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Heavy Metals and Human Health

Simone Morais[1], Fernando Garcia e Costa[2]
and Maria de Lourdes Pereira[3]
[1]REQUIMTE, Instituto Superior de Engenharia do Porto, Porto,
[2]Departamento de Morfologia e Função, CIISA, Faculdade de Medicina Veterinária,
Universidade Técnica de Lisboa, Lisboa,
[3]Departamento de Biologia & CICECO, Universidade de Aveiro, Aveiro,
Portugal

1. Introduction

Metals occur naturally in the earth's crust, and their contents in the environment can vary between different regions resulting in spatial variations of background concentrations. The distribution of metals in the environment is governed by the properties of the metal and influences of environmental factors (Khlifi & Hamza-Chaffai, 2010). Of the 92 naturally occurring elements, approximately 30 metals and metalloids are potentially toxic to humans, Be, B, Li, Al, Ti, V, Cr, Mn, Co, Ni, Cu, As, Se, Sr, Mo, Pd, Ag, Cd, Sn, Sb, Te, Cs, Ba, W, Pt, Au, Hg, Pb, and Bi. Heavy metals is the generic term for metallic elements having an atomic weight higher than 40.04 (the atomic mass of Ca) (Ming-Ho, 2005). Heavy metals enter the environment by natural and anthropogenic means. Such sources include: natural weathering of the earth's crust, mining, soil erosion, industrial discharge, urban runoff, sewage effluents, pest or disease control agents applied to plants, air pollution fallout, and a number of others (Ming-Ho, 2005). Although some individuals are primarily exposed to these contaminants in the workplace, for most people the main route of exposure to these toxic elements is through the diet (food and water). The contamination chain of heavy metals almost always follows a cyclic order: industry, atmosphere, soil, water, foods and human. Although toxicity and the resulting threat to human health of any contaminant are, of course, a function of concentration, it is well-known that chronic exposure to heavy metals and metalloids at relatively low levels can cause adverse effects (Agency for Toxic Substance and Disease Registry [ATSDR], 2003a, 2003b, 2007, 2008; Castro-González & Méndez-Armenta, 2008). Therefore, there has been increasing concern, mainly in the developed world, about exposures, intakes and absorption of heavy metals by humans. Populations are increasingly demanding a cleaner environment in general, and reductions in the amounts of contaminants reaching people as a result of increasing human activities. A practical implication of this trend, in the developed countries, has been the imposition of new and more restrictive regulations (European Commission, 2006; Figueroa, 2008).

Considering the importance of this subject, this chapter gives an overview of the main features of heavy metals and their health effects. The early part of this chapter is dedicated to the most found and toxic heavy metals, lead, cadmium, mercury, and arsenic. The next

piece deals with several approaches for assessment of human exposure, namely the use of biomarkers. The most widely applied separation and detection techniques for quantification of these elements in biological and environmental samples is included, as they provide valuable toxicological data for hazard and risk assessments. Then, finally, the example of the wood preservative chromated copper arsenate (CCA) illustrates the effect of some hazardous substances on the health of humans and the environment.

2. Heavy metals

Lead (Pb), cadmium (Cd), mercury (Hg), and arsenic (As) are widely dispersed in the environment. These elements have no beneficial effects in humans, and there is no known homeostasis mechanism for them (Draghici et al., 2010; Vieira et al., 2011). They are generally considered the most toxic to humans and animals; the adverse human health effects associated with exposure to them, even at low concentrations, are diverse and include, but are not limited to, neurotoxic and carcinogenic actions (ATSDR, 2003a, 2003b, 2007, 2008; Castro-González & Méndez-Armenta, 2008; Jomova & Valko, 2011; Tokar et al., 2011).

2.1 Lead

Lead as a toxicologically relevant element has been brought into the environment by man in extreme amounts, despite its low geochemical mobility and has been distributed worldwide (Oehlenschläger, 2002). Lead amounts in deep ocean waters is about 0.01-0.02 µg/L, but in surface ocean waters is *ca.* 0.3 µg/L (Castro-González & Méndez-Armenta, 2008). Lead still has a number of important uses in the present day; from sheets for roofing to screens for X-rays and radioactive emissions. Like many other contaminants, lead is ubiquitous and can be found occurring as metallic lead, inorganic ions and salts (Harrison, 2001). Lead has no essential function in man.

Food is one of the major sources of lead exposure; the others are air (mainly lead dust originating from petrol) and drinking water. Plant food may be contaminated with lead through its uptake from ambient air and soil; animals may then ingest the lead-contaminated vegetation. In humans, lead ingestion may arise from eating lead-contaminated vegetation or animal foods. Another source of ingestion is through the use of lead-containing vessels or lead-based pottery glazes (Ming-Ho, 2005). In humans, about 20 to 50% of inhaled, and 5 to 15% of ingested inorganic lead is absorbed. In contrast, about 80% of inhaled organic lead is absorbed, and ingested organic Pb is absorbed readily. Once in the bloodstream, lead is primarily distributed among blood, soft tissue, and mineralizing tissue (Ming-Ho, 2005). The bones and teeth of adults contain more than 95% of the total body burden of lead. Children are particularly sensitive to this metal because of their more rapid growth rate and metabolism, with critical effects in the developing nervous system (ATSDR, 2007; Castro-González & Méndez-Armenta, 2008).

The Joint FAO/ World Health Organization Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) for lead as 0.025 mg/kg body weight (bw) (JECFA, 2004). The WHO provisional guideline of 0.01 mg/L has been adopted as the standard for drinking water (WHO, 2004a).

2.2 Cadmium

The use of cadmium by man is relatively recent and it is only with its increasing technological use in the last few decades that serious consideration has been given to cadmium as a possible contaminant. Cadmium is naturally present in the environment: in air, soils, sediments and even in unpolluted seawater. Cadmium is emitted to air by mines, metal smelters and industries using cadmium compounds for alloys, batteries, pigments and in plastics, although many countries have stringent controls in place on such emissions (Harrison, 2001).

Tobacco smoke is one of the largest single sources of cadmium exposure in humans. Tobacco in all of its forms contains appreciable amounts of the metal. Because the absorption of cadmium from the lungs is much greater than from the gastrointestinal tract, smoking contributes significantly to the total body burden (Figueroa, 2008; Ming-Ho, 2005).

In general, for non-smokers and non-occupationally exposed workers, food products account for most of the human exposure burden to cadmium (ExtoxNet, 2003). In food, only inorganic cadmium salts are present. Organic cadmium compounds are very unstable. In contrast to lead and mercury ions, cadmium ions are readily absorbed by plants. They are equally distributed over the plant. Cadmium is taken up through the roots of plants to edible leaves, fruits and seeds. During the growth of grains such as wheat and rice, cadmium taken from the soil is concentrated in the core of the kernel. Cadmium also accumulates in animal milk and fatty tissues (Figueroa, 2008). Therefore, people are exposed to cadmium when consuming plant- and animal-based foods. Seafood, such as molluscs and crustaceans, can be also a source of cadmium (Castro-González & Méndez-Armenta, 2008; WHO 2004b; WHO 2006).

Cadmium accumulates in the human body affecting negatively several organs: liver, kidney, lung, bones, placenta, brain and the central nervous system (Castro-González & Méndez-Armenta, 2008). Other damages that have been observed include reproductive, and development toxicity, hepatic, haematological and immunological effects (Apostoli & Catalani, 2011; ATSDR, 2008).

The Joint FAO/WHO has recommended the PTWI as 0.007 mg/kg bw for cadmium (JEFCA, 2004). The EPA maximum contaminant level for cadmium in drinking water is 0.005 mg/L whereas the WHO adopted the provisional guideline of 0.003 mg/L (WHO, 2004a).

