Official Newsletter of the **Utah Poison Control Center**

TOXICOLOGY TODAY

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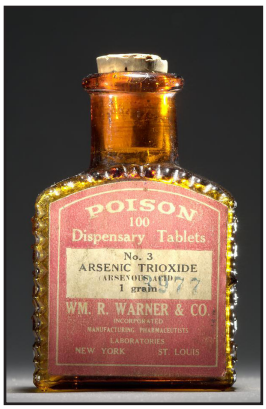
ARSENIC: EVALUATION AND DIAGNOSTIC MARKERS

by Rian Davis, PharmD



Arsenic toxicity, a rare but serious condition, typically presents with non-specific symptoms that make diagnosis difficult. A brief discussion of the sources of arsenic, clinical presentation, mechanism of toxicity, and toxicokinetics is presented to help the clinician understand what diagnostic tests are appropriate for a patient with suspected arsenic toxicity.

Sources

The major exposure threat world-wide is drinking water,[1] however, sources vary greatly by region. Inorganic arsenic, typically arsenic trioxide, occurs naturally in soil, rocks, minerals, and ores.[2] It can leach into water through runoff, and enters air through the smelting of ores, and by coal-burning plants. Arsenic is used for industrial purposes: as pesticides and insecticides, added to metal alloys for lead-acid batteries, and was used as a wood preservative prior to 2003.[2]

Food is also a major source of arsenic. Small amounts of arsenic are ingested daily without apparent toxicity.[2] Major food sources include fish and seafood, mushrooms, and poultry. Fish and seafood mostly contain organic, non-toxic forms of arsenic: arsenobetaine and arsenocholine. Herbal supplements may also be contaminated with arsenic, especially products imported from other countries.

Clinical Presentation

The symptoms for arsenic toxicity differ depending on the degree and duration of exposure. The main symptoms are summarized below:

Acute: Gastrointestinal effects manifesting as abdominal pain, vomiting and watery diarrhea are usually the first signs of toxicity after ingestion. Large ingestions may be followed by cardiac instability with hypotension, tachycardia that may progress to shock. Other manifestations of acute toxicity may include encephalopathy, seizures, hemolytic anemia and acute respiratory distress syndrome. Peripheral neuropathy, which is often painful, and muscle weakness is usually delayed 1-2 weeks after acute exposure, and may be irreversible.

Chronic: The main concern following chronic exposure is carcinogenicity. Studies in India and Bangladesh have shown associations of chronic arsenic exposure with skin, lung, liver, kidney, and bladder cancer.[3] However, non-cancerous effects are evident in nearly all body systems. Chronic arsenic toxicity is associated with vascular disease, diabetes mellitus, restrictive and obstructive respiratory conditions, peripheral neuropathy, and palmar and plantar keratosis with hyperpigmentation. Some skin effects may be latent for up to 60 years. Similar to other heavy metals, arsenic toxicity can also cause behavioral changes, confusion, and memory loss. Vomiting and diarrhea are episodic in chronic exposures.

Mechanism of Toxicity

Pentavalent arsenic (As V) has a similar structure and shares similar properties with phosphate and exerts its toxic effect by replacing phosphate in various biochemical reactions, such glycolysis. Trivalent arsenic (As III), is highly reactive with sulfhydryl and thiol groups, interfering with pyruvate dehydrogenase (PDH) and glutathione. By binding PDH, ATP production and gluconeogensis is limited. Depleting glutathione causes the disruption of cellular redox potential and induces oxidative stress.[4]

The methylated metabolites may also contribute to the toxic effects of arsenic. For example, monomethyl arsonic acid has greater affinity for PDH than the other arsenicals. Dimethylated arsenic is carcinogenic.[4]

Toxicokinetics

The oral bioavailability of arsenic is about 60-80%.[5] *(cont. on pg. 2)*

IN THIS ISSUE

POISONS UNDER YOUR NOSE

Inhalant abuse typically starts in elementary years and peaks in middle school. The 2008 National Survey on Drug Use and Health noted that an average of 593,000 12 -17 year olds used inhalants for the first time.[1] The Monitoring the Future 2008 survey results noted that while many drugs showed a decline in use, inhalant use held steady.[2] The 2009 Utah Student Health and Risk Prevention survey showed that inhalants are the 2nd most commonly abused substance of 6th graders in their lifetime.[3] A recent inhalant abuse case in the Tri-County area required a 4-day stay in ICU for a young teen.[4]

Inhalants are breathable chemical vapors or gases that produce psychoactive effects when misused. Most inhalants are readily available, inexpensive or free, and usually legal to purchase and possess. Many youth do not perceive them as harmful and don't understand the consequences. Education should start before abuse peaks.

