

This document provides guidelines to all Florida County Health Departments (CHDs) about the interpretation and use of case report forms developed for arsenic poisoning reporting. These guidelines will help to identify cases and to report them in a systematic manner so that control measures can be initiated promptly and effectively.

I. General Information: Arsenic: ¹

A. Acute Exposure

Acute arsenic poisoning rarely occurs in the workplace today; it usually results from unintentional ingestion, suicide, or homicide. The fatal dose of ingested arsenic in humans is difficult to determine from case reports and depends upon many factors (*e.g.*, solubility, valence state, etc.). The signs and symptoms of acute arsenic poisoning include the following:

- Gastrointestinal: severe abdominal pain, nausea and vomiting, and bloody or rice-water diarrhea
- Cardiovascular and respiratory: hypotension, shock; ventricular arrhythmia; congestive heart failure; and pulmonary edema
- Neurologic: light-headedness; headache; weakness, lethargy; delirium; encephalopathy; convulsions; coma; and sensorimotor peripheral neuropathy
- Hepatic and renal: elevated liver enzymes; hematuria, oliguria, proteinuria; and acute tubular necrosis, renal cortical necrosis
- Hematologic: anemia, leukopenia, thrombocytopenia, and disseminated intravascular coagulation
- Other: rhabdomyolysis*, garlic odor on the breath, and delayed appearance of transverse white striae (pale bands) on the nails called Mees lines.

As a result of inorganic arsenic's direct toxicity to the epithelial cells of the gastrointestinal tract and its systemic enzyme inhibition, profound gastroenteritis, sometimes with hemorrhage, can occur within minutes to hours after acute ingestion. Symptoms may last for several days. Difficulty in swallowing, abdominal pain, vomiting, diarrhea, and dehydration may result. In subacute poisoning, however, the onset of milder GI symptoms may be so insidious that the possibility of arsenic intoxication is overlooked.

Arsenic has deleterious effects on the heart and peripheral vascular system. Capillary dilation with fluid leakage may cause severe hypovolemia and hypotension. Cardiac manifestations have included cardiomyopathy, ventricular dysrhythmias (atypical ventricular tachycardia and ventricular fibrillation), and congestive heart failure.

- Onset of peripheral neuropathy may be delayed several weeks after the initial toxic insult.

A delayed sensorimotor peripheral neuropathy may occur after acute arsenic poisoning. Symptoms are initially sensory and may begin 2 to 4 weeks after resolution of the first signs of intoxication resulting from ingestion (shock or gastroenteritis).

(* Rhabdomyolysis is an acute, fulminant, potentially fatal disease that destroys skeletal muscle and is often accompanied by the excretion of myoglobin in the urine.)

Commonly reported initial symptoms include numbness, tingling and "pins and needles" sensations in the hands and feet in a symmetrical "stocking-glove" distribution, and muscular tenderness in the extremities. Clinical involvement spans the spectrum from mild paresthesia with preserved ambulation to distal weakness, quadriplegia, and, in rare instances, respiratory muscle insufficiency.

Other findings in acute arsenic poisoning may include fever and facial edema.

Several months after poisoning, Mees lines (or Aldrich-Mees lines) may be seen, reflecting transient disruption of nail plate growth during acute poisoning. In episodes of multiple acute exposures, several Mees lines may occur within a single nail. In some cases, the distance of the lines from the nail bed may be used to roughly gauge the date of the poisoning episode. However, Mees lines are not commonly seen; of 74 patients with acute and chronic arsenic poisoning, Mees lines occurred in only 5% of the patients.

Respiratory tract irritation (cough, laryngitis, mild bronchitis, and dyspnea) may result from acute exposure to airborne arsenic dust. Nasal septum perforation, as well as conjunctivitis and dermatitis, has also been reported.

