HUMAN HEALTH RISK ASSESSMENT OF TOXIC METALS

Ph.D. THESIS

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ABBREVIATIONS OF NOTES

ADD	Average Daily Dose
AT	Average Time
ATSDR	Agency for Toxic Substances and Disaese Registry
BCF	Bioconcentration Factor
BW	Body Weight
C	Concentration
DEFRA	Department for Environment, Food and Rural Affairs
ED	Event Duration
EF	Event Frequention
EHC	Environmental Health Criteria
HQ	Hazard Quotient
IR	Ingestion Rate
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
NOAEL	No Observed Adverse Effect Level
RfC	Reference Concentration
RfD	Reference Dose
RDA	Recommended Dietery Allowances
US EPA	United States Environmental Protection Agency
WHO	World Health Organization
WMU	Waste Management Unit

1. INTRODUCTION

1.1. Theory of risk assessment

People are exposed to a variety of potentially harmful agents in the air they breathe, the liquids they drink, the food they eat, the surfaces they touch and the products they use. An important aspect of public health protection is the prevention or reduction of exposures to environmental agents that contribute, either directly or indirectly, to increased rates of premature death, disease, discomfort or disability (WHO, 2000).

Chemicals have become an indispensable part of human life, sustaining activities and development, preventing and controlling many diseases, and increasing agricultural productivity. Despite their benefits, chemicals may, especially when misused, cause adverse effects on human health and environmental integrity. The widespread application of chemicals throughout the world increases the potential of adverse effects. The growth of chemical industries, both in developing as well as in developed countries, is predicted to continue to increase. In this context, it is recognized that the assessment and management of risks from exposure to chemicals are among the highest priorities in pursuing the principles of sustainable development (WHO, 1999).

Since about 1970 the field of risk assessment has received widespread attention within both the scientific and regulatory communities (Paustenbach, 2002). Risk assessment is a conceptual framework that provides the mechanism for a structured review of information relevant to estimating health or environmental outcomes. In conducting risk assessments, the National Academy of Sciences risk assessment paradigm has proven to be an useful tool (National Reasearch Council, 1983). This paradigm divides the risk assessment process into four distinct steps: hazard identification, dose-response assessment, exposure assessment and risk characterization (Cirone and Duncan, 2000).

The purpose of hazard identification is to evaluate the weight of evidence for adverse effects in humans based on assessment of all available data on toxicity and mode of action. It is designed to address primarily two questions: (1) whether an agent may pose a health hazard to human beings, and (2) under what circumstances an identified hazard may be expressed. Hazard identification is based on analyses of a

variety of data that may range from observations in humans to analysis of structure-activity relationships. The result of the hazard identification exercise is a scientific judgement as to whether the chemical evaluated can, under given exposure conditions, cause an adverse health effect in humans. Generally, toxicity is observed in one or more target organ(s). Often, multiple end-points are observed following exposure to a given chemical. The critical effect, which is usually the first significant adverse effect that occurs with increasing dose, is determined.

Dose-response assessment is the process of characterizing the relationship between the dose of an agent administered or received and the incidence of an adverse health effect. For most types of toxic effects (i.e. organ-specific, neurological/behavioural, immunological, non-genotoxic carcinogenesis, reproductive or developmental), it is generally considered that there is a dose or concentration below which adverse effects will not occur (i.e. a threshold). For other types of toxic effects, it is assumed that there is some probability of harm at any level of exposure (i.e. that no threshold exists). At the present time, the latter assumption is generally applied primarily for mutagenesis and genotoxic carcinogenesis.

If a threshold has been assumed, traditionally, a level of exposure below which it is believed that there are no adverse effects, based on a NOAEL/LOAEL (no/lowest-observed adverse effect level) and uncertainty factors, has been estimated. Alternatively, the magnitude by which the NOAEL/LOAEL exceeds the estimated exposure (i.e. the "margin of safety") is considered in light of various sources of uncertainty. In the past, this approach has often been described as a "safety evaluation". Therefore, the dose that can be considered as a first approximation of the threshold is critical. Increasingly, however, the "benchmark dose", a model-derived estimate (or its lower confidence limit) of a particular incidence level for the critical effect, is being proposed for use in quantitative assessment of the dose-response for such effects. There is no clear consensus on appropriate methodology for the risk assessment of chemicals for which the critical effect may not have a threshold (i.e. genotoxic carcinogens and germ cell mutagens). Indeed, a number of approaches based largely on characterization of dose-response have been adopted for assessment in such cases. Therefore, the critical data points are those that define the slope of the dose-response relationship (rather than the NOAEL, which is the first approximation of a threshold).

The third step in the process of risk assessment is the exposure assessment, which has the aim of determining the nature and extent of contact with chemical substances experienced or anticipated under different conditions. Multiple approaches can be used to conduct exposure assessments. Generally, approaches include indirect and direct techniques, covering measurement of environmental concentrations and personal exposures, as well as biomarkers. Questionnaires and models are also often used. Exposure assessment requires the determination of the emissions, pathways and rates of movement of a substance and its transformation or degradation, in order to estimate the concentrations to which human populations or environmental spheres (water, soil and air) may be exposed. Depending on the purpose of an exposure assessment, the numerical output may be an estimate of either the intensity, rate, duration or frequency of contact exposure or dose (resulting amount that actually crosses the boundary). Three main exposure routes are determined in exposure assessment: dermal, oral and respiratory. For risk assessments based on dose-response relationships, the output usually includes an estimate of dose. It is important to note that the internal dose, not the external exposure level, determines the toxicological outcome of a given exposure. The general equation of selected exposure route is the following:

$$\mathrm{ADD} = \frac{\mathrm{C} \times \mathrm{IR} \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{BW} \times \mathrm{AT}}.$$

In this equation C is concentration in the media (mg kg^{-1}), IR is ingestion rate (kg day^{-1}), EF is exposure frequency (days $year^{-1}$), ED is exposure duration (years), BW is body weight (kg), AT is average time (days).

The term "worst case exposure" has historically meant the maximum possible exposure, or where everything that can plausibly happen to maximize exposure, happens. While in actuality, this worst case exposure may fall on the uppermost point of the population distribution, in most cases, it will be somewhat higher than the individual in the population with the highest exposure. The worst case represents a hypothetical individual and an extreme set of conditions; this will usually not be observed in an actual population (US EPA, 1992).

Therfore in most risk assessments the "weakest link" is the exposure assessment (Bridges, 2003). In one hand the uncertainty of exposure assessment is caused by the calculation of residues in soil, water or air, which is often not a good indicator of

bioavailability. The use of biomarkers may provide our information about the pollution (Kakkar and Jaffery, 2005). In the other hand pollution often occurs in hotspots due to point sources and it is inadequate to assume that the whole population is exposed to the same, maybe average, contaminant level. By maintinaing the spatial distribution of soil contaminant levels and receptors, it is possible, via the source-pathway-receptor paradigm to calculate more realistic contaminant intake and hence risks (Gay and Korre, 2006). Site-specific risk assessment is based on location specific exposure patways and land-uses, hence get more realistic results, but often is limited to high-profile studies and large projects (Lester et al., 2007).

Risk characterization is the final step in risk assessment. It is designed to support risk managers by providing, in plain language, the essential scientific evidence and rationale about risk that they need for decision-making. In risk characterization, estimates of the risk to human health under relevant exposure scenarios are provided. Thus, a risk characterization is an evaluation and integration of the available scientific evidence used to estimate the nature, importance, and often the magnitude of human and/or environmental risk, including attendant uncertainty, that can reasonably be estimated to result from exposure to a particular environmental agent under specific circumstances.

The term "risk management" encompasses all of those activities required to reach decisions on whether an associated risk requires elimination or necessary reduction. Risk management strategies/or options can be broadly classified as regulatory, non-regulatory, economic, advisory or technological, which are not mutually exclusive. Key decision factors such as the size of the population, the resources, costs of meeting targets and the scientific quality of risk assessment and subsequent managerial decisions vary enormously from one decision context to another.

It is also recognized that risk management is a complex multidisciplinary procedure which is seldom codified or uniform, is frequently unstructured, but which can respond to evolving input from a wide variety of sources. Increasingly, risk perception and risk communication are recognized as important elements, which must also be considered for the broadest possible public acceptance of risk management decisions (WHO, 1999; WHO, 2000; Paustenbach, 2002).

1.2. Main properties of metals

1.2.1. Arsenic

Arsenic (atomic number 33; relative atomic mass 74.91) is a metalloid widely distributed in the earth's crust and present at an average concentration of 2 mg kg^{-1}. It occurs in trace quantities in all rock, soil, water and air. Arsenic can exist in four valency states: –3, 0, +3 and +5. Under reducing conditions, arsenite (As^{3+}) is the dominant form; arsenate (As^{5+}) is generally the stable form in oxygenated environments. Elemental arsenic is not soluble in water. Arsenic salts exhibit a wide range of solubilities depending on pH and the ionic environment (WHO, 2001b).

Arsenic is the main constituent of more than 200 mineral species, of which about 60% are arsenate, 20% sulfide and sulfosalts and the remaining 20% include arsenides, arsenites, oxides and elemental arsenic. The most common of the arsenic minerals is arsenopyrite (FeAsS), and arsenic is found associated with many types of mineral deposits, especially those including sulfide mineralization (Alloway, 1995). Volcanic action is the most important natural source of arsenic, followed by low-temperature volatilization. Inorganic arsenic is found in groundwater used as drinking-water in several parts of the world: in Taiwan (Chen et al., 1994), West Bengal, India (Mandal et al., 1996) and more recently in most districts of Bangladesh (Dhar et al., 1997; Biswas et al., 1998). Mining, smelting of non-ferrous metals and burning of fossil fuels are the major industrial processes that contribute to anthropogenic arsenic contamination of air, water and soil. Historically, use of arsenic-containing pesticides has left large tracts of agricultural land contaminated. The use of arsenic in the preservation of timber has also led to contamination of the environment.

Background concentrations in soil range from 1 to 40 mg kg^{-1}, with a mean value of 5 mg kg^{-1}. Naturally elevated levels of arsenic in soils may be associated with geological substrata such as sulfide ores. Terrestrial plants may accumulate arsenic by root uptake from the soil or by adsorption of airborne arsenic deposited on the leaves. Arsenic levels are higher in biota collected near anthropogenic sources or in areas with geothermal activity.

Non-occupational human exposure to arsenic in the environment is primarily through the ingestion of food and water. Of these, food is generally the principal contributor to the daily intake of total arsenic. In some areas arsenic in drinking-water is a significant source of exposure to inorganic arsenic. In these cases, arsenic in drinking-water often constitutes the principal contributor to the daily arsenic intake. Contaminated soils such as mine tailings are also a potential source of arsenic exposure (Alam et al., 2003; Caussy, 2003).

The US EPA has determined that the reference dose (RfD) for inorganic arsenic is 0.0003 mg kg^{-1} day^{-1}. This RfD is derived from the NOAEL of 0.009 mg l^{-1} using an uncertainty factor of 3. The NOAEL was established based on the occurrence of skin lesions in humans exposed to arsenic. Skin lesions are the most sensitive indicator of systemic toxicity resulting from chronic oral exposure (LeCoultre, 2001; DEFRA, 2002a).

1.2.2. Cadmium

Cadmium (atomic number 48; relative atomic mass 112.40) is a metallic element belonging to group IIb of the periodic table. Some cadmium salts, such as the sulfide, carbonate and oxide, are practically insoluble in water; these can be converted to water-soluble salts in nature. The sulfate, nitrate, and halides are soluble in water. The speciation of cadmium in the environment is of importance in evaluating the potential hazard (WHO, 1992a).

Cadmium is closely associated with Zn in its geochemistry; both elements have similar ionic structures and both are strongly chalcophile. The most abundant sources of cadmium are the ZnS minerals sphalerite and wurtzite and secondary minerals, such as $ZnCO_3$ (smithsonite) (Alloway, 1995).

Values for total cadmium concentrations in unpolluted soils vary from <0.01 to 2.50 mg kg^{-1}. European studies reported that the Cd concentrations in European soils ranged from 0.06 mg kg^{-1} in Finland to 0.50 mg kg^{-1} in the UK, depending on the nature of the parent material (Jensen and Bro-Rasmussen, 1992; Krishnamurti et al., 2005).

Cadmium is readily accumulated by many organisms, particularly by microorganisms and molluscs where the bioconcentration factors are in the order of thousands. Soil invertebrates also concentrate cadmium markedly. Most organisms show low to moderate concentration factors of less than 100. Cadmium is bound to proteins in many tissues. Specific heavy-metal-binding proteins (metallothioneins) have been isolated from cadmium-exposed organisms. The concentration of cadmium is the greatest in the kidney, gills, and liver (or their equivalents). Elimination of the metal from organisms probably occurs principally via the kidney, although significant amounts can be eliminated via the shed exoskeleton in crustaceans. In plants, cadmium is concentrated primarily in the roots and to a lesser extent in the leaves. Cadmium affects the growth of plants in experimental studies, although no field effects have been reported. The metal is taken up into plants more readily from nutrient solutions than from soil; effects have been mainly shown in studies involving culture in nutrient solutions. Stomatal opening, transpiration, and photosynthesis have been reported to be affected by cadmium in nutrient solutions (WHO, 1992b).

Exposure to cadmium produces a wide variety of effects involving many organs and systems. From the point of view of preventive medicine, the detection of early effects on the kidneys more serious renal effects and those on the lungs or bones. The discovery that Cd pollution from a basic metal mining operation could cause serious illness and possibly death has led to public anxiety as well as medical interest, owing to reports from Japan of "Ouch-Ouch" (Itai-Itai in Japanese) disease (Emmerson, 1970).

The RfD is determined using the NOAEL and an uncertainty factor of 10. The uncertainty factor is used to take into account biological variability. EPA has established RfDs for Cd of 0.001 mg kg^{-1} day^{-1} for food and 0.0005 mg kg^{-1} day^{-1} for water. These amounts represent an estimated daily oral exposure that is likely not to cause adverse health effects (WHO, 1992a; WHO, 1992b; DEFRA, 2002b).

1.2.3. Lead

Lead (atomic number 82; relative atomic mass 207.19) is a soft, silvery grey metal, melting at 327.5°C. It is highly resistant to corrosion, but is soluble in nitric and hot sulfuric acids. The usual valence state in inorganic lead compounds is +2. Solubilities in water vary, lead sulfide and lead oxides being poorly soluble and the nitrate, chlorate and chloride salts are reasonably soluble in cold water. Lead also forms salts with such organic acids as lactic and acetic acids, and stable organic compounds such as tetraethyllead and tetramethyllead (WHO, 1989).

The level of lead in the earth's crust is about 20 mg kg^{-1}. It is seldom found in its elemental form; however, it is part of several ores including its own (galena, PbS). Lead in the environment may derive from either natural or anthropogenic sources. Natural sources of atmospheric lead include geological weathering and volcanic emissions and have been estimated at 19 000 tonnes per year, compared to an estimate of 126 000 tonnes per year emitted to the air from the mining, smelting and consumption of over 3 million tonnes of lead per year. Ambient air levels over 10 μg m^{-3} have been reported in urban areas near a smelter, whereas lead levels below 0.2 μg m^{-3} have been found in cities where leaded petrol is no longer used. Background levels of lead in soil range between 10 and 70 mg kg^{-1} and a mean level near roadways of 138 mg kg^{-1} has been reported. Present levels of lead in water rarely exceed a few μg l^{-1}; the natural concentration of lead in surface water has been estimated to be 0.02 μg l^{-1}. Lead and its compounds may enter the environment at any point during mining, smelting, processing, use, recycling or disposal. Major uses are in batteries, cables, pigments, petrol (gasoline) additives, solder and steel products. Lead and lead compounds are also used in solder applied to water distribution pipes and to seams of cans used to store foods, in some traditional remedies, in bottle closures for alcoholic beverages and in ceramic glazes and crystal tableware. In countries where leaded petrol is still used, the major air emission is from mobile and stationary sources of petrol combustion (urban centres). Areas in the vicinity of lead mines and smelters are subject to high levels of air emissions. Airborne lead can be deposited on soil and water, thus reaching humans through the food chain and in drinking-water (WHO, 1995; LeCoultre, 2001).

In the general non-smoking adult population, the major exposure pathway is from food and water. Airborne lead may contribute significantly to exposure, depending upon such factors as use of tobacco, occupation, proximity to motorways, lead smelters, etc., and leisure activities (e.g. arts and crafts, firearm target practice). Food, air, water and dust/soil are the major potential exposure pathways for infants and young children. For infants up to 4 or 5 months of age, air, milk, formulae and water are the significant sources of lead exposure. Lead intake from air can vary from 4 μg day^{-1} to more than 200 μg day^{-1}. The level of dietary exposure to lead depends upon many lifestyle factors, including foodstuffs consumed, processing technology, use of lead solder, lead levels in water, and use of lead-glazed ceramics. Inhalation is the dominant pathway for lead exposure of workers in industries producing, refining, using or disposing of lead and lead compounds. During an 8-h shift, workers can absorb as much as 400 μg lead, in addition to the 20-30 μg day^{-1} absorbed from food, water and ambient air; significant intake may occur from ingestion of large inhaled particulate material (WHO, 1989; WHO, 1995).

The US EPA considered that it was inappropriate to set a RfD for ingestion of inorganic lead (US EPA, 2006). They noted that "by comparison to most other environmental toxicants, the degree of uncertainty about the health effects of lead is quite low. It appears that some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold" (DEFRA, 2002c). JECFA set the provisional tolerable weekly intake (PTWI) for all age groups at 25 μg kg^{-1} $week^{-1}$, thus the PTWI/7 formula can replace the RfD (JECFA, 1993).

1.2.4. Zinc

Zinc (atomic number 30; relative atomic mass 65.38) is a metallic element belonging to group IIb and the fourth period of the periodic table. Zinc is a chalcophilic element like copper and lead, and a trace constituent in most rocks. Zinc rarely occurs naturally in its metallic state, but many minerals contain zinc as a major component from which the metal may be economically recovered. Sphalerite (ZnS) is the most important ore mineral and the principal source for zinc production (WHO, 2001a).

For non-contaminated soils worldwide, Adriano reported average zinc concentrations of 40–90 mg kg^{-1}, with a minimum of 1 mg kg^{-1} and a maximum of 2000 mg kg^{-1}. Low levels are found in sandy soils (10–30 mg kg^{-1}), while high contents are found in clays (95 mg kg^{-1}) (Adriano, 1986).

