COMPREHENSIVE REVIEW

Acute Cyanide Poisoning in Prehospital Care: New Challenges, New Tools for Intervention

Tee Guidotti, MD, MPH, DABT

Professor and Director, Division of Occupational Medicine and Toxicology, Department of Medicine, School of Medicine and Health Sciences, The George Washington University Medical Center, Washington, DC USA

Correspondence:
E-mail: eohtlg@gwumc.edu

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Abbreviations:
ATP = adenosine triphosphate
CAK = Cyanide Antidote Kit

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Abstract
Effective management of cyanide poisoning from chemical terrorism, inhalation of fire smoke, and other causes constitutes a critical challenge for the prehospital care provider. The ability to meet the challenge of managing cyanide poisoning in the prehospital setting may be enhanced by the availability of the cyanide antidote hydroxocobalamin, currently under development for potential introduction in the United States. This paper discusses the causes, recognition, and management of acute cyanide poisoning in the prehospital setting with emphasis on the emerging profile of hydroxocobalamin, an antidote that may have a risk:benefit ratio suitable for empiric, out-of-hospital treatment of the range of causes of cyanide poisoning. If introduced in the US, hydroxocobalamin may enhance the role of the US prehospital responder in providing emergency care in a cyanide incident.

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Introduction

Perhaps because of its perceived rarity, cyanide poisoning historically has received scant attention in the medical literature. In recent years, however, cyanide poisoning has become a subject of increasing interest in the prehospital care and healthcare arenas.[1–5] The present attention to cyanide poisoning in the United Statess may be attributed to several developments, particularly: (1) recent attempts by terrorists to use cyanide as a chemical weapon; (2) increased understanding of the important role of cyanide in smoke inhalation-associated deaths; and (3) the potential availability of an antidote that can be administered as empiric therapy in the prehospital and hospital settings for the range of causes of cyanide poisoning. As the first line of medical care in cyanide events, the prehospital responder must understand these developments and their impact on the management of acute cyanide poisoning.

Effective management of cyanide poisoning from chemical terrorism and inhalation of fire smoke, constitutes a particularly critical challenge for the prehospital care provider.[6,7] In the US, the ability to effectively manage cyanide poisoning from these and other causes soon may be enhanced in the prehospital setting by the availability of the cyanide antidote hydroxocobalamin. The causes, recognition, and management of acute cyanide poisoning in the prehospital setting are discussed in this paper with emphasis on the emerging profile of hydroxocobalamin, which may enhance the ability of the prehospital responder to provide emergency care in a cyanide incident.

Forms of Cyanide

Cyanide exists in several forms, including the gases hydrogen cyanide and cyanogen chloride; soluble potassium and sodium cyanide salts; and insoluble mercury, copper, gold, and silver cyanide salts (Table 1).[8,9] Halogenated forms also exist. Properties of hydrogen cyanide, which is the most common form of cyanide involved in cases of acute poisoning, are listed in Table 2.[10] Hydrogen cyanide, a colorless gas, is lighter than air and may be perceived by

Compound	Commercial Use	Fatal Dose (Threshold Limit Value)
Acetonitrile	Solvent	120 mg/kg
Acrylonitrile	Synthetic fibers and plastics	35 to 90 mg/kg (20 ppm)
Calcium cyanamide	Fertilizer	40 to 50 g
Calcium cyanide	Fumigant, pesticide	5 mg/kg
Cyanogen	Fumigant, blast furnace	13 ppm
Cyanogen bromide	Fumigant	13 ppm
Cyanogen chloride	Organic synthesis	13 ppm
Dimethyl cyanamide	Organic synthesis	75 mg/kg
Hydrocyanic acid	Fumigant	0.5 mg/kg (10 ppm)
Nitroprusside	Antihypertensive, analytic reagent	10 mg/kg
Potassium cyanate	Herbicide, chemical reagent	1 g/kg
Potassium cyanide	Electroplating, organic synthesis	2 mg/kg
Potassium ferrocyanide	Metallurgy, graphic arts	1.6 mg/kg
Sodium cyanide	Electroplating, organic synthesis	2 mg/kg

