

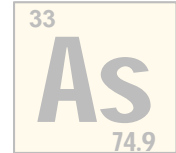


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## INFORMATION FOR HEALTH CARE PROFESSIONALS ARSENIC EXPOSURE & TOXICITY

*Revised: January 2009*

This document is designed for health care providers and summarizes information on the sources, exposure pathways, laboratory testing, recognition, and reporting of arsenic exposure and/or poisoning. Louisiana Law requires the [reporting](#) of all cases of arsenic poisoning and all arsenic laboratory test results to the Louisiana Department of Health and Hospital's Office of Public Health.



### EXPOSURE TO ARSENIC

Arsenic is a naturally occurring metal released into the environment by natural and unnatural (industrial and commercial) processes. Arsenic compounds can be classified into three major forms: inorganic, organic, and arsine gas.

Inorganic arsenic may be formed with either trivalent (+3, arsenite) or pentavalent (+5, arsenate) arsenic. The most common inorganic trivalent arsenic compounds are arsenic trioxide, sodium arsenite, and arsenic trichloride. Pentavalent inorganic compounds are arsenic pentoxide, arsenic acid, and arsenates such as lead arsenate and calcium arsenate. Inorganic arsenic compounds are used in metal alloy manufacturing, electronics manufacturing (semiconductors), and as wood preservatives. They are also formed as by-products during the smelting of metals and coal combustion (ATSDR, 2007).

Organic arsenic compounds are formed when arsenic combines with carbon. Organic arsenic compounds may be trivalent (+3, arsenite) or pentavalent (+5, arsenate). Most organic arsenic compounds found in the environment are methylated as a result of biomethylation by organisms in soil or water. Organic arsenics, such as disodium methylarsenate (DSMA) and monosodium methylarsenate (MSMA), are used as herbicides. Organic arsenic compounds are registered for use as medicinal animal feed additives. Arsenobetaine or "fish arsenic", an organic form of arsenic, is found in seafood and is nontoxic (ATSDR, 2007).

Arsine gas is formed by the reaction of hydrogen with arsenic and can have a garlic-like or fishy odor at high concentrations. Arsine gas is used commercially in the semiconductor industry, during the synthesis of organic arsenic compounds, and in the manufacture of crystals for computer chips and fiber optics. Arsine gas can be generated accidentally during the smelting and refining of nonferrous metals and in mining processes.

**Occupational Exposure:** Exposure to arsenic may occur in several industries: refining or smelting of metal ores, microelectronics, wood preservation, wood joinery shops, battery manufacturing, and working in power plants that burn arsenic-rich coal. Occupational exposure occurs primarily through inhalation of dust or fumes containing inorganic arsenic. Ingestion and dermal exposure to inorganic and organic arsenic compounds may occur in certain situations. Most occupational exposure to arsine occurs following inhalation of the gas that has been accidentally generated when arsenic-containing crude ores or metals are treated with acid. Acute high-dose exposures to arsine gas can be particularly harmful. It is rare for workers to be exposed to arsenic alone. The exposure usually occurs in combination with other metals (ATSDR, 2007).

Occupational Exposures to Arsenic			
	Arsine Gas	Inorganic Arsenic	Organic Arsenic
Battery Manufacturing		X	
Camera, watch, and musical instrument repair	X		
Coal-fired power plant	X	X	
Electrical and electronic technicians	X	X	
Electronics manufacturing (semiconductors, solar cells, space research)	X	X	X
Furnace, kiln, and oven operators	X		
Glass manufacturing (decolorizer, fining agent)		X	
Grinding/abrading/polishing machine operators		X	X
Industrial truck and tractor equipment operators		X	
Mechanical engineers		X	
Metal Plating		X	
Pesticide manufacturing/application	X		X
Painting and paint spraying machine operators, paint manufacturing	X	X	
Smelting/Refining non ferrous metals	X	X	
Soldering/brazing	X	X	
Use/manufacture of arsenic-treated wood		X	

This is not a complete list of exposure sources. The above information was compiled from: CDC, 1983; ATSDR, 2007.

**Take-Home Exposure:** Workers can transport arsenic on shoes and work clothes into their homes or automobiles (NIOSH, 1997). "Take-home" arsenic puts children and spouses at risk for arsenic exposure.