2.3 Mercury

Mercury is one of the most toxic heavy metals in the environment (Castro-González & Méndez-Armenta, 2008). Man released mercury into the environment by the actions of the agriculture industry (fungicides, seed preservatives), by pharmaceuticals, as pulp and paper preservatives, catalysts in organic syntheses, in thermometers and batteries, in amalgams and in chlorine and caustic soda production (Oehlenschläger, 2002; Zhang & Wong, 2007). Exposure to high levels of metallic, inorganic, or organic mercury can permanently damage the brain, kidneys, and developing fetus (ATSDR, 2003b).

The toxicity of mercury depends on its chemical form (ionic < metallic <organic) (Clarkson, 2006). Up to 90% of most organic mercury compounds are absorbed from food (Reilly, 2007).

Mercury can be detected in most foods and beverages, at levels of < 1 to 50 µg/kg (Reilly, 2007). Higher levels are often found in marine foods. Organic mercury compounds easily pass across biomembranes and are lipophilic. Therefore elevated mercury concentrations are mainly found in liver of lean species and in fatty fish species. Methyl mercury has a tendency to accumulate with fish age and with increasing trophic level. This leads to higher mercury concentrations in old fatty predatory species like tuna, halibut, redfish, shark, and swordfish (Oehlenschläger, 2002). In the year 2003, the JECFA revised its risk assessment on methylmercury in fish and adopted a lower PTWI of 1.6 µg/kg body weight/week to replace the previous PTWI of 3.3 µg/kg b.w./week of total mercury for the general population (Castro-González & Méndez-Armenta, 2008; JECFA, 2004). This risk assessment was based on two major epidemiology studies which investigated the relationship between maternal exposure to mercury through high consumption of contaminated fish and seafood and impaired neurodevelopment in their children (Castro-González & Méndez-Armenta, 2008; Grandjean et al., 1997; Murata et al., 2007). Because of the extreme health effects associated with mercury exposure, the current standards for drinking water were set by EPA and WHO at the very low levels of 0.002 mg/L and 0.001 mg/L, respectively (WHO, 2004a).

2.4 Arsenic

Arsenic is a metalloid. It is rarely found as a free element in the natural environment, but more commonly as a component of sulphur-containing ores in which it occurs as metal arsenides. Arsenic is quite widely distributed in natural waters and is often associated with geological sources, but in some locations anthropogenic inputs, such as the use of arsenical insecticides and the combustion of fossil fuels, can be extremely important additional sources. Arsenic occurs in natural waters in oxidation states III and V, in the form of arsenous acid (H_3AsO_3) and its salts, and arsenic acid (H_3AsO_5) and its salts, respectively (Sawyer et al., 2003).

The toxic effects of arsenic depend specially on oxidation state and chemical species, among others. Inorganic arsenic is considered carcinogenic and is related mainly to lung, kidney, bladder, and skin disorders (ATSDR, 2003a). The toxicity of arsenic in its inorganic form has been known for decades under the following forms: acute toxicity, subchronic toxicity, genetic toxicity, developmental and reproductive toxicity (Chakraborti et al., 2004), immunotoxicity (Sakurai et al., 2004), biochemical and cellular toxicity, and chronic toxicity (Mudhoo et al., 2011; Schwarzenegger et al., 2004). Drinking water is one of the primary routes of exposure of inorganic arsenic (Mudhoo et al., 2011; National Research Council, 2001). Ingestion of groundwater with elevated arsenic concentrations and the associated human health effects are prevalent in several regions across the world. Arsenic toxicity and chronic arsenicosis is of an alarming magnitude particularly in South Asia and is a major environmental health disaster (Bhattacharya et al., 2007; Chakraborti et al., 2004; Kapaj et al., 2006). Chronic arsenic ingestion from drinking water has been found to cause carcinogenic and noncarcinogenic health effects in humans (ATSDR, 2003a; Mudhoo et al., 2011; USEPA 2008, 2010a, 2010b). The growing awareness of arsenic-related health problems has led to a rethinking of the acceptable concentration in drinking water (Sawyer et al., 2003). Following a thorough review and in order to maximize health risk reduction, the USEPA in 2001 decided to reduce the drinking water maximum contaminant limit (MCL) to 0.010 mg/L, which is now the same as the WHO guidelines (USEPA, 2005a).

The adverse effects of arsenic in groundwater used for irrigation water on crops and aquatic ecosystems are also of major concern. The fate of arsenic in agricultural soils is less characterized compared to groundwater. However, the accumulation of arsenic in rice field soils and its introduction into the food chain through uptake by the rice plant is of major concern mainly in Asian countries (Bhattacharya et al., 2007; Duxbury et al., 2003). In foods, the major source of arsenic is mainly fish and seafood. The organic arsenic in food and seafood appears to be much less toxic than the inorganic forms (Uneyama et al., 2007). The presence of arsenic in fish has been detected in several species such as; sardine, chub mackerel, horse mackerel (Vieira et al., 2011) blue fish, carp, mullet tuna, and salmon (Castro-González & Méndez-Armenta, 2008). The results show that arsenic concentration is low in most fish, being always its highest concentration in muscle (Vieira et al., 2011). The JECFA established a PTWI for inorganic arsenic as 0.015 mg/kg body weight (FAO/WHO, 2005, JECFA 2004). Organo-arsenic intakes of about 0.05 mg/kg body weight/day seemed not to be associated to hazardous effects (Uneyama et al., 2007).

3. Assessment of exposure to heavy metals

Human exposure is defined by WHO as the amount of a substance in contact, over time and space, with the outer boundary of the body (WHO, 2000). The assessment of human exposure to contaminant chemicals in the environment can be measured by two major methods, each based on different data profiles, thus permitting the verification and validation of the information. One approach involves environmental monitoring i.e., determining the chemical concentration scenario. The second methodology is based on estimations of exposure through the use of biomarkers (Peterson, 2007).

Biomarkers are relevant indices in human health studies and are defined by the National Institute of Health (NIH) as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" (NIH, 2001). Biomarkers may be used at any level within biological organization (eg. molecular, cellular, or organ levels). These tools may be used to identify exposed individuals or groups, quantify the exposure, assess the health risks, or assist in diagnosis of environmental or occupational disease (Aitio et al., 2007).

A crucial measure for the assessment of exposure to hazardous chemicals, such as those from waste sites is evaluation of potentially exposed populations. This step also includes the degree, incidence extent, and routes of potential exposure. A most significant direct approach to assess exposure to hazardous substances within potentially exposed populations is to determine chemicals or their metabolic products on some biological fluids such as blood or urine, with certain defined levels being a reliable indicator of metal exposure.

However, long term storage of some toxic metals takes place in hard tissues such as teeth and bones. Additionally, samples of keratinous tissue components such as hair and nails are commonly used for routine clinical screening and diagnosis of longer-term exposure of metals. For example, the levels of lead in bones, hair, and teeth increase with age, suggesting a gradual accumulation of lead in the body. Therefore, contamination of food with lead and the possibility of chronic lead intoxication through the diet need constant monitoring

(Janssen, 1997). In addition, during mineralization of teeth cadmium and lead may persist within the matrix (Fischer, 2009).

Most of ingested arsenic is rapidly excreted via the kidney within a few days. However, high levels of arsenic are retained for longer periods of time in the bone, skin, hair, and nails of exposed humans (Mandal et al., 2003). Studies of arsenic speciation in the urine of exposed humans indicate that the metabolites comprise 10–15% inorganic arsenic and monomethylarsonic acid and a major proportion (60–80%) of dimethylarsenic acid (Bhattacharya et al., 2007). Recent studies have found monomethylarsonous acid and dimethylarsinous acid in trace quantities in human urine (Bhattacharya et al., 2007; Mandal et al., 2003).

