INSIGHTS

PERSPECTIVES

A Bangladeshi woman collects potable water from a hand pump. The health toll from arsenic in water justifies global solutions.

PUBLIC HEALTH

Global solutions to a silent poison

Modeling arsenic in domestic well water highlights large data gaps in testing

By **Yan Zheng**

Severe public health consequences of worldwide geogenic arsenic occurrence in groundwater have been recognized since the late 1990s (*1*). The population affected by groundwater arsenic from domestic well supplies has been frequently stated to exceed 100 million. However, this compilation is fraught with uncertainties due to incomplete and unreliable records on domestic wells that supply drinking water and incomplete testing for arsenic. On page 845 of this issue, Podgorski and Berg use statistical models to estimate that 94 million to 220 million people, with 94% in Asia, are at risk of drinking well water containing arsenic concentrations >10 μg/liter (*2*). In Bangladesh, a 2009 national drinking-water quality survey found that about 20 million and 45 million people were exposed to concentrations greater than 50 and 10 μg/liter, respectively, with an arsenic-related mortality rate of 1 in every 18 adult deaths (*3*). This global threat demands multisector solutions.

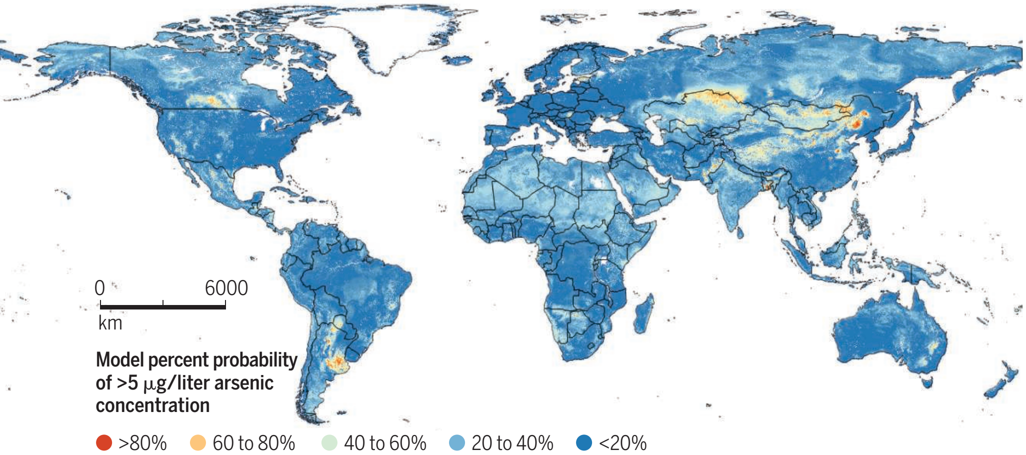
The 2017 edition of the World Health Organization's *Guidelines for Drinking-Water Quality* retained its provisional value of 10 μg/liter for inorganic arsenic, a recommendation based on treatment performance and analytical achievability. Many countries have adopted this value as their drinking-water quality standard over the past two decades. Although the European Union has set the standard at 10 μg/liter, Denmark's is more protective at 5 μg/liter. The Association of Dutch Drinking Water Companies voluntarily agreed on a guideline of <1 μg/liter in 2015 (*4*). The U.S. Environmental Protection Agency adopted 10 μg/liter in 2001 for the federal maximum contaminant level (MCL) on the basis of cost-benefit analyses, effective 2006. However, the state of New Jersey opted for 5 μg/liter effective 2006, and New Hampshire adopted 5 μg/liter in 2020. The world's two most populous countries, China and India, lowered their MCL, effective 2007 and 2012, respectively, from 50 to 10 μg/liter. However, 50 μg/liter is permissible in the absence of alternate sources in India and remains the MCL for Bangladesh and for small, dispersed rural supplies in China. This order-of-magnitude disparity in the MCL is concerning because new health evidence suggests that even 10 μg/liter may not be protective enough, especially during early, biologically vulnerable stages of life.

School of Environmental Science and Engineering, Southern University of Science and Technology, Shenzhen 518055, China. Email: yan.zheng@sustech.edu.cn

PHOTO: A. M. AHAD/AP PHOTO

A world model for groundwater arsenic risk

Lowering arsenic concentrations in drinking water helps avoid a range of adverse health outcomes. Modeling the probability of groundwater arsenic with excess risks helps guide testing. Podgorski and Berg developed global models for groundwater arsenic concentrations exceeding 5 and 10 μg/liter.



Health effects in adults

General health effects
Mortality
DNA methylation
Gene expression

Nervous system
Movement and motor function
Neuropathy

Immune system
Infections

Respiratory system
Bronchiectasis
Lung cancer

Cardiovascular system
Heart and vascular disease
High blood pressure
Stroke

Endocrine system
Diabetes

Soft organs
Kidney cancer
Bladder cancer
Liver cancer

Skin
Skin lesions
Skin cancer

Health effects in children

General health effects
Infant mortality
Reduced birth weight
DNA methylation
Gene expression

Nervous system
Neurological impairment

GRAPHIC: X. LIU/*SCIENCE* FROM (2)

