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Review

A global health problem caused by arsenic from natural sources

Jack C. Ng *, Jianping Wang, Amjad Shraim

National Research Centre for Environmental Toxicology, The University of Queensland, 39 Kessels Road, Coopers Plains, Brisbane, Queensland 4108, Australia

Abstract

Arsenic is a carcinogen to both humans and animals. Arsenicals have been associated with cancers of the skin, lung, and bladder. Clinical manifestations of chronic arsenic poisoning include non-cancer end point of hyper- and hypo-pigmentation, keratosis, hypertension, cardiovascular diseases and diabetes. Epidemiological evidence indicates that arsenic concentration exceeding 50 $\mu g l^{-1}$ in the drinking water is not public health protective. The current WHO recommended guideline value for arsenic in drinking water is 10 $\mu g l^{-1}$, whereas many developing countries are still having a value of 50 $\mu g l^{-1}$. It has been estimated that tens of millions of people are at risk exposing to excessive levels of arsenic from both contaminated water and arsenic-bearing coal from natural sources. The global health implication and possible intervention strategies were also discussed in this review article.

Keywords: Arsenic; Coal; Speciation; Environmental health; Arsenicosis; Arsenism; Carcinogen; Cancer

Contents

1. Introduction

Arsenic is a ubiquitous element in the environment. It is produced commercially by reduction of arsenic trioxide with charcoal. Arsenic trioxide is a by-product of metal smelting operations and also present in flue dust from the roasting of ores, especially those produced in copper smelting. Because of its prevalence in nature and its toxicity, the potential for arsenic contamination of water, air, and soil from both geological and anthropogenic sources is a significant environmental health concern.

Inorganic arsenicals have been classified as Group I carcinogens based on human epidemiological data (IARC, 1987). The evidence for arsenic carcinogenicity

* Corresponding author. Tel.: +61-7-3274-9020; fax: +61-7-3274-9003.

E-mail address: j.ng@mailbox.uq.edu.au (J.C. Ng).

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in animals was very limited until sodium arsenate was found to cause tumours in mice (Ng et al., 1999).

The clinical manifestations of chronic arsenicosis in humans include non-cancer effects of hyper- and hypopigmentation, keratosis, hypertension, cardiovascular diseases and diabetes; and cancer end point typically skin, lung and bladder cancers. Cancers involving other organs have also been implicated (IPCS, 2001).

Inorganic arsenic was regarded as the number one toxin in the USEPA list of prioritised pollutants. It has been generally accepted that arsenic contamination in the environment is causing a significant global health problem. It has been estimated that about 60–100 million people in India and Bangladesh are currently at risk as a result of drinking arsenic-contaminated waters (Ahmad, 2001; Chakraborti et al., 2001). Arsenicosis is also prevalent in certain areas of PR China (e.g. Shanxi, Xinjiang, and Inner Mongolia) (Wang et al., 2000; Guo et al., 2001), Taiwan (Chen et al., 1999), Vietnam (Berg et al., 2001) and recently Nepal (Tandukar and Neku, 2002). For these endemic areas, the major arsenic exposure pathway is believed to be from drinking contaminated groundwater whereas the contribution of arsenic from food is relatively low.

Guizhou Province of PR China has a rich resource of coal. Unfortunately, in this province elevated natural arsenic concentrations are found in coal and arsenicosis is prevalent among the residents. For this area, the major exposure pathway has been linked to ingestion of food that is contaminated by arsenic deposition during the burning of coal for cooking, drying of crops, and heating purposes (Liu et al., 2002).

A summary of the global health problems caused by chronic exposure poisoning from natural sources is reported. Possible intervention strategies to minimise the adverse health effects caused by arsenic are also discussed.

2. Chronic arsenic toxicity in animals

There is a noticeable absence of two-year carcinogenicity studies in animals for either the inhalation or oral route of exposure (ATSDR, 1998). Results so far published in the literature provide very limited supportive evidence of arsenic carcinogenicity in animals (IARC, 1987). In light of the ongoing controversy over that arsenic has been classified as a carcinogen based essentially on human epidemiological data, we established a two-year mouse model successfully to demonstrate arsenic carcinogenicity (Ng et al., 1999) and mutagenicity (Ng et al., 2001). The key strategy of the study was to select a strain of mice (C57BL/6J), which had a very low incidence of spontaneous tumours, and to expose animals to concentrations of arsenic in drinking water commonly found in endemic areas where arsenic concentration of such water is seen as a problem. The highest tumour incidences were found in lungs (17.5%) and the intestinal tract (14.4%) of treated C57BL/6J mice, while 3.3% of the mice had skin cancers. A recent study on humans conducted in Taiwan (Hsueh et al., 1995) reported that the prevalence of skin cancer was 6.1% (almost twofold higher than mice), and that there was a significant dose–response relationship between skin cancer prevalence and duration of residence in the endemic area. Our mice (unlike humans) were not exposed to sunlight, and/or interspecies differences between humans and rodents may explain the lower skin cancer incidence observed in laboratory animals. The average daily dosage of arsenic in the treated mice was about 2 μg per animal, which equates to 67 $\mu g\,kg^{-1}$ body weight for a 30 g mouse. This dose rate is similar to the current exposure levels in people who live in areas of endemic arsenic concentration in Bangladesh. Chronic oral exposure data from epidemiological studies in humans indicates that the LOAEL (lowest observable adverse effect level) for skin lesions and other effects is probably about 10–20 μg As $kg^{-1}\,day^{-1}$, and that the NOAEL (no observable adverse effect level) is probably between 0.4 and 0.9 μg As $kg^{-1}\,day^{-1}$ (ATSDR, 1998). Neither the LOAEL nor the NOAEL can be calculated from our study, which involved only a single fixed dose rate. The daily dose rate used in our study is about 3–6 times higher than the calculated LOAEL for humans.

