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# Arsenic-related mortality in Bangladesh

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More than 30 years after the installation of tube wells in Bangladesh, Maria Argos and colleagues[1] report a prospective cohort study in *The Lancet* today in which they investigated all-cause and chronic-disease mortalities related to arsenic exposure in well water. In previous studies by these and other investigators, associations were noted with skin lesions and malignant diseases (eg, skin, bladder, and lung cancer).[2,3] New findings from the Health Effects of Arsenic Longitudinal Study (HEALS)[1] cohort inform us of increased overall mortality and chronic-disease mortality associated with arsenic in drinking water in the Araihazar region. The investigators estimate that more than 20% of deaths could be attributed to well arsenic concentrations greater than 10·0 μg/L.

35–77 million of roughly 125 million inhabitants of Bangladesh have been drinking the contaminated well water. In the HEALS cohort, more than 55% consumed amounts greater than 50 μg/L, the current Bangladesh standard, and more than 75% consumed more than the WHO recommended 10·0 μg/L; however, not everyone was exposed. Concentrations ranged from 0·1 μg/L (the limit of detection) to 864·0 μg/L. The beauty of the HEALS cohort is that it includes concentrations at the low end of the dose-response curve and concentrations at the high end at which known health effects arise. Such data are rarely available, yet they are important for establishing rational guidelines.

An increase of nearly 70% in all-cause mortality was noted among those exposed to the highest concentration of arsenic in water (150·1–864·0 μg/L) relative to those exposed to not more than 10·0 μg/L. Importantly, however, the investigators report a dose-related trend in mortality risk with exposure to increasing concentrations, as opposed to a threshold effect. Perhaps with further follow-up the investigators might be able to provide a precise estimation of the continuous dose-response curve and the magnitude of its slope.

A carefully designed population-based epidemiological study in Bangladesh might be expected to be a daunting task: trained physicians travelled the tropical landscape over wooden bridges to do interviews, clinical examinations, and obtain urine samples for nearly all eligible residents in the region. This well-wrought design enabled the investigators to adjust for potentially confounding factors (eg, body-mass index, blood pressure, and cigarette smoking). Additionally, all (nearly 6000) wells in the region were tested to establish the arsenic concentration of the water source used by each participant. Quantification of arsenic exposure and other characteristics at an individual level along with the integration of biomarkers represents a substantial advance over previous ecological studies that were at risk of ecological fallacy, misclassification, and confounding.

Residents were revisited every 2 years. The good news is that after two 2-year follow-ups (ie, 4 years), about 40% of those with urinary arsenic concentrations greater than the median reverted to concentrations below the median. The bad news is that their mortality risk did not decline. Nonetheless, a long period of cessation with greater statistical power to note a reduction in mortality rate, or a more refined analysis, might be needed to fully understand the implications of remediation efforts.

Aside from chronic diseases, concerns have been raised about the effects of arsenic on pregnancy outcomes. A trend of reduced birthweight in relation to arsenic concentrations in drinking water was noted in a cohort study of pregnant women from a different region of Bangladesh, but only at concentrations below 100 μg/L.[4] Further, increasing evidence has raised awareness of the effect of the intrauterine environment on adult-onset diseases—eg, in mice the incidence of cancers is elevated among offspring exposed to arsenic in utero;[5] the findings of a recent ecological analysis from Chile support this possibility.[6]

Moreover, infectious diseases remain a significant cause of mortality worldwide, and indeed prompted the installation of the wells in Bangladesh as a means of supplying pathogen-free drinking water. Recent evidence suggests that environmental toxins, such as arsenic, might affect immune response.[7,8] Thus far, the repercussions of arsenic exposure on the occurrence and virulence of infectious diseases have not been realised entirely.

An estimated 20% of the world's population lacks access to safe drinking water.[9] In 2010, we are reminded once again of the effect of the earth's drinking water supply on the human lifespan and the challenges of securing this scarce resource.

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