Cyanide and Modern Fires:

Scientific and Practical Fundamentals for Fire Professionals

Cyanide, a Ubiquitous Product of Combustion in Modern Fires

Where There's Fire, There's Smoke!

Smoke and Fire: Recognizing Cyanide as a Toxic Agent

EMD

Cyanide and Modern Fires:

Scientific and Practical Fundamentals for Fire Professionals

TABLE OF CONTENTS

One Team Together
Improving Capabilities In Emergency Response

The risk of acute cyanide poisoning related to smoke inhalation in structural fires or as a potential chemical terrorism weapon is underappreciated by most emergency response and emergency medicine professionals. This is due in large part to the fact that current treatment options have limitations.

EMD Pharmaceuticals, Inc., the North American Affiliate of Merck KGaA of Darmstadt, Germany, is developing a cyanide antidote in the United States. For more information on the use of cyanide antidotes in response to industrial accidents, smoke inhalation, or potential terrorist activities, please contact one of the following:

In North America:
Elizabeth Field, PhD, Senior Director, Medical Communications
EMD Pharmaceuticals, Inc.
3211 Shannon Road, Suite 500
Durham, NC 27707
Tel: 919-401-7238 Fax: 919-401-7180
Email: elizabeth.field@emdpharmaceuticals.com

In Europe:
Emmanuel Eumont, Senior Global Operations Manager
Global Special Projects
Merck S.A. – France
37, rue Saint-Romain
Lyon Cedex 08 – F 69379
Tel: 33-(0)-472-78-2813 Fax: 33-(0)-472-78-0939
Email: emmanuel.eumont@merck.fr

EMD

Cyanide and Modern Fires:

Scientific and Practical Fundamentals for Fire Professionals

Fire professionals know that hydrogen cyanide is among the most rapidly acting and lethal of poisons, but they may not be aware that the most common cause of acute cyanide poisoning is fire smoke.

The contribution of hydrogen cyanide to smoke inhalation–associated injury and death has historically been overshadowed by a focus on carbon monoxide, another important toxicant in fire smoke. However, the role of cyanide is becoming better understood every day as the body of evidence establishing its pervasiveness as a combustion product and its toxicity in the fire setting has grown. The evidence demonstrates that hydrogen cyanide is an important contributor to the up to 10,000 deaths per year attributed to smoke inhalation in the United States. To improve the survival of fire victims, it is imperative that the contribution of cyanide to injury and death associated with smoke inhalation no longer go unnoticed.

Fire professionals are often the first to encounter and to administer to victims of cyanide poisoning associated with smoke inhalation. In many cases, whether victims of smoke inhalation live or die depends largely on the fire professional's knowledge and skills. This supplement, a collaborative effort of experts in prehospital emergency medicine, public health and safety, and disaster preparedness, discusses scientific data and practical information on cyanide in modern fires. In three articles, the supplement addresses the basic questions about cyanide and fire smoke:

- How common is cyanide as a combustion product in modern fires?

- What are the sources of cyanide released during combustion?

- How does cyanide cause injury and death in smoke-inhalation victims?

- How does the role of cyanide compare with that of carbon monoxide in smoke inhalation–associated morbidity and mortality?

- How is smoke inhalation–associated cyanide poisoning managed in the prehospital setting?

- What are the unmet needs in management of smoke inhalation–associated cyanide poisoning?

- What is on the horizon for improving the prehospital care of victims of smoke inhalation–associated cyanide poisoning?

Armed with answers to these questions, fire professionals will be well equipped to help reduce death and injury from cyanide poisoning and to protect themselves from being overcome by cyanide in the fire setting. ◆

Cyanide

A UBIQUITOUS PRODUCT OF COMBUSTION IN MODERN FIRES

Donald W. Walsh, PhD, EMT-P
International Emergency Medicine Disaster Specialists
Chicago Fire Department
Chicago, Illinois

Tragedy in West Warwick: The Rhode Island Nightclub Fire

Approximately 440 people were in The Station nightclub in West Warwick, Rhode Island, that Friday night in February 2003 when a fire broke out in the single-story, wood-frame building.[1] The fire started just after 11 PM, when pyrotechnics used by Great White, the band performing that night, ignited polyurethane foam lining the walls of the stage area. The blaze quickly spread to the ceiling and then ignited the wood paneling on its way to becoming a full-blown structural fire.

