Empiric Management of Cyanide Toxicity Associated with Smoke Inhalation

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Abstract

Enclosed-space smoke inhalation is the fifth most common cause of all unintentional injury deaths in the United States. Increasingly, cyanide has been recognized as a significant toxicant in many cases of smoke inhalation. However, it cannot be emergently verified. Failure to recognize the possibility of cyanide toxicity may result in inadequate treatment. Findings suggestive cyanide toxicity include: (1) a history of an enclosed-space fire scene in which smoke inhalation was likely; (2) the presence of oropharyngeal soot or carbonaceous expectorations; (3) any alteration of the level of consciousness, and particularly, otherwise inexplicable hypotension (systolic blood pressure ≤90 mmHg in adults). Prehospital studies have demonstrated the feasibility and safety of empiric treatment with hydroxocobalamin for patients with suspected smoke inhalation cyanide toxicity. Although United States Food and Drug Administration (FDA)-approved since 2006, the lack of efficacy data has stymied the routine use of this potentially lifesaving antidote. Based on a literature review and on-site observation of the Paris Fire Brigade, emergency management protocols to guide empiric and early hydroxocobalamin administration in smoke inhalation victims with high-risk presentations are proposed.

Introduction

Deaths from fires and burns are the fifth most common cause of all unintentional injury deaths in the United States. In 2006, US fire departments responded to 412,500 house fires that claimed the lives of a total of 2,580 persons and injured an additional 12,925.[1] Most of these fatalities are due to inhalation of smoke and toxic gases.[2]

Accurate description of the toxic threats associated with the enclosed-space smoke inhalation is difficult because the composition of the environment is quite complex. The amount of oxygen or other oxidizer available for combustion or pyrolysis, the nature and origin of the fuel sources, the fire temperature, the size and nature of the fire space, as well as the complex interplay of all of these factors create a highly variable and changing environment,

Abbreviations:
ABGs = Arterial blood gases
ACLS = Advanced cardiac life support
AED = Automatic external defibrillator
ALS = Advanced Life Support
BLS = Basic Life Support
BP = Blood Pressure
CN = Cyanide
CO = Carbon monoxide
CPR = Cardiopulmonary resuscitation
D5W = Five percent dextrose in water solution
FR = First Responders
GCS = Glasgow Coma Scale
HBO = Hyperbaric oxygen therapy
ICU = Intensive Care Unit

IV = Intravenous
LOC = Loss of consciousness
PEA = Pulseless electricity acitivity
PPE = Personal Protective Equipment
SBP = Systolic blood pressure
VF = Ventricular Fibrillation
VT = Ventricular Tachycardia

with the potential to release or generate a wide variety of toxic substances, including carbon monoxide and cyanide.[3–6]

The acute medical management of victims of smoke inhalation focuses primarily on airway management, oxygenation, and managing hemodynamic instability using intravenous volume support and vasopressor agents.[7] Although thermal injury, oxygen depletion, and carbon monoxide have been known to be significant causes of smoke inhalation injury and toxicity, recent studies have found that hydrogen cyanide and respiratory tract irritants such as hydrogen chloride are major toxicants.[8]

The prehospital and emergency department management of potential cyanide exposure in smoke inhalation victims has been problematic for several reasons. There is no readily available method to diagnose cyanide poisoning in smoke inhalation victims in the prehospital setting or in the emergency department. Once absorbed, cyanide rapidly disappears from the blood, with a half-life of one to three hours, and terminal elimination is estimated at 44 hours, making it difficult to accurately measure peak cyanide concentrations. Also, as it takes several days to confirm levels, treatment must be based on clinical suspicion alone. The literature describing the incidence of cyanide exposure due to smoke inhalation, as well as co-toxicity with carbon monoxide also is conflicting. Cadaver-based studies have suggested that cyanide is variably present in post-mortem studies of victims of smoke inhalation.[9–10] Other studies of fire victims have shown that elevated cyanide levels are common in those with smoke inhalation and in some instances, may be the primary toxicant.[11–12] There also is conflicting evidence about a correlation between carboxyhemoglobin levels (or carbon monoxide concentrations) and cyanide concentrations. In a prospective study of 18 deaths from building fires, Linquist *et al* found that 17 of 18 cases had detectable cyanide levels, although only nine were considered toxic. Sixteen of 18 victims had blood carboxyhemoglobin concentrations >20%. However, there was no correlation between carboxyhemoglobin and cyanide levels.[13] Likewise, an analysis of 364 fire deaths found only a weak correlation between carboxyhemoglobin and cyanide levels.[14] Collectively, these studies show that while cyanide exposure in smoke inhalation is common (ranging from 78–100% of cases), and carbon monoxide poisoning may be concomitant, carboxyhemoglobin levels cannot be used to predict cyanide toxicity.

