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Review

Arsenic in Water Systems: Ecotoxicological Effects and Their Relevance to Human Health

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Arsenic is a naturally occurring metalloid element that is found in soil, air and water. Environmental arsenic exists in both organic and inorganic states. Organic arsenicals are generally considered non toxic, whereas inorganic forms are toxic. The most acutely toxic form is arsine gas. Inorganic arsenic exists predominantly in trivalent (As^{3+}) and pentavalent (As^{5+}) forms, where trivalent compounds are more toxic than pentavalent ones. Human activities have also intensified arsenic accumulation in the environment. Organs most susceptible to arsenic toxicity are those involved with absorption, accumulation or excretion, including the skin, circulatory system, gastrointestinal tract, liver and kidney. Arsenic is associated with multiple health effects, including Blackfoot diseases, diabetes, hypertension, peripheral neuropathy and multiple vascular diseases. Other effects include anemia, liver damage, portal cirrhosis, hematopoietic depression, anhydremia, sensory disturbance and weight loss. In addition to acute toxicity, long-term exposure to inorganic arsenic is associated with certain forms of cancer of the skin, lung, colon, bladder, liver and breast. Understanding the ecotoxicological effects of arsenic in the environment is paramount to mitigating its deleterious effects on ecological and human health. This paper is therefore a review of the ecotoxicological effects of arsenic on human and ecological health.

Key words: Arsenic, ecotoxicology, hydrosphere, human health, ecological health.

INTRODUCTION

Arsenic is a naturally occurring metalloid element that is found in soil, air and water (Huang et al., 2004; Duker et al., 2005). Environmental arsenic exists in both organic and inorganic states. Organic arsenicals are generally considered non toxic (Gochfeld, 1995), whereas inorganic forms are toxic. The most acutely toxic form is arsine gas (Leonard, 1991). Inorganic arsenic exists predominantly in trivalent (As^{3+}) and pentavalent (As^{5+}) forms, where trivalent compounds are more toxic than pentavalent ones (Cervantes et al.,1994; Smedley et al., 1996). Both trivalent and pentavalent arsenicals are soluble over a wide pH range (Bell, 1998) and are routinely found in surface and groundwater (Feng et al., 2001). Under aerobic conditions, pentavalent arsenic is more stable and predominates, whereas trivalent species predominate under anaerobic conditions (Duker et al., 2005).

Arsenic ranks 20th in abundance in relation to other elements in the earth's crust and high concentrations are found in granite and in many minerals including copper, lead, zinc, silver and gold (NAS, 1977). The geochemistry of arsenic in the environment was recently reviewed (Duker et al., 2005). Arsenic naturally accumulates as both organic and inorganic forms in soil, surface and groundwater (Attrep and Anirudhan, 1977; Lloyd-Smith and Wickens, 2000) and seawater (Penrose et al., 1977).

The primary source of arsenic in soil is the parent rock (Smedley and Kinniburgh, 2002) additionally, volcanoes are a major natural source of arsenic released into the environment (Nriagu et al., 1988; Nriagu, 1989) that can generate high arsenic concentrations in natural waters (Smedley and Kinniburgh, 2002). The chemistry of arsenic in aqueous environments has been reviewed (Ferguson and Gavis, 1972). Arsenic concentrations in lakes are often less than in rivers, due to adsorption by iron oxides, although changes in water levels (Smedley and Kinniburgh; Nimick et al., 1998) and geothermal

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activity can enhance concentrations in some cases (Duker et al., 2005; Aggett and Kriegman, 1988).

Groundwater from alluvial and deltaic watersheds generally has high arsenic concentration due to predominantly reducing conditions (Smedley and Kinniburgh, 2002). Human activities have intensified arsenic accumulation in the environment (Bell, 1998) such as fossil fuel combustion and metal smelting, as well as the semiconductor and glass industries. Arsenic is also an ingredient in many commonly used materials including wood preservatives, pigments, insecticides, herbicides, rodenticides and fungicides (Hathaway et al., 1991). Although most arsenic in soil is derived from the parent rock, the application of arsenic compounds in agriculture and forestry practices may lead to extreme soil contamination and subsequent groundwater contamination, while the burning of coal and smelting of metals may be major sources of airborne arsenic. Mining activities may result in high levels of arsenic contamination in soil, surface water, groundwater and vegetation (Smedley et al., 1996; Smedley and Kinniburgh, 2002; Amasa, 1975).