The fate and transport of zinc (Zn^{2+}) in the environment is dependant on cation exchange capacity, pH, organic matter content, nature of complexing ligands, and the concentration of the metal in the soil. As pH increases, there is an increase in negatively charged binding sites on soil particles, which facilitates the adsorption of zinc ions and removal from solution. The zinc concentration in the soil and clay content are positively correlated. The most common form of zinc in anaerobic soils is the insoluble zinc sulfide. Therefore, mobility is limited in anaerobic conditions. Zinc mobility increases with low pH under oxidizing conditions and low cation exchange capacity. The presence of competing metal ions and organic ions such as humic material may cause the adsorption of Zn^{2+} ions to the soil, particularly in soils with an elevated pH, via ligand exchange reactions. These reactions reduce the solubility of zinc in the soil solution and, therefore, reducing its mobility and limit its bioavailability (LeCoultre, 2001).

Studies have shown that the uptake of zinc by terrestrial plants is significantly increased at a low soil pH, but reduced when there is a high content of organic matter. Normal levels of zinc in most crops and pastures range from 10 mg kg^{-1} to 100 mg kg^{-1}. Some plant species are zinc accumulators, but the extent of the accumulation in plant tissues varies with soil properties, plant organ and tissue age. Zinc toxicity in plants generally causes disturbances in metabolism, which are different from those occurring

in zinc deficiency. The critical leaf tissue concentration of zinc for an effect on growth in most species is in the range 200–300 mg kg^{-1} (WHO, 2001a).

Zinc is an essential element in the human diet thus zinc deficiency in the diet may be more detrimental to human health. The human health effects associated with zinc deficiency are numerous, and include neurosensory changes, oligospermia, impaired neuropsychological functions, growth retardation, delayed wound healing, immune disorders and dermatitis. These conditions are generally reversible when corrected by zinc supplementation. A disproportionate intake of zinc in relation to copper has been shown to induce copper deficiency in humans, resulting in increased copper requirements, increased copper excretion and impaired copper status. Pharmacological intakes of zinc have been associated with effects ranging from *leukopenia* and/or *hypochromic microcytic anaemia* to decreases in serum high-density lipoprotein concentrations. These conditions were reversible upon discontinuation of zinc therapy together with copper supplementation (Institute of Medicine, 2001).

The recommended dietary allowance (RDA) for zinc is 11 mg day^{-1} in men and 8 mg day^{-1} in women; these correspond to approximately 0.16 mg kg^{-1} day^{-1} for men and 0.13 mg kg^{-1} day^{-1} for women. Higher RDAs are recommended for women during pregnancy and lactation. The RfD is determined using the LOAEL (60 mg day^{-1}) and an uncertainty factor of 3. US EPA has established RfD for Zn of 0.3 mg kg^{-1} day^{-1} calculating with average bodyweight (70 kg) (US EPA, 2006).

1.3. Health effect of metals

1.3.1. Arsenic

The most characteristic effect of long-term oral exposure to inorganic arsenic compounds is the development of skin lesions; these lesions are often used as diagnostic criteria for arsenicosis. The three lesions most often associated with chronic arsenicosis are hyperkeratinization of the skin (especially on the palms and soles), formation of multiple hyperkeratinized corns or warts, and hyperpigmentation of the skin with interspersed spots of hypopigmentation. Numerous studies of long-term, low-level exposure to inorganic arsenic in humans have reported the presence of these lesions. In general, they begin to manifest at chronic exposure levels >0.02 mg kg^{-1} day^{-1}. Chronic oral studies of lower exposure levels, ranging from 0.0004 to 0.01 mg kg^{-1} day^{-1}, have generally not reported dermal effects. The mechanism by which inorganic arsenic causes dermal effects is not well-understood. Elucidating the mechanism of dermal effects has been particularly difficult because the dermal effects common in humans have not been seen in studies in animals. Dermal effects have also been reported following inhalation exposures to inorganic arsenic, although they are not as diagnostic as for oral exposure. Direct dermal contact with inorganic arsenicals may cause irritation and contact *dermatitis*. Usually, the effects are mild (*erythema* and swelling), but may progress to papules, vesicles, or necrotic lesions in extreme cases; these conditions tend to heal without treatment if exposure ceases (Holmquist, 1951; ATSDR, 2007a).

A large number of studies in humans have reported cardiovascular effects following oral exposure to inorganic arsenic compounds. The cardiac effects of arsenic exposure are numerous, and include altered myocardial depolarization (prolonged QT interval, nonspecific ST segment changes), cardiac arrhythmias, and ischemic heart disease. These effects have been seen after acute and long-term exposure to inorganic arsenic in the environment, as well as side effects from intravenous therapy with arsenic trioxide for acute promyelocytic leukemia. Exposure levels for environmental exposures have not been well characterized, but intravenous doses for arsenic trioxide therapy are generally on the order of 0.15 mg kg^{-1} day^{-1}. Chronic exposure to inorganic arsenic has

also been shown to lead to effects on the vascular system. The most dramatic of these effects is "blackfoot disease," a disease characterized by a progressive loss of circulation in the hands and feet, leading ultimately to necrosis and gangrene. Blackfoot disease is endemic in an area of Taiwan where average drinking water levels of arsenic range from 0.17 to 0.80 ppm, corresponding to doses of 0.014–0.065 mg kg^{-1} day^{-1}. Arsenic exposure in Taiwan has also been associated with an increased incidence of cerebrovascular and microvascular diseases and ischemic heart disease. While blackfoot disease itself has not been reported outside of Taiwan, other vascular effects are common in areas with high arsenic exposures, and include such severe effects as increases in the incidences of Raynaud's disease and of cyanosis of fingers and toes as well as hypertension, thickening and vascular occlusion of blood vessels, and other unspecified cardiovascular conditions (Little et al., 1990; Chen et al., 1994; Cullen et al., 1995; Mumford et al., 2007).

While case reports and small cohort studies have routinely reported an increase in respiratory symptoms of humans exposed occupationally to inorganic arsenic, dose-response data for these symptoms are generally lacking. The only study that evaluated respiratory effects (changes in chest X-ray or respiratory performance) reported an exposure estimate did not report significant changes at an exposure level of 0.613 mg m^{-3}. Exposed workers often report irritation of the mucous membranes of the nose and throat, which may lead to *laryngitis*, *bronchitis*, or *rhinitis*. Increased mortality due to respiratory disease has been reported in some cohort mortality studies of arsenic-exposed workers, but no conclusive evidence of an association of these diseases with arsenic exposure has been presented. It is not known whether respiratory effects following inhaled inorganic arsenic compounds are due to a direct effect of arsenic on respiratory tissues, general effects of foreign material in the lungs, or an effect of arsenic on the pulmonary vasculature. Respiratory effects have also been reported following oral exposure of humans to inorganic arsenic. In general, respiratory effects have not been widely associated with long-term oral exposure to low arsenic doses. However, some studies have reported minor respiratory symptoms, such as cough, *sputum*, *rhinorrhea*, and sore throat, in people with repeated oral exposure to 0.03–0.05 mg kg^{-1} day^{-1}. More serious respiratory effects, such as *bronchitis* and sequelae (*bronchiectasia, bronchopneumonia*) have been observed in patients

chronically exposed to arsenic and at autopsy in some chronic poisoning cases (Milton and Rahman, 2002).

Both short-term and chronic oral exposures to inorganic arsenicals have been reported to result in irritant effects on gastrointestinal tissues. Numerous studies of acute, high-dose exposure to inorganic arsenicals have reported *nausea*, vomiting, diarrhea, and abdominal pain, although specific dose levels associated with the onset of these symptoms have not been identified. Chronic oral exposure to 0.01 mg $kg^{-1}day^{-1}$ generally results in similar reported symptoms. For both acute and chronic exposures, the gastrointestinal effects generally diminish or resolve with cessation of exposure. Similar gastrointestinal effects have been reported after occupational exposures to inorganic arsenicals, although it is not known if these effects were due to absorption of arsenic from the respiratory tract or from mucociliary clearance resulting in eventual oral exposure (WHO, 2001b; ATSDR, 2007a).

A common effect following both oral and inhalation exposure to inorganic is the development of peripheral neuropathy. Following occupational exposure to inorganic arsenic in pesticide plants or smelters, exposed workers have shown increased incidence of neurological changes, including altered nerve conduction velocities. Histological features of the neuropathy include a dying-back axonopathy and demyelinisation. Following removal from exposure, the neuropathy is only partially reversible and what recovery does occur is generally slow. Reports of neurological effects at lower arsenic levels (0.004–0.006 mg $kg^{-1}day^{-1}$) have been inconsistent, with some human studies reporting fatigue, headache, depression, dizziness, insomnia, nightmare, and numbness while others reported no neurological effects. Some studies also have reported that exposure to arsenic may be associated with intellectual deficits in children. The mechanism of arsenic-induced neurological changes has not been determined (Gerr et al., 2000).

There is clear evidence from studies in humans that exposure to inorganic arsenic by either the inhalation or oral routes increases the risk of cancer. Numerous studies of copper smelters or miners exposed to arsenic trioxide have reported an increased risk of lung cancer. Increased incidence of lung cancer has also been observed at chemical plants where exposure was primarily to arsenate. Other studies suggest that residents living near smelters or arsenical chemical plants may have increased risk of

lung cancer, although the reported increases are small and are not clearly detectable in all cases. There is convincing evidence from a large number of epidemiological studies and case reports that ingestion of inorganic arsenic increases the risk of developing skin cancer. The most common tumors seen are squamous cell carcinomas, which may develop from the hyperkeratotic warts or corns commonly seen as a dermal effect of oral inorganic arsenic exposure. Early studies of populations within the United States did not suggest an increased risk of cancer from oral inorganic arsenic exposure. Later studies have found suggestive evidence that the possibility of arsenic-induced skin cancers cannot be discounted based on an association between toenail arsenic levels and incidence of skin cancer. There is increasing evidence that long-term exposure to arsenic can result in the development of bladder cancer, with transitional cell cancers being the most prevalent. While studies have noted statistical dose-response trends in arsenic-induced bladder cancers, reliable quantitative assessments of dose-response relationships have not been presented. Several studies have also shown that chronic oral exposure to arsenic results in the development of respiratory tumors, making lung cancer an established cause of death from exposure to arsenic in drinking water (Chen et al., 1988; Moore et al., 1994; Enterline et al., 1995; ATSDR, 2007a).

1.3.2. Cadmium

Acute inhalation exposure to cadmium at concentrations above about 5 mg m^{-3} may cause destruction of lung epithelial cells, resulting in pulmonary *oedema*, *tracheobronchitis*, and *pneumonitis*. The respiratory response to cadmium is similar to the response seen with other agents that produce oxidative damage. There typically is an alveolar pneumocyte type 2 cell hyperplasia in response to type 1 cell damage and necrosis. Long-term inhalation exposure at lower levels also leads to decreased lung function and *emphysema*. Some tolerance to cadmium-induced lung irritation develops in exposed humans, and respiratory function may recover after cessation of cadmium exposure. Another effect of long-term inhalation cadmium exposure is damage to the olfactory function. Nonoccupational exposure to cadmium is unlikely to be high enough to cause significant respiratory effects (Leduc et al., 1993; Sorahan and Lancashire, 1997).

Conflicting evidence has been obtained for the effect of cadmium exposure on the cardiovascular system. In some studies on rats, rabbits, and monkeys, cadmium exposure was shown to increase blood pressure, or to cause cardiac lesions. However, studies of exposed humans have found positive, negative and no association between cadmium exposure and hypertension. This suggests that if cadmium does affect blood pressure, the magnitude of the effect is small compared to other determinants of hypertension. Death rates for cardiovascular disease do not appear to be elevated in populations exposed to cadmium by inhalation or in the diet. Overall, the weight of evidence suggests that cardiovascular effects are not a sensitive end point indicator for cadmium toxicity (Kopp, 1982; Steassen and Lauwerys, 1993).

The gastrointestinal tract is the target organ for high-level, acute, oral exposure to cadmium in both humans and animals, due to direct irritation of the gastric epithelium. The main symptoms following ingestion of cadmium at doses above about 0.07 mg kg^{-1} in humans are *nausea*, vomiting, and abdominal pain. Gastrointestinal toxicity is not observed after lower levels of oral exposure or after inhalation exposure to cadmium, indicating that gastrointestinal effects are not likely to occur from environmental exposures to cadmium (Shipman, 1986).

Both oral and inhalation exposure to cadmium can cause *anaemia*. Oral exposure to cadmium has been shown to reduce uptake of iron from the diet in animals. It is likely that cadmium transported to the gastrointestinal system from the lung following inhalation exposure would also reduce iron absorption. Therefore, *anaemia* induced by inhalation exposure to cadmium is likely to be caused by reduced iron absorption (Friberg et al., 1985).

Prolonged inhalation or ingestion exposure of humans to cadmium causing renal dysfunction can lead to painful and debilitating bone disease in individuals with risk factors such as poor nutrition. Evidence from human studies suggests that low-level chronic exposure to cadmium causes alternations in renal metabolism of vitamin D, which then may cause milder bone effects *(osteoporosis*). These effects may be compounded by loss of calcium and phosphate with more severe renal damage, leading to *osteomalacia*. A recent large-scale cohort study in Belgium found that increased urinary calcium excretion was significantly associated with urinary cadmium levels, an index of kidney cadmium burden. This evidence suggests that either cadmium may have a direct effect on bone at levels lower than those causing kidney damage, or that interference with vitamin D metabolism in the proximal tubule may be a more sensitive indicator of cadmium-induced renal damage than *proteinuria* (Jarup et al., 1998; Steassen et al., 1999).

The kidney is the main target organ for cadmium toxicity following intermediate- or chronic-duration exposure by the inhalation or oral routes, as has been shown by numerous studies. The first manifestation of kidney damage is decreased reabsorption of filtered low molecular-weight proteins, indicating damage to the renal tubules. Production of tubular *proteinuria* is a relatively specific effect of cadmium on the kidneys and has been observed even following acute parenteral exposure in animals. This damage has been associated with increased urinary levels of β2-microglobulin, retinol-binding protein, or other low-molecular-weight proteins. At higher levels or durations of exposure, increased excretion of high molecular-weight proteins occurs, indicating either glomerular damage or severe tubular damage. The sensitivity of the kidney to cadmium is related to the metabolism of cadmium in the body. Except for extremely high-dose exposure, cadmium exists in the body primarily bound to metallothionein. The Cd-metallothionein complex is readily filtered at the glomerulus

and reabsorbed in the proximal tubule. Within the tubular cells, the metallothionein is degraded in lysosomes and free cadmium is released. The synthesis of endogenous metallothionein by the tubular cells is then stimulated, but when the total cadmium content in the renal cortex exceeds approximately 200 μg g^{-1} wet weight, the amount of cadmium not bound to metallothionein becomes sufficiently high to cause tubular damage (Waalkes and Goering, 1990; Buchet et al., 1999)

The health significance of the early kidney damage is difficult to assess. The decreased resorption of low molecular-weight proteins is not adverse in and of itself, but may be indicative of increased excretion of other solutes. Deaths from renal failure due to cadmium exposure are rare, but even after cadmium exposure ceases, the renal damage continues to progress. Evidence that cadmium exposure may affect kidney vitamin D metabolism with subsequent disturbances in calcium balance and bone density suggests that decreased bone density, particularly in elderly women, may be a significant adverse effect of kidney cadmium accumulation (WHO, 1992a; WHO, 1992b; ATSDR, 1999).

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1.3.3. Lead

The adverse hematological effects of lead are mainly the result of its perturbation of the heme biosynthesis pathway (Figure 1). The activity of δ-aminolevulinic acid synthase (ALAD), an enzyme occurring early in the heme synthesis pathway, is negatively correlated with blood Pb levels between 50 and 950 μg l^{-1}. Although inhibition of ALAD occurs at very low exposure levels, there is some controversy as to the toxicological significance of a depression in ALAD activity in the absence of a detectable effect on hemoglobin levels (WHO, 1989).

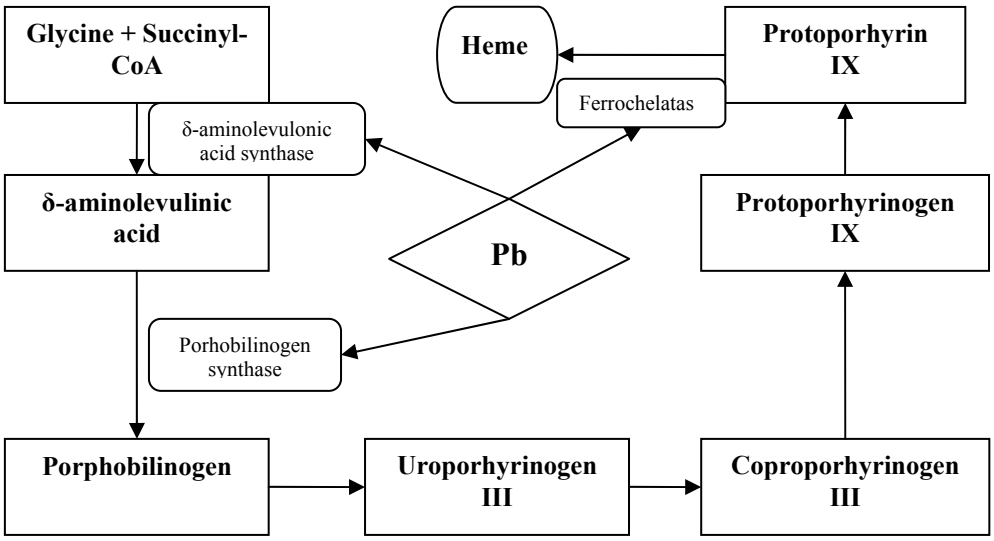

Figure 1. Heme biosynthesis and the effects of lead
(Modified figure from Voet et al., 1999)

Nevertheless, because the impairment of heme synthesis has a far-ranging impact not limited to the hemopoietic system, there is concern that developing organisms might be particularly susceptible. A potential consequence of the inhibition of heme synthesis is a decreased formation of mixed function oxidases in the liver resulting in impaired metabolism of endogenous compounds, as well as impaired detoxification of xenobiotics. Mitochondrial cytochrome oxidase is another heme-requiring protein that could be affected by heme synthesis inhibition. In addition, tryptophan pyrrolase, a hepatic hemerequiring enzyme system, is inhibited via the

reduction in the free hepatic heme pool (Kwong et al., 2004). This could ultimately lead to increased levels of the neurotransmitter serotonin in the brain and increased aberrant neurotransmission in serotonergic pathways. Inhibition of heme synthesis also results in increased levels of δ-aminolevulinic acid (ALA), which has a structure similar to that of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), and therefore, interferes with GABA neurotransmission (Sakai, 2000). Anemia occurs at blood Pb levels of ≥200 μg l^{-1}. The combined effects of rudeced heme body pool is demonstrated in Figure 2 (WHO, 1995; ATSDR, 2007b).