The mechanism of cyanide toxicity has been long known: cyanide induces oxidative cell death by binding to cytochrome oxidase and arresting cellular respiration. The organs most vulnerable to cyanide poisoning are those most dependent on high levels of oxygen delivery, including the brain, heart, and lungs. This manifests clinically as hyperventilation, headache, confusion, cardiac dysrhythmias; severe toxicity results in cardiovascular collapse and obtundation. Acidosis ensues as oxygen no longer is available to bind with hydrogen to form water.[15]

Accordingly, plasma lactate levels ≥10 mmol/L in smoke inhalation victims correlate with the presence of a significant cyanide poisoning component.[16–18] A small series of acute cyanide poisonings excluding smoke inhalation demonstrated that a plasma lactate concentration of >8 mmol/L was associated with a sensitivity of 94%, a specificity of 70%, a positive predictive value of 98% and a negative predictive value of 98%, for cyanide blood concentrations greater than ≥1.0 mg/L.[19] In contrast, in a study of pure carbon monoxide poisoning of varying severity in 183 patients, Benaissa *et al* showed that while lactate levels did correlate with carboxyhemoglobin levels, there only were mild increases in plasma lactate concentrations (median 2.3 mmol/L) even in victims with severe neurological impairment (coma or transient loss of consciousness (LOC)) and blood carbon monoxide concentrations usually considered toxic.[20]

Although confirming cyanide exposure from fire smoke is difficult, serious cyanide toxicity may be more common than initially appreciated. In March 2006, an unusual cluster of cyanide poisonings in firefighters was reported. While working a fire at a fast food restaurant, a firefighter began complaining of headache, dizziness, difficulty breathing, and cough, and began to speak incoherently. He was transported to a hospital, and subsequently found to have a whole blood cyanide level of 57 ug/dl (≥20 ug/dl toxic).[21] The following day, another firefighter suffered a heart attack and collapsed at the scene of a working fire. His whole blood cyanide level was 66 mg/dl. Based on these two incidents, 28 other firefighters who were involved in three industrial and residential fires were tested for whole blood cyanide levels. Eight demonstrated toxic (≥20 ug/dl) whole blood cyanide levels.

Once cyanide toxicity from smoke inhalation is suspected, prompt administration of antidotes are recommended. Historically, commonly used antidotes include 4-dimethylaminophenol (4-DMAP), and amyl or sodium nitrite which function as methemoglobin inducers. Methemoglobin reverses the cyanide inhibition of cytochrome oxidase activity by complexing with cyanide to form cyanmethemoglobin. (Cyanide has a greater affinity for binding with methemoglobin and thus, is displaced from cytochrome oxidase). When combined with the sulfur donor, sodium thiosulfate, cyanide is released from cyanmethemoglobin, forming the non-toxic compound thiocyanate, and is excreted in the urine.[22] However, the induction of non-oxygen transporting methemoglobin in victims of smoke inhalation who often have concomitant carbon monoxide poisoning, is less than desirable, as they already have decreased oxygen transport from formation of carboxyhemoglobin. Fatalities due to hypoxia from over-production of methemoglobinemia have been reported with the use of sodium or amyl nitrite. In addition, if sodium nitrite is administered too rapidly intravenously, it acts as a potent vasodilator resulting in hypotension, which can lead to serious adverse outcomes and further compromise the hemodynamic status in subjects already hypotensive due to cyanide toxicity.[16] On its own, sodium thiosulfate has the potential use for treatment of cyanide poisoning in smoke inhalation, but contradictory conclusions about efficacy in animal models and concerns about a slow onset of action in humans have limited any recommendations for empiric use.[23]

