A Review of Acute Cyanide Poisoning With a Treatment Update

Jillian Hamel, MS, ACNP-BC, CCNS, CCRN

Cyanide causes intracellular hypoxia by reversibly binding to mitochondrial cytochrome oxidase a_3. Signs and symptoms of cyanide poisoning usually occur less than 1 minute after inhalation and within a few minutes after ingestion. Early manifestations include anxiety, headache, giddiness, inability to focus the eyes, and mydriasis. As hypoxia progresses, progressively lower levels of consciousness, seizures, and coma can occur. Skin may look normal or slightly ashen, and arterial oxygen saturation may be normal. Early respiratory signs include transient rapid and deep respirations. As poisoning progresses, hemodynamic status may become unstable. The key treatment is early administration of 1 of the 2 antidotes currently available in the United States: the well-known cyanide antidote kit and hydroxocobalamin. Hydroxocobalamin detoxifies cyanide by binding with it to form the renally excreted, nontoxic cyanocobalamin. Because it binds with cyanide without forming methemoglobin, hydroxocobalamin can be used to treat patients without compromising the oxygen-carrying capacity of hemoglobin. (*Critical Care Nurse.* 2011;31[1]:72-82)

A patient who has occupational access to cyanide arrives in the intensive care unit (ICU) after ingesting the compound in an apparent suicide attempt. Although initially awake when emergency technicians were called to the scene, the patient became unresponsive and pulseless en route. After 2 rounds of cardiopulmonary resuscitation and injections of epinephrine and atropine, the patient has regained a pulse. At the hospital, the emergency department team administers hydroxocobalamin and a sedative, intubates the patient, and transfers him to the ICU. The complex process of managing a patient with acute cyanide poisoning begins as the critical care nurse notes the patient has cool, gray skin; blood pressure 100/50 mm Hg; heart rate 128/min; and oxygen saturation 98% on 100% fraction of inspired oxygen.

CE Continuing Education

This article has been designated for CE credit. A closed-book, multiple-choice examination follows this article, which tests your knowledge of the following objectives:

1. Understand the pathophysiology of acute cyanide poisoning
2. Recognize the importance of immediate antidote administration in the setting of acute cyanide poisoning
3. Differentiate the 2 available acute cyanide poisoning antidotes

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Knowledge of the pathophysiology of acute cyanide poisoning and its antidotes in combination with the ability to tailor management of a patient's care to this unique situation will be critical to the patient's recovery. In this article, I discuss the pathophysiology of acute cyanide poisoning and detail the benefits and challenges of the antidotes currently available.

Life-threatening cyanide poisoning is treatable when quickly recognized and immediately countered with an antidote. A delay in administration of an antidote can be devastating, allowing time for hypoxic brain injury, cardiovascular compromise, and death within minutes to hours.[1] Ideally, an antidote should be administered at the scene immediately after the patient is removed from the source of cyanide.[1] Unfortunately, no tests for rapid confirmation of cyanide poisoning exist, so treatment must be based on a presumptive diagnosis. Because treatment of persons exposed to cyanide is most often away from a hospital and provided by medical personnel with limited resources and time, the ideal cyanide antidote would be quickly

effective and have little to no treatment-limiting adverse effects.[2]

Cyanide is traditionally known as a poison and has been used in mass homicides, in suicides, and as a weapon of war. A fruit-flavored drink (Kool-Aid) laced with potassium cyanide was the causative agent in the mass suicide of the members of the People's Temple in Jonestown, Guyana, in 1978.[3] During World War II, the Nazis used cyanide as an agent of genocide in gas chambers.[4] Unintentional exposures to cyanide are also possible, as in smoke inhalation in fires in enclosed spaces or in occupations in which cyanide is used in industrial processes.[5]

Cyanide's molecular structure consists of a cyano group (a carbon triple-bonded to nitrogen) in combination with other elements such as potassium or hydrogen. Cyanide can be a salt, a liquid or a gas. Once it enters the bloodstream, cyanide rapidly reacts with metals such as ferric ions, binding to and halting critical enzymatic cascades, leading to central nervous system and cardiovascular impairment.[5]

The annual report of the National Poison Data System of the American Association of Poison Control Centers documented 247 reported cases of chemical exposures to cyanide in the United States in 2007; of the 247, 5 were fatal.[6] The number of reported cases is relatively small because poisonings in adults, occupational exposures, and fatalities are typically underreported to the National Poison Data System. Nevertheless, the small number does not diminish the devastating effect of acute cyanide poisoning, the rapid progression of the poisoning, and the need for quick recognition and intervention. Health care providers must be alert for suspected poisoning and provide prompt administration of empiric antidotal therapy for successful treatment.