Potential biomarkers include DNA and protein adducts, mutations, chromosomal aberrations, genes that have undergone induction and a host of other "early" cellular or subcellular events thought to link exposure and effect. Silins & Högberg (2011) in their review focus on three classes of biomarkers (exposure, effect and susceptibility). Biomarkers of exposure include measurements of parent compound, metabolites or DNA or protein adducts, and reflect internal doses, the biologically effective dose or target dose. Biomarkers of effects could be changes on a cellular level, such as altered expression of metabolic enzymes, and may also include markers for early pathological changes in complex disease developments, such as mutations and preneoplastic lesions. Biomarkers of susceptibility indicate an often constitutive ability of an individual to respond to specific exposures. The three categories of biomarkers cited above were exemplified by Nordberg (2010) in studies of health effects after heavy metal exposures.

Progress in the fields of genomics and proteomics is also reported, and more recent attention is focussed on proteomics technologies involved in finding new and relevant biomarkers for metal assessment. For example, preclinical changes in people exposed to heavy metals were recently monitored by proteomics biomarkers. In addition to urine and blood analysis proteomic profiling of serum samples, one representing the metal-exposed group and the other a control group, revealed three potential protein markers of preclinical changes in humans chronically exposed to a mixture of heavy metals (Kossowska et al., 2011). In this scope, and using these new tools, the effects of arsenic on human health were also illustrated (Vlaanderen et al., 2010).

Other symptoms associated with heavy metal exposure may also be evaluated such as effects on human skin damage, namely stress signals. For example, heavy metals down-regulated the phosphorylation levels of HSP27, and the ratio of p-HSP27 and HSP27 may be a sensitive marker or additional endpoint for the hazard assessment of potential skin irritation caused by chemicals and their products (Zhang et al., 2010).

Middendorf & Williams (2000) have critically reviewed early indicators of cadmium damage in kidneys, such as a low-molecular-weight protein (2-microglobulin), usually reabsorbed by the proximal tubules. Glycosuria, aminoaciduria, and the reduced ability of the kidney to secrete PAH are also indicators of nephrons damage by cadmium. An increase in urinary excretion of low- and high-molecular-weight proteins occurs as damage increases, reflecting the decline in glomerular filtration rate. This review also underlines that cadmium renal damage may occur after many years in workers removed from exposure in factories where nickel/cadmium was excessive.

More recently, some cellular functions have been used as biomarkers. For example, the autophagy pathway was proposed as a new sensitive biomarker for renal injury induced by cadmium (Chargui et al., 2011).

Non-invasive or a minimally invasive monitoring techniques are nowadays preferred, although these assays may require further improvement and validation. For example, the use of the buccal micronucleus assay as a biomarker of DNA damage is a contribution for epidemiological studies (Ceppi et al., 2010). Previously, children hand rinsing was used as a biomarker of short term exposure to As (Shalat et al., 2006). This method, added to the determination of total arsenic analyses in next morning urine was described by those authors for children using playground equipments treated with CCA.

In addition to the biomarkers mentioned above, various other groups of indicators have become widely used and play a significant role in trend analysis of exposures and chemical management response strategies. For example, higher plants, fungi, lichens, mosses, molluscs, and fish are important biomonitors for heavy metals contamination within the environment.

Another key point for human health risk evaluation is the mode of action analysis (MOA), defined by USEPA (2005b) as ''a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation''. The description of the adverse reactions in animal bioassays may provide relevant information for a better understanding of human health risk. In a recent review Thompson and co-workers (2011) focused on this parameter to illustrate the role of hexavalent chromium on human health assessment. Moreover, the relevance of animal testing data to humans is well established. However, the differences in metabolism between species, added to some intra-specific differences (e.g. gender, nutritional status, age, genetic predisposition, and frequency of exposure) are some limitations. In order to overlap these differences, a safety margin must be considered.

Finally, the complexity and number of available potential biomarkers for heavy metals exposure may be led to the development of improved prognostic and diagnostic tools.

4. Heavy metals analytical methods

4.1 Quantitative determination

Various approaches are described in the literature for detailed analysis of heavy metals in environmental, biological and food samples. Analytical methods frequently require sample preconcentration and/or pretreatment for the destruction of the organic matrix such as wet digestion, dry ashing, and microwave oven dissolution or extraction. Research has been carried out in sample collection, preservation, storage, pre-treatment, quantitative determination, speciation and microscopic analysis. Most of the new information about chemistry of heavy metals results mainly from continuing improvements in speciation and microscopic trace element analysis (Ortega, 2002). It is a tremendous challenge to develop sensitive and selective analytical methods that can quantitatively characterize trace levels of heavy metals in several types of samples (Rao, 2005). Table 1 summarizes the optical and the electrochemical methods applied for heavy metals determination (Karadjova et al., 2007; Draghici et al., 2010).

Technique	Principle	type of analysis	Applications
Atomic absorption spectrometry (AAS)	absorption of radiant energy produced, by a special radiation source, by atoms in their electronic ground state	-single element; -multielement analysis (2-6 elements)	widely used
Inductively coupled plasma with atomic emission spectrometry (ICP-AES)	measures the optical emission from excited atoms	simultaneous multielement analysis	widely used method for environmental analysis
Inductively coupled plasma with mass spectrometry (ICP-MS)	- argon plasma used as ion source; –used for separating ions based on their mass-to charge ratio	simultaneous multielement analysis	-widely used; -isotope determination
Atomic fluorescence spectrometry (AFS)	measures the light that is reemitted after absorption	single element	-mercury, arsenic, and selenium; -complementary technique to AAS
X-ray fluorescence (XRF)	-X-rays –primary excitation source; -elements emit secondary X-rays of a characteristic wavelength	simultaneous determination of most elements	-non-destructive analysis; -less suitable for analysis of minor and trace elements
Neutron activation analysis (NAA)	-conversion of stable nuclei of atoms into radioactive ones; -measurement of the characteristic nuclear radiation emitted by the radioactive nuclei	simultaneous multielement analysis	-most elements can be determined; - highly sensitive procedure
Electrochemical methods	-controlled voltage or current; -polarography; -potentiometry; - stripping voltammetry;	consecutive analysis of different metal ions	-analysis for transition metals and metalloids (total content or speciation analysis)

Table 1. Most usual methods applied for heavy metals determination (adapted from Draghici et al., 2010)

Atomic absorption spectrometry (AAS) and atomic emission spectrometry (AES) are the most widely used techniques for heavy metals quantitative analysis in environmental samples.

Several AAS can be distinguished depending on the mode of sample introduction and atomization. Flame (FAAS), graphite furnace (GFAAS), hydride generation (HGAAS), and cold vapor (CVAAS) systems have been described extensively (Ortega, 2002). FAAS and GFAAS are applicable for quantitative analysis of nearly 70 and 60 elements, respectively. Detection limits of GFAAS are approximately 100 times lower than those for FAAS. In HGAAS, the analyte is reduced to its volatile hydride and this technique is only applicable for the elements forming covalent gaseous hydrides, Ge, As, Se, Sn, Sb, Te, Bi, and Pb. Finally, CVAAS applies solely to Hg as it is the only analyte that has an appreciable atomic vapour pressure at room temperature (Ortega, 2002).

AES measures the optical emission from excited atoms to determine analyte concentration. Nowadays, Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) has clearly superseded FAAS because it is a truly multi-element technique.