Hyperbaric oxygen therapy (HBO) occasionally has been administered to patients with severe cyanide poisoning, and anecdotal results indicate that it may be efficacious.[16] However, transporting an unstable patient for the sole purpose of HBO therapy generally is considered to be unwarranted, as long as 100% normobaric oxygen can be provided at the initial treatment hospital. The role of hyperbaric oxygen for the management of carbon monoxide poisoning in smoke inhalation continues to evolve with conflicting conclusions. The American College of Emergency Medicine clinical policy on hyperbaric oxygen for acute carbon monoxide poisoning is given a Level C recommendation.[24] Likewise, the Cochrane Review concluded that there was no evidence to support hyperbaric oxygen for treatment of patients with carbon monoxide poisoning.[25]

Hydroxocobalamin (vitamin B12a) is a cyanide antidote that detoxifies cyanide by binding with it and forming

cyanocobalamin, which is then excreted in the urine. It has been used in France for pre-hospital and emergency in-hospital treatment of suspected cyanide poisoning from smoke inhalation since the 1980s.[26–27] In the retrospective review by Fortin *et al*, patients treated with hydroxocobalamin had improvement or reversal of neurologic compromise, and restoration of hemodynamic parameters with average systolic blood pressure rising 15 mmHg and diastolic rising 10 mmHg within 30 minutes of infusion. However, despite an initial favorable return of spontaneous circulation, a majority of patients who presented in shock later died due to multiorgan failure or sepsis.[26] In a prospective, empiric treatment trial by Borron *et al*, survival was 67% in patients subsequently proven to have had toxic cyanide levels (>39mmol/L), with no serious adverse side effects. Minor adverse effects included transient chromaturia, alterations in renal function, reddish skin discoloration, hypertension, and rarely allergic reactions.[27] Results of normal human volunteer safety studies suggest that the safety profile of hydroxocobalamin is favorable for prehospital or emergency department use in smoke inhalation victims with cyanide toxicity.[28–30]

Methods
The objective of this study was to review published and recently presented studies on the empiric prehospital and emergency department treatment of suspected cyanide poisoning in smoke inhalation victims and to develop treatment protocols for clinical use in the US.

It was hypothesized that although hydroxocobalamin is FDA-approved for use, the lack of familiarity or use in prehospital settings, coupled with scant outcomes data, demanded a critical analysis and on-site observation in order to reach a consensus on when to use it empirically. All of the authors previously have participated in meetings of the Cyanokit® Advisory Board and/or Speakers' Bureau for the two previous US Distributors, EMD Pharmaceuticals, Inc. and Dey, LP. In addition, two of the authors (DW, AH) participated in a fact-finding group that traveled to Paris for meetings with the Brigade de Sapeurs-Pompiers de Paris (Paris Fire Brigade), including spending time accompanying mobile intensive care unit (ICU) personnel during prehospital care of patients.

Results
Based on the analysis of the literature, as well as the French experience with the use of specific antidotes for smoke inhalation toxicity, and the fact-finding visit to the Brigade de Sapeurs-Pompiers de Paris (Paris Fire Brigade), the authors developed prehospital and emergency department protocols for the treatment of victims with enclosed-space fire smoke inhalation, based on the presenting signs and symptoms and patient history, such that the relative risks of significant cyanide exposure and toxicity may be identified (Figure 1; please see online supplemental material). Treatment protocols emphasize injury severity and patient selection in order to optimize outcomes and reduce potential treatment side effects.

Recommended Treatment for Mild Smoke Inhalation
Victims extricated from an enclosed-space fire who present awake and normotensive or hypertensive with non-specific symptoms that include confusion, tachypnea, headache, dyspnea, nausea, and/or vomiting with the presence of soot around the mouth or nose may have symptoms of smoke inhalation, but may not warrant empiric antidotal treatment for cyanide toxicity. These patients should be managed with basic and advanced life support measures as necessary, to include high-flow oxygen, monitoring for progressive airway compromise, evaluation for associated trauma-related conditions, and transportation to definitive emergency department and hospital care. When possible, it is recommended that a blood sample for carboxyhemoglobin (or carbon monoxide concentration), as well as a plasma lactate levels be obtained.

