Arsine (AsH_3)
CAS 7784-42-1; UN 2188

- **Persons exposed only to arsine gas pose no serious risks of secondary contamination to personnel outside the Hot Zone.**
- **Arsine is a flammable and highly toxic gas with a garlic-like or fishy odor that does not provide adequate warning of hazardous levels.**
- **Inhalation is the major route of arsine exposure. There is little information about absorption through the skin or toxic effects on the skin or eyes. However, contact with liquefied arsine may result in frostbite injury.**

Description

Arsine is a colorless, flammable, and highly toxic gas. It has a garlic-like or fishy odor that can be detected at concentrations of 0.5 ppm and above. Because arsine is nonirritating and produces no immediate symptoms, persons exposed to hazardous levels may be unaware of its presence. Arsine is water soluble. It is generally shipped in cylinders as a liquefied compressed gas (NIOSH 2005). Exposure may occur when arsine gas is generated while metals or crude ores containing arsenic impurities are treated with acid (HSDB 2007).

Routes of Exposure

Inhalation

Inhalation is the major route of exposure. The odor threshold of arsine is 10-fold greater than the Occupational Safety and Health Administration (OSHA) permissible exposure limit. **Odor is not an adequate indicator of arsine's presence and does not provide reliable warning of hazardous concentrations.** Arsine is heavier than air and hazardous concentrations may develop quickly in enclosed, poorly ventilated, or low-lying areas. Initial symptoms (malaise, dizziness, nausea, abdominal pain, and dyspnea) may develop within several hours of exposure to 3 ppm of arsine (AIHA 1999).

Children exposed to the same levels of arsine as adults may receive larger doses because they have relatively greater lung surface area:body weight ratios and higher minute volumes:weight ratios. In addition, they may be exposed to higher levels than adults in the same location because of their short stature and the higher levels of arsine found nearer to the ground.

Skin/Eye Contact

There is little information about direct toxic effects of arsine on the skin or eyes, or about absorption through the skin (AIHA 1999). Exposure to liquefied arsine (the compressed gas) can result in frostbite (NIOSH 2005).

Ingestion

Ingestion of arsine itself is unlikely because it is a gas at room temperature. However, metal arsenides are solids that can react with acidic gastric contents, releasing arsine gas in the stomach.

Sources/Uses

Arsine gas is formed when arsenic-containing materials react with freshly formed hydrogen in water or acids (NIOSH 2005). Exposure may result when arsenic containing metals (i.e., metal vats) undergo acid washes. Unintentional exposures have also occurred during refining of ores (e.g., lead, copper, zinc, iron, and antimony ores) that contain arsenic. Arsine is used as a doping agent in the semiconductor industry and in the manufacture of crystals for fiberoptics and computer chips. It is used infrequently in galvanizing, soldering, etching, burnishing, and lead plating (HSDB 2007; IPCS 1997).

Standards and Guidelines

OSHA PEL (permissible exposure limit) = 0.05 ppm (averaged over an 8-hour workshift) (OSHA 2006).

NIOSH IDLH (immediately dangerous to life or health) = 3 ppm (NIOSH 2005). NIOSH considers arsine to be a potential occupational carcinogen.

EPA AEGL-2 (Acute Exposure Guideline Level-2) for arsine = 0.3 ppm (10-minute) to 0.02 ppm (8-hour); AEGL-1 not recommended due to steep dose-response relationship, mechanism of toxicity, and because toxicity occurs at or below the odor threshold (EPA 2007).

Physical Properties

Description: Colorless, nonirritating gas at room temperature.

Warning properties: Inadequate; garlic-1ike or fishy smell; odor threshold of 0.5 ppm (IPCS 1997)

Molecular weight: 77.9 daltons (HSDB 2007)

Boiling point (760 mm Hg): -80.5 E F (-62.5 EC) (HSDB 2007)

Vapor pressure: 11,000 mm Hg at 68 EF (20 EC) (HSDB 2007)

Gas density: 2.7 (air = 1) (NIOSH 2005)

Water solubility: 28 mg/100 mL at 68 EF (20 EC) (HSDB 2007)

Flammability: Extremely flammable; may be ignited by heat, sparks, or flames. Vapors may travel to a source of ignition and flash back (HSDB 2007).