The band and the nightclub patrons first recognized the fire hazard approximately half a minute after ignition of the foam and nearly immediately thereafter began to evacuate the nightclub—primarily through the main entrance at the front of the building.

Figure 1 shows the timeline of the Rhode Island Nightclub Fire and of the emergency response, which was rapid and well executed.[1] In response to 911 calls made approximately 35 seconds and 1 minute after the fire ignited, four engine companies, a tower-ladder truck, a rescue unit, and a battalion chief were dispatched to the scene. Engine 4, the first responding unit, arrived at the scene less than 5 minutes after the initial 911 call and began applying water to the fire with a booster hand line approximately 1 minute thereafter. Ambulance units and additional engine/ladder companies were dispatched, and a mass casualty plan was implemented within 10 minutes of the arrival of Engine 4 on the scene. A triage area was established in the nightclub parking lot and inside the nearby Cowesett Inn. By 12 to 16 minutes after ignition, two engines were applying water from master streams, and these efforts were supplemented by at least three hose lines within 20 minutes of ignition. Rhode Island Governor Don Carcieri estimated that fire and rescue crews saved as many as 100 lives by pulling people from the burning building.[2]

Despite the rapid and capable emergency response, which is credited with saving many lives, 100 people perished in the fire, and scores of others were seriously injured. Why was the number of fatalities so high in this disaster, and why did many of the occupants perish so quickly? The US Department of Commerce's the spread of fire and smoke through the nightclub.[1,3] The experiments were conducted in a test room having dimensions and containing materials similar to those of the nightclub on the night of the fire. The fire simulation

Figure 1. Timeline of the Rhode Island Nightclub Fire and emergency response to it.[1]

National Institute of Standards and Technology (NIST), which is responsible for investigating building-related failures leading to substantial loss of life, was deployed on a fact-finding mission to answer these questions and to recommend improvements for future fire disasters.

As part of its efforts, the NIST conducted experiments to simulate experiments measured temperature as well as concentrations of various combustion gases in both sprinklered and un-sprinklered conditions. The un-sprinklered condition reproduced that of The Station nightclub, which did not have a sprinkler system. Building code did not require The Station to have a sprinkler system given the size of the nightclub (footprint of approximately 4500 square feet) and the date it was built. Given the similarity of the test conditions to conditions on the night of the fire, it is likely that the ex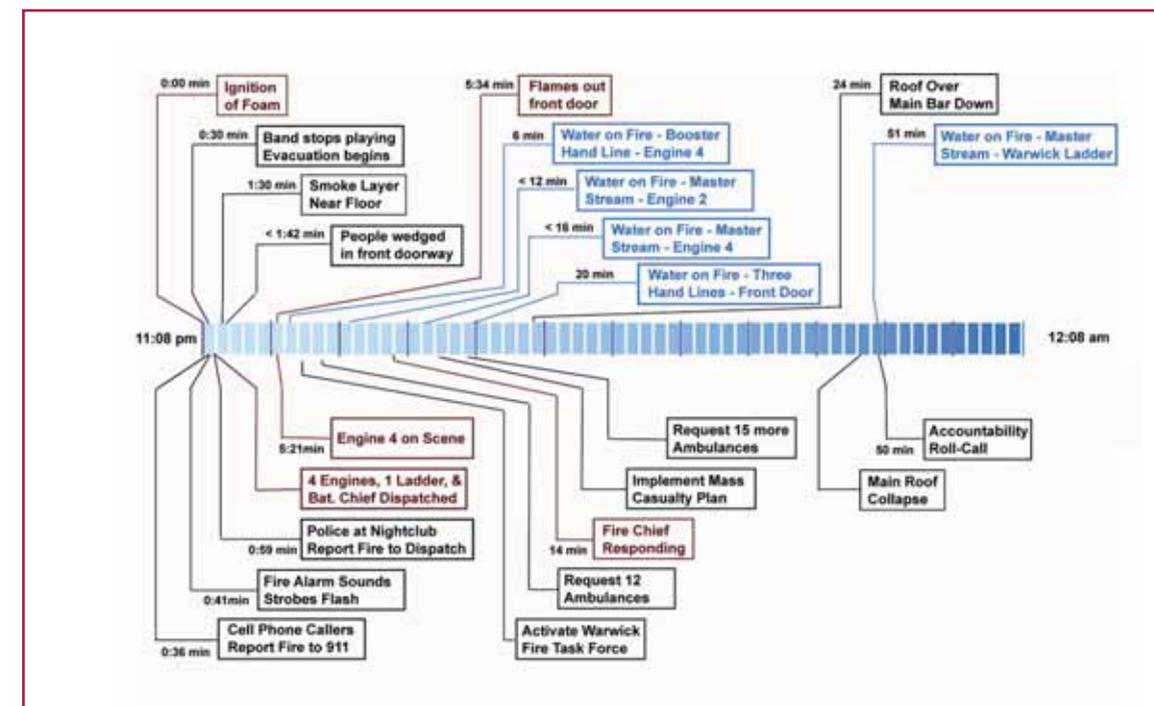perimental observations closely reflect what happened on the night of the fire. However, the simulations do not allow definitive conclusions about the actual fire because of the inability to replicate exactly the nightclub conditions.