Recommended Treatment for Moderate Smoke Inhalation
Victims of smoke inhalation who present mildly obtunded (Glasgow Coma Scale [GCS] score >8) with similar signs and symptoms as described for mild smoke inhalation, with the presence of soot around the mouth or nose and carbonaceous expectorations may have more significant toxicant exposure, but may not yet warrant empiric antidote treatment for cyanide poisoning in the field. However, at any sign of neurological or cardiovascular deterioration (e.g., dropping blood pressure or increased confusion) hydroxocobalamin should be administered empirically by trained personnel. It also is recommended to obtain blood samples for the measurement of cyanide and plasma lactate levels. Upon arrival to the emergency department, reassessment for empiric treatment or administration of a repeat dose of hydroxocobalamin will depend on the victim's cardiovascular and neurological status or the presence of acidosis.

Recommended Treatment for Severe Smoke Inhalation
Victims of smoke inhalation who present severely obtunded (GCS score <8) with mydriasis, seizures, hypotension or cardiovascular collapse, or with non-cardiogenic pulmonary edema, and with the presence of soot around the mouth or nose or in the larynx and carbonaceous expectorations following extrication from an enclosed-space fire scene warrant empiric treatment for cyanide poisoning. Patients should be managed with basic and advanced life support measures to include high flow oxygen, monitoring for progressive airway compromise, evaluation for associated trauma-related conditions, and transportation for definitive emergency department or hospital care. Prehospital treatment should include 100% oxygen by mask or endotracheal tube as necessary, especially when carbon monoxide poisoning is suspected. Due to the red color of hydroxocobalamin, modest interference with colorimetrically determined laboratory tests may occur; therefore, it is recommended that blood specimens be collected before the antidote is infused.[31–32]

Hydroxocobalamin is administered intravenously in adults at a dose of 5 grams in 200 mL solution, at 15 mL/minute.[33] Faster administration rates have sometimes been used for patients with severe cyanide poisoning. If the clinical response to the initial 5 gram dose is incomplete, a second dose of 5 grams may be administered in the same manner up to a maximum of 15 grams for adults. While pediatric doses have not been established, a dose of 70 mg/kg has been recommended based on a small number of pediatric clinical cases and extrapolation from adult doses and animal studies.[34–36]

Recommended Treatment for Smoke Inhalation with Cardiac Arrest
Victims of enclosed-space fire smoke inhalation who present in pulseless-apneic arrest represent the most critical subset of this patient population. It is reasonable to establish an airway

and to provide oxygenation. Standard advanced cardiac life support (ACLS) drugs should be administered as indicated.

Although data do exist on the administration of hydroxocobalamin to patients in cardiopulmonary arrest and do suggest some efficacy, data are limited.[26] However, given the generally favorable risk:benefit of hydroxocobalamin, it should be administered as described above. It must be remembered that confirmed brain-dead cyanide poisoning victims have been successful organ donors.[37–38]

Hydroxocobalamin Administration Instuctions (Package Insert, 2006)[33]
The Cyanokit® contains two clear glass 250 mL vials, each containing 2.5 grams of lyophilized hydroxycobalamin (a dark red crystalline powder) plus two sterile transfer spikes, one sterile intravenous (IV) infusion set, one quick infusion guide, and one package insert. A diluent such as 0.9% sodium chloride (normal saline), is not provided in the Cyanokit®. If normal saline is not available, D5W or Ringer's Lactate solutions may be used. Each hydroxocobalamin vial has a line demarcating the level for 100 mL of diluent. The transfer spike is used to transfer 100 mL of diluent from a small IV bag to the 2.5 gram hydroxocobalamin vial. Once reconstituted by at least 30 seconds of gentle inversion, swirling, or rocking, hydroxocobalamin solution is ready to be infused. Caution is advised to avoid shaking the vials, as bubbles may form rendering the antidote unsuitable for IV administration.