Steps to prevent take-home arsenic contamination:

- Change shoes and clothes at work before getting into the car or going home. Put dirty work clothes and shoes in a plastic bag.
- Wash face and hands prior to leaving work.
- Shower and wash hair immediately upon arriving home (or before leaving work).
- Wash work clothes separately from all other clothes and run the washing machine again to rinse residual arsenic.

**Exposure Risks to the General Population:** The general population may be exposed to small amounts of arsenic through ingestion of arsenic-containing drinking water and in some food, particularly seafood. High levels of naturally occurring arsenic are found in soil and rocks in some areas of the country; this arsenic may lead to unacceptable levels of arsenic in drinking water that may require action. There are arsenic regulations for public water systems and there are no risks for people drinking from a public water system. Arsenic is present in fish and other seafood, however it exists primarily in an organic form, arsenobetaine, which is non-toxic and is rapidly excreted in urine (ATSDR, 2007).

Other non-occupational sources of exposure also exist. Sawing or burning arsenic-treated wood (e.g. CCA-treated wood) could result in inhalation of arsenic-containing sawdust or smoke. Some folk medicines, herbal preparations and non-regulated supplements may contain arsenic. People who live near hazardous waste sites, landfills, or industrial arsenic sources (smelting operations, coal-burning power plants) may also be at an increased risk of exposure

Environmental Sources of Arsenic
Contaminated drinking water
Wood working/building/remodeling with arsenic-treated wood
Burning of arsenic-treated wood or coal in the home
Paints/pigments
Asian homeopathic medicines, folk remedies-asiatic pill, yellow root
Antiparasitic drugs-carbasone
Kelp-containing health foods (mainly organic)
Fish (organic)
Gardening- herbicides, (organic)

This is not a complete list of potential exposure sources. Unless otherwise noted, the above are sources of inorganic arsenic exposure. This information was compiled from ATSDR, 2007.

through air, soil, dust, or water contamination (ATSDR, 2007). Another consideration in evaluating arsenic exposure is the possibility of intentional poisoning. Arsenic has been a classic poison for suicidal, malicious or homicidal intent.

**Arsenic Toxicity in Children:** Children may be exposed to arsenic from environmental sources. In the past, some playground equipment was made of green wood, or pressed wood treated with chromated copper arsenate (CCA). It is possible for arsenic to leach from CCA-treated wood into the soil. Children who play on or near these wooden structures may ingest arsenic-containing residue, dust, or soil via hand-to-mouth activity. Ingestion of contaminated soil may also be a concern for children who live near hazardous waste sites, landfills, or industrial arsenic sources.

Health effects in children are similar to those in adults and include irritation of the GI tract, vascular damage, skin changes, and reduced nerve function. There is evidence that children may be less efficient at converting inorganic arsenic to the less harmful organic forms. For this reason, children may be more susceptible to health effects from inorganic arsenic than adults (ATSDR, 2007).

**Special Considerations for Adults of Reproductive Age:** There is suggestive evidence that arsenic can interfere with normal fetal development, however, these data are inconclusive. Inorganic arsenic crosses the placenta and has been found in fetal tissue. Umbilical cord blood levels of arsenic are similar to maternal blood levels and arsenic is found at low levels in breast milk. Chronic exposure of humans to inorganic arsenic in drinking water has been associated with an increased incidence of miscarriages, stillbirths, preterm births, and infants with low birth weights. Studies in animals demonstrate large doses of inorganic arsenic that cause illness in pregnant females can also cause low birth weight, fetal malformations, and even fetal death (ATSDR, 2007).

## TOXICITY OF ARSENIC

The toxicity of arsenic varies widely based on route of exposure and form. Ingestion and inhalation are the primary routes of both acute and chronic exposures; inorganic arsenic is not readily absorbed by the skin. Arsine gas is one of the most toxic forms and is readily absorbed into the body by inhalation. Inorganic forms of arsenic are more toxic than organic forms. Of inorganic arsenic compounds, the more toxic trivalent form reacts with sulfhydryl groups causing enzyme disruption and reduced oxidative phosphorylation; the pentavalent form is less toxic and, through phosphorus substitution, "uncouples" oxidative phosphorylation.

