
Arsenic Trioxide (As₂O₃)

CAS 1327-53-3; UN 1561

Synonyms include arsenic oxide, arsenious acid, arsenious oxide, arsenious trioxide, arsenous acid anhydride, crude arsenic, arsenolite, and white arsenic.

- **Persons whose clothing or skin is contaminated with arsenic trioxide can secondarily contaminate rescuers by direct contact or through release of inhalable dust.**
- **Arsenic trioxide is an odorless, tasteless, white or transparent nonflammable solid.**
- **Arsenic trioxide is readily absorbed if inhaled or ingested, but only slowly absorbed through the skin. Toxicity usually results from ingestion.**

Description

There are many forms of arsenic, but this medical Management Guideline focuses specifically on arsenic trioxide (As₂O₃), one of the most toxic and prevalent forms. 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 which is highly toxic.

Routes of Exposure

Inhalation

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. Thus, odor provides no warning of hazardous airborne concentrations.

Skin/Eye Contact

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.

Ingestion

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.

Sources/Uses

Arsenic is ubiquitous in the natural environment. Arsenic trioxide is one of the arsenites (inorganic forms of arsenic in the trivalent state $[\text{As}^{3+}]$), found in nature and is produced mainly from by-products of copper smelting. It is no longer commercially manufactured in the United States, but is imported primarily for use in manufacturing other arsenic compounds used as wood preservatives, insecticides, and herbicides. It is also used in metallurgical processes, and in the manufacturing of glass and ceramics. Arsenic compounds were formerly used medicinally in humans (e.g., Fowler's solution), but these uses have largely been abandoned. Inorganic arsenic compounds, however, can be found in some homeopathic and folk remedies.

Standards and Guidelines

OSHA PEL (permissible exposure limit) = $10 \mu\text{g}/\text{m}^3$ (averaged over an 8-hour workshift) for inorganic arsenic compounds.

NIOSH IDLH (immediately dangerous to life or health) = $5 \text{ mg As}/\text{m}^3$ (for all inorganic arsenic compounds).

Physical Properties

Description: white or transparent solid in the form of glassy, shapeless lumps or a crystalline powder that resembles sugar.

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.

Molecular weight: 197.84 daltons

Boiling point (760 mm Hg): $869 \text{ }^\circ\text{F}$ ($465 \text{ }^\circ\text{C}$)

Sublimes at $379 \text{ }^\circ\text{F}$ ($193 \text{ }^\circ\text{C}$)

Melting point: $594 \text{ }^\circ\text{F}$ ($312 \text{ }^\circ\text{C}$)

Vapor pressure: 66.1 mm Hg at $594 \text{ }^\circ\text{F}$ ($312 \text{ }^\circ\text{C}$)

Density (solid): 3.74 (water = 1.00)

Water solubility: Low solubility in water (37 g/L at $20 \text{ }^\circ\text{C}$, 115 g/L at $100 \text{ }^\circ\text{C}$); slightly soluble in alcohol; soluble in dilute HCl solutions.

Flammability: not flammable, but emits highly toxic arsine gas and oxides of arsenic fumes when burned.

Incompatibilities

Flammable reactions can occur in the presence of strong oxidizers. If arsenic trioxide is exposed to hydrogen gas or to the combination of acid (acid fumes) or water and active metals, the reaction can form toxic arsine gas (see *Medical Management Guideline for Arsine*).

Health Effects

- **Toxic effects of arsenic trioxide usually result from ingestion. Small amounts of arsenic trioxide can lead to multiple organ damage and death. Acute signs and symptoms include nausea, vomiting, diarrhea, gastrointestinal hemorrhage, cerebral edema, tachycardia, dysrhythmias, and hypovolemic shock. Symptoms are dose dependent and can be delayed.**
- **Dermal contact and inhalation of airborne arsenic trioxide can cause localized irritation and usually does not result in systemic effects.**

Acute Exposure

The toxic effects caused by acute exposure to arsenic trioxide are due in large part to its ability to bind to cellular proteins containing sulfhydryl groups. This inhibits the production of energy needed to maintain tissue functions, and results in a decrease in glutathione, which is necessary for the metabolic detoxification of arsenic. 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 trioxide has direct toxic effects on endothelial cells, increasing the permeability of small blood vessels.

