Journal of Life Sciences & Biomedicine, vol. 2(75), No 1, p. 38-46 (2020)

The effects of heavy metals on biochemical processes in the human body (review)

R.I. Ibrahimov

Azerbaijan Medical University, 23 Bakikhanov Str., Baku AZ 1022, Azerbaijan
For correspondence: iri-71@mail.ru
Accepted for publication: 05 June 2020

Environment and human health are closely related. Heavy metals are priority pollutants, as they are highly toxic to living organisms in relatively low concentrations. The World Health Organization considers them to be the most dangerous xenobiotics for human health. The paper reviews research on the toxic effects of heavy metals on biochemical processes in the human body and the clinical analysis of diseases caused by them. The author has presented the various mechanisms of heavy metal toxicity at the molecular level and shown the role of oxidative stress in the pathogenesis of diseases of the cardiovascular, nervous and respiratory systems, associated with the action of heavy metals, on a sufficiently large material. The analysis of literature data demonstrates the significant role and necessity of further study of biochemical mechanisms of the development of pathological processes under chronic exposure to various toxic heavy metals in order to develop effective methods of chronic diseases treatment.

Keywords: *Heavy metals, bioaccumulation, toxicity, biochemical disorders, complexing ability, oxidative stress*

Environmental pollution by toxic heavy metals is increasing worldwide and poses a growing threat to both the environment and human health. Intensive development of industry and chemicalization of agriculture led to accumulation of toxic for human organism chemical compounds in biosphere in large quantities. Today, due to the increasing anthropogenic load on the environment, the contamination of soil, water and wastewater with heavy metals is a worldwide problem (Теплая, 2013; Argos et al., 2010; Ogundiran et al., 2008). Dangerous levels of heavy metal pollution are observed in many industrialized areas of the world. (Гора, 2007; Дускаев и др., 2014; Теплая, 2013; Cheng, 2003).

Ecology and human health are closely interconnected. Heavy metals are priority pollutants, as they are highly toxic to living organisms in relatively low concentrations. Heavy metal ions do not disappear from the biological cycle from an ecotoxicological point of view, their toxicity does not decrease, but rather increases with increasing concentration. They possess high cumulative ability, therefore their danger lies in the possible long-term consequences (Рыбкин и др., 2014; Улахович и др., 2010; Фрумин, 2002; Batariova et al., 2006; Cheng, 2003).

It was found out that metals and their compounds accumulate in soil relatively quickly, are persistent and are removed from it very slowly (Мудрый, 2008). A lot of research is devoted to the study of heavy metals in soil. Sources of heavy metals entering the soil are examined in detail, and the content of a number of metals is analyzed. It is shown that the main anthropogenic sources of metals are various fuel installations, ferrous and non-ferrous metallurgy enterprises, mining enterprises, cement plants, chemical enterprises, galvanic industries and transport. The sources of heavy metals in soil are considered in detail and the content of a number of metals is analyzed. The heavy metals accumulated in soil and water undergo biomagnification in the food chain and then bioaccumulate in living organisms (Дускаев и др., 2014; Chiocchetti et al., 2017; Ogundiran et al., 2008; Rai et al., 2003).

According to scientific studies, the special place of metals among the priority chemicals polluting

doi.org/10.29228/jlsb.40

the biosphere is due to the following reasons (Батян и др., 2009; Фрумин, 2002):

• The rate of extraction of metals from the Earth's crust by humans is higher than the geological rate of their extraction (Table 1).

• Unlike organic pollutants undergoing decomposition processes, metals are capable of redistribution between the individual components of the geographic envelope.

Table 1. Recovery rate of metals from the Earth's crust (tons / year)

Element	«Geological speed» Vg	extraction rate by Humans Vh	Vh/Vg
Iron	$2{,}5 \cdot 10^7$	$3{,}2 \cdot 10^8$	12,8
Copper	$3{,}8 \cdot 10^5$	$4{,}5 \cdot 10^6$	11,8
Zinc	$3{,}7 \cdot 10^5$	$3{,}9 \cdot 10^6$	10,5
Lead	$1{,}8 \cdot 10^5$	$2{,}3 \cdot 10^6$	12,7
Manganese	$4{,}4 \cdot 10^5$	$1{,}6 \cdot 10^6$	3,6
Tin	$1{,}5 \cdot 10^3$	$1{,}7 \cdot 10^5$	113
Molybdenum	$1{,}3 \cdot 10^4$	$5{,}7 \cdot 10^4$	4,4
Mercury	$3{,}0 \cdot 10^3$	$7{,}0 \cdot 10^3$	2,3
Silver	$5{,}0 \cdot 10^3$	$7{,}0 \cdot 10^3$	1,4

Metals are relatively easy to accumulate in the soil, but are difficult and slow to remove from it. Half-removal period of zinc is up to 500 years, cadmium - up to 1100 years, copper - up to 1500 years, lead - up to several thousand years.