Table 1—Examples of cyanide-containing compounds[8]

Chemical and Physical Properties	
Boiling point	25.7°C
Flashpoint (closed cup)	-17.8°C
Vapor pressure	740 mmHg
Autoignition temperature	538°C
Density: Vapor Liquid	 0.99 at 20°C 0.68 g/mL at 25°C
Volatility	1.1 x 106 mg/m^3 at 25°C
Appearance and color	Gas: odor of bitter almonds or peach kernels (only detected by some individuals)
Solubility: In water In other solvents	 Complete at 25°C Completely miscible in almost all organic solvents
Environmental and Biological Properties	
Detection	ICAD; M254A1 kit
Persistency: In soil On material	 <1 hour Low
Skin decontamination	Water; soap and water
Biologically effective amount: Vapor (mg x min/m^3) Liquid (mg/kg)	 LCt_{50}: 2500 to 5000 (time-dependent) LD_{50} (skin): 100

Table 2—Chemical, physical, biological, and environmental properties of hydrogen cyanide[10]

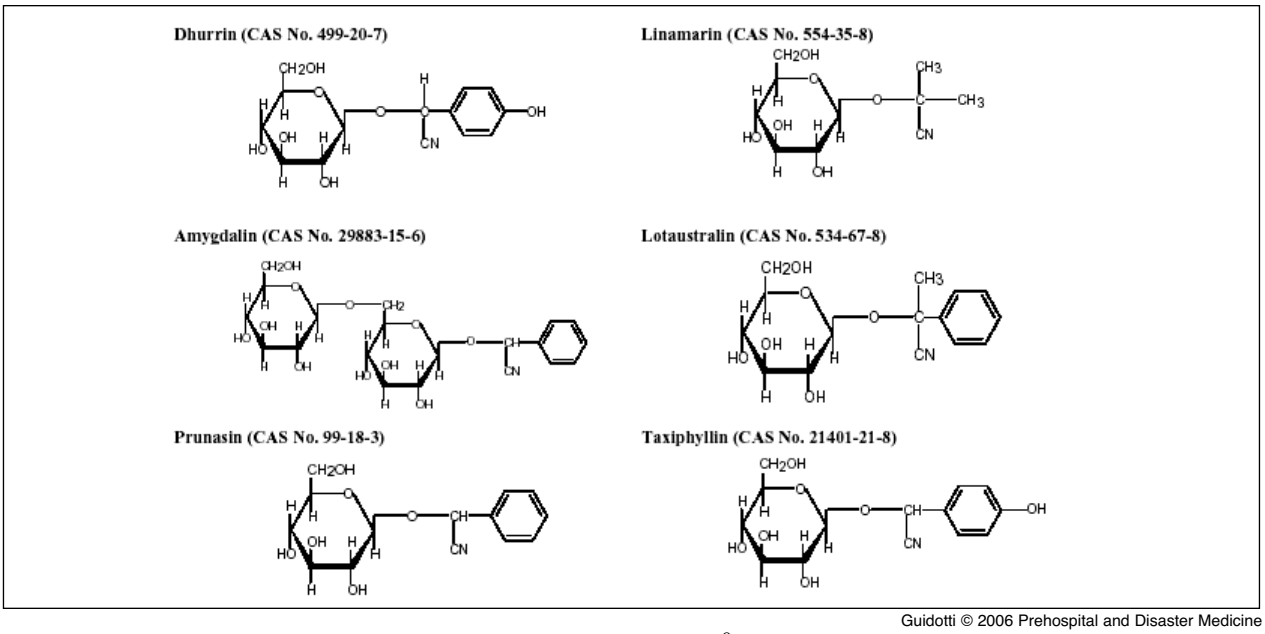

Figure 1—Cyanogenic glycosides in some edible plant contituents.[9] Dhurrin occurs in sorghum, linamarin in cassava, amygdalin in almonds, lotaustralin in cassava and lima beans, prunasin in pitted fruits, and taxiphyllin in bamboo shoots.

