



Arsine

September 2003

Introduction

Arsine, known chemically as arsenic hydride, is the arsenical analog to ammonia and is a lethal gaseous form of arsenic. In nature, it is produced by certain fungi that grow on decaying material or by sewage containing arsenic, and whenever arsenic-containing metallic ores come in contact with hydrogen ions from the action of an acid on the metal. The first case of arsine poisoning was reported in 1815 after a German chemist died from an exposure to arsine in his laboratory. From 1815 to 1928, 247 cases of arsine poisoning were reported, but the mortality rate is unknown. From 1928 to 1974 an additional 207 cases were reported, of which 51 (25%) were fatal.

It should be noted that while this presentation discusses arsine, stibine, or antimony hydride, acts like arsine in the body and is equally or more lethal. Fortunately, it is a more unstable compound and rarely seen.

Arsine – Overview

Arsine, first identified in 1775, is a highly poisonous gas that is colorless, non-irritating, and flammable. It has a mild odor likened to garlic or onion that is noticeable at concentrations of 0.5 parts per million and above, but this odor cannot be relied upon for detection. It is also two and a half times heavier than air and will settle to low-lying areas. It is readily soluble in water, but only slightly soluble in alcohol or alkaline solutions. Commercially, it is used mainly in organic synthesis and in the processing of solid-state electronics, but can be encountered during metallic ore processing.

Arsine – Toxicity

Arsine is the most acutely toxic form of arsenic, acting much faster than any solid arsenide or even pure arsenic. It is known as a blood gas agent because it binds preferentially to hemoglobin and prevents oxygen exchange within the body. In

addition, it oxidizes into an arsenic-dihydride intermediate and elemental arsenic, both of which are potent hemolytic agents. Arsine also inhibits catalase, leading to the accumulation of hydrogen peroxide, which, as an oxidizer, destroys red cell membranes and aids the arsine-induced conversion of iron from the ferrous to the ferric state. These actions further impair oxygen transport. Toxicity involves depletion of reduced glutathione, so glucose-6-phosphate-dehydrogenase (G6PD) deficient people are more susceptible to hemolysis. While most of arsine's toxicity can be explained by red cell destruction, it also has a direct and severe effect on the liver, spleen, kidneys, lungs, and other organs.

Arsine – Toxicity

As a gas, arsine's main route of toxicity is by inhalation. Since arsine is heavier than air, children are considered to be more vulnerable due their short stature, smaller airway diameters, increased minute volume per kilogram of weight, and greater lung surface area to body weight ratio. Arsine is not known to affect the skin or to have dermal absorption, although in solution, arsenic can be absorbed through the skin. 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 parts per million, or 0.2 mg/m³ 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/m³ of air as determined by a 15-minute sampling period.

Although the mean lethal dose of arsine in man is unknown, inhalation of 250 parts per million, or 800 mg/m³, of arsine gas is instantly lethal. Exposures of 25 to 50 parts per million for 30 minutes, or 10 parts per million for 1 to 2 hours, are also known to be lethal. In fact, a single inhalation at 30 parts per million can produce symptoms. Victims who receive sub-lethal doses of arsine will typically recover without sequelae, but those receiving lethal doses cannot be expected to survive, even with therapy.

Protective Equipment

Since arsine is a gas and does not affect the skin, chemical protective clothing is typically not required. Respiratory protection, however, is necessary and there are three options: a positive-pressure, self-contained breathing apparatus, a supplied-air respirator with a full facepiece, or an air-purifying, full facepiece respirator, a gas mask, with a chin-style, front- or back-mounted canister.

Detection

As stated earlier, you cannot rely upon the sense of smell for the detection of arsine. A variety of arsine monitors and gas sensors are commercially available. These units typically detect arsine at levels as low as 0.05 parts per million.

Decontamination

Victims exposed only to arsine gas do not need decontamination, but should be removed immediately from the contaminated environment. The presence of a solid arsenical compound or elemental arsenic, however, may require decontamination.

