A recent publication describes the case of a teenager who arrived at a community emergency room in a hemodynamically unstable, apneic, and unresponsive state and later died in a pediatric intensive care unit. The cause of death, confirmed by laboratory results available 2 days after the onset of symptoms, was cyanide poisoning. The 17-year-old male was previously healthy, was not taking medications, and had no history of drug abuse. Toxicity was manifested suddenly and dramatically by seizures and loss of consciousness while the boy was visiting at a classmate’s house. Supportive care was initiated in the emergency room beginning shortly after the onset of toxicity and continued in the intensive care unit; however, the patient did not receive antidotal therapy until cyanide poisoning was presumptively diagnosed approximately 4 hours after symptom onset—far too late, the authors later concluded, to be effective, particularly given the amount of cyanide to which the patient was exposed.1

This case illustrates many of the challenges in the recognition and treatment of acute cyanide poisoning. Because cyanide poisoning can rapidly culminate in incapacitation and death, prompt recognition of cyanide toxicity and early initiation of treatment are necessary for saving lives and reducing morbidity.2-4 However, the nonspecific nature of the signs and symptoms of cyanide poisoning and the inability of most hospital laboratories to rapidly confirm the presence of cyanide make diagnosis difficult. These challenges notwithstanding, acute cyanide poisoning can be successfully treated. As part of the first line of care for the critically ill patient in the prehospital and hospital settings, the emergency nurse can play an integral role in the recognition and treatment of acute cyanide poisoning. This article discusses the recognition and treatment of acute cyanide poisoning.
cyanide poisoning with emphasis on information that prepares the emergency nurse to respond to a cyanide emergency.

Causes of Acute Cyanide Poisoning

A detailed discussion of the potential causes of acute cyanide poisoning—inhalation of fire smoke, accidental ingestion, occupational exposure, industrial incidents, homicide or suicide attempts, terrorism, and ingestion of cyanogenic substances—is presented by Schnepp elsewhere in this supplement.5 In western countries, the most common cause of cyanide poisoning is inhalation of smoke from structural fires. As hydrogen cyanide is produced during combustion of carbon- and nitrogen-based materials, it is generated in nearly every fire.6 Modern structural fires, in particular, can produce high concentrations of hydrogen cyanide because of the abundance of substrates such as plastics and other polymers, synthetic fibers, wool, and silk. In keeping with the pervasiveness of cyanide in modern fires, cyanide is found, often at toxic-to-lethal concentrations, in the blood of most fire victims in which its presence is assessed.7 Toxicologic evidence suggests that cyanide is at least as important as carbon monoxide as cause of smoke-inhalation morbidity and mortality in many fires.6-9 Besides fire smoke, other causes of cyanide poisoning include occupational and industrial incidents and use in suicide, murder, and terrorism. The 17-year-old described above was poisoned by intentional adulteration of a beverage with 1.5 g potassium cyanide.1

Recognition of Acute Cyanide Poisoning

Clinical manifestations and laboratory findings in acute cyanide poisoning reflect hypoxia caused by cyanide’s deactivation of cellular oxygen-utilization mechanisms.10 Cyanide inhibits the activity of mitochondrial cytochrome oxidase, an enzyme necessary for the normal use of oxygen in cellular metabolism, and thereby prevents cells from extracting and using oxygen from arterial blood.

CLINICAL MANIFESTATIONS

Development of toxicity is generally rapid, at a rate dependent on the form of cyanide and the amount and route of exposure.11 Exposure to large doses, particularly by inhalation or ingestion, can produce marked symptoms nearly immediately and can result in death in minutes. Less rapid progression of symptoms with survival times of several hours has also been reported, particularly in cases of exposure by ingestion.12 The variability in absorption and onset of toxicity can be explained by the presence or absence of food in the stomach, the solubility of the cyanide salt involved, and other factors. In the case of ingestion of nitriles, which release cyanide when they are metabolized, onset of toxicity may be delayed for hours. These observations illustrate the existence of a window of time, albeit narrow, for effective intervention.

In western countries, the most common cause of cyanide poisoning is inhalation of smoke from structural fires.

The clinical presentation in acute cyanide poisoning can change quickly.13 Health care providers typically first encounter patients after severe toxicity has developed. Severe or advanced poisoning is manifested by hypotension, seizures, coma, respiratory depression, cardiovascular collapse, and cardiorespiratory arrest (Table 1).2-4,13,14 In a series of 101 patients treated by the Paris Fire Brigade for smoke inhalation-associated cyanide poisoning from 1995 to 2003, 37.6% were found in cardiac arrest, and 45.5% were neurologically impaired.15 Respiratory depression is generally not accompanied by cyanosis because of increased venous oxygen saturation.10,11 Often very transitory, early signs and symptoms include hypertension with reflex bradycardia; neurologic symptoms such as faintness, confusion, headache, and anxiety; and tachypnea and dyspnea.2-4,10,11,13,14 As these signs and symptoms illustrate, the heart and the brain are especially vulnerable to cyanide poisoning because of their high requirements for oxygen.

