The 'King of Poisons' Journeys Underground in Search of Water

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Historically popular for deliberate poisoning because of its innocuous looks, lack of odor and taste, and availability as a rat poison, arsenic soon fell out of favor with prospective poisoners as chemistry advanced far enough to detect metallic substances.[1,2] Nevertheless, the element still influences human health today. Humans are exposed to mostly innocuous forms of arsenic through the environment, pesticides, commercial products, and even some forms of cancer treatment. However, naturally high levels of arsenic in groundwater are a significant public health concern, affecting more than 140 million people worldwide as of 2018.[3,4]

At the molecular level, arsenic obstructs enzymes that facilitate cellular energy production and DNA repair; it also blocks voltage-gated potassium channels, which leads to cardiovascular and neurological problems. There is also evidence that arsenic induces changes to DNA and gene expression.[4] These mechanisms of action manifest differently for acute and chronic toxicities.

Up until two centuries ago, an unhappy individual would stir arsenic into someone's food or drink and depart satisfied that the additive was effective. That many of these cases involved high-profile deaths contributed to the dramatic sobriquet "king of poisons."[4] The development of the Marsh test and expansion of toxicology accelerated the decline of such nefarious activities. Today, acute arsenic poisoning would most likely occur via oral ingestion of pesticides. While toxicity varies with the type of arsenic compound, the most commonly encountered compound, arsenic trioxide, has a median lethal dose of around 150 mg/kg for adult humans weighing an average of 75 kg.[5] To put this in perspective, imagine a group of one hundred people attending a gathering. Tea is served. If each person added just over two teaspoons of arsenic to a cup of their favorite tea, they would all enjoy their beverages; within a few days' time, fifty of them would perish, but not before undergoing disagreeable effects.

PATHOPHYSIOLOGY

Telltale signs of acute arsenic poisoning involve the digestive system. Most of the arsenic is absorbed in the small intestine, where it then travels to the liver to be

Figure 1: Paris Green. *Paris Green contains harmful levels of arsenic and was once widely used as a pigment and pesticide. Licensed under CC BY-SA 3.0.*

broken into less hazardous compounds.[4] Ingested arsenic will accumulate in high concentrations for a few days before being excreted in urine. Thus, all the aforementioned tea drinkers, including those who survive the acute poisoning, would experience unpleasant symptoms. Even five milligrams of arsenic could induce abdominal pain, diarrhea, nausea, and vomiting. Watery, bloody diarrhea is the characteristic feature of acute poisoning, but other symptoms include weakness, bluish digits, and fluid buildup in the lungs.[6] For those less fortunate, bloody lesions in the gastrointestinal tract and extreme amounts of fluid loss result in dehydration and cardiovascular failure, eventually leading to death.

Unlike the tea drinkers who ingested a single large serving of arsenic, most people encounter arsenic in far smaller dosages, spread over their lifetimes. Known as chronic exposure, this gradual arsenic intake manifests as its own set of symptoms. While abdominal pain and diarrhea are present, chronic exposure also causes affected individuals to develop darkened skin, white lines in nails, and rough patches of potentially cancerous skin growths.[6] However, the most significant long term effects are cancers.

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ARSENIC IN GROUNDWATER

Arsenic works some of its most insidious exposures through groundwater contamination. In the 1970s, researchers in Taiwan noticed considerable disparities in cancer mortality between villages with different concentrations of arsenic in their drinking water.[7] Scientists have since found that elevated levels of arsenic in water lead to the highest known mortality rate for environmental exposures, near the mortality rate from cigarette smoking.[8] Long term health effects persist even decades after exposure to arsenic has been sharply reduced. The risk of fatal heart attacks only lessened ten years after decreased exposure, while lung, kidney, and bladder cancer mortality rates remained high even forty years after. Thus, public health efforts focus on eliminating arsenic from drinking water. South Asia houses some of the world's most severe cases of groundwater arsenic exposure.[9] Some wells in West Bengal, a state in eastern India, have had high concentrations ranging from 60 to more than 300 micrograms of arsenic per liter, far higher than the World Health Organization's recommended upper limit of ten micrograms per liter.[3,10] Such immense concentrations in areas where people rely on wells for drinking, cooking, daily life, and crop irrigation lead to considerable ramifications.