Incompatibilities

Arsine reacts with strong oxidizers, chlorine, and nitric acid. Arsine decomposes above 446 EF (230 EC) (NIOSH 2007).

Health Effects

- **Arsine is a highly toxic gas and may be fatal if inhaled in sufficient quantities. Its primary toxic effect is due to hemolysis resulting in renal failure.**
- **Common initial symptoms of exposure include malaise, headache, thirst, shivering, abdominal pain, and dyspnea. These symptoms usually occur within 30–60 minutes with heavy exposure, but can be delayed for 2–24 hours. Absence of early symptoms does not necessarily indicate a nontoxic exposure.**
- **Hemoglobinuria usually occurs within hours, jaundice within 1 or 2 days.**

Acute Exposure

After absorption by the lungs, arsine enters red blood cells (RBC) where different processes may contribute to hemolysis and impairment of oxygen transport. Inhibition of catalase may lead to accumulation of hydrogen peroxide which, as an oxidizer, destroys red cell membranes and may contribute to arsine-induced conversion of Fe^{+2} to Fe^{+3}, which also impairs oxygen transport. Arsine preferentially binds to hemoglobin, and is oxidized to an arsenic dihydride intermediate and elemental arsenic, both of which are hemolytic agents. Arsine toxicity involves depletion of reduced glutathione. Therefore, people deficient in the enzyme glucose-6-phosphate-dehydrogenase (G6PD) are more susceptible to hemolysis following arsine exposure. Pre-existing cardiopulmonary or renal conditions, iron deficiency, and/or pre-existing anemia may result in more severe outcomes if hemolysis occurs (AIHA 1999; Beliles 1994; Woods 1995).

Contact with the skin or eyes is not expected to result in systemic toxicity. Ingestion of arsine is unlikely, but ingestion of metallic arsenides can lead to arsine gas production and toxicity.

Hematologic

Acute intravascular hemolysis develops within hours and may be severe during the first 2 or 3 days following exposure. Free hemoglobin levels in plasma rise (levels greater than 2 g/dL have been reported). Anemia ensues subsequent to hemolysis. Anemia may develop quickly and be severe. Leukocytosis and signs of intravascular coagulation can be observed during the hemolytic phase (IPCS 1997). Methemoglobinemia can be of concern in infants and toddlers. Children may be more vulnerable to loss of effectiveness of hemoglobin because of their relative anemia compared to adults.

Respiratory

A garlic odor may be present on the breath. Delayed accumulation of fluid in the lungs may occur after massive exposure. Dyspnea may be due to lack of oxygen secondary to hemolysis (HSDB 2007; IPCS 1997).

Children may be more vulnerable to gas exposure because of relatively higher minute ventilation per kg and failure to recognize the need to promptly evacuate an area when exposed.

Renal

Kidney failure due to acute tubular necrosis is a significant sequela of arsine exposure. Hemoglobin in the urine is thought to be the major cause of damage to the kidneys; however, a direct toxic effect of arsine or deposition of the arsine-hemoglobin-haptoglobin complex may also play a role. Urinalysis shows large amounts of protein and free hemoglobin usually without intact RBCs. Urine may be unusually colored (e.g., brown, red, orange, or greenish). Decreased urinary output may develop within 24–48 hours (HSDB 2007; IPCS 1997).

Gastrointestinal

Nausea, vomiting, and crampy abdominal pain are among the first signs of arsine poisoning. Onset varies from a few minutes to 24 hours after exposure (HSDB 2007).