The medical complications from both acute and chronic abuse include severe and potentially life threatening effects. "Sudden sniffing death syndrome" is a well recognized consequence of inhalant abuse characterized by sudden cardiac arrest and can occur the 1st time or the 100th time a person abuses inhalants. A recent Poison Pearl on Inhalant Abuse discusses the clinical consequences of inhalant abuse (Toxicology Today. 2009, volume 11, issue 4).

Early education is key to preventing inhalant abuse. Inhalants should be viewed as poisons, pollutants, and fire and explosion hazards. Parents need to talk with their children about products that can be harmful if misused. Emphasis should be placed on fire safety and poison awareness

Age appropriate messages:

- Pre-K – 3rd grade – stress that smelling household chemicals can be dangerous
- 4th – 8th grade – address the poisonous effects on the environment and body in science and health classes.

Parents should demonstrate and follow product usage guidelines, supervise children's use of products, and work with school administrators to include inhalants in school drug policies.

The UPCC has elementary lessons plans for inhalant abuse prevention in the following website: http://uuhsc.utah.edu/poison/publiced/inhalant.htm

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(cont. from pg. 1)

Arsenate (As V) and arsenite (As III) are readily interconverted in the liver by arsenate reductase.[6] Specific methyltransferases and reductases convert arsenite to methylated arsenic.[6] Arsenic is excreted renally primarily as methylated organic arsenic and to a lesser extent as inorganic arsenic.

Diagnosis

If the clinical presentation is consistent with arsenic several laboratory tests are available to confirm the diagnosis. Table 1 summarizes the tests available through ARUP as well as their indications and limitations. The preferred specimen is urine and the toxic threshold for total inorganic and methylated arsenic is 35 µg/L.[7] The most meaningful arsenic levels are "fractionated" (speciated) that differentiate the concentrations of nontoxic (organic) and toxic (inorganic) arsenic. Random (spot) urine total arsenic can be useful as a screening test for outpatients with low a probability of exposure and no seafood ingestion for several days.

Table 1. Laboratory tests available to detect arsenic.
Adapted from ARUP Consult[7] unless otherwise indicated.

Specimen	Indication	Limitation	Comment
Urine, 24 hour	Suspected acute or chronic arsenic exposure	Must be within 2 weeks of exposure, less reliable if > 1 week	• Automatically fractionates if result > 50 µg/d. • Instruct patient to abstain from fish and seafood for 3-4 days prior.[8]
Urine, 24 hour Fractionated	Determines content of inorganic, methylated, and organic forms of arsenic	• Less reliable if > 1 week post exposure • Does not detect all arsenic species • Not reliable if level below < 10 µg/L	Instruct patient to abstain from fish and seafood for 3-4 days prior.[8]
Blood	Recent (<24 hours), large oral exposure to arsenic, or if urine sample cannot be produced	Does not fractionate types	
Hair, 0.5 g	Chronic exposures[9]	• Large intra- and inter- hair variability • Hair may be contaminated by environment[8]	Gather at least 3 inches of hair from nape of neck
Nails, 1 g	Chronic exposure	Must be within 1 year of exposure	Toenails take longer to grow thus provide a wider time window for testing

Treatment

The standard treatment includes metal chelators, such as dimercaprol (British anti-Lewisite—BAL) or 2,3-dimercaptosuccinic acid (succimer). These compounds are sulfhydryl donors that serve to bind and remove arsenic from the body.[10] Succimer is a water-soluble compound that is administered orally. BAL is available as a parenteral solution in peanut oil and therefore, can only be given by intramuscular injection. The lipophilic nature of this drug allows it to penetrate the CNS to remove arsenic. Succimer is an acceptable chelator for acute arsenic *(cont. on pg. 3)*

(cont. from pg. 2)
exposures in patients with a functioning GI tract.

Summary

Acute arsenic toxicity presents with relatively non-specific symptoms, often suggestive of an acute GI illness, and is followed by peripheral sensory-motor deficits. The diagnosis should encompass patient history, clinical presentation, and laboratory analysis. Interpretation of laboratory results and the decision to treat should be discussed with a toxicologist or poison control center.

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POISON PEARLS

MARIJUANA ALTERNATIVES OR "SPICE"

Adam Bowman, MD
Emergency Medicine, PGY2

Spice originally appeared in Europe in 2001. It is marketed over the Internet and in local smoking shops as either incense or "herbal smoking blend." It is widely available and there are no restrictions on its purchase. It is commonly known as a "legal high" or legal marijuana alternative within the drug abuse sub-culture.

Smoking herbal spice blends are reported to produce a relaxing, euphoric, marijuana-like effect. This effect is purportedly caused by the unique herbal mixtures. Studies analyzing the chemical composition of "Spice" products in Germany found them to contain synthetic cannabinoids (JWH-018, HU-210, and CP 47-497). These designer drugs act at cannabinoid (CB1, CB2) receptors with increased affinity relative to THC.

