

Arsenic (As) and Inorganic Arsenic Compounds

- **Persons whose clothing or skin is contaminated with arsenic may secondarily contaminate others by direct contact or through release of inhalable dust.**
- **Elemental arsenic is usually a steel grey metal-like material without characteristic taste or smell. Arsenic trioxide (an odorless, tasteless, white or transparent, nonflammable solid) is one of the most toxic and prevalent forms of arsenic. The water solubility of arsenic salts varies depending on the salt.**
- **Arsenic trioxide is readily absorbed if ingested or inhaled, but only slowly absorbed through the skin. Toxicity usually results from ingestion. Acute signs and symptoms include nausea, vomiting, diarrhea, gastrointestinal hemorrhage, cerebral edema, tachycardia, dysrhythmias, and hypovolemic shock. The toxicity of a particular arsenic compound depends in part on its solubility.**

Description

Arsenic compounds exist in a number of inorganic and organic forms. This Medical Management Guideline focuses on arsenic trioxide (As_2O_3), one of the most toxic and prevalent forms. Other inorganic arsenic compounds may vary somewhat in relative toxicity, and organic arsenic compounds appear to be essentially nontoxic. Physical and chemical properties vary among the various arsenic compounds of toxicological concern. The physical and chemical properties of arsenic trioxide are presented in this Medical Management Guideline; the guidelines for decontamination and medical treatment are applicable for exposure to arsenic and inorganic arsenic compounds, including arsenic trioxide.

Arsenic trioxide is a white or transparent solid in the form of glassy, shapeless lumps or a crystalline powder that resembles sugar. It has no odor or taste. It forms readily when elemental metallic arsenic is heated to high temperatures or burned. When arsenic trioxide is burned, it releases toxic fumes and arsine gas (see arsine Medical Management Guideline), which is highly toxic (ATSDR 2005; HSDB 2007).

Routes of Exposure

<i>Inhalation</i>	Arsenic trioxide dust is readily absorbed from the lungs, but inhaled quantities are usually insufficient to cause acute systemic toxicity. Arsenic trioxide has no odor and thus provides no warning of hazardous airborne concentrations. Inhalation may present a relevant exposure hazard for other arsenic compounds such as lead arsenate and arsenic sulfide (ATSDR 2005; HSDB 2007).
<i>Dermal</i>	Direct contact with arsenic trioxide dust can cause localized skin irritation, but systemic absorption through the skin is negligible. Skin contact is unlikely to cause systemic effects unless the dermal barrier is compromised. Arsenic trioxide dust is irritating to the eyes (ATSDR 2005; HSDB 2007).
<i>Ingestion</i>	Ingestion is the most important route of acute exposure of arsenic trioxide. Ingested arsenic trioxide is quickly absorbed and can be extremely hazardous. Significant tissue and organ damage and death may result. Most acute intoxications are from suicidal or homicidal ingestion. Ingestion is the main route of exposure to other arsenites and arsenates for the general population. Overexposure may result from relatively high levels of arsenic in drinking water and foods. Contaminated soil may also be a source of significant arsenic exposure in children, although it is not likely that children would ingest sufficient arsenic-contaminated soil to cause significant acute toxicity. The human diet is a source of exposure to small (nontoxic) amounts of inorganic arsenic (ATSDR 2005; HSDB 2007).

Sources/Uses

Arsenic occurs naturally in soil and many kinds of rock (especially minerals and ores that contain copper and lead) as inorganic arsenic. Arsenic trioxide is produced during the smelting of ores that contain arsenic. Arsenic trioxide has been used to produce the wood preservative CCA (copper chromated arsenic); however, this treatment process has been phased out in the United States. Inorganic arsenic compounds have been used as pesticides, but can no longer be used in agriculture. Some organic arsenic compounds may be used as pesticides or as additives in animal feed. Small quantities of arsenic metal are used in alloys in products such as lead-acid batteries. Some arsenic compounds may also be found in semiconductors and light-emitting diodes (ATSDR 2005; HSDB 2007).

Standards and Guidelines

OSHA PEL (permissible exposure limit) = $10 \mu\text{g}/\text{m}^3$ as an 8-hour TWA concentration (as As) for inorganic arsenic (OSHA 2006).

NIOSH IDLH (immediately dangerous to life or health) = $5 \text{ mg}/\text{m}^3$ (as As) (NIOSH 2005).