Toxicology quick facts about arsenic:

- Arsine gas is extremely toxic.
- Inorganic arsenics are more toxic than the organic forms.
- Trivalent arsenic compounds tend to be more toxic than pentavalent arsenic compounds.
- Metalloid arsenic is nontoxic because it is insoluble in water and body fluids.
- Arsenobetaine is the primary form of arsenic found in fish and is nontoxic.

**Inorganic Arsenic:** Often, there will be a garlic smell to the breath and tissue fluids of people exposed to inorganic arsenic. Effects of acute inorganic arsenic poisoning include fever, anorexia, hepatomegaly, melanosis, cardiac arrhythmia and eventual cardiovascular failure, upper respiratory track symptoms, peripheral neuropathies, gastrointestinal and hematopoietic effects. Sensory loss in the peripheral neurons may appear 1-2 weeks after large exposures. Dermal contact with high concentrations of inorganic arsenic compounds may result in skin irritation, redness, and swelling. High acute exposures may cause cholera-like gastrointestinal symptoms of vomiting (often times bloody) and severe diarrhea (which may be rice-watery in character and often bloody); these patients will experience acute distress, dehydration (often), and hypovolemic shock. Ingestion of large doses of inorganic arsenic (70 to 180 mg) may be fatal (ATSDR, 2007).

Chronic toxicity is insidious as the symptoms are vague and take time to appear. Dermal or neurological symptoms may occur. Dermal effects may include hyperpigmentation with a classical "raindrops on a dusty road" appearance, a characteristic pattern of darkened skin patches with scattered pale spots. Hyperkeratosis, may follow with small "corns" or "warts", appearing most often on the palms, soles and torso. Peripheral neuropathy may appear with painful paresthesia that is symmetrical and stocking-glove in distribution. Neurotoxicity begins with sensory changes, paresthesia and muscle tenderness, followed by weakness which progresses from proximal to distal muscle groups. Whitish lines (Mees lines) may be seen on the fingernails. Chronic hepatic and renal damage is common; jaundice may occur with liver injury.

**Basic mechanisms of inorganic arsenic toxicity:** Trivalent arsenic inhibits numerous cellular enzymes through sulfhydryl group binding. Trivalent arsenic inhibits cellular glucose uptake, gluconeogenesis, fatty acid oxidation, and decreases production of cellular ATP and further production of acetyl CoA. Trivalent arsenic also blocks the production of glutathione, which prevents cellular oxidative damage. Effects of pentavalent inorganic arsenic are partially due to its transformation to trivalent arsenic. The most important mechanism of pentavalent arsenic results from its similarity to inorganic phosphate and the potential for it to substitute for phosphate in glycolytic and cellular respiration pathways. Arsenic cannot form the high-energy phosphate bonds that are needed and oxidative phosphorylation is uncoupled. Therefore, ATP with its high-energy phosphate bonds is not formed. Because arsenic affects these fundamental mechanisms, very few organ systems are unaffected by arsenic. The signs and symptoms of arsenic may vary with the route of exposure, the dose, the duration of exposure, and the time elapsed since the exposure.

**Arsine Gas:** Arsine gas is the most acutely toxic form of arsenic. Symptoms are often delayed 2-24 hours after exposure and manifest with an acute hemolytic anemia and striking chills. Initial symptoms include chills, malaise, dizziness, nausea, abdominal pain and dyspnea, bloody urine, and jaundice. Hemoglobinuria causes the urine to appear black. Hemolysis leads to hypoxia and ultimately renal failure. Chronic exposure to arsine gas is rare. Of the few reported cases, symptoms include a progressive drop in the number of red blood cells, shortness of breath on exertion, and a general feeling of weakness (ATSDR, 2007).

**Organic Arsenic:** Most of the available information regarding arsenic toxicity in humans involves exposure to inorganic arsenic compounds or arsine gas. Laboratory studies suggest organic compounds are less toxic than inorganic compounds and that some organic arsenic compounds (such as those found in fish) are virtually nontoxic. However, very high doses of certain organic compounds may be metabolized to inorganic arsenic and result in some of the same effects as exposure to inorganic compounds: nerve injury, stomach irritation, and lung irritation.