Additionally, human modifications to the natural hydrograph, including the construction of dams (Armah et al., 1998) wastewater recycling and irrigation practices (Siegel, 2002) can potentiate arsenic accumulation in soil and in water supplies. Many microorganisms have adapted to arsenic-rich environments, including soils and waters and may be important factors in arsenic biotrans-formation (Siegel, 2002; Nakahara et al., 1977; De Vicente et al., 1990; Cervantes et al., 1994; Ahmann, et al., 1994; Laverman et al., 1995; Saltikov et al., 2002) and mobilization (Cummings et al., 1999; Shariatpanahi et al., 1981) in the environment. Under anaerobic condi-tions, some microbes can reduce the less toxic arsenate to the more toxic arsenite (Andreae, 1979; Nies and Silver, 1995; Rensing et al., 1999) through an energy-ge-nerating process (Ilyaletdinov and Abdrashitova, 1981).

Additionally, other microbes are able to methylate arsenic compounds (Gadd, 1993), which may serve as a detoxification process. Seasonal variations in temperature and water levels can have strong effects on arsenic concentration and speciation in soil and water due to changes in microbial uptake (Andreae, 1979; Andreae, 1978). During warm, dry periods arsenic compounds are often oxidized (Maest et al., 1992), potentially increasing toxicity (Savage et al., 2000), while during wet periods oxidized arsenic is solubilized and distributed throughout the environment (McLaren and Kim, 1995; Rodriguez et al., 2004). The hydrosphere consists of the bodies of water that cover 71 percent of the earth surface. The largest of these are the oceans, which contain over 97 percent of all water on earth. Glaciers and the polar ice caps contain just over 2 percent of earth water in the form of solid ice. Only about 0.6 percent is under the surface as groundwater. Nevertheless, ground- water is 36 times more plentiful than water found in lakes, inland seas, rivers, and in the atmosphere as water vapor. Only 0.017 percent of all the water on earth is found in lakes and rivers. And a mere 0.001 percent is found in the atmosphere as water vapor. Most of the water in glaciers, lakes, inland seas, rivers, and groundwater is fresh and can be used for drinking and agriculture. Dissolved salts compose about 3.5 percent of the water in the oceans, however, making it unsuitable for drinking or agriculture unless it is treated to remove the salts.

Arsenic compounds have been used directly on humans for treating many diseases including skin conditions, malaria, ulcers, syphilis, sleeping sickness and some forms of leukemia (Luh et al., 1973; Nevens et al., 1990; Zhang, 1999; Miller et al., 2002) although it is now rarely used medicinally (Azcue and Nriagu, 1994). Organs most susceptible to arsenic toxicity are those involved with absorption, accumulation or excretion, including the skin, circulatory system, gastrointestinal tract, liver and kidney (Duker et al., 2005). The primary symptom of arsenic exposure is dermal lesions (Zaloga et al., 1985). Skin localizes and stores arsenic, presumably due to high levels of sulfhydryl-rich keratin (Kitchin, 2001), potentially explaining this response.

Arsenic is associated with multiple health effects, including Blackfoot disease (Abernathy et al., 1999), diabetes (Longnecker and Daniels, 2001), hypertension (Chen et al., 1995), peripheral neuropathy and multiple vascular diseases (Duker et al., 2005). Other effects include anemia (Agency for Toxic Substances and Disease Registry, 2000), liver damage, portal cirrhosis, hematopoietic depression, anhydremia, sensory disturbance and weight loss (Webb, 1966). It has been suggested that multiple factors, including genetics and nutrition, affect susceptibility to arsenic and disease manifestation (Mandal et al., 1996; Hseuh et al., 1998.). In addition to acute toxicity, long-term exposure to inorganic arsenic is associated with certain forms of cancer of the skin, lung, colon, bladder, liver and breast (Duker et al., 2005; Abernathy et al., 1999; Huang et al., 2004; Nemery, 1990) although effects may not appear until more than 20 years after exposure (Jackson and Grainge, 1975).

It has been suggested that arsenic may act as a carcinogen through DNA hypomethylation and over expression of protooncogenes (Zhao et al., 1997). Cancer may be induced by alteration of DNA-repair mechanisms, thus interfering with cell division, differentiation and tumor suppression (Chen et al., 1996; Goering et al., 1999.). Additionally, arsenic may induce certain forms of cancer by enhancing the carcinogenic effects of other sub-stances and by affecting metabolic pathways (Huang et al., 2004).