Dermal

The characteristic bronze tint of the skin caused by arsine toxicity is induced by hemolysis and may be caused by hemoglobin deposits. The bronze coloration is not jaundice, although jaundice may develop later as a result of significant hemolysis (HSDB 2007).

Contact with liquefied arsine (compressed gas) can cause frostbite (HSDB 2007).

CNS

Headache is often an early sign of exposure. CNS disorders can develop several days after severe exposure; signs include restlessness, memory loss, disorientation, and agitation. Some exposed persons experience signs of peripheral nerve damage 1–2 weeks after exposure. There are case reports of polyneuropathy developing 1–6 months after arsine exposure (AIHA 1999; Reigart and Roberts 1999).

Hepatic

Right upper quadrant pain, hepatomegaly, elevated serum globulin, elevated liver enzymes and prolonged prothrombin time have been observed (AIHA 1999).

Musculoskeletal

Skeletal muscle injury or necrosis have been reported (HSDB 2007). Muscle pain and twitches, myoglobinuria, elevated levels of serum creatine phosphokinase (CPK), and aldolase have been observed.

Cardiovascular

Cardiovascular effects may include moderate and transient sinus tachycardia secondary to hemolysis or anemia, hypovolemia or acute pulmonary edema, hypotension and cardiovascular shock due to direct effects on the myocardium and hyperkalemia, elevation of the T-wave (ECG) and various degrees of heart block, and general vasoconstriction due to peripheral hypoxia (IPCS 1997).

Ophthalmic/Ocular

Watery eyes, photophobia, blurred vision, and red staining of the conjunctiva may appear early after exposure (IPCS 1997).

Chronic Exposure

Chronic arsine exposure can result in gastrointestinal upset, anemia, and damage to lungs, kidneys, liver, nervous system, heart, and blood-forming organs (HSDB 2007; IPCS 1997). There is little information regarding health effects of chronic low-level exposures to arsine.

Carcinogenicity

There are no data on the carcinogenicity of arsine in humans or in experimental animals. However, arsine is oxidized to the same trivalent and pentavalent forms of arsenic as those seen after drinking-water or inhalation exposure to arsenic compounds known to present a cancer hazard. The Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), and the Environmental Protection Agency (EPA) have classified inorganic arsenic as a human carcinogen based on sufficient evidence from human data.

Reproductive and Developmental Effects

Arsine should be treated as a potential teratogenic agent. Although the reproductive effects of acute or chronic exposure to arsine are unknown, some related inorganic arsenicals produce a broad spectrum of adverse developmental effects in animals. Animal studies indicated that in arsine-exposed mothers, arsenic crosses the placenta and reaches the fetus (AIHA 1999); however, no adverse developmental effects were observed.

Prehospital Management

- **Although small amounts of arsine gas can be trapped in the victim's clothing or hair after an overwhelming exposure, these quantities are not likely to create a hazard for response personnel outside the Hot Zone.**
- **The odor of arsine is not always detected during serious exposures. Since symptoms may be delayed, ALL exposure victims should be evaluated at a medical facility.**
- **Toxic effects may be delayed for up to 2–24 hours after exposure.**
- **There is no specific antidote for arsine. Treatment is symptomatic and consists of measures to support respiratory, vascular, and renal function.**

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

Arsine is a highly toxic systemic poison.

Respiratory Protection: Positive-pressure, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to potentially unsafe levels of arsine (NIOSH 2005).

Skin Protection: Chemical-protective clothing is not generally required because arsine gas is not absorbed through the skin and does not cause skin irritation. However, contact with the liquid (compressed gas) can cause frostbite injury to the skin or eyes (NIOSH 2005).

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

Victims who have exposure only to arsine gas do not need decontamination. They may be transferred immediately to the Support Zone. In rare cases of liquefied arsine-contamination, remove and double-bag contaminated clothing.

In rare cases of liquefied arsine dermal contamination, immediately flush exposed areas with running water for at least 15 minutes (IPCS 1997).