Spice products are about twice as expensive as marijuana and its safety threshold is not known. It is not detected on urine drug screens allowing users to abuse these products for their euphoric effects without fear of being detected by employers or legal authorities. This property may provide sufficient reason for users to accept the increased risk and cost of using these products.

There have been over 20 "Spice" cases reported to the Utah Poison Control Center of patients presenting to area emergency departments with symptoms of agitation, confusion, respiratory depression, seizure-like activity, and tachycardia that are not consistent with traditional marijuana use. These adverse effects usually last 8-12 hours but have persisted for 48-72 hours. Treatment is supportive.

Spice products are not illegal in the US. However, if they truly contain synthetic cannabinoids, they may fall under the Federal Analog Act, which outlaws any compound designed to mimic a Schedule I or Schedule II substance. Most Spice products are labeled "not for human consumption" to avoid this law, which only applies to compounds intended for use in humans.

POISON PEARLS

THE TOXICOLOGY OF VITAMINS

Sarah Sliva, MD
Emergency Medicine Resident

Vitamins and herbs are very accessible and considered by many people to be innocuous. In 2007, 44% of Americans reported taking vitamins and dietary supplements but few are aware of the effects of excessive vitamin supplementation.

Any vitamin in large doses can cause non-specific effects such as vomiting, abdominal pain, diarrhea and rash. Vitamins A, D, E and K are fat-soluble and have higher potential for toxicity due to accumulation in the body. Vitamin A toxicity is associated with alopecia, bone fractures, and pseudotumor cerebri. Vitamin D causes hypercalcemia and secondary effects such as hypertension, renal failure and arrhythmias. Vitamin E in large quantities is associated with a weakness, headache and increased bleeding tendency. Vitamin K given intravenously can result in life-threatening anaphylactoid reactions in an unmonitored setting. Some water-soluble vitamins are also associated with toxicities in high doses. Niacin can cause flushing and liver dysfunction. Pyridoxine is associated with peripheral nerve injury and decreased seizure threshold. Vitamin C can precipitate gout and nephrolithiasis.

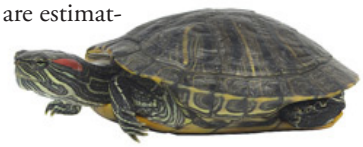
Health care workers should be familiar with the common vitamin toxidromes, and educate patients about proper administration as well as storage of these agents away from children.

DID YOU KNOW?

Compact Fluorescent Lights (CFLs) contain mercury, a toxin that can cause adverse health effects. If a bulb breaks, open the windows for at least 15 minutes, shut off central air systems, and call the Utah Poison Control Center for help (1-800-222-1222). Don't vacuum up the debris. Follow proper disposal guidelines: www.epa.gov/mercury/spills

TOXINS IN THE NEWS

- Severe liver injury and death has been associated with use of **diclofenac 1% gel**. Most reactions occur during the first 1-2 month of therapy but may occur anytime therapy.
- **Pet turtles** carry salmonella and are estimated to cause up to 70,000 cases of human infection per year.



DID YOU KNOW?

Medicine Mishaps Put Children at Risk:

Each year, more than 71,000 children end up in hospital emergency departments from medicine overdoses. Most of these poisonings occur in children less than 6 years of age. The majority of the overdoses are a result of children getting into medicine while unsupervised or as a result of adult errors.

—Am J Prev Med 2009

Checkout our website for more poison prevention information at **www.utahpoisoncontrol.org**

MEET THE UPCC STAFF

JEANNETT MADSEN, RN, ASN joined the Utah Poison Control Center as a Specialist in Poison Information (SPI) in February 2009. She graduated from The Salt Lake Community College Nursing program in 1996. Her nursing career originally started at Primary Children's Medical Center as a LPN and continued working there as a RN. She has been a Travel Nurse off and on for over 12 years which has given her the opportunity to explore the world. She has worked in many different hospitals located in places like NYC, Chicago, Boston, San Francisco and even Sydney, Australia. Jeannett enjoys working with the younger generations and has focused her nursing career in Pediatrics and NICU, with 9 years in the Pediatric ICU. Since her change in focus to toxicology Jeannett says her biggest challenge was the learning curve. In her free time Jeannett loves cooking, gardening, photography and continuing to travel. Her favorite poison exposure call to receive is anything non-toxic because they have minimal clinical effects and no one has to go to the hospital. To top it all off she gets to recommend a popsicle or ice cream as a therapy and staying up past their bed time for observational purposes.

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*CSPI denotes Certified Specialist in Poison Information.

THANK YOU

The Utah Poison Control Center expresses its sincere thanks to the health care professionals, public health officials and toxicology colleagues that work together to treat and prevent poisonings.

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POISON HELP 1-800-222-1222