Conclusions
Smoke inhalation occurs when partially burned or pyrolized products of combustion are breathed during a fire, producing a myriad of inhaled toxicants. Although the exact composition of fire smoke cannot be predicted, a significant cyanide poisoning component from enclosed-space fires is becoming increasingly recognized as contributing to morbidity and mortality in these patients. Generally, there are no available laboratory methods to emergently confirm the presence of cyanide poisoning in this setting. Prehospital and emergency department personnel must suspect the diagnosis of a cyanide poisoning component in smoke inhalation victims by awareness that the enclosed smoke-fire environment may contain cyanide gas, and by knowledge of the signs and symptoms most suggestive of cyanide poisoning.

The decision of whether or not to administer a specific cyanide antidote must be made on clinical grounds. Elevated plasma lactate levels (≥ 10 mmol/L) are correlated with the possibility of a cyanide poisoning component. While it may take days to confirm toxic serum cyanide levels, obtaining them pre-treatment will help clarify the diagnosis and add to our understanding of the incidence of cyanide poisoning from enclosed space fire smoke inhalation.

In the US, there are two available cyanide antidotes: Kits containing the combination of amyl nitrite or sodium nitrite with sodium thiosulfate (not FDA-approved), and hydroxocobalamin.

The available literature suggests that only hydroxocobalamin is proven to be safe for cyanide poisoning due to smoke inhalation. Specifically, unlike the nitrate based antidotes, hydroxocobalamin does not induce methemoglobin, and does not compromise oxygen delivery. Also, the transient hypertension caused by hydroxocobalamin through induction of nitric oxide [39–40] may be advantageous for patients suffering the ill effects of hypotension due to cyanide toxicity. Accordingly, hydroxocobalamin was approved as an orphan drug by the FDA in 2006 for use in "proven" or "suspected" cyanide toxicity under the Animal Efficacy rule, which allows for drug approval based on effectiveness in animals when adequate human clinical trials cannot be conducted for ethical reasons [41.] Additionally, there are more published data regarding potential efficacy for hydroxocobalamin than for the other antidotes.[26–30,42]

Despite the safety and feasibility of administration of hydroxocobalamin demonstrated in the French studies, the lack of controlled efficacy data for the empiric use of hydroxycobalamin in smoke inhalation victims has led some to suggest that such administration may be unwarranted,[43] or at least not indicated for all victims of enclosed-space fire smoke inhalation.[44] Opponents to empiric use suggest cautiously considering use only for patients who are comatose, or *in extremis*, rationalizing that treatment risks will be outweighed by potential benefit in these patients. However, any antidote might be predictably less efficacious when given late in the clinical course, as the downstream effects of hypoxia and tissue necrosis causing liberation of endotoxin and inflammatory cytokines may result in irreversible injury.

Therefore, the empiric use of hydroxocobalamin in victims of enclosed space smoke inhalation and suspected cyanide toxicity, with signs and symptoms of neurologic or cardiovascular deterioration is advised (Figure 2). It is most predictable that benefit from hydroxocobalamin will be achieved if given as *early* as possible, especially to patients who are not moribund. Any hesitation in the empiric use may have the unintended consequence of missed opportunity to save additional lives. Although randomized controlled trials of empiric use will remain very challenging, efficacy can be extrapolated from additional well-designed prospective, observational studies: such trials would emphasize severity of presentation, presence of acidosis, and verification of cyanide levels, in addition to treatment response with outcomes compared to historical controls or control patients who do not receive the antidote. Until such studies are available, absent any immediate means to objectively determine and document the presence of cyanide toxicity in smoke inhalation victims, it appears justifiable to administer hydroxocobalamin empirically to subjects with a high likelihood of cyanide poisoning. Coordination of academic medical centers and on-scene emergency care providers is essential for effective prehospital management of smoke inhalation victims. Consensus opinion derived treatment protocols should serve to guide the empiric use of hydroxocobalamin.