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

Support Zone

Support Zone personnel require no specialized protective gear if the victim has been exposed only to arsine gas.

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. Evaluate for respiratory tract irritation, bronchitis, or pneumonitis (HSDB 2007).

In cases of dermal and ocular exposure, immediately flush exposed areas with running water for at least 15 minutes (IPCS 1997).

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

Advanced Treatment

In cases of respiratory compromise, secure airway and support respiration according to advanced life support (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.. Monitor fluid balance and avoid fluid overload if renal failure supervenes (Reigart and Roberts 1999); monitor plasma electrolytes to detect disturbances (particularly hyperkalemia) as early as possible. Monitor hematocrit.

Because of possible severe hemolysis, ensure adequate oxygenation by arterial blood gas measurement or pulse oxygenation monitoring. Ensure adequate hydration by starting intravenous fluids. The use of diuretics such as furosemide to maintain urinary flow is an important consideration and should be performed under medical base control.

Transport to Medical Facility

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.

Multi-Casualty Triage

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

It is difficult to determine at the scene which persons have had the most serious exposures and are likely to develop severe hemolysis; therefore, *all* persons who have potential exposure should be transported to a medical facility for evaluation.

Persons who have smelled a garlic- or fish-like odor should be transported first.

Emergency Department Management

- **Although small amounts of arsine gas can be trapped in the victim's clothing or hair after an overwhelming exposure, these quantities are not likely to create a hazard for hospital personnel away from the scene.**
- **Arsine poisoning causes acute intravascular hemolysis, which may lead to renal failure. Arsine gas does not produce acute arsenic intoxication.**
- **Even if arsine's odor was not detected at the scene, those present could have been seriously exposed. All exposure victims should be evaluated and observed.**
- **There is no specific antidote for arsine. Treatment consists of measures to support vascular, renal, hematologic, and respiratory function.**

Critical Care Area

Patients exposed only to arsine gas do not need decontamination.

ABC Reminders

Evaluate and support airway, breathing, and circulation according to ALS protocols. Establish intravenous access in symptomatic patients. Monitor cardiac rhythm.

Monitor fluid balance carefully to avoid fluid overload if renal failure supervenes (Reigart and Roberts 1999); monitor plasma electrolytes to detect disturbances (particularly hyperkalemia) as early as possible, and monitor hematocrit.

Patients who are comatose or hypotensive should be treated in the conventional manner.

Consider dopamine for hypotension or oligonuria, or norepinephrine in cases of severe resistant shock.

Observe patients who have inhaled arsine for up to 24 hours. Follow up as clinically indicated.

Inhalation Exposure

Administer supplemental oxygen by mask to patients who have respiratory symptoms. 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). Arsine 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.

If hemolysis develops, initiate urinary alkalinization. Add 50–100 mEq of sodium bicarbonate to one liter of 5% dextrose in 0.25 normal saline and administer intravenously at a rate that maintains urine output at 2 –3 mL/kg/hour. Maintain alkaline urine (i.e., pH >7.5) until urine is hemoglobin free. Closely monitor serum electrolytes, calcium, BUN, creatinine, hemoglobin, and hematocrit (Ellenhorn 1997).

Consider hemodialysis if renal failure is severe. (Although hemodialysis will assist the patient who has renal failure, it will not effectively remove the arsine-hemoglobin or arsine-haptoglobin complexes deposited in the renal tubules.) Blood transfusions may be necessary if hemolysis causes severe anemia (Reigart and Roberts 1999).

Skin Exposure

In case of frostbite injury, irrigate with lukewarm (42 EC) water according to standard treatment.

Eye Exposure

In case of frostbite injury, ensure that thorough warming with lukewarm water or saline has been completed. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have corneal injuries.

Antidotes and Other Treatments

There are no antidotes for arsine poisoning.

Do not administer arsenic chelating drugs. Although BAL (British Anti-Lewisite, dimercaprol) and other chelating agents are acceptable for arsenic poisoning, they are not effective antidotes for arsine poisoning and are not recommended (HSDB 2007).