3. Chronic arsenic toxicity in humans

There are numerous epidemiological studies in humans that have demonstrated the carcinogenic effects of inorganic arsenic from inhalation exposure (Ferreccio et al., 1996) and oral exposure (Tseng, 1977).

Long-term exposure to arsenic results in chronic arsenic poisoning (arsenicosis). This has been reported to occur in people who live in endemic areas with high arsenic concentrations in drinking water or in burning coal (Hopenhayn-Rich et al., 2000; Pi et al., 2000; Berg et al., 2001; Liu et al., 2002). Arsenicosis has also been reported in people due to occupational exposure to arsenic (Ng et al., 1998). Occupational exposure to arsenic can result in reduction of methylation capacity as indicated by elevation of unmetabolised inorganic arsenic in the urine (Ng et al., 1998). Skin lesions, which include change of pigmentation (e.g. melanosis) and keratosis of the hands and feet are characteristics of chronic arsenic poisoning and usually appear after 5–15 years after exposure (Tseng, 1977). Chronic arsenic poisoning may also lead to damages of internal organs the respiratory, digestive, circulatory, neural, and renal systems (ATSDR, 2000; IPCS, 2001). The most significant consequence of chronic exposure to arsenic is the occurrence of cancers in various organs especially the skin, lung,

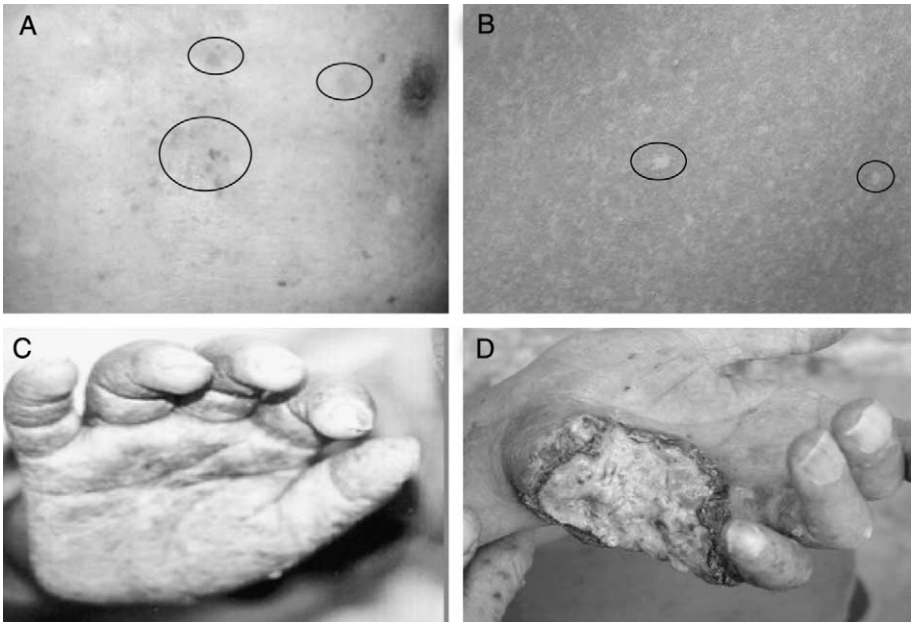

Fig. 1. Typical skin lesions and skin cancer found in patients who have been chronically exposed to arsenic: (A) hyperpigmentation, (B) hypopigmentation, (C) keratosis, and (D) skin cancer.

and bladder (ATSDR, 2000; IPCS, 2001). Examples of arsenicosis are shown in Fig. 1. In Taiwan, where residents were chronically exposed to high levels of arsenic in their drinking water, Black Foot Disease (BFD) has been the most severe manifestation associated with this type of exposure (Chen et al., 1985; Tseng, 1977). Peripheral neuropathy has also been reported to occur but after long-term exposure to inorganic arsenic in drinking water (Hindmarsh et al., 1977). More over, people occupationally exposed to arsenic and through contaminated water are reported to have an increased risk of diabetes (Rahman and Axelson, 1995; Tseng et al., 2002).

