

# Environmental exposure of Arsenic and related health hazards-a review

\*Agrawal Prashant, \*Mittal Anugya, \*\*Prakash Rajiv, \*Kumar Manoj, \*Tripathi S.K.

\*Department of Forensic Medicine & Toxicology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, \*\* School of Material Science & Technology, Institute of Technology, Banaras Hindu University, Varanasi

## Abstract

Arsenic is historically the poison of choice for many murders, in reality and in fiction. Here, arsenic is dealt with only as mineral specimens and is not to be ingested. Although it has been used as a poison, arsenic has many chemical uses and is quite an important element. Exposure to higher than average levels of arsenic occur mostly in the workplace, near hazardous waste sites, or in areas with high natural levels. At high levels, inorganic arsenic can cause death. Exposure to lower levels for a long time can cause a discoloration of the skin and the appearance of small corns or warts. Arsenic has been found in at least 1,149 of the 1,684 National Priority List sites identified by the Environmental Protection Agency.

**Key words:** Arsenic, exposure, hazards.

## Introduction

Arsenic, a naturally occurring element, is found throughout the environment. It is released in to the environment through natural as well as anthropogenic sources. Natural sources include volcanoes, the weathering of arsenic-containing minerals and ores. Smelting of non-ferrous metals such as copper smelting, mining, coal burning and the production of energy from fossil fuel are the major industrial processes that lead to Arsenic contamination of air, water and soil. High arsenic levels can also come from certain fertilizers and animal feeding operations.

For most people, food is the major source of exposure. Inorganic Arsenic is present in groundwater used for drinking in several countries all over the world (e.g. Bangladesh, Chile and China), whereas organic Arsenic compounds (such as arsenobetaine) are primarily found in fish, which thus may give rise to human exposure.

Acute (short-term) high-level inhalation exposure to arsenic dust or fumes has resulted in gastrointestinal effects (nausea, diarrhea, abdominal pain); central and peripheral nervous system disorders have occurred in workers acutely exposed to inorganic arsenic. Chronic (long-term) inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes. Chronic oral exposure has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyper pigmentation, and liver or kidney damage in humans. Inorganic arsenic exposure in humans, by the inhalation route, has been shown to be strongly associated with lung cancer, while ingestion of inorganic arsenic in humans has been linked to a form of skin cancer and also to bladder, liver, and lung cancer. USEPA has classified inorganic arsenic as a Group A, human carcinogen.

## Occurrence of Arsenic in Nature

Arsenic is a semi-metal element and was first documented by Albertus Magnus in 1250.<sup>(1)</sup> It is odorless and tasteless.<sup>(2)</sup> Arsenic is widely distributed in the earth's crust and present at an average concentration of 2 mg/kg. It occurs in trace quantities in all rock, soil, water and air. Inorganic arsenic is a naturally occurring element in the earth's crust. Pure inorganic

## Reprints Requests: Prashant Agrawal

Research Scholar

Department of Forensic Medicine & Toxicology

Institute of Medical Sciences

Banaras Hindu University, Varanasi, U.P.

Email. prashantagrawala@gmail.com

arsenic is a gray-colored metal.

Arsenic combined with elements such as oxygen, chlorine, and sulfur forms inorganic arsenic; inorganic arsenic compounds include arsenic pentoxide, arsenic trioxide, and arsenic acid. Arsenic combined with carbon and hydrogen forms organic arsenic; organic arsenic compounds include arsanic acid, arsenobetaine, and dimethylarsinic acid.<sup>(3)</sup>

The most important compounds of arsenic are arsenic (III) oxide,  $As_2O_3$ , ("white arsenic"), the yellow sulfide orpiment ( $As_2S_3$ ) and red realgar ( $As_4S_4$ ), Paris green, calcium arsenate, and lead hydrogen arsenate. Elemental Arsenic is not soluble in water. Arsenic salts exhibit a wide range of solubility depending on pH and the ionic environment.<sup>(4)</sup>

### **Arsenic and Environment**

Inorganic arsenic is found throughout the environment; it is released into the air by volcanoes, the weathering of arsenic-containing minerals and ores, and by commercial or industrial processes.<sup>(3,5)</sup> For most people, food is the largest source of arsenic exposure (about 25 to 50 micrograms per day [ $\mu\text{g}/\text{d}$ ]), with lower amounts coming from drinking water and air. Among foods, some of the highest levels are found in fish and shellfish; however, this arsenic exists primarily as organic compounds, which are essentially nontoxic.<sup>(3)</sup>