some to have an almond-like odor. It can be produced by the contact of cyanide salts such as sodium or potassium cyanide with acids or acid salts, by the hydrolysis of other cyanide gases such as cyanogen chloride, and by the hydrolysis of cyanogenic glycosides, which are natural products of constituents in plants such as cassava, lima beans, pitted fruits, and bamboo shoots (Figure 1).[9]

Sources of Cyanide

Cyanides come from a wide range of natural and human-made sources.[8,9,11,12] Both gaseous and solid forms of cyanide are used extensively, often in very large quantities, in industries including metallurgy, electroplating, and metal cleaning. Cyanide also is used in the recovery of gold and silver from mineral ores and of silver from photographic materials; in the production of plastics, pigments, and dyes; and as a pesticide. Other sources of cyanide include emissions from production of iron and steel, coal burning, vehicle exhaust, and cigarette smoke. Moreover, hydrogen cyanide is released as a product during the combustion of plastics and other polymers, silks, wool, cotton, and many other nitrogen-containing substances. According to the Toxics Release Inventory, nearly 2.8 million pounds of hydrogen cyanide were released from 76 facilities in 1998. Air emissions result in the release of the majority of these compounds (2.06 million pounds) followed by release by underground injection (approximately 600,000 pounds) and in landfills (approximately 113,000 pounds).[13]

Numerous substances are cyanogenic when burned or when metabolized in the body.[9,14] For example, nitriles, used as solvents and in the manufacturing of plastics, can release hydrogen cyanide during combustion or when they are metabolized after absorption through the skin or gastrointestinal tract. Some drugs (e.g., sodium nitroprusside, benzylisothiocyanate, and amygdalin [a fraudulent cancer remedy]) and plant constituents (e.g., those in cassava or Puerto Rican lima beans) can generate cyanide in the body when they are metabolized. Some of these sources, such as cyanogenic plant constituents, are more likely to cause chronic toxicity when ingested over a period of time and typically are not responsible for acute cyanide toxicity.

Human Exposure to Cyanide

Cyanide poisoning can occur under heterogeneous circumstances including occupational exposure, industrial accidents, natural catastrophes (e.g., fire resulting from an earthquake), suicide and murder attempts, chemical warfare, and terrorism. Cyanide exposure from combustion of nitrile plastics and other nitrogen sources is a common, but sometimes overlooked hazard in firefighting.

Occupations with potential exposure to cyanides are listed in Table 3.[15] Violation of occupational exposure standards for cyanide in the US is punishable by law. In 1990 in Illinois, a cyanide-related death was prosecuted as murder in light of evidence that an employee of Film Recovery Systems (the defendant in the case) died after inhaling cyanide while working in a plant owned by Film Recovery Systems. Plant workers were not informed that they were working with cyanide, the plant was poorly ventilated, and workers were not provided with protective clothing.[16]

Of the approximately 2.7 million incidents of poisoning reported to the American Association of Poison Control Centers in 2002, cyanide accounted for 224.[17] This number substantially under-represents the actual incidence of acute cyanide poisoning, because it represents only voluntary, unsolicited reports and does not include reports of cyanide poisoning arising from smoke inhalation, which is the most common cause of acute cyanide poisoning in the

Acid dippers	Gold refiners
Acrylate makers	Heat treateres
Acrylonitrile makers	Hexamethylenediamine makers
Adipic acid makers	Hydrocyanic acid makers
Adiponitril makers	Hydrogen cyanide workers
Aircraft workers	Insecticide and rodenticide makers
Almond flavor makers	Jewelers
Ammonium salt makers	Laboratory technicians
Art printing workers	Metal cleaners
Blacksmiths	Metal polishers
Blast furnace workers	Methacryalate makers
Bone distillers	Mirror silverers
Bronzers	Mordanters
Browners	Nylon makers
Cadmium platers	Organic chemical synthesizers
Case hardeners	Oxalic acid makers
Cellulose product treaters	Phosphoric acid makers
Cement makers	Photoengravers
Coal tar distillery workers	Photographers
Coke oven operators	Pigment makers
Cyanide workers	Plastic workers
Cyanogen makers	Polish makers
Disinfectant makers	Rayon makers
Dye makers	Rubber makers
Eletroplaters	Silver extractors
Executioners	Silver refiners
Exterminators	Solderers
Fertilizer makers	Steel carburizers
Firefighters	Steel hardeners
Fulminate mixers	Steel galvinizers
Fumigant makers	Tannery workers
Fumigators of fruit trees, apiaries, soil, ships, railway cars, warehouses, stored foods	Temperers
Galvanizers	Tree sprayers
Gas purifiers	White cyanide makers
Gilders	Zinc platers
Gold extractors	Zinkers

