleming M. 2006. Steap proteins are metalloreductases. Blood 108: 1388-1394.

Molloy S, Kaplan J. 2009. Copper-dependent recycling of hCTR1, a high-affinity copper transporter in human. J Biol Chem284: 29704-29713.

Petris M, Smith K, Lee J, Thiele D. 2003. Copper-stimulated endocytosis and degradation of the human copper transporter hCtr1. J Biol Chemistry278: 9639-9646.

Clifford R, Maryon E, Kaplan J. 2016. Dynamic internalization and recycling of a metal ion transporter: Cu homeostasis and CTR1, the human Cu1 transport system. J Cell Science129:1711-1721.1 Nose Y, Wood L, Kim B, Prohaska J, Fry R, Spears J, Thiele D. 2010. An apical copper

transporter controlled at the level of protein stability in mammalian intestinal epithelial cells in vivo. J Biol Chemistry285: 32385-32392.

Nose Y, Kim B, Thiele D. 2006. Ctr1 enhances intestinal copper absorption and is required for growth, iron metabolism and newborn heart function. Cell Metabolism4: 235-244.

Harrison M, Jones C, Dameron C. 1999. Copper chaperones: Function, structure and copper binding properties. Biol Inorganic Chemistry4: 145-153.

Vulpe C, Levinson B, Whitney S, Packman S, Gitschier J. 1993. Isolation of a candidate gene for Menkes disease and evidence that it encodes a copper-transporting ATPase. Nat Genet3: 7-13.

Kaler S. 2011. ATP7A-related copper transport diseases, emerging concepts and future trends. Nat Rev Neurol7: 15-29.

Greenough M, Pase L, Voskoboinik I, Petris M, O'Brien A, Camakaris J. 2004. Signals regulating trafficking of the Menkes (MNK; ATP7A) copper translocated P-type ATPase in polarized MDCK cells. Am J Physiol Cell Physiol 287:C1463-C1471.

Nyasae L, Bustos R, Braiterman L, Eipper B, Hubbard A. 2007. Dynamics of endogenous ATP7A (Menkes protein) in intestinal epithelial cells: copper-dependent redistribution between two intracellular domains. Am J Physiol Gastrointest Liver Physiol292:G1181-1194. 35.Veldhuis N, Gaeth A, Pearson R, Gabriel K, Camakaris J. 2009. Multilayer regulation of copper translocated P-type ATPases. BioMetals22: 177-190.

Pierson H, Lutsenko S, Tumer Z. 2015. Copper metabolism, ATP7A and Menkes disease. eLS: 1-15

Wan, D., Han, Z., Liu, D., Yang, J., 2016. Risk Assesments of Heavy Metals in House Dust from a Typical Industrial Area in Central China. Human and Ecological Risk Assessment. Vol:22, No:2 489-501

Akbal A, Resorlu H, Savaş Y (2015) Toxic Effects of Heavy Metals on Bone Tissue. Turkish Journal of Osteoporosis; 21: 30-3

Akbal A, Tutkun E, Yilmaz H. (2014) Lead exposure is a risk for worsening bone mineral density in middle-aged male workers. Aging Male, 17:189-93.

Bellinger DC. Lead. Pediatrics, (2004); 113: 1016-1022.

Boldyrev M. (2018) Lead: properties, history, and applications. WikiJournal of Science, 1(2):7

Boskabady M, Marefatib, Farkhondeh T, Shakeric F, Alieh Farshbafd A, Boskabady MH. The effect of environmental lead exposure on human health and the contribution of inflammatory mechanisms, a review. (2018) Environment International. 08.013

Campbell C, Osterhoudt KE. (2000); Prevention of childhood lead poisoning. Current Opinion in Pediatrics. 12: 428-437.

Centro Laboratories: (2014)." Lead Poisoning", Lab Tests Online, Debnath B, Singh WS, Manna K (2019). Sources and toxicological effects of lead on human health. Indian Journal of Medical Specialities. 10.232.74.27.

Dursun A, Yurdakok K, S Yalcin S. S., Tekinalp G., Aykut O, Orhan G., Morgil G. K. (2016). Maternal risk factors associated with lead, mercury and cadmium levels in umbilical cord blood, breast milk and newborn hair. The Journal of Maternal-Fetal & Neonatal Medicine; 29 (6):954-61

Dündar Y. Aslan R. (2005). The Effects of Heavy Metal Lead Surrounding Life. Kocatepe Medical Journal 6: 1-5

Çaylak E, Hakifeoğlu İ. (2010). Effects of lead on antioxidant enzymes in children and the therapeutic/protective role of antioxidants. Journal of Pediatrics. 53: 159-173.

Erickson L, Thompson T. (2005). A review of a preventable poison: pediatric lead poisoning Journal for Specialists in Pediatric Nursing. 10: 171-182.

Fişek AG, Piyal B. (1991) Worker health guide. 3rd edition. Ankara. Turkish Medical Association Publication Yorum Basım, 22-7.