• Metals are well accumulated by human organs and tissues, warm-blooded animals and aquatic animals.

• Metals, especially heavy metals, are highly toxic for various biological objects.

More than 40 metals of D.I. Mendeleev's periodic table of elements with atomic mass of more than 50 atomic units are considered to be heavy metals (Куценко, 2004; Лысенко и др., 2015; Фрумин, 2002). In terms of their toxicity, prevalence and ability to accumulate in food chains, 10 elements are recognized as priority pollutants of the biosphere and are subject to priority control. These are Pb, Cu, Zn, Ni, Cd, Co, Sb, Sn, Bi, Hg. The maximum permissible concentrations of trace elements in the human body are established (Table 3).

The amplitude of the content of an element in different organisms may significantly exceed the specified concentrations. The concentration factor has a determining character for evaluation of the physiological action of the element. It is known that each element has an inherent safe exposure range that supports optimal tissue concentrations and functions. Each element has its own toxic range when its safe exposure is exceeded (Батян и др., 2009; Куценко, 2004; Лысенко и др., 2015; Фрумин, 2002). To assess the degree of hazard of heavy metals in toxicological chemistry, according the Mertz rule all metals are divided into three groups (the smaller the range, the "more dangerous"): (I) As, Be, Cd, Hg, Pb, Tl, Zn; (II) B, Co, Cr, Cu, Mo, Ni, Sb, Sc; (III) Ba, Mn, Sr, V, W.

It is generally recognized that the most dangerous elements for humans, and indeed for warm-blooded animals, are cadmium, mercury and lead (Оберлис и др., 2008; Полина, 2012; Улахович и др., 2010; Фрумин, 2002; Bjermo et al., 2013; Martinez et al., 2011). A chemical element is considered vital if, in its absence or inadequate intake into the body, normal vital activity is disrupted, development stops. As a result of exposure to toxic elements, intoxication syndrome develops in the body. Each element has its own operating concentration range, which allows vital functions to be performed. If there is a deficiency or excess of an element, the work of the enzymes that are dependent on them suffers first. Homeostasis of metals and ligands is disturbed, pathological changes develop.

Heavy metals are considered by the World Health Organization as the most dangerous to human health xenobiotics. Daily prolonged exposure to contaminated food and water leads to the accumulation of metals in the human body and the development of various severe diseases (Jomova et al., 2011; Kyrre et al., 2017; Martinez et al., 2011; Young-Seoub et al., 2014). Heavy metal pollution more often is recognized as dramatic in many countries of the developing world. There are a significant number of large-scale studies in various countries to determine the content of heavy metals in the environment and biological fluids and human tissues to assess toxicity (Batariova et al., 2006; Bibi et al., 2015; Bjermo et al., 2013; Cheng, 2003; Forte et al., 2011).

It has been shown that the main sources of exposure to heavy metals are food, water and airborne particulates, including smoke (Улимбашев и др., 2012; Hyun-Jun et al., 2017; Kyrre et al., 2017; Rahmani et al., 2018).