Table 3—Occupations with potential exposure to cyanide[1]

US. Cyanide is thought to be a significant contributor to up to 10,000 deaths attributed to smoke inhalation each year in the US.[12]

Biological Effects of Cyanide

Depending on its form, cyanide can enter the body via inhalation, ingestion, or absorption through the skin.[12,14] The body can detoxify small amounts of cyanide by several mechanisms including metabolism in the liver by the enzyme rhodanese to non-toxic thiocyanate, which is excreted in the urine, and conversion of cyanide to cyanocobalamin by binding to hydroxocobalamin (Figure 2).[14] These mechanisms are overwhelmed by exposure to all but very small concentrations of cyanide.

Cyanide is thought to cause toxicity by inactivating mitochondrial cytochrome oxidase.[14,18] Cyanide binds to ferric

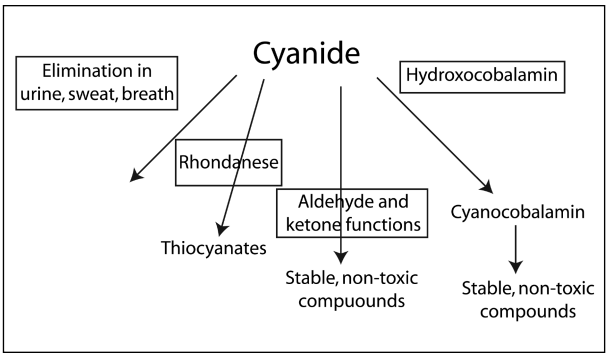

Figure 2—Metabolic pathways for detoxifying small amounts of cyanide[14]

iron (Fe^{3+}) of cytochrome oxidase a3 to inhibit the oxidative function of this enzyme and thereby to block cells from using oxygen, which is the substrate of normal cellular respiration. Cyanide causes cells to switch from aerobic (or oxygen-dependent) metabolism that yields the cellular energy source adenosine triphosphate (ATP) to anaerobic (or oxygen-independent) energy production, which generates toxic byproducts such as lactic acid instead of ATP. The heart, brain, and liver particularly are vulnerable to cyanide poisoning because of their requirement for a continuous supply of oxygen and ATP generated from aerobic metabolism.

The time between initial exposure to cyanide and symptom onset can vary from seconds to hours depending primarily on the concentration of cyanide exposure. Exposure to moderate to high concentrations of cyanide can cause the loss of consciousness in seconds, and respiratory depression and cardiac arrest can follow within minutes. Because cyanide poisoning can culminate in death so quickly, the success of intervention critically depends on early recognition of potential cyanide poisoning and prompt initiation of treatment.

Recognition and Management of Cyanide Poisoning in the Prehospital Setting

No laboratory test, including measurement of blood cyanide concentrations, can confirm the presence of acute cyanide poisoning within the time period required to initiate intervention. Therefore, in the prehospital setting, cyanide poisoning is diagnosed clinically on the basis of symptoms and signs. A diagnosis of cyanide poisoning is suggested strongly by rapid loss of consciousness or development of coma and cardiovascular instability in the presence of conditions consistent with the possibility of cyanide exposure.[12,14] The presence of elevated concentrations of plasma lactate, a toxic byproduct of anaerobic energy production, in addition to impaired consciousness and cardiovascular instability, increase confidence in the diagnosis. Other diagnostic clues include a recent history consistent with cyanide exposure. For example, the presence of cyanides in the workplace is consistent with possible occupational exposure. Exposure to smoke from fires suggests the possibility of cyanide poisoning. Cyanide poisoning should be suspected in any individual exposed to fire smoke in a structural or other confined-space fire.[7]