The toxicity of arsine gas is quite different from the toxicity of other arsenicals, requiring different emphases in the medical history, physical examination, and patient management. Arsine is most commonly used in the semiconductor and metals refining industries.² Arsine is a powerful hemolytic poison in both acute and chronic exposures. The clinical signs of hemolysis may not appear for up to 24 hours after acute exposure, thereby obscuring the relationship between exposure and effect. Initial symptoms of arsine poisoning may include headache, nausea, abdominal pain, and hematuria.

B. Chronic Exposure

- Neuropathy may be the first sign of chronic arsenic toxicity.

Skin lesions and peripheral neuropathy are the hallmarks of arsenic ingestion, and their presence should result in an aggressive search for this etiology. Neuropathy can occur insidiously in chronic toxicity without other apparent symptoms. However, careful evaluation usually reveals signs of multiorgan and multisystem involvement such as anemia, leukopenia, skin changes, or elevated liver function tests.

- Hyperpigmentation and hyperkeratosis are delayed hallmarks of chronic arsenic exposure.
- Anemia often accompanies skin lesions in patients chronically poisoned by arsenic.

Manifestations of chronic arsenic ingestion depend on both the intensity and duration of exposure. An intense exposure of several milligrams a day results in anemia, neuropathy, and hepatotoxicity within a few weeks to months. Hematologic and neurologic signs may occur after a similar latency period. Skin lesions, however, take longer to manifest (3 to 7 years for pigmentation changes and keratoses; up to 40 years for skin cancer) and may occur after lower doses than those causing neuropathy or anemia.

- Lung cancer and skin cancer are serious long-term concerns in cases of chronic arsenic exposure.

Chronic arsenic dust inhalation may be accompanied by upper respiratory symptoms, nasal perforation, and lung cancer; however, since permissible workplace arsenic levels have been lowered, these conditions are rarely encountered in workers.

II. Case Classification

A. Arsenic Poisoning:

Clinical Description

Arsenic intoxication may affect multiple organ systems. Acute exposure to toxic amounts of arsenic may include signs and symptoms such as vomiting, abdominal pain, diarrhea, light-headedness, headache, weakness, and lethargy. These signs and symptoms may rapidly lead to dehydration, hypotension, pulmonary edema, congestive heart failure and shock. Different clinical manifestations might follow, including dysrhythmias (prolonged QT, T-wave changes), altered mental status, and multisystem organ failure which may ultimately lead to death.

Laboratory criteria for diagnosis

Elevated inorganic or total urinary arsenic levels (>50 µg/L total for a 24-hr urine) as determined by laboratory test.

If laboratory results for urine are reported in µg As/g creatinine (mcg/g creat) and are >15 µg/g creatinine, then results must be converted to µg As/Liter of urine using the following formula and conversion factor.

$$\frac{\text{_____}}{\text{given}} (\mu\text{g As/g creat}) \times \frac{\text{_____}}{\text{given}} (\text{mg creat/dL}) \times 0.01 = \frac{\text{_____}}{\text{calculated}} (\mu\text{g As/Liter urine})$$

