
Chemical Terrorism Fact Sheet

Blood Agents - Arsines
(Arsenic Hydride, AsH_3)

Protective Equipment/Detection

A positive-pressure, self-contained breathing apparatus (SCBA) or supplied-air respirator with a full-facepiece, or an air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted canister, is recommended for protection. Chemical-protective clothing is not required because arsine gas is not absorbed through the skin and does not cause skin irritation.

Decontamination

Victims exposed only to arsine gas do not need decontamination, but should be removed immediately from the contaminated environment.

Signs and Symptoms

Arsine is the most acutely toxic form of arsenic and preferentially binds to hemoglobin. Inhibition of catalase may lead to the accumulation of hydrogen peroxide, which, as an oxidizer, destroys red cell membranes and aids the arsine-induced conversion of Fe^{+2} to Fe^{+3} , which further impairs oxygen transport. Arsine is oxidized to an arsenic-dihydride intermediate and elemental arsenic, both of which are also hemolytic agents. Toxicity involves depletion of reduced glutathione, so glucose-6-phosphate-dehydrogenase (G6PD) deficient people are more susceptible to hemolysis.

The characteristic features of acute poisoning are abdominal pain, bloody urine, and jaundice. Initial symptoms include headache, thirst, shivering, malaise, weakness, dizziness, dyspnea, abdominal and back pain, hepatomegaly, nausea, and vomiting. These can develop within 30 - 60 minutes after heavy exposure, but more typically occur 2 - 24 hours after exposure. The characteristic garlicky odor of arsine may be detectable in the breath. CNS disorders can develop several days after severe exposure with signs including restlessness, memory loss, disorientation, and agitation. Signs of peripheral nerve damage may occur 1 to 2 weeks after exposure. EKG changes and dysrhythmias associated with hypocalcaemia, and hypotension (with severe exposure) can also occur.

Hematuria, light to dark red, is usually seen 4 - 6 hours after exposure, followed by jaundice 12-48 hours later. Hemolysis can persist for up to 4 days. An unusual bronze discoloration of the skin may be observed as well. With severe exposure, the products of red blood cell and hemoglobin destruction will clog the kidneys, producing acute tubular destruction and renal failure.

Other toxic effects of arsine include liver and heart damage, either by direct actions of arsine in these cells or from the formation of arsenic. The skin is not generally affected by arsine, other than the potential for frostbite injury with exposure to the compressed liquid form.

Once inhaled, arsine breaks down and releases inorganic arsenic into the system. When ingested, arsenic compounds can cause nausea, vomiting and diarrhea within a few hours. Chronic arsenic intoxication can produce dermatitis, increased pigmenta-



Arsine has a mild garlic odor.
Photo courtesy of the Garlic Information Center, UK

Chemical Overview

First identified in 1775, arsine is a highly poisonous, colorless, nonirritating, flammable gas with a mild garlic odor at concentrations of 0.5 ppm and above (a level 10-fold greater than OSHA permissible levels). Two and one half times heavier than air, it will settle to low-lying areas. It is soluble in water, and slightly soluble in alcohol and alkalis.

Arsine results when nascent hydrogen is generated in the presence of arsenic, or when water reacts with a metallic arsenide. Fungi in the presence of arsenic (especially in sewage) can also produce arsine. Stibine (SbH_3), a toxic gas that is formed when antimony is exposed to nascent hydrogen, equals or surpasses arsine in toxicity and causes a specific toxic action similar to arsine. Stibine is less stable than arsine, so fewer cases of stibine poisoning have been reported.

Arsine is commercially used in organic synthesis and the processing of solid-state electronic components. Most cases of arsine poisoning have been associated with the use of acids and crude metals or ores that contain arsenic impurities, and are the result of arsine's accidental formation during smelting, refining, galvanizing, soldering, etching and lead plating operations.

The current OSHA standard for occupational exposure to arsine is 0.05 ppm (0.2 mg/m^3 of air) and to stibine is 0.1 ppm (0.5 mg/m^3 of air), as a time-weighted average in any 8-hour work shift of a 40-hour workweek. NIOSH recommends that exposure to inorganic arsenic and to arsine be limited to 0.002 mg (2.0 μ) of arsenic/ m^3 of air as determined by a 15-minute sampling period. Children are at higher risk because of their greater lung surface area to body weight ratio, increased minute volume to weight ratio, and shorter stature.