Early symptoms of acute cyanide poisoning include neurological manifestations such as giddiness, confusion, headache, and dizziness; nausea and vomiting; palpitations and hyperventilation or shortness of breath; and eye irritation. These symptoms reflect neurologic and respiratory stimulation occurring as a reflexive attempt to compensate for tissue hypoxia. Later symptoms of acute cyanide poisoning reflect neurological, respiratory, and cardiovascular depression arising from inability to compensate for the tissue hypoxia. Seizures, coma, respiratory arrest, and cardiac arrest can occur within minutes after exposure to moderate to high concentrations of cyanide.

Other signs that sometimes are present in acute cyanide poisoning include cherry-red complexion and bright-red retinal veins and arteries. These signs are attributed to high oxygenation of venous blood (as well as arterial blood) because of the inability of cells to extract oxygen from arterial blood. Cyanosis, which can be an indication of poorly oxygenated blood, typically is not present because of the elevated venous oxygen levels. Breath may have a bitter, almond-like odor attributed to excretion of unmetabolized cyanide; however, this odor may be undetectable.

Although cyanide poisoning is dangerous and frequently lethal, effective intervention is possible with supportive care and treatment using antidotes. Management of acute cyanide poisoning entails removing the victim from the source of cyanide, basic supportive measures (e.g., administration of 100% oxygen, cardiopulmonary resuscitation) intended to gain or maintain cardiac and respiratory function, and administration of an antidote (Table 4).[12,14,18,19] Supportive care beyond basic cardiopulmonary support is administered depending on the specific needs of the victim: (1) anticonvulsants are given for seizures; (2) continuous infusion of pressors may be administered for cardiovascular collapse; (3) antiarrhythmics are administered for cardiac rhythm abnormalities; and (4) sodium bicarbonate is given in an attempt to correct metabolic acidosis.

Cyanide Antidotes

Cyanide Antidote Package

Several cyanide antidotes are available around the world. Cyanide antidotes include the Cyanide Antidote Package (also known as the Cyanide Antidote Kit (CAK), Lilly kit, Taylor kit, and Pasadena kit), hydroxocobalamin (or Cyanokit®), and other antidotes such as dicobalt edetate (EDTA) and 4-dimethylaminophenol (4-DMAP). The CAK, the only cyanide antidote currently available in the US, is composed of amyl nitrite (available as pearls), sodium nitrite, and sodium thiosulfate.[10,14] Sodium nitrate and sodium thiosulfate are administered intravenously, whereas amyl nitrate often is given via a mechanical ventilation device and is required to stabilize the victim before the administration of the other components of the antidote kit. Sodium nitrate reduces blood cyanide levels by causing the formation of methemoglobin, to which cyanide binds with higher affinity than it does to the cytochrome oxidase enzyme. Binding of cyanide to methemoglobin liberates cytochrome oxidase, which is necessary for aerobic cellular respiration. Sodium thiosulfate binds the cyanide ion to form thiocyanates, which are much less toxic than cyanide and are excreted by the kidneys.

Measure	Action
Reduction or elimination of sources of cyanide	- For inhalation exposure, move victim from site of suspected exposure - For exposure by ingestions, undertake gastric decontamination with activated charcoal
Supportive measures	- Cardiopulmonary support and/or resuscitation - Administration of 100% oxygen - Sodium bicarbonate to correct metabolic acidosis - Anticonvulsants, epinephrine, antiarrhythmics as needed
Antidotal treatment	- Amyl nitrate + sodium nitrate + thiosulfate in cases of poisioning by ingestion - Antidote should be administered with caution in hemodynamically unstable victims, particularly those with low blood pressure, because of potential for antidote to induce severe hypotension