Other findings that can, but do not always, occur in cyanide poisoning include bright-red retinal veins because of elevated venous oxygen concentration; and a bitter-almond odor of victims’ breath or gastric contents.11 As the gene necessary for detecting the bitter-almond odor is absent in approximately half of the population, absence of the bitter-almond odor does not necessarily reflect the absence of cyanide toxicity. The almond odor may be masked by the odor of smoke in the case of smoke inhalation.

LABORATORY FINDINGS

Hallmark laboratory findings in acute cyanide poisoning are metabolic acidosis with markedly elevated plasma
Elevations in plasma lactate are caused by the shift of cyanide-poisoned cells from aerobic metabolism to anaerobic metabolism, which generates lactate as a toxic by-product. Plasma lactate concentration normally ranges from 0.5 to 2.2 mmol/L. A concentration ≥8 mmol/L suggests the possibility of cyanide poisoning. However, elevated plasma lactate is not specific to cyanide poisoning and therefore does not definitively signify cyanide toxicity. For example, plasma lactate concentration is also elevated in cardiac arrest of any cause and in carbon monoxide poisoning, which, like cyanide poisoning, is common in smoke-inhalation victims. The elevation of lactate observed in pure carbon monoxide poisoning is generally less than that in cyanide poisoning such that markedly elevated plasma lactate in the setting of smoke inhalation is more suggestive of cyanide.

**Severe or advanced cyanide poisoning is manifested by hypotension, seizures, coma, respiratory depression, cardiovascular collapse, and cardiorespiratory arrest.**

Based on the observation of a direct relationship between plasma lactate concentration and clinical indices of cyanide toxicity, plasma lactate concentration has been suggested as a marker of severity of cyanide toxicity both immediately after poisoning and during recovery. Plasma lactate may be influenced by factors other than cyanide toxicity in the critically ill patient. In one study, for example, the specificity of a plasma lactate concentration for a toxic blood cyanide concentration (≥1.0 mg/L) was affected by whether or not catecholamines (e.g., epinephrine, norepinephrine, dobutamine, dopamine) had been given. Specificity was 85% in patients who had not been treated with catecholamines compared with 70% in the overall sample, which included both patients who had received catecholamines and patients who had not.

**Hallmark laboratory findings in acute cyanide poisoning are metabolic acidosis with markedly elevated plasma lactate and excessive venous oxygenation.**

Excessive venous oxygenation, the second main laboratory finding in acute cyanide poisoning, is reflected in a low (<10 mm Hg) arteriovenous oxygen saturation difference (SaO$_2$-SvO$_2$) on arterial and venous blood gas analysis. Excessive venous oxygenation is attributed to the inability of cells to extract and use oxygen from arterial blood.
Blood cyanide concentrations currently have only a confirmatory role in the initial management of acute cyanide poisoning because the results of standard assays are generally not available within the time required to initiate intervention. Although blood cyanide concentrations are not practical in initial management, they are used to confirm toxicity. Cyanide should be measured in whole blood because red blood cells concentrate cyanide more than other constituents of blood do. The usefulness of blood cyanide concentrations depends on early sampling and careful storage and analysis because of the rapid metabolism of cyanide, its instability in blood samples, and the vulnerability of cyanide assays to multiple sources of interference.

For cyanide in whole blood, the toxicity threshold for cyanide alone ranges from 0.5 to 1.0 mg/L, and the lethal threshold ranges from 2.5 to 3.0 mg/L.


diagnosis. The relative ease of obtaining cyanide can facilitate concealment of contextual clues in cases of intentional poisonings such as suicide, murder, and terrorism. In recent poisonings, such as the March 5, 2006, suicide of a Minnesota State University student, individuals otherwise unlikely to be in a position to procure cyanide ordered it over the Internet. In the case of the 17-year-old described above, contextual clues available at the time of poisoning did not lead to suspicion of cyanide toxicity. The previously healthy victim with no history of depression was visiting a classmate’s house when he complained of feeling unwell and lost consciousness. Only after the window of opportunity for effective intervention had passed did investigators learn that the patient was poisoned by intentional adulteration of a beverage with potassium cyanide that the perpetrator had purchased via the Internet.


diagnosis based on index of suspicion and clinical presentation. Rapid loss of consciousness or development of coma and cardiovascular instability in the presence of elevated (>8 mmol/L) plasma lactate suggest the possibility of acute cyanide poisoning.