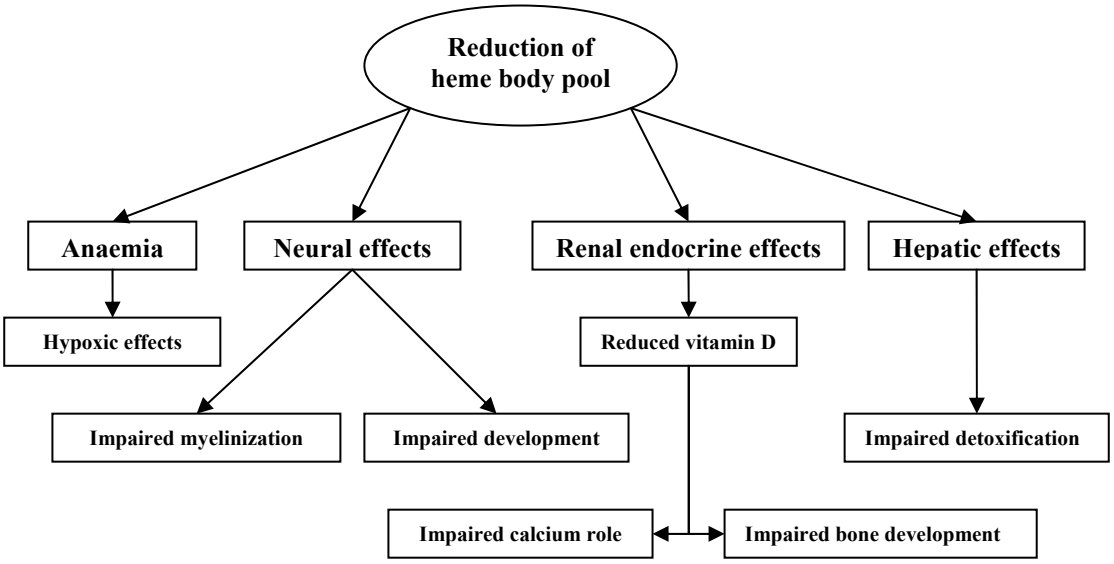

Figure 2. The effects of reduced heme body pool
(Modified figure from WHO, 1995)

Lead can impair cognitive function in children and adults, but children are more vulnerable than adults. Although the inhalation and oral routes are the main routes of exposure for both adults and children, children are more likely to have contact with contaminated surfaces due to playing on the ground and to hand-to-mouth activities. However, perhaps more important is the fact that the developing nervous system is especially susceptible to lead toxicity. During brain development, lead interferes with the trimming and pruning of synapses, migration of neurons, and neuron/glia interactions. The time of exposure-specific response appears to have contributed to the failure to identify a "behavioral signature" of lead exposure. Other factors that may affect individual vulnerability are certain genetic polymorphisms, such as that for the

vitamin D receptor, the lead-binding enzyme ALAD, or the ApoE genotype. One important additional factor shown to influence the toxicity of lead is the characteristics of the child's rearing environment, a modifying factor. Most importantly, no threshold for the effects of lead on IQ has been identified (Davis and Svendsgaard, 1987; Goering, 1993; Schwartz, 1994).

Although lead has been shown to produce various cardiovascular and renal effects in animals, end points of greatest concern for humans at low exposures and low blood Pb levels are elevations in systemic blood pressure and decrements in glomerular filtration rate. These effects may be mechanistically related and, furthermore, can be confounders and covariables in epidemiological studies. Decrements in glomerular filtration rate may contribute to elevations in blood pressure, and elevated blood pressure may predispose people to glomerular disease. Meta-analyses of the epidemiological findings have found a persistent trend in the data that supports a relatively weak, but significant association. Quantitatively, this association amounts to an increase in systolic blood pressure of approximately 1 Hgmm with each doubling of blood Pb level. The results of more recent epidemiology studies indicate that the lead contribution to elevated blood pressure is more pronounced in middle age than at younger ages. Lead poisoning in childhood has also been associated with hypertension during adulthood in the absence of clinically significant renal disease and discernable elevations in blood Pb level (Hertz-Picciotto and Croft, 1993; WHO, 1995).

Classic lead nephrotoxicity is characterized by proximal tubular nephropathy, *glomerular sclerosis, interstitial fibrosis* and related functional deficits, including *enzymuria*, low- and high-molecular weight *proteinuria*, impaired transport of organic anions and glucose, and depressed glomerular filtration rate. In humans, the overall dose-effect pattern suggests an increasing severity of nephrotoxicity associated with increasing blood Pb level, with effects on glomerular filtration evident at blood Pb level below 100 μg l^{-1}, *enzymuria* and *proteinuria* becoming evident above 300 μg l^{-1}, and severe deficits in function and pathological changes occurring in association with blood Pb level exceeding 500 μg l^{-1}. Furthermore, as noted previously, hypertension can be both a confounder in studies of associations between lead exposure and creatinine clearance as well as a covariable with lead exposure. (Bernard and Becker, 1988; Goyer, 1993; ATSDR, 2007b).

1.3.4. Zinc

Zinc is an essential nutrient for humans that is necessary for the function of a large number of metalloenzymes, including alcohol dehydrogenase, alkaline phosphatase, carbonic anhydrase, leucine aminopeptidase, and superoxide dismutase. Zinc deficiency has been associated with *dermatitis*, anorexia, growth retardation, poor wound healing, hypogonadism with impaired reproductive capacity, impaired immune function, and depressed mental function; an increased incidence of congenital malformations in infants has also been associated with zinc deficiency in the mothers. Zinc deficiency may also have an impact on the carcinogenesis of other chemicals, although the direction of the influence seems to vary with the carcinogenic agent (Institute of Medicine, 2001).

The effects of inhalation exposure to zinc and zinc compounds vary somewhat with the chemical form of the zinc compound, but the majority of the effects seen will occur within the respiratory tract. Following inhalation of zinc oxide, and to a lesser extent zinc metal and many other zinc compounds, the most commonly reported effect is the development of "metal fume fever." Metal fume fever, a well-documented acute disease induced by inhalation of metal oxides, especially zinc, impairs pulmonary function but does not usually progress to chronic lung disease. Symptoms generally appear within a few hours after acute exposure, usually with dryness of the throat and coughing. The most prominent respiratory effects of metal fume fever are substernal chest pain, cough, and *dyspnoe*. The impairment of pulmonary function is characterized by reduced lung volumes and a decreased diffusing capacity of carbon monoxide. Leukocytosis persisting for approximately 12 hours after the fever dissipates is also a common manifestation of metal fume fever. In general, the symptoms of metal fume fever resolve within 1–4 days after cessation of exposure and do not lead to long-term respiratory effects. The exact mechanism behind the development of metal fume fever is not known, but it is believed to involve an immune response to the inhaled zinc oxide. It has been suggested that the zinc oxide causes inflammation of the respiratory tract and the release of histamine or histamine-like substances. In response, an allergen-antibody complex is formed that may elicit an allergic reaction upon subsequent exposure to the allergen. In response to the allergen-antibody complex, an anti-antibody is formed. The

anti-antibody dominates with continued exposure to the zinc oxide, thereby producing a tolerance. When the exposure is interrupted and re-exposure occurs, the allergen-antibody complex dominates, producing an allergic reaction and symptoms of metal fume fever (Malo et al., 1990; Lindahl et al., 1998).

Nausea has been reported by humans exposed to high concentrations of zinc oxide fumes (300–600 mg m^{-3}) and zinc chloride (~120 mg m^{-3}) smoke, as well as following oral exposure to zinc chloride and zinc sulfate. Other gastrointestinal symptoms reported in cases of excess zinc exposure include vomiting, abdominal cramps, and diarrhea, in several cases with blood. In general, oral exposure levels associated with gastrointestinal effects of zinc have not been reliably reported, but the limited available data suggest that oral concentrations of 910 mg l^{-1} or single-dose exposures of ~140–560 mg (acute oral doses of 2–8 mg kg^{-1} day^{-1}) are sufficient to cause these effects. The noted effects are consistent with gastrointestinal irritation. It is unclear in the majority of human studies whether the gastrointestinal effects seen following zinc inhalation were due to systemic zinc or were the result of direct contact with the gastrointestinal tract following mucociliary clearance of inhaled zinc particles and subsequent swallowing (WHO, 2001a; ATSDR, 2005).

Following longer-term exposure to lower doses (~0.5–2 mg kg^{-1} day^{-1}) of zinc compounds, the observed symptoms generally result from a decreased absorption of copper from the diet, leading to early symptoms of copper deficiency. When ingested zinc levels are very high, zinc is believed to inhibit copper absorption through interaction with metallothionein at the brush border of the intestinal lumen. Both copper and zinc appear to bind to the same metallothionein protein; however, copper has a higher affinity for metallothionein than zinc and displaces zinc from metallothionein protein. Copper complexed with metallothionein is retained in the mucosal cell, relatively unavailable for transfer to plasma, and is excreted in the feces when the mucosal cells are sloughed off. Thus, an excess of zinc can result in a decreased availability of dietary copper, and the development of copper deficiency. This fact has been used therapeutically in the treatment of Wilson's Disease. Zinc supplementation is used to substantially decrease the absorption of copper from the diet, which can aggravate the disease. Copper is incorporated into metalloenzymes involved in hemoglobin formation, carbohydrate metabolism, catecholamine biosynthesis, and

cross-linking of collagen, elastin, and hair keratin. The copper-dependent enzymes, which include cytochrome C oxidase, superoxide dismutase, ferroxidases, monoamine oxidase, and dopamine β-monooxygenase, function mainly to reduce molecular oxygen. Excess zinc may alter the levels or activity of these enzymes before the more severe symptoms of copper deficiency, which include *anaemia* and *leucopenia,* begin to manifest. Numerous studies in humans receiving 40–50 mg zinc day^{-1} (0.68–0.83 mg kg^{-1} day^{-1}) have reported decreases in erythrocyte superoxide dismutase, mononuclear white cell 5'-nucleotidase, and plasma 5'-nucleotidase activities (Hewitt, 1988; ATSDR, 2005).

High-dose zinc administration has also resulted in reductions in leukocyte number and function. Some studies have also found decreases in high-density lipoprotein (HDL) levels in humans exposed to increased levels of zinc; however, not all studies have confirmed this observation. Long-term consumption of excess zinc may also result in decreased iron stores, although the mechanism behind this effect is not presently clear. In most cases, dermal exposure to zinc or zinc compounds does not result in any noticeable toxic effects (Hughes at Samman, 2006).

Available studies have not presented evidence of reproductive or developmental effects in humans following inhalation of zinc compounds. Effects on reproductive or developmental end points have been noted in oral-exposure animal studies, but generally only at very high doses (>200 mg kg^{-1} day^{-1}). Available studies of zinc-induced carcinogenic effects in humans following both oral or inhalation exposure have not adequately demonstrated an increase in cancer incidence. The EPA currently classifies zinc and compounds as carcinogenicity group D (not classifiable as to human carcinogenicity) (WHO, 2001a; ATSDR, 2005).

1.4. Risk assessment of metals

Inorganic metals and metal compounds have unique characteristics that should be considered when assessing their risks. Metals are neither created nor destroyed by biological or chemical processes; they are transformed from one chemical form to another. Native (zero valence) forms of most metals and some metal compounds are not readily soluble, and as a result, toxicity tests based on soluble salts may overestimate the bioavailability and toxicity of these substances. Some metals (e.g. copper, selenium, and zinc) are nutritionally essential elements at low levels but toxic at higher levels, and others (e.g. lead, arsenic, and mercury) have no known biological functions. Because metals are naturally occurring, many organisms have evolved mechanisms to regulate accumulations, especially accumulations of essential metals (Fairbrother et al., 2007).

The "soil–plant barrier" concept was introduced to communicate how metal addition, soil chemistry, and plant chemistry affect risk to human from metals mixed in soil (Chaney, 1980). Plants access metals through the pore water although mycorrhyzae, protons, and phytosiderophores released by the root can significantly influence the microenvironment and change uptake rates of metals. Furthermore, plants have both active and passive mechanisms for taking up or excluding metals, depending on internal concentrations and whether or not the metal is an essential micronutrient, or whether it is mistaken for an essential micronutrient. The different routes of plant uptake is found in Figure 3 (US EPA, 2003; Fairbrother et al., 2007).

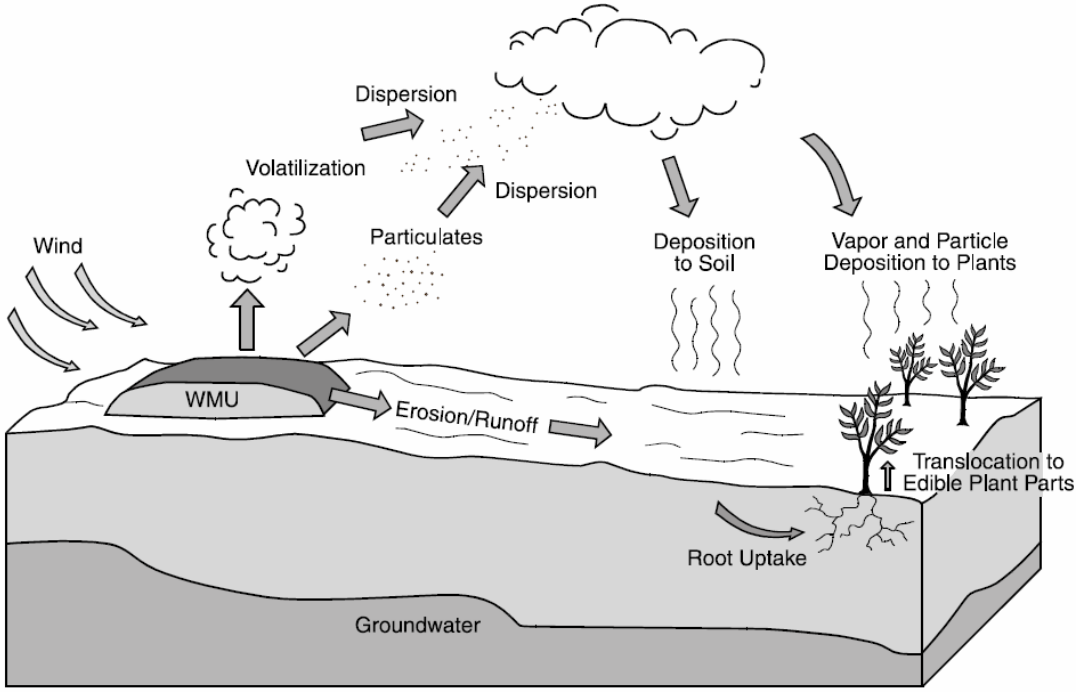

Figure 3. Release, exposure, and uptake mechanisms of contaminants in plants (US EPA, 2003)

The risk assessor should consider the default approach to estimating exposure of plants to metal as measuring metal concentrations in bulk soil (top 0–12 cm). It is very clear that strongly acidic soils increase plant uptake of zinc, cadmium, nickel, cobalt and increase the potential for phytotoxicity from copper, zinc, and nickel. Alkaline soil pH increases uptake of molibdene and selenium, while lead and chromium are not absorbed to any significant extent at any pH (Kabata-Pendias and Pendias, 1985).

The general concepts of risk assessment might to be modified to make a correct approach of metal risk assessment. Figure 4 illustrates this concept. In this concept the "weakest link" is the exposure model. Two main parts of this model is the bioaccumulation model and the dietery exposure model. The most important source for direct human exposure is the "econosphere", which contains food and drinking water (Baker et al., 2003). Trophic transfer can be an important route of exposure for metals, although biomagnification of inorganic forms of metals in food webs is generally not a concern in metals assessments.

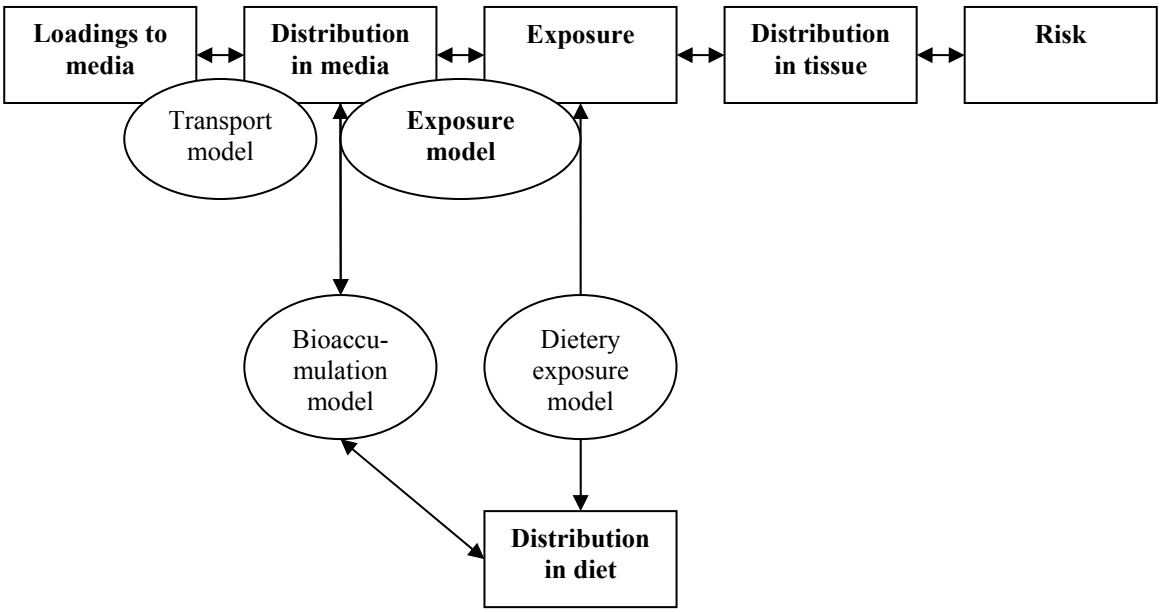

Figure 4. Generic conceptual model for metals risk assessment
(Modified figure from Fairbrother et al., 2007)

Infants and children can have enhanced exposures to metals through the pathway of surface dust because they crawl and play in close proximity to surface dust and they often mouth their hands (e.g. finger sucking) and objects in their environment. This causes an intake of surface dust that is generally greater than that which is normally found in adults. Few studies of soil ingestion in adults have been conducted; however, the estimates support the assumption that average daily soil ingestion rates of adults who do not participate in activities in which intensive exposure to surface dust and soil occur (e.g. occupational gardening, construction work) are lower than those of children (Fairbrother et al., 2007).