The results of the simulations under un-sprinklered conditions dramatically demonstrate how quickly conditions in the nightclub may have become deadly. Within seconds of ignition of the fire, concentrations of the toxic combustion products carbon monoxide and hydrogen cyanide soared and oxygen levels plummeted to create conditions incompatible with sustaining life (Figure 2).[3]

The striking differences in

"The high temperatures, low oxygen, high carbon monoxide, and high hydrogen cyanide levels within the test room in the absence of a sprinkler all contribute to a non-tenable condition . . . within 90 s after ignition."

National Institute of Standards and Technology report[3] on an experiment simulating the Rhode Island Nightclub Fire

temperature and in concentrations of oxygen, carbon monoxide, and hydrogen cyanide between the sprinklered condition and the un-sprinklered condition support the judgment of on-the-scene firefighters who contended that the lack of a sprinkler system cost many lives (Figure 2).[3] Whereas temperature and oxygen levels were maintained at nearly ambient levels from the floor to approximately 1.4 meters above floor level in the sprinklered

"If there were sprinklers in this building, we wouldn't be here right now."

Fire Chief Charlie Hall of the aftermath of the Rhode Island Nightclub Fire[2]

condition, flashover conditions occurred approximately 60 seconds after ignition in the un-sprinklered condition. These findings contributed to the NIST's primary recommendations that model codes require sprinkler systems for all new and existing nightclubs regardless of size and that state and local authorities adopt this provision.[1]

A ROLE OF CYANIDE IN SMOKE-INHALATION DEATH?