EPA AEGL-2 (Acute Exposure Guideline Level-2) for arsenic trioxide = $3.7 \text{ mg}/\text{m}^3$ (10-minute) to $1.2 \text{ mg}/\text{m}^3$ (8-hour); AEGL-1 not recommended due to the lack of human or animal data for AEGL-1 end points (EPA 2007)

Physical Properties

Description: Arsenic is a usually a steel grey metal-like material with no characteristic taste or smell. Arsenic trioxide is a white or transparent solid in the form of glassy, shapeless lumps or a crystalline powder that resembles sugar. Other arsenic compounds vary in color (ATSDR 2005; HSDB 2007).

Warning properties: Inadequate; odorless and tasteless. Airborne arsenic trioxide may produce a burning sensation to the nose, mouth, and eyes and cause coughing, shortness of breath, headache, sore throat, and dizziness (ATSDR 2005; HSDB 2007).

Molecular weight (arsenic trioxide): 197.84 daltons (ATSDR 2005).

Boiling point (arsenic trioxide): 460°C (860°F) (ATSDR 2005).

Melting point (arsenic trioxide): 274°C (525°F) arsenolite; 313°C (595°F) claudetite (ATSDR 2005).

Vapor pressure (arsenic trioxide): 2.47×10^{-4} mmHg at 25 °C (ATSDR 2005)

Density (arsenic trioxide): 3.86 or 4.15 g/cm³ as cubes or crystals, respectively (ATSDR 2005).

Water solubility (arsenic trioxide): 17g/L at 16 °C (ATSDR 2005).

Flammability limits (arsenic trioxide): no data (ATSDR 2005).

Incompatibilities

Arsenic is flammable in the form of dust when exposed to heat or flame or by chemical reaction with powerful oxidizers. Arsenic is slightly explosive in the form of dust when exposed to flame. When heated or on contact with acid or acid fumes, arsenic emits highly toxic fumes, including arsine gas. Arsenic can react vigorously on contact with oxidizing materials. Arsenicals can react violently with strong oxidizing materials and active metals (HSDB 2007; NIOSH 2005). Hydrogen gas can react with inorganic arsenic to form the highly toxic gas, arsine (see the Medical Management Guideline for Arsine).

Health Effects

- **Acute signs and symptoms of arsenic trioxide systemic toxicity following oral exposure include nausea, vomiting, diarrhea, gastrointestinal hemorrhage, cerebral edema, tachycardia, dysrhythmias, hypovolemic shock, coma, and even death. Symptoms are dose dependent and can be delayed. Similar effects would be expected following oral exposure to toxic levels of other arsenic compounds.**
- **Dermal contact and inhalation of airborne arsenic trioxide and other arsenic compounds may cause localized irritation, but usually do not result in systemic effects.**

Acute Exposure

The toxic effects caused by acute exposure to arsenic are due in large part to its inhibition of pyruvate and succinate oxidation, which leads to decreased production of acetyl-CoA and succinyl-CoA, impaired gluconeogenesis, and disruption of oxidative phosphorylation. Arsenic accumulates in mitochondria and damages mitochondrial membranes. As(V) mimics phosphate anions, which leads to loss of high-energy phosphate bonds, uncoupling of ATP synthesis, and decreased mitochondrial respiration. The primary target organs are the gastrointestinal tract, heart, brain, and kidney. Eventually the skin, bone marrow, and peripheral nervous system are also affected. Arsenic has direct toxic effects on endothelial cells, increasing the permeability of small blood vessels (ATSDR 2005; HSDB 2007).

Children do not always respond to chemicals in the same manner as adults. Different protocols for managing their care may be needed.

This medical management guide focuses specifically on arsenic trioxide (an arsenite), which is one of the most toxic forms of arsenic. As little as 1–2.5 mg/kg of arsenic trioxide is a potentially fatal dose. Toxicity from natural sources of arsenic is rare except from drinking highly contaminated groundwater or from breathing highly contaminated air (e.g., from burning of arsenic-containing coal indoors without adequate ventilation). Other inorganic forms of arsenic called arsenates are in the pentavalent state (As^{5+}) and are several times less toxic than the arsenites. Elemental

arsenic has a gray metal-like appearance, is insoluble in water or body fluids, and is not considered poisonous. Small amounts of arsenic can be found in grains, meat, fish, and poultry. Organic arsenic, also known as fish or seaweed arsenic (arsenocholine, arsenobetaine, or arsenosugars) is mostly found in seafood such as bivalves, bottom-feeding fish, and seaweed and usually considered nontoxic (ATSDR 2005; HSDB 2007).