Hızel S, Şanlı C. (2006). Nutrition and Lead Interaction in Children. Journal of Pediatrics. 49: 333-338.

Kasten-Jolly J. Heo Y. Lawrence AD. (2010). Impact of Developmental Lead Exposure on Splenic Factors. Toxicology and Applied Pharmaco- 133 logy. 247(2):105-15.

Levin, S.M., Goldberg, M. (2000) Clinical evaluation and management of lead-exposed construction workers. American Journal of Industrial Medicine. 37: 23-43.

McKinney PE (2003). Lead neurotoxicity in children: basic mechanisms and clinical correlates. Brain. 126(1): 5-19.

Mohammadyan M, Moosazadeh M, Borji A, Khanjani N & Moghadam SR. (2019). Investigation of occupational exposure to lead and it's relation with blood lead levels in electrical solderers. Environmental Monitoring and Assessment. 4;191(3):126.

Needleman H. 2004. Lead poisoning. Annu Rev Med. 55: 209-222. Needlman HL, Gatsonis CA. 1990. Low level lead exposure and the IQ of children. JAMA. 263: 673-678.

Orr SE and Bridges CC. (2017). Chronic Kidney Disease and Exposure to Nephrotoxic Metals. International Journal of Molecular Sciences. 18(5): 1039.

Özbolat G, Tuli T. (2016) Effects of Heavy Metal Toxicity on Human Health. Journal of Archival Resource Search. 25(4): 502-521.

Papanikolaou N,. Hatzidaki EG, Belivanis S, Tzanakakis GN, Tsatsakis AM. (2005); Lead toxicity update. A brief review. Medical Science Monitor, 11(10): 329-336.

Piomelli S. (2002); Childhood lead poisoning. Pediatric Clinics of North America. 49: 1285-1304.

Rebelo FM, Caldas ED (2016) Arsenic, lead, mercury and cadmium: Toxicity, levels in breast milk and the risks for breast fed infants. Environmental Research; 151: 671-688.

Rocha A. Trujillo K. (2019) Neurotoxicity of low-level lead exposure: History, mechanisms of action, and behavioral effects in humans and preclinical models. Neurotoxicology; 73: 58-80.

Rosin A. (2009). The Long-term Consequences of Exposure to Lead. Israel Medical Association Journal. 11:689-94.

Sanborn MD, Abelsohn A, Campbell M, Weir E. (2002). Identifying and managing adverse environmental health effects: 3. Lead exposure. Canadian Medical Association Journal 166(10):1287-1292.

Seven T, Can B, Darende BN, Ocak S. (2018). Heavy Metal Pollution in Air and Soil. National Research Journal of Environmental Sciences, Issue 1(2): 91-103.

Shih RA, Glass TA, Bandeen-Roche K, Carlson MC, Bolla K, Todd AC, Schwartz BS. (2006) Environmental lead exposure and cognitive functi-134 on in community-dwelling older adults. Neurology. 14;67(9): 1556-1562.

De Souza LD de Andrade AS, Dalmolin RJS. (2018) Lead-interacting proteins and their implication in lead poisoning. Critical Reviews in Toxicology. 48(5): 375-386.

Şanlı C. Hızel S. Albayrak M. (2005). Lead and Child Health. Journal of Continuing Education Medicine. 14;4: 70- 75.

Simsek HG, Onal AE. (2019). The Effects of Lead, an Environmentally Toxic Heavy Metal, on Fetal Health. Turkish Journal of Family Medicine and Primary Care. 13(3): 363-370.

Tchounwou PB, Yedjou CG, Patlolla AK, and Sutton DJ. (2012) Heavy Metals Toxicity and the Environment. Molecular, Clinical and Environmental Toxicology; 101: 133-164.

Vijayakumar S, Sasikala M, Ramesh R. (2012). Lead Poisoning - An Overveiw. International Journal of Pharmacology and Toxicology. 2(2): 70-82.

Vlasaka T, Jordakieva G, Gnambsc T, Augnere C, Crevennab R, Winker R, Barth A. (2019). Blood lead levels and cognitive functioning: A meta-analysis. Science of the Total Environment. 03.052.

Vaziri ND, Gonick HC, (2008) Cardiovascular effects of lead exposure, Indian Journal of Medical Research. 128: 426-431.

Wani AL, Ara A, Usmani JA. (2015) Lead toxicity: a review. Interdisciplinary Toxicologyol. 8(2): 55-64.

(WHO 2019). Exposure To Lead: Major Public Health Concern. Preventing Disease Through Healthy Environments. Department of Public Health, Environmental and Social Determinants of Health World Health Organization.

WHO (2000). Air Quality Guidelines-Second Edition. WHO Regional Office for Europe, Denmark;

WHO (2001) Lead. Regional Office for Europe, Copenhagen, Denmark, Chapter 6.7 Yapıcı G., Can G., Şahin Ü. 2002). Asymptomatic Lead Poisoning in Children, Cerrahpaşa Medical Journal. 33(3): 197-204.