Table 1 Potential sources of cyanide exposure[a]

Industrial sources
Insecticides
Photographic solutions
Metal polishing materials
Jewelry cleaners
Acetonitrile
Electroplating materials
Synthetic products such as rayon, nylon, polyurethane foam, insulation, and adhesive resins
Natural sources
Seeds and fruit pits of *Prunus* species (eg, apple seeds and cherry and apricot pits)
Environmental sources
Smoke inhalation in closed-space fires
Iatrogenic sources
Sodium nitroprusside infusion

[a] Based on data from Borron,[7] Schnepp,[8] and Shepherd and Velez.[9]

Etiology of Cyanide Poisoning

Cyanide has many natural, industrial, and even household sources (Table 1). Smoke inhalation from structural fires is the most common cause of cyanide poisoning in Western countries.[7] Materials such as wool, silk, and synthetic polymers contain carbon and nitrogen and may produce cyanide gas when exposed to high temperatures during thermal breakdown.[8-10] Although carbon monoxide is traditionally associated with morbidity and mortality from smoke inhalation, prospective studies[5,11] in which cyanide concentrations after smoke exposure were measured indicated that cyanide poisoning can contribute independently and markedly to illness and death.

Cyanide is used in industrial processes that require electroplating and the polishing of metals. Cyanide salts such as mercury cyanide, copper cyanide, gold cyanide, and silver cyanide produce hydrogen cyanide gas when combined with acids, creating the opportunity for industrial accidents or purposeful harmful exposures.[8,9] Cyanide is also found in insecticides used for some commercial mass fumigations.[8]

Iatrogenic sources of cyanide include administration of the intravenous antihypertensive sodium nitroprusside. Nitroprusside can be cyanogenic; it is 44% cyanide by molar weight. Cyanide groups are released from the nitroprusside molecule nonenzymatically. In the liver, the enzyme rhodanese then catalyzes the conversion of cyanide

Author

When this article was written, Jillian Hamel was a nurse practitioner in cardiology at the University of Maryland Medical Center in Baltimore.

Corresponding author: Jillian Hamel, MS, ACNP-BC, CCNS, CCRN, Division of Cardiology, University of Maryland Medical Center, 22 S. Greene Street, Baltimore, MD 21201 (e-mail: jillian.hamel@gmail.com).

to thiocyanate, which is normally excreted through the kidneys. Poisoning may be due to a defect in cyanide metabolism or to an accumulation of thiocyanate during an administration period of several days or more.[4,12] Particularly in patients with impaired renal function, cyanide poisoning may occur because the patients are unable to excrete thiocyanate at a sufficient rate.[4] Careful screening of renal function may aid in avoiding poisoning in patients who require sodium nitroprusside infusions. Serial monitoring can reveal elevations in the serum level of cyanhemoglobin or cyanmethemoglobin. Levels greater than 10 mg/dL confirm thiocyanate poisoning and are an indication to stop therapy.[12]

Nitriles are a form of cyanide found in solvents and glue removers. Acetonitrile and propionitrile are the most commonly encountered nitriles. Metabolized to cyanide in the liver, acetonitrile is the active ingredient in artificial nail removers and has been linked to cases of cyanide poisoning.[8,11]

Although not a common cause of poisoning, natural sources can produce cyanide poisoning when taken in large quantities or when they are packaged as alternative medicines, such as Laetrile. Cyanide occurs naturally in amygdalin, a cyanogenic glucoside. Amygdalin occurs in low concentrations in the seeds and fruit pits (eg, apple seeds, cherry pits, bitter almonds, and apricot pits) of *Prunus* species.

Pathophysiology of Acute Cyanide Poisoning

Cyanide is highly lethal because it diffuses into tissues and binds to target sites within seconds.[9] Intravenous and inhaled exposures produce more rapid onset of signs and symptoms than does oral ingestion because the first 2 routes provide fast diffusion and direct distribution to target organs via the bloodstream.[13] Oral or transdermal ingestion may produce a delay in signs and symptoms as concentrations increase in the bloodstream.[5]

The primary mechanism of cyanide excretion is formation of thiocyanate within the liver. Rhodanese catalyzes the conversion of cyanide to thiocyanate, and thiocyanate is then excreted via the kidneys[9] (Figure 1). This mechanism is overwhelmed by high doses of cyanide in acute poisoning or in patients with decreased kidney function.[13]

The toxicity of cyanide is largely attributed to the cessation of aerobic cell metabolism. Cyanide causes intracellular hypoxia by reversibly binding to the cytochrome oxidase a_3 within the mitochondria. Cytochrome oxidase a_3 is necessary for the reduction of oxygen to water in the fourth complex of oxidative phosphorylation. Binding of cyanide to the ferric ion in cytochrome oxidase a_3 inhibits the terminal enzyme in the respiratory chain and halts electron transport and oxidative phosphorylation[5] (Figure 2). This downward cascade is fatal if not reversed. Oxidative phosphorylation is essential to the synthesis of adenosine triphosphate (ATP) and the continuation of cellular respiration.