Gastrointestinal

Initial symptoms of acute arsenic trioxide poisoning (occurring within 30 minutes to several hours) include burning of the lips, pharyngeal constriction, severe abdominal pain, and nausea. A metallic or garlic taste and intense thirst also occur. Inflammation and necrosis of the mucosa and submucosa can lead to bloody or “rice water” diarrhea, vomiting, and gastrointestinal perforation and bleeding. Bleeding and/or fluid loss can result in electrolyte abnormalities, shock, and death (ATSDR 2005; HSDB 2007).

CNS

Encephalopathy (cerebral edema), headache, lethargy, delirium, hallucinations, seizures, or coma can occur. Cerebral lesions consisting of multiple, symmetrical foci of hemorrhagic necrosis occur in the gray and white matter (ATSDR 2005; HSDB 2007).

Peripheral neurologic

Peripheral neuropathy resembling Guillain-Barré syndrome (ascending flaccid paralysis) is common acutely or subacutely. Sensory symptoms predominate early, with patients complaining of “pins and needles” or electrical shock like pains in the lower extremities. This may be followed by numbness and motor weakness (ATSDR 2005; HSDB 2007).

Cardiovascular

Increased capillary permeability (third-spacing and vasodilation) can result in hypovolemic shock. Sinus tachycardia can be an early sign of poisoning. Polymorphous ventricular tachycardia, ventricular fibrillation, and congestive heart failure can occur. Electrocardiographic findings can include, prolongation of the QT interval, ST depression, and flattened T waves (ATSDR 2005; HSDB 2007).

<i>Respiratory</i>	<p>Pulmonary edema, acute respiratory distress syndrome (ARDS), and respiratory failure due to weakness of the respiratory muscles can occur following ingestion. Coughing, chest pain, dyspnea, and general irritation of the upper respiratory tract can occur following inhalation (ATSDR 2005; HSDB 2007).</p> <p>Children may be more vulnerable because of relatively higher minute ventilation per kg and failure to recognize the need to promptly evacuate an area when exposed.</p>
<i>Musculoskeletal</i>	<p>Myalgia, weakness, muscular atrophy, and rhabdomyolysis can occur (ATSDR 2005; HSDB 2007).</p>
<i>Renal</i>	<p>Initial glomerular damage leading to proteinuria is common following high arsenic exposure. Tubular necrosis and degeneration, oliguria with proteinuria, hematuria, and acute renal failure are also frequently observed (ATSDR 2005; HSDB 2007).</p>
<i>Hepatic</i>	<p>Hepatocellular injury after acute exposure to inorganic arsenicals is uncommon, but fatty infiltration of the liver, central necrosis, and cirrhosis may occur. Hepatitis may also develop due to altered intrahepatic heme metabolism, increased synthesis of bilirubin, and altered interhepatocyte protein transport (ATSDR 2005; HSDB 2007).</p>
<i>Dermal</i>	<p>Flushing, diaphoresis, edema (especially periorbital), hyperkeratosis, and brawny desquamation or exfoliative dermatitis can occur (ATSDR 2005; HSDB 2007).</p>
<i>Ocular</i>	<p>Conjunctivitis, photophobia, and dimness of vision, diplopia, and lacrimation can occur (ATSDR 2005; HSDB 2007).</p>
<i>Potential Sequelae</i>	<p>If the immediate effects of acute arsenic poisoning are survived, a variety of delayed effects, including peripheral neuropathy and bone marrow suppression (anemia, leukopenia, pancytopenia), may develop. New or persistent encephalopathy, dysrhythmias, and nail changes (Mee's lines) can also occur. Peripheral neuropathy involves sensory and motor neurons in a</p>

stocking-glove distribution. Initially painful dysesthesias (i.e., “pins and needles” or an electric shock-like sensation) are prominent. Early treatment with the chelator dimercaprol, also known as BAL (British AntiLewisite), may not eliminate the risk of delayed effects. Survival of the acute phase of arsenic poisoning is highly dependent on the dose received and the timing and extent of treatment. Recovery from subsequent peripheral neuropathy is usually only partial and may require months to years (ATSDR 2005; HSDB 2007).