Table 2. Toxic effects of heavy metals and the diseases caused by them

Metal	Acute	Chronic	Toxic Concentration
Arsenic	Nausea, vomiting, "rice-water" diarrhea, encephalopathy, MODS, LoQTS, painful neuropathy	Diabetes, hypopigmentation/ hyperkeratosis, cancer: lung, bladder, skin, encephalopathy	24-h urine: ≥50 μg/L urine, or 100 μg/g creatinine
Bismuth	Renal failure; acute tubular necrosis	Diffuse myoclonic encephalopathy	No clear reference standard
Cadmium	Pneumonitis (oxide fumes)	Proteinuria, lung cancer, osteomalacia	Proteinuria and/or ≥15 μg/ g creatinine
Chromium	GI hemorrhage, hemolysis, acute renal failure (Cr^{6+} ingestion)	Pulmonary fibrosis, lung cancer (inhalation)	No clear reference standard
Cobalt	Beer drinker's (dilated) cardiomyopathy	Pneumoconiosis (inhaled); goiter	Normal excretion: 0.1-1.2 μg/L (serum) 0.1-2.2 μg/L (urine)
Copper	Blue vomitus, GI irritation/ hemorrhage, hemolysis, MODS (ingested); MFF (inhaled)	Vineyard sprayer's lung (inhaled); Wilson disease (hepatic and basal ganglia degeneration)	Normal excretion: 25 μg/24 h (urine)
Iron	Vomiting, GI hemorrhage, cardiac depression, metabolic acidosis	Hepatic cirrhosis	Nontoxic: < 300 μg/dL Severe: >500 μg/dL
Lead	Nausea, vomiting, encephalopathy (headache, seizures, ataxia, obtundation)	Encephalopathy, anemia, abdominal pain, nephropathy, foot-drop/ wrist-drop	Pediatric: symptoms or [Pb] ≥45 μ/dL (blood); Adult: symptoms or [Pb] ≥70 μ/dL
Manganese	MFF (inhaled)	Parkinson-like syndrome, respiratory, neuropsychiatric	No clear reference standard
Mercury	Elemental (inhaled): fever, vomiting, diarrhea, ALI; Inorganic salts (ingestion): caustic gastroenteritis	Nausea, metallic taste, gingivo-stomatitis, tremor, neurasthenia, nephrotic syndrome; hypersensitivity (Pink disease)	Background exposure "normal" limits: 10 μg/L (whole blood); 20 μg/L (24-h urine)
Nickel	Dermatitis; nickel carbonyl: myocarditis, ALI, encephalopathy	Occupational (inhaled): pulmonary fibrosis, reduced sperm count, nasopharyngeal tumors	Excessive exposure: ≥8 μg/L (blood) Severe poisoning: ≥500 μg/L (8-h urine)
Selenium	Caustic burns, pneumonitis, hypotension	Brittle hair and nails, red skin, paresthesia, hemiplegia	Mild toxicity: [Se] >1 mg/L (serum); Serious: >2 mg/L
Silver	Very high doses: hemorrhage, bone marrow suppression, pulmonary edema, hepatorenal necrosis	Argyria: blue-grey discoloration of skin, nails, mucosae	Asymptomatic workers have mean [Ag] of 11 μg/L (serum) and 2.6 μg/L (spot urine)
Thallium	Early: Vomiting, diarrhea, painful neuropathy, coma, autonomic instability, MODS	Late findings: Alopecia, Mees lines, residual neurologic symptoms	Toxic: >3 μg/L (blood)
Zinc	MFF (oxide fumes); vomiting, diarrhea, abdominal pain (ingestion)	Copper deficiency: anemia, neurologic degeneration, osteoporosis	Normal range: 0.6-1.1 mg/L (plasma) 10-14 mg/L (red cells)

MODS- multi-organ dysfunction syndrome; MFF- metal fume fever; GI-gastrointestinal; LoQTS-long QT syndrome and a rare inborn heart condition; ALI-acute lung injury.

The most dangerous non-degradable elements, toxic even in trace amounts, according to the FAO/ WHO Food Codex Commission (Codex Alimentarius), are Hg, Cd, Pb, Sn, V, Mo, As, Co (www.fao.org/fao-who-codexalimentarius).

Health problems due to environmental pollution by heavy metals are becoming a serious problem today in the world and are widely studied. Heavy metals entering the human body violate the regulation of many physiological functions, biochemical and morphological disorders are identified (Jomova et al., 2011; Young-Seoub et al., 2014). They disrupt metabolic processes (Planchart et al., 2018) have a toxic effect on many systems of the human body, including the nervous (Jomova et al., 2010), immune (Балабекова и др., 2015; Tasleem et al., 2015) and cardiovascular systems (Prozialeck et al., 2008), kidneys (Reyes et.al., 2013) and other.

Table 3. Maximum permissible concentrations of trace elements in the human body.