Results of the NIST experiments are consistent with the possibility that an elevated level of hydrogen cyanide was among the causes of incapacitation and death in the Rhode Island Nightclub Fire. Hydrogen cyanide is a highly toxic combustion product that is formed during combustion of any material containing nitrogen[4]— that is to say, during combustion of almost any material found or used in the construction of human dwellings. The possibility that cyanide contributed to morbidity and mortality in the Rhode Island Nightclub Fire was not considered by at least some of the
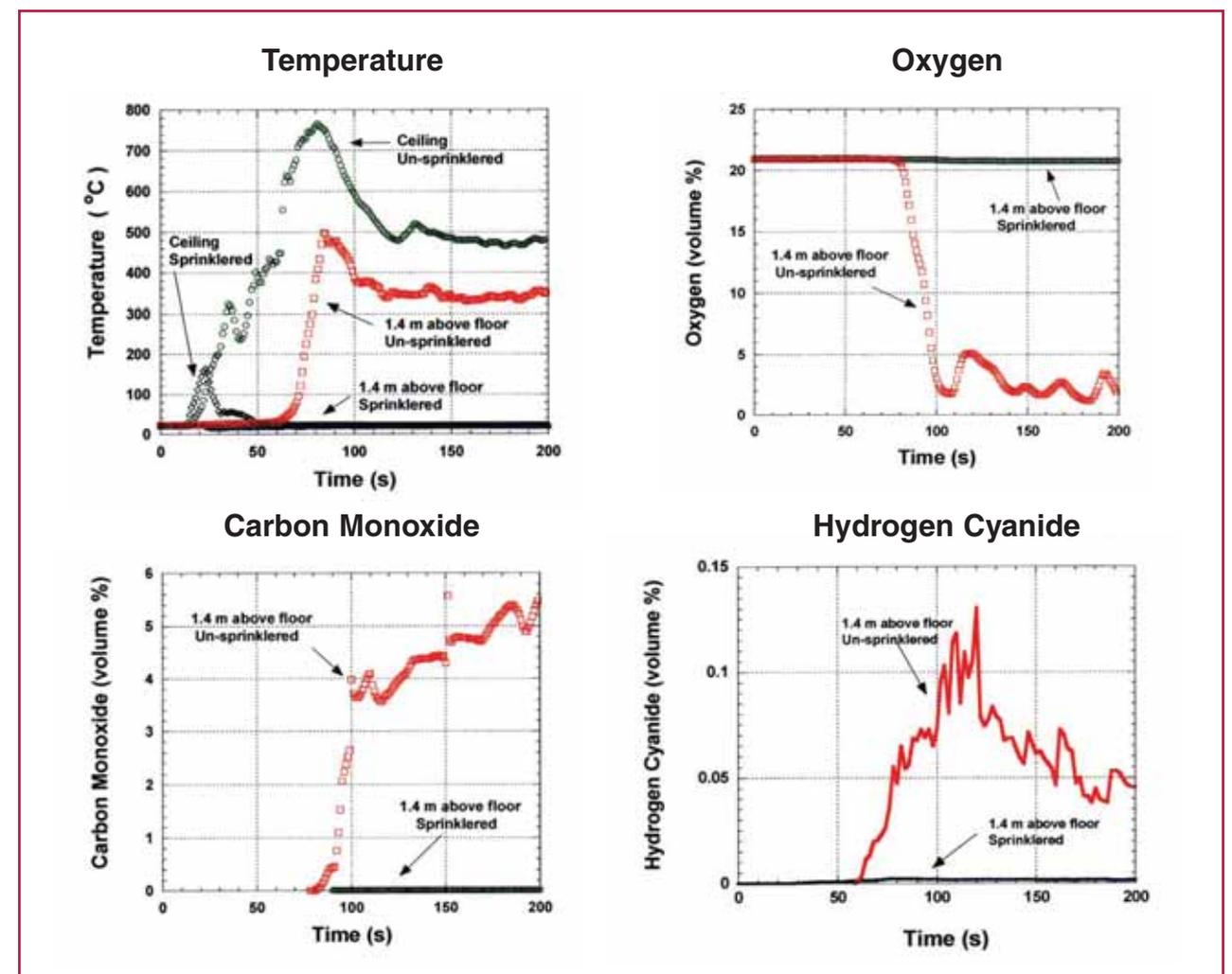
health care providers administering to fire victims as illustrated by a case report published in the *New England Journal of Medicine* in 2004.[5] The authors assessed and treated a woman severely burned in the Rhode Island Nightclub Fire for carbon monoxide poisoning but did not report evaluating her for toxicity arising from other combustion products including hydrogen cyanide. Furthermore, although the authors discussed several aspects of managing burn- and smoke inhalation–related injury in their case report, they did not discuss cyanide toxicity despite the presence of several signs and symptoms suggesting the possible presence of cyanide poisoning. The failure to consider cyanide as a potential cause of fire-related morbidity and mortality characterizes much of the

medical literature on the management of smoke inhalation.

Why this lack of awareness of the importance of cyanide as a toxic combustion product? Researchers at the Swedish National Testing and Research Institute (SNTRI), which has conducted pioneering work identifying toxicants in fire smoke, suggest that the pervasive and relatively well recognized hazard of carbon monoxide can blind researchers and clinicians to the possibility that other toxicants, too, can be important in causing smoke-inhalation injury.[6] In effect, cyanide has not been found because it has not been sought.

