World Health Organization

PREVENTING DISEASE THROUGH HEALTHY ENVIRONMENTS

EXPOSURE TO ARSENIC: A MAJOR PUBLIC HEALTH CONCERN

Soluble inorganic arsenic is highly acutely toxic. Intake of inorganic arsenic over a long period can lead to chronic arsenic poisoning (arsenicosis). Effects, which can take years to develop depending on the level of exposure, include skin lesions, peripheral neuropathy, gastrointestinal symptoms, diabetes, cardiovascular disease, developmental toxicity, and cancer of the skin and internal organs. Organic arsenic compounds, which are abundant in seafood, are less harmful to health and are rapidly eliminated by the body.[1,2]

Human exposure to elevated levels of inorganic arsenic occurs mainly through the consumption of groundwater containing naturally high levels of inorganic arsenic, food prepared with this water, and food crops irrigated with high-arsenic water sources. Public health actions need to be continued to reduce human exposure to arsenic, particularly in areas with naturally high levels in groundwater.

Sources of exposure to arsenic[1-3]

Arsenic is widely distributed throughout the Earth's crust, generally as arsenic sulfide or as metal arsenates and arsenides. In water, arsenic occurs in one of two main forms: arsenite As(III) under reducing conditions and arsenate As(V) if the water is oxygenated. It can be released to the atmosphere, primarily as the trioxide, mainly by high-temperature processes or through volatilization from aerated soils. In the atmosphere, it is mainly adsorbed on particles, which are dispersed by winds and deposited on land and water.

Arsenic can be released into the atmosphere and water in the following ways:

- natural activities, such as volcanic activity, dissolution or desorption of minerals (particularly into groundwater), exudates from vegetation and wind-blown dusts;
- human activities, such as metal smelting, combustion of fossil fuels (especially coal), mining, timber treatment with preservatives, and, historically, agricultural pesticide production and use;
- remobilization of historic sources, such as mine drainage water; and
- mobilization into drinking-water from geological deposits by drilling of tube wells.

Drinking-water

Drinking-water poses the greatest threat to public health from arsenic. In 2002, it was estimated that at least 140 million people in 50 countries have been drinking water containing arsenic at levels above the WHO provisional guideline value of 10 µg/L.[3] Inorganic arsenic is naturally present at high levels in the groundwater of a number of countries, such as Argentina, Chile, China, India (West Bengal), Mexico, the United States of America, and particularly Bangladesh, where it was estimated that in 2012 approximately 19 million people were exposed to drinking-water concentrations above the national standard of 50 µg/L and 39

million people were drinking water with levels of arsenic above 10 µg/L.[4] In 2010, 21.4% of all deaths in a highly affected area of Bangladesh were attributed to arsenic levels of above 10 µg/L in drinking-water,[5] while another analysis published in 2012 for all districts indicated an annual total of nearly 43 000 deaths (about 5.6% of all deaths) attributable to chronic arsenic exposure.[6]

Industrial processes

Most arsenic in industrial processes is used to produce antifungal wood preservatives, which can lead to soil contamination. Other current or historical uses include in the pharmaceutical and glass industries, in the manufacture of alloys, sheep dips, leather preservatives, arsenic-containing pigments, antifouling paints and poison baits and, to a diminishing extent, in the production of agrochemicals (especially for use in orchards and vineyards). Arsenic compounds are also employed in limited amounts in the microelectronics and optical industries. High arsenic levels in air can be found in the working environment as well as the general environment around non-ferrous metal smelters, where arsenic trioxide may be formed, and some coal-fired power plants (especially those using low-grade brown coal).[7]

Food

In areas where arsenic is not naturally present at high levels, food usually contributes most to the daily intake of arsenic. Fish, shellfish, meat, poultry, dairy products and cereals are the main sources of dietary intake. However, the arsenic in fish and shellfish is usually in the form of organic compounds (e.g. arsenobetaine) that are of low toxicity.[1] In areas where arsenic is naturally present at high levels, food (e.g. rice) prepared with high arsenic-containing water and food crops irrigated with contaminated water also contribute to total daily intake.

Smoking

Exposure of smokers to arsenic arises from the natural inorganic arsenic content of tobacco. Exposures were higher in the past when tobacco plants were treated with lead arsenate insecticide.

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World Health Organization (WHO) arsenic guidelines

Tolerable intake level

In a review of the latest scientific evidence conducted in 2010, the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) determined the lower limit on the benchmark dose for a 0.5% increased incidence of lung cancer ($BMDL_{0.5}$) from epidemiological data to be 3.0 µg/kg body weight per day (2–7 µg/kg body weight per day based on the range of estimated total dietary exposure). The Committee noted that the previously established provisional tolerable weekly intake (PTWI) of 15 µg/kg body weight (equivalent to 2.1 µg/kg body weight per day) for inorganic arsenic was in the region of the $BMDL_{0.5}$ and therefore was no longer appropriate. This PTWI was therefore withdrawn by the Committee.[8] No new tolerable intake level could be established. In areas where levels in water are below the WHO drinking-water guideline value, human health effects are unlikely.

Drinking-water

The provisional guideline value is 10 µg/L, in light of practical difficulties in removing arsenic in drinking water).[2,9] Every effort should therefore be made to keep concentrations as low as reasonably possible and below the guideline when resources are available.