Elevated levels of inorganic arsenic may be present in soil, either from natural mineral deposits or contamination from human activities, which may lead to dermal or ingestion exposure. Workers in metal smelters and nearby residents may be exposed to above-average inorganic arsenic levels from arsenic released into the air (3). Other sources of inorganic arsenic exposure include burning plywood treated with an arsenic wood preservative or dermal contact with wood treated with arsenic.<sup>(5)</sup> Most arsenic poisoning incidents in industry have involved the production of arsine, a short-lived, extremely toxic gas.<sup>(6)</sup> Humans are exposed to arsenic through air, drinking water, and food (meat, fish, and poultry); this food is usually the largest source of arsenic. Arsenic was also found in wine if arsenic pesticides are used in the vineyard.

High arsenic levels can also come from certain

fertilizers and animal feeding operations. Industry practices such as copper smelting, mining and coal burning also contribute to arsenic in our environment. Smelting of non-ferrous metals and the production of energy from fossil fuel are the two major industrial processes that lead to Arsenic contamination of air, water and soil.<sup>(7)</sup>

### **Arsenic and Human beings**

Arsenic is well absorbed by oral and inhalation routes, widely distributed and excreted in urine; most of a single, low-level dose is excreted within a few days after consuming any form of inorganic arsenic. Remains of arsenic in nails and hair can be detected even after years and years after the exposure.<sup>(4)</sup>

Arsenic (or metabolites) concentrations in blood, hair, nails and urine have been used as biomarkers of exposure. Arsenic in hair and nails can be useful indicators of past Arsenic exposure, if care is taken to avoid external Arsenic contamination of the samples. Speciated metabolites in urine expressed as either inorganic Arsenic or the sum of metabolites is generally the best estimate of recent Arsenic dose. However, consumption of certain seafood may confound estimation of inorganic Arsenic exposure, and should thus be avoided before urine sampling.<sup>(8)</sup>

Arsenic and many of its compounds are especially potent poisons. Arsenic disrupts ATP production through several mechanisms. At the level of the citric acid cycle, arsenic inhibits pyruvate dehydrogenase and by competing with phosphate it uncouples oxidative phosphorylation, thus inhibiting energy-linked reduction of  $NAD^+$ , mitochondrial respiration, and ATP synthesis. Hydrogen peroxide production is also increased, which might form reactive oxygen species and oxidative stress. These metabolic interferences lead to death from multi-system organ failure probably from necrotic cell death, not apoptosis. A post mortem reveals brick red colored mucosa, due to severe hemorrhage. Although arsenic causes toxicity, it can also play a protective role.<sup>(9)</sup>

Absorption of Arsenic in inhaled airborne particles is highly dependent on the solubility and the size of particles. Soluble arsenic

compounds are easily absorbed from the gastrointestinal tract. However, inorganic Arsenic is extensively methylated in humans and the metabolites are excreted in the urine.<sup>(8)</sup>

### **Arsenic and Health Hazards**

The importance of arsenic as a health hazard, which is also known as 'slow killer' is now well recognised. The most obvious signs are the blisters on the palms of the hands and soles of the feet, which can eventually turn gangrenous and cancerous. Meanwhile, the poison also attacks internal organs, notably the lungs and kidneys, which can result in a battery of illnesses including cancers.<sup>(10)</sup>

### **Inorganic Arsenic: Acute Effects**

Acute inhalation exposure of workers to high levels of arsenic dusts or fumes has resulted in gastrointestinal effects (nausea, diarrhea, abdominal pain), while acute exposure of workers to inorganic arsenic has also resulted in central and peripheral nervous system disorders.<sup>(3)</sup>

Acute oral exposure to inorganic arsenic, at doses of approximately 600 micrograms per kilogram body weight per day ( $\mu\text{g}/\text{kg}/\text{d}$ ) or higher in humans, has resulted in death. Oral exposure to lower levels of inorganic arsenic has resulted in effects on the gastrointestinal tract (nausea, vomiting), central nervous system (CNS) (headaches, weakness, delirium), cardiovascular system (hypotension, shock), liver, kidney, and blood (anemia, leukopenia).<sup>(3)</sup>  
<sup>5)</sup> Acute animal tests in rats and mice have shown inorganic arsenic to have moderate to high acute toxicity.<sup>(11)</sup>

### **Chronic Effects (Non cancer)**

Chronic inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes (dermatitis, conjunctivitis, pharyngitis, and rhinitis). Chronic oral exposure to inorganic arsenic in humans has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyper pigmentation, gangrene of the extremities, vascular lesions, and liver or kidney damage.<sup>(3,5)</sup>