Element	Blood (mkg/ml)	Urine (mkg/ml)
Mn (Manganese)	0,06	0,07
Ag (silver)	0,1	0,06
As (arsenic)	0,2	0,004
Va (barium)	0,08	0,8
Cd (cadmium)	0,005	0,04
Bi (bismuth)	0,03	0,02
Cr (chrome)	0,004	0,02
Cu (copper)	0,9	0,1
Pb (lead)	0,25	0,08
Tl (Thallium)	0,01	0,002
Zn (zinc)	1,2	1,2

The physiological and biochemical effect of heavy metals on the human body is different and depends on the nature of the metal, the type of compound in which it exists in the natural environment, as well as its concentration. Not all heavy metals are equally dangerous to human health. According to a classification that takes into account the physiological role, chemical elements are divided into (Куценко, 2004; Оберлис и др., 2008):

- essential: Fe, I, Cu, Zn, Co, Cr, I, Mo, Se, Mn;
- conditionally essential: As, B, Br, F, Li, Ni, Si;
- toxic: Al, Cd, Pb, Hg, Be, Ba, Bi, Tl;
- potentially toxic: Ag, Au, In, Ge, Rb, Ti, Te, U, W, Sn, Zr.

Among heavy metals, some are essential for the vital functions of man and other living organisms. They are referred to as essential nutrients and are called trace elements (Оберлис и др., 2008)). They participate in the biochemical processes of the human body and are necessary for its normal functioning. Such metals include iron, zinc, molybdenum, copper, etc. However, in large quantities, these metals and their compounds are toxic and can have harmful effects on the body. It should be remembered that each trace element has its own working range of concentrations, which allows it to perform vital functions. Deficiency or excess of an element leads at first to disturbance the activity of the enzymes in which they are included. The homeostasis of metals and biological molecules is disrupted, pathological changes develop.

Other heavy metals are not used by the body, are highly toxic and can accumulate in tissues, leading to poisoning or even death (Батян и др., 2009; Дускаев др., 2014; Лысенко и др., 2015; Оберлис и др., 2008). These metals are called toxic and belong to the class of xenobiotics, that is alien to living organisms and are considered systemic toxicants. The toxicity of “metallic poisons” is explained by their binding to the relevant functional groups of protein and other vital compounds in the body. As a result, the normal functions of the relevant cells and tissues in the body are disrupted. Clinical symptoms vary depending on the metal, its dose and whether the exposure was acute or chronic (Table 2).

Although toxicity resulting from exposure to significant amounts of toxic metals usually affects many organ systems, the severity of the health consequences depends on the type of chemical structure and element shape, the route and duration of exposure, and, to a greater extent, depends on the individual's susceptibility (Батян и др., 2009; Полина, 2012). For example, barium sulfate is generally non-toxic, however barium is rapidly absorbed and cause deep, potentially fatal hypokalemia. Mercury is relatively inert in the gastrointestinal tract and is also poorly absorbed through intact skin, but inhalation or injection of mercury can be disastrous.

Age also influences toxicity. For example, younger children are more susceptible to heavy metals, and even short-lived effects can affect the child's development processes (Blaurock-Busch et al., 2011; Molina-Villalba et al., 2015). Experimental studies have shown that blood concentrations of Pb, As, Cd and Mn in animals varied significantly between young and older age groups. All components except Mn were higher in older age groups (Тухватшин и др., 2017).

Chronic poisoning due heavy metal of lead acetate and potassium dichromate in experimental animals disrupts carbohydrate and fat metabolism, as well as changes in protein metabolism and the enzyme system in animals, especially older ones, in which recovery processes are less pronounced (Балабекова и др., 2015; Тухватшин и др., 2017). It was found that the course of aseptic inflammation under conditions of preliminary poisoning of rats with heavy metal compounds without treatment is aggravated by a tendency to the chronization of the process (Тухватшин и др., 2017).

Heavy metals are characterized by high permeability and the ability to be absorbed into the blood and after spread to organs, tissues and settling in them. The liver and kidneys, which filtering out toxins and removing them, take the main blow. If these organs suffer greatly, their functions were violated - from this moment the removal of metal compounds from the body is impossible. As a result, intoxication does not decrease, and toxins without interference affect the nervous, cardiovascular and respiratory systems.

The cardiovascular system, also the kidneys, is one of the first to be exposed to the toxic effects of xenobiotics. There is an increase in cardiovascular and renal pathology in the population in ecologically unfavorable areas. In addition, as a result of detailed studies conducted over the past decade, it has been revealed that heavy metals play a role in the emergence and development of such widespread diseases as hypertension, diabetes mellitus, and a number of neurological and oncological diseases (Jomova et al., 2010; Sharma et al., 2006; Waisberg et al., 2003).