Chronic Exposure

Chronic exposure is characterized by malaise, peripheral sensorimotor neuropathy, anemia, jaundice, gastrointestinal complaints, and characteristic skin lesions including hyperkeratosis (small corn-like elevations) and hyperpigmentation. Hyperkeratosis usually appears on the palms or soles. Pigmentation changes and hyperkeratosis can take 3–7 years to appear. Chronic inhalation can also lead to conjunctivitis, irritation of the throat and respiratory tract, and perforation of the nasal septum. Chronic exposure can cause allergic contact dermatitis (ATSDR 2005; HSDB 2007). Chronic exposure may be more serious for children because of their potential longer life span.

Carcinogenicity

The Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), the Environmental Protection Agency (EPA), and the National Toxicology Program (NTP) have classified arsenic as a human carcinogen based on sufficient evidence from human data. Arsenic trioxide causes skin and lung cancer, and may cause internal cancers such as liver, bladder, kidney, colon, and prostate cancers.

Reproductive and Developmental Effects

Arsenic ions released from arsenic trioxide within the body can cross the placenta and affect the developing fetus; arsenic is also excreted in breast milk. Experimental animal studies support an association between high ingested arsenic dose and fetal toxicity (ATSDR 2005; HSDB 2007).

Special consideration regarding the exposure of pregnant women may be warranted, since arsenic trioxide has been shown to be mutagenic and clastogenic, and is suspected of being teratogenic; thus, medical counseling is recommended for the acutely exposed pregnant woman.

Prehospital Management

- **Exposed persons whose skin or clothing is contaminated with arsenic trioxide can contaminate rescuers by direct contact or through release of inhalable dust.**
- **There is no serious risk of secondary contamination after clothing is removed and the skin is washed.**
- **Arsenic trioxide is irritating to the skin, eyes, and respiratory tract. Systemic effects may include severe gastrointestinal injury, life-threatening shock, and nerve damage and are usually associated with oral exposure.**
- **There is no specific antidote for arsenic trioxide. Prehospital treatment consists of supportive care and gastric decontamination. Chelation therapy is strongly recommended.**

Hot Zone

Rescuers should be trained and appropriately attired before entering the Hot Zone. If the proper equipment is not available, or if rescuers have not been trained in its use, assistance should be obtained from a local or regional HAZMAT team or other properly equipped response organization.

Rescuer Protection

Arsenic trioxide dust is readily absorbed through inhalation and can irritate the respiratory tract. Although it is poorly absorbed dermally, skin contact should be avoided because arsenic trioxide can irritate the skin.

Respiratory Protection: Positive-pressure, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to potentially unsafe levels of arsenic trioxide or combustion products (arsine and arsenic trioxide fumes) (HSDB 2007).

Skin Protection: Chemical-protective clothing is recommended when contact with arsenic trioxide is expected because skin irritation might occur (HSDB 2007).

ABC Reminders Quickly establish a patent airway, ensure adequate respiration and pulse. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible. Apply direct pressure to stop any heavy bleeding.

Victim Removal If victims can walk, lead them out of the Hot Zone to the Decontamination Zone. Victims who are unable to walk may be removed on backboards or gurneys; if these are not available, carefully carry or drag victims to safety.

Victims with chemically-induced acute disorders may suffer from anxiety, especially children who may be separated from a parent or other adult.

Decontamination Zone

All victims exposed to arsenic trioxide require decontamination (see *Basic Decontamination*, below).

Rescuer Protection If exposure levels are determined to be safe, decontamination may be conducted by personnel wearing a lower level of protection than that worn in the Hot Zone (described above).

ABC Reminders Quickly establish a patent airway, ensure adequate respiration and pulse. Stabilize the cervical spine with a collar and a backboard if trauma is suspected. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device if necessary. Apply direct pressure to control bleeding.

Basic Decontamination Victims who are able may assist with their own decontamination. Quickly remove and double-bag contaminated clothing and personal belongings.

Wash exposed skin and hair with mild soap and water (preferably under a shower). Rinse thoroughly with water. Use caution to avoid hypothermia when decontaminating victims, particularly children or the elderly. Use blankets or warmers after decontamination as needed.