4. Drinking water containing naturally high levels of arsenic

Globally, arsenic contamination in drinking water is a major public health issue. Groundwater is a major source of drinking water in many part of the world, especially the South East Asia Region Countries (SEAR). Arsenic contamination of groundwater has been reported in many SEAR countries including Bangladesh and India (Chatterjee et al., 1995; Ahmad, 2001; Shraim et al., 2002), Vietnam (Berg et al., 2001), Nepal (Tandukar and Neku, 2002), Taiwan (Chen et al., 1999), and PR China (Wang et al., 1993; Guo et al., 2001; Lin et al., 2002), where arsenic is from a natural source. Table 1 shows elevated concentrations of arsenic in drinking water and burning coal from arsenic endemic areas around the world.

Ingesting inorganic arsenic through drinking water can cause multi-site cancers in the human body. For people who are exposed to arsenic levels >50 $\mu g l^{-1}$ in drinking water, the cancer risk could be as high as 1 in 100 (Morales et al., 2000). Populations with exposures to arsenic in drinking water, generally at levels of several hundreds micrograms per litre or higher, are reported to have increased risks of skin, bladder, and lung cancers in Taiwan (Chen et al., 1985), Argentina (Hopenhayn-Rich et al., 1996b), and Chile (Smith et al., 1998). The current evidence also suggests that the risks of liver and kidney cancer may also be increased following exposure to inorganic forms of arsenic. The first studies of dose-dependent effects of arsenic associated with skin cancer were observed in Taiwan (Tseng, 1977). Tseng's reports and other similar studies on exposure to arsenic such as through drinking water (Cebrian et al., 1983) and medicines (Cuzick et al., 1982) led the US EPA to use skin cancer as the endpoint classifying inorganic arsenic as a human carcinogen (group A) by the oral route (USEPA, 1984). Currently, the WHO recommended guideline value for arsenic in drinking water is 10 $\mu g l^{-1}$, and the value in Australia has been set at 7 $\mu g l^{-1}$ (NHMRC, 1996). In 2001, the government of USA has reduced its standard from 50 to 10 $\mu g l^{-1}$. However, many developing countries still have their standards set at 50 $\mu g l^{-1}$. It has been generally accepted that $\geqslant 50$ μg

Table 1
Arsenic contaminations in groundwater and coal and population at risk around the world

Country or area	Population at risk	Groundwater concentration (μg As l^{-1})	Guidelines (μg As l^{-1})	Discovery date	References
Argentina	2 000 000	100–1000	50	1981	Sancha and Castro (2001)
Bangladesh	50 000 000	<1–4700	50	1980s	Ahmad (2001)
Bolivia	20 000		50	1997	Sancha and Castro (2001)
Chile	437 000	900–1040	50	1971	Sancha and Castro (2001)
China, Guizhou[a]	20 000	100–10 000 (mg kg^{-1})	8 mg kg^{-1}	1950s	An et al. (1997)
China, Inner Mongolia	600 000	1–2400	50	1990s	Guo et al. (2001)
China, Xinjiang Province	100 000	1–8000	50	1980s	Wang (1997)
Hungary	220 000	10–176	10	1974	Sancha and Castro (2001)
India, West Bengal	1 000 000	<10–3900	50	1980s	Chakraborti et al. (2001)
Mexico	400 000	10–4100	50	1983	Sancha and Castro (2001)
Nepal	Unknown	Up to 456	50	2002	Tandukar and Neku (2002)
Peru	250 000	500	50	1984	Sancha and Castro (2001)
Romania	36 000	10–176	10	2001	Gurzau and Gurzau (2001)
Taiwan	200 000	10–1820	10	1950s	Tseng (1977)
Thailand, Ronpibool	1000	1–5000	50	1980s	Choprapwon and Porapakkham (2001)
USA	Unknown	10–48 000	10	1988	Welch et al. (1988)
Vietnam	Millions	1–3050	10	2001	Berg et al. (2001)

[a] Guizhou is the only known arsenicosis endemic area caused by arsenic contamination in coal.

As l^{-1} in drinking water is not public health protective (Morales et al., 2000).

5. Coal containing naturally high levels of arsenic

Generally coal contains low arsenic concentration that poses no health risks to humans, as the arsenic content in most coals is less than 5 mg kg^{-1}. However, some coals may contain up to 35 000 mg kg^{-1} (Ding et al., 2001). Power plants using high arsenic-containing coal as a fuel, especially in India and Czechoslovakia, could be a major source of pollution in the environment. The wastewater discharged from such power plants is also highly contaminated with arsenic (Wang, 1997). Using high arsenic-containing coal can also cause arsenic poisoning in humans from consumption of contaminated food and inhalation of contaminated indoor air, such as the case in Guizhou Province in PR China where contaminated coal is used for heating, cooking and drying of crops (An et al., 1997; Finkelman et al., 1999; Liu et al., 2002; Shraim et al., 2003).