Case classification

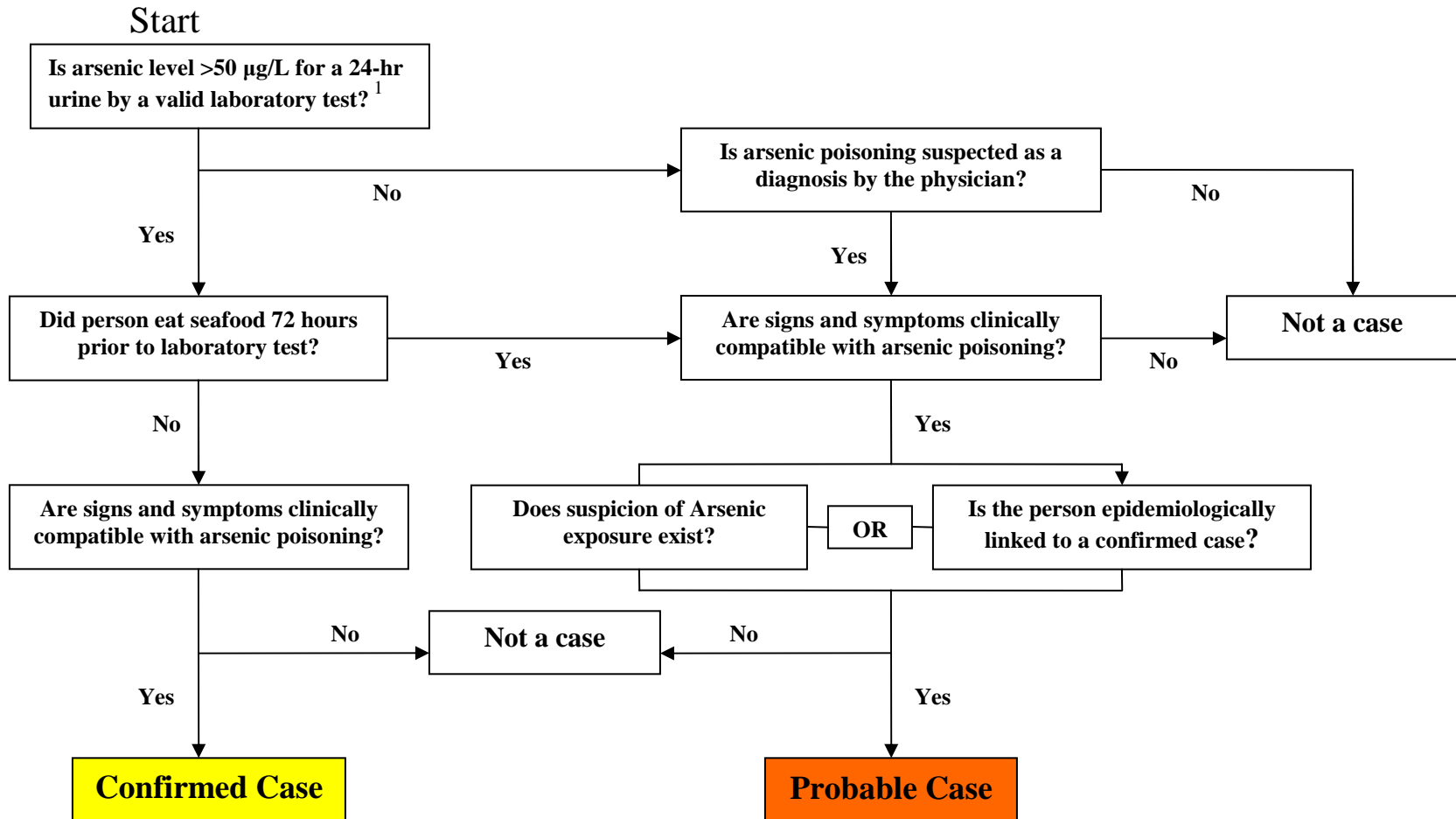
Confirmed: a clinically compatible case that meets the laboratory criteria for diagnosis.

Probable: a clinically compatible case in which a high index of suspicion, (patient's exposure history regarding location and time) exists or an epidemiologic link exists between this case and a confirmed case.

Comment

Most cases of arsenic-induced toxicity in humans are due to exposure to inorganic arsenic. Humans may be exposed to organic arsenicals used in agriculture or those found in fish and shellfish. Organic arsenic found in fish is not believed to be toxic. Total arsenic tests do not distinguish between organic and inorganic arsenic (the more toxic form). For this reason, positive total arsenic laboratory test results from specimens taken within 72 hours of consumption of seafood do not meet the laboratory criteria for diagnosis. If this person is symptomatic, please recommend to have health care provider retest after 3-5 days of no fish consumption.

