

## Elevated Blood and Urine Arsenic Levels in Michigan

Reasons that clinicians order arsenic blood or urine levels include: 1) Neurologists when evaluating a patient with a peripheral neuropathy where they have ruled out more common causes of peripheral neuropathy such as diabetes; 2) Occupational doctors when they have a patient/worker exposed to arsenic; 3) Clinicians when requested by their patient because the patient is aware their well water has an elevated arsenic level, or the patient is on a diet where they are eating excessive brown rice; or 4) Clinicians trying to assess exposure to a particular metal such as mercury but the laboratory will not allow testing for a single metal to be ordered and only allows the mercury level to be ordered as part of a heavy metal panel that also includes arsenic.

In 2005, Michigan promulgated a rule that required laboratories to report elevated blood and urine arsenic levels to the state health department (R325.61 - R325.68). These reports have been used to identify public health issues and direct interventions to reduce exposures. Follow up of these arsenic results has provided useful clinical insights.

- 1) The most common source of elevated arsenic levels in individuals tested in Michigan from 2006 - 2024 was from the ingestion of fish; 75.1%, then work exposure 13.9%, then drinking water 5.8%, and then other non-work exposure (e.g., supplements (ayurvedics), rice, spice, herbicide ingestion, wine) 5.2%. Fish, especially shellfish, absorb arsenic from the environment, which accumulates in fish tissue and then is consumed by people. Unlike the mercury found in fish that can cause adverse health effects in humans, approximately 90% of the arsenic found in fish and shellfish is a non-toxic organic form, arsenobetaine, (ATSDR, 2007; Luvonga et al., 2020; Wolle et al., 2019) and no clinical follow up other than reassuring the patient is indicated for elevated levels of organic arsenic. To reduce the need for additional testing and anxiety in patients, clinicians ordering arsenic levels should:
  - Ask patient not to eat seafood for 48 hours prior to blood or urine collection. The half-life of inorganic arsenic in urine is four days and in blood 4-6 hours in contrast to organic arsenic where the half-life in blood is 20-30 hours and 4-6 hours in urine.
  - Currently, all the reference laboratories, except Quest, which analyze for arsenic automatically speciate the results if the total arsenic level is elevated. If the total arsenic level is elevated, clinicians should review the speciated results, which provide the inorganic and organic levels. Only if the inorganic level is elevated, is clinical follow up indicated. Quest has indicated that sometime in 2026 they will begin to routinely speciate arsenic results. Until then, if the total arsenic level is elevated and the testing was done by Quest, the ordering provider needs to ask Quest to speciate the results.
- 2) The likelihood of work-related exposure to arsenic in Michigan is unlikely. There has not been a well-documented case of work-related arsenic poisoning in Michigan identified through the laboratory tracking system. The 13.5% of the cases attributed to work were based on total arsenic levels so the elevated levels could have been from fish ingestion. Previous work-related exposures to arsenic either no longer occur or are less common; the last smelter in the U.S. that produced arsenic closed in 1985, Lead arsenate, an insecticide widely used in apple orchards, was banned in 1988 (the few remaining organic arsenic pesticides have very limited use), Chromium copper arsenate (CCA) a wood preservative that was responsible for 65% of the arsenic used in the US was banned from wood used in residential settings in 2004 and is now limited to industrial uses. The ongoing potential for work-related arsenic exposure in Michigan would be in glass and ceramics manufacturing, production of lead acid batteries, and the manufacturing of semiconductor chips and circuit boards (Baker et al., 2018).

- 3) The symptoms and physical signs of inorganic poisoning occur at higher levels than the 95% confidence limit reference values used by laboratories. This means that usually the treatment of patients with inorganic arsenic above the reference range is to identify the source and cease exposure to arsenic rather than the administration of a chelating agent such as BAL or penicillamine. Most of the acute adverse health effects of inorganic arsenic are non-specific; nausea, vomiting, diarrhea, peeling of the skin, changes in skin pigmentation, tingling in the hands and feet, as is the cardiovascular diseases and cancers of the bladder, skin and lung cancer which are increased in those with chronic arsenic exposure (ATSDR, 2007; Meliker et al., 2006). However, the constellation of subjective symptoms in the presence of the physical findings of Mees lines (horizontal white bands on nails) and keratosis (corn-like, yellowish, hyperkeratotic papules and plaques, primarily affecting the palms and soles) would be an indication of inorganic arsenic toxicity.

