Heavy metals toxicity.

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ABSTRACT: Even though heavy metals are the oldest known toxins harmful to humans, heavy metal toxicity is still a topic that requires further investigation. This paper aims το provid an overview on the most dangerous heavy metals and their negative effects on the human health.
Arsenic (As) contaminated underground water and arsenic based agricultural products have generated a worldwide increase of illnesses and deaths that are mainly due to various types of cancer and skin disorders. Industrialization and manufacturing made ead (Pb) poisoning a common occurrence, forcing governments to take measures to decrease lead usage. Mercury (Hg), being highly bioaccumulative and with an increasing presence in the environment, when consumed through food is proven to be especially harmful to lactating mothers, fetuses and children. The vast use of admium (Cd) for technological and agricultural purposes poses a high risk of occupational and non-occupational exposure of humans to that element, since it has been confirmed to cause carcinogenesis. Public awareness of the topic is necessary in order to prevent future increase of heavy metal related human diseases and deaths.

Key Words: Heavy metals, Toxicity, Health effects.

INTRODUCTION

Although heavy metals are considered as the oldest known toxins harmful to humans, heavy metal toxicity remains a very general subject due to the variety of symptoms caused by heavy metal poisoning. Arsenic (As), Cadmium (Cd), Mercury (Hg) and Lead (Pb) are some of the most commonly found metals associated with several adverse effects to humans due to their accumulation in the human body caused through any dietary products (Table 1). Exposure to heavy metals usually has symptoms that are chronic and subtle and in many cases resemble those of other diseases[1].

The wasteful use of pesticides during the last decades as well as the industrial pollution, have caused an extensive contamination of the aquifer layer and of the soil with pollutants that are very toxic to humans. The accumulation of such elements in the environment, especially in the aquatic media, followed by their uptake by plants and finally their consumption by humans necessitate not only a close monitoring of toxic elements but also further and extensive research on the subject[1].

ARSENIC TOXICITY

Arsenic (As), from the viewpoint of occurrence in the environment, toxic activity and probability of exposure to humans, is considered as one of the most dangerous pollutants[5]. Many organic and inorganic arsenic species are present in food and water and this variety makes As a heavy metal of great significance. The most important arsenic species that have a toxicological interest include the oxidation states As (III) and As (V), monomethylarsonic (MMA), dimethylarsinic (DMA), arsenobetaine and arsenocholine[1].

In most cases, arsenic exposure deactivates the human enzyme system as it causes binding through various biological lingands[1]. Epidemiological studies throughout the years revealed that chronic exposure to As may cause peripheral artery disease, various types of cancer such as skin, lung and bladder cancer, skin

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Table 1. Heavy metals and their potential effects on human health[18].

ELEMENT	POTENTIAL HEALTH EFFECTS FROM EXPOSURE
Antimony	Increase in blood cholesterol; decrease of glucose levels
Arsenic	Skin damage or problems with circulatory systems, and may increase risk of cancer development
Barium	Increases blood pressure levels
Beryllium	Intestinal lesions
Cadmium	Kidney damage
Chromium (total)	Allergic dermatitis
Copper	Short term exposure: Gastrointestinal distress. Long term exposure: Liver or kidney damage. People with Wilson's Disease should consult their personal physician if the amount of copper in their water supplier exceeds the permitted action level
Lead	Children: Delays in physical or mental development; children could show slight deficits in attention span and learning abilities; Adults: Kidney problems; high blood pressure levels
Mercury, inorganic	Kidney damage
Selenium	Hair or fingernail loss; numbness in fingers or toes; blood circulatory problems
Thallium	Hair loss; pathology in blood; kidney, intestine, or liver problems
Uranium	Increased risk of cancer, kidney toxicity

disorders, vascular disease and diabetes mellitus[2].

The common route of arsenic intake is through the contamination of underground water. In the past, the use of arsenic-based agricultural products such as herbicides, fungicides and insecticides was extensive and worldwide. Arsenic's persistent nature and wide distribution makes it present in most human foods[1]. Air intoxication derives primarily from industrial activity and has a lesser adverse result than oral contamination.

