The Tox Box

from *Critical Decisions in Emergency Medicine*

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About the Editor-in-Chief

Dr. Tomaszewski is the section editor of the Tox Box in *Critical Decisions in Emergency Medicine*. He is a professor of clinical emergency medicine and serves as the chief medical officer for a community hospital affiliated with the University of California San Diego (UCSD).

Originally trained as a marine biologist, he maintains his connection to the ocean through diving and surfing, and he integrates this passion into his clinical work as an attending physician in hyperbaric medicine. Dr. Tomaszewski also practices medical toxicology and previously served as editor-in-chief of the *Journal of Medical Toxicology*. A long-time oral board examiner and developer of written examinations for the American Board of Emergency Medicine, he currently contributes to the specialty's new on-site certifying examination.

He spent several years abroad developing and overseeing emergency medicine systems in the Middle East. He currently provides emergency care primarily in San Diego. His research interests include novel treatments for carbon monoxide poisoning and pioneering the use of insulin therapy for cardiotoxicity caused by calcium channel blockers and β-blockers.

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Tox Box

Aconite Poisoning

Introduction
Aconitine and related alkaloids are natural plant toxins. Poisoning can occur from accidental or intentional ingestion of wild plants (monkshood, wolfsbane) or through improper use in some herbal medications. Two grams of root are potentially lethal.

Kinetics
- Absorbed rapidly after ingestion
- Half-life up to ~24 hr

Mechanism
- Binds to open state of voltage-sensitive sodium channels
- Contains aconitine, mesaconitine, and hypaconitine
- Potent cardiovascular and neurovascular toxin

Clinical Manifestations
- ***CNS:*** paresthesia, perioral or limb numbness, and muscle weakness
- ***Cardiovascular:*** hypotension and variety of dysrhythmias, with ventricular tachycardia as the most serious (eg, torsades de pointes, atrial fibrillation, bidirectional)
- ***GI:*** hypersalivation, nausea, vomiting, abdominal pain, and diarrhea
- ***Respiratory:*** respiratory paralysis

Diagnostics
- Screening glucose, electrolytes, calcium, and magnesium levels and ECG
- Aconitine is detectable in urine or blood as send out.

Treatment
- Oral activated charcoal if <1 hr post ingestion and can protect airway
- Atropine for symptomatic bradycardia
- IV fluid bolus for hypotension; norepinephrine for fluid-unresponsive hypotension
- Correct electrolyte abnormalities (ie, hypokalemia, hypomagnesemia).
- Amiodarone or flecainide is the preferred antidysrhythmic for ventricular tachycardias; lidocaine and cardioversion have less success.
- Refractory hypotension may require cardiopulmonary bypass.

Disposition
- If asymptomatic, patient may be observed at home.
- If symptomatic (usually GI) or worse, monitor until resolution.

Aliphatic Hydrocarbon Ingestion

Introduction

Aliphatic hydrocarbons include a variety of petroleum distillates, including gasoline, and are present in many household cosmetics and chemicals (eg, lamp oils, furniture polish, paint thinner). Most ingestions are unintentional pediatric exposures that can result in life-threatening pulmonary complications, especially if accompanied by vomiting. In addition, halogenated hydrocarbons (eg, chloroform, trichloroethylene), which are usually inhaled, can lead to sudden death.

Mechanism

- Aspiration of low-viscosity agents leading to surfactant destruction
- General anesthetic effects on the CNS
- Increased myocardial sensitivity to epinephrine (halogenated)

Clinical Manifestations

- ***CNS:*** slurred speech, disorientation, dizziness, and ataxia
- ***Cardiac:*** dysrhythmias (halogenated)
- ***GI:*** nausea, vomiting, abdominal pain, and diarrhea
- ***Respiratory:*** cough and dyspnea
- ***Dermatologic (spill):*** irritation, defatting, and full-thickness burns

Diagnostics

- Chest x-ray (may not show changes until ~6 hr)
- Pulse oximetry
- ECG (optional)
- Acetaminophen level in intentional ingestions
- Rule out life-threatening coingestants (camphor, halogenated or aromatic hydrocarbons, metals, or pesticides) and treat accordingly.