B. Arsenic Poisoning Flow Chart:



¹ Valid Laboratory test: Only urine (24 hrs) and urine creatinine tests are valid for arsenic.

Environmental Health Acute Arsenic Poisoning Case Report Form

Florida Department of Health
DOH/Division of Environmental Health
Bureau Office of Environmental Public Health Medicine

Merlin Case Number: _____
Telephone number: (850) 245-4299
Fax number: (850) 922-8473

Demographic Information

Name: _____ Date of Birth: (mm/dd/yyyy) ____/____/____

Street Address: _____

City: _____ County: _____ Zip: _____

Name of Employer OR School: _____

Telephone #: Home: _____ Work: _____ Other: _____

Gender: Male Female
Race/Ethnicity: White Black Asian Native American
 Hispanic Other: _____

Exposure Information

Did you eat fish or shellfish at some point during the three days before you were tested for arsenic? Yes No

***If Yes- review reporting guidelines before continuing interview.**

Within a week of your illness, have you been?

Exposed to agricultural pesticides Drinking well water Taking homeopathic medicines
 Exposed to CCA-treated wood Smoking _____ (n cigarettes/ per day)
 Exposed to other possible arsenic sources (list sources) _____ Unknown

Poisoning intent: Unintentional Intentional (suicide, homicide) Unknown

If the exposure is potentially work-related, indicate the industry:

Agriculture Industrial processing plant Emergency response
 Smelter industry Glass manufacturing plant Laboratory
 Coal-burning facility Waste incinerator plant Mining industry
 Battery recycling Computer Circuit board manufacturing
 Other: _____ Unknown

Type of work performed? _____

Case Number: _____ County: _____ Patient initials: _____

* Review the Health Effect and Medical Information (page 2). Continue interview only if case is clinically compatible, in which a high index of suspicion exists, (patient's exposure history regarding location and time) or an epidemiologic link exists between this case and a confirmed case. Recommend retesting of urine after 72 hours of abstinence from seafood.

Health Effects and Medical Information

Date of illness onset (mm/dd/yyyy): ____/____/____

Unknown

Signs and Symptoms (Check all that apply):

- Severe abdominal pain
- Nausea
- Vomiting
- Diarrhea (bloody/rice-water)
- Garlic odor on breath
- Anemia
- 'Pins & needles' sensation
- Other: _____
- Numbness
- Light-headedness
- Headache
- Weakness
- Delirium
- Convulsion
- Mee's lines
- Pulmonary edema
- Hypotension
- Shock
- Ventricular arrhythmia
- Hyperpigmentation of fingernails
- Hyperkeratosis of skin

Do you have a preexisting illness with any of these (the mentioned) signs and symptoms?

Yes (specify) _____ No Unknown

Name of diagnosing physician: _____ Telephone #: () _____

Was the person hospitalized? Yes No Unknown

If yes, name of medical facility and address: _____

Date of admission: (mm/dd/yyyy) ____/____/____ Diagnosis (if known): _____

What was the medical outcome? Survived Died Unknown

Date of discharge/death: (mm/dd/yyyy) ____/____/____

Are you pregnant? Yes No Unknown

Test/Laboratory Information

Was a test ordered to confirm arsenic poisoning? Yes No Unknown

If yes, which test(s) were conducted? Total urine (24 hrs) Urine creatinine

If urine creatinine test was conducted, was the concentration level > 15 µg/g? Yes No

If yes, results must be converted to µg As/Liter of urine using the following formula and conversion factor.

$$\frac{\text{Given}}{\text{Given}} (\mu\text{g As/g creat}) \times \frac{\text{Given}}{\text{Given}} (\text{mg creat/dL}) \times 0.01 = \frac{\text{Calculated}}{\text{Calculated}} (\mu\text{g As/Liter urine})$$

If urine test was conducted, was the arsenic concentration level > 50 µg/L? Yes No

Investigator's name (Please print): _____ Phone: () _____

Please submit the completed survey to the Office of Environmental Public Health Medicine, Division of Environmental Health, Department of Health, Bald Cypress Way, Bin A08, Tallahassee, FL. Or FAX 850-922-8473

III. Instructions for completing the case report form- Arsenic

A. Demographic Information- All demographic information needs to be filled out in full.

B. Exposure Information- Please ask this series of questions to complete the exposure section.

Did you eat fish or shellfish at some point during the three days before you were tested for arsenic?