Flush exposed or irritated eyes with plain water or saline for at least 15 minutes. Remove contact lenses if easily removable without additional trauma to the eye. Continue eye irrigation during other basic care and transport. If pain or injury is evident, continue irrigation while transferring the victim to the Support Zone.

In cases of ingestion, **do not induce emesis**. Aggressive decontamination with gastric lavage is recommended within 1 hour of ingestion of a life-threatening amount of poison.

Provide reassurance to chemically-contaminated victims during decontamination, particularly children who may suffer separation anxiety if separation from a parent occurs.

Transfer to Support Zone

As soon as basic decontamination is complete, move the victim to the Support Zone.

Support Zone

Be certain that victims have been decontaminated properly (see *Decontamination Zone*, above). Victims who have undergone decontamination pose no serious risks of secondary contamination to rescuers. In such cases, Support Zone personnel require no specialized protective gear.

ABC Reminders

Quickly establish a patent airway, ensure adequate respiration and pulse. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible. Administer supplemental oxygen as required and establish intravenous access if necessary. Place on a cardiac monitor.

Additional Decontamination

Continue irrigating exposed skin and eyes, as appropriate.

In cases of ingestion, **do not induce emesis**. Aggressive decontamination with gastric lavage is recommended within 1 hour of ingestion of a life-threatening amount of poison.

Advanced Treatment

In cases of respiratory compromise, secure airway and support respiration according to advanced life support (ALS) protocols.

Treat patients who have bronchospasm with an aerosolized bronchodilator such as albuterol. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Arsenic trioxide poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Patients who are comatose, hypotensive, or having seizures or cardiac arrhythmias should be treated according to ALS protocols.

If evidence of shock or hypotension is observed, begin fluid administration. For adults with systolic pressure less than 80 mm Hg, bolus perfusion of 1,000 mL/hour intravenous saline or lactated Ringer's solution may be appropriate. Higher adult systolic pressures may necessitate lower perfusion rates. For children with compromised perfusion, administer a 20 mL/kg bolus of normal saline over 10–20 minutes, followed by reassessment and further management as clinically appropriate.

Transport to Medical Facility

Only decontaminated patients or patients not requiring decontamination should be transported to a medical facility. "Body bags" are not recommended.

Report to the base station and the receiving medical facility the condition of the patient, treatment given, and estimated time of arrival at the medical facility.

If arsenic trioxide has been ingested, prepare the ambulance in case the victim vomits. Have ready several towels and open plastic bags to quickly clean up and isolate vomitus.

Multi-Casualty Triage

Consult with the base station physician or the regional poison control center for advice regarding triage of multiple victims.

Patients with evidence of significant exposure and all patients who have ingested arsenic trioxide should be transported to a medical facility for evaluation.

Asymptomatic patients who have not had direct exposure to arsenic trioxide may be discharged from the scene, after their names, addresses, and telephone numbers are recorded. These patients should be advised to seek medical care promptly if symptoms develop (see *Patient Information Sheet* below).

Emergency Department Management

- **Patients whose skin or clothing is contaminated with arsenic trioxide can contaminate rescuers by direct contact or through release of inhalable dust.**
- **Patients do not pose a serious risk of secondary contamination after their clothing is removed and their skin is washed.**
- **Arsenic trioxide is irritating to the skin, eyes, and respiratory tract. Systemic effects may include severe gastrointestinal injury, life-threatening shock, and nerve damage and are usually associated with oral exposure.**
- **There is no specific antidote for arsenic trioxide. Treatment consists of supportive care and gastric decontamination. Chelation therapy is strongly recommended.**

Decontamination Area

Previously decontaminated patients and patients who have no skin or eye irritation may be transferred immediately to the Critical Care Area. Others require decontamination as described below. Because arsenic trioxide can irritate the skin, thus increasing the probability of dermal absorption, chemical protective clothing is recommended when contact with arsenic trioxide is expected.

Be aware that use of protective equipment by the provider may cause anxiety, particularly in children, resulting in decreased compliance with further management efforts.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants that react with the skin. Also, emergency room personnel should examine children's mouths because of the frequency of hand-to-mouth activity among children.

ABC Reminders

Evaluate and support airway, breathing, and circulation according to ALS protocols.