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Figure 1—Suggested management protocol

Fire Smoke Inhalation—(Mild)
Carbon monoxide (CO), cyanide (CN⁻) and other toxicants which can be part of fire smoke exposure are associated with significant morbidity and mortality in severe fire smoke inhalation exposures. Definitive diagnosis is not possible in the pre-hospital or emergency department environment. All symptomatic patients should be treated for CO intoxication. Patients should be monitored for development of severe neurological impairment or cardiovascular collapse that may suggest CN⁻ poisoning.

SIGNS:
- Confusion
- GCS = 15
- Tachypnea/Hyperpnea
- Normotension/Hypertension
- Vomiting

SYMPTOMS:
- Headache
- Dyspnea
- Chest Tightness
- Nausea

SCENE SIZE-UP:
- Protect yourself from the toxic environment and use personal protective equipment (PPE)
- Remove the patient from the toxic environment
- **Indication assessment for antidotal therapy:**
  - Was this an enclosed-space fire smoke inhalation exposure?
  - Is there soot in the victim's Presence of soot in the nose, mouth, or larynx or are there carbonaceous expectorations?

BASIC LIFE SUPPORT (BLS) AND FIRST RESPONDER (FR) ORDERS:
- Administer high-flow, 100% oxygen by non-rebreather mask for inhalation injury or any serious burn. Consider the possibility of carbon monoxide poisoning or other toxic inhalation exposure. Note that pulse oximeter oxygen saturations may be falsely elevated.
- For related trauma:
  - Follow Trauma and Burn Management Protocols
- Consider ALS intercept.

ADVANCED LIFE SUPPORT (ALS) ORDERS:
- Airway management as appropriate and trained
  - Be alert for signs of inhalation injury (i.e., stridor, muffled voice, singed facial/nasal hairs, soot in the nose, mouth, throat or larynx, carbonaceous expectorations, extrication for an enclosed space fire scene with potential smoke inhalation.
- Establish a patent intravenous line
- If possible, collect 5–7 mL of venous blood in each of a gray and lavender-top tube and place in an ice pack for whole blood cyanide and plasma lactate levels to be measured in the hospital.
- Initiate cardiac monitoring
- If patient deteriorates, follow Severe Smoke Inhalation protocol.

EMERGENCY DEPARTMENT MANAGEMENT:
- Determine carboxyhemoglobin or carbon monoxide levels
- Determine Plasma Lactate Levels (Plasma Lactate levels >/= 10 mmol/L strongly suggest a significant cyanide poisoning component).
- Determine whole blood cyanide levels for confirmation of a significant cyanide poisoning component.
- Failure to respond to conservative management or evidence of progressive neurological or cardiovascular deterioration may warrant empiric treatment with hydroxocobalamin

Fire Smoke Inhalation (Moderate)
Carbon monoxide (CO), cyanide (CN⁻) and other toxicants which can be part of fire smoke exposure are associated with significant morbidity and mortality in severe fire smoke inhalation exposures. Definitive diagnosis is not possible in the pre-hospital or emergency department environment. All symptomatic patients should be treated for CO intoxication. Patients should be monitored for development of severe neurological impairment or cardiovascular collapse that may suggest CN⁻ poisoning.

SIGNS:
- Confusion
- Disorientation
- GCS > 8
- Tachypnea/Hyperpnea
- Normotension/Hypertension
- Vomiting

SYMPTOMS:
- Headache
- Dyspnea
- Chest Tightness
- Nausea

SCENE SIZE-UP:
- Protect yourself from the toxic environment and use personal protective equipment (PPE)
- Remove patient from the toxic environment
- **Indication assessment for antidotal therapy:**
  - Was this an enclosed-space fire smoke inhalation exposure?
  - Is there soot in the victim's Presence of soot in the nose, mouth, or larynx or are there carbonaceous expectorations?

