Approach Considerations

Administer a cyanide antidote if the diagnosis of cyanide toxicity is strongly suspected, without waiting for laboratory confirmation. Available antidotes are hydroxocobalamin (Cyanokit) and sodium thiosulfate and sodium nitrite (Nithiodote). Both are given intravenously.

Patients who present with more than minimal symptoms that resolve without treatment should be admitted for observation and supportive care. In patients with acute poisoning from hydrogen cyanide (HCN) gas or soluble salts, the principal acute care concerns are hemodynamic instability and cerebral edema. The continuous cardiac monitoring, respiratory and cardiovascular support, and frequent neurologic evaluation these patients require is generally best provided in an intensive care unit.

Conversely, acute poisoning from cyanogens (nitriles) or poorly soluble salts may not manifest or become life-threatening for several hours after exposure. These patients require a 24-hour observation period.\[24, 25\]

Oxygenation should be optimized and continuous cardiac monitoring provided. Depending on the severity of symptoms, endotracheal intubation may be necessary to optimize oxygen delivery and protect the airway. Serum lactate concentrations, chemistries, and arterial or venous blood gases should be monitored.

Patients should be reevaluated 7-10 days after discharge from the hospital.\[26\] Delayed onset of Parkinson-like syndrome or neuropsychiatric sequelae may be noted on followup.

Special concerns in pregnancy

Fetal demise is possible in cyanide poisoning. Aggressive support and antidotal treatment of the mother is paramount. An obstetric evaluation following stabilization of the mother is essential. Therapeutic abortion may be indicated in the presence of fetal demise.

Prehospital Care

Use of personal protective equipment is essential at many cyanide exposure scenes. Respiratory protection against hydrogen cyanide gas may be needed at fires and industrial accidents. Certain cyanide compounds can be absorbed dermally; emergency services personnel should wear gloves and other forms of skin protection.

Appropriate prehospital measures may include the following\[6, 6\]:

- Rescue from the cyanide source (on the assumption that rescuers have the highest level of respiratory protection [level A])
- Removal of contaminated clothing and decontamination of the skin as required with soap and water
- Administration of high-flow oxygen, airway management, and ventilatory support as required
- Establishment of intravenous (IV) access
- Continuous cardiac monitoring
- Advanced cardiac life support (ACLS) measures as indicated for dysrhythmias
Aggressive airway management with delivery of 100% oxygen can be lifesaving. (Although theoretically useless, supportive care with administration of oxygen alone has proven effective in a number of poisonings.) It can also treat concomitant carbon monoxide exposure, pending measurement of blood levels.

Administer cyanide antidotes as soon as possible. While not carried by all emergency medical technicians, some first responders do have protocols to administer hydroxocobalamin in the field. As a temporizing measure, amyl nitrite ampules can be crushed and their contents poured onto a gauze pad and placed in front of the patient's mouth, if the patient is breathing spontaneously, or ventilated into an apneic patient using a bag-valve-mask.

**Emergency Department Care**

Initial emergency department care for patients with cyanide exposure is identical to that provided in the prehospital phase. Provide supportive care, including the following:

- Airway control, ventilation, and 100% oxygen
- Crystalloids and vasopressors, as needed, for hypotension
- Sodium bicarbonate, titrated according to arterial blood gas (ABG) and serum bicarbonate level

Decontaminate the patient with removal of clothing/skin flushing and/or activated charcoal (1g/kg), as appropriate. Activated charcoal should be given after oral exposure in alert patients who are able to protect the airway or after endotracheal intubation in unconscious patients. In recent ingestions, activated charcoal may be preceded by gastric lavage. The gastric aspirate may cause secondary contamination and should be viewed as hazardous.

Administer hydroxocobalamin or sodium thiosulfate and sodium nitrite if the diagnosis is strongly suspected. Do not wait for laboratory confirmation.

**Cyanide Antidotes**

Antidotes to cyanide include hydroxocobalamin and sodium nitrite and sodium thiosulfate. Sodium thiosulfate may be given in combination with sodium nitrite or hydroxocobalamin, or may be given alone. These agents are administered intravenously.

**Hydroxocobalamin**

Hydroxocobalamin, which is considered the drug of choice in continental Europe and Australia, is approved by the US Food and Drug Administration (FDA) for treating known or suspected cyanide poisoning. Coadministration of sodium thiosulfate (through a separate line or sequentially) has been suggested to have a synergistic effect on detoxification.

Hydroxocobalamin combines with cyanide to form cyanocobalamin (vitamin B-12), which is renally cleared. Alternatively, cyanocobalamin may dissociate from cyanide at a slow enough rate to allow for cyanide detoxification by the mitochondrial enzyme rhodanese.

A review by Hall et al notes that hydroxocobalamin has not been associated with clinically significant toxicity in antidotal doses compared with other cyanide antidotes. Hydroxocobalamin has a rapid onset of action, neutralizes cyanide without interfering with cellular oxygen use, is conducive to prehospital use due to its tolerability and safety profiles, and is safe for use in patients with smoke inhalation.

Adverse effects of hydroxocobalamin administration include transient hypertension (a benefit in hypotensive patients), reddish brown skin, mucous membrane and urine discoloration, and rare anaphylaxis and anaphylactoid reactions. Because of its bright red color, it also interferes with co-oximetry (about a 5% increase in carboxyhemoglobin levels) and blood chemistry testing (bilirubin, creatinine kinase and possibly liver enzymes, creatinine, phosphorus, glucose, magnesium, and iron levels). It can also interfere with hemodialysis.

Certain medications should not be administered simultaneously or through the same line as hydroxocobalamin. These include diazepam, dopamine, dobutamine, and sodium thiosulfate.