Inductively coupled plasma-mass spectrometry (ICP-MS), a more recent technology, can also be used for rapid ultratrace multielement analysis. It consists of an ICP ion source, a quadrupole or magnetic sector mass filter, and an ion detection system. The detection sensitivity of ICP-MS is generally better than the graphite furnace AAS. One important feature is that it can detect and quantify small variations on isotopic compositions in geological and environmental samples (Zhang & Zhang, 2003). However, trace element quantification in biological and clinical samples present analytical complications associated with these sample types, such as non-spectroscopic interferences from the complex salt- and protein-rich matrix.

Atomic fluorescence spectrometry is a single-element technique that measures the light that is reemitted after absorption. It is a complementary technique to AAS that allows the determination of mercury, arsenic and selenium (after mineralization of the samples) using a specific atomic fluorescence spectrometer equipped with hydride generation (Biziuk & Kuczynska, 2007). The limits of detection are about 0.5 μg/L.

Radiochemical methods such as X-ray fluorescence spectrometry and neutron activation analysis are also strictly connected with atomic structure.

X-ray fluorescence analysis, one of the oldest nuclear techniques, is based on subjecting the sample to electromagnetic radiation of sufficient energy to remove electrons from the inner orbitals (Biziuk & Kuczynska, 2007). The fluorescence X-radiation is characteristic for each element and thus enables determination of elements with high selectivity. This radiation, however, has a low energy, that easily can be absorbed by the sample matrix; therefore, this technique is more suitable for very thin, very flat, and homogenous samples. USEPA published a standard method for elemental analysis using a field X-ray fluorescence analyzer (Poley, 1998). Applications include the *in situ* analysis of metals in soil, sediments, air monitoring filters, and lead in paint. Fluorescence radiation can also be obtained after bombardment of atoms with protons or charged particles produced by accelerator (Particle-Induced X-ray Emission; PIXE) (Biziuk & Kuczynska, 2007).

The sensitivity of X-ray spectrometry is lower than that of the neutron activation method (NAA). NAA is a non-destructive technique that is, in general, appropriate for materials that

are difficult to convert into a solution for analysis. The required amount of samples is *ca.*, maximally, 200 mg and is simply packaged in an irradiation container (quartz, polyethylene, or aluminium foil), sealed, and irradiated with neutrons for a time determined by the half-life of the radionuclide or the composition of the sample (Biziuk & Kuczynska, 2007). NAA can be applied for analysis of several heavy metals by measuring the gamma activities of their activated radioisotopes such as: ^{76}As; ^{115}Cd; ^{122}Sb, ^{124}Sb; and ^{203}Hg (Ortega, 2002; Chéry, 2003). The limits of detection may as low as 0.1 ng/g.

Another group of detection techniques is the electroanalytical methods. This group has gained considerable ground in the environmental and health analysis because of the simplicity, rapidity, and relative low cost of the techniques. Many of them exhibit excellent detection limits coupled with a wide dynamic range. They usually enable the determination of metals concentration at the level of their occurrence in the environment (Szyczewski, 2009). Measurements can generally be made on very small samples, typically in the microliter volume range. The principal methods include polarography, potentiometry and voltammetry. Stripping voltammetric analysis (especially the differential pulse anodic stripping voltammetry and adsorptive stripping voltammetry) is the most common and interesting option for the quantitation of heavy metals. Advantages of this technique include its sensitivity (10^{-10} mol/L in some cases) and accuracy; typically, minimal pretreatment of the sample is required. One major difficulty in the application of electroanalytical techniques to complex real-world samples has been the susceptibility of the electrode surface to fouling by surface active material in the sample. Metals commonly analyzed with this technique include Al, Fe, Cr, Co, Mo, Cd, Pb, Zn, Cu, and Ni, although others have also been reported. Typical results compare well with those obtained by GFAAS.

International organisation such as USEPA (http://www.epa.gov/), European Environment Agency (EEA; http://www.eea.eu.int/), WHO (http://www.who.int/peh/site map.htm), Occupational Safety and Health Administration (OSHA; http://www.osha.gov/), The National Institute for Occupational Safety and Health (NIOSH; http://www.cdc.gov/niosh/homepage.html), National Institute of Standards and Technology (NIST; http:// nvl.nist.gov/) and national structures established sampling and analytical techniques for pollutants determinations in different matrixes, different types of limits of pollutants in different matrixes and other regulations. Specialised laboratories use previously mentioned analytical methods but is also entitled to use other validated techniques.

4.2 Speciation analysis

The chemical species of an element are the specific forms of an element defined as to molecular, complex, or nuclear structure, or oxidation state (Ortega, 2002). The main analytical challenges concern speciation determination of redox and organometallic forms of arsenic and antimony, protein-bound cadmium, organic forms of lead (i.e. alkyllead compounds), organomercury compounds, inorganic platinum compounds, inorganic and organometallic compounds of selenium, organometallic forms of tin, and redox forms of chromium and vanadium. Recently, speciation analysis plays a unique role in the studies of biogeochemical cycles of chemical compounds, determination of toxicity and ecotoxicity of selected elements, quality control of food products, control of medicines and pharmaceutical products, technological process control, research on the impact of technological installation

on the environment, examination of occupational exposure and clinical analysis (Kot & Namiesnik, 2000; Michalski, 2009). The fields of health and nutrition benefit tremendously from the information that speciation analysis provides (Rao & Talluri, 2007).

Chromatographic methods (liquid chromatography (LC), ion chromatography (IC) and gas chromatography (GC) and capillary electrophoresis (CE) are the most popular separation techniques which are mainly combined with AAS, AES, ICP-AES or ICP-MS (X. Zhang & C. Zhang, 2003). Table 2 presents the more relevant separation methods and hyphenated techniques for metal speciation.

Technique	Principle	Type of analysis	Applications
Liquid chromatography (LC)	repartition of the analyte between a stationary phase and a mobile liquid one	simultaneous multielement analysis	-environmental metal speciation; - hyphenated techniques for speciation: LC-AAS, LC-AES, LC-ICP-AES, LC-ICP-MS
Gas chromatography (GC)	repartition of the analyte between a stationary phase and a mobile gas one	simultaneous multielement analysis	-volatile or thermally stable compounds (Hg, Sn, Pb alkyl compounds); - techniques for speciation: GC-AAS, GC-AES, GC-MS
Ion chromatography (IC)	LC technique which uses ion- exchange resins	simultaneous multielement analysis	-lack of selectivity control; -hyphenated techniques for metal speciation: IC-AAS, IC-ICP-AES, IC-ICP-MS
Capillary electrophoresis (CE)	differential migrationof charged analytes along a capillary filled with a suitable conducting electrolyte	simultaneous multielement analysis	-cations, organic and inorganic compounds of the same metal, metalloids; - hyphenated techniques: CE-MS, CE-ICP-MS

Table 2. More relevant separation methods and hyphenated techniques for metal speciation.

Most of the current approaches to As, Pb and Hg speciation analysis rely on complete (or partial) extraction of species, with or without previous de-fatting and clean up of crude extracts, followed by high performance liquid chromatographic (HPLC) or CE separation and element-selective detection (Karadjova et al., 2007). Widely used extractants are water, methanol (MeOH)–water and MeOH–chloroform. HPLC separations or CE with ICP-MS detection are mostly used, while HGAAS detection for As and Pb is gradually declining because of poorer sensitivity (*ca.* 10-fold) (Leermakers et al., 2006; Mattusch & Wennrich, 2005). Volatile compounds of Pb, Hg, Sn and Se may be also detected by gas chromatography coupled with AAS, AES or mass spectrometric detection.

Concerning speciation studies for cadmium, several methods have been applied being the most used in soils IC followed by FAAS or ICP-AES (Ortega, 2002). For protein-bound cadmium speciation, size-exclusion chromatography and ICP-MS are the preferred methods (Rao & Talluri, 2007).