The toxicity of heavy metals at the molecular level has three mechanisms. The first mechanism is determined by the ability of heavy metals to bind functional groups of biologically important substances in the body, primarily to block sulfhydrilic groups of SH-enzymes (Куценко, 2004; Forte et al., 2011; Winterbourn et al**.,** 2008). As a result of the reaction of metal ions with SH-groups of enzymes, are formed weakly dissociating and insoluble compounds - mercaptides. The formation of mercaptides is accompanied by damage to proteins, a violation of their function, which initiates the development of a toxic process. Damage to intra-protein bonds leads to their denaturation, thereby changing their main functions - transport, structural and enzymatic. In this case, thiol poisons and their compounds interact with SH-groups of amino acids that form proteins with carboxyl groups.

The second mechanism of the toxic effect of heavy metals is based on the displacement of biogenic metals from metal-containing complexes (Jacobson et al., 2012; Sharma et al., 2011; Tamas et al., 2014). If the stability of a metal-containing complex is greater than that of biogenic metals, the equilibrium shifts to the right and toxic metals accumulate in the body, which leads to disruption of normal body function. This mechanism is due to the proximity of the geometric dimensions and charges of ions of biogenic and toxic metals. It should be noted that strength of chemical bonds of proteins and other biologically important components of blood with ions of any metal is sufficient for considerable part of time of its stay in organism metal was in the form of complex with proteins, amino acids and other biologically active compounds. Therefore, if an excess of metals enters the body, the latter can cause a violation of its functions, poisoning or death. The degree of such influence depends not only on the concentration exceeding a certain level, but also on the nature of the metal, primarily its complexing ability. Thus, if the complex-forming ability of the metal-toxicant is large enough, it can displace the biogenic metal-catalyst from the active center as a result of competitive interaction or bind with itself the overwhelming part of biologically active compounds used for the synthesis of this or that vital enzyme. Heavy metals can cause disruption in cellular processes by displacing irreplaceable metals from their respective locations. Oxidative degradation of biological macromolecules has been found to be mainly associated with metal binding to DNA and nuclear proteins (Реутова, 2015; Abilev et al., 2013; Flora et al., 2008; Ghosh et al., 2012).

The third mechanism is caused by the development of oxidative stress under the influence of heavy metals (Cuypers et al., 2010; Ercal et al., 2001; Jacobson et al., 2012; Leonardo et al., 2017; Sharma et al., 2014). Redox active metals such as iron, copper and chromium, as active redox agents, directly enhance redox reactions, while redox inactive metals such as lead and cadmium, mercury and others deplete the main antioxidants in cells, especially thiol-containing antioxidants and enzymes, while cadmium, arsenic and lead exhibit their toxic effects by binding to sulfhydride protein groups and depleting glutathione (Jomova et al., 2011). Silver nanoparticles have been shown to induce oxidative stress and chromosome aberrations (Ghosh et al., 2012).

It is believed that the factor of metal toxicity and carcinogenicity is the formation of reactive oxygen species that cause lipid peroxidation, membrane destruction and damage to proteins, carbohydrates and DNA.

It has been established that chronic exposure to metals leads to protein damage, which contributes to the progression of neurodegenerative diseases. A detailed understanding of the oxidative damage to proteins caused by metal is provided by Reyes et al (2013) and Tamas et al. (2014) and others (Ghezzi, 2005; Sharma et al., 2014; Valko et al., 2006; Winterbourn et al., 2008). Thus, the analysis of literature data shows the significant role and necessity of further study of biochemical mechanisms of pathological processes development under chronic exposure of various toxic heavy metals in order to develop effective methods of chronic diseases treatment.

REFERENCES

Багандова Л. М., Астарханова Т. С., Ашурбекова Т. Н. (2011) Биоэкологический мониторинг антропогенных воздействий при разных видах хозяйственной деятельности. *Юг России: экология, развитие*, **6 (3):** 99-101.

Балабекова М.К., Рыспекова Н.Н., Жукешева М.К. и др. (2015) Динамика течения воспаления, вызванного на фоне металлиндуцированной иммунодепрессии. *Ж. Современные проблемы науки и образования*, **6:** 276 с.

Батян А. Н., Фрумин Г. Т., Базылев В. Н. (2009) Основы общей и экологической токсикологии. СПб.: СпецЛит., 352 с.

Гора Е.П. (2007) Экология человека. Учебное пособие. М., 540 с.

Дускаев Г. К., Мирошников С. А., Сизова Е. А. и др. (2014) Влияние тяжелых металлов на организм животных и окружающую среду обитания (обзор). *Вестник мясного скотоводства*, **3:** 7-11.

Куценко С.А. (2004) Основы токсикологии. М.: Фолиант, 570 с.