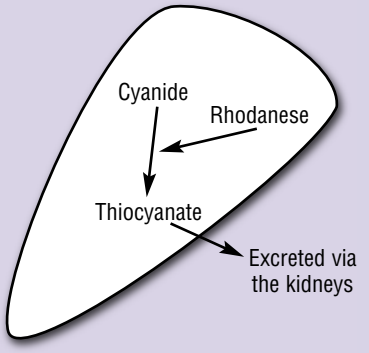

Figure 1 Metabolism of cyanide: the enzyme rhodanese catalyzes conversion of cyanide to the nontoxic thiocyanate in the liver, and the thiocyanate is then excreted via the kidneys.

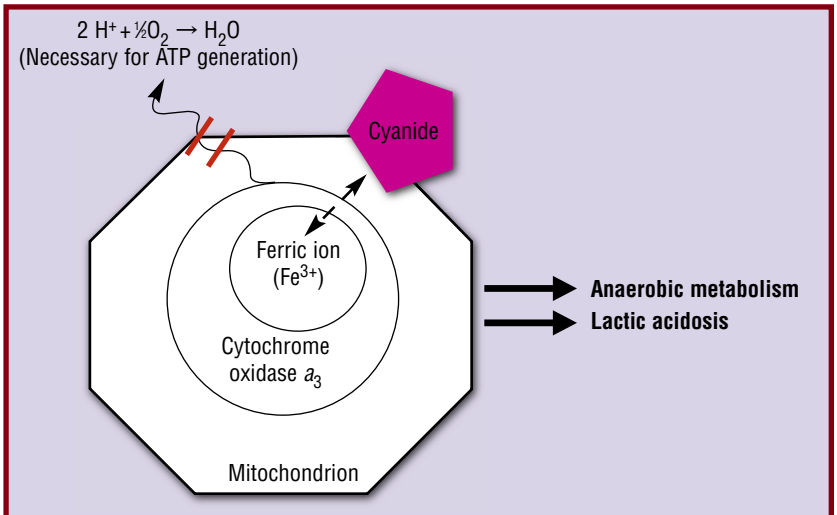

Figure 2 Effect of cyanide on cellular respiration: cyanide reversibly binds to the ferric ion in cytochrome oxidase a_3 within the mitochondria, effectively halting cellular respiration by blocking the reduction of oxygen to water.

Abbreviation: ATP, adenosine triphosphate.

As supplies of ATP become depleted, mitochondria cannot extract or use the oxygen they are exposed to. As a result, metabolism shifts to glycolysis through anaerobic metabolism, an inefficient mechanism for energy needs, and produces lactate. Production of lactate results in a high-anion-gap metabolic acidosis.[5,9] Poor oxygen extraction associated with cessation of aerobic cellular respiration also leads to an accumulation of oxygen in the venous supply. In this situation, the problem is not delivery of oxygen but extraction and utilization of oxygen at the cellular level. The increased oxygenation of venous blood also explains the presence of elevated venous level of oxygen indicated by blood gas analysis and a reduced arteriovenous oxygen saturation difference (<10 mm Hg).[13] Some cyanide also binds to the ferric form of hemoglobin (a transient physiological form of methemoglobin), which accounts for normally 1% to 2% of all hemoglobin. Binding of cyanide to the ferric form makes this type of hemoglobin incapable of transporting oxygen.[5]

Clinical Manifestations

The clinical manifestations of cyanide poisoning are largely a reflection of intracellular hypoxia (Table 2). The onset of signs and symptoms is usually less than 1 minute after inhalation and within a few minutes after ingestion.[5] Early neurological manifestations include anxiety, headache, and giddiness. Patients may be unable to focus their eyes, and mydriasis may develop because of hypoxia. As hypoxia progresses, patients may experience progressively lower levels of consciousness, seizures, and coma.[4,13]

Table 2 Clinical manifestations of cyanide's toxic effect[a]

System	Manifestations
Central nervous	Early (due to hypoxia) Anxiety Headache Giddiness Dizziness Confusion Mydriasis Bright retinal veins (elevated venous Po_2) Late Decreased consciousness Seizures Paralysis Coma
Respiratory	Early Hyperventilation and tachypnea (due to hypoxic stimulation of peripheral and central chemoreceptors) Late Absence of cyanosis (caused by an increase in oxygen content in venous blood) Hypoventilation Apnea (cells cannot take up oxygen)
Cardiovascular	Early Tachycardia Late Hypotension Supraventricular tachycardia Atrioventricular blocks Ventricular fibrillation Asystole

[a] Based on data from DesLauriers et al,[4] Hall et al,[5] and Nelson.[13]

In acute cyanide poisoning, the skin may have a normal or a slightly ashen appearance despite tissue hypoxia, and arterial oxygen saturation may also be normal. Early respiratory signs of cyanide poisoning include transient rapid and deep respirations.[4,5] This respiratory change reflects stimulation of peripheral and central chemoreceptors within the brain stem in an attempt to overcome tissue hypoxia.