Wells extending into groundwater gained popularity in late-20th century Bangladesh because they were safe from disease-causing microbes present in surface water sources.[1,10] Unfortunately, high concentrations of arsenic posed an unexpected issue as arsenic had not yet been included in water testing procedures.[11] Surveys in the late 1990s estimated that around 20 million people in Bangladesh were consuming contaminated water. The Bangladeshi government identified contaminated wells and encouraged the use of safe water sources, mostly arsenic-safe tube wells. Other options included deeper tube wells reaching into uncontaminated water, rainwater harvesters, and aerated sand filters that adsorb arsenic.[9,10] Despite these federal efforts, around one-third of these arsenic-safe water systems fell into disrepair within a few years.

Since there is currently no treatment for prolonged arsenic exposure, changing water sources has shown the most striking changes in arsenic concentration, followed by maintaining the sources and monitoring the population for adverse health effects.[10,11] The city of Antofagasta in northern Chile has provided an insightful chronicle of arsenic's long-term health effects, especially the consequences of switching to, rather than away from, a contaminated source of water.[8] Arsenic concentration in 1930s Antofagasta had averaged around 90 micrograms per liter. However, the city replaced its source of water in 1958. Arsenic concentrations surged up to 860 micrograms per liter, staying at such astronomical levels until the city installed an arsenic removal plant in 1970. The level then fell to 110 micrograms over the course of the 1970s, and then to 10 micrograms by the early 2000s. Unfortunately, the damage had already been done, and Antofagasta would show high cancer mortality in the decades following its sudden decrease in arsenic exposure.

From an effective means of intentional poisoning to a significant groundwater pollutant, arsenic's role as a toxin has accompanied the shift from acute to chronic exposure. Sinister stories have given way to widespread public health problems and significant mortality, as discovered by epidemiological studies

Figure 2: Medical illustration. *A lithograph from 1859 depicts bodily harm from exposure to green arsenic. Licensed under CC-BY-4.0.*

"Long term health effects persist even decades after exposure to arsenic has been sharply reduced."

on arsenic's long term effects. The most urgent action concerning contaminated groundwater is providing safe water sources to reduce exposure to arsenic.[3] Community involvement and education are needed for successful interventions, while additional studies on arsenic's health effects can determine the impact of reducing exposure. Further research may lead to more successful interventions and author the next chapter of humanity's association with arsenic.

REFERENCES

1. Ferrie, J. E. (2014). Arsenic, antibiotics and interventions. International *Journal of Epidemiology*, *43*(4), 977–982. https://doi.org/10.1093/ije/dyu152
2. Griffin, J. D. (2016). Blood's 70th anniversary: Arsenic—from poison pill to magic bullet. *Blood*, *127*(14), 1729–1730. https://doi.org/10.1182/blood-2015-10-638650
3. World Health Organization. (2018, February 15). *Arsenic*. https://www.who.int/news-room/fact-sheets/detail/arsenic
4. Hughes, M. F., Beck, B. D., Chen, Y., Lewis, A. S., & Thomas, D. J. (2011). Arsenic exposure and toxicology: A historical perspective. *Toxicological Sciences*, *123*(2), 305–332. https://doi.org/10.1093/toxsci/kfr184
5. Benramdane, L., Accominotti, M., Fanton, L., Malicier, D., & Vallon, J. J. (1999). Arsenic speciation in human organs following fatal arsenic trioxide poisoning—A case report. *Clinical Chemistry*, *45*(2), 301–306. https://doi.org/10.1093/clinchem/45.2.301
6. Gehle, K., & Agency for Toxic Substances & Disease Registry. (2009). *Arsenic Toxicity: What are the Physiologic Effects of Arsenic Exposure* [Lecture notes]. Centers for Disease Control. https://www.atsdr.cdc.gov/csem/arsenic/docs/arsenic.pdf
7. Chen, C.-J., Kuo, T.-L., Wu, M.-M. (1988). Arsenic and cancers. *The Lancet*, *331*(8582), 414–415. https://doi.org/10.1016/s0140-6736(88)91207-x
8. Smith, A. H., Marshall, G., Roh, T., Ferreccio, C., Liaw, J., & Steinmaus, C. (2017). Lung, bladder, and kidney cancer mortality 40 years after arsenic exposure reduction. *Journal of the National Cancer Institute*, *110*(3), 241–249. https://doi.org/10.1093/jnci/djx201
9. Ahmad, A., Van Der Wens, P., Baken, K., De Waal, L., Bhattacharya, P., & Stuyfzand, P. (2020). Arsenic reduction to <1 µg/L in Dutch drinking water. *Environment International*, 134, Article 105253. https://doi.org/10.1016/j.envint.2019.105253
10. Ahmad, S. A., Khan, M. H., & Haque, M. (2018). Arsenic contamination in groundwater in Bangladesh: Implications and challenges for healthcare policy. *Risk Management and Healthcare Policy*, *2018*(11), 251–261. https://doi.org/10.2147/RMHP.S153188
11. Smith, A. H., Lingas, E. O., & Rahman, M. (2000). Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. *Bulletin of the World Health Organization*, *78*(9), 1093–1103. https://www.who.int/bulletin/archives/78%289%291093.pdf

