



Cyanides

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Cyanides – Introduction

Cyanide has long been known as a rapidly lethal poison that can be found in a variety of salts or in its most volatile form, hydrocyanic acid. The discoverer of this acid, chemist Karl Wilhelm Scheele, died from its vapors, which can kill within minutes after inhalation.

Hydrocyanic acid and its derivatives are more commonly found than many might expect. Cyanides are used commercially and in the home as fumigants, metal cleaners, silver polish and rodenticides, as well as in ore refining and the production of synthetic rubber and plastics. In nature, cyanide is found in the seeds of the apple, peach, plum, apricot, cherry, and almond in the form of amygdalin. One hundred grams of moist peach seed contains 88 mg of cyanide, while an equivalent amount of apricot seed holds 217 mg. Apricot kernels have been promoted in health food stores as a medicinal product and have been linked to accidental cyanide poisonings in this country. Amygdalin is also sold as the pharmaceutical Laetrile[®], which has been linked to several deaths from overuse. Another commonly used medication that contains cyanide is nitroprusside and its excess use has been reported to cause cyanide toxicity and metabolic acidosis. The suffix 'prusside' comes from the common name of hydrocyanic acid, prussic acid.

Cyanides – Overview

Of the various cyanide compounds, two weapons are known to hold the military's interest as potential warfare agents. As such, we must also expect that they could have potential as terrorist weapons. Hydrocyanic acid and its derivative cyanogen chloride, their military designations are HCN and CK, respectively. Both are highly volatile and exist as a gas in warm temperatures. Even in their liquid state, however, they are easily dispersed as aerosols that are as deadly as their gaseous forms. In addition, they are readily soluble and stable in water. While inhalation is the main route of exposure, they can be absorbed through the skin, eyes, and GI

tract. Both have an aroma of bitter almond or marzipan, but it is estimated that between 25 and 50 percent of all people cannot detect it. CK does differ from HCN in several ways. One difference is that it can have a cumulative effect on its victims, which poses a higher risk of chronic poisoning.

Cyanides – Toxicity (1)

Cyanide's toxicity is due to its inhibition of oxidizing enzymes containing ferric iron, particularly cytochrome oxidase, which results in interference with aerobic respiration. Although hemoglobin is the highest reservoir of iron in the body, this is ferrous iron and is not affected by cyanide. With the inhibition of aerobic respiration, lactic acid accumulates and cells die from a histotoxic anoxia. Cyanide is also reported to alter calcium metabolism and increased intracellular calcium is suggested as a contributor to cell death.

Cyanides – Toxicity

Both HCN and CK are highly toxic. While exposure to 60 mg-min/m³ of HCN in air generally causes no serious symptoms, tripling that exposure to roughly 200 mg-min/m³ is fatal within 10 minutes, and ten times that dose is immediately fatal. One of the other main differences between HCN and CK is that CK also possesses lung irritant properties much like phosgene or chlorine. These irritant effects are present at very low exposure rates. Just 2.5 mg-min/m³ of CK produces eye and upper airway irritation within 10 minutes and doubling that dose is intolerable at the 10 minute mark. CK requires an exposure of 400 mg-min/m³ to cause death within 10 minutes.

Protective Equipment

Since cyanide can be absorbed through the skin and mucous membranes, chemical-protective clothing must be used in areas of exposure. A military-style gas mask is required for protection from inhalation, and to neutralize the cyanide, the mask's filter must contain silver oxide. Because the silver oxide is used up deactivating the cyanide, the filter must be changed after exposure.

Detection

Since so many people cannot detect the aroma of these cyanide gases, odor alone is unreliable for detection of these agents. There are several analytical methods that can be used to detect HCN and CK, but the mainstay of both lab and mobile field detection is a combination of gas chromatography and mass spectrometry.

Decontamination

The immediate priority of decontamination is to remove the victim from the area of exposure. Upon reaching a safe area, the victims skin can be decontaminated

with a thorough washing with soap and water. The eyes can be cleansed by irrigation with copious amounts of water or saline. Because these agents are so volatile, decontamination of clothing and equipment is usually not required.

Signs and Symptoms

Typically, the diagnosis of cyanide poisoning is one made by the history; the abrupt, sometimes catastrophic, onset of symptoms, and the odor of bitter almonds on the victim's breath. In mild, non-lethal exposures the victim might experience headache, vertigo and nausea for several hours before complete recovery. At low concentrations the victim may sense apprehension, experience dyspnea, headache and vertigo, and notice a metallic taste. Convulsions and coma can follow and may last for hours or days depending on the duration of exposure. If coma is prolonged, there may be residual central nervous system damage, manifested by irrationality, altered reflexes and an unsteady gait. These symptoms can last for several weeks or longer. Temporary or permanent nerve deafness has also been described.

Signs and Symptoms

At high concentrations, victims notice a sensation of throat constriction, giddiness, confusion and decreased vision. A vice-like gripping of the temples and pain in the back of the neck and chest may occur. Unconsciousness soon follows and the individual falls. By this time, continued exposure can be fatal within 2-3 minutes, preceded by brief convulsions and respiratory failure. At lower but still lethal concentrations, the severity of symptoms may increase over an hour or more. Victims notice an immediate and progressive sense of warmth due to vasodilatation with visible flushing. Prostration then ensues, with nausea, vomiting, headache, dyspnea, and chest tightness. Unconsciousness and asphyxia will follow if exposure continues. At very high concentrations, hyperventilation is the main initial symptom, followed by loss of consciousness, convulsions, and loss of corneal reflex, with death caused by cardiac and/or respiratory arrest.