Cyanide has a profound hypoxic effect on the cardiovascular system. Patients may initially have palpitations, diaphoresis, dizziness, or flushing. They may have an initial increase in cardiac output and blood pressure associated with catecholamine release. Vasodilatation, hypotension, and a decrease in the inotropic ability of the heart ensue, with shunting of blood to the brain and heart.[4] Cyanide depresses the sinoatrial node, causes an increase in arrhythmias, and decreases the force of contraction of the heart.[4] As poisoning progresses, patients' hemodynamic status may become unstable, with ventricular arrhythmias, bradycardia, heart block, cardiac arrest, and death.[4]

Serum concentrations of cyanide greater than 0.5 mg/L are typically associated with acute cyanide poisoning.[7] Unfortunately this finding is not helpful in the initial diagnosis and management of acute poisoning because of cyanide's rapid action and lethality. Furthermore, measurement

Table 3 Management of patients with acute cyanide poisoning[a]

Decontamination	Basic Life Support/Advanced Cardiac Life Support (ACLS)	Antidotal therapy	Supportive care
Smoke inhalation Remove from source into fresh air Remove contaminated clothing Dermal exposure[b] Remove wet clothing Wash skin with soap and water or water alone Irrigate exposed eyes with water or saline Remove contact lenses Ingestion Do not induce emesis Activated charcoal may be administered if the victim is alert and the ingestion occurred within 1 hour Isolate emesis (it may emit hydrogen cyanide)	Establish ABCs (airway, breathing, circulation) Establish intravenous access Start cardiac monitoring Start ACLS if respiratory or cardiovascular compromise evident	Administer the cyanide antidote kit or hydroxocobalamin once an airway has been secured	Admit to an intensive care unit for cardiac monitoring, respiratory and cardiovascular support Perform routine laboratory testing, including arterial blood gas analysis, serum lactate levels, complete blood cell counts, serum glucose level, a serum cyanide level (confirmatory), and electrolyte levels Monitor and treat dysrhythmias Monitor for and treat adverse effects of antidotal therapy

[a] Based on data from Koschel.[14]
[b] Protection of responders from contamination is essential with the use of personal protective equipment such as face masks, eye shields, and frequent double gloving or the use of butyl rubber gloves.

of serum cyanide levels may require several days, depending on the laboratory facility.[5] Serum cyanide concentrations also do not correlate with specific degrees of severity. Borron[7] addressed this issue by examining serial lactate levels as an alternative way to assess the severity of cyanide poisoning. He reported that serum lactate levels greater than 8 mmol/L are associated with acute poisoning and may aid in determining the need for repeated antidotal therapy. However, lactic acidosis is not specific to cyanide poisoning, and future research is still needed to find a rapid test to aid in diagnosis of this poisoning.

Management

Initial management of patients with acute cyanide poisoning requires rapid assessment and identification of the most likely route of exposure to determine proper decontamination (Table 3). Patients with suspected inhalation exposure should first undergo decontamination by being evacuated from the contaminated area and having affected clothing removed.[5,9,14] For patients with oral ingestion who have vomited or spilled liquid on their skin or clothing, care must be taken by health care providers to avoid secondary contamination. Providers should use personal protective equipment per the hospital standard. During decontamination, the protective steps may include using face masks, eye shields, and double gloving, with frequent replacement of gloves or the use of butyl rubber gloves, which have a breakthrough time of 1 to 4 hours.[7,14] Emesis should not be induced in patients with suspected ingestion. Activated charcoal may be administered if the patient is alert, the time is within 1 hour of the suspected oral ingestion, and administration is not otherwise contraindicated. Although it may not be effective in countering acute cyanide poisoning because of the high potency of cyanide, the rapid onset of poisoning, and the small size of cyanide molecules, activated charcoal may be useful in patients who may have ingested another poison in addition to cyanide.[9]

Because cyanide causes a decrease in oxygen utilization, the administration of 100% oxygen by nonrebreather mask or endotracheal tube is indicated in acute poisoning.[10] Although 100% oxygen will not correct the problem, it may enhance the effectiveness of antidotal therapy by competing with cyanide for the cytochrome oxidase binding sites.[10]

After decontamination and life-support measures are started, the

Table 4 The cyanide antidote kit and hydroxocobalamin[a]