Air

A safe level of arsenic in air cannot be established.[10]

Health effects[2,11]

Ill effects associated with elevated exposures to inorganic arsenic via the oral route are most likely to occur through consumption of arsenic-contaminated drinking-water. In contrast, exposure to inorganic arsenic from the diet is generally much lower. The intake of small quantities of less toxic organic arsenic compounds, such as from consumption of seafood, does not pose a health risk.

Acute effects

- The immediate symptoms of acute arsenic poisoning include vomiting, abdominal pain and diarrhoea. These are followed by numbness and tingling of the extremities, muscle cramping and, in extreme cases, death.

Effects of long-term exposure

- During long-term exposure to high levels of inorganic arsenic (e.g. through drinking-water), the first changes are usually seen in the skin: pigmentation changes and then skin lesions and hard patches on the palms of the hands and soles of the feet, which may be a precursor to skin cancer.
- Inorganic arsenic is one of the few substances that have been shown to cause cancer in humans through consumption of drinking-water. However, effects may take many years to occur, as increased risks of cancers were still found in a population in northern Chile 40 years after reduction of exposure.[12] Arsenic can cause cancers of

the skin, bladder and lungs, and there is limited evidence that it may also cause cancers of the kidney, liver and prostate.[13] The International Agency for Research on Cancer (IARC) has classified arsenic and arsenic compounds as *carcinogenic to humans* (Group 1), which means that there is sufficient evidence for their carcinogenicity in humans.[13] The organic arsenic compounds monomethylarsonic acid and dimethylarsinic acid are the active ingredients of some herbicides and are metabolites of inorganic arsenic. On the basis of sufficient evidence of cancer in experimental animals, and because monomethylarsonic acid is extensively metabolized to dimethylarsinic acid, both compounds are classified as *possibly carcinogenic to humans* (Group 2B). Arsenobetaine and other organic compounds that are not metabolized in humans are *not classifiable as to their carcinogenicity* (Group 3).[13] Furthermore, IARC has stated that arsenic in drinking-water is *carcinogenic to humans* (Group 1).[13] There is some evidence that the combined effect of smoking and arsenic exposure on lung cancer risk may be greater than additive, based on studies in smelter workers and populations exposed to arsenic in the drinking-water.[13,14]

- Arsenic alters DNA repair and causes genomic instability, inducing oxidative DNA damage aneuploidy, and gene amplification.[13] It also induces epigenetic alterations.[13]
- Other effects of long-term exposure to high inorganic arsenic levels include peripheral neuropathy, gastrointestinal symptoms, conjunctivitis, diabetes, enlarged liver, high blood pressure and cardiovascular disease. “Blackfoot disease”, a severe disease of blood vessels leading to gangrene has been found uniquely in Taiwan, China; malnutrition may contribute to its development.
- Arsenic can pass through the placenta. Pregnant women chronically exposed to arsenic-contaminated drinking-water are at increased risk for spontaneous abortion, stillbirth and preterm birth. In utero and/or early-life exposures to arsenic have been linked to increases in deaths due to multiple cancers, lung disease, heart attacks and kidney failure as well as effects on cognitive development, intelligence and memory later in life.[15,16]

Risk mitigation recommendations[2]

Long-term actions are required to reduce exposure to arsenic from mining, metal smelting and refining, combustion of low-grade coal, pesticide use and timber treatment. In particular, action is needed to reduce the intake of arsenic from drinking-water and food in areas with naturally high levels in the groundwater.

The following actions are needed:

- Make available drinking-water with arsenic concentrations below the WHO provisional drinking-water guideline value of 10 µg/L in areas where the level is higher. Possible measures include:
  - testing water for arsenic levels and informing users of the results;
  - installing arsenic removal systems, either centralized or domestic, and ensuring appropriate disposal of the removed arsenic;
  - substituting high-arsenic sources, such as groundwater, with low-arsenic, microbiologically safe sources such as rainwater and treated surface water. Low-

arsenic water can be used for drinking, cooking and irrigation purposes, whereas high-arsenic water can be used for other purposes such as bathing and washing clothes;

  - discriminating between high-arsenic and low-arsenic sources by testing water for arsenic levels and painting tube wells or hand pumps different colours (e.g. red and green); and
  - blending low-arsenic water with higher-arsenic water to achieve an acceptable arsenic concentration level.

- Reduce occupational exposure to arsenic and its compounds.
- Make both the general public and the health sector aware of the harmful effects of high arsenic intake and the sources of exposure (including use of high-arsenic water for crops irrigation or food preparation) and how to avoid these sources.
- Monitor high-risk populations for early signs of arsenic poisoning, usually skin problems. It should be noted that total urinary arsenic does not differentiate between inorganic arsenic, which is toxic, and organic arsenic, some of which is not. Where possible, arsenic speciation should be attempted in order to differentiate these two forms (and their metabolites).
- The WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene monitors progress towards global targets on drinking-water. Under the new 2030 Agenda for Sustainable Development, the indicator of “safely managed drinking water services” calls for tracking the population accessing drinking-water that is free of faecal contamination and priority chemical contaminants, including arsenic.

References

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