Ultraviolet and visible molecular absorption spectrometry depends on the chemical form of the element and gives information about its speciation. It is based on the formation of coloured compounds with appropriate reagents, and on the absorption of characteristic electromagnetic wavelength by this compound. Formations of metal–organic complex are well characterized (Biziuk & Kuczynska, 2007). The use of specific complexing agents and solid phase extraction has improved the technique's selectivity and lowered its limits of detection to the sub-µg/L level. It is the cheapest method for the speciation determination of Al(III), V(V), Cr(VI), Fe(II), Se(IV), Sn(IV), Pt(II), Pt(IV) and Tl(III) (Szyczewski, 2009). Examples include Cr (III) and Cr(VI) species in soil extracts (Jankiewicz & Ptaszyński, 2005) and water samples (Michalski, 2005).

Electro-analytical techniques find their main application in the investigation of dissolved species in environmental samples. They are species selective rather than element selective that can be deployed *in situ* with minimal sample perturbation. If the main targets of speciation analysis are grouped into redox states, metal(loid) complexes and organometal(loid) compounds, analytes in all three areas can be determined by electroanalysis (Town et al., 2003).

5. Case study: The wood preservative chromated copper arsenate

Chromated copper arsenate (CCA) has been used extensively in the past as a chemical wood preservative, and several risks for human and environmental health have been associated with its widespread use. CCA type C (34.0% As_2O_5, 47.5% CrO_3 and 18.5% CuO, w/w), was the most frequently used chemical formulation due to the products durability, performance, and leach resistance. The high durability of CCA-treated wood, added to the persistence of CCA residues from chemical industries within the environment (water, soil, food crops) thus creating a great danger to the public health, including cancer. Furthermore the disposal of CCA-treated wood remains a public health problem, due to elevate arsenic levels released into the environment. For this reason a better understanding of chemical-induced target toxicity on both humans, and other animals is progressively becoming an important part of the impact of hazardous substances on human health.

5.1 Inherent toxicity associated to chemical components in CCA

The characterization of the components of CCA is relevant to better understand the hazards of CCA-treated wood on human health. In this mixture, arsenic and copper act as insecticide, and fungicide, respectively. In addition, chromium plays a key role in the fixation of copper and arsenic to the wood. The toxicity of chromium, copper and arsenic compounds was reviewed by Katz & Salem (2005) in different taxa of animals, and humans. The effects of CCA on aquatic and agricultural environment were also mentioned by these authors. Both arsenic and hexavalent chromium are hazardous chemicals, and detailed arsenic effects on human health were described at the beginning of this chapter.

Cr(VI) has been classified as a human carcinogen by inhalation routes of exposure (IARC, 1990). Although hexavalent chromium may occur naturally in the environment, it is commonly generated by production industries (eg. stainless steel, painting, welding, leather tanning, and electroplating, among others). Previously, an elegant review performed by Costa (1997) underlined the hazards of chromium compounds on animals and human systems, and organs (e.g. respiratory, gastrointestinal, immune, liver, and kidney). More recently, a great number of laboratory and epidemiological studies were reviewed focussing on the health hazards induced by hexavalent chromium-based chemicals (Singh et al., 1999; Thompson et al., 2011). An increased incidence of lung cancer was described in those studies on workers exposed to chromate dust (Tokar et al., 2011). In addition, several adverse changes on haematological parameters were noted in tannery workers (Ramzan et al., 2011).

Copper is a naturally occurring element and a well recognized essential nutrient for human health, since it is involved in several biological processes. It is present within a wide range of food sources such as beef/calf liver, shrimp, nuts, avocados, and beans (ATSDR, 2004). Relevant aspects of whole body copper metabolism, cell and molecular basis for copper homeostasis were recently reviewed by De Romaña and co-workers (2011). In addition, as a brief summary, copper essentiality and toxicity were also reported, and, although acute or chronic copper poisoning is not common, adverse reactions on liver after chronic copper exposure were underlined in this review. The potential health hazards associated to varying levels of copper intake was also recently described (Stern, 2010).

Acute nephrotoxicity of CCA compounds per se, $Na_2Cr_2O_7$, Na_3AsO_4 and $CuSO_4$ was previously described on rats by Mason and Edwards (1989). Although these authors had reported the synergistic effect of different dosage of those compounds, experimental evidences on the nephrotoxicity of CCA on mice have also been described. For example, a set of experiments was designed to study the effects of arsenic pentoxide and chromium trioxide on kidneys, based on histopathology, and histochemistry. In addition, chromium and arsenic analyses (ICP-MS and GFAAS) were used for evaluation. Acute tubular necrosis and the individual effects of those compounds were reported after administration of CCA solution (Matos et al., 2009a, 2009b, 2010).

The sensitizing activity of CCA, namely lymphocyte proliferation was reported in mice using the local lymph node assay (Fukuyama et al., 2008).

5.2 Human exposure to chromated copper arsenate

Human contact with CCA is mainly due to environmental and/or occupational exposures. It occurs during the handling of treated wood and related equipment. Skin exposure and

ingestion are the main routes of absorption, and inhalation is another probable route (Cocker et al., 2006). This investigation correlates exposure data based on urinary arsenic and chromium from workers.

Consequently, concerns have been raised owing to the high levels of arsenic and chromium concentrations in CCA treated wood, due to the potential human contact in occupational environments and to the ecological exposure (Chou et al., 2007; Zartarian et al., 2006). In this perspective, concerns about the safety of children have prompted more attention. In fact, children's exposure to these hazardous compounds may occur through hand-to-mouth playing activities. These include incidental ingestion of residues and dermal contact with the soil or sand beneath structures made of CCA-treated wood. Owing to this problem, a model was used in order to estimate children's absorbed dose of arsenic from CCA, using dermal contact and ingestion of soil (The probabilistic Stochastic Human Exposure and Dose Simulation model for wood preservatives - SHEDS-Wood) (Barraj et al., 2007; Xue, et. al., 2006; Zartarian et al., 2006).

6. Conclusion

Heavy metals have been proved to be toxic to both human and environmental health. Owing to their toxicity and their possible bioaccumulation, these compounds should be subject to mandatory monitoring. Several suitable separation and detection methods are available for laboratories engaged daily in routine analysis of a large number of biological or environmental samples. Also, the rapid development of molecular biological methods is bringing valuable advantages to the analytical field. Governments should promote harmonized data collection, research, legislation and regulations, and consider the use of indicators. Each of the two assessment methods outlined above (determining the chemical concentration scenario and the use of biomarkers) provide useful data helping to set standards and guideline values designed to protect human and environmental health from heavy metals contaminants. Exposure measurements are essential for the protection of high risk populations and subgroups. Furthermore, governments should, when setting acceptable levels or criteria related to chemicals, take into consideration the potential enhanced exposures and/or vulnerabilities of children.

7. Acknowledgment

8. References

Agency for Toxic Substance and Disease Registry (ATSDR). (2003a). Toxicological Profile for Arsenic U.S. Department of Health and Humans Services, Public Health Humans Services, Centers for Diseases Control. Atlanta.

Agency for Toxic Substance and Disease Registry (ATSDR). (2003b). Toxicological Profile for Mercury U.S. Department of Health and Humans Services, Public Health Humans Services, Centers for Diseases Control. Atlanta.

Agency for Toxic Substances and Disease Registry (ATSDR). (2004). Toxicological Profile for Copper. U.S. Department of Health and Humans Services, Public Health Service, Centers for Diseases Control. Atlanta.

Agency for Toxic Substance and Disease Registry (ATSDR). (2007). Toxicological Profile for Lead U.S. Department of Health and Humans Services, Public Health Humans Services, Centers for Diseases Control. Atlanta.