The distribution of metals in human tissues determined by oral bioavailability. This depends on soil and mineral characteristics and also toxicological profiles. Historically, relative bioavailability estimates for metals in soil have been based on *in vivo* studies in laboratory animals. In recent years the main goals are to establish *in vitro* extraction tests, which are rapid and inexpensive methods (Ruby et al., 1999).

2. AIMS

The purpose of my study was to refine the human health risk assessment and exposure assessment of metal contaminated sites.

In this approach the main objects were:

- to analyse the arsenic, cadmium, lead and zinc content of soil and homegrown vegetables in the area of an abandoned lead-zinc mine,
- to model the plant uptake of metals with the most accumulating vegetable species in polluted and unpolluted soil,
- to develop a more reasonable method for risk assessment,
- to determine the differences in soil pollution and human health risk between the flooded and non-flooded vegetable gardens in the village of Gyöngyösoroszi using site-specific and default exposure parameters.

3. MATERIALS AND METHODS

3.1. Area description

The studied area is located in the South-Western part of Mátra Mountains, North-Eastern Hungary along the left side of the Toka creek. The creek flows from North to South through the village Gyöngyösoroszi (47.826°N, 19.894°E) and collects the runoff of the abandoned metal site. The territory is the Southern part of the biggest collapse caldera in the Western Mátra. The mountain mostly consists of amphibole andesite, its pyroclastics and pyroxene andesite at the top together with 500-2000 m thickness. The stratovolcanic andesite series is containing more than 1% Pb-Zn concentration in the 0.5-1 m thick dikes (Nagy, 1986). In the Gyöngyösoroszi area the most frequent ore minerals are galenite (PbS), sphalerite (ZnS), pyrite (cubic FeS_2), marcasite (rhombic FeS_2) and chalcopyrite ($CuFeS_2$) (Vető, 1988). The mining activities were based on these minerals.

Mining began in the Middle Ages and was expanding rapidly throughout the 19th century until 1929. After two decades of interruption, mining continued more intensively and between 1954 and 1985 the total amount of 3920089 tons of ore were mined and transported to the flotation plant near Gyöngyösoroszi (Nagy, 1986; Kovács et al., 2006). To meet the water demand of the flotation technology an industrial water reservoir was constructed in the valley of the Toka creek. The mining activity has ceased, but the final closing of the mine and remediation of the site has not been carried out yet. The sulphide minerals in the old drifts and headings have been oxidized and sulfurous acid is formed by infiltration. The acidic mine drainage is continuously limed and the lime-precipitate is settled and dumped in open reservoirs. Before the establishment of the neutralization plant, the mine outflow entered directly into the surface water system, where it was *in situ* neutralized, and this lime precipitate has been part of the sediment of Toka creek and water reservoirs. In 1996 a remarkable precipitation event (105 mm) occurred during one day, the water overflowed the dams and caused a huge flood in the village. The toxic sediment was spread over the surrounding vegetable gardens.

3.2. Field experiment

Sampling of soils and vegetables was carried out at 44 sampling sites from flooded and non-flooded vegetable gardens in the village Gyöngyösoroszi. The flooded gardens are near to the bank of Toka creek; the non-flooded gardens are 100-400 m from the creek. Soil samples were collected also from the taling dump at 13 sampling sites. The sampled locations are marked on Figure 5. At each sampling site duplicate samples were collected by random sampling method according to MSZ 21470-1 (Hungarian Standard Institution, 1998), 1 kg soil samples were packed into polyethylene bags.

Vegetable samples were taken from flooded and non-flooded vegetable gardens in the village according to the type of harvest. Six vegetable species were selected for this study; these were representative of species consumed in the studied area: tomato (*Lycopersicon lycopesicum*), squash (*Cucurbita pepo*), bean (*Phaseolus vulgaris*), onion (*Allium cepa*), carrot (*Daucus carota ssp. sativus*) and sorrel (*Rumex rugosus*). Good quality vegetable samples were selected using a random sampling procedure, packed into polyethylene bags and transported to the laboratory. The sampling amount of vegetables were the following: 0.3-0.5 kg tomato, 1-2 kg squash, 0.2-0.3 kg bean, 0.4-0.6 kg onion, 0.3-0.5 kg carrot and 0.1-0.2 kg sorrel.

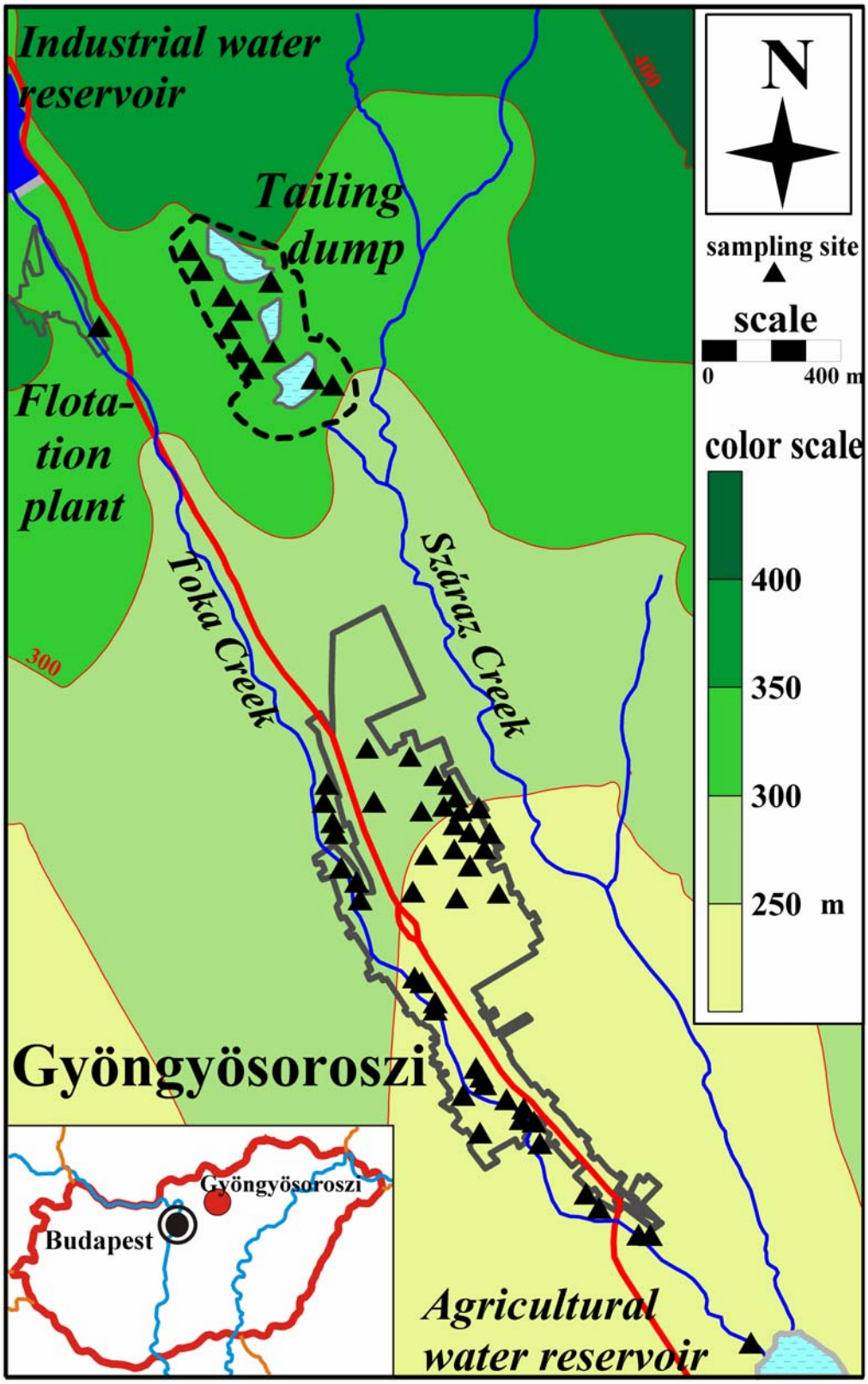

Figure 5. Topographical map and sampling points in the studied area

3.3. Pot experiment

The pot experiment was planned on the basis of field experiment. Two soils were used: one was collected from non-flooded vegetable garden in the village (UP). This soil is a typical unpolluted soil with relevant background concentrations. The other soil sample (P) was a mixture of reference soil (80%) and tailing material (20%). This mixture modelled the flooding processes.

6-6 black plastic pots were filled with 1000 g air-dried soil (Figure 6). There were three replications of each sample in a randomized block design. Vegetable seeds were sowed into the pots: sorrel (*Rumex acetosa*) (100 seeds) and carrot (*Daucus carota*) (100 seeds). These were the most accumulating vegetables in the field experiment. The germination ability had defined in test before the experiment and the sowing number of seeds calculated. The water holding capacity of the soils was measured and the water supply was determined as 70% of the saturation. The evaporated water was supplemented at every 2nd day. Nitrogen and phosphorus were added as 3-3 ml 50 g l^{-1} $(NH_4)_2HPO_4$ solution per pots on the 65th and 86th day. The plant fresh weight and toxic metal content was measured after harvesting. The seedling number was determined on the 6th, 8th, 10th, 13th, 15th, 17th, 20th day.

The experiment was carried out in climate chamber for 106 days with 400 W m^{-2} light and 24°C for 16 hours and darkness and 16°C for 8 hours.

Figure 6. Arrangement of the pots

3.4. Laboratory analyses

Soil samples were dried at 30°C until constant weight and sieved through 2-mm nylon mesh according to MSZ 21470-2 (Hungarian Standard Institution, 1981).

The vegetable samples were washed with distilled water three times to eliminate the air-borne pollutants and soil particles and then blotted dry with tissue paper. Only the edible part of each vegetable was used for analytical purposes; the non-edible parts were removed using a plastic knife. The cook-ready vegetables were weighed, dried at 30°C until constant weight, weighed again to determine water content and then ground using a ceramic-coated grinder.

1 g of dried soil and vegetable samples were treated with 4 ml of *aqua regia* (HNO_3:HCl=1:3) in hermetic Teflon bombs and placed in a microwave digester (Milestone 1200 MEGA) under a power-controlled program. Solutions were filtered and made up to 25 ml with deionized water. The arsenic, cadmium, mercury, lead and zinc contents were measured by inductively coupled-mass spectrometry (Agilent HP4500 Plus) according to method 6020 (US EPA, 1994). The limits of detection (LOD) for soils and vegetables were the following: 0.005 mg kg^{-1} for Cd, Pb and Zn; 0.01 mg kg^{-1} for Hg; and 0.05 mg kg^{-1} for As. The accuracy of the methodology was checked by determining the levels in duplicate samples as well as those of blanks. For quality control standard reference materials (GBW07404 and LGC6138) were used. The recovery rates ranged from 89 to 110%.

3.5. Questionnaire, statistical analyses and geochemical mapping

A standardized questionnaire (q.v. Appendix) was constructed to set the site-specific parameters for risk assessment. The door-to-door survey method was operated with open response and multiple choices. The age, gender, body weight, family members and the average yield of the home-produced vegetables were asked. The survey included 67 vegetable gardens in the village and 90 participants (43 male and 47 female).

Median concentrations and median absolute deviation were calculated and compared to their Hungarian pollution limit value. In analyzing the differences among the two territory types the Mann-Whitney test was used for the statistical analysis taking $p<0.05$ as significant. The statistical parameters were prepared using Statistica 6.0 (StatSoft, Tulsa, OK, 2001).

Base map was created from the topographic map at the scale 1:10000 of the Hungarian Cartographical Company. An area of 10 km^2 was selected around Gyöngyösoroszi, which United Hungarian Projection (EOV) coordinates with geographical grid of parallels and meridians were the following: EOV X between 712000 and 714500, EOV Y between 275000 and 279000.

The sampling points were digitalized according to their GPS coordinates. Separated geochemical maps were created for arsenic, cadmium, lead and zinc concentrations using the grid based graphics program Surfer 8.0 (Golden Software, Golden, CO, 2002). The data were weighted by interpolation with inverse distance to a power method: the influence of one sampling site relative to other declines with distance from the grid node (Mueller et al., 2004).

3.6. Risk assessment

The average daily dose was calculated in two selected exposure routes by default and site-specific equations. The default equations and exposure factors were derived from databases (US EPA, 1992; US EPA, 1997). The default equations were the following:

(1) Ingestion of soil: $$ADD = \frac{C_S \times IR_{SOIL} \times EF \times ED}{BW \times AT}$$

(2) Ingestion of vegetables: $$ADD = \frac{C_S \times BCF \times F_{HP} \times IR_{VEG} \times EF \times ED}{BW \times AT}$$

C_S is concentration in soil (mg kg^{-1}), BCF is bioconcentration factor (-), F_{HP} is the fraction of home-produced vegetables (-), IR_{SOIL} is ingestion rate of soil (kg day^{-1}), IR_{VEG} is ingestion rate of vegetables (kg day^{-1}), EF is exposure frequency (days $year^{-1}$), ED is exposure duration (years), BW is body weight (kg), AT is average time (days). The average daily dose of soil ingestion was calculated separately for adults and children, because of differences in bodyweight and ingestion rate soil.

The site-specific equation of ingestion of vegetables was created from quastionairre derived data. The equation of ingestion of soil was the same as the default:

(3) Ingestion of soil: $$ADD = \frac{C_S \times IR_{SOIL} \times EF \times ED}{BW \times AT}$$

(4) Ingestion of vegetables: $$ADD = \frac{\sum (C_{VEG} \times \frac{Y_{VEG}}{n}) \times ED}{BW \times AT}$$

C_S is concentration in soil (mg kg^{-1}), C_{VEG} is concentration in vegetable (mg kg^{-1} fresh weight), Y_{VEG} is the average yield of the selected vegetable in the garden (kg $year^{-1}$), n is the average family size (-), IR_{SOIL} is ingestion rate of soil (kg day^{-1}), EF is exposure frequency (days $year^{-1}$), ED is exposure duration (years), BW is body weight (kg), AT is average time (days).

The average daily dose of soil ingestion was calculated separately for men, women and children, because of differences in bodyweight and ingestion rate soil. The average daily dose of vegetable ingestion for men and women was calculated separately, because of differences in bodyweight. All of the parameters applied in the calculations were site-specific and derived from a population survey, except the

parameter ingestion rate soil, which was 16.7 mg day^{-1} for children and 10 mg day^{-1} for adults (Wcislo et al., 2002).

The non-carcinogenic risk was characterized using a hazard quotient (HQ), which is the ratio of the average daily dose (ADD) to the reference dose (RfD). The applied reference doses were the following: 0.0003 mg kg^{-1} day^{-1} for As; 0.001 mg kg^{-1} day^{-1} for Cd; 0.035 mg kg^{-1} day^{-1} for Pb; and 0.3 mg kg^{-1} day^{-1} for Zn. If HQ is bigger than 1, then the ADD of particular metal exceeds the RfD, indicating that there is a potential risk associated with that metal. The hazard index (HI) is the sum of hazard quotient for each exposure route and metal (Paustenbach, 2002).

4. RESULTS

4.1. Arsenic and heavy metal content of soils

The results obtained for the median, median absolute deviation (MAD), minimum and maximum for soil samples are presented in Table 1.

Table 1. Arsenic and heavy metal content of soil samples (mg kg^{-1})

Sample type	Parameters	As	Cd	Pb	Zn
Tailing dump	Median	55.7	1.46	125.5	436
	MAD	29.3	0.40	49.5	114
	Minimum	24.5	0.97	66.0	297
	Maximum	365.0	9.08	658.0	1110
Flooded vegetable gardens	Median	46.6	1.31	85.2	366
	MAD	9.9	0.50	37.8	98
	Minimum	24.4	0.33	29.2	120
	Maximum	142.0	13.60	694.0	2050
Non-flooded vegetable gardens	Median	31.4	0.43	27.8	142
	MAD	3.0	0.12	6.4	28
	Minimum	23.8	0.22	20.5	97
	Maximum	37.4	0.70	40.1	225
Pot experiment polluted soil	Median	202.5	0.49	391.5	159
	MAD	27.5	0.06	36.0	11
	Minimum	132.0	0.28	305.0	142
	Maximum	241.0	0.70	448.0	173
Pot experiment unpolluted soil	Median	34.5	0.27	30.8	124
	MAD	3.2	0.06	5.7	13
	Minimum	28.2	0.21	23.2	108
	Maximum	40.2	0.43	44.3	145
	Pollution limit value	15.0	1.00	100.0	200

MAD: Median absolute deviation

The median concentrations were compared to the Hungarian pollution limit value. The arsenic and metal content of flooded vegetable gardens exceeded these thresholds, with the exception of lead, whereas the contents of non-flooded vegetable gardens were, bar arsenic, under these thresholds. The flooded and non-flooded vegetable gardens show highly significant differences ($p<0.0005$ for As, $p<0.00005$ for Cd, Hg and Zn, and $p<0.00001$ for Pb), but the difference between the tailing dump and flooded vegetable gardens was non significant. The arsenic content of soils in the pot experiment also exceeded the Hungarian pollution limit value, but the cadmium and

zinc content were under these thresholds. The difference was significant ($p<0.01$ for Cd, $p<0.005$ for Zn and $p<0.001$ for As). The differences between the non-flooded vegetable gardens and unpolluted soil were non significant, but between the polluted soil and flooded vegetable gardens or tailing dump was significant ($p<0.005$ for As and Pb, and $p<0.0005$ for Cd and Zn).