Signs and Symptoms

When exposure to these agents occurs through the skin or GI tract, the symptoms of exposure can take 15 to 30 minutes to develop, even at lethal doses. The symptoms are also slower to progress which allows time for the administration of an antidote and other therapies.

As stated previously, CK is also a lung irritant. With eye exposure, there is lacrimation and blepharospasm, while exposure of the respiratory tract produces irritation of the nose and throat, cough, dyspnea, chest tightness, and ultimately pulmonary edema with concentrations of CK between 50 and 300 mg-min/m³. Slowed breathing will be followed by collapse, coma and death. Of course, at higher exposures the predominant effect will become that of the cyanide and the

victim could die before any pulmonary symptoms become evident. It should also be noted that liquid cyanogen chloride can cause second and third degree burns following skin contact.

Laboratory / Diagnostics

In terms of lab and diagnostic testing, useful lab findings include a high anion gap metabolic acidosis, and elevated lactate, methemoglobin, and urinary thiocyanate levels. The victims EKG will typically show cardiac manifestations such as atrial fibrillation, ectopic ventricular beats, and abnormal QRS waves with the T wave originating high on the R wave.

Treatment

Victims of cyanide gas exposure who remain asymptomatic after several minutes usually do not require oxygen or antidotes. However, anyone displaying acute effects such as convulsions or dyspnea, and those recovering from acute exposure who remain unconscious but breathing, require supportive care, oxygen, and antidote therapy, which we discuss in subsequent slides.

In addition, those who have been exposed to CK require additional care for the irritant effects of the agent. Exposed eyes may be irrigated with a weak boric acid solution, while mildly injured skin may respond to soothing lotions and cool compresses. Severe skin injuries should be treated as thermal burns. Supplemental oxygen is required and the early use of intermittent positive pressure breathing, a continuous positive end-expiratory pressure mask, or intubation may delay or minimize the resultant pulmonary edema and hypoxia.

Treatment

As stated, these agents are stable in water and can cause exposure by ingestion. In these cases, gastric lavage using large amounts of water is required. If potassium permanganate is available, use a 1:5000 solution for the lavage.

As mentioned a moment ago, there are antidotal therapies for cyanide. These work by dissociating the cyanide from oxidative enzymes such as cytochrome oxidase. This is most commonly achieved by creating methemoglobin which holds iron in the ferric state and attracts the cyanide ion away from the cellular enzymes. The resulting cyanmethemoglobin holds the cyanide ion until the natural enzyme rhodanase can convert it to thiocyanate. Sodium nitrite is the recommended therapy. For adults, 10 mL of a 3% solution (300 mg) is given intravenously over a period of 3 minutes. For children, the dose is 0.33 mL of the 10% solution per kilogram of body weight. Amyl nitrite is also promoted as a therapy because it is available in a capsule that can be broken for inhalation through the mouth or nose. However, little is actually absorbed from these capsules and it is only effective when used in a closed respiratory system. Also,

amyl nitrite produces methemoglobin more slowly than sodium nitrite, so it should be used only as an interim therapy until sodium nitrite can be given. DMAP, 4-dimethylaminophenol-hydrochloride, is also effective and is given at a dose of 250 mg slowly injected intravenously. With DMAP, muscular necrosis may follow IM injection, so that route should be avoided.

Treatment

In addition to the therapies that form methemoglobin, chelating therapies utilizing cobalt are also available. Hydroxocobalamin (vitamin B12a) binds cyanide to form cyanocobalamin (vitamin B12) which is excreted in the urine when in excess in the body. It is only given intravenously, in large doses of 4 g intravenously over 30 minutes in adults. Also effective is dicobalt edetate, given intravenously as 40 ml of a 1.5% solution in glucose and water, a dose of 600mg. Exercise caution when using this therapy because cobalt edetate is toxic to the kidney and may cause hypotension.

These therapies are life saving, but not curative. Following their administration, sodium thiosulfate must be given to aid clearance of the cyanide by enhancing the activity of rhodanase which uses the thiosulfate group to combine with cyanide and form thiocyanate, a harmless chemical excreted by the kidneys. The dose in adults is 12.5 grams, or 50 mL of a 50% solution, administered intravenously over ten minutes. For children, the dose is 1.65 mL/kg of a 25% solution.

Long-term Medical Sequelae

While low concentration exposures generally cause no long-term problems, near lethal exposures can cause prolonged CNS effects secondary to cyanide's effects on cellular respiration. These include deterioration in intellect, confusion, loss of concentration and Parkinsonism. Also, an ataxic neuropathy can be seen in victims of chronic cyanide poisoning. As for developmental and reproductive effects, mutagenicity or carcinogenicity, specific data are not available, although many cyanide derivatives have well established carcinogenicity and teratogenicity.

Environmental Sequelae

Hydrocyanic acid is highly volatile and is usually removed from the environment in less than an hour. Cyanogen chloride is even less persistent.

Summary

In summary, hydrogen cyanide (HCN) and cyanogen chloride (CK) are highly lethal cyanide gases with military, and thus terrorist, potential. Inhalation is the main route of exposure; but skin, eye, and GI absorption also occur – with rapid absorption by all routes. Decontamination with soap and water must begin

immediately. The cyanides inhibit cellular aerobic respiration by inhibiting cytochrome oxidase, preventing cells from utilizing oxygen. Cyanide's symptoms are immediate, reflect the dose and route of exposure, and are consistent with tissue anoxia so respiratory and CNS symptoms appear initially. Besides supportive care, antidotes are available to chelate the cyanide ion or to dissociate the cyanide ion from cytochrome oxidase and bind it to methemoglobin, and to accelerate the natural activity of rhodanase in removing cyanide from the body.