CYANIDE PRODUCTION IN MODERN FIRES: DATA FROM THE SWEDISH NATIONAL TESTING AND RESEARCH INSTITUTE

Data from studies conducted by the SNTRI are consistent with NIST data in showing that cyanide is a major combustion product generated during burning of materials commonly found in domestic

Figure 2. Temperature and oxygen, carbon monoxide, and hydrogen cyanide concentrations in an experiment simulating the Rhode Island Nightclub Fire.[3] Temperature and gas concentrations were measured 1.4 meters above the floor and 1.6 meters away from the stage where the fire started.

structures. In one series of experiments, the SNTRI assessed the emission of hydrogen cyanide and carbon monoxide under both non-flaming (i.e., pyrolyzing) and flaming (i.e., fire) conditions during burning of wool, nylon, synthetic rubber, melamine, and polyurethane foam.[6] The results show that all of these substances liberated high quantities of cyanide when burned—particularly under pyrolyzing conditions characterized by low oxygen. Carbon monoxide was also emitted during the burning of these substances. Noting that hydrogen cyanide is approximately 35 times more

toxic than carbon monoxide during acute exposure, the authors emphasized the need for increased recognition of the contribution of cyanide to smoke toxicity.[6]

The SNTRI conducted other experiments to identify factors that affect the amount of cyanide generated in a fire.[4] They developed combustion models that take into account the observations that oxygen content in the air near a fire is lower than that of fresh air; that air in the fire contains combustion products that reduce the efficiency of burning and result in

incomplete combustion; and that growth of a fire increases the contents of combustion products in the air. Using these models, they identified two conditions that increased the probability of cyanide formation in a fire. First, recycling of combustion products within a confined space increased the formation of hydrogen cyanide. Second, lowered ventilation rate to the fire increased the formation of hydrogen cyanide by 6 to 10 times relative to conditions of higher ventilation rate. Carbon monoxide formation was also increased under these two conditions, which are particularly likely
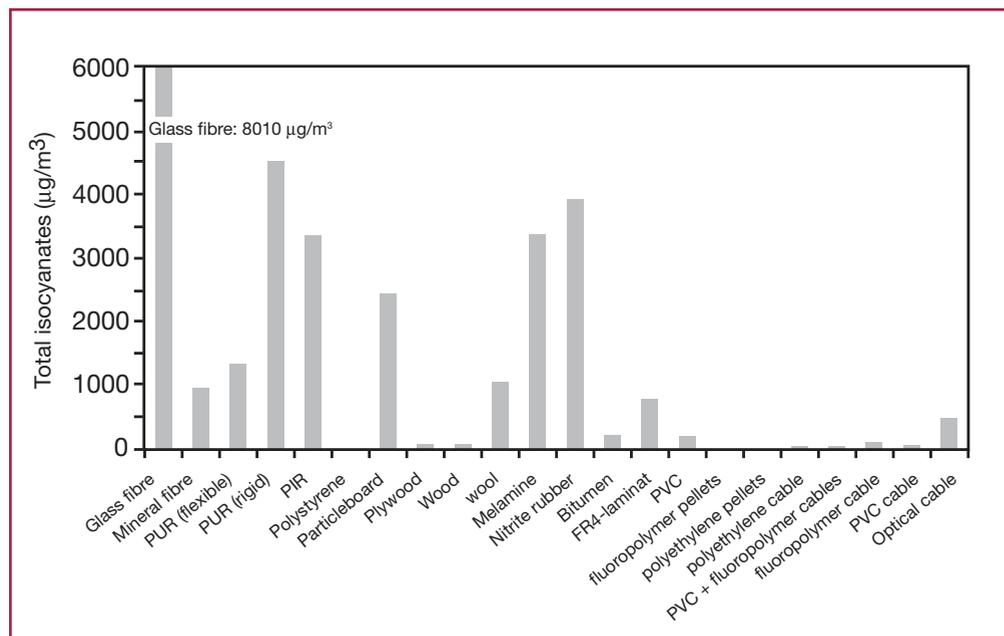
Glass fibre: 8010 µg/m³

Figure 3. Total isocyanate concentrations in Cone calorimeter tests.[10]

to apply to closed-structure fires.

Other research demonstrates the frequent presence of cyanide at toxic-to-lethal concentrations in the blood of fire victims.[7,8] Studies described by Dr. James Augustine in his article *Smoke and Fire: Recognizing Cyanide as a Toxic Agent* on Pages 18 to 23 in this supplement show that cyanide from smoke inhalation contributes significantly to fire-related deaths and may in some cases be a more important contributor to morbidity and mortality than carbon monoxide.