Contextual clues to cyanide poisoning can provide pivotal diagnostic information when considered in conjunction with the clinical presentation. Information useful for assessing the possibility of cyanide poisoning includes the patient’s occupation, the patient’s mental status before poisoning, and the location and circumstances of the poisoning. Occupations with potential exposure to cyanide include laboratory scientists and technicians, metal workers and miners, aircraft workers, firefighters, exterminators, and fumigators. Exposure to fire smoke, in particular, increases the clinical suspicion of cyanide poisoning. Acute cyanide poisoning should be suspected in anyone who inhales smoke in a closed-space fire, particularly in the presence of soot in the mouth, altered mental status, and hypotension. Smoke-inhalation victims are likely to suffer concurrent cyanide and carbon monoxide poisoning.

Although contextual clues such as exposure to fire smoke can be critical in diagnosing acute cyanide poisoning, the apparent absence of such clues does not exclude a
although this diagnostic tool is unlikely to be available at the incident scene.

**Treatment of Acute Cyanide Poisoning**

Acute cyanide poisoning is treated by terminating exposure and administering supportive care and antidotal therapy (Table 2). These aspects of care are discussed further in this supplement in Koschel’s article, Management of the Cyanide-Poisoned Patient.

**DECONTAMINATION**

Termination of cyanide exposure can entail removal of the patient from the contaminated environment in the case of inhalation exposure, removal of contaminated clothing and rinsing of the skin in the case of dermal exposure, and gastric lavage and administration of activated charcoal in the case of ingestion unless contraindicated.

**SUPPORTIVE CARE**

Initial supportive care involves the basic life support airway, breathing, and circulation (ABC) triad. Administration of 100% oxygen is viewed as an important component of supportive care despite the fact that cyanide poisoning involves deficient oxygen utilization rather than deficient oxygen availability. It is hypothesized that increased oxygen delivery could increase respiratory excretion of cyanide, reactivate mitochondrial enzymes inhibited by cyanide, and activate oxidative systems other than mitochondrial cytochrome oxidase. Administration of 100% oxygen is essential to effective treatment of concurrent carbon monoxide exposure. Advanced life support for acute cyanide poisoning includes endotracheal intubation for comatose patients, epinephrine infusion for cardiovascular collapse, sodium bicarbonate for metabolic acidosis and anticonvulsants for seizures.

**ANTIDOTAL THERAPY**

Several cyanide antidotes are available in one or more countries around the world, but the Cyanide Antidote Kit (CAK) is the only one currently available in the United States. The CAK is composed of amyl nitrite, sodium nitrite, and sodium thiosulfate. Amyl nitrite, available as perles, is given by inhalation, sometimes via a mechanical ventilation device to initiate methemoglobin formation before intravenous administration of sodium nitrite and sodium thiosulfate. The nitrites reduce blood cyanide concentrations by forming methemoglobin, to which cyanide binds with higher affinity than it binds cytochrome oxidase. Binding of cyanide to methemoglobin liberates cytochrome oxidase, which is necessary for aerobic cellular respiration. Another mechanism of action of nitrite therapy is generation of nitric oxide, which is also involved in cellular respiration.

**TABLE 2**

Management of acute cyanide poisoning

<table>
<thead>
<tr>
<th>Measure</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination of exposure</td>
<td>• For inhalation exposure, removal of victim from site of exposure, using appropriate personal protective equipment</td>
</tr>
<tr>
<td></td>
<td>• For exposure by ingestion, gastric lavage and activated charcoal unless contraindicated</td>
</tr>
<tr>
<td></td>
<td>• For dermal exposure, decontamination of skin with soap and water</td>
</tr>
<tr>
<td>Supportive care</td>
<td>Basic Life Support</td>
</tr>
<tr>
<td></td>
<td>• 100% oxygen</td>
</tr>
<tr>
<td></td>
<td>• Cardiopulmonary support or resuscitation</td>
</tr>
<tr>
<td></td>
<td>Advanced Life Support</td>
</tr>
<tr>
<td></td>
<td>• Sodium bicarbonate for metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td>• Anticonvulsants for seizures</td>
</tr>
<tr>
<td></td>
<td>• Epinephrine for cardiovascular collapse</td>
</tr>
<tr>
<td>Antidotal treatment</td>
<td>Cyanide Antidote Kit (amyl nitrite + sodium nitrite + thiosulfate) (not generally recommended in smoke-inhalation victims)</td>
</tr>
<tr>
<td></td>
<td>Hydroxocobalamin (proposed antidote in the United States; can be used regardless of suspected cyanide source, including fire smoke)</td>
</tr>
</tbody>
</table>
thiosulfate enhances transformation of cyanide to less toxic thiocyanates, which are renally excreted.  