In summary, the effects of arsenic on health include various mechanisms of acute and chronic toxicity, enzymetic and genetic effects, and/or increasing susceptibility to multiple types of disease, both cancerous and non cancerous. Although it is clear that exposure to arsenic alters normal biological functions, resulting in the direct initiation of disease or, at least, predisposition of an organism to it. Understanding the ecotoxicological effects of

arsenic in the environment is paramount to mitigating its deleterious effects on ecological and human health. This paper is therefore a review of the ecotoxicological effects of arsenic on human and ecological health.

BIOACCUMULATION AND METABOLISM OF ARSENIC IN THE HYDROSPHERE

Arsenic accumulates across highly diverse environments within the soil, water and air where it is subsequently taken up and processed by microbes, plants and animals. Soluble arsenic taken up by plants rapidly accumulates in the food chain (Green et al., 2001). Freshwater plants and peat moss have been shown to contain considerable amounts of arsenic (Minkkinen and Yliruokanen, 1978). High arsenic concentrations have been found in the tissues of wild birds (Fairbrother et al.,1994) and in many marine organisms, including algae (Lunde, 1972), crustaceans (Edmonds et al.,1977), cetaceans, pinni-peds, sea turtles and sea birds (Kubota et al., 2003). Ecotoxicants released into the environment, including arsenic, often accumulate most rapidly in aquatic habitats where they enter the biota and are subsequently transferred to higher trophic levels and, in many cases, eventually to humans. Extremely high levels of arsenic have been observed in many fish taxa (Bosnir et al., 2003; Juresa and Blanosa, 2003) and have been shown to be toxic (Suhendrayatna et al., 2002; Tisler and Zagorc-Koncan, 2002). Some species possess specific arsenic-binding proteins (Oladimeji, 1985), that may increase bioaccumulation. Monitoring arsenic levels and their associated health effects in aquatic organisms, particularly in taxa at high trophic levels such as fish, may provide insight into overall ecosystem health (Zelikoff et al., 2000) as well as into potential impacts on human health (Zelikoff, 1998; Adams and Greeley, 1999).

Exposure from air and soil is usually minimal in humans. The major sources of exposure for humans are food and water (Bernstam and Nriagu, 2000). Once ingested, arsenic that is not eliminated from the body may accumulate in the muscles, skin, hair and nail (Kitchin, 2001; Ishinishi et al., 1986). Food contains both organic and inorganic arsenic, whereas water primarily contains inorganic forms. Seafood may provide higher concentrations of arsenic when compared with terrestrial food products (Sakurai et al., 2004), presumably due to increased bioaccumulation through generally longer trophic chains. As elemental arsenic is poorly absorbed, it is predominantly eliminated from the body unchanged (Duker et al., 2005). Inorganic arsenic is absorbed through the gastrointestinal tract and is eliminated via renal function (Hindmarsh and McCurdy, 1986); however, a small amount is biotransformed into "detoxified" forms via methylation and reduction in the liver (Bernstam and Nriagu, 2000; Winski and Carter, 1995). Once thought to be a purely detoxification process, it has been shown that methylation of arsenic may, in some cases, actually increase arsenic toxicity in humans and rodents (Petrick et al., 2001). Variation in arsenic metabolism has been shown to occur in humans (Abernathy et al., 1999). Interestingly, some mammals, including non human primates, are deficient in arsenite methyltransferases necessary for effective methylation (Aposhian, 1997). They may also show different tissue-specific expression (Abernathy et al., 1999). The relationships between arsenical exposure, methylation and toxicity are paramount to understanding the risks posed to humans.

BIOGEOCHEMISTRY OF ARSENIC

Arsenic has a complex marine biogeochemistry that has important implications for its toxicity to marine organisms and their consumers, including humans. The average concentration of total arsenic in the ocean is about 1.7 µg/L, about two orders of magnitude higher than the U.S Environmental Protection Agency on human health criterion (fish consumption) value of 0.0175 µg/L. The dominant form of arsenic in oxygenated marine and brackish waters is arsenate (As 5). The more toxic and potentially carcinogenic arsenite (As 3) rarely accounts for more than 20% of total arsenic in seawater. Uncontaminated marine sediments contain from 5 to about 40 µg/g dry weight total arsenic. Arsenate domi-nates in oxidized sediments and is associated primarily with iron oxyhydroxides. In reducing marine sediments, arsenate is reduced to arsenite and is associated primarily with sulfide minerals. Marine algae accumulate arsenate from seawater, reduce it to arsenite, and then oxidize the arsenite to a large number of organoarsenic compounds. The algae release arsenite, methylarsonic acid, and dimethylarsinic acid to seawater. Dissolved arsenite and arsenate are more toxic to marine phytoplankton than to marine invertebrates and fish. This may be due to the fact that marine animals have a limited ability to bioconcentrate inorganic arsenic from seawater but can hioaccumulate organoarsenic compounds from their food. Tissues of marine invertebrates and fish contain high concentrations of arsenic, usually in the range of about 1 to 100 µg/g dry weight, most of it in the form of organoarsenic compounds, particularly arsenohe-taine. Organoarsenic compounds are bioaccumulated by human consumers of seafood products, but the arsenic is excreted rapidly, mostly as organoarsenic compounds. Arsenohetaine, the most abundant organoarsenic com-pound in seafoods, is not toxic or carcinogenic to mammals. Little of the organoarsenic accumulated by humans from seafood is converted to toxic inorganic arsenite. Therefore, marine arsenic represents a low risk to human consumers of fishery products (Neef, 1997).

