

Arsenic

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PubH 243

April 18, 2000

Arsenic

- Inorganic arsenic compounds
 - contain oxygen, chlorine, and sulfur
- Organic arsenic
 - combines with carbon and hydrogen in plants and animals
 - usually less harmful than inorganic arsenic

Common Sources-1

- Ubiquitous in nature
- Geologic inputs from mineral weathering processes
- Smelting of nonferrous metal ores
- Volcanoes

Common Sources-2

- Elevated soil levels from mineral deposits or contamination
- Ground water contamination
 - bedrock
 - pesticide runoff
 - cemeteries
 - burning treated wood

Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Arsenic. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1989.

---. Case Studies in Environmental Medicine. Arsenic Toxicity. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

Common Sources-3

- Ecological effects in environment
- Leaching potential and environmental fate
 - arsenic-based wood preservatives
 - aquatic ecosystems

Exposure-1

- Dermal Contact
- Ingestion
- Inhalation

Dermal Contact

- Corrosive effect to dermal layers
- Prolonged contact exposure can result in focal hyperemia

Ingestion

- Appearance of symptoms dependent upon dose and medium
- Food is largest source, followed by drinking water and air

Grossblatt N, ed. Arsenic: Medical and Biological Effects of Environmental Pollutants. Washington, DC: National Academy Press, 1977.

Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Arsenic. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1989.

Inhalation

- Inflammation of mucous membranes
- Process may be delayed because of lower concentrations

Toxicokinetics-1

- Arsenic remains inert until contact with air or water
- Inorganic forms are more toxic than organic forms
- Trivalent forms are more toxic
- Pentavalent forms are less toxic

Toxicokinetics-2

- Inorganic arsenic readily absorbed in the GI tract
- Poorly absorbed through intact skin
- Binds externally to skin and hair

Toxicokinetics-3

- Absorbed arsenic is transported in blood
- Part is bound to transferrin
- Most is rapidly cleared
 - three-exponential clearance curve

Toxicokinetics-4

- Excretion is mainly via the urine
- Small amounts removed elsewhere
 - skin
 - sweat
 - hair
 - breast milk
- Half-time of about 4 days

Toxicokinetics-5

- Inorganic arsenic is methylated in liver to
 - monomethylarsonic acid (MMA)
 - dimethylarsinic acid (DMA)
- Involves addition of methyl groups from *S*-adenosylmethionone to arsenic in its trivalent oxidation state

Toxicodynamics-1

- Concentration of arsenic metabolites serves as a better marker of exposure measurement
- Total urinary arsenic is a less useful biomarker

Toxicodynamics-2

- Arsenic accumulates in hair and nails
- Used as indicators of exposure rather than markers of absorbed dose

Effects Introduction

- Dependent upon chemical form
- Organ-specific effects

Effects-1

- Acute exposures present with symptoms that mimic cholera
 - severe diarrhea
 - dehydration
 - hypovolemic shock
 - possible hemorrhagic gastroenteritis

Effects-2

- Other GI effects include
 - inflammation
 - vesicle formation
 - and eventual sloughing of mucosa in mouth, pharynx, and esophagus

Effects-3

- Acute or subacute exposure to inorganic arsenic induce appearance of cardiovascular manifestations
 - hypotension
 - congestive heart failure
 - cardiac arrhythmia
 - cyanosis

Effects-4

- Acute intoxication can be followed by delayed central or peripheral nervous system involvement
 - 1 to 5 days after poisoning
 - range from headache to coma

Effects-5

- Chronic toxicity presents in classic cutaneous manifestations
 - hyperpigmentation
 - palmar-plantar hyperkeratoses
 - Mees lines on finger nails
 - peripheral neuropathy

Effects-6

- Chronic hepatic and renal damage
 - proteinuria
 - acute tubular necrosis in severe cases
- Hematological abnormalities
 - anemia
 - leukopenia

Crossgrove RD, ed. Arsenic in Drinking Water. Washington, DC: National Academy Press, 1999.

Reigart JR, et al. Recognition and Management of Pesticide Poisonings, fifth edition. "Arsenical Pesticides." US EPA, 1999.

Effects-7

- Increased frequency of chromosomal abnormalities
- No endocrine disruption
- Act as contact allergens

Effects-8

- Chronic health effects
 - organ damage
 - neurotoxicity
 - reproductive toxicity and teratogenicity
 - immunotoxicity

Carcinogenicity-1

- DHHS deemed arsenic a known carcinogen
- EPA classified as a class A, or known human carcinogen
- Arsenic has a latency period of greater than 6 years

Environmental Protection Agency. Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

Ostrowski SR, et al. Latent effects and developmental deficits in humans and animals. *Toxicol Ind Health* 1999 Nov; 15(7):602-44.

Carcinogenicity-2

- Inhaled arsenic is a recognized cause of lung cancer
- Arsenic ingestion or inhalation has been reported to increase the risk of cancer in a number of organs

Regulatory Policy-1

- NIOSH considers arsenic to be a potential occupational carcinogen.
- NIOSH usually recommends that occupational exposures to carcinogens be limited to the lowest feasible concentration.

Regulatory Policy-2

- OSHA established a maximum permissible exposure limit (PEL) for workplace airborne arsenic of $10 \mu\text{g}/\text{m}^3$
- NIOSH Recommended Exposure Limit:
15-Min Ceiling Value: $0.002 \text{ mg}/\text{m}^3$
- EPA set a limit of 0.05 ppm for arsenic in drinking water

Environmental Protection Agency. Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997.

Regulatory Policy-3

- Periodic Health Surveillance for potentially exposed workers
- The EPA set limits on amounts of arsenic industrial sources can release
- EPA has also canceled/restricted many uses of arsenic in pesticides