Agency for Toxic Substance and Disease Registry (ATSDR). (2008). Draft Toxicological Profile for Cadmium U.S. Department of Health and Humans Services, Public Health Humans Services, Centers for Diseases Control. Atlanta.

Aitio, A., Bernard, A., Fowler, B.A. & Nordberg, G.F. (2007). Biological monitoring and biomarkers. In: *Handbook on the Toxicology of Metals*, Nordberg, G.F., et al. (Eds.), pp. 65-78, Academic Press/Elsevier, 3rd ed., ISBN 0-123694132, USA.

Apostoli, P. & Catalani, S. (2011). Metal ions affecting reproduction and development. *Metal Ions in Life Science*, 8, 263-303.

Barraj, L.M., Tsuji, J.S. & Scrafford, C.G. (2007). The SHEDS-Wood Model: incorporation of observational data to estimate exposure to arsenic for children playing on CCA-treated wood structures. *Environmental Health Perspectives*, 115, 781-786.

Bhattacharya, P., Welch, A.H., Stollenwerk, K. G., McLaughlin, M.J., Bundschuh, J. & Panaullah, G. (2007). Arsenic in the environment: Biology and Chemistry, *Science of the Total Environment*, 379, 109–120.

Biziuk, M. & Kuczynska, J. (2007). Mineral Components in Food — Analytical Implications, In: *Mineral Components in Foods*, Szefer P. And Nriagu J.O. (Eds), pp. 1-31, Taylor & Francis Group, ISBN 978-0-8493-2234-1, Boca Raton, FL.

Castro-González, M.I. & Méndez-Armenta, M. (2008). Heavy metals: Implications associated to fish consumption. *Environmental Toxicology & Pharmacology*, 26, 263-271.

Ceppi, M., Biasotti, B., Fenech, M., & Bonassi, S. (2010). Human population studies with the exfoliated buccal micronucleus assay: statistical and epidemiological issues. *Mutation Research*, 705, 11-19.

Chakraborti, D., Sengupta, M.K., Rahaman, M.M., Ahamed, S., Chowdhury, U.K. & Hossain M.A. (2004). Groundwater arsenic contamination and its health effects in the Ganga–Megna–Brahmaputra Plain. *Journal of Environmental Monitoring*, 6, 74–83.

Chargui, A., Zekri, S., Jacquillet, G., Rubera, I., Ilie, M., Belaid, A., Duranton, C., Tauc, M., Hofman, P., Poujeol, P., El May, M.V. & Mograbi, B. (2011). Cadmium-induced autophagy in rat kidney: an early biomarker of subtoxic exposure. *Toxicology Science*, 121, 31-42.

Chéry, C. C. (2003). Gel Electrophoresis for Speciation Purposes, In: *Handbook of Elemental Speciation: Techniques and Methodology*, Cornelis, R., Caruso, J. Crews, H. & Heumann, K. (Eds), pp. 224-239, John Wiley & Sons Ltd, ISBN: 0-471-49214-0, West Sussex, England.

Clarkson, T. (2006). The toxicology of mercury and its chemical compounds. *Critical Reviews in Toxicology*, 36, 609–662.

Cocker, J., Morton, J., Warren, N., Wheeler, J.P., & Garrod, A.N. (2006). Biomonitoring for chromium and arsenic in timber treatment plant workers exposed to CCA wood preservatives. *Annals of Occupational Hygiene*, 5, 517-525.

Costa, M. (1997). Toxicity and carcinogeneicity of Cr(VI) in animal models and humans. *Critical Review in Toxicology*, 27, 431-442.

Chou, S., Colman, J., Tylenda, C., & De Rosa, C. (2007). Chemical-specific health consultation for chromated copper arsenate chemical mixture: port of Djibouti. *Toxicology & Industrial Health,* 23, 183-208.

De Romaña, D.J., Olivares, M., Uauy, R. & Araya, M. (2011). Risks and benefits of copper in light of new insights of copper homeostasis. *Journal of Trace Elements in Medicine and Biology*, 25, 3–13.

Draghici, C., Coman, G., Jelescu, C., Dima, C. & Chirila, E. (2010). Heavy metals determination in environmental and biological samples, In: Environmental Heavy Metal Pollution and Effects on Child Mental Development- Risk Assessment and Prevention Strategies, NATO Advanced Research Workshop, Sofia, Bulgaria, 28 April-1 May 2010.

Duxbury, J.M, Mayer, A.B., Lauren, J.G. & Hassan, N. (2003). Food chain aspects of arsenic contamination in Bangladesh: effects on quality and productivity of rice. *Journal of Environmental Science Health Part A, Environmental Science Engineering & Toxic Hazard Substance Control*, 38, 61–69.

European Commission (2006). Regulation (EC) No 1881/2006. JO L364, 20.12.06, pp. 5-24.

ExtoxNet. (2003) Cadmium contamination of food, Available from http://ace.orst.edu/ info/extoxnet/faqs/foodcon/cadmium.htm2003

FAO/WHO Expert Committee on Food Additives, Arsenic. (2005). Available from http://www.inchem.org/documents/jecfa/jeceval/jec_159.htm

Fischer, A., Wiechuła, D., Postek-Stefańska, L. & Kwapuliński, J. (2009). Concentrations of metals in maxilla and mandible deciduous and permanent human teeth. *Biology of Trace Elements Research*, 132, 19–26.

Figueroa, E. (2008). Are more restrictive food cadmium standards justifiable health safety measures or opportunistic barriers to trade? An answer from economics and public health. *Science of the Total Environment*, 389, 1-9.

Fukuyama, T., Ueda, H., Hayashi, K., Tajima, Y., Shuto, Y., Kosaka, T. & Harada, T. (2008). Sensitizing potential of chromated copper arsenate in local lymph node assays differs with the solvent used. *Journal of Immunotoxicology*, 5, 99-106.

Grandjean, P., Weihe, P., White, R.F., Debes, F., Araki, S., Yokoyama, K., Murata, K., Sorensen, N., Dohl, R. & Jorgensen, P.J. (1997). Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicology & Teratol*ogy, 19, 417-428.

Guney, M., Zagurya, G.J., Doganb, N. & Onayb, T.T. (2010). Exposure assessment and risk characterization from trace elements following soil ingestion by children exposed to playgrounds, parks and picnic areas. *Journal of Hazardous Materials*, 182, 656–664.

Harrison, N. (2001). Inorganic contaminants in food, In: Food Chemical Safety Contaminants, Watson, D.H. (Ed.), pp. 148-168, Ltd, first Edition, Woodhead Publishing ISBN 1-85573-462-1, Cambridge.

International Agency for Research on Cancer (IARC). (1990). Chromium, nickel and welding. IARC Monographs Evaluation on Carcinogenic Risks Human, 49, 1–648.

Janssen, M.M.T. (1997). Contaminants, In: *Food Safety and Toxicity*, Vries, J. (Ed.), pp. 61-71, CRC Press LLC, ISBN 0-8493-9488-0, first edition, Boca Raton, USA.

Jankiewicz, B. & Ptaszyński, B. (2005). Determination of chromium in soil of łódź gardens. *Polish Journal of Environmental Studies* 14, 869-875.

Joint FAO/WHO Expert Committee on Food Additives (JECFA). (2004). Safety evaluation of certain food additives and contaminants. WHO Food Additives Series No 52.

Jomova, K. & Valko, M. (2010). Advances in metal-induced oxidative stress and human disease. *Toxicology*, 283, 65–87.