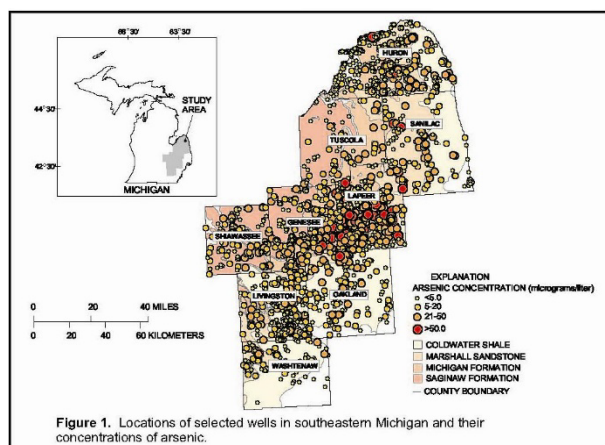
## Arsenic Toxicity

Inorganic arsenic has been known by the Greeks as a poison since the first century. Multiple books have been written about its use as a poison (e.g., *The King of Poison*, *The History of Arsenic*) and in murder mysteries (e.g., *Arsenic and Old Lace*). The minimal lethal oral dose has been estimated to be 130 mg (2 mg/kg). Despite its toxicity, arsenic has had multiple uses including as a foaming agent in beer, to treat psoriasis (Fowler's solution), and to treat syphilis, as a pesticide, as a wood preservative and is still used in certain industrial processes. Arsenic is a naturally occurring element found in water, soil, rocks, and minerals. It is released into the environment from copper and lead mining and ore smelting, and the burning of coal. There are two different types of arsenic compounds, inorganic and organic. Arsenic in combination with elements such as oxygen, sulfur, and chlorine is referred to as inorganic arsenic, whereas arsenic combined with carbon and hydrogen is called organic arsenic.

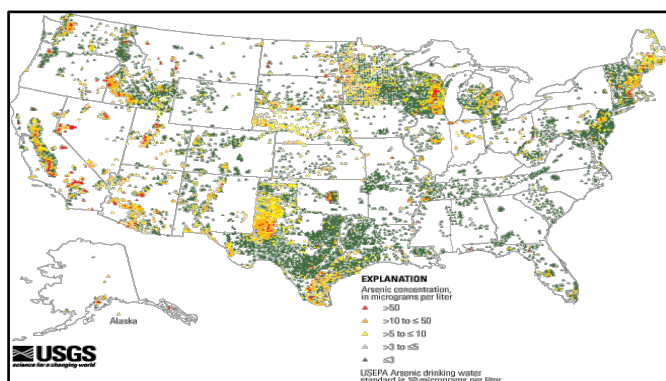
Contaminated drinking water from sandstone bedrock aquifers, with well water concentrations as high as 335ppb was identified as the major source of inorganic arsenic exposure among residents in eleven southeastern Michigan counties (Meliker et al., 2006). The second major source in Michigan was rice consumption, as rice more readily absorbs inorganic arsenic than other grains (Meliker et al., 2006). Brown rice has higher concentrations of inorganic arsenic than white rice because the two outer layers that absorb the arsenic, the bran and germ, are removed during the refining process of white but not brown rice (Su et al., 2023). Besides natural sources, irrigation of crops with groundwater that has been contaminated from old lead arsenate pesticide applications or fallout from emissions of coal burning power plants can increase exposure to people (Shrivastava, 2021).

In the United States, the EPA Safe Drinking Water Act requires drinking water arsenic levels  $\leq 10$ ppb. OSHA has a permissible exposure level of  $10 \mu\text{g}/\text{m}^3$  8-hour time weighted average while NIOSH recommends a maximum level of  $2 \mu\text{g}/\text{m}^3$  over 15 minutes. Figure 1 shows how the thumb area in Michigan has the highest arsenic levels in drinking water in the state and Figure 2 shows how areas of the country with the highest levels.

**Figure 1. Arsenic in Groundwater in Michigan**



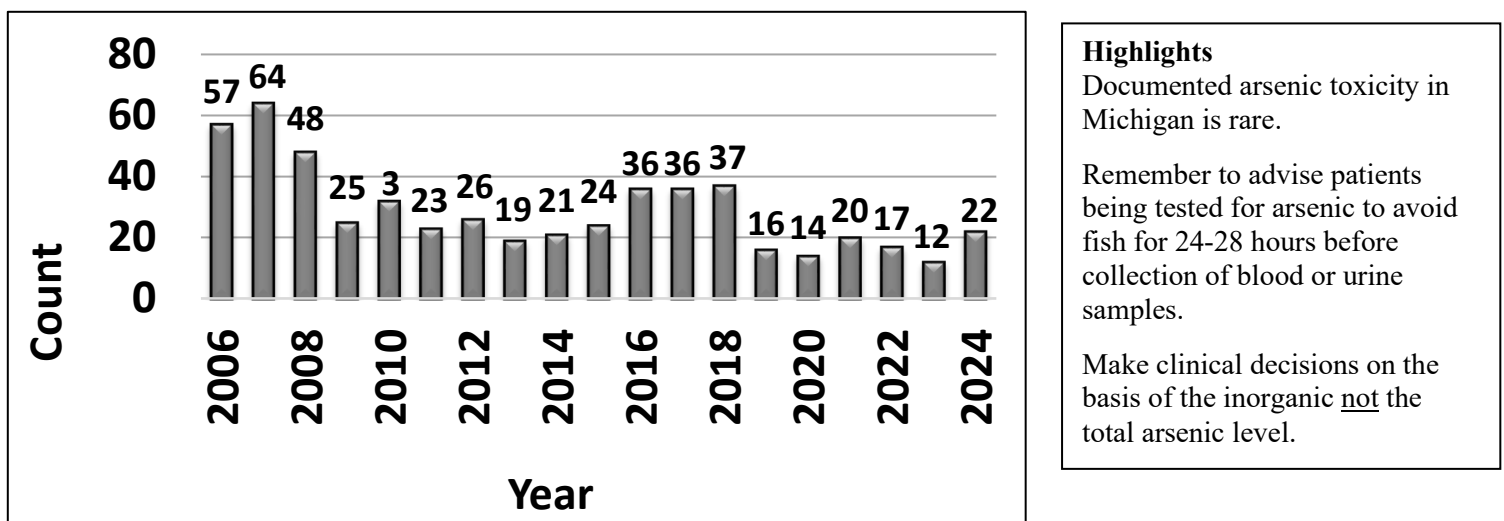
**Figure 2. Arsenic in Groundwater in the United States**



