BLOOD AGENTS

Cyanide
Cyanide is a chemical that is widely utilized, manufactured, and transported in the U.S. Over 300,000 tons of cyanide is produced annually. It is used in printing, agriculture, photography, and in the manufacture of paper and plastics. It is also a combustion product of burning synthetic materials. Rail cars with 30,000-gallon tanks of cyanide represent potential transportation and terrorist threats. A large amount of cyanide is needed to cause death on the battlefield; therefore, it is not a very good military weapon. Terrorist use in confined spaces such as a subway care, shopping center, convention center or high-rise building would be far more effective.

Characteristics
Cyanide is stored and utilized in the liquid or solid state. It may have an odor of bitter almonds, but the ability to smell the cyanide exists in only 40 percent of the population.

Three types of cyanide may be encountered: hydrogen cyanide (AC), cyanogen chloride (CK), and cyanide salts. The term cyanide refers to the anion, CN-, or to its acidic form, hydrocyanic acid (HCN). Cyanogen (CN2) is formed by the oxidation of cyanide anions. However, the term cyanogen has also come to mean a substance that forms cyanide upon metabolism and produces the biological effects of free cyanide. Cyanogen chloride is a pungent, heavier-than-air vapor, which can cause irritation of the eyes, nose, and throat. This is in distinct contrast to hydrogen cyanide, which has no irritant properties.

Cyanide salts (for example, NaCN) are compounds that dissociate into the cyanide anion (CN-) and a cation (Na+). Salts are most dangerous following ingestion; onset of action is slower and more prolonged. Cyanide salts generate hydrogen cyanide gas on contact with a strong acid (e.g., sulfuric acid).

Mechanism of Action
Cyanide exists normally in human tissues and is usually metabolized by sulfur in the presence of a hepatic enzyme, rhodanese, into thiocyanante, which is excreted in the urine.

Under normal conditions, the cyanide anion is attracted to iron in the ferric state (Fe+++). In the mitochondrion of the human cell, cytochrome A3 in the cytochrome oxidase complex contains Fe+++. Cyanide is bound to cytochrome A3 and thus inhibits the effect of cytochrome oxidase. This enzyme complex is responsible for the utilization of oxygen within the cell. In the presence of cyanide, even though there is plenty of dissolved oxygen in the blood, the cells cannot use the available oxygen. As a result, cells must utilize anaerobic metabolism, or the creation of energy without the benefit of oxygen, which causes severe lactic acidosis. When cells cannot get enough energy, they die. Cells in the brain and heart are affected initially.

Acute cyanide poisoning occurs after inhaling the agent, but may also occur after drinking solutions of cyanide (it is sometimes used with suicidal intent) or by skin contact with large amounts of liquid cyanide.

Clinical Effects
After inhalation of a low concentration, the patient may become anxious, will often hyperventilate, and typically develops a headache with dizziness and vomiting. Skin color may initially be flushed but may also be normal or cyanotic. A cherry-red skin color is characteristic of cyanide, but this is not always seen. If a victim is exposed to a low concentration of vapor and removed from the source of the cyanide, the symptoms should not progress.

In about 15 seconds after inhaling a large amount of cyanide, victims become anxious and start to hyperventilate. Thirty seconds after exposure, the patient may begin to convulse. In 3 to 5 minutes, breathing ceases. Asystole, or cessation of heart activity, occurs in 6 to 10 minutes,
followed by death. The patient may have normal sized or dilated pupils. Death can occur within 8 minutes of exposure.

**Laboratory**
Normal oxygen saturation may be noted when using a pulse oximeter, despite the fact that the patient may be in severe respiratory distress. There is high arterial oxygen content to venous blood because oxygen is not extracted from arterial blood by the cells. Metabolic (lactic) acidosis may also be present from the lack of oxygen to the tissues. Cyanide toxicity can be measured at the hospital by checking serum cyanide concentrations. These values may, however, only be available after a delay of several hours and of no value in the initial management of acute severe poisoning.

**Medical Management**
Patients who have inhaled significant doses of cyanide must be rapidly treated with appropriate antidotes to prevent brain damage. Cyanide is attracted to iron (Fe+++), in a form of hemoglobin called methemoglobin. In fact, cyanide will preferentially leave the cytochrome oxidase enzyme in the cell and bind to circulating methemoglobin. Drugs such as amyl nitrite and sodium nitrite, which are found in the cyanide treatment kit, increase blood concentrations of methemoglobin and are antidotal. Adding sodium thiosulfate completes the detoxification process.

Patients should be treated with IV saline for hydration; sodium bicarbonate and intubation with hyperventilation should be used for the metabolic acidosis. Oxygenation should be maintained with high-flow oxygen by mask or by endotracheal tube. Monitor and treat significant arrhythmias.

**The Cyanide Antidote Kit**
This kit (formerly known as the Lily Cyanide Kit and now produced by Taylor Pharmaceuticals) contains amyl nitrite, sodium nitrite, and sodium thiosulfate.

**Amyl nitrite**
Amyl nitrite is available in perles, more commonly referred to as ampules, which are broken and placed in either a gauze bandage, or in the bag mask, and inhaled for 15 seconds, then taken away for 15 seconds (although, if the patient is breathing, he probably does not need the antidote). This is the initial step in antidote therapy. Amyl nitrite forms methemoglobin and reduces the elevated total peripheral resistance caused by the acidosis and cyanide. This should be used only until the IV drugs can be given. Inhalation of amyl nitrite will cause orthostatic hypotension. However, if the patient can stand, he or she does not need the antidote.

**Sodium nitrite**
Sodium nitrite is a strong methemoglobin former that is available for IV use in a dose of 300 mg in 10 cc. This dose is injected over 2 to 4 minutes and has the potential side effect of orthostatic hypotension. Normal saline infusion and supine posture can help to correct the hypotension. However, if patients can stand, they do not need the sodium nitrite. The pediatric dosage is 0.2 cc/kg, not to exceed 10 cc.

**Sodium thiosulfate**
This compound is a cofactor for the enzyme rhodanese for detoxification (to change cyanide to a form that can be excreted by the kidneys). The drug is administered in a 50cc ampule (12.5 gm) over 5 minutes by IV.

**Treatment**

**General:**
Remove from the area of exposure and remove clothing
**Mild exposure:**
If conscious and breathing, give O2 and IV fluids. Observe and monitor no antidotes are necessary.

**Severe exposure:**
If unconscious, whether breathing or not, give O2, and bag mask ventilate with 100 percent O2. Cardiac monitor. Oxygen saturation may or may not be normal. Administer the following medications:

**Amyl nitrite:**
Crush into a 4 x 4 piece of gauze and place over face or in a bag mask (however, if patients are breathing, they probably do not need the drug). Add another ampule every few minutes.

*Give only until IV drugs are available.*

**Sodium nitrite:**
When IV established, give 300 mg (10 cc ampule) over 5 minutes for adults. For children, use 0.22 to 0.33 ml/kg of the 3 percent solution. Watch for orthostatic hypotension (however, if patient can stand, they do not need this).

**Sodium thiosulfate:**
Give 12.5 gm (50 cc) IV (administered after sodium nitrite). For children, use 1.65 ml/kg of the 25 percent solution.