Children do not always respond to chemicals in the same way that adults do. 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 to 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. 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 has a lower toxicity.

Gastrointestinal

Initial symptoms 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.

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.

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.

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.

Respiratory 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.

Exposure to certain chemicals can lead to Reactive Airway Dysfunction Syndrome (RADS), a chemically- or irritant-induced type of asthma.

Children may be more vulnerable because of relatively increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Musculoskeletal Myalgia, weakness, muscular atrophy and rhabdomyolysis can occur.

Renal 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.

<i>Hepatic</i>	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.
<i>Dermal</i>	Flushing, diaphoresis, edema (especially periorbital), hyperkeratosis, and brawny desquamation or exfoliative dermatitis can occur.
<i>Ocular</i>	Conjunctivitis, photophobia, and dimness of vision, diplopia, and lacrimation can occur.

Potential Sequelae

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 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.

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 to 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. Chronic exposure may be more serious for children because of their potential longer latency period.

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

*Reproductive and
Developmental Effects*

internal cancers such as liver, bladder, kidney, colon, and prostate cancers.

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. Arsenic trioxide is not included in *Reproductive and Developmental Toxicants*, a 1991 report published by the General Accounting Office (GAO) that lists 30 chemicals of concern because of widely acknowledged reproductive and developmental consequences.

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 can occur from all routes of exposure and may include severe gastrointestinal injury, life-threatening shock, and nerve damage.
- 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 the rescuers have not been trained in its use, call for assistance 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).

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

ABC Reminders

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

Victim Removal

If victims can walk, lead them out of the Hot Zone to the Decontamination Zone. Victims who are unable to walk should

be removed on backboards or gurneys. If these are not available, carefully carry or drag victims to safety.

Consider appropriate management of chemically contaminated children, anticipate separation anxiety if a child is 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 required in the Hot Zone (described above).

ABC Reminders

Quickly access for a patent airway, ensure adequate respiration and pulse. Maintain adequate circulation. If trauma is suspected, manually maintain cervical immobilization and apply a cervical collar and a backboard when feasible. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device if necessary. Apply direct pressure to control any bleeding.

Basic Decontamination

Victims 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 children or the elderly. Use blankets or warmers when appropriate.

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. 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. The effectiveness of activated charcoal in binding arsenic trioxide is questionable, but administration of a charcoal slurry is recommended pending further evaluation in cases of ingestion of unknown quantities (at 1 gm/kg, usual adult dose 60–90 g, child dose 25–50 g). A soda can and straw may be of assistance when offering charcoal to a child.

Consider appropriate management of chemically contaminated children at the exposure site. Also, provide reassurance to the child during decontamination, especially if separation from a parent occurs. If possible, seek assistance from a child separation expert.

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 risk of secondary contamination to rescuers. In such cases, Support Zone personnel require no specialized protective gear.

ABC Reminders

Quickly access for a patent airway, ensure adequate respiration and pulse. If trauma is suspected, manually maintain cervical immobilization and apply a cervical collar and a backboard when feasible. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device, if necessary. Maintain adequate circulation. Apply direct pressure to control any bleeding. Establish intravenous access, if necessary. Place on a cardiac monitor.

If evidence of shock or hypotension is observed begin fluid administration. For adults, bolus 1,000 mL/hour if blood pressure is under 80 mm Hg; if systolic pressure is over 90 mm Hg, an infusion rate of 150 to 200 mL/hour is sufficient. For children with compromised perfusion administer a 20 mL/kg bolus of normal saline over 10 to 20 minutes, then infuse at 2 to 3 mL/kg/hour.