Organic arsenic found in fish is not believed to be toxic. Total arsenic tests do not distinguish between organic and inorganic arsenic (the more toxic form). For this reason, positive total arsenic laboratory test results from specimens taken within 72 hours of consumption of seafood do not meet the laboratory criteria for diagnosis.

If Yes- Go to the Health Effects and Medical Information section (Page 2).

- Discontinue interview if it is apparent from clinical evaluation and patient interview that increased in total urine arsenic is due to consumption of seafood.
- Recommend retesting of total urine arsenic of all the patients with signs and symptoms compatible with arsenic poisoning. This is voluntary retesting after 72 hours of abstinence from seafood by patient's health care provider.

If No- Continue to next question.

If seafood consumption status is unknown, complete the case report form based on information available.

Within a week of your illness, have you been?

Exposed to agricultural pesticides: Insecticides, herbicides (weed killers and defoliants), fungicides and cotton desiccants are potential sources of arsenic exposure.

Drinking well water: Well water contaminated by natural sources such as arsenic-containing bedrock has been reported to be the cause of arsenic toxicity. There are a number of areas in Florida that are associated with arsenic-containing bedrock. Groundwater may also contain elevated concentrations of arsenic due to contamination from runoff of arsenical pesticide. The United States (U.S.) Environmental Protection Agency's (EPA) maximum contaminant level for arsenic in drinking water is 50 ppb.

Taking homeopathic medicines: Arsenic is found in some homeopathic and naturopathic preparations, and in folk remedies such as *kushtay*, a tonic used in Asian cultures to cure various sexual disorders.

Exposed to CCA-treated wood: Check if patient was exposed to CCA-treated wood. CCA wood - also called pressure treated wood - is the green-tinged lumber found in docks, picnic tables, decking, etc. It has the indisputable benefit of being highly resistant to rot and insects. The lumber is treated with a pressurized solution containing copper, chromates and arsenic, hence the name CCA lumber. CCA pressure-treated wood contains arsenic which can be released from the wood in several ways:

- During wood burning
- Through mechanical abrasion
- Direct dermal contact
- When acid contacts the treated lumber and leaching of arsenic results

Smoking: Smokers may also inhale small amounts of arsenic as a result of pesticide residue on tobacco leaves.

Exposed to other possible arsenic sources:

Sources of Arsenic³

- Environmental sources of arsenic exposure include food, water, soil, and air.

Arsenic is everywhere in the environment. It is released into the air by volcanoes, through weathering of arsenic-containing minerals and ores, and by commercial or industrial processes. In industry, arsenic is a by-product of the smelting process for many metal ores such as lead, gold, zinc, cobalt, and nickel. Other potential sources of arsenic exposure are:

- Natural sources: arsenic-containing mineral ores and groundwater (especially near geothermal activity).
- Commercial products: wood preservatives, insecticides, herbicides (weed killers and defoliants), fungicides, cotton desiccants, cattle and sheep dips, paints and pigments, antifouling paints, leaded gasoline, and fire salts (multicolored flame).
- Food: wine (grapes sprayed with arsenic-containing pesticides), tobacco (plants sprayed with arsenic-containing pesticides), and seafood (especially bivalves, certain cold water and bottom-feeding finfish, and seaweed).
- Industrial processes: purifying industrial gases (removal of sulfur), burning fossil fuels, burning wood treated with arsenic preservatives, electronics manufacturing (microwave devices, lasers, light-emitting diodes, photoelectric cells, and semiconductor devices), hardening metal alloys, preserving animal hides, bronze plating, and clarifying glass and ceramics.
- Medicinals: Fowler's solution (potassium arsenite), antiparasitic drugs (carbasone), Donovan's solution, folk remedies ("Asiatic pill," *kushtay*, yellow root), kelp-containing health foods, some naturopathic remedies.