Table 4—Management of acute cyanide poisoning[12,14,18,19]

The CAK is associated with risks that limit its prehospital empiric use.[11,20,21] First, the nitrite components of the kit displace oxygen from hemoglobin to form methemoglobin. Although methemoglobin is beneficial in that it neutralizes cyanide, this effect may be counterproductive because it reduces the oxygen-carrying capacity of the blood. Nitrite-induced methemoglobinemia may exacerbate ischemia in patients with low cardiopulmonary reserve, and may be harmful or fatal in smoke-inhalation victims who have pre-existing hypoxia because of carbon monoxide poisoning. Second, sodium nitrite and amyl nitrite in the CAK cause potent vasodilation leading to hypotension and, potentially, shock. Cyanide-poisoned victims have marked hemodynamic instability, and the additive effects of nitrite-induced vasodilation can be harmful or fatal. The sodium thiosulfate component of the CAK is limited by its slow onset of action. Therefore, it is most often used in conjunction with other rapidly acting agents rather than as a single antidote.

Induction of methemoglobinemia with the nitrite components of the CAK can be particularly dangerous in victims of cyanide poisoning arising from smoke inhalation.[10,11,20,21] Smoke-inhalation victims almost always have carbon monoxide toxicity. Like nitrites, carbon monoxide displaces oxygen from hemoglobin. Carbon monoxide displaces oxygen from hemoglobin to form carboxyhemoglobin, whereas nitrites in the CAK displace oxygen from hemoglobin to form methemoglobin. The additive oxygen-depriving effects of nitrites and carbon monoxide can be lethal. Therefore, use of the nitrite components of the CAK is not recommended in victims of cyanide poisoning arising from smoke inhalation.

Dicobalt-EDTA, 4-DMAP

Other antidotes including dicobalt-EDTA and 4-DMAP are typically not used in the US. Like the CAK, these two antidotes are not well-suited for prehospital empiric treatment of acute cyanide poisoning because of their risk:benefit ratios. Dicobalt-EDTA can cause severe hypotension, particularly in patients without cyanide poisoning,[11] and 4-DMAP is associated with severe methemoglobinemia.[22]

Hydroxocobalamin

In order to address the unmet need in the US and other countries to find an antidote suitable for use as an empiric out-of-hospital intervention, use of the antidote hydroxocobalamin, a precursor of vitamin B_{12} seems appropriate (Table 5; Figure 3).[23–25] Another form of hydroxocobalamin currently is used in the US to treat vitamin B_{12} deficiency, but the formulation for this use is too dilute to be used as a cyanide antidote. Hydroxocobalamin has been recognized as a cyanide antidote for almost 50 years. It was granted regulatory approval for marketing in 1996 in France, where it is the antidote of choice and is commercially available as Cyanokit® (Merck Santé s.a.s.). In France, hydroxocobalamin is used for empiric prehospital treatment of cyanide poisoning and in smoke-inhalation victims as well as in hospitalized victims.[14,23]

Each kit includes two vials of 2.5 g hydroxocobalamin lyophilizate for reconstitution with 100 mL saline per vial before use and two sterile transfer kits. The initial adult dose of hydroxocobalamin in France is typically 5 g. In Europe, an additional 5 g dose can be given according to the clinical status of the patient. Dosing recommendations for the US (should hydroxocobalamin be introduced there) are not yet established.

Hydroxocobalamin detoxifies cyanide by binding with it to form cyanocobalamin, or vitamin B_{12}, which is excreted in urine.[14] Hydroxocobalamin pharmacokinetics in humans have not been studied extensively, but the currently available data show significant intra-individual variability. In a prospective study conducted in 11 smoke-inhalation

Chemical name	Cobinamide hydrochloride dihydrogen phosphate (ester) inner salt 3'-ester with 5,6-dimethyl-1-α-D-ribofuranosyl-1H-benzimidazole
Molecular formula	$C_{62}H_{89}N_{13}O_{15}P$
Molecular weight	1346
Physical and chemical properties	Dark red powder readily soluble in water and ethanol and practically insoluble in acetone