Arsenic contamination has been reported in many countries throughout the World. Bangladesh, Mexico, Chile and Cambodia are just a few regions which are confronting major problems derived by arsenic contamination. The extensive use of arsenic contaminated tube wells for drinking water, used for cooking purposes, as well as livestock feeding by Bangladeshi people, has led to the increase of acute gastrointestinal illnesses and deaths the last decades[3,13]. Studies have shown that more than 60% of tube wells' water has an arsenic content higher than the permissible limit set by the World Health Organization (WHO). Effects of arsenic exposure to human health appeared at first in the 1950s and included vascular, respiratory and skin lesions in both children and adults after the intake of contaminated water[4]. In the following years there has been a considerable effort to develop methods to constrain or eliminate arsenic contamination by using treatment with plants to remove arsenic from water and by regulating the arsenic emissions[4].

LEAD TOXICITY

Lead is a typically cumulative toxic element and therefore during the last decades there has been a considerable awareness regarding lead (Pb) usage and lead exposure. Although ead's appearance as a natural plain element is very rare, it has been used heedlessly in the past for industrial purposes. In the 1980's, 25 megatons of lead were mined in order to be used for the manufacturing of batteries, pigments, pipes etc. Industrialization and gas emissions from cars using leaded gasoline maximized the presence of lead in

the environment rapidly increasing lead intoxications worldwide[5]. The anti-knocking additive tetraethyllead [$(C_2H_5)_4Pb$] which was used to increase the octane level of gasoline was converted by combustion into PbO and $PbCl_2$ two intoxicating lead compounds that were found in high concentrations in a close proximity to roads and highways[5]. It has now been proven that environmental lead exposure heightens the incidence rate of brain cancer in the human population[22]. For that reason, governments were forced to decrease lead's usage and substitute it with less toxic elements[5].

According to EFSA (European Food Safety Authority) lead dietary exposure ranges from 0.36 to 1.24, up to 2.43 μg/kg body weight (b.w.) per day in high consumers in Europe while exposure of infants ranges from 0.21 to 0.94 μg/kg b.w. per day and of children from 0.80 to 3.10 (average consumers), up to 5.51 (high consumers) μg/kg b.w. per day[15].

Toxic effects caused by lead exposure are usually detected in the kidney, the nervous, hematopoietic and gastrointestinal systems, male and female reproductive organs as well as other soft tissues, with a long term deposition of lead usually accumulating into the bones[6]. Several studies have shown that maternal exposure to lead is highly responsible for miscarriages and birth defects in the fetuses and also has adverse effects on the cognitive development of children[20,21]. Furthermore, in vivo studies also showed that there is a close relationship between lead exposure and alteration of antioxidant defense systems in animals and occupationally exposed workers. Lead poisoning seems to affect the prooxidant-antioxidant balance that exists in humans by producing reactive oxygen species inducing oxidative stress in human tissues, DNA, proteins and the human antioxidant mechanism[7].

More analytical research has been undertaken during the last years in order to examine this behavior and determine the lowest lead dose that could induce oxidative stress. Moreover, the case of antioxidants such as vitamin C or vitamin E is being examined to determine their role in preventing oxidative stress by preserving the prooxidant/oxidant balance in normal levels[16].

MERCURY TOXICITY

Mercury (Hg) is a ubiquitous, very persistent element which can be found literally everywhere. The high levels of mercury concentration in a great variety of foods and its bioaccumulation in the environment, especially the aquatic chain, make mercury an element of great scientific interest as it is considered to be one of the most dangerous heavy metals for human consumption. Mercury can be found in three different forms: elemental or metallic mercury (Hg^0), inorganic mercury compounds (I-Hg), primarily mercuric chloride, and the most intoxicating organic mercury such as methyl mercury (MeHg)[1]. All forms of mercury entering the aquatic environment are converted into methyl-mercury by microorganisms and subsequently concentrated in fish and other aquatic species. When taken in through food, methyl-mercury compounds are readily absorbed up to 95% by the gut effectively entering biological membranes such as the peripheral nerves, the blood brain barrier, the spinal cord, and the placenta[8,9]. Inside the body, methyl-mercury is bound mostly to proteins containing sulphur amino acids and it can induce toxic effects in several organs such as the nervous system, the kidney, the liver and the reproductive organs[14].