TOXICOLOGY OF ARSENIC

Acute and chronic arsenic toxicities have been shown in a variety of organisms, and the data suggest that most

inorganic arsenicals are more toxic than organic forms (Duker et al., 2005; Abernathy et al., 1999). Toxic effects of inorganic arsenic include denaturing of cellular enzymes through interaction with sulfhydryl groups (Graeme and Pollack, 1998) causing cellular damage through increased reactive oxygen species (ROS) (Ahmad et al., 2000), and altering gene regulation (Abernathy et al.,

1999). Arsenic is known to inhibit more than 200 enzymes (Abernathy et al., 1999), and has been implicated in multisystemic health effects via interference with enzy-matic function and transcriptional regulation (National Research Council, 1995). A variety of inhibitory effects on cellular metabolism has been shown, affecting mitochon-drial respiration (Abernathy et al., 1999), and synthesis of adenosine triphosphate (ATP) (Winship, 1984). Other effects of arsenic include activation of the estrogen receptor, inhibition of angiogenesis and tubulin polymeri-zation, induction of heat-shock proteins, and oxidation of glutathione (Bernstam and Nriagu, 2000). Due to its structural similarity to phosphate, arsenate may replace phosphorus in bone (Ellenhorn and Barceloux, 1988).

Among fish taxa, arsenic has been shown to induce apoptosis of fin cells (Wang et al., 2004), to cause liver inflammation, hyperplasia and necrosis (Pedlar et al., 2002), gall bladder inflammation, fibrosis and edema (Pedlar et al., 2002; Cockell et al., 1991) kidney fibrosis, and the induction of various heat-shock proteins. Arsenic has been shown to cause morphological changes, as well as to increase numbers of necrotic bodies, abnormal lysosomes and autophagic vacuoles in fish hepatocytes (Sorensen et al., 1985). Additionally, effects on reproduction in fishes include disrupting ovarian cell cycles (Wang et al., 2004), inhibiting ovarian follicle development, impairing spermatogenesis and changing testicular architecture (Shukla and Pandey, 1984).

There is clear evidence that arsenic can disrupt gene expression, particularly through its effects on signal transduction (Abernathy et al., 1999). Arsenic can interact directly with the glucocorticoid receptor (GR), selectively inhibiting GR-mediated transcription (Kaltreider et al., 2001). It has been suggested that arsenic can disrupt cell division by deranging the spindle apparatus (Abernathy et al., 1999). Arsenic induces large deletion mutations (Hei et al., 1998), chromosome damage and aneuploidy (Abernathy et al., 1999), and causes micronucleus formation, DNA–protein cross-linking, and sister chromatid exchange (Huang et al., 2004). It is known to inhibit DNA repair (Brochmoller et al., 2000), and even to exacerbate the effects of other mutagenic agents (Abernathy et al., 1999), thereby increasing susceptibility to multiple diseases (Duker et al., 2005).

CONCLUSION

Arsenic often accumulates most rapidly in aquatic habitats. Monitoring arsenic levels and their associated health effects in aquatic animals may not only provide insight into overall ecosystem health (Zelikoff et al., 2000) but may also act as a sentinel for potential impacts on human health (Zelikoff, 1998; Adams and Greeley, 1999). In summary, the effects of arsenic on health include various mechanisms of acute and chronic toxicity, enzy-matic and genetic effects, and/or increasing susceptibility to multiple types of disease, both cancerous and non cancerous. It is clear that exposure to arsenic alters normal biological functions, resulting in the direct initiation of disease or, at least, predisposition of an organism to it. Understanding the ecotoxicological effects of arsenic in the environment is paramount to mitigating its deleterious effects on ecological and human health, particularly on the immune response.

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