Kapaj, S., Peterson, H., Liber, K. & Bhattacharya, P. (2006). Human health effects from chronic arsenic poisoning — a review. *Journal of Environmental Science Health Part A, Environmental Science Engineering Toxic Hazard Substance Control*, 41, 2399–2428.

Karadjova, I.B., Petrov, P.K, Serafimovski, I., Stafilov, T. & Tsalev, D.L. (2007). Arsenic in marine tissues — The challenging problems to electrothermal and hydride generation atomic absorption spectrometry. *Spectrochimica Acta Part B*, 62, 258–268.

Katz, S.A. & Salem, H. (2005). Chemistry and toxicology of building timbers pressure-treated with chromate copper arsenate: a review. *J. of Applied Toxicology*, 25, 1-7.

Khlifi, R. & Hamza-Chaffai, A. (2010). Head and neck cancer due to heavy metal exposure via tobacco smoking and professional exposure: A review. *Toxicology & Applied Pharmacology*, 248, 71–88.

Kossowska, B., Dudka, I., Bugla-Płoskońska, G., Szymańska-Chabowska, A., Doroszkiewicz, W., Gancarz, R., Andrzejak, R. & Antonowicz-Juchniewicz, J. (2010). Proteomic analysis of serum of workers occupationally exposed to arsenic, cadmium, and lead for biomarker research: A preliminary study. *Science of the Total Environment*, 408, 5317–5324.

Kot, A. & Namiesnik, J. (2000). The role of speciation in analytical chemistry. *Trends in Analytical Chemistry*, 19, 69–79.

Leermakers, M., Baeyens, W., De Gieter, M., Smedts, B., Meert, C., De Bisschop, H.C., Morabito, R. & Quevauviller, P.H. (2006). Toxic arsenic compounds in environmental samples: speciation and validation, *Trends in Analytical Chemistry*, 25, 1–10.

Mandal, B.K., Ogra, Y. & Suzuki, K.T. (2003). Speciation of arsenic in human nail and hair from arsenic-affected area by HPLC-inductively coupled argon plasma mass spectrometry. *Toxicology &Applied Pharmacology*, 189, 73–83.

Mason, R.W., & Edwards, I.R. (1989). Acute toxicity of combinations of sodium dichromate, sodium arsenate and copper sulphate in the rat. *Comparative Pharmacology & Toxicology*, 93, 121-125.

Matos, R.C., Vieira, C., Morais, S., Pereira, M.L., & Pedrosa de Jesus, J.P. (2009a). Nephrotoxicity of CCA-treated wood: a comparative study with As_2O_5 and CrO_3 on mice. *Environmental Toxicology & Pharmacology*, 27, 259–263.

Matos, R.C., Vieira, C., Morais, S., Pereira, M.L., & Pedrosa de Jesus, J.P. (2009b). Nephrotoxicity effects of the wood preservative chromium copper arsenate on mice: histopathological and quantitative approaches. *Journal of Trace Elements in Medicine & Biology*, 23, 224–230.

Matos, R.C., Vieira, C., Morais, S., Pereira, M.L., & Pedrosa de Jesus, J.P. (2010). Toxicity of chromated copper arsenate: A study in mice. *Environmental Research*, 110, 424–427.

Mattusch, J. & Wennrich, R. (2005). Novel analytical methodologies for the determination of arsenic and other metalloid species in solids, liquids and gases. *Mikrochimica Acta*, 151, 137–139.

Michalski, R. (2005). Trace level determination of Cr(III)/Cr(VI) in water samples using ion chromatography with UV detection. *Journal of Liquid Chromatography & Related Technologies*, 28, 2849–2862.

Michalski, R. (2009). Applications of ion chromatography for the determination of inorganic cations. *Critical Reviews in Analytical Chemistry*, 39, 230–250.

Middendorf, P.J. & Williams, P.L. (2000). Nephrotoxicity: Toxic Responses of the Kidney, In: *Principles of Toxicology Environmental & Industrial Applications*, Williams, P.L., James, R.C., Roberts, S.M. (Eds), pp. 129-143, John Wiley & Sons, Inc., ISBN 0-47129321-0, New York.

Ming-Ho, Y. (2005). *Environmental Toxicology: Biological and Health Effects of Pollutants*, Chap. 12, CRC Press LLC, ISBN 1-56670-670-2, 2nd Edition, BocaRaton, USA.

Mudhoo, A., Sharma, S.K., Garg, V.K. & Tseng, C-H. (2011). Arsenic: an overview of applications, health, and environmental concerns and removal processes. *Critical Reviews in Environmental Science & Technology*, 41, 435–519.

Murata, K., Grandjean, P. & Dakeishi, M. (2007). Neurophysiological evidence of methylmercury neurotoxicity. *Am.J.Int.Med.*, 50, 765-771.

National Institute of Health. (2001). Biomarkers Definitions Working Group. Biomarkers and Surrogate endpoints: preferred definitions and conceptual framework. *Clinical Pharmacology & Therapeutics*, 69, 89-95.

National Research Council. (2001). Arsenic in drinking water—Update. Washington DC, National Academy Press.

Nordberg, G.F. (2010). Biomarkers of exposure, effects and susceptibility in humans and their application in studies of interactions among metals in China. *Toxicology Letters*, 192, 45-49.

Oehlenschläger, J. (2002). Identifying heavy metals in fish In: *Safety and Quality issues in fish processing*, Bremner, H.A. (Ed), pp. 95-113, Woodhead Publishing Limited, 978-1-84569-019-9, Cambridge.

Ortega, R. (2002). Analytical Methods for Heavy Metals in the Environment: Quantitative Determination, Speciation, and Microscopic Analysis, In: *Heavy Metals in the Environment*, Sarkar, B. (Ed), pp. 35-68, Marcel Dekker Inc., ISBN 0-8247-0630-7, New York.

Peterson, P.J. (2007) Assessment of Exposure to Chemical Pollutants in Food and Water, In: *Mineral Components in Foods*, Szefer P. And Nriagu J.O. (Eds), pp. 413-431, Taylor & Francis Group, ISBN 978-0-8493-2234-1, Boca Raton, FL.

Poley, G.J. (1998). Environmental Technology Verification Report. Field Portable X-ray Fluorescence Analyzer. Washington, DC: USEPA, EPA/600/R-97/145.

Ramzan, M., Malik, M.A., Iqbal, Z., Arshad, N., Khan, S.Y. & Arshad, M. (2011). Study of hematological indices in tannery workers exposed to chromium in Sheikhupura (Pakistan*). Toxicology & Industrial Health*, Apr 19. [Epub ahead of print].

Rao, R.N. & Talluri, M.V.N.K. (2007). An overview of recent applications of inductivelycoupled plasma-mass spectrometry (ICP-MS) in determination of inorganic impurities in drugs and pharmaceuticals. *Journal of Pharmaceutical & Biomedical Analysis*, 43, 1–13.

Rao, T.P., Metilda, J. & Gladis, M. (2005). Overview of analytical methodologies for sea water analysis: Part I—Metals. *Critical Reviews in Analytical Chemistry*, 35, 247–288.

Reilly, C. (2007). Pollutants in Food —Metals and Metalloids, In: *Mineral Components in Foods*, Szefer P. And Nriagu J.O. (Eds), pp. 363-388, Taylor & Francis Group, ISBN 978-0-8493-2234-1, Boca Raton, FL.

Sakurai, T., Kojima, C., Ochiai, M., Ohta, T. & Fujiwara, K. (2004). Evaluation of in vivo acute immunotoxicity of a major organic arsenic compound arsenobetaine in seafood. *International Immunopharmacology*, 4, 179–184.

Sawyer, C.N., McCarty, P.L. & Parkin, G.F. (2003). *Chemistry for environmental and Engineering and Science* (fifth Edition), Mc Graw Hill, ISBN 0-07-248066-1, NY.

