International Research on Arsenic Contamination and Health

Some historical notes

Arsenikon, the Greek word meaning arsenic, was used during the Renaissance to mean potent or male. Hippocrates (460 BC), the father of modern medicine, and Galen (129 AD), the two most famous physicians of the Roman Empire, are said to have used a paste containing arsenic tetrasulphide to treat ulcers (1,2).

Inorganic arsenic compounds have been used in medicine since these ancient times. Over the past 150 years, arsenic has been used for treating dermatitis herpetiformis, asthma, syphilis, epilepsy, psoriasis, trypanosomiasis, amoebiasis, and other conditions (3-6). In 1786, Thomas Fowler introduced his own ‘Liquor Arsenicalis’—a 1% solution of potassium arsenite, coloured with a tincture of lavender—which contained a very high concentration (5,000,000 ppb) of arsenic (7). Fowler’s treatment involved 24 doses, and the total course of 280 drops was equivalent to about 60 mg of arsenic, especially psoriasis. During the decades, following the introduction of Fowler’s solution, arsenic is still used in homeopathic (8) and herbal medicine (9-11), although enormous adverse effects of this medication have been reported (3-6). It has also been recognized as a modern intravenous treatment for acute promyelocytic leukaemia (12). Results of recent research suggest that arsenic trioxide, in combination with other agents, may have therapeutic uses for other malignancies (13).

Arsenic compounds have also been used, since ancient times, as poisons. The death of the French emperor Napoleon Bonaparte, on 5 May 1821, was believed to be due to slow poisoning with arsenic (14). He was exiled on the Island of St. Helena in the middle of the Atlantic Ocean following his defeat at the Battle of Waterloo in 1816.

Studying exposure in the general populations

Arsenic, a ubiquitous element in the earth’s crust, is a constituent of many different minerals. Concentrations of arsenic vary in the environment, e.g. 0.03-0.25 part per million (ppm) in soil, 0.023-0.25 ppm in plants, up to 55 ppm in groundwater, 0.001-0.08 ppm in seawater, 3-170 ppm in fish, 0.008-0.85 ppm in wine, and up to 0.00049 or 0.63 mg/m³ in urban air (3-6). One in every 60 people (~100 million people) on the planet is living in an area where they may be exposed to 50 µg/L of arsenic or above in drinking-water, and one in every 30 people may quaff water with 10 µg/L of arsenic or above which is the WHO guideline for drinking-water (15).

Twenty-six papers on health effects of arsenic exposure and mitigation of arsenic contamination have been assembled in the two issues (June and September) of the Journal. In these two special issues, seven studies are reported from North and South America (16-19). North and South America have large tracts of arsenic-rich groundwater. Exposure is spotty in areas of the Pampean Plain of Argentina, which is much bigger than Bangladesh and West Bengal. In Argentina, the first arsenic-induced skin lesion was recorded in 1917 (3-5). The disease was named Bel Ville disease after the name of the town in which the cases were reported. In Chile, the first case was recorded in 1962 (3-5).

Arsenic contamination of water in several Asian countries are also reported in the two special issues (20-25). In Asia, the first health effects from arsenic contamination in drinking-water were reported in Taiwan (26,27). In South Asia, the Bengal Basin, encompassing the world’s largest delta, is geologically very young, comprising the convergent Ganges, Brahmaputra, and Meghna rivers. The first health effects were discovered in West Bengal by dermatologist K.C. Saha who diagnosed patients as having arsenic-caused skin lesions in 1982 (28). Skin-lesion patients from Bangladesh were also first identified by him in Kolkata in 1984 (29). The Department of Public Health Engineering (DPHE) of Bangladesh first reported arsenic contamination of groundwater in Bangladesh in 1993 (30). Unique exposure from burning of arsenic-rich coal in the Guizhou province (21,23), widespread contamination in China (22,23) and Nepal (24) are also reported in this issue. Other countries with arsenic-rich groundwater include Mexico, Cambodia, Viet Nam, Thailand, and Ghana (32-36). Mukarjee et al. highlighted the situation of arsenic contamination round the globe with special mention of the Asian situation (37).
Skin lesions and cancer

In this issue, arsenic-induced skin lesions are reported from China, Bangladesh, and Nepal (20,23-25). In Nepal, the prevalence of skin lesions is 22 per 1,000 people (24). Skin lesions, which include pigmentation changes and thickening of the outer, horny layer of skin, are the most obvious effects resulting from high exposure to arsenic (38,39). For reasons not understood, men are more likely than women to be found with skin lesions in all countries in which skin lesions have been reported. In Inner Mongolia, Guo et al. found an increased risk of arsenic-induced skin lesions among participants with elevated concentrations of arsenic in water (23). The adjusted risks were 5.2 (95% confidence interval [CI] 1.32-83.24), 11 (95% CI 1.50-79.95), and 10 (95% CI 1.39-71.77) for exposure to water containing <50-199, 200-499, and ≥500 µg/L respectively. In another study in Bangladesh, the prevalence of skin keratosis was also reported to be 13 per 1,000 people (25). The prevalence and incidence of skin lesions are highly variable from one country to another.

A study of the association between arsenic exposure and the prevalence of skin cancer is also reported in this issue (16). Knobeloch et al. reported the prevalence of skin cancer at low exposure which is increased by high exposure (16). Arsenic was one of the first chemicals recognized as a cause of cancer (3-6). In 1887, Jonathan Hutchinson described arsenic-induced skin lesions and cancers in patients who were treated with arsenic-containing medication (40). In the 1930s, evidence suggested arsenic as causing skin cancer (41). Results of dozens of epidemiological studies based on populations in Asia (42,43), South America (44), North America (45), and Europe (46,47) showed a causal association between well-water containing inorganic arsenic and occurrence of skin cancer. The elevated risk persisted years after the cessation of exposure. All these studies found an increased risk of non-melanocytic skin cancer, but not melanocytic skin cancer, in relation to arsenic exposure. A recent case-control study conducted in Iowa, USA, reported an association between concentrations of arsenic in toenails and risk of melanoma (48).