Medication	Dosing	Mechanism of action
Amyl nitrite	Crushed 0.3-mL ampule inhaled for 15 seconds; may repeat 3-5 minutes until intravenous access established Amyl nitrite should be discontinued once intravenous access is obtained and sodium nitrite infusion is started	Induces methemoglobinemia via oxidation to bind cyanide
Sodium nitrite	300 mg (10 mL in a 3% solution) or 10 mg/kg given intravenously for 3-5 minutes (a rate of 2.5-5 mL/min) in adults 6-8 mL/m^2, or 0.2 mL/kg in children, not to exceed 10 mL	Induces methemoglobinemia via oxidation to bind cyanide
Sodium thiosulfate	1 ampule, or 12.5 g in 50 mL, given intravenously for 30 minutes in adults The dosage for children is 7 g/m^2, not to exceed 12.5 g	Combines with unbound cyanide to form renally excreted thiocyanate
	Hydroxocobalamin	
Hydroxocobalamin	5 g for adults, administered intravenously for 15 minutes, repeat a half dose if needed; 70 mg/kg in children	Combines with unbound cyanide to form cyanocobalamin

[a] Based on data from Koschel.[14]

key to treatment of cyanide poisoning is early administration of an antidote.[2] The decision to administer the antidote must often be made empirically, without full knowledge of the patient's underlying health status or complicating factors. The available antidotes are discussed in detail in the following section.

Additional supportive care includes controlling seizures with anticonvulsants, cardiac monitoring to evaluate and treat dysrhythmias and conduction defects, and blood pressure support with fluids and vasopressors. Care should be taken when administering intravenous fluids, because noncardiogenic pulmonary edema can develop in patients with cyanide poisoning. Hyperbaric oxygen may have a role in therapy, but its use remains controversial and is not standard practice.

Routine laboratory studies include arterial blood gas analysis, measurement of serum lactate levels, a complete blood cell count, measurement of serum glucose and electrolyte levels, and determination of the serum cyanide level for confirmation. Common laboratory findings in cyanide poisoning include metabolic acidosis, plasma lactate level greater than 8 mmol/L, and reduced arteriovenous oxygen saturation difference (<10 mm Hg).

Antidotes

Currently, 2 antidotes for acute cyanide poisoning are available in the United States: the cyanide antidote kit, which has been in use in the United States for decades, and hydroxocobalamin, which was approved by the Food and Drug Administration in December 2006. Approval of hydroxocobalamin is significant; because of its low incidence of adverse events, it is a potentially acceptable choice in prehospital settings.[1,8,9] Hydroxocobalamin also appears to be safer than the cyanide antidote kit in patients who have preexisting hypotension, inhaled the poison in smoke in a closed space, or are pregnant. An understanding of both available antidotes and their respective benefits, contraindications, side effects, and monitoring requirements is essential to the proper care and management of patients with acute cyanide poisoning.

Cyanide Antidote Kit

The cyanide antidote kit has been used for decades in the United States for acute cyanide poisoning on the basis of the animal studies and clinical reports of Chen and Rose in the mid-twentieth century.[9,15] Death rates in the United States associated with cyanide poisoning have decreased since the 1930s, most likely because of the use of the cyanide antidote kit.[10] This kit consists of 3 medications given together for their synergistic effect: amyl nitrite, sodium nitrite, and sodium thiosulfate. Amyl nitrite is administered via inhalation over 15 to 30 seconds while intravenous access is established. Sodium nitrite is then administered intravenously over 3 to 5 minutes, and then intravenous sodium thiosulfate over 30 minutes (Table 4).

The 2 nitrites are administered to form methemoglobin and bind cyanide.[9] Nitrites oxidize the iron in hemoglobin to form cyanmethemoglobin (Figure 3). Because cyanide

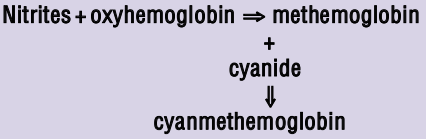

Figure 3 Nitrites oxidize the iron in hemoglobin to form cyanmethemoglobin.

appears to bind preferentially to the ferric ion of methemoglobin rather than to the ferric ion of the cytochrome oxidase a_3 in the mitochondria, cyanmethemoglobin draws cyanide away from the mitochondria. This process frees the mitochondria for electron transport and return to aerobic cellular respiration. The cells are able to generate ATP, and the production of lactic acid ceases. Sodium thiosulfate is administered in combination with the nitrites to clear cyanide by acting as a sulfhydryl donor.[9] The unbound, extracellular cyanide binds with sulfur of thiosulfate to form the renally excreted thiocyanate.[9]

When the cyanide antidote kit is used, critical care nurses must watch for vasodilatation and hypotension, important adverse effects of nitrites[9] (Table 5). Sodium nitrite must be administered slowly, over at least 3 to 5 minutes, with frequent blood pressure monitoring. Hypotension can be treated with intravenous fluid and vasopressors.