HYDROGEN CYANIDE AS AN ESCAPE INHIBITOR
Cyanide poisoning from fire smoke can be directly lethal or, as the SNTRI and other researchers emphasize, can indirectly cause death by incapacitating a fire victim.[6,9] Hydrogen cyanide and other toxicants in sublethal concentrations appear to act as *escape inhibitors* in modern fires.[6,9] Exposure to low cyanide concentrations in a fire can cause unconsciousness that makes

self-directed escape from the fire very difficult.[6] The victim of cyanide-associated incapacitation may continue to inhale increasing amounts of carbon monoxide and other noxious gases. Carbon monoxide poisoning may eventually be the direct cause of death. However, as the carbon monoxide poisoning might not have occurred without cyanide-induced incapacitation, hydrogen cyanide arguably is the cause of death in this example. The role of hydrogen cyanide as an escape inhibitor is supported by results of fire modeling experiments as well as animal research that Captain Robert Schnepp describes in his article *Where There's Fire, There's Smoke!* on Pages 12 to 17 of this supplement.

SISTERS OF CYANIDE: ISOCYANATES GENERATED DURING COMBUSTION
Other findings from the SNTRI suggest that the impact of cyanide as isocyanates should be considered in estimating the cyanide-associated hazards of fire

smoke.[10] Derived from cyanide and hydrocarbons, isocyanates are commonly found in plastics and adhesives. They are generated during the thermal decomposition of urethanes and, it is hypothesized, during the incomplete combustion of nitrogen-containing compounds.[10] The SNTRI assessed the formation of isocyanates in small-scale combustion experiments involving 18 standard materials used in building and in large-scale experiments involving 2 domestic products (i.e., a sofa and a mattress). Other combustion products including carbon monoxide, sulfur dioxide, hydrogen fluoride, hydrogen chloride, and hydrogen cyanide were also measured.

The small-scale experiments involved highly ventilated conditions under which generation of large quantities of dangerous combustion products such as carbon monoxide and hydrogen cyanide was neither expected nor observed. In these small-scale experiments, isocyanates were

found to be present at a concentration that made them potentially more dangerous to humans than the other combustion products that were tested (Figure 3).[10] The results suggest that elevated isocyanate levels in a fire can result in life-threatening conditions even when hydrogen cyanide and carbon monoxide remain at nondangerous levels.

The large-scale experiments differed from the small-scale experiments in that combustion generated high concentrations of dangerous products such as hydrogen cyanide and carbon monoxide. Isocyanates were also present at high levels in these large-scale experiments. For example, in a large-scale test in which a sofa in an enclosed room was ignited, isocyanates reached approximately 17% of the concentration that is immediately dangerous to life and health (IDLH), and carbon monoxide reached 30% of the IDLH value during the test period. The authors concluded based on these results that the contribution of isocyanates should be included in estimating the toxic effect of a gas mixture.[10]

CONCLUSIONS
Results of fire modeling experi-

ments including simulations of the February 2003 Rhode Island Nightclub Fire suggest that cyanide is a ubiquitous toxicant in modern fires. Depending on the fire conditions, hydrogen cyanide is formed as an interme-

Hydrogen cyanide is formed during combustion of any material containing nitrogen—that is, during combustion of almost any material found or used in the construction of human dwellings.

diate combustion product and/or an end product. Isocyanates, too, are formed during combustion and should be considered in estimating cyanide-related hazards from fire smoke. The amount of cyanide produced can vary from fire to fire and from one location to another in a given fire depending on factors such as the composition of the burning material, the rate of burning, the absolute temperature, and ambient oxygen level.