Лысенко Н. Н., Догадина М. А. (2015) Основы экотоксикологии: учеб. пособие. Орел ГАУ, 460 с.

Мудрый И.В. (2008) Влияние химического загрязнения почвы на здоровье населения. *Гигиена и санитария*, **4:** 32-37.

Оберлис Д., Харланд Б., Скальный А. (2008) Биологическая роль макро- и микроэлементов у человека и животных. СПб.: Наука, 544 с.

Полина И. Н. (2012) Токсикология: учебное пособие. Сыктывкар: СЛИ, 2012: 128 с.

Ревич Б.А. (2007) Проблемы прогнозирования, «горячие точки» химического загрязнения окружающей среды и здоровье населения России. Под ред. В.М.Захарова. Москва, 192 с.

Реутова Н. В. (2015) Мутагенный потенциал ряда тяжелых металлов. *Экологическая генетика,* **13 (3):** 70-75.

Рыбкин В.С., Богданов А.Н., Чуйков Ю.С., Теплая Г.А. (2014) Тяжелые металлы как фактор возможных экологически обусловленных заболеваний в астраханском регионе. *Гигиена и санитария*, **2:** 27-31.

Теплая Г. А. (2013) Тяжелые металлы как фактор загрязнения окружающей среды. *Астраханский вестник экологического образования*, **1 (23):** 182-192.

Тухватшин Р.Р., Аумолдаева З.М., Абаева Т.С., Исупова А.А. (2017) Биохимические показатели крови у животных различного возраста при отравлении тяжелыми металлами. *Патологическая физиология*, **1 (35):** 39-44 .

Улахович Н.А., Кутырева М.П., Медянцева Э.П., Бабкина С.С. (2010) Экотоксиканты : учеб.-метод. пособие для лекционного курса «Химия в экологии». Казань: Казанский Государственный Университет, 56 с.

Улимбашев М. Б., Тхашигугова М. С. (2012) Концентрация тяжелых металлов в сельскохозяйственной продукции, полученной в различных экологических зонах. *Достижения вузовской науки*, **1:** 110-114.

Фрумин Г.Т. (2002) Экологическая химия и экологическая токсикология: учеб. пос. СПб.: РГГМУ, 107-111.

Abilev S., Glazer V. (2013) Geneticheskaja toksikologija: itogi i problemy. [Genetic toxicology: results and problems]. *Russian journal of gene,* **49 (1):** 81-93.

Argos M., Kalra T., Rathouz P. et al. (2010) Arsenic exposure from drinking water, and all-cause and chronic-disease mortalities in Bangladesh (HEALS): a prospective cohort study. *Lancet*, 376 **(9737):** 252-258.

Batariova A., Spevackova V., Benes B. et al. (2006) Blood and urine levels of Pb, Cd and Hg in the general population of the Czech Republic and proposed reference values. *Int. J. Hyg. Environ. Health*, **209:** 359-366.

Bibi M., Hashmi M., Malik R. (2015).The level and distribution of heavy metals and changes in oxidative stress indices in humans from Lahore district, Pakistan. *Hum. Exp. Toxicol.*, **35 (1):** 78-90.

Blaurock-Busch E., Amin R. O., Rabah T. (2011) Heavy Metals and trace elements in hair and urine of a sample of Arab children with autistic spectrum. *Disorder Maedica (Buchar.)*, **6(4):** 247-257.

Bjermo H., Sand S., Nalsen C. et al. (2013) Lead, mercury, and cadmium in blood and their relation to diet among Swedish adults. *Food Chem. Toxicol.*, 57**:** 161-169.

Cheng S. (2003) Heavy metal pollution in China: Origion, pattern and control. *Environ. Sci. Pollut. Res. Int.*, **10:** 192–198.

Chiocchetti G., Jadán-Piedra C., Vélez D., Devesa V. (2017) Metal (loid) contamination in seafood products. *Crit. Rev. Food Sci. Nutr.*, **57 (17):** 3715-3728.

Cuypers A., Plusquin M., Remans T. et al. (2010) Cadmium stress: an oxidative challenge. *Biometals*, **23:** 927-940.

Ercal N., Gurer-Orhan H., Aykin-Burns N. (2001) Toxic metals and oxidative stress part I: mechanisms involved in metal-induced oxidative damage. *Curr. Top. Med. Chem.*, **1(6):** 529-539.

Flora S., Mittal M., Mehta A. (2008) Heavy metal induced oxidative stress and its reversal by chelation therapy. *Ind. J. Med. Res.*, **128:** 501-523.