Another important consideration is the production of methemoglobin. Although this process frees cells to continue aerobic metabolism, methemoglobinemia reduces the level of functional circulating hemoglobin and may exacerbate conditions in certain patients, such as those with concurrent carbon monoxide poisoning or those with poor cardiopulmonary reserve, by worsening the patients' deficit in oxygen-carrying capacity.[5,9] Nitrites should also be avoided in pregnant patients because of the oxidative stress on fetal hemoglobin.[9] Sodium thiosulfate occasionally causes a hypersensitivity reaction and hypotension, depending on the rate of infusion. Although sodium thiosulfate is a relatively efficacious antidote for cyanide poisoning, its slow onset of action is a disadvantage for its use as the sole medication in antidotal therapy.[9]

Hydroxocobalamin

The Food and Drug Administration approved hydroxocobalamin (Cyanokit) for the treatment of acute cyanide poisoning in December 2006.[16,17] Each kit contains two 250-mL glass vials, and each vial contains 2.5 g of lyophilized hydroxocobalamin. The kit also contains 2 sterile transfer spikes and 1 sterile intravenous infusion set. The manufacturer recommends storing the powder form at room temperature, or approximately 25°C (77°F). Once it is reconstituted, the medication can be kept at room temperature, but it must be used within 6 hours. An initial starting dose for adults is 5 g (two 2.5-g vials) diluted in 0.9% saline and administered over 15 minutes (Table 4). A second 5-g dose can be given over 15 minutes to 2 hours thereafter if deemed necessary for reversal of signs and symptoms of cyanide poisoning.[5,17]

Hydroxocobalamin detoxifies cyanide by binding with it to form the renally excreted, nontoxic

Table 5 Nursing considerations for the cyanide antidote kit and hydroxocobalamin[a]

Antidote	Adverse effects	Other considerations
Cyanide antidote kit	Potent vasodilatation from the nitrites may lead to hypotension Methemoglobinemia may be harmful or even lethal in patients who already have a deficiency of oxygen-rich blood, such as those exposed to carbon monoxide	Monitoring of methemoglobin levels is indicated and should not exceed 20% Contraindicated in smoke-inhalation patients Is not considered safe in pregnant patients
Hydroxocobalamin	May cause transient hypertension Most common adverse effects include reddening of the skin and urine	Is safe for smoke-inhalation patients May be used in pregnant patients May interfere with colorimetric tests because of its red color Effect on blood pressure may be beneficial in patients in shock

[a] Based on data from Shepherd and Velez[8] and Koschel.[14]

cyanocobalamin (vitamin B_{12}). Cyanocobalamin releases cyanide at a rate that is slow enough to allow the enzyme rhodanese to detoxify the cyanide in the liver.[4] Cyanide has a greater affinity for hydroxocobalamin than for the cytochrome oxidase within the mitochondria and so frees the mitochondria for cellular respiration. This characteristic makes hydroxocobalamin an effective antidote against cyanide poisoning.[9] Because it binds with cyanide without forming methemoglobin, hydroxocobalamin also can be used to treat patients with cyanide poisoning without compromising the oxygen-carrying capacity of hemoglobin.[5] This property is especially important for patients who already have decreased concentration of useful hemoglobin because of exposure to carbon monoxide or who are pregnant.

Hydroxocobalamin has been used outside the United States for acute cyanide poisoning for more than 30 years.[5] Licensed in 1996 in France, the medication is used there for empiric prehospital and in-hospital treatment of acute cyanide poisoning.[18] A study[19] in 2006 of the safety and effects of hydroxocobalamin in healthy volunteers supports empiric, prehospital administration and indicated few side effects. The results of the study cannot be directly applied to the prehospital treatment of acute cyanide poisoning in the United States because, unlike in the United States, first responders in France are nurses and physicians. However, the study did confirm that unlike the nitrites, hydroxocobalamin does not interfere with tissue oxygenation.[5,18,20]

Reddening of the skin and urine are the most common drug-related side effects of treatment with hydroxocobalamin. These effects occurred in more than 60% of 136 healthy volunteers who were given hydroxocobalamin in a double-blind, randomized, placebo-controlled study[18] of the safety of the medication and patients' tolerance to it. The 2 main effects are due to the color of the drug itself and appear to resolve within 2 to 3 days of administration of the drug (Table 5). Of note, hydroxocobalamin can also interfere with certain colorimetric tests, such as those for bilirubin, creatinine, magnesium, serum iron, serum aspartate aminotransferase, carboxyhemoglobin, methemoglobin, and oxyhemoglobin, but such interference has not been associated with any clinically meaningful changes.[8,21]