Laboratory Tests

If significant exposure is a possibility and transfusion is considered, obtain a blood sample for type and screen. Laboratory tests to determine hemolysis include CBC with peripheral smear, urinalysis, and plasma free hemoglobin and haptoglobin analyses. These tests should be performed in all cases of suspected poisoning. Other useful studies include renal-function tests (e.g., BUN, creatinine), and determinations of serum electrolytes and bilirubin levels. Urinary arsenic may be elevated for a few weeks following arsine exposure and may provide some index of the extent of exposure.

Disposition and Follow-up

Decisions to admit or discharge a patient should be based on exposure history, physical examination, and test results.

Delayed Effects

All patients who have suspected arsine exposure should be carefully observed for 24 hours, including hourly urine output. Onset of hemolysis may be delayed for up to 24 hours, and acute renal failure may not become evident for as long as 72 hours after exposure.

Patient Release

Patients who have no signs of hemolysis may be discharged after 24 hours of observation with instructions to seek medical care promptly if symptoms develop (see the *Arsine—Patient Information Sheet* below). Released patients should also be instructed to rest and to drink plenty of fluids.

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.

All patients should have repeat urine and blood laboratory tests in 12–24 hours. Patients who have corneal injuries should be reexamined within 24 hours.

If severe hemolysis has occurred, anemia may persist for several weeks (AIHA1999).

Polyneuropathy and alteration in mental status are reported to have followed arsine poisoning after a latency of 1–6 months (Reigart and Roberts 1999). Depending on the severity of arsine exposure, patients should be evaluated periodically by their physician for several months; these examinations should include hematological and urinalysis tests.

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 Appendix III for a list of agencies that may be of assistance.

Arsine
Patient Information Sheet

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

What is arsine?
Arsine is a colorless, flammable and non-irritating gas with a garlic-like or fishy smell, but exposure to levels below the odor threshold may present a health hazard. Arsine is used in a variety of processes during the manufacturing of electronic products. If water or acid contacts ores or metals that contain arsenic, they may release arsine gas at hazardous levels.

What immediate health effects can result from arsine exposure?
Breathing in arsine gas can be very harmful, even in small quantities. The main effect of arsine poisoning is to destroy red blood cells, causing anemia (lack of red blood cells) and kidney damage. Within hours after a serious exposure, symptoms such as headache, weakness, shortness of breath, and back or stomach pain with nausea and vomiting may develop; the urine, skin, and eyes may become discolored. Although arsine is related to arsenic, it does not produce the usual signs and symptoms of arsenic poisoning.

Can arsine poisoning be treated?
There is no antidote for arsine, but its effects can be treated. A doctor may give the exposed patient fluids through a vein to protect the kidneys from damage. For severe poisoning, blood transfusions and cleansing of the blood (hemodialysis to prevent additional kidney damage) may be needed.

Are any future health effects likely to occur?
After a serious exposure, symptoms usually begin within 2–24 hours (see the *Follow-up Instructions*). Most people do not develop long-term effects from a single, small exposure to arsine. In rare cases, permanent kidney damage or nerve damage has developed after a severe exposure. Repeated exposures to arsenic may cause skin or lung cancer; however, similar results from long-term exposure to arsine have not been reported..

What tests can be done if a person is exposed to arsine?
Specific tests can show the amount of arsenic in urine, but this information may or may not be helpful to the doctor. Standard tests of blood, urine, and other measures of health may show whether exposure has caused serious injury to the lungs, blood cells, kidneys, or nerves. Since toxic effects of arsine poisoning may be delayed, testing should be done in all cases of suspected exposure.

Where can more information about arsine be found?
More information about arsine 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:

- unusual fatigue or weakness
- shortness of breath
- abnormal urine color (red or brown)
- stomach pain or tenderness
- unusual skin color (yellow or bronze)

[ ] 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 _____

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