Chronic effects, such as lung and bladder cancers, were reported in Chile (18). High rates of lung cancer were first reported in 1879 in Saxony miners, and higher risks were attributed at least in part to arsenic (49,50). The International Agency for Research on Cancer recently classified arsenic in drinking-water as a ‘Group I’ human carcinogen based on evidence of increased risks of skin, bladder and lung cancers (4). Lung cancer is actually the main long-term cause of death, resulting from ingestion of inorganic arsenic in drinking-water.

Vascular and other effects

A link between arsenic in drinking-water and elevated risks of several vascular diseases, including blackfoot disease, systemic hypertension, cerebrovascular disease, and ischaemic heart disease has been suggested (51-57). From an occupational and environmental health point of view, arsenic exposure has attracted great interest in the past few decades, especially lung cancer, among copper smelter workers, but also the risk of skin, lung and bladder cancers seen in connection with exposure through drinking-water. Other findings reported in this issue include the newly-proposed risk of carotid atherosclerosis (58) and ECG abnormalities (59). The common carotid atherosclerosis represents a marker of pre-clinical atherosclerosis. An intima-medial thickness (IMT) measure of >0.75 mm is considered an indicator for significant coronary artery disease. The odds ratios (ORs) for carotid IMT are 1.61 (95% CI 0.2-8.8) and 2.84 (95% CI 0.3-20.9) when compared with the lowest-tertiles exposure group. Data concerning nerve conduction velocity is also presented in a cross-sectional study (60). A three-time increased risk (OR=2.9; 95% CI 1.1-7.5) was observed for the development of slow nerve conduction velocity of the sural sensory action potentials.

One study reported reproductive effects, including birth-defects and low birth-weight (61). A small but statistically significant association was observed between arsenic exposure and birth-defects. No association was observed between arsenic exposure and stillbirth, low birth-weight, childhood stunting, and child under-weight while investigating 2,006 pregnant women who were chronically exposed to arsenic. Earlier studies, including increased infant mortality (18-34%), and reduction in birth-weight, were reported from Chile (62,63). Higher negative pregnancy outcomes have been observed in Bangladesh (64,65), Hungary (66), and Taiwan (67). However, none of these studies showed increased birth-defects. The birth-defect findings need to be confirmed ideally in a prospective pregnancy cohort study.

Variation of exposures

Temporal variation in concentrations of arsenic has important implications for public-health research. In quantification and retrospective assessments of human exposure, current measurements in well-water are used for estimating past concentrations which study participants were exposed to. Two studies are reported on
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The West Bengal study showed the evidence of variation over time in high concentrations of arsenic in tubewells (68). In Argentina, concentrations of arsenic in well-water were reported to be the same over a decade (17) which was also similar to what was found in a study in the USA (69). In Bangladesh, little temporal variation was reported over a short period in low concentration of arsenic in wells (70). If variations in concentrations of arsenic over time are confirmed, concentrations of arsenic in tubewell water may need to be monitored periodically. Further investigations are needed for temporal variability in concentrations of arsenic in well-water.

Huq et al. have shown that arsenic-laced irrigation-water can substantially increase the arsenic content of rice and vegetables (71). Around 150 mg/kg of arsenic was found in arum which is a green watery leafy vegetable, and concentrations of arsenic have been found in soil as high as 80 mg/kg in an area receiving arsenic-contaminated irrigation. Foods, soil, and air are the other potential sources of arsenic exposure. The public-health impact of these exposures is largely unknown as epidemiologic focus has only been given on exposure via drinking-water.

**Strategies reducing exposure in different settings**

The first and most obvious necessity is to measure the levels of arsenic in any groundwater intended for human use. The next useful step would be to purify water contaminated with arsenic or to provide alternative sources of water.

We have reported several mitigation options (72,73) and a risk assessment of these options (74) in the September issue of the Journal. The use of a sanitary (dug) well is a satisfactory and reliable solution for the provision of water free of bacteria and arsenic. This option needs a suitable site and strict adherence to sanitary standards, ensuring community participation, ownership, and maintenance of each sanitary well (72). A simple flow-through system has been described which makes the use of wasted heat generated in traditional clay-ovens (challis) to pasteurize surface water and to provide a safe alternative source of drinking-water (90 litres per day) in arsenic-contaminated areas (73). This simple system can also have wider application wherever people consume microbiologically-contaminated water.

Estimating the burden of disease associated with each technology in disability-adjusted life years (DALYs) is also reported in the September issue of the Journal (74). Van Geen et al. have shown that mobile-phone technology could optimize interventions by guiding the choice of the drilling method that is likely to reach a safe aquifer and by identifying those villages where exploratory drilling is needed (75).

**Lessons to be learnt**

The discovery of arsenic in drinking-water in many areas, including Argentina, Chile, India, Taiwan, the United States, Bangladesh, China, Nepal, and other countries, illustrates that this is a global problem (76). Elevated risk of adverse health effects persists years after the cessation of exposure, and an understanding of prevention strategies for arsenic-induced health effects is needed in both scientific and public-health arenas. It is now clear that all sources of groundwater used for drinking-water should be tested for arsenic.

**REFERENCES**


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