Bangladesh is the country most affected by arsenic-contaminated groundwater with 50 million residents, about one-third of the population, at risk of exposure (Ahmad et al., 2018). In the mid-20<sup>th</sup> century, tubewells were installed across the country in response to the high rates of cholera and other diarrheal diseases that occurred from drinking surface water from nearby rivers, lakes, and ponds. Studies in the late 1990's revealed that about 29% of the tubewells were contaminated with the arsenic concentrations ranging from 100ppb to 300ppb, with the highest concentration identified at 4,700ppb (Ahmad et al., 2018). Rice is a staple food in Bangladesh and increases the exposure to arsenic (Shrivastava, 2021). Adverse health effects reported from arsenic in Bangladesh included reproductive complications, decreased cognitive function, hypertension, changes in skin pigmentation, peripheral neuropathy, non-pitting edema, gangrene, diabetes, peripheral vascular disease, and cancers of the skin and lungs (Ahmad et al., 2018; ATSDR, 2007).

The laboratory reference range varies by lab. For example, the Mayo reference lab will speciate any urine value greater than 10 µg/L, while Quest's normal reference range ≤80 µg/L. To prioritize follow up on elevated results, a higher threshold level was used; Blood levels >70 µg/L for all and urine levels >100 µg/L for adults and >50 µg/L in children under the age of 18 for total arsenic. From 2006-2024, 554 individuals had 611 elevated blood or urine arsenic tests. Of the 554 individuals, 329 (59.4%) were male and (95.8%) were ≥18 years. The total number of individuals with elevated blood or urine arsenic levels that exceeded the action thresholds trended downward from 2006 but plateaued since 2019 (Figure 3). Most individuals (97.8%) had a urine test for arsenic and almost all the elevated levels were for total, non-specified arsenic (99.8%).

**Figure 3. Number of Individuals with Elevated Arsenic Levels above Action Thresholds, Michigan 2006-2024**



Contact Kenneth Rosenman MD if you have questions about diagnosing or managing a patient with possible arsenic toxicity, [rosenman@msu.edu](mailto:rosenman@msu.edu), 1-800-446-7805.

## References

- Ahmad SA, Khan MH, Haque M. Arsenic contamination in groundwater in Bangladesh: Implications and challenges for healthcare policy. *Risk Management and Healthcare Policy* 2018;11: 251–261.
- Baker BA, Cassano VA, Murray C, ACOEM Task Force on Arsenic Exposure. Arsenic Exposure, Assessment, Toxicity, Diagnosis, and Management: Guidance for Occupational and Environmental Physicians. *J Occup Environ Med* 2018; 60: e634–e639.
- Hardin J, Seltzer J, Suhandynata R, Spiegel B, Silver R, Thomas D, et al. Severe arsenic poisoning due to Ayurvedic supplements. *Clin Case Rep* 2023 Jul 23;11(7):e7733.
- Luvonga C, Rimmer CA, Yu LL, Lee SB. Organoarsenicals in Seafood: Occurrence, Dietary Exposure, Toxicity, and Risk Assessment Considerations – A Review. *J Agr Food Chem* 2020;68:943–960.
- Meliker, J R, Franzblau A, Slotnick MJ, Nriagu JO. Major contributors to inorganic arsenic intake in southeastern Michigan. *Int J Hyg Environ Health* 2006;209:399–411.
- Shrivastava A. Dietary Arsenic Exposure: Sources and Risks. In N. Kumar (Ed.), *Arsenic Toxicity: Challenges and Solutions*. pp. 95–125. Springer Nature.
- Su LJ, Chiang TC, O'Connor S N. Arsenic in brown rice: Do the benefits outweigh the risks? *Front Nutr* 2023;10:1209574.
- Wolle MM, Stadig S, Conklin SD. Market Basket Survey of Arsenic Species in the Top Ten Most Consumed Seafoods in the United States. *J Agr Food Chem* 2019; 67:8253–8267.

Michigan Thoracic Society