The differences in maximum concentrations are highest in the case of cadmium (19 times) and lead (17 times), and lowest in the case of arsenic (3.8 times). These could confirm that the origin of the high Cd and Pb content of flooded vegetable gardens is the floods of Toka creek.

Figure 7, Figure 8, Figure 9, and Figure 10 show the median arsenic and metal contents of soil samples. The tailing dump and the polluted soil in the pot experiment have the highest concentration values; the non-flooded vegetable gardens and the unpolluted soil in the pot experiment have the lowests. Mixing the soil with tailing material (polluted soil) principally increased the lead and arsenic content in the pot experiment.

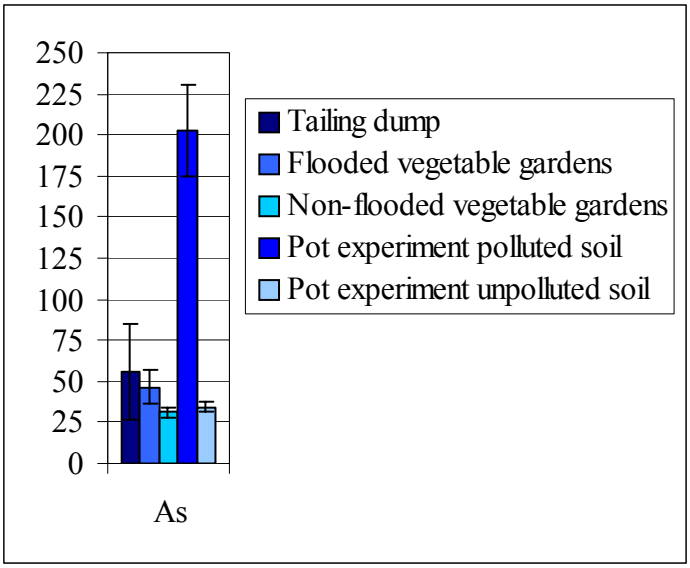

Figure 7. Arsenic content of soil samples

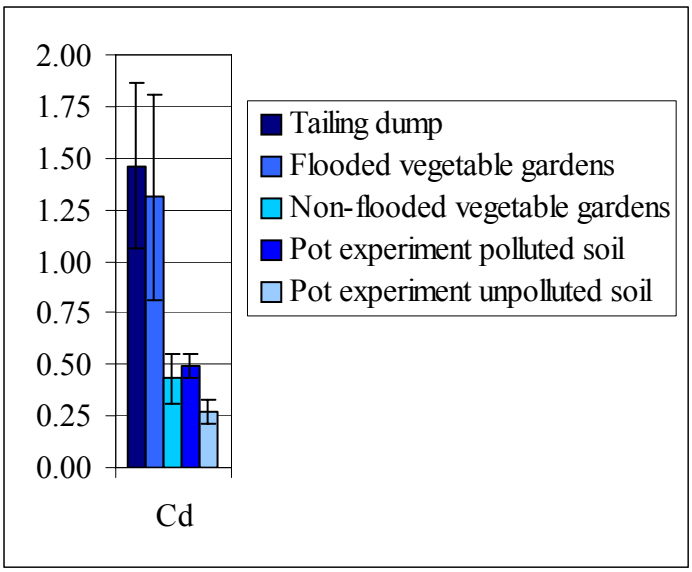

Figure 8. Cadmium content of soil samples

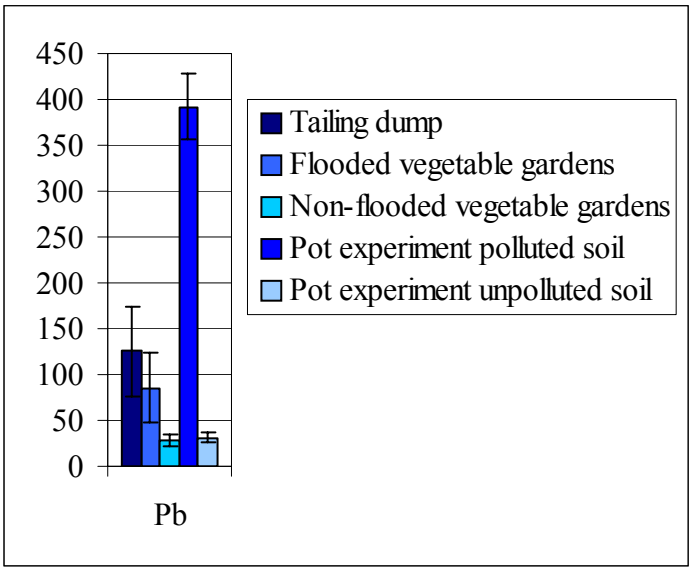

Figure 9. Lead content of soil samples

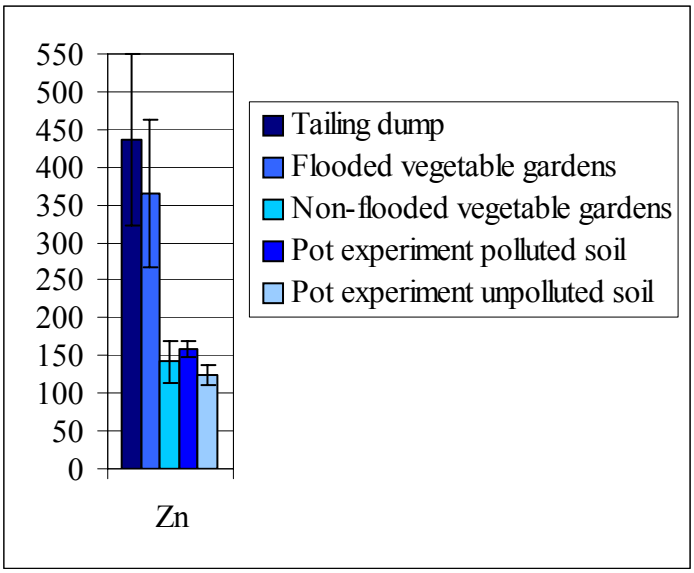

Figure 10. Zinc content of soil samples

Arsenic, cadmium, lead and zinc distribution are shown on contour maps (Figure 11). The first step of color scale is the natural background of the area: 15 mg kg^{-1} for arsenic, 0.1 mg kg^{-1} for cadmium, 20 mg kg^{-1} for lead and 70 mg kg^{-1} for zinc (Ódor et al., 1998), the second step is the Hungarian pollution limit value. The tailing dump show high concentration values and the contour lines draw plum configuration in the direction of the village. The concentration maps reflect the flooding plain with higher concentration values in the village.

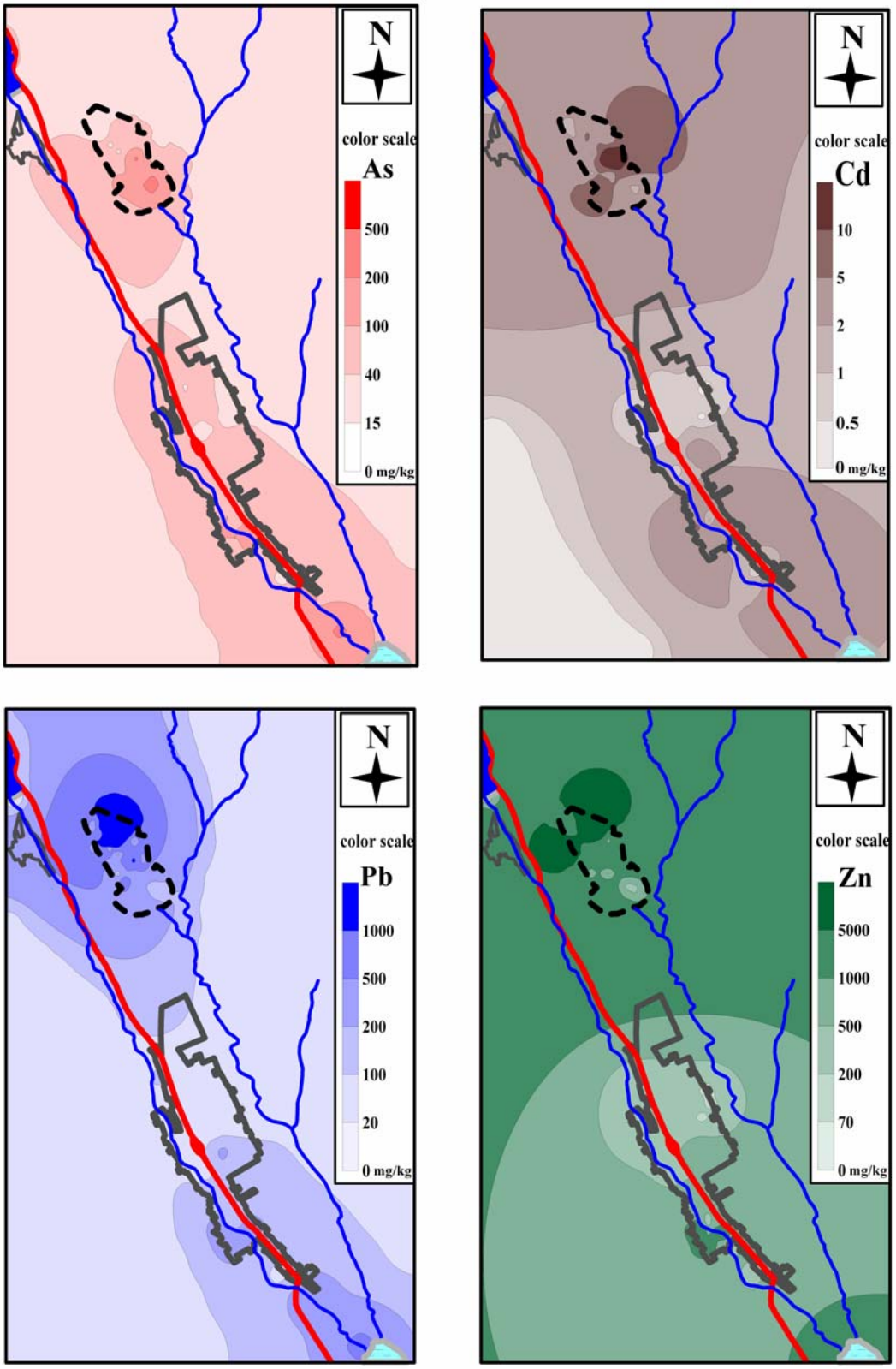

Figure 11. Concentration maps

4.2. Arsenic and heavy metal content of plants

The results of vegetable analyses are shown on Table 2 and Table 3. The arsenic content of vegetables was under the limit of detection in every cases in the field experiment.

Table 2. Arsenic and heavy metal content of vegetable samples (mg kg^{-1})

	Tomato		Squash		Bean	
	NF	F	NF	F	NF	F
As	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Cd	†0.008	†0.060	0.005	0.033	0.010	0.020
Pb	†0.083	†0.480	†0.079	†0.673	0.141	0.260
Zn	†3.16	†18.00	†1.41	†30.90	†7.70	†30.5
	Onion		Carrot		Sorrel	
	NF	F	NF	F	NF	F
As	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Cd	0.056	0.070	0.068	0.130	0.101	0.115
Pb	†0.130	†1.060	0.278	0.810	†0.295	†0.990
Zn	17.20	42.20	11.80	27.60	29.30	60.50

†$p<0.05$
NF: non-flooded vegetable gardens
F: flooded vegetable gardens
LOD: limit of detection

Table 3. Arsenic and heavy metal content of vegetables in pot experiment (mg kg^{-1})

	Carrot		Sorrel	
	UP	P	UP	P
As	<LOD	1.214	<LOD	<LOD
Cd	†0.063	†0.300	†0.164	†1.273
Pb	†0.149	†7.720	2.109	8.570
Zn	†16.59	†27.82	†43.18	†139.57

†$p<0.05$
UP: unpolluted soil
P: polluted soil
LOD: limit of detection

The measured heavy metal levels were higher in vegetables grown in flooded vegetable gardens in every case, but it was significant ($p<0.05$) in the Cd content of tomato, the Pb content of tomato, squash, onion and sorrel, and the Zn content of tomato, bean and squash. We have not found any significant differences in the case of carrot. The highest concentration of Cd was found in carrot, the highest concentration of Zn found in sorrel, and the highest Pb content found in onion.

In the case of pot experiment the arsenic content was measurable in the carrot grown in polluted soil. The heavy metal levels were higher in carrot and sorrel grown in polluted soil, and the differences were significant, with the exception of lead content of sorrel. The highest concentrations were found in sorrel grown in polluted soil.

The yield of vegetables was also measured in the pot experiment. The yield of carrot was 12.148 grams in unpolluted soil, and 8.759 grams in polluted soil. The quality of vegetables also differed (Figure 12 and Figure 13). The yield of sorrel was hardly differed (10.539 grams in unpolluted soil and 10.642 grams in polluted soil).

The seedling capacity is significantly differed between the polluted and unpolluted soils in case of sorrel. (8.7 vs 4 in case of sorrel and 26 vs. 24 in case of carrot.)

Figure 12. Carrot grown in unpolluted soil

Figure 13. Carrot grown in polluted soil

4.3. Bioconcentration factors

The bioconcentration factor (BCF) was calculated from the ratio of the metal concentration of the vegetable (fresh weight) and the metal concentration of the soil. Figure 14 illustrates the BCFs of different species in flooded and non-flooded vegetable gardens and Figure 15 illustrates the BCFs of the pot experiment.

The calculated BCFs were low in the field experiment (0.003-0.012 for lead, 0.012-0.235 for cadmium and 0.010-0.206 for zinc). The BCFs of pot experiment were much higher (0.004-0.069.1 for lead, 0.232-2.59 for cadmium and 0.133-0.882 for zinc) than the BCFs of field experiment. The BCF was higher than 1 only in one case, the cadmium bioconcentration factor of sorrel in polluted soil.

The highest bioaccumulation capacity has the sorrel in both experiments. In the field experiment higher BCFs were found in the non-flooded vegetable gardens, but in the pot experiment the BCFs of polluted soils were higher. In our experiments cadmium and zinc were the mobile elements, cadmium was more mobile than zinc in the pot experiment. In the field experiment zinc was more mobile in less bioaccumulating vegetables (tomato, squash and bean).

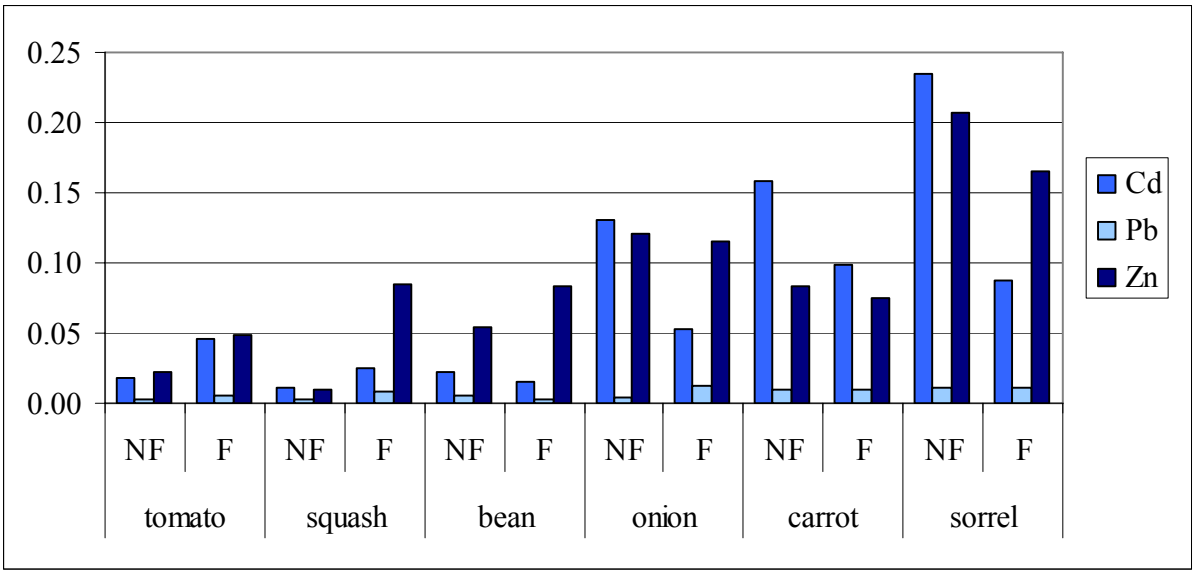

Figure 14. Bioconcentration factors of vegetable gardens

NF: non-flooded vegetable gardens
F: flooded vegetable gardens

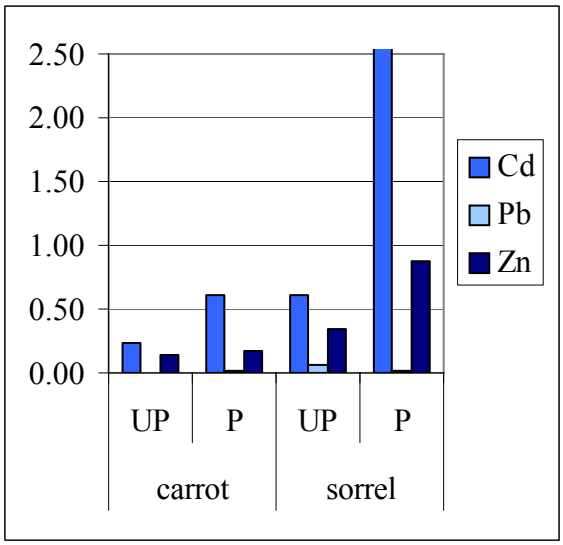

Figure 15. Bioconcentration factors of pot experiment

UP: unpolluted soil
P: polluted soil

4.4. Risk assessment

The default exposure parameters were demonstrated in Table 4. The yearly consumption of home-produced vegetables is about 42 kg with default data, the holidays amounted 2 weeks, and the average bodyweight is 70 kg. The bioconcentration factors are set only for different metals and the type of vegetable is unregarded. Table 5 illustrates the site-specific exposure parameters, which were derived from the questionnaire survey method. Holidays amounted to only 1 week per year, therefore the exposure frequency was 358 days. Home gardening is a traditional family food production system in the village of Gyöngyösoroszi. Home-produced vegetables are for family consumption and not for commercial purposes, therefore in the calculation formula the yield of vegetables was divided by the average family size in the village. The yearly consumption of vegetables per capita was the following: 7.68 kg tomato, 6.21 kg squash, 2.74 kg bean, 2.44 kg onion, 2.15 kg carrot and 1.32 kg sorrel.