Signs and Symptoms

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 to 60 minutes after heavy exposure, but more typically are noted 2 to 24 hours after exposure. The characteristic garlicky odor of arsine may be detectable in the breath. EKG changes and dysrhythmias associated with hypocalcemia are likely to occur and, after severe exposure, hypotension will develop. If the exposure is not immediately lethal, CNS disorders can develop several days after severe exposure with signs including restlessness, memory loss, disorientation, and agitation. Signs of peripheral nerve damage may appear 1 to 2 weeks after exposure.

Signs and Symptoms

As a result of the hemolysis process, hematuria, from light to dark red, is usually seen 4 to 6 hours after exposure, followed by jaundice 12 to 48 hours later. Hemolysis can persist for up to 4 days, and in time, an unusual bronze discoloration of the skin may be observed. With severe exposure, the products of red blood cell and hemoglobin destruction will clog the kidneys, producing acute tubular destruction and renal failure.

As already mentioned, arsine can have a direct and severe effect on other organs. Other toxic effects of arsine include lung, 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.

Laboratory

As the hemolytic 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, however, is usually unremarkable. Coombs and Ham tests are negative, and red blood cell fragility is normal. Urinalysis reveals myoglobinuria, large amounts of protein and free hemoglobin usually without intact red blood cells, and the urine may be colored brown, red, orange, or even greenish. Elevated serum globulin, serum creatine phosphokinase (CPK) and liver enzymes, as well as prolonged prothrombin times, have been observed.

Treatment

Clearly, all toxic exposures require basic first aid and arsine exposure is no different. In acute exposure, prompt medical attention is critical and victims should be rushed to an appropriate medical facility. With no specific antidote for arsine, treatment is supportive of respiratory, vascular, and renal function. This includes supplemental oxygen and fluids, and the use of aerosolized bronchodilators for those with acute bronchospasm. For children with stridor, 0.25 to 0.75 mL of 2.25% racemic epinephrine solution in water should be used and repeated every 20 minutes as needed. 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 for BAL is 3-5 mg/kg IM every 4 hours for four doses. However, it must be understood that some authorities advise against the use of dimercaprol or other arsenic chelating drugs, saying that they are not effective in arsine poisoning, particularly 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.

Treatment

If hemolysis develops, initiate urinary alkalinization by administering a solution of 50 to 100 mEq of sodium bicarbonate in one liter of 5% dextrose in quarter normal saline at a rate that maintains urine output at 2 to 3 mL/kg/hour. Adjust the bicarb dose to maintain an alkaline urine, defined as a urinary pH >7.5, until urine is hemoglobin free. Throughout this period, closely monitor serum electrolytes, calcium, BUN, creatinine, hemoglobin, and hematocrit. Dialysis

should be started for patients with severe renal damage. Though often life saving, dialysis does not remove arsenic from the patient, so BAL or other arsenic chelating treatments should be considered if there is suspicion of toxic levels of arsenic.

Long Term Medical Sequelae

If severe hemolysis has occurred, anemia may persist for several weeks. Be aware, also, that after a latency of 1 to 6 months polyneuropathy and alterations in mental status have been reported following arsine poisoning. 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.

Summary

In summary, arsine has potential for terrorist use because it is highly lethal and can be dispersed as a gas. It is the most acutely toxic form of arsenic, preferentially binds to hemoglobin, and is oxidized to an arsenic-dihydride intermediate and elemental arsenic, both hemolytic agents. Characteristic features of acute poisoning are abdominal pain, bloody urine, and jaundice with a severe hemolytic anemia. The resultant hematuria, ranging in color from light to dark red, is seen within 4 to 6 hours, followed by jaundice 12-48 hours later, and, with severe exposure, acute tubular destruction and renal failure develop. There is no antidote and treatment is supportive, including dialysis if there is severe renal damage.