Treat patients who have bronchospasm with an aerosolized bronchodilator such as albuterol. The use of bronchial sensitizing agents in situations of multiple

chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Arsenic trioxide poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Patients who are comatose, hypotensive, or have seizures or ventricular arrhythmias should be treated according to established emergency department protocols.

Basic Decontamination

Patients who are able may assist with their own decontamination. Remove and double-bag contaminated clothing and all personal belongings.

Wash exposed skin and hair with mild soap and water (preferably under a shower). Rinse thoroughly with water.

Use caution to avoid hypothermia when decontaminating victims, particularly children or the elderly. Use blankets or warmers after decontamination as needed.

Flush exposed or irritated eyes with plain water or saline for at least 15 minutes. Remove contact lenses if easily removable without additional trauma to the eye. Continue eye irrigation during other basic care and transport. If pain or injury is evident, continue irrigation while transferring the victim to the Support Zone.

In cases of ingestion, **do not induce emesis**. Consider gastric lavage for recent large ingestion. Consider administering a slurry of activated charcoal at a dose of 1 g/kg (infant, child, and adult dose) (HSDB 2007). (More information is provided in *Ingestion Exposure* under *Critical Care Area* below).

Critical Care Area

Be certain that appropriate decontamination has been carried out (see *Decontamination Area* above).

ABC Reminders

Evaluate and support airway, breathing, and circulation as in ABC Reminders above under *Decontamination Zone*. Establish intravenous access in seriously ill patients if this has not been done previously. Continuously monitor cardiac rhythm.

Patients who are comatose, hypotensive, or have seizures or cardiac arrhythmias should be treated in the conventional manner.

Inhalation Exposure

Administer supplemental oxygen by mask to patients who have respiratory complaints. For serious exposure, respiratory tract irritation can progress to pulmonary edema; maintain adequate oxygenation and provide mechanical support if needed.

Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Also consider the health of the myocardium before choosing which type of bronchodilator should be administered. Dopamine or norepinephrine may be appropriate in management of shock; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Arsenic trioxide poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Skin Exposure Dermal exposure to arsenic trioxide may cause skin irritation. Treat symptomatically.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants affecting the skin.

Eye Exposure Ensure that adequate eye irrigation has been completed. Test visual acuity. Examine the eyes for corneal damage and treat appropriately. Consult an ophthalmologist for patients who have apparent or suspected corneal injury.

Ingestion Exposure Fluid repletion should begin as soon as possible in severe acute poisoning. Central venous or pulmonary wedge pressure monitoring can be useful in managing severe exposures where hypotension is a risk.

In cases of ingestion, **do not induce emesis**. Aggressive decontamination with gastric lavage is recommended within 1 hour of ingestion of a life threatening amount of poison. If activated charcoal has not been given previously, consider administering a slurry at a dose of 1 g/kg (infant, child, and adult dose) if the patient is alert and able to swallow.

Arsenic is radiopaque and an abdominal radiograph should be obtained in cases of ingestion. If opacities compatible with arsenic are noted on the radiograph, consider whole bowel irrigation (e.g., with a polyethylene glycol [PEG-3350] electrolyte lavage solution).

Consider alkalization of urine (pH 7.5) to protect kidney from deposition of red cell breakdown products. Assure adequate renal function before administering sodium bicarbonate.

Antidotes and Other Treatments

Chelation therapy curtails the distribution of arsenic in the body and reduces the body burden. The decision to chelate for a patient should be made only by professionals experienced in the use of chelation, preferably in consultation with a regional poison control center or a medical toxicologist. Patients with a clear history of exposure to arsenic with significant GI and/or cardiovascular symptoms may require chelation

before laboratory confirmation. As time increases after exposure, chelation therapy becomes less effective in reducing the severity of poisoning and in reducing the risks of serious delayed effects. Do not chelate asymptomatic patients without the guidance of a 24-hour urinary arsenic level.

In acutely ill patients, the agent most frequently recommended is dimercaprol, also known as BAL (British AntiLewisite). The standard dosage regimen is 3–5 mg/kg IM every 4–6 hours until the 24-hour urinary arsenic level falls below 50 µg/L, unless an orally administered chelating agent (e.g., DMSA, see below) is substituted. This regimen may be adjusted depending upon the severity of the exposure and the symptoms.

Contraindications to BAL include preexisting renal disease, pregnancy (except in life-threatening circumstances) and concurrent use of medicinal iron (BAL and iron together form a complex that is very toxic).