Experience with the Rhode Island Nightclub Fire, in which cyanide is likely to have contributed to morbidity and mortality, and data from studies reviewed elsewhere in this supplement show that cyanide can be rapidly lethal—a daunting challenge for first

responders working to save lives. While daunting, the challenge is not insurmountable. Effective management of cyanide poisoning in a fire emergency is possible. The first responder's awareness that cyanide poisoning is highly probable in smoke-inhalation victims of closed-structure fires constitutes a first step in effective management of smoke inhalation–associated cyanide poisoning. Specific measures to help victims of smoke inhalation–associated cyanide poisoning in the prehospital setting are discussed elsewhere in this supplement by Dr. James Augustine and Captain Robert Schnepp. ◆

References
1. Grosshandler WL, Bryner N, Madrzykowski D, et al. Draft report of the technical investigation of The Station nightclub fire. US Department of Commerce, Technology Administration, National Institute of Standards and Technology. March 2005.
2. Anonymous. At least 96 killed in nightclub inferno. Available at www.cnn.com. CNN news report, 21 February 2003. Accessed 17 March 2005.
3. Madrzykowski D, Bryner NP, Grosshandler WL, et al. Fire spread through a room with polyurethane foam-covered walls. *Interflam* 2004. International Interflam Conference, 10th Proceedings; Volume 2; July 5-7, 2004.
4. Tuovinen H, Blomqvist P. Modeling of hydrogen cyanide formation in room fires. Brandforsk project 321-011. SP Swedish National Testing and Research Institute. *SP Report 2003:10*. Borås, Sweden, 2003.
5. Sheridan RL, Schulz JT, Ryan CM, et al. Case 6-2004: A 35-year-old woman with extensive, deep burns from a nightclub fire. *New Engl J Med.* 2004;350:810-821.
6. SP Swedish National Testing and Research Institute. Formation of hydrogen cyanide in fires. *SP Report 2000:27*. Borås, Sweden, 2000.
7. Baud F, Barriot P, Toffis V, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med.* 1991;325:1761-1766.
8. Alarie Y. Toxicity of fire smoke. *Crit Rev Toxicol.* 2002;32:259-289.
9. Peacock RD, Averill JD, Reneke PA, et al. Characteristics of fire scenarios in which sublethal effects of smoke are important. *Fire Technology.* 2004;40:127-147.
10. Hertzberg T, Blomqvist P, Dalene M, et al. Particles and isocyanates from fires. Brandforsk project 324-021. SP Swedish National Testing and Research Institute. *SP Report 2003:05*. Borås, Sweden, 2003.

Where There's Fire, There's Smoke!

Robert Schnepp, EMT-P
Alameda County Fire Department
Hazardous Materials Specialist, FEMA Urban Search and Rescue Region 4 Task Force

Smoke is omnipresent on the third rock from the sun. In every nook and cranny of the planet and every second of every day, smoke is wisping, wafting, or billowing from some point of origin. Smoke has had a long-standing impact on the world. Scientists theorize that a gigantic cloud of smoke and dust caused by a meteorite colliding with the Earth contributed to the extinction of the dinosaurs eons ago.

Sometimes smoke signifies warmth, comfort, and progress. Other times smoke signifies menace and danger. All of the time, smoke is to one degree or another harmful to breathe. During the Industrial Revolution, the belching smokestacks of nineteenth-century England were signs of progress and innovation: factories provided jobs, consumer products, and revenue. On the other hand, that same smoke, full of soot and toxic byproducts of combustion, stained the landscape and sickened the surrounding population. The unforgettable images of thick black smoke pouring from the World Trade Center and Pentagon on September 11, 2001, are a modern-day example of the menacing and dangerous aspects of smoke.

Smoke continues to be underestimated as a source of toxic poisoning. The fire service knows that smoke is everywhere, but do fire professionals understand thoroughly what is in the smoke or why people die from smoke inhalation? Nationwide, fire academies and fire science programs teach the basics of combustion chemistry, and it is well known that smoke kills more people than flames. However, many firefighters would be hard pressed to name five products of combustion from a typical residential structure fire. Carbon monoxide is frequently identified, but others seldom come to mind. Rarely recognized are compounds such as ammonia, hydrogen chloride, sulfur dioxide, hydrogen sulfide, carbon dioxide, the oxides of nitrogen, and soot. Even less frequently named are cyanide compounds, particularly hydrogen cyanide, which has recently been established as a major contributor to fatal smoke-inhalation exposures.[2,3] This article reviews basic information about the toxic components of smoke, especially cyanide, and discusses a potential new approach to treating smoke-inhalation victims in the prehospital setting.