The potential for toxicity caused by the CAK is significant. At antidotal doses, sodium nitrite can cause profound vasodilation associated with syncope, hypotension, tachycardia, dizziness, and nausea and vomiting. Nitrite-induced methemoglobinemia, one therapeutic mechanism of amyl nitrite and sodium nitrite, reduces the ability of blood to transport oxygen to the cells. Nitrite-induced methemoglobinemia may be particularly dangerous for smoke-inhalation victims, who likely also have carboxyhemoglobinemia secondary to concomitant carbon monoxide poisoning. Like methemoglobinemia, carboxyhemoglobinemia reduces the ability of blood to transport oxygen to the cells. Nitrite-induced methemoglobinemia superimposed on carboxyhemoglobinemia from carbon monoxide exposure could lead to potentially fatal reduction in the oxygen-carrying capacity of the blood. Because of the potential for dangerous disruption of oxygen transport to the cells, the CAK is generally considered unsuitable for prehospital use in victims of smoke inhalation, the most common cause of cyanide poisoning.

The Clinical Dilemma: to Treat or Not to Treat in the Context of an Uncertain Diagnosis

Successful treatment of acute cyanide poisoning is greatly enhanced by antidotal treatment. Supportive care alone impacts signs and symptoms but does not affect the body’s cyanide burden or the time course of cyanide in the body. In cases of suspected cyanide poisoning, the need for rapid administration of an antidote in the context of an uncertain diagnosis creates a predicament for the clinician deciding whether or not to administer the CAK. Use of the CAK entails the risk of causing harm to nonpoisoned patients if the presumptive diagnosis is incorrect. However, the consequences of failure to use the CAK because of an uncertain diagnosis include death if cyanide toxicity is present.

In an attempt to improve the risk:benefit ratio in the antidotal treatment of cyanide poisoning, the vitamin B_{12} precursor hydroxocobalamin has been proposed for introduction in the United States. Hydroxocobalamin detoxifies cyanide by binding it to form vitamin B_{12}, which is excreted in urine. First licensed as an antidote in France in 1996, hydroxocobalamin has been used safely and effectively in both prehospital and hospital settings to treat acute cyanide poisoning associated with smoke inhalation, industrial exposure to cyanide gas, and ingestion of cyanide salts.

Hydroxocobalamin has a favorable tolerability profile. It does not impair blood oxygenation and seems to generally improve hemodynamic stability victims of cyanide poisoning. The most common side effects are caused by the red color of the compound: hydroxocobalamin is associated with transient pink discoloration of the urine and mucous membranes and may interfere with some colorimetric laboratory tests. These effects have limited clinical impact and typically resolve within a few days of administration of hydroxocobalamin. Transient elevations in blood pressure rarely requiring treatment may also occur after treatment with hydroxocobalamin. Hydroxocobalamin, like all medications, has been associated with occasional allergic reactions, primarily with long-term, low-dose use for applications other than cyanide poisoning.

The apparently low risk of introducing significant harm with hydroxocobalamin could allow for more confident empiric treatment of acute cyanide poisoning than is currently possible in the United States and could enhance the feasibility of early prehospital treatment of suspected cyanide poisoning from all causes including smoke inhalation.

Conclusions

Acute cyanide poisoning constitutes a formidable clinical challenge. The need for early intervention and the lack of a point-of-care test for confirming cyanide toxicity necessitate administration of antidotal therapy based on a presumptive diagnosis. Rapid presumptive diagnosis is difficult because of the relatively nonspecific nature of signs and symptoms. The differential diagnosis is broad. Cyanide poisoning should be considered in any individual with rapid loss of consciousness or development of coma and cardiovascular instability in the presence of elevated (>8 mmol/L) plasma lactate—especially in the presence of a recent history consistent with possible exposure. Altered mental status or hemodynamic instability after exposure to smoke in a structural fire, suggests the probability of cyanide poisoning. When cyanide poisoning is strongly suspected, rapid administration of an antidote is required.
The decision to administer an antidote for presumptive cyanide poisoning involves consideration of the risk of antidote-induced toxicity as well as the risk of withholding treatment if cyanide poisoning is present. The introduction of hydroxocobalamin may help to improve the risk/benefit ratio in the antidotal treatment of cyanide poisoning in the United States.

Acknowledgment

The author acknowledges the assistance of Jane Saiers, PhD, in writing this manuscript. Dr. Saiers and the author’s work on this manuscript was funded by EMD Pharmaceuticals.

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