An increased risk for hemolysis should also be considered when administering BAL to patients with glucose-6-phosphate dehydrogenase deficiency; arsenic trioxide is itself an inhibitor of G-6-PD.

Chelation therapy should be continued until the 24-hour urinary arsenic level falls below 50 µg/L. Alkalization of the urine stabilizes the dimercaprol metal complex and has been proposed to protect the kidneys during chelation therapy. If any degree of acute renal insufficiency develops during chelation, hemodialysis should be considered to remove the dimercaprolarsenic complex. The main side effect of BAL administered at 2.5 mg/kg is pain at the injection site. At an intramuscular dose of 5 mg/kg, the effects can include hypertension, nausea, vomiting, headache, lacrimation, rhinorrhea, salivation, and diaphoresis.

Oral agents such as 2,3-dimercaptosuccinic acid (DMSA or Succimer[®]) or D-penicillamine have been used as alternatives to BAL. DMSA is approved for the treatment of pediatric lead poisoning in the United States; it also has been used successfully to chelate arsenic in humans, and is being further evaluated for this use. Water-soluble chelating agents like DMSA are less toxic than BAL and are often substituted when the patient's condition improves. DMSA might also be preferable for patients with renal insufficiency, but GI motility is a prerequisite, as well as GI decontamination (to prevent increased arsenic absorption).

The use of D-penicillamine as an oral chelating agent is controversial. It has been used successfully in children, but should be avoided in penicillin-allergic patients.

Laboratory Tests

Routine laboratory studies for seriously exposed patients include CBC, serum electrolytes, urinalysis, and liver enzyme and kidney function tests. Chest radiographs and pulse oximetry (or ABG measurements) are recommended for patients who have respiratory symptoms. An abdominal radiograph can detect radiopaque ingested arsenic. Additionally, 24-hour urine arsenic levels are useful for monitoring symptomatic patients. A chelated or non-chelated level above 100 µg is usually considered abnormal. Normal total urinary arsenic levels are less than 50 µg/L in the absence of recent consumption of seafood that contains organic forms of arsenic (i.e., fish arsenic).

A high blood arsenic level (normal being less than 7 µg/100 mL) might confirm a diagnosis of poisoning. However, arsenic moves quickly out of the bloodstream (its initial half-life in blood is 1–2 hours) and a normal value does not exclude poisoning. If the blood arsenic level is normal, but the 24-hour urinary arsenic excretion is elevated, and there is a compatible clinical presentation, the diagnosis can still be made.

Note: If the patient has eaten seafood containing organic arsenic (fish arsenic) within the past 48 hours, total urinary arsenic might be significantly elevated

(urinary arsenic of up to 1,700 µg/L has been measured following a large shellfish meal). Some laboratories can speciate arsenic into the nontoxic organic arsenics found in seafood and the toxic inorganic forms, although results are often not quickly available.

Disposition and Follow-up

Hospitalize patients who present with typical symptoms of arsenic poisoning and those for whom chelation therapy is indicated.

Delayed Effects

Delayed effects can occur after an acute arsenic exposure that resulted in significant acute effects. Delayed effects include peripheral neuropathy, bone marrow suppression (anemia, leukopenia, pancytopenia), encephalopathy, cardiomyopathy, and dermatologic lesions. Although timely chelation therapy reduces the occurrence of delayed effects, follow-up should include particular attention to these organ systems.

Patient Release

Asymptomatic patients who have minimal exposure, normal initial examinations, and no signs of toxicity after 6 to 8 hours of observation may be discharged with instructions to seek medical attention promptly if symptoms develop (see the *Arsenic Trioxide—Patient Information Sheet* below).

Follow-up

Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor. Patients who remain asymptomatic after exposure require no follow-up. Discharged patients who had relatively minor or transient symptoms following an ingestion exposure should initiate a 24-hour urine collection for arsenic measurement. Follow-up should include evaluation of urinary arsenic levels, and consultation with the regional poison center regarding outpatient chelation. For severely exposed patients with significant symptoms of acute poisoning, follow-up evaluation of neurologic, circulatory, renal, pulmonary, hematologic, and hepatic function should be arranged. Patients who have corneal lesions should be reexamined within 24 hours.