Treatment

- Avoid activated charcoal because of vomiting and aspiration risk.
- Administer supplemental oxygen or intubate as needed.
  - Steroids and antibiotics are routinely unhelpful.
  - Bronchoalveolar lavage is controversial.
  - Instillation of surfactant or extracorporeal membrane oxygenation may help severe cases.
- Short-acting β-blockers for ventricular dysrhythmias

Aliphatic Hydrocarbon Ingestion (cont.)

Disposition

- If asymptomatic, patients may be observed at home.
- Evaluate deliberate ingestions or symptomatic cases.
  - Discharge asymptomatic cases at 6-8 hr.
  - Admit if persistent pulmonary or CNS symptoms.

Tox Box

Arsenic Toxicity

Introduction

Arsenic is a metalloid (atomic number 33) with similar physicochemical properties to phosphorus. Arsenic is nonpoisonous in its typically silvery-grey elemental state but can form several inorganic salts or oxides of exquisite toxicity, including realgar (As_4S_4), orpiment (As_2S_3), and arsenic trioxide (AsO_3). Arsenic naturally occurs throughout the earth's crust in various ores, typically as a sulfide and in association with other metals such as iron and copper. It has industrial utility in the manufacture of computer chips, in the doping of semiconductors, and as an increasingly uncommon herbicide. Medicinal purposes include the use of inorganic forms (AsO_3) for treating acute promyelocytic leukemia, and the use of organic forms (melarsoprol) for treating African trypanosomiasis and as a veterinary antihelminthic (thiacetarsamide). Toxicity typically occurs after ingestion of an inorganic salt and can manifest as prominent GI effects that can progress to multisystem organ failure associated with neurologic, cardiovascular, dermatologic, and hepatorenal effects.

Sources of Exposure

- Organic arsenicals of low toxicity (eg, arsenobetaine) from fish, crustaceans, or algae
- Inorganic salts in contaminated water or soil-derived produce (eg, rice) can lead to chronic toxicity.
- Acute toxicity typically from surreptitious addition of inorganic salts to food or beverages

Mechanism of Action (Toxicity)

- Inhibition of pyruvate dehydrogenase leads to decreased acetyl-coenzyme A and ATP.
- Inhibition of glutathione synthetase and G6PD leads to hemolysis and decreased hemoglobin.
- Inhibition of cardiac potassium channels leads to dysrhythmias.

Pharmacokinetics and Toxicokinetics

- Inorganic and organic forms are well absorbed from the GI tract (small intestine > colon).
- Hepatic metabolism (methylation, redox) leads to renal elimination of metabolites.

Risk Stratification

- Urine arsenic levels: >50 µg/L, >100 µg/g creatinine, or >100 µg total arsenic is abnormal

Arsenic Toxicity (cont.)

Clinical Manifestations (Acute)

- ***GI:*** abdominal pain, nausea or vomiting, and diarrhea ("rice water" or "cholera-like")
- ***Cardiovascular:*** tachycardia, hypotension, and ventricular dysrhythmias
- ***Neurologic:*** delirium, coma, or seizures
- ***Other:*** fever, acute respiratory distress syndrome, hepatitis, acute kidney injury, rhabdomyolysis, and erythroderma or desquamation

Diagnostics

- CBC, comprehensive metabolic panel, creatine phosphokinase level, ECG, abdominal x-ray, urine arsenic test (spot, 24 hr with speciation)

Treatment

- Positive abdominal x-ray — treat with gastric lavage followed by whole bowel irrigation
- Severe, acute toxicity — treat with chelation with British anti-Lewisite IM (4 mg/kg every 4 hr)
- Less symptomatic or chronic toxicity — treat with dimercaptosuccinic acid PO (10 mg/kg 3 times a day)

Disposition

- Acutely symptomatic with more than isolated GI manifestations — admit to ICU
- No GI signs or symptoms within 6-12 hr of ingestion — unlikely to develop severe manifestations