Several studies have shown how burning of high arsenic coals can contaminate the indoor environment. For example the effect of coal burning on the residents of Guizhou Province, PR China (An et al., 1997) was investigated. Samples of coal, water, air, food, urine and hair were collected from endemic and controlled areas and analysed for arsenic. The mean arsenic concentrations in coal (mg kg^{-1}), water (μg l^{-1}), urine (μg l^{-1}), and hair (mg kg^{-1}) in the polluted areas were 2166.7, 5.2, 137, and 3.08 and for control areas were 2.5, 2.4, 23, and 0.97 respectively. Elevated concentrations of arsenic in hair samples (7.99 ± 8.16 mg kg^{-1}, $n = 36$, control < 2.0 mg kg^{-1}) collected from individuals who lived in the same endemic coal-burning areas were also reported (Shraim et al., 2003). The overall estimated mean daily intake of arsenic per person was 31 mg in the polluted city and only 1.34 mg in the control. More than half of the study subjects in the polluted city were found to have clear symptoms of arsenicosis (An et al., 1997). In another study (Wei et al., 1997), the extent of arsenic contamination was measured in the kitchen air, corn and chilli in endemic village in Guizhou Province. The

reported arsenic concentrations in the kitchen air, corn and chilli were 455 ± 304 $\mu g\,m^{-3}$ (control < 1), 4.1 ± 2.8 and 512 ± 300 $mg\,kg^{-1}$ respectively.

6. Urinary arsenic concentrations

Urinary arsenic is widely used as a biomarker for arsenic exposure in humans. Total arsenic concentrations were reported to correlate with increases in arsenic exposure (Valentine et al., 1979; Hopenhayn-Rich et al., 1996a; Ng et al., 1998; Mandal et al., 2001).

Human bodies methylate the ingested inorganic arsenic [InAs = As(III) + As(V)] to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), which are less reactive with the tissue constituents than the parent InAs and therefore are more rapidly excreted into the urine (Vahter, 1999). Low percentages of MMA and DMA in urine are related to a low rate of methylation and therefore a low rate of excretion of the adsorbed arsenic, which is likely to correspond to an increased risk of toxic level (Vahter, 2000). Speciation of arsenic in urine is therefore essential for estimating the capacity of the human body to methylate the ingested InAs and for assessing the extent of exposure to these toxic forms of arsenic (Ng et al., 1998; Vahter, 1999).

The reported percentages of the four metabolites in human urine irrespective of the type and extent of exposure were 10–30%, 60–80% and 10–20% for InAs, DMA and MMA respectively (Hsu et al., 1997; Vahter, 1999). In a recent investigation (Shraim et al., 2003), urine samples were collected from residents of a coal-burning arsenic endemic area in Guizhou Province and analysed for arsenic species. Similar percentages of the four metabolites were reported, however gender variation was observed in the population of that study. Females were found to have a higher DMA but lower percentages of InAs and MMA in their urine than males. This may indicate that the females' methylation capacity is higher than males. Similar findings were also reported by other research groups in subjects exposed to arsenic through drinking water (Hsu et al., 1997; Hsueh et al., 1998).

7. Possible intervention

Currently there are some countries where arsenic contamination in the groundwater has reached a very alarming level and requires immediate attention, especially in Bangladesh and India. The present situation in Bangladesh demands a thorough screening of tubewells to assess the arsenic concentrations, identify hot spots, and implement suitable intervention programs. Intervention options may include dug wells and deep tubewells, where low arsenic concentrations are usually present. Other watershed management strategies have included the use of rainwater harvesting, pond sand filtration, low cost domestic filtration systems, and arsenic removal technologies such as iron hydroxide precipitation (Meng et al., 2001, 2002). For arsenic-contaminated coal endemic areas, possible intervention options are to use coals with arsenic concentration that does not pose any health risk and to improve the indoor air ventilation systems. In China and Taiwan, alternative safe water sources have been implemented and post intervention follow up studies are being conducted by various researchers to evaluate the health outcomes. Small to medium scale intervention studies are being conducted in Bangladesh and India by various governmental, non-governmental organizations and academic institutions. The intervention approaches include arsenic removal technologies based on adsorption–coprecipitation using iron or aluminum salts; adsorption on activated alumina, activated carbon, and activated bauxite; reverse osmosis, and ion exchange; and other alternative water supplies and watershed management strategies (Viraraghavan et al., 1999; Meng et al., 2002; Zaw and Emett, 2002).

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