ARSENIC TOXICITY

Information source:
http://www.emedicine.com/med/topic168.htm

"Background: Arsenic is a heavy metal with a name derived from the Greek word *arsenikon*, meaning potent. Arsenic is ubiquitous, found in air, water, fuels, and marine life. The daily human intake of arsenic contained in food ranges from 0.5-1 mg, with the greatest concentrations coming from fish and crustaceans. Arsenic has been used for a variety of purposes. For a long time, arsenic was considered the perfect poison because it is odorless, tasteless, and resembles sugar. Throughout history, arsenic was thought to have claimed the lives of many, including Britanicus, Pope Pius III, Pope Clemente XIV, and Napoleon Bonaparte. Arsenic has been used for the treatment of ulcers, tuberculosis, syphilis, and many other ailments. More recently, arsenic has been used as an insecticide, fungicide, rodenticide, and wood preservative. Arsenic also has been used to manufacture glass and semiconductors.

Pathophysiology: Arsenic exists in metalloid, arsenite (trivalent), and arsenate (pentavalent) valences and in arsine gas. The inorganic (trivalent) compound is absorbed more readily than the organic (pentavalent) forms because of its high lipid solubility. Absorption primarily occurs through the gastrointestinal tract; however, some absorption occurs through the skin. Once arsenic is in the body, it binds to hemoglobin, plasma proteins, and leukocytes and is redistributed to the liver, kidney, lung, spleen, and intestines. Over a period of weeks, deposits may be found in skin, hair, nails, bone, muscle, and even nervous tissue.

Arsenic produces cellular damage through a variety of mechanisms. Arsenic binds to enzyme sulfhydryl groups and forms a stable ring, which deactivates the enzyme. The process of deactivating the enzyme causes widespread endothelial cell damage, vasodilation, and leakage of plasma. Massive transudation of fluid into the bowel lumen, mucosal vesicle formation, and tissue sloughing may result in large gastrointestinal fluid losses. Arsenic binds to dihydrolipoic acid, a pyruvate dehydrogenase cofactor, blocking the conversion of pyruvate to acetyl coenzyme A and inhibiting gluconeogenesis. Arsenic competes with phosphates for adenosine triphosphate, forming adenosine diphosphate monoarsine, causing the loss of high-energy bonds.

In some forms, arsenic is caustic, exerting a direct toxic effect on blood vessels and large organs. Long-term exposure results in nerve damage and may lead to lung, skin, or liver cancer. Once inhaled, arsine gas combines with hemoglobin in RBCs, causing severe hemolysis and anemia. Patients develop hemoglobinuria and hematuria within several hours of exposure.

Frequency:

- **In the US:** Approximately 1000 cases of arsenic exposure are reported annually. Many more cases of chronic arsenic exposure probably go unreported.
- **Internationally:** Thousands of people are exposed to arsenic in the form of contaminated drinking water, foodstuffs, and industrial pollution.

Mortality/Morbidity:

- Acute arsenic intoxication resulting in a fatality is rare. Survivors may have severe disabilities secondary to organ damage.
- Chronic exposure, from weeks to months, can have devastating effects. Patients may

develop encephalopathy, painful paresthesias, myocarditis, pericarditis, peripheral vascular disease (ie, blackfoot disease), lung cancer, renal failure, anemia, brittle nails exhibiting Mees lines, or hyperpigmentation (especially of the eyelids, neck, axillae, and groin)".

"**Physical:**

- Findings depend on the chronicity of exposure.
    - Patients with acute exposure present with gastrointestinal distress characterized by nausea, vomiting, abdominal pain, and profuse watery or bloody diarrhea. Patients often are hypotensive and tachycardic and may complain of a metallic taste in their mouth and have a garlic odor on their breath. Patients frequently exhibit signs of delirium upon examination.
    - Patients with chronic arsenic exposure often present with the complaint of painful paresthesias. Neuropathy results in diminished sensitivity to pinprick, light touch, temperature, and vibration and in motor deficits in a stocking-glove distribution. Muscle wasting and foot drop sometimes are noted. Other examination findings include cyanosis of distal extremities, pallor from anemia, hyperpigmentation of skin, and Mees lines. Patients may develop cardiovascular effects, diabetes mellitus, or cancer as well.
    - Patients with acute arsine gas exposure present with headache, nausea, vomiting, diarrhea, and abdominal pain. Patients often develop dyspnea and severe jaundice.

Causes:

- Accidental or intentional ingestion of insecticides, rodenticides, and other compounds containing arsenic is more likely to result in an acute intoxication.
- Environmental exposure to contaminated drinking water or food and industrial exposures are more likely to result in chronic effects".

Medical Care:

Chelation therapy is the definitive treatment for arsenic poisoning. During chelation, arsenic is incorporated into a heterocyclic ring. This stable, water-soluble, less toxic compound is more easily eliminated from the body by the excretory system. Chelation is not an effective treatment for arsine gas exposure, and it may increase urinary arsenic excretion without preventing hemolysis.

Initiate therapy in all symptomatic patients and in all patients whose speciated urine arsenic level exceeds 200 mcg/L. Patients who are minimally symptomatic and have chronic arsenic poisoning may be removed from the source of their exposure without chelation therapy. Chelation may be of greatest benefit to patients exposed to high levels of arsenic over short periods or to patients with chronic poisoning who recently were exposed to high levels that were superimposed on their chronic toxicity. Chelating agents are used only when necessary because they are toxic and have many adverse effects. If renal failure occurs, initiate hemodialysis and continue chelation.

Patients presenting with acute arsenic ingestion and evidence of a radiopaque bariumlike substance on abdominal radiographs should receive whole-bowel irrigation. If tolerated, polyethylene glycol solution may be used for irrigation at a rate of 1 L/h and continued until opacities no longer are present.

- Remove the patient from the source of exposure.
- For recent ingestion, decontaminate the patient with gastric lavage.
- Consider whole-bowel irrigation if lavage does not achieve desired results.

- Initiate supportive care with aggressive fluid resuscitation for hypovolemia, and monitor the patient's electrolyte levels.
- Initiate cardiac monitoring for arrhythmia. Torsade de pointes may be treated with magnesium sulfate or overdrive pacing with isoproterenol in addition to the measures usually recommended to treat ventricular tachycardia.
- Maintain high urine output with intravenous fluids (IVF) to facilitate arsenic excretion. Consider adding bicarbonate to IVF to maintain a urine pH of at least 7.5 in an attempt to prevent renal failure secondary to myoglobinuria.

Consultations:

- Nephrologist (early) - To discuss possible need for hemodialysis
- Toxicologist - Regarding use of chelating agents
- Psychiatrist - In the case of suicide attempts
- Neurologist - For patients with chronic toxicity".