**Carcinogenesis:** Arsenic has been classified as a known human carcinogen by multiple agencies based on the increased prevalence of lung and skin cancer observed in human populations exposed to arsenic. Ingestion of arsenic has been primarily associated with an increased risk of skin cancer. Inhaled arsenic has been associated with an increased risk of lung cancer (ATSDR, 2007).

Possible Health-Effects of Arsenic Exposure in Adults		
	Acute	Chronic
<b>Inorganic</b>	Neurological: light-headedness, headache, weakness, lethargy, delirium, encephalopathy, convulsions, coma, peripheral neuropathy	Peripheral and CNS: paraesthesia, muscle tenderness, muscle weakness, peripheral neuropathy, anorexia
	Hepatic and renal effects: elevated liver enzymes, oliguria, proteinuria, acute tubular necrosis, renal cortical necrosis	Hepatic jaundice, cirrhosis, ascites
	Cardiovascular and respiratory hypotension, shock; ventricular arrhythmia; congestive heart failure; pulmonary edema	Peripheral vascular disease; acrocyanosis, Raynaud's phenomenon, endarteritis obliterans
	GI: abdominal pain, nausea, vomiting, bloody stools, gastroenteritis	GI hemorrhagic gastroenteritis
	Hematological: anemia, leukopenia, thrombocytopenia	Dermal: hyperpigmentation, hyperkeratosis of hands/feet
	Death	Metallic taste, garlicky breath Diabetes mellitus Mees lines
		Increased risk of skin, lung, liver, kidney and bladder cancers, lymphomas and leukemias
<b>Arsine Gas</b>	Hemolytic anemia, chills, malaise, nausea, vomiting, abdominal pain, jaundice, renal failure	Shortness of breath, general feeling of weakness

Information obtained from: ATSDR, 2007 WHO, 2000, 2001.

## EVALUATION OF ARSENIC POISONING

Assessment of a patient for arsenic poisoning requires the following

- Work history and identification of possible arsenic exposure sources
- Medical history
- Laboratory testing for arsenic

**Work and Exposure History:** Often, patients do not recognize that they have been exposed to arsenic unless directly asked about their work environment and activities. A detailed occupational and environmental exposure history is a fundamental step toward acquiring information on possible exposure to arsenic.

- A full work history is necessary to identify jobs with possible arsenic exposures. Ask patients about their job (where they work and what they do), potential exposure occurring in current and previous jobs, hygiene practices in the workplace, and use of any personal protective equipment. If the individual is employed in a job that may involve exposure to arsenic, further questions on length of time at the job, frequency of tasks handling arsenic materials, and descriptions of how they carry out their work should be asked.
- An environmental history can identify other potential exposure sources. Questions about recent activities associated with arsenic provide information on possible risks. Questions may include: sawing or burning of arsenic-treated wood in the home; use of folk remedies (e.g. "Asiatic pill", kushta, yellow root); spouse's occupation and the potential for "take-home" arsenic exposure; and proximity of residence to hazardous waste sites, smelting operations, or other industries.

The Agency for Toxic Substances & Disease Registry (ATSDR) offers a self-instructional module on "[Taking an Exposure History](#)" which provides an exposure history form in Appendix 1 of the document.

**Medical History:** A medical history may help recognize possible symptoms associated with arsenic poisoning. Health effects of arsenic poisoning may include respiratory irritation, nausea, skin effects, and neurological effects. Laboratory testing for arsenic should be considered if the exposure history indicates possible arsenic exposure and/or the patient is experiencing symptoms that suggest possible arsenic poisoning. A laboratory test is the only means to confirm arsenic exposure.

**Laboratory Tests:** Detection of arsenic in blood and urine will confirm recent arsenic exposure. Interpretation of the results of arsenic testing must take into account toxicokinetics as arsenic is rapidly cleared from the body. Arsenic is deposited in hair and nails, however, the results of hair or fingernail analysis must be interpreted carefully.