Table 4. Default exposure parameters

Parameter	Value	Origin
Ingestion $rate_{vegetable}$ (kg day^{-1})	0.301	US EPA, 1997
Ingestion $rate_{soil\ adult}$ (kg day^{-1})	0.00005	US EPA, 1997
Ingestion $rate_{soil\ children}$ (kg day^{-1})	0.0001	US EPA, 1997
BCF_{As}	0.021	Bockting and van den Berg, 1992
BCF_{Cd}	0.37	Bockting and van den Berg, 1992
BCF_{Pb}	0.013	Bockting and van den Berg, 1992
BCF_{Zn}	0.22	Bockting and van den Berg, 1992
$Fraction_{home\text{-}produced\ vegetables}$	0.4	US EPA, 1997
Exposure frequency (days)	350	US EPA, 1997
$Bodyweight_{adult}$ (kg)	70	US EPA, 1997
$Bodyweight_{children}$ (kg)	15	US EPA, 1997

Table 5. Site-specific exposure parameters

Parameter	Value
$Yield_{tomato}$ (kg $year^{-1}$ $garden^{-1}$)	21.56
$Yield_{squash}$ (kg $year^{-1}$ $garden^{-1}$)	17.43
$Yield_{bean}$ (kg $year^{-1}$ $garden^{-1}$)	7.68
$Yield_{onion}$ (kg $year^{-1}$ $garden^{-1}$)	6.85
$Yield_{carrot}$ (kg $year^{-1}$ $garden^{-1}$)	6.04
$Yield_{sorrel}$ (kg $year^{-1}$ $garden^{-1}$)	3.70
Family size ($garden^{-1}$)	2.8
Exposure frequency (days)	358
$Bodyweight_{men}$ (kg)	80.07
$Bodyweight_{women}$ (kg)	73.66

The results of human health risk assessment with default values are shown in Table 6 and Figure 16.

Table 6. Hazard indices of flooded and non-flooded vegetable gardens (default parameters)

Flooded vegetable gardens	Ingestion soil	Ingestion vegetable	Hazard index
As	0.18239	0.53801	0.72040
Cd	0.00154	0.07994	0.08148
Pb	0.02858	0.05219	0.08077
Zn	0.00143	0.04427	0.04570
Hazard index	0.21394	0.71441	0.92835

Non-flooded vegetable gardens	Ingestion soil	Ingestion vegetable	Hazard index
As	0.12290	0.36252	0.48542
Cd	0.00051	0.02624	0.02675
Pb	0.00933	0.01703	0.02636
Zn	0.00056	0.01718	0.01774
Hazard index	0.13330	0.42297	0.55627

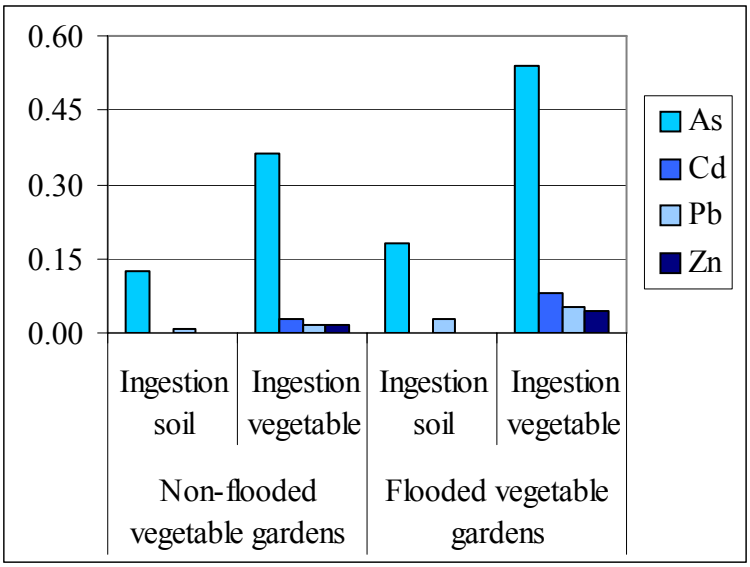

Figure 16. Distribution of hazard indices of flooded and non-flooded vegetable gardens (default parameters)

The summarized hazard index of flooded vegetable gardens is 0.92835 and of non-flooded vegetable gardens is 0.55627, which is an indicated acceptable risk. The largest contribution to hazard index was from arsenic both in the flooded and non-flooded vegetable gardens. In all cases most hazard index was attributable to ingestion of home-produced vegetables (77% in the case of flooded vegetable gardens and 76% in the case of non-flooded vegetable gardens). The contribution to the hazard index from soil ingestion was largest for children in flooded-vegetable gardens and 90% of the risk is derived from arsenic.

The results of human health risk assessment with site-specific parameters are shown in Table 7 and Figure 17. The summarized hazard index of flooded vegetable gardens is 0.3275 and of non-flooded vegetable gardens is 0.0922, both of them are indicated acceptable risk. The largest contribution to hazard index was from lead both in the flooded and non-flooded vegetable gardens. In all cases most hazard index was attributable to ingestion of home-produced vegetables (83% in the case of flooded vegetable gardens and 72% in the case of non-flooded vegetable gardens). The contribution to the hazard index from soil ingestion was largest for children in flooded-vegetable gardens and 90% of the risk is derived from arsenic.

Table 7. Hazard indices of flooded and non-flooded vegetable gardens (site-specific parameters)

Flooded vegetable gardens	Ingestion soil	Ingestion vegetable	Hazard index
As	0.05140	-	0.05140
Cd	0.00020	0.04730	0.04750
Pb	0.00534	0.14500	0.15034
Zn	0.00025	0.07800	0.07825
Hazard index	0.05719	0.27030	0.32749

Non-flooded vegetable gardens	Ingestion soil	Ingestion vegetable	Hazard index
As	0.02350	-	0.02350
Cd	0.00011	0.01900	0.01911
Pb	0.00165	0.02870	0.03035
Zn	0.00011	0.01910	0.01921
Hazard index	0.02537	0.06680	0.09217

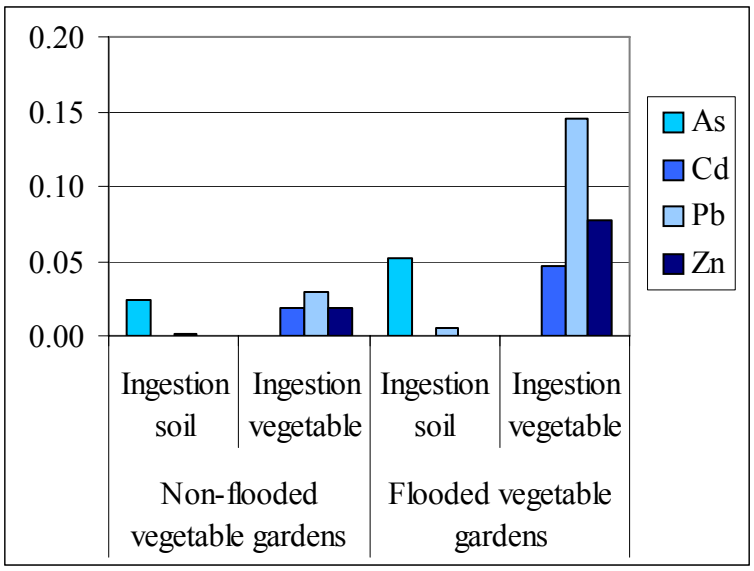

Figure 17. Distribution of hazard indices of flooded and non-flooded vegetable gardens (site-specific parameters)

5. DISCUSSION

Metals are widely used, and their sources are numerous. Major sources are smelters, mining activities, hazardous waste sites and even natural sources (Calderon et al., 2003). Our studied area –the area of a former lead/zinc mine– is a typical metal polluted site, where the main pollutants are arsenic, lead, cadmium and zinc. The metal contamination in Gyöngyösoroszi area is well-documentated, but these are mainly analysed the soil pollution (Horváth and Gruiz, 1996; Ódor et al., 1998; Fügedi, 2004; Kovács et al., 2006) or the possibility of phytoremediation (Máthé-Gáspár and Anton, 2005; Simon, 2005). The health effect of pollution and risk assessment is rarely investigated.

Arsenic, cadmium and lead contamination have been reported in smelter and mining areas located in different coutries, among them Poland (Ullrich et al., 1999, Weislo et al., 2002), Spain (Grimalt et al., 1999), China (Liu et al., 2005, Zheng et al., 2007b), Korea (Lee et al., 2001, Jung, 2001, Kim et al., 2005), Slovakia (Rapant et al., 2006) and Romania (Lacatusu, 1996). These studies are completed with risk assessment.

In our study the measured concentrations are the "pseudo-total metal contents", which accounts for the *aqua regia* digestion not completely destroying silicates (Manta et al., 2002). This method is widely used in environmental geochemistry studies and recommended by the Hungarian Standards Institution. High arsenic concentrations were found in all samples, also found in lower layers (28 mg kg^{-1}), and are thought to represent the natural background (Ódor et al., 1998). Generally lead and zinc are contained in the dikes of the Badenian while copper is dominantly in the Karpatian coarsely crystalline stratovolcanic andesite series and arsenic occurs mainly in the dikes of the small porphyritic andesite (kalitrachite or tuffs) series (Nagy, 1986). This can be one interpretation of high arsenic concentration in the area. On the other hand, the most frequented lead ore mineral is galenite, where lead can be substituted by silver, copper and zinc, rarely arsenic as microscopical inclusions.

The statistical analyses emphasize the relevance of floods in the contamination of vegetable gardens in the village and the origin of this contamination is the tailing dump. The high median absolute deviation in the soil of tailing dump and flooded

vegetable gardens shows the inhomogeneous distribution of soil contamination. The statistical analysis suggested that the mixing of unpolluted soil with tailing material neither modelling the flooded vegetable gardens and nor the soil of the tailing dump.

The geochemical maps of the studied area tried to predict pollutant concentrations at sites where measurements had not been taken (Morra et al., 2006). The modeling methods have been greatly strengthened by the use of geographical information system (GIS) and geostatistical techniques. These techniques have been used to model local pollution patterns on the basis of monitored data (Nieuwenhuijsen et al., 2006). In the studied area the highest values are found in the tailing dump, but the patterns of elements are not similar, only the mobile elements like cadmium and zinc have similar patterns. The created isoconcentration maps help to visualize the soil pollution from the measured data. These predicted the most polluted area in the village and may enhance exposure assessment in environmental epidemiology studies (Jarup, 2004).

Despite of the arsenic concentration being high in the soil, in the vegetables it was under the limit of detection. In contrast with our results, other studies found elevated levels of arsenic in vegetables and crops cultivated in metal-contaminated soils (Queirolo et al., 2000; Lee and Chon, 2003; Rapant et al., 2006). The different mineralogy form and the presence of bioleaching microbes could explain the various phyto- and bioavailability of arsenic (Ruby et al., 1999; Mahimairaja et al., 2005).

In our study the most mobile metals were cadmium and zinc. Our results agree with Ullrich et al., who found that the potential phytoavailability of Pb, Zn and Cd in the topsoils between pH 5 and 7 declines in the order Cd, Zn and Pb (Ullrich et al., 1999). The order of bioconcentration capacity of metals was Cd>Zn>>Pb and this strongly agrees with the literature data (McBride, 2003; Cui et al., 2004; Liu et al., 2005).

Sorrel was the most contaminated vegetable while the lowest concentration was measured in bean. Other studies found spinach, which is very similar to sorrel, had the highest bioconcentration capacity among vegetables (Mattina et al., 2003; Wang et al., 2006) and bean had one of the lowest (Liu et al., 2005). Generally, the BCFs are lower in flooded vegetable gardens, this is in agreement with BCF values decreasing as the metal concentration in soil increasing (Alam et al., 2003; Wang et al., 2004). In case of

low accumulating vegetables (tomato, squash and bean) this effect was not predominating. Results indicated different characters of species for element uptake. Zheng et al. found similar BCF values for vegetables in China (Zheng et al., 2007a).

In the pot experiment the important pollutant elements were the same as in the field experiment and the seeded vegetables were the most bioaccumulating vegetables: carrot and sorrel. The rates of metal concentration were higher than the field experiment in polluted soil and unpolluted soil, too. Cadmium content increased at a higher rate in both species compared to zinc content. Increase of cadmium content of sorrel caused the highest BCF. In contrast with the field experiment, the bioconcentration values of polluted soil were higher, than the unpolluted soil. Other studies also tried to model the contaminated soil by mixing the unpolluted soil with other materials (Dudka et al., 1996). In our study this approach does not model the contamination process, the flooding. The high accumulating capacity in pot experiment can generate by the pH decreasing. The increased metal concentration in tailing material can decrease the pH of soil and hence stimulate the accumulating capacity (Chunilall et al., 2006).

Two exposure pathways were selected due to the site-specific land uses and the feature of metals: ingestion of soil and ingestion of home-produced vegetables. The inhalation and dermal exposure routes were neglected in accordance with other studies (Granero and Domingo, 2002; Hough et al., 2004; Nadal et al., 2004; Grasmück and Scholz, 2005; Hellström et al., 2007).

The bodyweight of women was significantly higher than the average bodyweight of Hungarian women (67.21 kg), but the bodyweight of men was nearly the same (80.84 kg) (Melles, 2004). Location-specific human data were also necessary to calculate actual human exposure through ingestion of vegetables (Albering et al., 1999). The yearly consumptions of vegetables are generally lower than Santos et al. found in Rio de Janeiro (5.4 kg tomato, 4.1 kg onion and 3.7 kg carrot) (Santos et al., 2004) or that is given in the US EPA Exposure Factor Handbook (12.57 kg tomato, 5.1 kg bean, 4.42 kg carrot, 2.7 kg onion) (US EPA, 1997), because home gardening partly covers the vegetable requirements of families. The daily consumption of home produced vegetables was 173.3 g day^{-1}, which is higher than found in Bangladesh (130 g day^{-1}) (Alam et al., 2003) or in China (105 g day^{-1}) (Liu et al., 2005).

The distribution of risk due to different exposure routes is similar to that found by Hough et al. in the United Kingdom (Hough et al., 2004). The elevated arsenic level of soil indicates the importance of soil ingestion pathway, especially for children (Rieuwerts et al., 2006). In order to reduce the uncertainty in estimating the risk associated with incidental ingestion of soil, further testing is necessary because the *in vivo* arsenic availability can vary widely (Juhasz et al., 2007). Our results, as do other studies (Hellström et al., 2007; Huang et al., 2007), also emphasize that the consumption of locally grown vegetables is an important exposure pathway in metal contaminated sites. Despite the high concentration levels in soil, the summarized hazard index was low in flooded vegetable gardens. Another study in Germany has similar suggestion (Wilhelm et al., 2005).

The result of risk assessment with default data was higher than with site-specific data. Our results approved the theory, that default risk assessment usually overestimate the real hazard and the necessity, that the risk assessment methods should be improved (Wentsel et al., 2002).

In our study the risk assessment was determined by special calculation with ingestion of vegetables and site-specific exposure parameters. Of special note is that the calculation using the concentration of vegetables could reproduce the real phytoavailability of metals in contaminated sites. The usage of yield of homegrown vegetables also refines the calculation because consumption of vegetables with higher BCF was much lower than with lower BCF. The latest scientific data on bioaccumulation do not currently support the use of bioconcentration factor (BCF) and bioaccumulation factor (BAF) values when applied as generic threshold criteria for the hazard potential of inorganic metals in human and ecological risk assessment.

Risk assessors should be aware that dietary pathways represent a major exposure route for metals (Choudhury et al., 2001). Estimation of intakes of metals occurring in food requires information on the levels of metals in food and the amount of food consumed. Although large-scale surveys of the metal contents of foods and food consumption patterns have been conducted, assessors should be aware that these surveys have several limitations for applications to human health risk assessment. Analysis is often conducted with "market basket" samples of packaged processed foods. Food consumption surveys are generally limited to short-term consumption (e.g. 1–3

days) and do not capture intra-individual variability that would affect long-term averages. Furthermore, dietary patterns may change over time (e.g. consumption of ethnic foods in childhood may change later), and, thus, patterns discerned at any given time may not accurately represent historical or future exposures. The correct estimation of dietery parameters is the key step in exposure assessment. Hence site-specific parameters might be applied instead of default parameters. On the other hand there are data gaps in the exposure factors such as the estimates of home prudeced vegetables and the consumption of homegrown vegetables (Moya and Phillips, 2002; Finster et al., 2004).

Many studies on the toxicity of heavy metals have shown that health risks to humans do not always correlate with the external exposure dose of metals. This is because virtually all risk estimates ignore the bioavailability component in the assessment process. The bioavailability is a critical point of exposure assessment (Caussy, 2003). The future role of exposure assessment will perhaps be marginalized because biomonitoring programs can directly measure the concentration of chemicals that are present in biologic matrices (Paustenbach and Galbraith, 2006).

Epidemiology has a special role to play in risk assessment of environmental exposures. This is because epidemiology is based on direct observations in humans. Environmental epidemiology studies the effects of environmental exposures on health and disease in the population (Brunekreef, 2008). In our studied area only one epidemiological study was carried on in 1988 (Gombkötő, 1988). These results did not found significant differences between Gyöngyösoroszi and Kisnána (another village in Heves county without industrial pollution source). The mortality rate was 13.8 in Gyöngyösoroszi and 17.4 in Kisnána per 1000 inhabitant. The mean blood lead level among the whole population was the following: 174.8 $\mu g\ l^{-1}$ in Gyöngyösoroszi and 174.0 $\mu g\ l^{-1}$ in Kisnána. Difference was found between the blood lead level among children. 95 $\mu g\ l^{-1}$ in Gyöngyösoroszi and 46 $\mu g\ l^{-1}$ in Kisnána.

The lifestyle-related factors (smoking and obesity) can modify the risk assessment process and the effect of environmental agents (Irigaray et al., 2007). In the studied area the 34.5% of men and 12.9% of women were smokers in 1988 and 35% of men and 17% of women in 2003. Our questionarrie derived data and the previuos

studies (Gombkötő, 1988) in this area also found eleveted bodyweight (78.65 kg for men and 69.19 kg for women) but compered the data the tendency is increasing.

The disturbances in the interpretations of results in the Gyöngyösoroszi area suggest new biomarker investigations and epidemiological studies as next chellanges.