Neurotoxicity is one the most acknowledged effects of methyl-mercury on humans, as it is rapidly transported through biological membranes and accumulates in the envelopes of nerve cells causing neurological damage (WHO/ food additives series 52). Protein synthesis is inhibited, cell division is affected, abnormal neuronal migration occurs, and microtubules in neuronal and astrocystic cells are destroyed. Delayed symptoms include sensory disturbance, constriction of visual field, deafness, motor aberrations, mental disorder, cramps, and paralysis, and in cases of acute poisoning nephrotoxicity has been observed. "Developing fetus" is the most vulnerable unit associated with lower level chronic exposure to methyl-mercury with at least four times greater sensitivity[10], and damage occurring in all parts of the brain. Methyl-mercury passes readily through the placenta to the fetus, with concentrations in the fetal blood and brain being generally greater (5-7 times) than the corresponding maternal concentrations at parturition while mercury could also be passed to the infants through their mother's milk. Children with serious symptoms died within two months of birth, whereas when the illness was prolonged, they were susceptible to other diseases such as pneumonia which was the primary

Table 2. Recommendations for consumption and highest permissible intake.

E.U.	❖ Max 100g /week of big fish (swordfish, shark, pike) ❖ Avoid consumption of other fishery products
FDA (Food and Drug Administration) and Environmental Protection Agency (EPA)	❖ Avoid consumption of shark, swordfish, King Mackerel or Tilefish. ❖ Up to 340 g (2 average meals) / week of fish and mollusks with low concentration of Hg ❖ Up to 170 g (1 average meal) / week of fresh tuna fish or canned tuna fish (albacore)
UK Food Standards Agency	❖ Avoid consumption of big fish ❖ Recommendation of max 140g /week of cooked tuna fish (or 170g raw tuna fish)
Ireland Food Standards Agency	❖ Recommendation of max 2 tuna fish /week

cause of death. Survivors were often found to be mentally retarded and epileptic. Lower concentrations of methyl-mercury during gestation have been associated with impediment of the cognitive development of young children[11]. Carcinogenicity, genotoxicity, reproductive toxicity, immunotoxicity and cardiotoxicity have also been associated with chronic methyl-mercury dietary exposure.

Among the recent examples of epidemic methyl-mercury poisoning are the Minamata bay incident in 1953 and the seed grain intoxication in Iraq in 1971-1972. Illegal mining and industrial waste disposal polluted the area of Minamata bay with high concentrations of methyl-mercury. It was not until the mid-1950 that people began to notice a strange behaviour from the Minamata victims. Many people were diagnosed with a degeneration of their nervous systems and in the following years things got worse as many foetuses were born with mental retardation, constricted vision and hearing disabilities.

In recent years, FDA, as well as other food and health organizations, started a campaign in order to reduce the amount of methyl-mercury in human diet, by reducing the amount of foodstuff that is highly contaminated (Table 2)[17]. Great interest has been shown towards groups of people such as underdeveloped children, women in reproductive age and lactating mothers due to exposure to methyl-mercury.

CADMIUM TOXICITY

Cadmium (Cd) is a non-essential highly toxic element, which emerges as a by-product of zinc production and is usually found in phosphate fertilizers. Due to its extensive technological and industrial applications, cadmium can be literally found everywhere, and is recognized as one of the most dangerous trace elements in the environment as it shows a high soil to plant transference rate[1,12]. Cadmium is widely used for alloy and amalgam production, paint pigments, electric cables, plastics and during the last decades for the production of Ni-Cd batteries[19].

In agriculture, the use of industrial waste water and sewage sludge as fertilizer, contaminates the soil with great concentrations of cadmium ions which unlike mercury (Hg^{+2}) and lead (Pb^{+2}) ions, are readily absorbed by plants and distributed in their tissues[5,8]. Certain plant species show a remarkable ability to absorb great amount of cadmium from soils of poor cadmium concentration[12].

For those people who are occupationally exposed to cadmium, the main entrance of the toxic element is through the respiratory system and secondarily by the gastrointestinal system and the skin.

Foodstuff and particularly meat, cereals and dairy products is the main source of non-occupational cadmium exposure to humans. Animals accumulate cadmium primarily in their internal organs, such as the

kidney and liver, and also in milk. According to WHO the weekly recommended intake of Cd should not exceed 400-500 **μ**g, where the daily air intake is about 1,5 **μ**g and the intake from drinking water is 10**μ**g per day[8].

