

Arsenic Fractionation

IDENTIFICATION AND TOXICOLOGICAL STRATIFICATION OF ARSENIC EXPOSURE

Test Highlights

- Detects and quantitates three major fractions of arsenic-containing compounds with differential clinical significance: inorganic (most toxic), methylated metabolites (moderately toxic), and organic (nontoxic).
- Used to determine if an elevated total arsenic result in urine reflects exposure to toxic or relatively nontoxic forms of arsenic.

Indications for ordering

- Elevated (>35 µg/L) arsenic (nonfractionated total) result in urine.
- Occupational monitoring for exposure to inorganic arsenic.
- Confirm or rule out suspicion of recent exposure to inorganic arsenic.
- Monitor elimination of arsenic after exposure has been confirmed.

Clinical Background

- Arsenic exists in more than 30 chemical forms or species that can be grouped into inorganic (e.g., arsenite, As⁺³; arsenate, As⁺⁵), methylated (e.g., monomethylarsonic acid, MMA; dimethylarsenic acid, DMA), and organic (e.g., arsenobetaine; arsenocholine) fractions. Inorganic species of arsenic occur naturally in rocks, soil, and groundwater, and are also found in many synthetic products, poisons, and industrial processes. Methylated species arise primarily from metabolism of inorganic species, but small amounts may arise directly from food. Organic species arise primarily from food such as fish, seaweed, and shellfish.
- Signs and symptoms of arsenic poisoning vary with time and extent of exposure, but may include abdominal pain, hyperpyrexia, polyneuropathy, tremor, hyperpigmentation, hepatomegaly, oliguria, and bone marrow hypoplasia.
- The toxic potential of arsenic is based on the forms of arsenic involved in an exposure and on the variable elimination kinetics of each form.

Arsenic fraction	Approximate LD ₅₀ * in mice (mg/kg)	Approximate elimination half-life** in human blood	Approximate detection window** in human urine
Inorganic	10	1-2 hours	10-20 hrs
Methylated metabolites	2,000	5-20 hours	1-20 days
Organic	10,000	4-6 hours	1-3 days

* LD₅₀ is the calculated lethal dose expected in 50 percent of animals tested

** Elimination kinetics apply to acute exposures; estimations presented in this table may not apply to chronic or very high exposures.

- Due to the short half-life of arsenic in the blood, urine is the preferred specimen for detection of arsenic exposure. For chronic or past exposures (>3 weeks), analysis of hair or nails may be useful.
- Fractionation is required for definitive diagnosis of moderate arsenic poisoning. Specimens with total arsenic >35 µg/L but <2,000 µg/L must be fractionated to determine the contribution of each arsenic fraction to the total arsenic burden, and associated clinical signs and symptoms. Specimens with arsenic concentrations of greater than 2,000 µg/L will most likely reflect an acute poisoning that requires medical attention, regardless of the distribution of species.

Methodology

- A two-step process is employed. First, high performance liquid chromatography (HPLC) is used to separate the arsenic species. Second, inductively coupled plasma mass spectrometry (ICP-MS) is used to detect and quantitate arsenic at mass 75 (100 percent abundance).
- No dietary restrictions are required to perform this test; most dietary forms of arsenic are separated and quantitated as part of the organic fraction.
- The well-recognized polyatomic interference from argon chloride is eliminated by chromatographic separation.

Limitations

- Not all species of arsenic can be identified in this test. As such, the sum of the fractions detected in this method may not equal the total arsenic concentration detected using another method.
- This test cannot determine the source of an arsenic exposure.
- Specimens preserved with acid are unacceptable due to pH-related changes in the chromatography and potential inter-conversion of species.
- Specimens collected from persons exposed to gadolinium-containing contrast agents should not be submitted for testing due to interference with quantification.
- Due to the relatively rapid clearance of arsenic and the analytical limit of quantification (LOQ = 10 µg/L), this test is best applied to acute evaluations of arsenic exposure. Therefore, the test will not reliably identify low-level exposures (< 10 µg/L) of arsenic that occurred more than one week prior to specimen collection.

Interpretation

- Organic arsenic species are eliminated within three days of exposure.
- In the absence of chelation or other treatment designed to accelerate elimination, inorganic arsenic will be eliminated in the urine over several days, primarily as methylated metabolites. Approximately 24 hours after an exposure to inorganic arsenic, the inorganic species may not be detected in urine. Instead, the concentration of methylated metabolites will predominate. The presence of methylated metabolites in urine is good evidence that exposure to inorganic arsenic has occurred.
- The Biological Exposure Index established by the American Conference of Governmental Industrial Hygienists (ACGIH) for the sum of inorganic and methylated metabolites of arsenic is 35 µg/L. However, clinical symptoms may not be evident at 35 µg/L. Toxic thresholds are not well established.
- Relation of clinical signs and symptoms to arsenic exposure depends on the duration and extent of the exposure to inorganic and methylated species of arsenic, as well as underlying clinical status of the patient.

References

1. 2007 TLVs and BEIs, a publication of the ACGIH.
2. Ellenhorn MJ, Schonwald S, Ordog G, and Wasserberger J. *Ellenhorn's Medical Toxicology*, Williams and Wilkins, Baltimore, MD,1997.
3. Kales SF, Huyck K, Goldman RH. Elevated urine arsenic: un-specified results lead to unnecessary concern and further evaluation. *J Anal Tox* 2006;30:80-5.
4. Feldmann J, Lae VWM, Cullen WR, Ma M, Lu X, Le X. Sample preparation and storage can change arsenic speciation in human urine. *Clin Chem* 1999;45(11):1988-97.
5. Reuter W, Davidowski L, Neubauer K. Speciation of five arsenic compounds in urine by HPLC/ICP-MS. Perkin Elmer Sciex Application Note, accessed October 2007 at www.perkinelmer.com.

Test Information

0020734 **Arsenic, Fractionated, Urine**

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.