IMAGE REFERENCES

1. *Banner*: *Two skeletons dressed as lady and gentleman* [Etching]. (1862). Wellcome Collection. https://catalogue.wellcomelibrary.org/record=b1194600
2. *Figure 1*: Goulet, C. (2008). *Paris Green (Schweinfurter Grün)* [Photograph]. Wikimedia Commons. https://commons.wikimedia.org/wiki/File:Paris_Green_(Schweinfurter_Gr%C3%BCn).JPG
3. *Figure 2*: Lackerbauer, P. (1859). *Annales d'hygiène publique et de médecine légale* [Accidents caused by the use of green arsenic, Lithograph]. Wellcome Collection. https://wellcomecollection.org/works/purtqgwv/images?id=yd6ya82w
4. *Figure 3*: Eishiya. (2017). *Arsenic contamination areas* [Infographic]. Wikimedia Commons. https://commons.wikimedia.org/wiki/File:Arsenic_contamination_areas.png

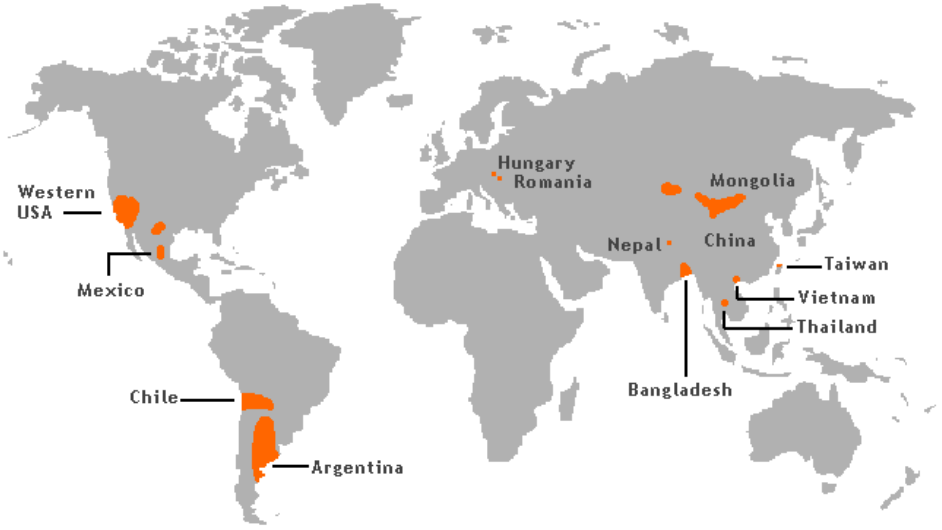

Figure 3: Global distribution of arsenic contamination. *Arsenic-contaminated groundwater in the orange-shaded areas pose disproportionately high levels of health risks to nearby populations. Licensed under CC BY-SA 4.0.*