In recent years, ingestion of inorganic arsenic from drinking water has emerged as an important scientific issue and public health concern. The International Agency for Research on Cancer has identified sufficient evidence in humans that inorganic arsenic causes lung, bladder, and nonmelanoma skin cancers (1) (summary at http://monographs.iarc.fr/). Reports by expert committees have suggested associations with several other cancer and noncancer outcomes (2–4). As a result, the US Environmental Protection Agency lowered the maximum contaminant level for arsenic in drinking water supplied by community water systems from 50 µg/L, a level set in 1942, to 10 µg/L, effective from January 2006. The reduction will necessitate changes to water systems serving approximately 13 million people (http://www.epa.gov/safewater/arsenic/compliance.html). The World Health Organization has similarly recommended 10 µg/L for arsenic in water as a “guideline value” for setting national standards (http://www.who.int/mediacentre/factsheets/fs210/en/index.html).

Substantial numbers of people worldwide are exposed to elevated concentrations of arsenic. An estimated 25 million people in Bangladesh (19% of the population) and 6 million people in West Bengal, India (8% of the population), consume water with arsenic exceeding 50 µg/L (5), with perhaps twice these numbers in these countries consuming water with arsenic levels exceeding 10 µg/L. High levels of inorganic arsenic are found in drinking water in many other parts of the world, including areas of Argentina (county means ranged to 178 µg/L) (6), the Inner Mongolia and Xinjiang autonomous regions in China (levels in excess of 600 µg/L) (7), Finland (levels were generally low but ranged to 64 µg/L) (8), northern Mexico (ranges in exposed areas to 160–740 µg/L) (9), and the United States (with some areas in California, Nevada, Alaska, Michigan, New England, New Mexico, and Utah exceeding 50 µg/L) (see US Geological Survey map of 31 350 ground water measurements at http://co.water.usgs.gov/trace/pubs/arsenic_fi g1.html). Drinking water arsenic levels in excess of 150 µg/L also occur in Nepal (10), Thailand (11), Vietnam (12), Hungary (13), Ghana (14), and elsewhere (15). Although arsenic contamination of water supplies arises mainly from natural sources, human activities such as mining and ore processing may also contribute to elevated arsenic levels in some areas.

Although ingestion of high levels of inorganic arsenic is most strongly linked to lung, bladder, and nonmelanoma skin cancers, there is evidence for associations with cancers of the kidney, liver, and possibly prostate (16). In addition, high levels of drinking water arsenic have been linked to cutaneous effects (hyperpigmentation, hypopigmentation, palmar–plantar hyperkeratoses, and leukomelanosis), gastrointestinal effects (gastrointestinal distress and liver cirrhosis), vascular effects (peripheral vascular diseases, such as blackfoot disease and Raynaud’s syndrome; arterial occlusions; cardiovascular disease; cerebrovascular disease; and hypertension), diabetes mellitus, and peripheral neuropathy (2), as well as to chronic cough, shortness of breath, and other respiratory effects (17). Arsenic can cross the placental barrier, and ingestion of high levels by pregnant women may cause adverse reproductive and developmental effects and increase rates of stillbirths, spontaneous abortions, low–birth weight deliveries, and neonatal and postneonatal mortality (18,19). Many of these associations were identified from ecologic studies conducted in a limited number of populations; there have been relatively few analytic studies. Thus, many of the associations between arsenic ingestion and cancers other than lung, bladder, and nonmelanoma skin cancers and noncancer outcomes have not been conclusively demonstrated, and additional studies are needed.

In this issue of the Journal, Marshall et al. (20) analyzed 50 years of mortality data for lung and bladder cancers, substantially extending a previous analysis (21). Data are ecologic and come from the climatologically and geographically unique setting of Region II in northern Chile. The climate is extremely arid, and the population lives primarily in cities and towns and relies almost exclusively on municipally supplied drinking water. Based on arsenic measurements made since the 1950s, arsenic levels within Region II have varied spatially and temporally, from highs of 870 µg/L during 1955–1970 in Antofagasta and 600 µg/L during 1950–1994 in San Pedro to current concentrations of 10–40 µg/L in most areas. Variation among regions and time periods created a natural experiment that permitted the authors to examine the health effects of arsenic in drinking water. Relative to Region V, where arsenic levels in the drinking water are low, standardized mortality ratios for lung cancer and bladder cancer in Region II were elevated starting 10–20 years after the time periods with the highest arsenic levels. Moreover, although arsenic levels declined steadily since the 1970s, risks for lung and bladder cancers remained elevated through the 1990s, suggesting an apparent persistence in arsenic effects. These temporal patterns are intriguing, and additional analyses could increase understanding of disease latency and the impact of reducing exposure. Finally, a recent

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See “Note” following “References.”

**DOI:** 10.1093/jnci/djm012

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Inorganic Arsenic in Drinking Water: An Evolving Public Health Concern

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analytic case–control study conducted in northern Chile reported increased odds ratios for lung cancer with increasing drinking water arsenic (22), providing confirmatory evidence of the ecologic results for lung cancer.

The process of arsenic metabolism in humans has not been fully elucidated. In the environment and in biologic systems, inorganic arsenic occurs primarily as pentavalent arsenate [As(V)] or under reducing conditions as trivalent arsenite [As(III)]. It has been proposed that after ingestion, inorganic arsenic cycles through a series of reduction and methylation reactions (23). Inorganic As(V) is rapidly reduced to As(III), which then accepts a methyl group from S-adenosylmethionine to produce the methylated pentavalent species monomethylarsonic acid (MMA), MMA(V), MMA(V) is reduced to trivalent MMA(III), and the cycle is repeated to produce the pentavalent species dimethylarsinic acid (DMA), DMA(V), which is in turn reduced to DMA(III). The trivalent species are the more bioactive, with toxicity resulting in part from an ability to bind with sulfhydryl groups, thus disrupting enzyme function (2).

Epidemiologic evidence supporting hypothesized mechanisms of action for arsenic, including susceptibility factors, is limited (2,3). Several studies have found an increased risk of bladder and skin cancers with increasing MMA to DMA ratios (24,25), although the genetic or other determinants of this ratio have not yet been elucidated. Arsenic may also exert its toxicity through the generation of reactive oxygen species (26). Detailed epidemiologic studies are currently underway.

Studies of populations and of individuals exposed to high levels of arsenic in drinking water raise the possibility of a causal relationship not only for lung, bladder, and nonmelanoma skin cancers but also for cancers of the kidney, liver, and possibly prostate, as well as several noncancer outcomes. The report by Marshall et al. (20) provides additional evidence linking arsenic to lung and bladder cancers and, perhaps more importantly, insights into the temporal patterns of arsenic effects. However, ecologic studies have recognized limitations and additional analytic studies are needed. With large numbers of people potentially exposed to arsenic in drinking water above 10 μg/L, the full scope of the public health consequences of arsenic in drinking water is not yet clear.

References


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Note

This work was supported by the Intramural Research Program of the National Institutes of Health and the National Cancer Institute.