Hydroxocobalamin also does not compromise hemodynamic stability. In the study[18] of the effects of hydroxocobalamin in healthy volunteers, 12 volunteers (18%) had an elevation in blood pressure greater than 180 mm Hg systolic or greater than 110 mm Hg diastolic. This transient increase in blood pressure is thought to be caused by the binding of hydroxocobalamin to nitric oxide and may actually benefit patients with acute cyanide poisoning who are hypotensive. The increase in blood pressure has also been linked anecdotally with improvement in patients' condition and does not require treatment.[2,18]

Summary of Patient Scenario

The patient in the clinical scenario at the beginning of this article received 5 g of hydroxocobalamin reconstituted in normal saline and administered intravenously over 15 minutes. During infusion, the patient's blood pressure gradually increased from 100/50 mm Hg to 156/90 mm Hg, and he experienced concurrent reflex bradycardia (heart rate of 128/min decreased to 100/min). These changes were transient and self-limiting and did not require treatment. The patient received normal saline intravenously for hydration but did not require vasopressor support in the resuscitation period. Because of the positive response to antidotal therapy, a second 5-g dose of hydroxocobalamin was not administered.

No serious adverse events were noted or attributed to the treatment with the antidote. Reddening of the skin and urine was visible on day 1 but subsided without treatment by day 3. Because of the red color of hydroxocobalamin, colorimetric laboratory values, such as those for bilirubin, creatinine, and magnesium, were thought to have been falsely elevated on day 1. These laboratory values were in the reference range by day 4, and no treatment was necessary.

The results of arterial blood gas analysis on admission were pH 7.21, Po_2 80 mm Hg, $Paco_2$ 55 mm Hg, and bicarbonate 18 mEq/L when the fraction of inspired oxygen was 100%. Serial blood gas monitoring after hydroxocobalamin infusion indicted a gradual resolution of metabolic acidosis, and on the morning of day 3, the patient was extubated. A neurological examination at that time revealed a drowsy but oriented and responsive patient. Case management, psychiatry, and spiritual services were consulted in preparation for transition out of the

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To learn more about toxicology, read "Free and Total Digoxin in Serum During Treatment of Acute Digoxin Poisoning With Fab Fragments: Case Study," by Eyer et al in the *American Journal of Critical Care,* 2010;19:391-387. Available at **www.ajcconline.org**.

ICU and to ensure that adequate support systems would be in place for a safe discharge home.

Summary

Although both the cyanide antidote kit and hydroxocobalamin are considered acceptable for treatment of cyanide poisoning in uncomplicated exposures, few data are available to compare the 2 in the United States.[5] The type of exposure and the risk-benefit profile of each antidote must be considered when deciding which antidote to administer. Although the cyanide antidote kit has been traditionally used in the United States, nurses may begin to see hydroxocobalamin used as an alternative, because the latter appears to be safer than the kit in patients who have preexisting hypotension, are pregnant, or inhaled smoke in a closed space. Barring new evidence to the contrary, hydroxocobalamin most likely will become the standard of care in the treatment of acute cyanide poisoning. ICU nurses must understand the current options and the adverse effects, contraindications, and monitoring requirements of each antidote for proper care and management of patients with acute cyanide poisoning. CCN

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Financial Disclosures
Note reported.

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A Review of Acute Cyanide Poisoning With a Treatment Update

Facts

Cyanide causes intracellular hypoxia by reversibly binding to mitochondrial cytochrome oxidase a_3. Signs and symptoms of cyanide poisoning usually occur less than 1 minute after inhalation and within a few minutes after ingestion. Early manifestations include anxiety, headache, giddiness, inability to focus the eyes, and mydriasis. As hypoxia progresses, progressively lower levels of consciousness, seizures, and coma can occur. Skin may look normal or slightly ashen, and arterial oxygen saturation may be normal. Early respiratory signs include transient rapid and deep respirations. As poisoning progresses, hemodynamic status may become unstable.

Initial management of patients with acute cyanide poisoning requires rapid assessment and identification of the most likely route of exposure to determine proper decontamination (see Table).

The key treatment is early administration of 1 of the 2 antidotes currently available in the United States: the well-known cyanide antidote kit and hydroxocobalamin. Hydroxocobalamin detoxifies cyanide by binding with it to form the renally excreted, nontoxic cyanocobalamin. Because it binds with cyanide without forming methemoglobin, hydroxocobalamin can be used to treat patients without compromising the oxygen-carrying capacity of hemoglobin.