Forte G., Madeddu R., Tolu P. et al. (2011) Reference intervals for blood Cd and Pb in the general population of Sardinia (Italy). *Int. J. Hyg. Environ. Health*, **214:** 102-109.

Ghezzi P. (2005) Oxidoreduction of protein thiols in redox regulation. *Biochem. Soc. Trans.*, **33:** 1378-1381.

Ghosh M., Manivannan J., Sinha S. et al. (2012) In vitro and in vivo genotoxicity of silver nanoparticles. *Mutat. Res.*, **749 (1-2):** 60-69.

http://www.fao.org/fao-who-codexalimentarius/about-codex/ru/#c453333

Hyun-Jun K., Hwan-Sub L., Kyoung-Ryul L. (2017) Determination of trace metal levels in the general population of Korea. *Int. J. Environ. Res. Public Health*, **14(7):** 702 p.

Jacobson T., Navarrete C., Sharma S.K. et al. (2012) Arsenite interferes with protein folding and triggers formation of protein aggregates in yeast. J. Cell Sci. **125 (Pt. 1):** 5073-5083.

Jomova K., Valko M. (2011) Advances in metal-induced oxidative stress and human disease. *Toxicology*, **283(2-3):** 65-87

Jomova K., Vondrakova D., Lawson M. (2010) Metals, oxidative stress and neurodegenerative disorders. Mol. Cell Biochem. **345 (1-2):** 91-104.

Kyrre S., Pacyna J., Elisabeth G. et al. (2017) Thorne Global Sources and Pathways of Mercury in the Context of Human Health. *Int. J. Environ Res Public Health*., **14(1):** 105.

Leonardo O. Bittencourt B., Senda C. et al. (2017) Oxidative biochemistry disbalance and changes on proteomic profile in salivary glands of rats induced by chronic exposure to methyl mercury. *Oxid. Med. Cell Longev*., **2017:** 5653291.

Martinez V., Vucic E., Becker-Santos D. et al. (2011) arsenic exposure and the induction of human cancers. *J. Toxicol*., **2011:** 431-487.

Molina-Villalba I., Lacasaña M., Rodríguez-Barranco M. et al. (2015) Biomonitoring of arsenic, cadmium, lead, manganese and mercury in urine and hair of children living near mining and industrial areas. *Chemosphere*, **124:** 83-91.

Ogundiran M., Osibanjo O. (2008) Heavy metal concentration in soils and accumulation in plants growing in a deserted slag dump site in Nigeria. *Afr. J. Biotechnol*., **7:** 3053-3060.

Planchart A., Green A., Hoyo C., Mattingly C. (2018) Heavy metal exposure and metabolic syndrome: Evidence from human and model system studies. *Curr. Environ. Health Rep*., **5(1):** 110-124.

Rai U., Tripathi R., Vajpayee P. et al. (2003) Cadmium accumulation and its phytoxicity in *Potamogeton pectinatus* L. (*Potamogetona-ceae*). *Bull. Environ. Contam. Toxicol*., **70:** 566-575.

Prozialeck W., Edwards J., Nebert D. et al. (2008) The vascular system as a target of metal toxicity. *Toxicol. Sci*., **102:** 207-218.

Rahmani J., Fakhri Y., Shahsavani A. et al. (2018) A systematic review and meta-analysis of metal concentrations in canned tuna fish in Iran and human health risk assessment. *Food Chem. Toxicol.*. **118:** 753-765.

Reyes J., Molina-Jijon E., Rodriguez-Munoz R. et.al (2013) Tight junction proteins and oxidative stress in heavy metals induced nephrotoxicity. *BioMed. Res. Int.*, **2013:** 730-789.

Sharma A., Talukder G. (1987) Effects of metals on chromosomes of higher organisms. *Environ. Mutagenesis*, **9:** 191-226.

Sharma B., Singh S., Siddiqi N. (2014) Biomedical implications of heavy metals induced imbalances in redox systems. *Biomed. Res. Int.*, **2014:** 640-654.

Sharma S., Goloubinoff P., Christen P. (2008) Heavy metal ions are potent inhibitors of protein folding. *Biochem. Biophys. Res. Commun.*, **372:** 341-345.

Sharma S., Goloubinoff P., Christen P. (2011) Non-native proteins as newly identified targets of heavy metals and metalloids. In: *G.Bánfalvi (ed.) Cellular Effects of Heavy Metals*. Germany, Heidelberg: Springer, p. 263-274.