- **Urinary Arsenic** is the most reliable means of detecting arsenic exposures occurring within the last several days. A urine spot test can be helpful in identifying elevated arsenic levels and a 24-hour urine collection for total arsenic excretion can be diagnostic. Urinary levels of arsenic may drop rapidly in the first 24 to 48 hours after an acute exposure or cessation of exposure. Elevated arsenic levels over time indicate an ongoing source of exposure. If a single urine test is high, a second test should be repeated within 2 weeks to determine if exposure is ongoing.

Critical Interference: Urine tests that monitor total arsenic can be misleading. Nutritional sources of arsenic, particularly seafood, are detected in total urine arsenic measurements and can lead to erroneously high levels of arsenic that may be diagnosed as arsenic poisoning. To determine the level of inorganic arsenic, the laboratory must "speciate" the arsenic into organic and inorganic fractions. Inorganic arsenic is responsible for the adverse health effects. Metabolites of inorganic arsenic can be separated from the nontoxic dietary organic forms (arsenobetaine and arsenocholine). It is imperative to ask the laboratory to speciate the arsenic as this is not routinely done in many laboratories. Failure to speciate and using total arsenic levels may lead to the misdiagnosis of arsenic poisoning and result in unnecessary treatment of patients. It is important to inquire about recent diet or advise individuals not to ingest seafood for at least 3 days prior to testing. If they have, it should be noted.

- **Arsenic in Blood** is rapidly cleared, is only useful for very recent exposures, and is not a useful indicator of chronic low level arsenic exposure. The reported half-life of arsenic in blood immediately following ingestion is hours, while whole-body clearance may be days or months and is dose-related.
- **Complete Blood Count:** As with many heavy metals, microcytic hypochromic anemia is common and a CBC with indices and reticulocyte is useful. Acute hemolytic anemia occurs with arsine gas exposure

- **Arsenic in Hair and Nails:** Arsenic may be detected in hair and nails of *chronically* exposed people and has been used to effectively identify arsenic poisoning post-mortem. Interpretation of levels of arsenic in hair or nails of living people need to be subjected to several factors: 1) the results are qualitative as there is wide variability in the growth of both hair and nails among individuals, seasons, type and color of hair; 2) the pharmacokinetics of deposition of arsenic in hair and nails has not been established; 3) few laboratories are capable of quantitative analysis due to difficulties in extraction and analysis; 4) there are no standards for comparison to determine relative levels; and 5) external contamination occurs from hair products, air pollution, and other sources.

## HEALTH-BASED REQUIREMENTS, RECOMMENDATIONS & GUIDELINES

**Occupational Safety and Health Administration:** The Occupational Safety and Health Administration (OSHA) promulgates and enforces regulations for toxic substances in the workplace. These regulations are enforceable by law. OSHA regulations are based on both air monitoring and biological monitoring of the worker. Air monitoring provides data on work place conditions, guides industrial hygiene measures and serves as the basis for requiring medical/biological monitoring of workers. Biological monitoring measures the uptake of arsenic into the body, reflects actual exposure and is used to assess health risk to workers (OSHA, 2004).

### Inorganic Arsenic Compounds

- OSHA promulgates and enforces regulations on **inorganic arsenic** exposure in the workplace.
- Workers exposed to levels of airborne arsenic levels  $> 5 \mu\text{g}/\text{m}^3$  (eight-hour time-weighted average) for more than 30 days per year must be placed in a medical surveillance program.
- Biological monitoring of arsenic levels is not explicitly required by this standard.

### Organic Arsenic Compounds

OSHA is currently developing medical surveillance regulations for individuals occupationally exposed to organic arsenic compounds. Until a complete standard is promulgated, OSHA has put-forth **recommended guidelines** for protection from the risk of illness resulting from exposure to organic arsenic:

- Workers cannot be exposed above the permissible exposure limit (PEL) of  $0.5 \text{ mg}/\text{m}^3$  of air expressed as a time-weighted average concentration for an 8-hour period.
- Organic arsenic can be measured in the urine. A biological exposure index (BEI) of  $50 \mu\text{g}/\text{gram}$  of creatinine should be used for exposure to organic arsenic compounds.

**American Conference of Governmental Industrial Hygienists:** The American Conference of Governmental Industrial Hygienists (ACGIH) is a non-profit, nongovernmental scientific organization which develops peer-reviewed guidelines for workplace exposures. These guidelines are considered best practices for protecting workers health, but are not legally enforceable (ACGIH, 2003).