Table Management of patients with acute cyanide poisoning[a]

Decontamination	Basic Life Support/Advanced Cardiac Life Support (ACLS)	Antidotal therapy	Supportive care
Smoke inhalation Remove from source into fresh air Remove contaminated clothing Dermal exposure[b] Remove wet clothing Wash skin with soap and water or water alone Irrigate exposed eyes with water or saline Remove contact lenses Ingestion Do not induce emesis Activated charcoal may be administered if the victim is alert and the ingestion occurred within 1 hour Isolate emesis (it may emit hydrogen cyanide)	Establish ABCs (airway, breathing, circulation) Establish intravenous access Start cardiac monitoring Start ACLS if respiratory or cardiovascular compromise evident	Administer the cyanide antidote kit or hydroxocobalamin once an airway has been secured	Admit to an intensive care unit for cardiac monitoring, respiratory and cardiovascular support Perform routine laboratory testing, including arterial blood gas analysis, serum lactate levels, complete blood cell counts, serum glucose level, a serum cyanide level (confirmatory), and electrolyte levels Monitor and treat dysrhythmias Monitor for and treat adverse effects of antidotal therapy

a Based on data from Koschel MJ. Management of the cyanide-poisoned patient. *J Emerg Nurs.* 2006;32(4 suppl):S19-S26.
[b] Protection of responders from contamination is essential with the use of personal protective equipment such as face masks, eye shields, and frequent double gloving or the use of butyl rubber gloves.

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CE Test

Test ID C111: A Review of Acute Cyanide Poisoning With a Treatment Update

Learning objectives: 1. Understand the pathophysiology of acute cyanide poisoning 2. Recognize the importance of immediate antidote administration in the setting of acute cyanide poisoning 3. Differentiate the 2 available acute cyanide poisoning antidotes

1. What is the most common source of cyanide poisoning in Western countries?
a. Insecticides
b. Acetonitrile
c. Sodium nitroprusside
d. Smoke inhalation

2. What enzyme catalyzes conversion of cyanide to nontoxic thiocyanate in the liver?
a. Rhodanese
b. Catalase
c. Glutathione peroxidase
d. Superoxide dismutase

3. Which routes of cyanide exposure produce the most rapid onset of signs and symptoms?
a. Oral and transdermal
b. Intravenous and transdermal
c. Inhaled and intravenous
d. Oral and inhaled

4. What acid-base imbalance results from cessation of aerobic cellular metabolism in cyanide poisoning?
a. Metabolic alkalosis
b. Respiratory alkalosis
c. Respiratory acidosis
d. Metabolic acidosis

5. Cyanide causes intracellular hypoxia by reversibly binding to the cytochrome oxidase a_3 within what intracellular organelle?
a. Mitochondria
b. Golgi complex
c. Lysosomes
d. Peroxisomes

6. What is a late central nervous system manifestation of cyanide's toxic effect?
a. Bright retinal veins
b. Headache
c. Mydriasis
d. Seizures

7. Which is correct about diagnostic testing in acute cyanide poisoning?
a. Serum cyanide levels correlate well with specific degrees of poisoning severity.
b. Research is needed to find a rapid diagnostic test.
c. Lactic acidosis is specific for acute cyanide poisoning.
d. Serum cyanide levels greater than 0.5 mg/L are helpful in initial diagnosis.

8. What are common laboratory findings in acute cyanide poisoning?
a. Plasma lactate level >8 mmol/L and arteriovenous oxygen saturation difference <10 mm Hg
b. Plasma lactate level >8 mmol/L and arteriovenous oxygen saturation difference >10 mm Hg
c. Plasma lactate level <8 mmol/L and arteriovenous oxygen saturation difference <10 mm Hg
d. Plasma lactate level <8 mmol/L and arteriovenous oxygen saturation difference >10 mm Hg

9. Which is correct about hydroxocobalamin?
a. It should be refrigerated immediately after reconstitution.
b. It binds with cyanide without forming methemoglobin.
c. It should be used within 24 hours after reconstitution.
d. It binds with cyanide to form vitamin B_9.

10. What combines with unbound cyanide to form renally excreted thiocyanate?
a. Amyl nitrite
b. Sodium nitrate
c. Sodium thiosulfate
d. Hydroxocobalamin

11. What is the initial intravenous dose of hydroxocobalamin in adults?
a. 2.5 mg
b. 5 mg
c. 2.5 g
d. 5 g

12. What are the most common drug-related side effects of hydroxocobalamin?
a. Yellow skin and amber urine
b. Blue-gray skin and orange urine
c. Red skin and red urine
d. Gray skin and blue-green urine

13. What is a nursing consideration for hydroxocobalamin?
a. It is contraindicated in patients with smoke inhalation.
b. It may cause transient hypertension.
c. It requires monitoring of methemoglobin levels.
d. It is not considered safe for pregnant patients.

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

1. ❑**a**	**2.** ❑**a**	**3.** ❑**a**	**4.** ❑**a**	**5.** ❑**a**	**6.** ❑**a**	**7.** ❑**a**	**8.** ❑**a**	**9.** ❑**a**	**10.** ❑**a**	**11.** ❑**a**	**12.** ❑**a**	**13.** ❑**a**
❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**	❑**b**
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