Inorganic arsenic is used as an antiparasitic agent in veterinary medicine in the United States and other countries.⁴

Arsine gas (AsH_3), used commercially in the microelectronics industry and may also be encountered accidentally in metallurgical and mining processes.

Arsenic production has greatly decreased in the United States, but imports have increased steadily and substantially in recent years. Currently, the principal use of arsenic is in products used for wood preservation. Most of the rest is used in the production of insecticides, herbicides, algicides, and growth stimulants for plants and animals. Gallium arsenide (GaAs) is used in integral components of discrete microwave devices, lasers, light-emitting diodes, photoelectric chemical cells, and semiconductor devices. The use of arsine gas (AsH_3) as a dopant in the production of semiconductors is also expected to

increase, although substitutes of lower toxicity such as tributylarsine have recently been used. A source of arsine exposure is accidental release during manufacture, transport, or use of the gas. More often, however, arsine forms unexpectedly when acid or other reducing substances are added to arsenic-containing compounds, such as metals in which arsenic is a low-level contaminant.

In the general population, the main route of arsenic exposure is via ingestion of arsenic-containing food. Intake from air, soil, and water is usually much smaller. It has been estimated that the average daily dietary intake of arsenic by adults in the United States is 11 to 14 milligrams per day. Meat, fish, and poultry account for 80% of dietary arsenic intake. Fish, seafood, and algae also contain high concentrations of arsenic in the form of arsenobetaine and arsenocholine, sometimes referred to as "fish arsenic." Fish arsenic has low toxicity to humans and is rapidly excreted in urine. Wine made from grapes sprayed with arsenic-containing pesticides may have appreciable levels of arsenic.

Poisoning intent: Subjective determination based on the patient's history and investigators judgment.

- **Unintentional:** Includes exposure of drinking well water, using medicines containing arsenic, and exposure to pesticides etc. where patient is unaware of potential exposure to arsenic.
- **Intentional:** Involves suicidal or homicidal use of arsenic.
- **Unknown:** Intent of arsenic poisoning is unknown.

If the exposure is potentially work-related, indicate the industry: Based on patient's occupation select appropriate industry from given options.

Type of work performed: Brief job description of patient.

C. Health Effects and Medical Information: Please ask full series of questions to complete health effects and medical information section

Date of illness onset: Month/ day/year that symptoms started, if patient is unsure or is unable to be contacted, please enter the first positive laboratory date and indicate that it is a laboratory date and not an onset date.

Signs and Symptoms (Check all that apply): Select appropriate signs and symptoms. All patients should have signs and symptoms consistent with arsenic poisoning to make a confirmed or probable case. *

Definition of selected clinical symptoms:

Pins & needles' sensation: An altered sensation often described pin and needle pricks.

Delirium: An altered state of mind often resulting in illusions and hallucinations

Mees lines: Lines of discoloration across the nails of the fingers and toes.

Hyperpigmentation of fingernails: Unusual darkening of nails.

Hyperkeratosis of skin: Thickening of the outer layer of the skin

*Signs and symptoms can not be entered in to Merlin.

Do you have a preexisting illness with any of these (the mentioned) signs and symptoms? Indicate if patient had experienced any of the signs and symptoms consistent with arsenic poisoning before being evaluated for/diagnosed with arsenic poisoning. Specify which signs and symptoms are experienced, these questions are asked to identify any underlying medical condition.