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. The effectiveness of activated charcoal in binding arsenic trioxide is questionable, but administration of a charcoal slurry is recommended pending further evaluation in cases of ingestion of unknown quantities (at 1 gm/kg, usual adult dose 60–90 g, child dose 25–50 g). A soda can and straw may be of assistance when offering charcoal to a child.

Advanced Treatment

In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, perform cricothyroidotomy if equipped and trained to do so.

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. 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 in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.

Patients who are comatose, hypotensive, or have seizures or cardiac dysrhythmias should be treated according to advanced life support (ALS) protocols.

If massive exposure is suspected or if the patient is hypotensive, infuse intravenous saline or lactated Ringer's solution. For adults, bolus 1,000 mL/hour if blood pressure is under 80 mm Hg; if systolic pressure is over 90 mm Hg, an infusion rate of 150 to 200 mL/hour is sufficient. For children with compromised perfusion administer a 20 mL/kg bolus of normal saline over 10 to 20 minutes, then infuse at 2 to 3 mL/kg/hour.

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 the patient has ingested arsenic trioxide, prepare the ambulance in case the patient vomits toxic material or has diarrhea. 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 can occur from all routes of exposure and may include gastrointestinal injury, life-threatening shock, and nerve damage.**
- **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 may be transferred directly 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 fear in children, resulting in decreased compliance with further management efforts.

Because of their relatively larger surface area:weight ratio, children are more vulnerable to toxicants absorbed through 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 the airway, breathing, and circulation. Secure airway and respiration via endotracheal intubation. If not possible, perform cricothyroidotomy if equipped and trained to do so.

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. 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 in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.

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

Basic Decontamination

Patients who are able and cooperative 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.

Flush exposed or irritated eyes with plain water or saline for at least **15 minutes**. Remove contact lenses if present and easily removable without additional trauma to the eye. If ocular pain or injury is evident, continue irrigation while transferring the victim to the Critical Care Area.

In cases of ingestion, **do not induce emesis**. Consider gastric lavage for recent large ingestion. (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 the airway, breathing, and circulation as in ABC Reminders above. Children may be more vulnerable to corrosive agents than adults because of the relatively smaller diameter of their airways. Establish intravenous access in symptomatic patients. Continuously monitor cardiac rhythm.

Patients who are comatose, hypotensive, or have seizures or cardiac dysrhythmias 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 in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.

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

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.

Do not induce emesis. In case of recent ingestion (less than 1 hour), and if spontaneous emesis has not occurred, consider performing gastric lavage to prevent further absorption. Insert an orogastric tube and begin lavage with water or normal saline as soon as possible. Continue lavage until the return is clear. Activated charcoal may not bind significant amounts but is recommended (at 1 gm/kg, usual adult dose 60–90 g, child dose 25–50 g).

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 to 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. Alkalinization 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 dimercaprol-arsenic complex. Side effects of BAL administered at 2.5 mg/kg are mostly 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 $\mu\text{g}/\text{L}$ 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 $\mu\text{g}/100\text{ mL}$) might confirm a diagnosis of poisoning. However, arsenic moves quickly out of the bloodstream (its initial half-life in blood is 1 to 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 $\mu\text{g}/\text{L}$ 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 have ingested a significant amount of arsenic trioxide, those who have had significant inhalation exposure, and those who require chelation therapy.

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 form 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 an element found naturally in the environment. There are many arsenic compounds of commercial importance. One of the most toxic of these is arsenic trioxide. Arsenic trioxide is a white or transparent solid that has no taste or odor and low flammability. Arsenic trioxide 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.

Intentional or unintentional swallowing of even a tiny amount of arsenic trioxide 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 done to confirm exposures. In cases of ingestion, arsenic might show up in the intestines or stomach on x-rays. Arsenic levels in urine can be monitored to tell when the arsenic has been eliminated from the body. Monitoring for past or long-term exposure can be carried out by analysis of arsenic levels in hair or nails.

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:

- vomiting, abdominal cramps, diarrhea
- 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 _____