The word arsenic originates from the Greek arsenikon, which means valiant, bold, or potent. Odorless and tasteless when dissolved in water, this silent poison became known as both "the king of poisons" and "the poison of kings." The acute toxicity of inorganic arsenic, classified as a group I carcinogen by the International Agency for Research on Cancer, has been appreciated since ancient times. Long-term exposure to water containing high concentrations (>100 μg/liter) of inorganic arsenic (arsenate and arsenite) is associated with nonmelanoma skin, lung, and bladder cancers, as well as noncancer outcomes. The Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh showed dose-response relationships between drinking-water arsenic and skin lesions, respiratory symptoms, cardiovascular disease, and reduced intellectual function in children (*5*). Long-term exposure to moderate concentrations (<50 μg/liter) has been associated with cardiovascular disease incidence and mortality in one of the largest studies in the United States (*6*). Epidemiologic evidence, consistent with experimental evidence, supports that arsenic affects birth outcomes and impairs neurodevelopment when exposure occurs during early life, even at moderate concentrations (<50 μg/liter) (*5*). In utero, arsenic exposure has been associated with alterations in gene expression pathways related to diabetes (*7*), which may contribute to adult diabetes risks. This supports the epigenome as a general mechanism involved in arsenic toxicity, consistent with evidence from a genome-wide DNA methylation study of 396 HEALS adults (*8*). Still, not enough is known about the mode of action of inorganic arsenic for extrapolating dose response to very low concentrations (<5 μg/liter).

Because three-dimensional (longitude, latitude, and depth) mapping of groundwater arsenic concentration often lacks the spatial resolution to characterize most aquifers, exposure assessment has turned to "predictive" models incorporating geo-environmental predictor variables. Podgorski and Berg utilized 58,555 aggregated well (<100-m depth) water arsenic average values, mapped to 1-km^2 grid cells based on >200,000 tests from 67 countries, to develop a random forest machine-learning model to globally quantify exposed populations. This represents a culmination of logistic regression (*9*, *10*) and machine-learning (*11*) modeling efforts (see the figure). The authors' efforts expose data gaps because few countries have conducted a nationwide groundwater arsenic survey. Testing data are also clustered with uneven and incomplete spatial coverage. More arsenic data and detailed predictor datasets will reduce the large and partially unknown uncertainties. Eleven out of 52 spatially continuous predictor variables representing various climatic, geologic, soil, and other parameters emerged through recursive feature elimination to create the simplest best model. Additional research is required to explain why these are important. Statistical models are not meant to predict individual well water arsenic concentrations. Their greatest value lies in identifying potential areas at risk that have not had testing.

This public health crisis leads to an urgent call to test all domestic well water for arsenic worldwide. Testing should prioritize the high-risk areas identified by models. Heterogeneous groundwater arsenic spatial distribution (10^1 to 10^3 m) should make wells that are close to known high-arsenic wells testing priorities. The combination of arsenic's toxicity and its wide distribution makes this task imperative. Disparities in coverage of regulatory requirements in the United States have left more than a million rural Americans unknowingly exposed to arsenic, with a high proportion belonging to socioeconomically and behaviorally vulnerable groups (*10*, *12*). Development of sensitive, reliable, inexpensive, and user-friendly testing methods for inorganic arsenic in water and urine, preferably with on-site rapid measurement capability, can further improve screening and identify exposed populations. Whereas many countries have succeeded in replacing noncompliant arsenic domestic wells with alternative supplies or treatment to reduce exposure, dispersed rural populations require sustained attention. Treatment of arsenic is not cheap, burdening rural households even in high-income countries. Geogenic arsenic in well water is forever, but our exposure to it should not be. ■

REFERENCES AND NOTES

1. D. K. Nordstrom, *Science* **296**, 2143 (2002).
2. J. Podgorski, M. Berg, *Science* **368**, 845 (2020).
3. S. V. Flanagan, R. B. Johnston, Y. Zheng, *Bull. World Health Organ*. **90**, 839 (2012).
4. A. Ahmad *et al*., *Environ. Int*. **134**, 105253 (2020).
5. National Research Council, "Critical aspects of EPA's IRIS assessment of inorganic arsenic: Interim report" (The National Academies Press, Washington, DC, 2013).
6. K. A. Moon *et al*., *Ann. Intern. Med*. **159**, 649 (2013).
7. A. Navas-Acien *et al*., *Curr. Diab. Rep*. **19**, 147 (2019).
8. K. Demanelis *et al*., *Environ. Health Perspect*. **127**, 057011 (2019).
9. L. Winkel *et al*., *Nat. Geosci*. **1**, 536 (2008).
10. J. D. Ayotte *et al*., *Environ. Sci. Technol*. **51**, 12443 (2017).
11. J. D. Ayotte *et al*., *Environ. Sci. Technol*. **50**, 7555 (2016).
12. Y. Zheng, S. V. Flanagan, *Environ. Health Perspect*. **125**, 085002 (2017).

ACKNOWLEDGMENTS

J. D. Ayotte, A. Navas-Acien, and D. K. Nordstrom provided comments. Figure courtesy of A. Bozack, Z. Tan, and B. Xu. Y.Z. is supported by Strategic Priority Research Program of the Chinese Academy of Sciences (XDA20060402), the National Natural Science Foundation (41831279), and the U.S. National Institute of Environmental Health Sciences, Superfund Research Program (P42 ES010349).

10.1126/science.abb9746

Global solutions to a silent poison

Yan Zheng

Science **368** (6493), 818-819.
DOI: 10.1126/science.abb9746

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. The title *Science* is a registered trademark of AAAS.