Several studies have suggested that women who work in, or live near, metal smelters may have higher than normal spontaneous abortion

rates, and their children may exhibit lower than normal birth weights. However, these studies are limited because they were designed to evaluate the effects of smelter pollutants in general, and are not specific for inorganic arsenic. Ingested inorganic arsenic can cross the placenta in humans, exposing the fetus to the chemical. Oral animal studies have reported inorganic arsenic at very high doses to be fetotoxic and to cause birth defects.<sup>(4)</sup>

### **Arsenic and Drinking water**

Inorganic Arsenic is present in groundwater used for drinking in several countries all over the world (e.g. Bangladesh, Chile and China), whereas organic Arsenic compounds (such as arsenobetaine) are primarily found in fish, which thus may give rise to human exposure.<sup>(8)</sup> Millions of persons in the world-including more than 3 million in the United States and more than 70 million in Bangladesh and adjoining West Bengal, India are chronically exposed to arsenic through drinking water. Epidemiological studies on children, living in the vicinity of a coal power plant in Czechoslovakia where coal that was used contained about 1000-1500 g arsenic per tonne, showed respiratory symptoms and hearing loss.<sup>(10)</sup> Arsenic contamination of groundwater has led to a massive epidemic of arsenic poisoning in Bangladesh and neighboring countries.

In India Arsenic contamination in ground water has been observed in some parts of the States of West Bengal, Bihar, Uttar Pradesh, Assam and Chhattisgarh. In West Bengal, occurrence of high concentration of arsenic in ground water has been observed in the depth range of 20 - 80 m in the area east of river Bhagirathi in parts of 8 districts viz. Malda, Murshidabad, Nadia, North 24 Parganas, South 24 Parganas, Hoogli, Howrah, and Bardhaman. Occurrence of Arsenic in excess of permissible limit in ground water has been observed in the alluvial aquifers in the depth range of 10-70 meter below ground level in parts of Patna, Bhojpur, Begusarai, Khagaria, Samastipur, Bhagalpur, Saran, Munger, Katihar, Buxar, Vaishali and Darbhanga districts. In Uttar Pradesh, arsenic contamination in ground water has been reported from parts of Gonda, Balia, Balrampur, Lakhimpur Kheri and

Siddharthnagar districts. In Assam, ground water in parts of Dhemaji District is reported to be affected by arsenic contamination. Occurrence of arsenic in these states is associated with sediments in Ganga - Brahmaputra basin. Localized occurrence of arsenic in ground water has been reported from parts of Rajnandgaon district of Chhattisgarh due to arsenopyrite mineralization in the fractured zones in hard rock terrain.<sup>(12)</sup>

Presently 42 major incidents around the world have been reported on groundwater arsenic contamination. It is estimated that approximately 57 million people are drinking groundwater with arsenic concentrations elevated above the World Health Organization's standard of 10 parts per billion. However, a study of cancer rates in Taiwan<sup>(13)</sup> suggested that significant increases in cancer mortality appear only at levels above 150 parts per billion. The arsenic in the groundwater is of natural origin, and is released from the sediment into the groundwater due to the anoxic conditions of the subsurface.<sup>(4)</sup>

The northern United States, including parts of Michigan, Wisconsin, Minnesota and the Dakotas are known to have significant concentrations of arsenic in ground water. Increased levels of skin cancer have been associated with arsenic exposure in Wisconsin, even at levels below the 10 part per billion drinking water standard.<sup>(14)</sup>

Epidemiological evidence from Chile shows a dose dependent connection between chronic arsenic exposure and various forms of cancer, particularly when other risk factors, such as cigarette smoking, are present. These effects have been demonstrated to persist below 50 parts per billion.<sup>(15)</sup>

Analyzing multiple epidemiological studies on inorganic arsenic exposure suggests a small but measurable risk increase for bladder cancer at 10 parts per billion (16). According to Peter Ravenscroft of the Department of Geography at the University of Cambridge roughly 80 million people worldwide consume between 10 and 50 parts per billion arsenic in their drinking water. If they all consumed exactly 10 parts per billion arsenic in their drinking water, the previously cited multiple epidemiological study analysis

would predict an additional 2,000 cases of bladder cancer alone.<sup>(4)</sup>

### **Arsenic and Carcinogenic effect**

Several studies have shown that inorganic Arsenic can increase the risk of lung cancer, skin cancer, bladder cancer, liver cancer, kidney cancer, and prostate cancer. The World Health Organization<sup>(17)</sup>, the Department of Health and Human Services<sup>(11)</sup> and the USEPA<sup>(6)</sup> have determined that inorganic Arsenic is a human carcinogen.