Reporting

If a work-related incident has occurred, you may be legally required to file a report; contact your state or local health department.

Other persons may still be at risk in the setting where this incident occurred. If the incident occurred in the workplace, discussing it with company personnel may prevent future incidents. If a public health risk exists, notify your state or local health department or other responsible public agency. When appropriate, inform patients that they may request an evaluation of their workplace from OSHA or NIOSH. See Appendices III and IV for a list of agencies that may be of assistance.

Arsenic trioxide (As₂O₃)

Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to arsenic trioxide.

What is arsenic trioxide?

Arsenic is a naturally occurring element. There are many arsenic compounds of commercial importance. One of the most toxic is arsenic trioxide, which is a tasteless and odorless white or transparent solid with low flammability. It is used in the manufacture of wood preservatives, as an insecticide and herbicide, in metallurgy, and in glass and ceramic manufacturing.

What immediate health effects can be caused by exposure to arsenic trioxide?

Breathing arsenic trioxide can cause nose and throat irritation, but generally, a person cannot inhale enough to severely harm internal organs. Skin or eye contact can cause irritation. Daily arsenic doses from typical U.S. diet and drinking water sources are <1 µg per kg body weight. Intentional or unintentional swallowing of arsenic trioxide at dose levels exceeding a few micrograms arsenic per kilogram body weight can cause severe vomiting, diarrhea, abdominal cramps, and shock, as well as seizures; coma; damage to the liver, kidneys, nerves, and bone marrow; and death.

Can arsenic trioxide poisoning be treated?

Washing arsenical residues from the skin or eyes usually reduces the irritant effect. If arsenic trioxide is swallowed, measures can be taken to remove it from the body. In severe cases, medicines called chelating agents are given to remove arsenic from the body and eliminate it in the urine. Severely affected individuals must be hospitalized. In some cases, permanent nerve damage can result even if chelation therapy is used.

Are any future health effects likely to occur?

Arsenic trioxide can cause adverse health effects in the liver, kidney, brain, nervous system, or bone marrow for months or years after a severe poisoning.

What tests can be done if a person is exposed to arsenic trioxide?

Blood and urine tests for arsenic can be performed. However, most arsenic is eliminated from the blood within a few hours and from urine within a few days following exposure. In cases of ingestion, arsenic might show up in the intestines or stomach on x-rays. Arsenic levels in hair or nails can be used to estimate past or long-term exposure, but results may be misleading due to adsorption to the external surfaces; this can often be overcome by washing the samples extensively.

Where can more information about arsenic trioxide be found?

More information about arsenic trioxide can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational and environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA) or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

☐ Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- abdominal pain, diarrhea, vomiting
- severe weakness
- rapid heart rate
- shortness of breath, coughing, or wheezing
- increased pain or discharge from injured eyes

☐ No follow-up appointment is necessary unless you develop any of the symptoms listed above.

☐ Call for an appointment with Dr. _____ in the practice of _____.

When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.

☐ Return to the Emergency Department/_____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.

☐ Do not perform vigorous physical activities for 1 to 2 days.

☐ You may resume everyday activities including driving and operating machinery.

☐ Do not return to work for _____ days.

☐ You may return to work on a limited basis. See instructions below.

☐ Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.

☐ Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.

☐ Avoid taking the following medications: _____

☐ You may continue taking the following medication(s) that your doctor(s) prescribed for you:

☐ Other instructions: _____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ or _____, or by checking out the following Internet Web sites: _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

References

- ATSDR. 2005. Toxicological profile for arsenic (draft for public comment). U.S. Department of Health and Human Services. Agency for Toxic Substances and Disease Registry.
- EPA. 2007. Arsenic trioxide results. Acute Exposure Guideline Levels (AEGLs). U.S. Environmental Protection Agency. <http://www.epa.gov/opptintr/aegl/pubs/rest165.htm>. October 11, 2007.
- HSDB. 2007. Arsenic compounds. Hazardous Substances Data Bank. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>. October 11, 2007.
- NIOSH. 2005. NIOSH pocket guide to chemical hazards. Atlanta, GA: National Institute for Occupational Safety and Health. <http://www.cdc.gov/niosh/npg/npgd0038.html>. October 11, 2007.
- OSHA. 2006. Limits for air contaminants. Occupational safety and health standards. Washington, DC: Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1910.1810. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10023. October 11, 2007.