Table 5—Hydroxocobalamin physical and chemical properties

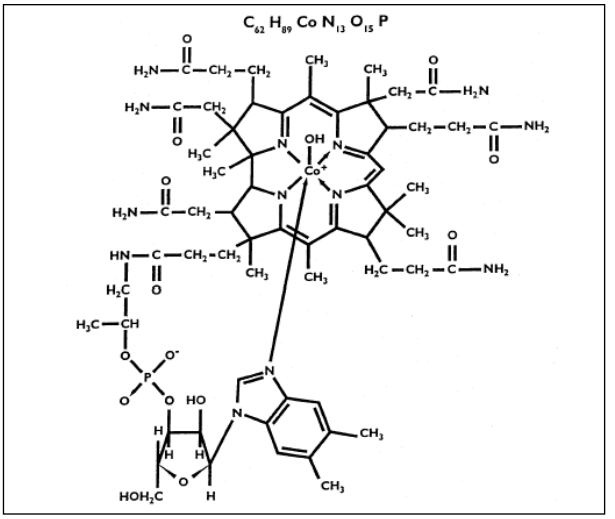

Figure 3—Structural formula of hydroxocobalamin

victims, serum hydroxocobalamin concentrations were measured for six days after a single 5g dose of the antidote.[24] The pharmacokinetic data fit a two-compartment model. The author concluded that the apparent volume of distribution suggests predominantly extracellular partitioning of the antidote. Distribution half-life was 1.89 ±0.34 hours (h); elimination half-life was 26.2 ±2.7 h; volume of distribution was 0.45 ±0.03 L/kg; renal clearance was 0.31 ±0.06 L/h; and total body clearance was 0.83 ±0.07 L/h.

The antidotal efficacy of hydroxocobalamin for acute cyanide poisoning was assessed in a prospective, open-label study of 69 smoke-inhalation victims in Paris, France and a retrospective study of nine victims of poisoning by large concentrations of ingested (n = 8) or inhaled (n = 1) cyanide.[25,26] The prospective Paris study, an open-label trial conducted from 1989–1994, enrolled adults who were at least 15 years of age and who were victims of smoke inhalation as determined by soot in the mouth and expectoration, and the presence of neurologic impairment.[25] The main exclusion criteria were presence of multiple traumatic injuries, second-degree (or more severe) burns exceeding 20% of body surface, and significant facial burns. After they were examined at the scene of the fire, patients received an intravenous infusion of hydroxocobalamin 5g (maximum total infusion dosage 15g) and supportive care. Oxygen was administered by mask or intubation. Some patients who were in shock or ventilatory arrest received additional hydroxocobalamin at the scene of the fire or during hospitalization.

Between 1989–1994, 69 patients were treated with hydroxocobalamin. The sample was divided approximately equally between men (n = 33) and women (n = 36). All but one patient had neurological impairment. More than half of the patients were comatose before the administration of hydroxocobalamin. Cardiorespiratory arrest initially was present in 14 of 69 patients (20.2%). Of the 69 patients treated with hydroxocobalamin, 50 (72%) survived. Among the 19 patients who died (28%), the main causes of death were decerebration related to anoxia and infectious complications unrelated to cyanide intoxication. Hemodynamic parameters, including arterial pressure and heart rate, remained relatively stable following the administration of hydroxocobalamin. Neurological impairment before administration of the antidote was present in 68 of 69 patients (98.6%). Among these patients, neurological recovery (defined as disappearance of neurological signs) was observed in 46 patients (68%).