BASIC LIFE SUPPORT (BLS) AND FIRST RESPONDER (FR) ORDERS:
- Administer high-flow 100% concentration oxygen by non-rebreather mask for potential inhalation injury or any serious burn. Consider the possibility of carbon monoxide or other toxic inhalation. Pulse oximeter oxygen saturation readings may be falsely elevated.
- *For Associated Trauma:*
  - Follow Trauma and Burn Management Protocols
- Consider ALS intercept

ADVANCED LIFE SUPPORT (ALS) ORDERS:
- Airway management as appropriate and trained
  - Be alert for signs of inhalation injury (i.e., stridor, muffled voice, singed facial/nasal hairs, soot in the nose, mouth, throat or larynx, carbonaceous expectorations, extrication for an enclosed space fire scene with potential smoke inhalation.
- Establish a patent intravenous line
- If possible, collect 5–7 mL of venous blood in each of a gray and lavender-top tube and place in an ice pack for whole blood cyanide and plasma lactate levels to be measured in the hospital.
- Initiate cardiac monitoring
- If patient deteriorates, follow Severe Smoke Inhalation protocol.

EMERGENCY DEPARTMENT MANAGEMENT:
- Determine carboxyhemoglobin or carbon monoxide levels
- Determine Plasma Lactate Levels (Plasma Lactate levels >/= 10 mmol/L strongly suggest a significant cyanide poisoning component).
- Determine whole blood cyanide levels for confirmation of a significant cyanide poisoning component.
- Determine Arterial Blood Gases (ABGs).
- Failure of the patient to respond to conservative management or evidence of progressive neurological or cardiovascular deterioration may warrant empiric treatment with hydroxocobalamin

**Fire Smoke Inhalation (Severe*)*
Carbon monoxide (CO), cyanide (CN^-) and other toxicants which can be part of fire smoke exposure are associated with significant morbidity and mortality in severe fire smoke inhalation exposures. Definitive diagnosis is not possible in the pre-hospital or emergency department environment. All symptomatic patients should be treated for CO intoxication. Patients with severe neurological impairment and/or extremis should be given hydroxocobalamin empirically, as soon as a patent intravenous line is established.

SIGNS:
- Seizures or Coma
- GCS < 8
- Mydriasis
- Vomiting
- Hypotension (Systolic BP < 90 mmHg in adults)
- Cardiovascular Collapse

SYMPTOMS:
- Extreme Confusion
- Dyspnea
- Nausea

SCENE SIZE-UP:
- Protect yourself from the toxic environment and use personal protective equipment (PPE)
- Remove patient from the toxic environment
- **Indication assessment for antidotal therapy:**
  - Was this an enclosed-space fire smoke inhalation exposure?
  - Is there soot in the victim's Presence of soot in the nose, mouth, or larynx or are there carbonaceous expectorations?

BASIC LIFE SUPPORT (BLS) AND FIRST RESPONDER (FR) ORDERS:
- Administer high-flow 100% concentration oxygen by non-rebreather mask for potential inhalation injury or any serious burn. Consider the possibility of carbon monoxide or other toxic inhalation. Pulse oximeter oxygen saturation readings may be falsely elevated.
- *For Associated Trauma:*
  - Follow Trauma and Burn Management Protocols
- Consider ALS intercept

ADVANCED LIFE SUPPORT (ALS) ORDERS:
- Airway management as appropriate and trained
  - Be alert for signs of inhalation injury (i.e., stridor, muffled voice, singed facial/nasal hairs, soot in the nose, mouth, throat or larynx, carbonaceous expectorations, extrication for an enclosed space fire scene with potential smoke inhalation.
- Establish two patent intravenous lines
- If possible, collect 5-7 mL of venous blood in each of a gray and lavender-top tube and place in an ice pack for whole blood cyanide and plasma lactate levels to be measured in the hospital.
- Initiate cardiac monitoring. Treat cardiac dysrhythmias with standard ACLS protocols or established directives.
- Administer Hydroxocobalamin 5-grams IV infusion per protocol. If the clinical response in insufficient, consider a second 5-gram hydroxocobalamin infusion.
- Treat shock – consider volume replacement and vasopressors.

Fire Smoke Inhalation – Cardiac Arrest

SIGNS AND SYMPTOMS:
- Pulseless Cardiopulmonary Arrest

SCENE SIZE-UP:
- Protect yourself from the toxic environment and use personal protective equipment (PPE)
- Remove patient from the toxic environment
- **Indication assessment for antidotal therapy:**
  - Was this an enclosed-space fire smoke inhalation exposure?
  - Is there soot in the victim's Presence of soot in the nose, mouth, or larynx or are there carbonaceous expectorations?