Tamas M., Sharma S., Ibstedt S. et al. (2014) Heavy metals and metalloids as a cause for protein misfolding and aggregation. *Biomolecules*, **4:** 252-267.

Tasleem A. Azam M., Siddiqui K. et al. (2015) Heavy metals and human health: Mechanistic insight into toxicity and counter defense system of antioxidants. *Int. J. Mol. Sci.*, **16 (12):** 2959-2963.

Valko M., Rhodes C.J., Moncol J., Izakovic M., Mazur M. (2006) Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chem. Biol. Interact.*, **160 (1):** 1-40.

Valko M, Jomova K, Rhodes C. et al. (2016) Redox- and non-redox-metal-induced formation of free radicals and their role in human disease. *Arch. Toxicol.*, **90 (1):** 1-37.

Waisberg M., Joseph P., Hale B., Beyersmann D. (2003) Molecular and cellular mechanisms of cadmium carcinogenesis. *Toxicology*, **192:** 95-117.

Winterbourn C., Hampton M. (2008) Thiol chemistry and specificity in redox signalling. *Free Radic. Biol. Med.*, **45:** 549-561.

Young-Seoub H., Ki-Hoon S., Jin-Yong C. (2014) Health effects of chronic arsenic exposure. *J. Prev. Med. Public Health*, **47(5):** 245-252.

Ağır metallar və onların insan orqanizmində biokimyəvi proseslərə təsiri

R.İ. İbrahimov

Azərbaycan Tibb Universiteti

Ekologiya və insan sağlamlığı biri-biri ilə sıx bağlıdır. Ağır metallar ətraf mühit çirkləndiriciləri arasında canlı orqanizmlər üçün ən zərərlilərdəndir, çünki onlar nisbətən aşağı konsentrasiyalarda öz toksiki təsirini göstərir. Ağır metallar Ümumdünya Səhiyyə Təşkilatı tərəfindən insan sağlamlığı üçün ən təhlükəli ksenobiotik kimi qəbul edilmişdir. Bu məqalə ağır metalların orqanizmdə biokimyəvi proseslərə təsiri və onların yaratdığı xəstəliklərin kliniki təhlili üzrə aparılan tədqiqatların icmalına həsr olunmuşdur. Ağır metalların toksikliyinin müxtəlif molekulyar mexanizmləri təqdim edilmişdir və kifayət qədər böyük materialda ağır metalların təsiri ilə bağlı ürək-damar, sinir və tənəffüs sistemləri xəstəliklərinin patogenezində oksidləşdirici stresin rolu müzakirə edilmişdir. Ədəbiyyat məlumatlarının təhlili göstərir ki, müxtəlif toksiki ağır metalların xroniki təsiri zamanı patoloji proseslərin inkişafının biokimyəvi mexanizmlərinin öyrənilməsi və gələcək araşdırılmaların zəruriliyi xroniki xəstəliklərin effektiv müalicə üsullarının işlənib hazırlanması məqsədləri üçün mühüm əhəmiyyətə malikdir.

Açar sözlər: *Ağır metallar, bioakkumulyasiya, toksiklik, biokimyəvi pozuntular, kompleksyaratma qabiliyyəti, oksidləşdirici stres*

Тяжелые металлы и их влияние на биохимические процессы в организме человека

Р.И. Ибрагимов

Азербайджанский медицинский университет

Экология и здоровье человека тесно взаимосвязаны. Тяжелые металлы являются приоритетными загрязнителями, поскольку они очень токсичны для живых организмов в относительно низких концентрациях. Тяжелые металлы рассматриваются Всемирной Организацией Здравоохранения как наиболее опасные для здоровья человека ксенобиотики. Данная статья посвящена обзору исследований по токсическому влиянию тяжелых металлов на биохимические процессы в организме и клиническому анализу вызванных ими болезней. Представлены различные механизмы токсичности тяжелых металлов на молекулярном уровне и, на достаточно большом материале, показана роль окислительного стресса в патогенезе заболеваний сердечно-сосудистой, нервной и дыхательной систем, связанных с действием тяжелых металлов. Анализ литературных данных свидетельствует о значительной роли и необходимости дальнейшего изучения биохимических механизмов развития патологических процессов при хроническом воздействии различных токсичных тяжелых металлов с целью разработки эффективных методов лечения хронических заболеваний.

Ключевые слова: *Тяжелые металлы, биоаккумуляция, токсичность, биохимические нарушения, комплексообразующая способность, окислительный стресс*