Signs and Symptoms (Continued)

tion, thickening of the skin on the palms and soles of the feet, ECG changes, anemia, and leukopenia, all of which regress once the exposure had ended. Acute arsine exposure will not usually produce the symptoms of chronic exposure.

Stibine also reacts with hemoglobin and victims experience symptoms similar to arsine exposure. Unlike arsine, however, stibine exerts a direct effect on brain cells, leading to various degrees of degeneration.

Laboratory: As anemia develops, the peripheral smear shows variation in the size and shape of the red blood cells, red-cell fragments, Heinz bodies, ghost cells, and cell components with an affinity for basic dyes. The bone marrow is usually unremarkable. Coombs and Ham tests are negative, and RBC fragility is normal. Urinalysis shows myoglobinuria, large amounts of protein and free hemoglobin usually without intact RBCs; and the urine may be colored (e.g., brown, red, orange, or greenish). Elevated serum globulin, serum creatine phosphokinase (CPK) and liver enzymes, as well as prolonged prothrombin times, have been observed.

Treatment

With no specific antidote for arsine/stibine, treatment is supportive of respiratory, vascular, and renal function. In acute exposure, prompt medical attention is critical. By NIOSH guidelines, treatment of severe arsine poisoning should include an immediate blood exchange transfusion to replace the destroyed red blood cells and to remove arsenic and the hemoglobin-arsine complex; followed by the administration of dimercaprol (BAL), which is available for deep, intramuscular injection. The standard dosing regimen is 3-5 mg/kg IM every 4 hours for four doses.

Some authorities advise against the use of dimercaprol or other arsenic chelating drugs, saying that they are not effective in arsine poisoning. This is possibly true in acute toxic events where significant levels of arsenic within the body are unlikely to develop. Since these drugs may have their own levels of systemic toxicity, you should assess the potential for systemic arsenic poisoning and consider monitoring urinary arsenic excretion to assess the severity of poisoning, and then weigh the risks against the benefits of using these agents. With sub-acute or chronic exposures, however, significant arsenic levels may develop and chelating agents would be warranted.

If hemolysis develops, initiate urinary alkalization by administering a solution of 50 to 100 mEq of sodium bicarbonate in one liter of 5% dextrose in 0.25 normal saline at a rate that maintains urine output at 2 - 3 mL/kg/hour. Maintain an alkaline urine (pH >7.5) until urine is hemoglobin free. Closely monitor serum electrolytes, calcium, BUN, creatinine, hemoglobin, and hematocrit. For patients with severe renal damage, dialysis should be started. Dialysis, though often life saving, does not remove arsenic from the patient, so treatments to remove arsenic from the victim's body should be considered.

Supportive care – supplemental oxygen, fluids, etc. -- should be provided as indicated.

Aerosolized bronchodilators should be administered for acute bronchospasm, with consideration of the health of the myocardium in choosing which type of bronchodilator should be used. Arsine poisoning is not known to add additional risk during the use of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. A dose of 0.25–0.75 mL of 2.25% racemic epinephrine solution in water, repeated every 20 minutes as needed, should be used.

Additional information and references available at <http://www.bioterrorism.slu.edu>



Chemical Overview (continued)

Inhalation of 250 ppm (800 mg/m³) of arsine gas is instantly lethal. Exposures of 25-50 ppm (80-160 mg/ m³) for 30 minutes, or 10 ppm (32 mg/m³) for longer (1-2 hours) exposures, are lethal. The mean lethal dose is unknown for man. The exposure limits for stibine are not reported.

Long-term Medical Sequelae

If severe hemolysis has occurred, anemia may persist for several weeks. Polyneuropathy and alteration in mental status have been reported following arsine poisoning after a latency of 1 to 6 months. Therefore, patients should be evaluated periodically for several months, including hematological and urinalysis tests.

Arsine has not been classified for carcinogenic effects, but arsenic compounds and metabolites are known human carcinogens. Arsine should also be treated as a potential teratogenic agent.

Environmental Sequelae

The environmental effects of arsine are not reported. However, on exposure to light, moist arsine decomposes quickly, depositing shiny black arsenic.

Disclaimer

Information contained in this fact sheet was current as of September 2002, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.

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