The data with smoke-inhalation victims are complemented by clinical data from a case series of nine severely ill patients (seven men, two women) admitted to the Toxicological Intensive Care Unit of the Hôpital Fernand Widal in France, who were treated with hydroxocobalamin after exposure to lethal doses of cyanide.[25] The subject subsequently were incorperated into a published study on lactic acidosis as a measure of severity of intoxication.[26] Seven of the patients had voluntarily ingested cyanide salts; one had voluntarily ingested acetonitrile; and one accidentally had been exposed to cyanogen bromide gas. The mean value for the age of the patients was 41.4 years. At admission, patients showed signs of severe cyanide poisoning. Five of the patients were comatose; six were in shock; and three were in cardiorespiratory arrest. Mean values for systolic blood pressure and plasma lactate were 81 mmHg and 20.6 mmol/L, respectively. Mean blood cyanide concentrations values ranged from 12.7–256.4 μmol/L. Hydroxocobalamin was administered intravenously in the emergency department at an average dose of 8.1 g (range 5–15 g).

Six of the nine patients survived after treatment with hydroxocobalamin (Table 6).[25] Of the three patients who died, all had been admitted several hours after the onset of intoxication when neurological impairment appeared to be irreversible. Hydroxocobalamin improved blood pressure in all patients admitted with shock or hypotension. Furthermore, neurologic parameters normalized in two of the five patients who were comatose at admission.

Hydroxocobalamin appears to be well-tolerated with no known major toxicities.[1,2,11,25] Hydroxocobalamin does

				Systolic Blood Pressure (mmHg)		
Patient #	Poison	Cyanide Level (μmol/L)	Cardio-respiratory arrest?	Pretreatment	After antidote	Outcome
1	Acetonitrile	104	No	80	160	Recovery
2	Potassium cyanide	256.4	Yes	40	130	Deferred death (septic shock on 11th day)
3	Gold and potassium cyanide	44	No	120	150	Recovery
4	Mercuric cyanide	217	No	80	120	Recovery
5	Potassium cyanide	158	No	140	155	Recovery
6	Potassium cyanide	238.7	Yes	0	160	Death by decerebration after 48 hours
7	Potassium cyanide	Not determined	No	80	120	Recovery
8	Cyanide salts	196	Yes	50	70	Death
9	Cyanogen bromide (inhalation)	12.7	No	140	150	Recovery

Table 6—Profiles of cyanide-poisoned patients treated with hydroxocobalamin[26]

not reduce the ability of the blood to carry oxygen or appear to cause hemodynamic instability, but instead, appears to improve hemodynamic parameters in disaster victims.[25] Because of the red color of the molecule, hydroxocobalamin turns mucous membranes, skin, and urine red, and it may interfere transiently with specific colorimetric clinical laboratory values including aspartate aminotransferase, total bilirubin, creatinine, and magnesium.[27,28] Use of hydroxocobalamin rarely has been associated with allergic response and anaphylactic reaction.[29–31]

Considered in aggregate, the prospective and retrospective studies describe the potential use of hydroxocobalamin as a cyanide antidote. Hydroxocobalamin was used empirically at the scene of fires to treat victims of smoke inhalation-associated cyanide poisoning and in the hospital to treat cyanide poisoning from other sources including inhalation and ingestion of cyanide salts or cyanogenic compounds. The administration of hydroxocobalamin is associated with an improvement of hemodynamic stability. Ongoing studies of efficacy in dogs and safety in healthy human volunteers will help to further define the therapeutic profile of hydroxocobalamin.

Conclusions

Sources of cyanide are ubiquitous, and cyanide poisoning can occur under heterogeneous circumstances, including occupational exposure, industrial accidents, murder and suicide attempts, chemical warfare, and terrorism. The prehospital emergency responder provides the first line of medical care for victims of cyanide poisoning, and therefore, plays a crucial role in saving lives. The earlier the prehospital emergency responder recognizes or suspects cyanide poisoning and initiates intervention, the greater the chance of a successful outcome. If introduced in the US, hydroxocobalamin potentially will facilitate the ability of prehospital responders to provide effective intervention for cyanide-poisoned victims. Hydroxocobalamin has been used in victims of smoke inhalation as well as other sources of cyanide poisoning, as empiric treatment, and as prehospital treatment. With this profile, hydroxocobalamin offers the potential for a cyanide antidote that can be administered in the prehospital setting as empiric therapy for the range of causes of cyanide poisoning. Data from ongoing studies will help to further define the profile of this antidote.

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