Human, inhalation studies have reported inorganic arsenic exposure to be strongly associated with lung cancer. Ingestion of inorganic arsenic in humans has been associated with an increased risk of nonmelanoma skin cancer and also to an increased risk of bladder, liver, and lung cancer. USEPA has classified inorganic arsenic as a Group A, human carcinogen.<sup>(3, 5, 18)</sup>

Arsenic ingestion has been reported to increase the risk of cancer at internal sites, especially lung, urinary bladder, kidney, and liver (19). Populations exposed to Arsenic via drinking water show excess risk of mortality from lung, bladder and kidney cancer, and the risk increasing with increasing exposure. There is also an increased risk of skin cancer and other skin lesions, such as hyperkeratosis and pigmentation changes<sup>(3)</sup>

### **Arsenic and Recommended Permissible Limits**

USEPA has set limits on the amount of Arsenic that industrial sources can release to the environment and has restricted or canceled many uses of Arsenic in pesticides. USEPA has set a limit of 0.01 parts per million (ppm) for Arsenic in drinking water. The Occupational Safety and Health Administration<sup>(20)</sup> have set limits of 10µg Arsenic per cubic meter of workplace air (10µg/m<sup>3</sup>) for 8 hour shifts and 40 hour work weeks.

### **References**

1. Emsley J. An A-Z Guide to the Elements. Oxford: Oxford University Press Nature's Building Blocks. 2001; 43: 513-529.
2. US Environmental Protection Agency. Arsenic in drinking water. accessed in 2008. Available from:

- <http://www.epa.gov/safewater/arsenic/index.html>.
3. Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Arsenic (Draft). U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA; 1998.
  4. Wikipedia- The free encyclopedia. Arsenic. accessed in 2008. available from: <http://en.wikipedia.org/wiki/Arsenic>.
  5. Agency for Toxic Substances and Disease Registry (ATSDR). Case Studies in Environmental Medicine. Arsenic Toxicity. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA; 1990.
  6. U.S. Environmental Protection Agency Health Assessment Document for Inorganic Arsenic. EPA/540/1-86/020. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Washington, DC; 1984.
  7. Chilvers DC, Peterson PJ. Global cycling of arsenic. In: Hutchinson TC, Meema KM, editors. Lead, mercury, cadmium and arsenic in the environment. SCOPE. John Wiley & Sons, 1987; 31: 279-301.
  8. Environmental Health Criteria (EHC). Arsenic and Arsenic Compounds; World Health Organization, Geneva; 2001: 124.
  9. Klaassen C, Watkins J. Casarett and Doull's Essentials of Toxicology. McGraw-Hill: 2003.
  10. Rai UN, Pal A. Health Hazards of Heavy Metals. Enviro news. News letter of ISEB India. 2002; 8(1)
  11. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD; 1993.
  12. Ministry of Water Resources. Ground Water Quality Scenario. India. accessed in 2008. Available from: <http://wrmin.nic.in/index3.asp?subsublinkid=782&langid=1&sslid=801>
  13. Lamm SH, Engel A, Penn CA, Chen R, Feinleib M. Arsenic cancer risk confounder in southwest Taiwan data set. Environ Health Perspect, 2006; 114 (7): 1077-82.
  14. Knobeloch LM, Zierold KM, Anderson HA. Association of arsenic-contaminated drinking-water with prevalence of skin cancer in Wisconsin's Fox River Valley. J Health Popul Nutr, 2006; 24 (2): 206-13.
  15. Ferreccio C, Sancha AM. Arsenic exposure and its impact on health in Chile. J Health Popul Nutr. 2006; 24 (2): 164-75.
  16. Chu HA, Crawford-Brown DJ. Inorganic arsenic in drinking water and bladder cancer: a meta-analysis for dose-response assessment. Int J Environ Res Public Health, 2006; 3 (4): 316-22.
  17. World Health Organization (WHO). Recommendations in Guidelines for Drinking Water Quality, vol. 1, Geneva, Switzerland; 1993.
  18. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on Arsenic. National Center for Environmental Assessment, Office of Research and Development, Washington, DC; 1999.
  19. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Arsenic and Cadmium. United States Department of Health and Human Services; 2000. Accessed October 2006. Available from: <http://www.atsdr.cdc.gov>
  20. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations; 1998.