Are you pregnant? Chronic exposure to arsenic through drinking water has the potential to cause adverse pregnancy outcomes. More data are required to establish a firm causal relationship between arsenic ingestion and adverse outcomes during pregnancy and on neonatal morbidity and mortality. In pregnant Andean women who consumed water with arsenic concentrations of about 200 µg/l, arsenic in cord blood (9 µg/l) was almost as high as in maternal blood (11 µg/l). In the same group placental arsenic was 34 µg/l compared with 7 µg/l in women unexposed to arsenic.⁵

D. Test/Laboratory Information:

Valid laboratory test: Only Urine (24 hrs) and urine creatinine tests are valid for arsenic. Speciations for inorganic and organic arsenic is not required but if available use only inorganic arsenic level to determine arsenic poisoning.

Was a test ordered to confirm arsenic poisoning? Yes/ No/Unknown

If yes, which test(s) were conducted? Choose between total urine (24 hrs) and urine creatinine test. No other test types are valid for confirmation of arsenic poisoning.

If a urine As/ g creatinine (urine creatinine) test was conducted, was the concentration level > 15 µg/g?

If no- Case does not match the laboratory criteria for arsenic poisoning

If yes- Results must be converted to µg As /Liter of urine using the following formula and conversion factor. Arsenic (µg As/g creat) and creatinine (mg creat/dL urine) values are given in laboratory report.

$$\frac{\text{_____}}{\text{Given}} (\mu\text{g As/g creat}) \times \frac{\text{_____}}{\text{Given}} (\text{mg creat/dL}) \times 0.01 = \frac{\text{_____}}{\text{Calculated}} (\mu\text{g As/Liter urine})$$

E.g. The heavy metals profile for urine shows that the level of urinary Arsenic (random urine) = 413.3 mcg As/g creat (µg /g creatinine) and Creatinine (random urine) = 51mg/dL. Using the above formula the calculated urinary arsenic level will be 210.78 µg/Liter.

$$413.3 \mu\text{g/g creat} \times 51 \text{ mg/dL} \times 0.01 = 210.78 \mu\text{g/Liter}$$

If urine test was conducted, was the arsenic concentration level > 50 µg/L?

If yes- Case matches the laboratory criteria for arsenic poisoning

If no- Case does not match the laboratory criteria for arsenic poisoning

Note: Laboratory may report arsenic, urine 24 hour as $\mu\text{g As} / 24 \text{ hours}$ instead of $\mu\text{g As} / \text{Liter}$ for 24 hour urine. The following instructions are helpful in order to interpret the results,

1. If the total volume of urine collected during 24 hour is not given: - lab values given in $\text{ug}/24 \text{ hr}$ should read as $\mu\text{g As} / \text{liter} / 24 \text{ hr}$.

E.g. Given only 24 hour urine arsenic value ($60 \text{ ug}/24 \text{ hour}$).

Then, the arsenic level for 24 hour urine will be $60 \mu\text{g} / \text{liter}$ for 24 hours.

2. If total volume of urine collected during 24 hour is given: - lab values given in $\mu\text{g As} / 24 \text{ hr}$ should be recalculated by dividing the arsenic value ($\mu\text{g As} / 24 \text{ hour}$) by the total volume of urine collected during 24 hours. The unit of total volume of urine is in liter.

E.g. Given total volume of urine ($2150\text{ml} = 2.15 \text{ liter}$) and a 24 hour urine arsenic value of $127 \text{ ug}/24 \text{ hour}$ then, the arsenic level/ L for the 24 hour urine will be $127 / 2.15 = 59 \mu\text{g} / \text{liter}$ for 24 hours.

Department of Health Contacts:

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*** YOU MUST ATTACH LAB REPORTS WITH THIS CASE REPORT FORM**

References

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- ⁵Concha G, Vogler G, Lezcano D, *et al.* Exposure to inorganic arsenic metabolites during early human development. *Toxicol Sci* 1998;44:185–90.