Schwarzenegger, A., Tamminen, T., & Denton, J.E. (2004). Public health goals for chemicals in drinking water arsenic. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

Shalat, S.L., Solo-Gabriele, H.M., Fleming, L.E., Buckley, B.T., Black, K., Jimenez, M., Shibata, T., Durbin, M., Graygo, J., Stephan, W. & Van De Bogart, G. (2006). A pilot study of children's exposure to CCA-treated wood from playground equipment. *Science of Total Environment*, 367, 80-88.

Silins, I. & Johan Högberg, J. (2011). Combined toxic exposures and human health: biomarkers of exposure and effect. *International Journal of Environmental Research & Public Health*, 8, 629-647.

Singh, J., Pritchard, D.E., Carlisle, D.L., Mclean, J.A., Montaser, A., Orenstein, J.M. & Patierno, S.R. (1999). Internalization of carcinogenic lead chromate particles by cultured normal human lung epithelial cells: formation of intracellular lead-inclusion bodies and induction of apoptosis. *Toxicology & Applied Pharmacology*, 161, 240–248.

Stern, B.R. (2010). Essentiality and Toxicity in Copper Health Risk Assessment: Overview, Update and Regulatory Considerations. *Journal of Toxicology & Environmental Health- Part A*, 73, 114-127.

Szyczewski, P., Siepak, J. , Niedzielski, P. & Sobczyński, T. (2009). Research on heavy metals in Poland. *Polish Journal of Environmental Studies*, 18, 755-768.

Tokar, E.J., Benbrahim-Tallaa, L. & Waalkes, M.P. (2011). Metal ions in human cancer development. *Metal Ions on Life Science*, 8, 375-401.

Thompson, C.H., Haws, L.C., Harris, M.A., Gatto, N. M. & Proctor, D. M. (2011). Application of the U.S. EPA mode of action framework for purposes of guiding future research: a case study involving the oral carcinogenicity of hexavalent chromium. *Toxicological Sciences*, 119, 20–40.

Town, R.M., Emons, H. & Buffle, J. (2003). Speciation Analysis by Electrochemical Methods, In: *Handbook of Elemental Speciation: Techniques and Methodology*, Cornelis, R., Caruso, J. Crews, H. & Heumann, K. (Eds), pp. 421-460, John Wiley & Sons Ltd, ISBN: 0-471-49214-0, West Sussex, England.

Uneyama, C., Toda, M., Yamamoto, M. & Morikawa, K. (2007). Arsenic in various foods: Cumulative data. *Food Additives & Contaminants*, 24, 447-534.

United States Environmental Protection Agency (USEPA). (2005a). Arsenic in drinking water fact sheet. 10.07.2011, Available from http://www.epa.gov/safewater/arsenic.html.

United States Environmental Protection Agency (USEPA). (2005b). Guidelines for carcinogen risk assessment EPA/630/P-03/001F.

United States Environmental Protection Agency (USEPA). (2008). Risk-Based Concentration Table, Available from http://www.epa.gov/reg3hwmd/risk/human/index.htm

United States Environmental Protection Agency (USEPA). (2009). Integrated Risk Information System (IRIS), Washington, DC 20005, Available from http://www.epa.gov/ncea/iris/.

United States Environmental Protection Agency (USEPA). (2010a). Mid-Atlantic Risk Assessment, available from http://www.epa.gov/reg3hwmd/risk/human/ rbconcentration_table/usersguide.htm

United States Environmental Protection Agency (USEPA). (2010b). Risk-Based Concentration Table. Region 3 Fish Tissue Screening Levels.

Vieira, C., Morais, S., Ramos, S., Delerue-Matos, C. & Oliveira, M.B.P.P. (2011). Mercury, cadmium, lead and arsenic levels in three pelagic fish species from the Atlantic Ocean: intra- and inter-specific variability and human health risks for consumption. *Food & Chemical Toxicology*, 49, 923-932.

Vlaanderen, J., Moore, L. E., Smith, M. T., Lan, Q., Zhang, L., Skibola, C. F., Rothman, N. & Vermeulen, R. (2010). Application of OMICS technologies in occupational and environmental health research; current status and projections. *Occupational & Environmental Medicine*, 67, 136-43.

WHO. (2004a). Guidelines for drinking-water quality. Sixty-first meeting, Rome, 10-19 June 2003. Joint FAO/WHO Expert Committee on Food Additives, Avaible from http://ftp.fao.org/es/esn/jecfa/jecfa61sc.pdf

WHO. (2004b). Evaluation of certain food additives contaminants. Sixty-first report of the joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, No. 922.

WHO. (2006). Evaluation of certain food contaminants. Sixty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, No. 930.

WHO/IPCS. (2000) Human Exposure Assessment, Environmental Health Criteria 214, WHO, Geneva.

Xue, J., Zartarian, V. G, Ozkaynak, H., Dang, W., Glen, G., Smith, L. & Stallings, C. (2006). A probabilistic arsenic exposure assessment for children who contact chromated copper arsenate (CCA)-treated playsets and decks, Part 2: Sensitivity and uncertainty analyses. *Risk Analysis*, 26, 533-541.

Zartarian, V., Jianping, X., Özkaynak, H., Dang, W., Glen, G., Smith, L., & Stallings, C. (2006). A Probabilistic Arsenic Exposure Assessment for Children Who Contact CCA-Treated Playsets and Decks. Part 1: Model Methodology, Variability Results, and Model Evaluation. *Risk Analysis*, 26, 515-531.

Zhang, I. & Wong, M.H. 2007. Environmental mercury contamination in China: sources and impacts. *Environment International*, 33, 108-121.

Zhang, X. & Zhang, C. (2003). Atomic Absorption and Atomic Emission Spectrometry, In: *Handbook of Elemental Speciation: Techniques and Methodology*, Cornelis, R., Caruso, J. Crews, H. & Heumann, K. (Eds), pp. 241-257, John Wiley & Sons Ltd, ISBN: 0-471-49214-0, West Sussex, England.

Zhang, Q., Zhang, L., Xiao, X., Su, Z., Zou, P., Hu, H., Yadong Huang, Y. & Qing-Yu, H. (2010). Heavy metals chromium and neodymium reduced phosphorylation level of heat shock protein 27 in human keratinocytes. *Toxicology In Vitro*, 24, 1098-1104.
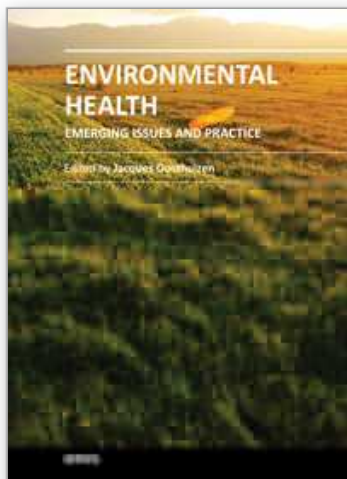
Environmental Health - Emerging Issues and Practice
Edited by Prof. Jacques Oosthuizen

Environmental health practitioners worldwide are frequently presented with issues that require further investigating and acting upon so that exposed populations can be protected from ill-health consequences. These environmental factors can be broadly classified according to their relation to air, water or food contamination. However, there are also work-related, occupational health exposures that need to be considered as a subset of this dynamic academic field. This book presents a review of the current practice and emerging research in the three broadly defined domains, but also provides reference for new emerging technologies, health effects associated with particular exposures and environmental justice issues. The contributing authors themselves display a range of backgrounds and they present a developing as well as a developed world perspective. This book will assist environmental health professionals to develop best practice protocols for monitoring a range of environmental exposure scenarios.

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