6. CONCLUSION

In conclusion, the results are supported the followings:

- The toxic metal contents in the Gyöngyösoroszi area exceed the Hungarian limit value.
- The high arsenic content of the area is due to the natural background and is not available by vegetables.
- There are significant differences between the flooded and non-flooded vegetable gardens. Origin of the pollution is the tailing dump and the flotation plant.
- The mixing of unpolluted soil with tailing material does not model the floodings.
- The most mobile elements are cadmium and zinc.
- The most accumulating vegetable is sorrel.
- Using the new equation $ADD = \frac{\sum (C_{VEG} \times \frac{Y_{VEG}}{n}) \times ED}{BW \times AT}$ can combine the amount of homegrown vegetables and the bioavailabilty of metals.
- Using site-specific parameters instead of default exposure parameters is more accurate in risk assessment process. The default processes overestimate the real hazard.
- The consumption of homegrown vegetables does not pose unacceptable risk to the population although the main exposure route is consumption of vegetables.

7. SUMMARY

The environmental research carried out in the village of Gyöngyösoroszi has documented increased concentrations of arsenic and heavy metals in the soil of vegetable gardens. The differences between the metal contents of flooded and non-flooded vegetable gardens were significant, which confirm that the floods of Toka creek spread the contamination over the flood-plain of the village. The source of pollution is the tailing dump and the flotation plant.

The metal contents of vegetables were low and the arsenic content was under the detection limit in every case. The sorrel cultivated in flooded gardens has the highest metal content. Significant differences were also found between the flooded and non-flooded vegetable gardens. The vegetable concentration results further support the view that soil metals are not always absorbed as well as soluble forms, therefore use of default bioconcentration factors in assessing human health risk may overestimate the hazard. In our study, all of the bioconcentration factors were under 0.25 and the mobile elements were cadmium and zinc. Generally, the bioconcentration factors of non-flooded vegetable gardens were higher; the sorrel was the most accumulating vegetable.

In the pot experiment the BCFs were higher, but the tendencies were the same. The most accumulating vegetable was sorrel and the most mobile element was cadmium and zinc. The arsenic contents were also immeasurable.

Site-specific exposure parameters and a newly created equation for ingestion of vegetables were applied in risk assessment process. The site-specific exposure factors were generated from the results of questionnaire survey in the village, while the equation was based on the cultivation habits of homegrown vegetables.

The outcome of risk assessment has indicated acceptable risk in the village of Gyöngyösoroszi, both in flooded and non-flooded vegetable gardens. The risk assessment process with default exposure parameters overestimated the risk. In contrast with previous study in the area, home gardening does not increase the risk for inhabitants at present. The most relevant exposure route was ingestion of homegrown vegetables. It is possible to further reduce the risk of human exposure to soil metal contamination by selecting leafy vegetables such as sorrel in home gardening.

ÖSSZEFOGLALÁS

A toxikus fémek a természetben káros hatásokat és sokszor már visszafordíthatatlan elváltozásokat okoznak veszélyeztetve ezzel az ott élő emberek egészségét.

Munkám során a Gyöngyösoroszi ércbánya által okozott toxikus fémszennyeződés egészségi kockázatát vizsgáltam a falu területén található kiskertekben. A területen átfolyó Toka-patak által elöntött kiskertek fémtartalma szignifikánsan különbözött a nem elöntött kiskertekétől, az előbbiek fémtartalma –az ólom kivételével- meghaladta a szennyezettségi határértéket. A kiskertekben termesztett zöldségek arzéntartalma minden esetben a kimutatási határ alatt volt. A számolt biokoncentrációs faktor (BCF) értékek is alacsonyak voltak, a szabadföldi vizsgálatban a leginkább akkumuláló zöldség a sóska volt, a legmobilisabb fémek a kadmium és a cink.

A tenyészedényes kísérletben sóska és sárgarépa bioakkumulációját vizsgáltam egy szennyezetlen és egy meddőanyaggal mesterségesen szennyezett talajon, a szabadföldi kísérlethez hasonló eredmények születtek. A legmobilisabb fém ebben az esetben is a kadmium és a cink volt, a legjobban akkumuláló növény a sóska. A kísérletben számolt BCF értékek azonban sokkal magasabbak voltak a területről származó mintákból számoltaknál.

Az egészségi kockázat számításánál alapértelmezett illetve helyspecifikus paraméterekkel végeztem számítást. A helyspecifikus értékeket kérdőívek segítségével határoztam meg, különös tekintettel a helyben termesztett zöldségek mennyiségére. A kockázat számítását ennek megfelelően általam módosított képlet segítségével végeztem. A kapott eredmények alapján a kiskertekben termesztett zöldségek fogyasztása illetve a talajszemcsék szervezetbe kerülése nem jelent kockázatot a területen élő populációra. A számítás alapján a legnagyobb veszélyt a talaj ólomtartalma jelenti, a legkockázatosabb expozíciós út a helyben termesztett zöldségek elfogyasztása.

A számítások összehasonlításakor egyértelművé vált, hogy az alapértelmezett paraméterek használata túlértékeli a kockázatot a helyspecifikus paraméterekkel szemben.

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9. REFERENCES

1. Adriano, D.C., 1986. Trace elements in the terrestrial environment. Springer, New York, NY.
2. Alam, M.G.M., Snow, E.T., Tanaka, A., 2003. Arsenic and heavy metal contamination of vegetables grown in Samta village, Bangladesh. Sci. Total Environ. 308, 83-96.
3. Albering, H.J., van Leusen, S.M., Moonen, E., Hoogewerf, J.A., Kleinjans, J.C.S., 1999. Human health risk assessment: A case study involving heavy metal soil contamination after the flooding of the River Meuse during the winter of 1993-1994. Environ. Health Perspect. 107, 37-43.
4. Alloway, B.J. (Ed.), 1995. Heavy metals in soils. Chapman and Hall, London.
5. ATSDR, 1999. Toxicological profile for cadmium. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disaese Registry, Atlanta, GA.
6. ATSDR, 2005. Toxicological profile for zinc. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disaese Registry, Atlanta, GA.
7. ATSDR, 2007a. Toxicological profile for arsenic. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disaese Registry, Atlanta, GA.
8. ATSDR, 2007b. Toxicological profile for lead. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disaese Registry, Atlanta, GA.
9. Baker, S., Herrchen, M., Hund-Rinke, K., Klein, W., Kördel, W., Peijnenburg, W., Rensing, C., 2003. Underlying issues including approaches and information needs in risk assessment. Ecotox. Environ. Safe. 56, 6-19.
10. Bernard, B.P., Becker, C.E., 1988. Environmental lead exposure and the kidney. Clin. Toxicol. 26, 1-34.
11. Biswas, B.K., Dhar, R.K., Samanta, G., Mandal, B.K., Chakraborti, D., Faruk, I., Islam, K.S., Chowdhury, M.M., Islam, A., Roy, S., 1998. Detailed study

report of Samta, one of the arsenic-affected villages of Jessore District, Bangladesh. Curr. Sci. 74, 134–145.

12. Bockting, G.J.M., van den Berg, R., 1992. The accumulation of trace metals in crops grown on contaminated soils. National Institute of Public Health and the Environment, Bilthoven.
13. Bridges, J., 2003. Human health and environmental risk assessment: the need for a more harmonised and integrated approach. Chemosphere 52, 1347-1351.
14. Brunekreef, B., 2008. Environmental epidemiology and risk assessment. Tox. Lett. doi:10.1016/j.toxlet.2008.05.012.
15. Buchet, J.P., Lauwerys, R., Roels, H., 1990. Renal effects of cadmium body burden of the general population. Lancet 336, 699-702.
16. Calderón, J., Ortiz-Pérez, D., Yánez, L., Diaz-barriga, F., 2003. Human exposure to metals. Pathways of exposure, biomarkers of effect, and host factors. Ecotox. Environ. Safe. 56, 93-103.
17. Caussy, D., 2003. Case studies of the impact of understanding bioavailability: arsenic. Ecotox. Environ. Safe. 56, 164-173.
18. Chaney, R.L., 1980. Health risks associated with toxic metals in municipal sludge. In: Bitton, G., Damron, B.L., Edds, G.T., Davidson, J.M. (Eds.), Sludge–health risks of land application. Ann Arbor Science Publishers, Ann Arbor, MI.
19. Chen, C.J., Kuo, T.L., Wu, M.M., 1988. Arsenic and cancers. Lancet, 1, 414–415.
20. Chen, S.L., Dzeng, S.R., Yang, M.H., Chiu, K.H., Shieh, G.M., Wai, C.M., 1994. Arsenic species in groundwaters of the blackfoot disease area, Taiwan. Environ Sci Technol. 28, 877–881.
21. Choudhury, H., Harvey, T., Thayer, W.C., Lockwood, T.F., Stiteler, W.M., Goodrum, P.E., Hassett, J.M., Diamond, G.L., 2001. Urinary cadmium elimination as a biomarker of exposure for evaluating a cadmium dietary exposure-biokinetics model. J. Toxicol. Environ. Health 63, 101–130.
22. Chunilall, V., Kindness, A., Jonnalagadda, S.B., 2006. Impact of coal mine dump contaminated soils on elemental uptake by *Spinacia oleracea* (spinach). J. Environ. Sci. Health B 41, 297-307.

23. Cirone, P.A., Duncan, P.B., 2000. Integrating human health and ecological concerns in risk assessments. J. Hazard Mater. 78, 1-17.
24. Cui, Y.J., Zhu, Y.G., Zhai, R.H., Chen, D.Y., Huang, Y.Z., Qui, Y., Liang, J.Z., 2004. Transfer of metals from soil to vegetables in an area near a smelter in Nanning, China. Env. Int. 30, 785-791.
25. Cullen, N.M., Wolf, L.R., St Clair, D., 1995. Pediatric arsenic ingestion. Am. J. Emerg. Med. 13, 432-435.
26. Davis, J.M., Svendsgaard, D.J., 1987. Lead and child development. Nature 329, 297-300.
27. DEFRA, 2002a. Contaminants in soil: Collation of toxicological data and intake values for humans. Arsenic. Environment Agency, Bristol.
28. DEFRA, 2002b. Contaminants in soil: Collation of toxicological data and intake values for humans. Cadmium. Environment Agency, Bristol.
29. DEFRA, 2002c. Contaminants in soil: Collation of toxicological data and intake values for humans. Lead. Environment Agency, Bristol.
30. Dhar, R.K., Biswas, B.K., Samanta, G., Mandal, B.K., Chakraborti, D., Roy, S., Fafar, A., Islam, A., Ara, G., Kabir, S., Khan, A.W., Ahmed, S.A., Hadi, S.A., 1997. Groundwater arsenic calamity in Bangladesh. Curr. Sci. 73, 48–59.
31. Dudka, S., Piotrowska, M., Terelak, H., 1996. Transfer of cadmium, lead, and zinc from industrially contaminated ssoil to crop plants: a field study. Environ. Poll. 94, 181-188.
32. Emmerson, B.T., 1970. "Ouch-Ouch" disease: the osteomalacia of cadmium nephropathy. Ann. Int. Med. 73, 854-855.
33. Enterline, P.E., Day, R., Marsh, G.M., 1995. Cancers related to exposure to arsenic at a copper smelter. Occup. Environ. Med. 52, 28-32.
34. Fairbrother, A., Randall, W., Sappington, K., Wood, W., 2007. Framework for metals risk assessment. Ecotox. Environ. Saf. 68,145-227.
35. Finster, M.E., Gray, A.K., Binns, H.J., 2004. Lead levels of edibles grown in contaminated residential soils: a field survey. Sci. Total Environ. 320, 245-257.
36. Friberg, L., Elinder, C.G., Kjellstrom, T., Nordberg, G.F. (Eds.), 1985. Cadmium and health: A toxicological and epidemiological appraisal. CRC Press, Boca Raton, FL.

37. Fügedi, U., 2004. Geochemical background and heavy metal pollution near Gyöngyösoroszi (NE Hungary). Bull. Hung. Geol. Soc. 134, 291-301.
38. Gay, J.R., Korre, A., 2006. A spatially-evaluated methodology for assessimg risk to a population from contaminated land. Environ. Poll. 142, 227-234.
39. Gerr, F., Letz, R., Ryan, P.B., Green, R.C., 2000. Neurological effects of environmental exposure to arsenic in dust and soil among humans. Neurotoxicology 21, 475-487.
40. Goering, P.L., 1993. Lead-protein interactions as a basis for lead toxicity. Neurotoxicology 14, 45-60.
41. Gombkötő, Gy. (Ed.), 1988. Gyöngyösoroszi HAF üzem környezetvizsgálati eredményei. Heves Megyei ÁNTSZ, Eger.
42. Goyer, R.A., 1993. Lead toxicity: Current concerns. Environ. Health Perspect. 100, 177-187.
43. Granero, S., Domingo, J.L., 2002. Levels of metals in soils of Alcalá de Henares, Spain: Human health risk. Environ. Int. 28, 159-164.
44. Grasmück, D., Sholz, R.W., 2005. Risk perception of heavy metal soil contamination by high-exposed and low-exposed inhabitants: The role of knowledge and emotional concerns. Risk. Anal. 25, 611-622.
45. Grimalt, J.O., Ferrer, M., Macpherson, E., 1999. The mine tailing accident in Aznacollar. Sci. Total Environ. 242, 3-11.
46. Hellström, L., Persson, B., Brudin, L., Petersson Grawé, K., Öborn, I., Järup, L., 2007. Cadmium exposure pathways in a population living near a battery plant. Sci. Total Environ. 373, 447-455.
47. Hertz-Picciotto, I., Croft, J., 1993. Review of the relation between blood lead and blood pressure. Epidemiol. Rev. 15, 352-373.
48. Hewitt, P.J., 1988. Accumulation of metals in the tissues of occupationally exposed workers. Environ. Geochem. Health 10, 113-116.
49. Holmqvist, I., 1951. Occupational arsenical dermatitis: A study among employees at a copper ore smelting work including investigations of skin reactions to contact with arsenic compounds. Acta Derm. Venerol. 31, 1-204.
50. Horváth, B., Gruiz, K., 1996. Impact of metalliferous ore mining activity on the environment in Gyongyosoroszi, Hungary. Sci. Total Environ. 184, 215-227.

51. Hough, R.L., Breward, N., Young, S.D., Crout, N.M., Tye, A.M., Moir, A.M., Thornton, I., 2004. Assessing potential risk of heavy metal exposure from consumption of home-produced vegetables by urban populations. Environ. Health Perspect. 112, 215-221.

52. Huang, S.S., Liao, Q.L., Hua, M., Wu, X.M., Bi, K.S., Yan, C.Y., Chen, B., Zhang, X.Y., 2007. Survey of heavy metal pollution and assessment of agricultural soil in Yangzhong district, Jiangsu Province, China. Chemosphere 67, 2148-2155.

53. Hughes, S., Samman, S., 2006. The effect of zinc supplementation in humans on plasma lipids, antioxidant status and thrombogenesis. J. Am. Coll. Nutr. 25, 285-291.

54. Hungarian Standard Institution, 1981. MSZ 21470-2. Environmental protection. Preparation of soil sample. Determination of electrical conduction, humidity and pH. Hungarian Standard Institution, Budapest.

55. Hungarian Standard Institution, 1998. MSZ 21470-1. Environmental protection. Testing of soils. Sampling. Hungarian Standard Institution, Budapest.

56. Institute of Medicine, 2001. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, silicon, vanadium, and zinc. National Academy Press, Washington, DC.

57. Irigaray, P., Newby, J.A., Clapp, R., Hardell, L., Howard, V., Montagnier, L., Epstein, S., Belpomme, D., 2007. Lifestyle-related factors and environmental agents causing cancer: An overview. Biomed. Pharmacother. 61, 640-658.

58. Jarup, L., Berglund, M., Elinder, C.G., Nordberg, G., Vahter, M., 1998. Health effects of cadmium exposure – a review of the literature and a risk estimate. Scand. J. Work. Environ. Health 24, 1-51.

59. Jarup, L., 2004. Health and environment information systems for exposure and disease mapping, and risk assessment. Environ. Health Perspect. 112, 995-997.

60. JECFA, 1993. Evaluation of certain food additives and contaminants: 41st report of the Joint FAO/WHO expert committee on food additives. World Health Organization, Geneva.

61. Jensen, A., Bro-Rasmussen, R., 1992. Environmental cadmium in Europe. Rev. Environ. Contam. Toxicol. 125, 101-181.

62. Juhasz, A.L., Smith, E., Weber, J., Rees, M., Rofe, A., Kuchel, T., Sansom, L., Naidu, R., 2007. Comparison of *in vivo* and *in vitro* methodologies for the assessment of arsenic bioavailability in contaminated soils. Chemosphere 69, 961-966.

63. Jung, M.C., 2001. Heavy metal contamination of soils and waters in and around the Imcheon Au-Ag mine, Korea. Appl. Geochem. 16, 1369-1375.

64. Kabata-Pendias, A., Pendias, H., 1984. Trace elements in soils and plants. CRC Press, Boca Raton, FL.

65. Kakkar, P., Jaffery, F.N., 2005. Biological markers for metal toxictiy. Environ. Toxicol. Phar. 19, 335-349.

66. Kim, J., Kim, K., Ahn, J.S., Ko, I., Lee, C., 2005. Investigation and risk assessment modeling of As and heavy metals contamination around five abandoned metal mines in Korea. Environ. Geochem. Hlth. 27, 193-203.

67. Kopp, S.J., Glonek, T., Perry, H.M., Erlanger, M., Perry, E.F., 1982. Cardiovascular actions of cadmium at environmental exposure levels. Science 217, 837-839.

68. Kovács, E., Dubbin, W.E., Tamás, J., 2006. Influence of hydrology on heavy metal speciation and mobility in a Pb-Zn mine tailing. Environ. Pollut. 141, 310-320.

69. Krishnamurti, G.S.R., McArthur, D.F.E., Wang, M.K., Kozak, L.M., Huang, P.M., 2005. Biogeochemistry of soil cadmium and the impact on terrestrial food chain contamination In: Biogeochemistry of Trace Elements in the Rhizosphere, Elsevier, Amsterdam.

70. Kwong, W.T., Friello, P., Semba, R.D., 2004. Interactions between iron deficiency and lead poisoning: Epidemiology and pathogenesis. Sci. Total Environ. 330, 21-37.