BASIC LIFE SUPPORT (BLS) AND FIRST RESPONDER (FR) ORDERS:
- Routine Patient Care – with focus on CPR
- Apply and use AED if available and indicated.
- *For Associated Trauma:*
  - Minimize on-scene time
- Consider ALS intercept.

ADVANCED LIFE SUPPORT (ALS) ORDERS:
- Follow Cardiac Arrest Protocol
- Document presenting cardiac rhythm in two (2) separate leads if possible.
- Consider the presence of treatable toxicants (such as CO and CN^-)
- If two IV lines are established, use one for administration of standard ACLS medications and the second to begin IV infusion of hydroxocobalamin 5-grams as described above. A second dose of 5-grams may be administered IV if there is an inadequate clinical response.
- Airway management as appropriate and trained.

- *For Ventricular Fibrillation (VF)/Pulseless Ventricular Tachycardia (VT):*
  - CPR for 5 cycles/2 minutes; then defibrillation (use 360 joules for monophasic and 120-200 joules for biphasic defibrillators); then CPR for 5 cycles/2 minutes; then rhythm check, then:
  - Epinephrine (1:10,000) 1 mg IV; repeat every 3–5 minutes.
  - Continue CPR for 5 cycles/2 minutes between interventions; stop only for defibrillation, rhythm check, or return of circulation.
- *For Asystole or Pulseless Electrical Activity (PEA):*
  - Continue CPR for 5 cycles/2 minutes.
  - Epinephrine (1:10,000) 1 mg IV; repeat every 3-5 minutes.
  - Atropine 1 mg IV for asystole or slow PEA; repeat every 3–5 minutes up to 3 doses.
  - Continue CPR for 5 cycles/2 minutes between interventions; stop only for rhythm check or return of circulation.
  - Advanced airway management.

	Mild Smoke Inhalation	Moderate Smoke Inhalation	Severe Smoke Inhalation
Patient Status (Key Signs and Symptoms)	• GSC = 15 • Respiratory Difficulty • Mild Confusion • Normotensive	• GSC > 8 • Tachypnea • Moderate Confusion • Normotensive	• GSC < 8 • ↑ Tachypnea, dyspnea • Mydriasis, severe • Confusion/obtunded • Hypotension (SBP,90mm HG) Cardiovascular collapse
Scene size-up	• Protect yourself from the toxic evironment • Use appropriate personal protective equipment • Remove patient from toxic environment Indication assessment for supportive or antidotal therapy: • Was this enclosed-space 'fire' smoke inhalation? • Is there soot in the patient's nose, mouth, larynx, or are there carbonaceous expectations?	SAME	SAME
BLS and First Responder Orders:	• Administer 100% oxygen by non-rebreather mask (Pulse oximetry may be falsely elevated) • Follow trauma and burn management protocols • Consider ALS Intercept	SAME	SAME
Advanced Life Support Orders:	• Advanced Airway Management as Indicated • Establish Intravenous Line • If possible, collect 5-7 ml venous blood in each a gray and lavender top tube/place in ice pack for whole blood cyanide and plasma lactate levels.	PLUS: • Initiate Cardiac Monitoring • **Consider empiric hydroxocobalamin for neurologic or cardiovascular deterioration.**	PLUS: • Establish second intravenous line for volume support. • Administer hydroxocobalamin per protocol
Emergency Department Management	• Determine carboxyhemoglobin or CO level • Determine plasma lactate levels (levels ≥ 10 mmol/L) strongly suggests cyanide poisoning component • Send out for whole blood cyanide levels • **Consider empiric hydroxocobalamin for neurologic or cardiovascular deterioration**	PLUS: • Obtain ABG • **Administer or repeat dose of hydroxocobalamin as indicated.**	PLUS: • **Repeat dose of hydroxocobalamin as indicated.** • Continue with management and treatment of injuries.

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Figure 2—Smoke inhalation treatment protocol