Non-occupational exposure to cadmium can cause a variety of pathological alterations in several organs and tissues. Cadmium has a broad carcinogenetic activity which can affect several organs such as the pancreas, kidneys, lungs, urinary bladder, breast and prostate and additionally it can induce diabetic complications, hypertension and osteoporosis[12].

CONCLUSION

To conclude, heavy metal toxicity poses a real and substantial danger to the human health. Arsenic contamination of underground water has caused major health issues in most countries of the World with an increase of acute gastrointestinal illnesses and deaths. It has also been found that arsenic exposure deactivates the human enzyme system making the body more susceptible at developing various types of cancer. Lead, due to its vast use for industrial purposes is another very dangerous toxic element that has the ability to induce oxidative stress to human tissues and DNA. Mercury is easily absorbed by the human body and is extremely harmful for all groups of people, especially women of reproductive age and children as it affects the fetus and the normal development of young individuals. Last, cadmium is easily accumulated by plants and animals and reaches humans through the food chain affecting many organs and causing serious illnesses. It is thus evident that heavy metal toxicity is a subject that requires the attention of scientists and policy makers in order to increase public understanding of the severity of conditions caused by toxic elements and help at minimizing heavy metal related illnesses and deaths.

Τοξικότητα βαρέων μετάλλων.

Μαρία Αχπαράκη, Ελισάβετ Θεσσαλονικέως, Ελένη Τσούκαλη, Ορθοδοξία Μαστρογιάννη, Ελένη Ζαγγελίδου, Φώτιος Χατζηνικολάου, Νικόλαος Βασιλειάδης, Νικόλαος Ράικος

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ΠΕΡΙΛΗΨΗ: Τα βαρέα μέταλλα είναι από τα παλαιότερα και πλέον γνωστά τοξικά στοιχεία παρόλα αυτά η τοξικότητα τους παραμένει ένα θέμα που χρήζει περαιτέρω έρευνας. Αυτή η εργασία έχει ως σκοπό την ανασκόπηση των επιδράσεων στην υγεία που προκαλεί η έκθεση του ανθρώπου στα πλέον επικίνδυνα βαρέα μέταλλα. Βαρέα μέταλλα με υψηλή τοξικότητα και ευρεία χρήση είναι το αρσενικό, ο μόλυβδος, ουδράργυρος και το κάδμιο.

Το επιμολυσμένο με αρσενικό (As) υπόγειο ύδωρ και τα φυτοφάρμακα που περιέχουν ενώσεις του στοιχείου αυτού έχουν προκαλέσει μία παγκόσμια αύξηση δερματικών διαταραχών και διαφόρων μορφών καρκίνου. Η βιομηχανοποίηση και η εκτενής χρήση του μολύβδου (Pb) έχουν ως αποτέλεσμα την έκθεση πολλών ανθρώπων στο στοιχείο αυτό και την εκδήλωση πολλών περιστατικών μολυβδίασης κυρίως σε επαγγελματικούς χώρους, αναγκάζοντας διάφορες κυβερνήσεις να πάρουν μέτρα για τη μείωση της χρήσης του. Ο υδράργυρος (Hg) είναι ιδιαίτερα επιβλαβής για τα έμβρυα και τα παιδιά έχει μεγάλη φυσική παρουσία στο περιβάλλον και παρουσιάζει υψηλή βιοσυσσώρευση με αποτέλεσμα την πρόσληψη του στοιχείου αυτού κυρίως δια της τροφικής αλυσίδας. Τέλος η ευρεία χρήση του καδμίου (Cd), το οποίο προκαλεί καρκινογένεση στον άνθρωπο, για τεχνολογικούς και γεωργικούς σκοπούς αποτελεί μεγάλο κίνδυνο επαγγελματικής κυρίως έκθεσης του ανθρώπου σε αυτό το στοιχείο. Η ενημέρωση του κοινού όσον αφορά νεότερα δεδομένα για τις τοξικές επιδράσεις των βαρέων μετάλλων στην υγεία του ανθρώπου και τους τρόπους έκθεσης σε αυτά είναι απαραίτητη για να αποφευχθεί περαιτέρω αύξηση των ασθενειών και των θανάτων σχετιζομένων με την χρόνια ή την οξεία τοξικότητα των βαρέων μετάλλων.

Λέξεις Κλειδιά: Βαρέα μέταλλα, Τοξικότητα, Επιδράσεις στην υγεία.

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