71. Lacatusu, R., Rauta, C., Carstea, S., Ghelase, I., 1996. Soil-plant-man relationship in heavy metal polluted areas in Romania. Appl. Geochem. 11, 105-107.

72. LeCoultre, T.D., 2001. A meta-analysis and risk assessment of heavy metal uptake in common garden vegetables, MSc Thesis, East Tennessee State University, Johnson City, TN.

73. Leduc, D., Francquen, P., Jacobovitz, D., Vandeweyer, R., Lauwerys, R., De Vuyst, P., 1993. Association of cadmium exposure with rapidly progressive emphysema in a smoker. Thorax 48, 570-571.

74. Lee, C.G., Chon, H.T., Jung, M.C., 2001. Heavy metal contamination in the vicinity of the Daduk Au-Ag-Pb-Zn mine in Korea. Appl. Geochem. 16, 1377-1386.

75. Lee, J.S., Chon, H.T., 2003. Exposure assessment of heavy metals on abandoned metal mine areas by ingestion of soil, crop plant and groundwater. J. Phys. IV. 107, 757-760.

76. Lee, J., Chon, H., Kim, K., 2005. Human risk assessment of As, Cd, Cu and Zn in the abandoned metal mine site. Environ. Geochem. Hlth. 27, 185-191.

77. Lester, R.R., Green, L.C., Linkov I., 2007. Site.specific applications on Probabilistic Health Risk Assessment: Review of the literature since 2000. Risk Anal. 27, 635-658.

78. Lindahl, M., Leanderson, P., Tagesson, C., 1998. Novel aspect on metal fume fever: zinc stimulates oxygen radical formation in human neutrophils. Hum. Exp. Toxicol. 17, 105-110.

79. Little, R.E., Kay,. G.N., Cavender, J.B., 1990. Torsade de pointes and T-U wave alternans associated with arsenic poisoning. PACE 13, 164-170.

80. Liu, H., Probst, A., Liao, B., 2005. Metal contamination of soils and crops affected by the Chenzhou lead/zinc mine spill (Hunan, China). Sci. Total Environ. 339, 153-166.

81. Mahimairaja, S., Bolan, N.S., Adriano, D.C., Robinson, B., 2005. Arsenic contamination and its risk management in complex environmental settings. Adv. Agron. 86, 1-82.

82. Malo, J.L., Malo, J., Cartier, A., Dolovichm, J., 1990. Acute lung reaction due to zinc inhalation. Eur. Respir. J. 3, 111-114.

83. Mandal, B.K., Chowdhury, T.R., Samanta, G., Basu, G.K., Chowdhury, P.P., Chanda, C.R., Lodh, D., Karan, N.K., Dhar, R.K., Tamili, D.K., Das, D., Saha, K.C., Chakraborti, D., 1996. Arsenic in groundwater in seven districts of West Bengal, India – The biggest arsenic calamity in the world. Curr. Sci. 70, 976–986.

84. Manta, D.S., Angelone, M., Bellanca, A., Neri, R., Sprovieri, M., 2002. Heavy metals in urban soils: a case study from the city of Palermo (Sicily), Italy. Sci. Total Environ. 300, 229-243.

85. Máthé-Gáspár, G., Anton, A., 2005. Phytoremediation study: Factors influencing heavy metal uptake of plants. Acta Biol. Szeg. 49, 69-70.

86. Mattina, M.I., Lannucci-Berger, W., Musante, C., White, J.C., 2003. Concurrent plant uptake of heavy metals and persistent organic pollutants from soil. Env. Poll. 124, 375-378.

87. McBride, M.B., 2003. Toxic metals in sewage sludge-amended soils: has promotion of beneficial use discounted risks? Adv. Environ. Res. 8, 5-19.

88. Melles, M. (Ed.), 2004. National Health Interview Survey 2003. Johan Béla National Center for Epidemiology, Budapest.

89. Milton, A.H., Rahman, M., 2002. Respiratory effects and arsenic contaminated well water in Bangladesh. Int. J. Environ. Health Res. 12, 175-179.

90. Moore, M.M., Harrington-Brock, K., Doerr, C.L., 1994. Genotoxicity of arsenic and its methylated metabolites. Environ. Geochem. Health 16, 191-198.

91. Morra, P., Bagli, S., Spadoni, G., 2006. The analysis of human health risk with a detailed procedure operating in a GIS environment. Environ. Int. 32, 444-454.

92. Moya, J., Phillips, L., 2002. Overview of the use of the U.S. EPA exposure factors handbook. Int. J. Hyg. Environ. Health 205, 155-159.

93. Mueller, T.G., Pusuluri, N.B., Mathias, K.K., Cornelius, P.L., Barnhisel, R.I., Shearer, S.A., 2004. Map quality for ordinary kriging and inverse distance weighted interpolation. Soil Sci. Soc. Am. J. 68, 2042-2047.

94. Mumford, J.L., Wu, K., Xia, Y., Kwok, R., Yang, Z., Foster, J., Sanders, W.E., 2007. Chronic arsenic exposure and cardiac repolarization abnormalities with QT interval prolongation in a population-based study. Environ. Health Perspect. 115, 690-694.

95. Nadal, M., Schuhmacher, M., Domingo, J.L., 2004. Metal pollution of soils and vegetation in an area with petrochemical industry. Sci. Total Environ. 321, 59-69.

96. Nagy, G., 1986. A középső és a nyugat-Mátra ércelőkutatása. Magyar Állami Földtani Intézet, Budapest.

97. National Research Council, 1983. Risk assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC.

98. Nieuwenhuijsen, M., Paustenbach, D., Duarte-Davidson, R., 2006. New developments in exposure assessment: The impact on the practice of health risk assessment and epidemiological studies. Environ. Int. 32, 996-1009.

99. Ódor, L., Wanty, R.B., Horváth, I., Fügedi, U., 1998. Mobilization and attenuation of metals downstream from a base-metal mining site in the Mátra Mountains, northeastern Hungary. J. Geochem. Explor. 65, 47–60.

100. Paustenbach, D.J. (Ed.), 2002. Human and ecological risk assessment: Theory and practice. John Wiley and Sons, New York, NY.

101. Paustenbach, D., Galbraith, D., 2006. Biomonitoring and biomarkers: Exposure assessment will never be the same. Environ. Health Perspect. 114, 1143-1149.

102. Queirolo, F., Stegen, S., Restovic, M., Paz, M., Ostapczuk, P., Schwuger, M.J., Muñoz, L., 2000. Total arsenic, lead and cadmium levels in vegetables cultivated at the Andean villages of northern Chile. Sci. Total Environ. 255, 75-84.

103. Rapant, E., Dietzová, Z., Cicmonová, S., 2006. Environmental and health risk assessment in abandoned mining area, Zlata Idka, Slovakia. Environ. Geol. 51, 387-397.

104. Rieuwerts, J.S., Searle, P., Buck, R., 2006. Bioaccessible arsenic in the home environment in southwest England. Sci. Total Environ. 371, 89-98.

105. Ruby, M.V., Schoff, R., Brattin, W., Goldade, M., Post, G., Harnois, M., Mosby, D.E., Casteel, S.W., Berti, W., Carpenter, M., Edwards, D., Cragin, D., Chappel, W., 1999. Advances in evaluating the oral bioavailability of inorganics in soil for use in human health risk assessment. Environ. Sci. Technol. 33, 3697-3705.

106. Sakai, T., 2000. Biomarkers of lead exposure. Ind. Health 38, 127-142.

107. Santos, E.E., Lauria, D.C., Port oda Silveira, C.L., 2004. Assessment of daily intake of trace elements due to the consumption of foodstuffs by adult inhabitants of Rio de Janeiro city. Sci. Total Environ. 327, 69-79.

108. Schwartz, J., 1994. Low-level lead exposure and children's IQ: A meta-analysis and search for a threshold. Environ. Res. 65, 42-55.

109. Shipman, D.L., 1986. Cadmium food poisoning in a Missouri school. J. Environ. Health 49, 89.
110. Simon, L., 2005. Stabilization of metals in acidic mine spoil with amendments and red fescue (*Festuca rubra* L.) growth. Environ. Geochem. Hlth. 27, 289-300.
111. Sorahan, T., Lancashire, R.J., 1997. Lung cancer mortality in a cohort of workers employed at a cadmium recovery plant in the united states: an analysis with detailed job histories. Occup. Environ. Med. 54, 194-201.
112. Staessen, J., Lauwerys, R., 1993. Health effects of environmental exposure to cadmium in a population study. J. Hum. Hypertens. 7, 195-199.
113. Staessen, J.A., Roels, H.A., Emelianov, D., Kuznetsova, T., Thijs, L., Vangronsveld, J., Fagard, R., 1999. Environmental exposure to cadmium, forearm bone density, and risk of fractures: prospective population study. Lancet 353, 1140-1144.
114. Ullrich, S.M., Ramsey, M.H., Helios-Rybicka, E., 1999. Total and exchangeable concentrations of heavy metals in soils near Bytom, an area of Pb/Zn mining and smelting in Upper Silesia, Poland. Appl. Geochem. 14, 187-197.
115. US EPA, 1992. Guideline for exposure assessment. Environmental Protection Agency, Office of Research and Development, Washington DC.
116. US EPA, 1994. Method 6020. Inductively Coupled Plasma – Mass Spectrometry. Environmental Protection Agency, Office of Solid Waste and Emergency Response, Washington DC.
117. US EPA, 1997. Exposure Factors Handbook. Environmental Protection Agency, Office of Research and Development, Washington DC.
118. US EPA, 2003. Multimedia, Multipathway, and Multireceptor Risk Assessment (3MRA) Modeling System. Environmental Protection Agency, Office of Research and Development, Washington DC.
119. US EPA, 2006. Integrated Risk Information System (IRIS). Available from: www.epa.gov/iris.
120. Vető, É., 1988. Conditions of Pb-Zn ore formation in the Carpathian Neogene volcanic arc: evidence from Gyöngyösoroszi mine, N-Hungary. In: Proceedings

of the seventh quadrennial IAGOD symposium. Schweitzerbart'sche Verlagsbuchandlung, Stuttgart.

121. Voet, D., Voet J.G., Pratt, C.W., 1999. Fundamentals of Biochemistry. John Wiley and Sons, New York, NY.

122. Waalkes, M.P., Goering, P.L., 1990. Metallothionein and other cadmium-binding proteins: Recent developments. Chem. Res. Toxicol. 3, 28l-288.

123. Wang, G., Su, M., Chen, Y., Kin, F., Luo, D., Gao, S., 2006. Transfer characteristics of cadmium and lead from soil to the edible parts of six vegetable species in southeastern China. Environ. Poll. 144, 127-135.

124. Wang, X., Shan, X., Zhang, S., Wen, B., 2004. A model for evaluation of the phytoavailability of trace elements to vegetables under the field conditions. Chemosphere 55, 811-822.

125. Wcislo, E., Ioven, D., Kucharski, R., Szdzuj, J., 2002. Human health risk assessment case study: an abandoned metal smelter site in Poland. Chemosphere 47, 507-515.

126. Wentsel, R.S., Blaney, B., Kowalski, L., Bennet, D.A., Grevatt, P., Frey, S., 2002. Future directions for EPA Superfund research. Int. J. Hyg. Environ. Health 205, 161-163.

127. Wilhelm, M., Wittsiepe, J., Schrey, P., Hilbig, A., Kersting, M., 2005. Consumption of homegrown products does not increase diatery intake of arsenic, cadmium, lead, and mercury by young children living in an industrialized area of Germany. Sci. Total Environ. 343, 61-70.

128. WHO, 1989. Environmental Health Criteria 85. Lead. Environmental Aspects, WHO, Geneva.

129. WHO, 1992a. Environmental Health Criteria 134. Cadmium, WHO, Geneva.

130. WHO, 1992b. Environmental Health Criteria 135. Cadmium. Environmental Aspects, WHO, Geneva.

131. WHO, 1995. Environmental Health Criteria 165. Inorganic Lead, WHO, Geneva.

132. WHO, 1999. Environmental Health Criteria 210. Principles for the Assessment of Risks to Human Health from Exposure to Chemicals. WHO, Geneva.

133. WHO, 2000. Environmental Health Criteria 214. Human Exposure Assessment. WHO, Geneva.
134. WHO, 2001a. Environmental Health Criteria 221. Zinc, WHO, Geneva.
135. WHO, 2001b. Environmental Health Criteria 224. Arsenic and Arsenic Compounds, WHO, Geneva.
136. Zheng, N., Wang, Q., Zheng, D., 2007a. Health risk of Hg, Pb, Cd, Zn, and Cu to the inhabitants around Huludao Zinc Plant in China via consumption of vegetables. Sci. Total Environ. 383, 81-89.
137. Zheng, N., Wang, Q., Zhang, X., Zheng, D., Zhang, Z., Zhang, S., 2007b. Population health risks due to dietary intake of heavy metals in the industrial area of Huludao city, China. Sci. Total Environ. 387, 96-104.

10. APPENDIX

Azonosító:……
Kitöltés ideje:……...

KÉRDŐÍV

Nem:	férfi ☐	nő ☐	
Életkor:	…..... év		
Testsúly:	……. kg		
Dohányzás:	igen ☐	nem ☐	ha igen, mennyit? ……
Alkohol:	naponta ☐	alkalmanként ☐	nem ☐

Foglalkozása:
- irodai dolgozó ☐
- ipari dolgozó ☐
- mezőgazdasági munkás ☐
- tanuló ☐
- egyéb:…….
- háztartásbeli ☐
- nyugdíjas ☐
- rokkant nyugdíjas ☐
- munkanélküli ☐

Kisegítő iskolába jár(t)-e? igen ☐ nem ☐

Legmagasabb iskolai végzettsége:
- 4 általános ☐
- 6 általános ☐
- 8 általános ☐
- gimnázium ☐
- szakiskola ☐
- főiskola, egyetem ☐

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Dolgozott-e a bányában vagy az ércelőkészítőben? bánya □ ércelőkészítő □ nem □
ha igen, hány évet? ……év

Mióta él a faluban? …… éve

Mennyi időt tartózkodik a faluban? egész nap □ dolgozni máshova jár □

Járt-e rendszeresen a meddőhányóhoz vagy a meddő kupacokhoz? igen □ nem □
ha igen, hányszor? …….

Lakótelek szomszédos a Toka-patakkal? igen □ nem □
ha nem, a pataktól kb. hány méterre van? ……. m

Van-e egyéb földje, ahol mezőgazdasági tevékenységet folytat? igen □ nem □
ha igen, hol?……

1996-ban az áradáskor a patak elárasztotta a földet? igen □ nem □
ha igen, melyiket?……

Fúrt vagy ásott kút van-e a telken? igen □ nem □
ha igen, hol?……
ha igen, használja-e ivásra, főzésre □
öntözésre □
tisztálkodásra □

Hányan élnek a családban?

felnőtt: 1. …….év	gyerek: 1. …….
felnőtt: 2. …….év	gyerek: 2. …….
felnőtt: 3. …….év	gyerek: 3. …….
felnőtt: 4. …….év	gyerek: 4. …….
felnőtt: 5. …….év	gyerek: 5. …….

Termesztett növények:

Mennyit termeszt belőle évente	a ház körül?	egyéb termőföldön?
paradicsom □	…… kg	…… kg
paprika □	…… kg	…… kg
sóska, spenót □	…… kg	…… kg
káposzta, kelkáposzta □	…… kg	…… kg
sárgarépa, petrezselyem □	…… kg	…… kg
bab, borsó □	…… kg	…… kg
hagyma □	…… kg	…… kg
szőlő □	…… kg	…… kg
málna □	…… kg	…… kg
egyéb: ……	…… kg	…… kg
egyéb: ……	…… kg	…… kg
egyéb: ……	…… kg	…… kg

A termesztett növényeket ki fogyasztja? családban felnőtt □ családban gyerek □
értékesíti □, ha igen, hanyad részét? ……

Milyen szabadidős tevékenységet folytat? ásványgyűjtés □ horgászat □
úszás a közeli tavakban □ vadászat □
motorozás □ bogyógyűjtés □

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Milyen orvoshoz jár? körzeti (házi) ☐ hova?……..…
üzemi ☐ hova?……..…
szakrendelő (SZTK) ☐ hova?……..…
kórház ☐ hova?……..…

Rendszeresen jelenleg jár-e gyógykezelésre? igen ☐ nem ☐
ha igen, hova és miért? ……

Feküdt-e már kórházban? (gyermekszülés kivételével) igen ☐ nem ☐
ha igen, miért és mikor?……..
……..
……..

Az alábbi megbetegedésekben szenved-e Ön illetve családtagja?
Ha tudja, kérjük írja le a pontos megbetegedést!

	Ön	Mióta?	családtagja
magasvérnyomás	☐	……....	☐
cukorbetegség	☐	……	☐
csont és ízületi problémák	☐	……	☐
vesebetegségek	☐	……	☐
májbetegségek	☐	……	☐
tüdőbetegségek	☐	……	☐
vérképző szervi megbetegedések	☐	……	☐
idegrendszeri problémák	☐	……	☐
daganatos megbetegedések	☐	……	☐

ha igen, milyen ……

Pontos megbetegedések, diagnózisok:

……
……
……
……
……
……
……
……
……
……
……....

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http://www.ch.bme.hu/agtct

11. PUBLICATIONS

1. **Sipter, E.**, Rózsa, E., Gruiz, K., Tátrai, E., Morvai, V., 2008. Site-specific risk asseessment in contaminated vegetable gardens. Chemosphere 71, 1301-1307.
   IF: 2.442
2. **Sipter, E.**, Auerbach, R., Gruiz, K., Máthé-Gáspár, G., 2008. Change of bioaccumulation of toxic metals in vegetable. Commun. Soil Sci. Plan. Accepted article.
   IF: 0.302
3. Máthé-Gáspár, G., **Sipter, E.**, Szili-Kovács, T., Takács, T., Máthé, P., Anton, A., 2008. Environmental impact of soil pollution with toxic element from the lead and zinc mine at Gyöngyösoroszi (Hungary).Commun. Soil Sci. Plan. Accepted article.
   IF: 0.302
4. Máthé, P., Máthé-Gáspár, G., Szili-Kovács, T., **Sipter, E.**, Anton, A., 2007. Changes in the parts of the rhizosphere phosphorus cycle influencing by heavy metal contamination. Cereal Res. Commun. 35, 761-764.
   IF: 1.037