- ACGIH develops Biological Exposure Indices (BEIs<sup>®</sup>) as guidance values for assessing biological monitoring results. The BEI<sup>®</sup> generally indicates a concentration below which nearly all workers should not experience adverse health effects.
- BEIs<sup>®</sup> are considered best practices, but are not legally enforceable.
- ACGIH has developed a BEI<sup>®</sup> of  $35 \mu\text{g}/\text{L}$  for inorganic arsenic and methylated-arsenic metabolites in urine.

**Centers for Disease Control and Prevention:** The US Public Health Service agencies provide guidance and set national goals for improving health and preventing disease and injury. The Centers for Disease Control and Prevention (CDC) has established **clinical case definitions** for chemical poisoning involving arsenic compounds for the general population. These definitions are based on biological monitoring results.

- A case of inorganic arsenic poisoning is confirmed when urinary arsenic levels are  $>50 \mu\text{g}/\text{L}$ .
- A case of arsine poisoning might be indicated when urinary arsenic levels are  $> 50 \mu\text{g}/\text{L}$  and signs of hemolysis are observed.

## Louisiana Arsenic Poisoning Reporting Requirements

The State of Louisiana mandates that all cases of arsenic poisoning and all laboratory arsenic test results (regardless of the arsenic levels) are reported to the Louisiana Office of Public Health. Arsenic poisoning cases are defined as, “any medical condition/visit resulting from exposure as determined from the exposure history or patient statement and/or acute, subacute, or chronic illness or injury resulting from inhalation, ingestion, dermal exposure or ocular contact.”

Cases of arsenic poisoning in adults and children must be reported to the Office of Public Health’s Section of Environmental Epidemiology and Toxicology via

fax (504)219-4582

telephone 888-293-7020 (business hours) or (504)219-4518

[Reporting Form](#)

### ACUTE MEDICAL MANAGEMENT GUIDELINES

The Agency for Toxic Substances and Disease Registry (ATSDR) has published [Medical Management Guidelines](#) for acute exposure to arsine gas and arsenic trioxide. These guidelines were developed to aid emergency department physicians and other emergency healthcare professionals who manage acute exposures resulting from chemical incidents. They provide instruction on effective decontamination of patients, protection from contamination during treatment, efficient transport of patients to a medical facility, and medical evaluation and treatment recommendations.

### CONTINUING EDUCATION

The Agency for Toxic Substances & Disease Registry (ATSDR) offers self-instructional [Case Studies in Environmental Medicine](#) designed to increase the health care provider’s knowledge of arsenic (and other hazardous substances) in the environment and to aid in the evaluation of potentially exposed patients. Continuing medical education credits, continuing nursing education units, and continuing education units are offered by ATSDR in support of this series.

### SOURCES OF INFORMATION

The [Agency for Toxic Substances and Disease Registry](#) (ATSDR) is a federal public health agency focused on providing trusted health information to prevent harmful exposures and diseases related to toxic substances. Succinct fact sheets, detailed documents, and educational resources regarding [arsenic](#) and [arsine](#) exposure and toxicity can be found on their website.

The [Electronic Library of Construction Occupational Safety and Health](#) (eLCOSH), developed and maintained by The Center for Construction Research and Prevention, provides accurate, user-friendly information about the safety and health of construction workers including two articles explaining the dangers of working with wood that has been preserved with arsenic compounds entitled “Hazards of Pressure-Treated Lumber” and “Wood Worries”.

The [US Environmental Protection Agency](#) provides the general public and professionals with information about arsenic hazards in drinking water and their prevention.

The [National Institute for Occupational Safety and Health](#) (NIOSH) is a federal agency established to help assure safe and healthful working conditions by providing research, information, education, and training in the field of occupational safety and health. Information on occupational arsenic exposure and take-home arsenic can be found on their website.

The [US Department of Labor’s Occupational Safety & Health Administration](#) (OSHA) develops and enforces regulations for toxic substances in the workplace. Occupational standards and medical monitoring standards for occupational arsenic exposure can be found on their website.

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