**Sodium nitrite and sodium thiosulfate**

Sodium nitrite and sodium thiosulfate are often used in combination and are currently considered second-line therapy after hydroxocobalamin. Sodium nitrite is rapidly effective but can cause life-threatening toxicity, whereas sodium thiosulfate has a somewhat delayed effect but is far safer.

Sodium nitrite induces methemoglobin in red blood cells, which combines with cyanide, thus releasing cytochrome oxidase enzyme. Sodium thiosulfate donates a sulfur atom necessary for the transformation of cyanide to thiocyanate by rhodanese, thus increasing the activity of the endogenous detoxification system. The thiocyanate is then renally excreted.

Sodium nitrite should not be used in patients with smoke inhalation unless their carboxyhemoglobin concentration is very low (<10%). The induction of methemoglobinemia by sodium nitrite compounds the effect of any existing carboxyhemoglobinemia, significantly reduces the oxygen-carrying capacity of blood. In addition, vasodilation from sodium nitrite may result in significant hypotension and cardiovascular collapse.

Appropriate dosing of sodium nitrite has not been established in children. Consequently, these patients are at increased risk for excessive methemoglobinemia, hypotension, or both.

Inpatient Care

Optimize oxygenation. Monitor disease resolution by clinical criteria, serial plasma lactate concentrations, and arterial and venous blood gases. Perform serial electrocardiograms (ECGs) for patients with cardiac dysrhythmias or complaints of chest pain. Monitor for delayed onset of pulmonary edema in those presenting with evidence of respiratory irritation. Discharge the patient when neurologic status and cardiovascular status have normalized and acidosis and other metabolic abnormalities have resolved.

Transfer

Avoid transfer of patients with acute cyanide toxicity. However, transfer the patient if antidotes and intensive care are unavailable and if rapid, appropriate medical transport can be assured. Ideally, transfer patients to a regional toxicology treatment center.

Provide medical stabilization (eg, airway, hemodynamic parameters) before transfer. Transfer with an advanced cardiac life support (ACLS) level of service under continuous cardiac monitoring with supplemental oxygen and intravenous access.

Deterrence and Prevention

Smoke alarms significantly reduce the incidence of serious smoke inhalation injury. Workplaces using cyanides should have engineering controls in place to avoid inadvertent exposures. Workers should be provided with personal protective equipment and training; they should be instructed to avoid contact between cyanide salts and mineral acids or other compounds with low pH.

Patients receiving sodium nitroprusside at high doses or for more than 5 days should have monitoring of blood cyanide or thiocyanate concentrations. Alternatively, these patients can be treated prophylactically with sodium thiosulfate or hydroxocobalamin to reduce the risk of iatrogenic cyanide poisoning.

Consultations

Consultation with a medical toxicologist or a poison control center is recommended. They should be contacted immediately upon consideration of cyanide as a diagnosis, given the critical nature of these cases. They can provide recommendations regarding the most effective available antidotal therapy, as well as insight into potential sources of poisoning (eg, industrial) that may place others at risk. Online resources may also be consulted (see the chart below).

Chemical terrorism agents and syndromes: signs and symptoms (PDF) (Copyright University of North Carolina at Chapel Hill)

Consult with law enforcement authorities and the Federal Bureau of Investigation (FBI) in any suspected terrorist incident.


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Summary

- Cyanide is a common product of combustion and thus must be included in the differential diagnosis for any patient with severe smoke inhalation.

- Prompt recognition of and intervention for acute cyanide poisoning from smoke inhalation are necessary for saving lives.

- CAK cannot be administered empirically to smoke inhalation victims who may already be hypoxic and have CO toxicity.

- Hydroxocobalamin now provides a safe and rapid alternative for treatment of known or suspected cyanide toxicity in the US.
Recognizing Cyanide Poisoning

Malcolm J. Estes, M.D.

Cyanide poisoning may result from inhalation, ingestion, or dermal exposure. Prior to administration of CYANOKIT, smoke-inhalation victims should be assessed for: exposure to fire or smoke in an enclosed area; presence of soot around the mouth, nose, or oropharynx, and altered mental status. In addition to CYANOKIT, treatment of cyanide poisoning must include immediate attention to airway patency, adequacy of oxygenation and hydration, cardiovascular support, and management of any seizure activity.

Use caution in the management of patients with known anaphylactic reactions to hydroxocobalamin or cyanocobalamin. Consideration should be given to use of alternative therapies, if available. Allergic reactions may include: anaphylaxis, chest tightness, edema, urticaria, pruritus, dyspnea, and rash. Allergic reactions including anaphylactic reactions have also been reported in postmarketing experience. Substantial increases in blood pressure may occur following CYANOKIT therapy. Elevations in blood pressure (~180 mmHg systolic or ~110 mmHg diastolic) were observed in approximately 10% of healthy subjects receiving hydroxocobalamin 5 g and 20% of subjects receiving 10 g.

Usage may interfere with some clinical laboratory evaluations. Also, because of its deep red color, hydroxocobalamin may cause hemodilution and lytes or 21+10 errors. In addition, an erroneous detection of a "blood leak" should be considered before hemodialysis is initiated in patients treated with hydroxocobalamin. Due to potential photosensitivity, patients should avoid direct sun until erythema resolves.

CYANOKIT is Pregnancy Category C and should be used during pregnancy only if the potential benefit justifies the potential risk. Safety and effectiveness of CYANOKIT have not been established in pediatric patients.

The most common adverse reactions (>5%) included transient chromaturia, erythema, rash (predominantly acneiform), increased blood pressure, nausea, headache, decreased lymphocyte percentage, and injection site reactions.

Please see single 5-g vial full Prescribing Information.

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