SMOKE SHOWING!

According to the National Fire Protection Association, smoke inhalation is responsible for up to 80% of the more than 4,000 fire-related deaths and more than 18,000 civilian and firefighter

The fatality toll for smoke inhalation in the United States roughly equates to that from three jumbo jet crashes each month for an entire year.

injuries that occur annually in the United States. By these statistics, the United States is one of the worst places to live in terms of fire-related death and injury.

Smoke production depends on several factors including the chemical composition of the burning material, the temperature of the combustion process, the oxygen content supporting combustion, and the presence or absence of ventilation. Combustion is a complex process, and the smoke from fires (especially closed-compartment residential structure fires) is a varied mixture of particulates, superheated air, and toxic chemical compounds.

Smoke is an aerosol of solid or liquid particles, usually resulting from incomplete combustion, accompanied by various fire gases. The gaseous constituents of fire smoke are largely dictated by the rate of burning and by the composition of the heated material. The extensive commercial and residential use of synthetic materials (plastics, nylons, and polymers such as Styrofoam and polyurethane foam) significantly impacts combustion and fire behavior and the composition of the smoke produced during a structural fire. The vast majority of synthetics are carbon based, bonded with various atoms

including hydrogen, nitrogen, chlorine, and sulfur. Synthetic substances ignite and burn quickly to cause rapidly developing fires and toxic smoke. The rapid development of these fires and the highly toxic nature of smoke make structural firefighting more dangerous today than ever before.

The example of a mattress fire in a small bedroom illustrates these points. A typical mattress is made primarily of polyurethane foam, which comprises many chemicals including polyol (an organic alcohol molecule and the majority of the polyurethane compound), toluene diisocyanate (commonly known as TDI), methylene chloride, and ammonia-based catalysts. When polyurethane foam is exposed to heat, the parent substances break down and bond with each other to create

> **Aerosol:** An assembly of liquid or solid particles suspended in a gaseous medium long enough to be observed and measured
>
> **Particle:** A small, discrete object with the same makeup and density as the parent substance

many new compounds. Some of the compounds are irritants, such as hydrogen chloride and ammonia, that cause eye irritation or airway problems in smoke exposures. Other compounds, such as carbon monoxide and cyanide, are toxic when inhaled. These toxicants can cause problems even when sublethal amounts are inhaled. Carbon monoxide, created from the incomplete combustion of carbon-based material, is partly responsible for incapacitating a smoke-inhalation victim. Cyanide,

formed by carbon-hydrogen-nitrogen bonding during the combustion process, disrupts the body's ability to use oxygen and causes asphyxia at the cellular level.

The example of the mattress is representative of what can occur during combustion of countless items found in a typical residential structure fire. Sofas, stereo cabinets, drapes, blankets, and carpeting all produce cyanide and other common byproducts of combustion. Additionally, vehicle fires, garage fires, and dumpster fires are capable of generating cyanide and other toxicants. It is prudent to assume, then, that firefighters are assaulted with toxic gases, including cyanide, in many fire scenarios.

CYANIDE AND SMOKE

Smoke is one of the first observable signs of a structure fire. Firefighters regard the volume and color of smoke and the force with which smoke exits a fire building as indicators of what the fire is doing inside. They use that information to implement appropriate fireground tactics. Firefighters often aggressively enter smoky buildings to search for victims without stopping to evaluate the toxic potential of the smoke and taking appropriate measures to protect themselves. The danger of this approach is illustrated by results of studies of fire scenes in Paris, France, and Dallas County, Texas.[3,4] These studies, which are discussed in detail by Dr. James Augustine on Pages 18 to 23 in

this supplement, show that cyanide and carbon monoxide were commonly found in the blood of victims of structural fires. In these studies,

- Cyanide and carbon monoxide were both important determinants of smoke inhalation–associated morbidity and mortality;

- Cyanide concentrations in the blood of smoke-inhalation victims were correlated with the probability of death;

- Cyanide poisoning appeared to be a more important contributor than carbon monoxide poisoning to causing death in certain fire victims;

- Cyanide and carbon monoxide may have potentiated the harmful effects of one another.

Other research shows that exposure to cyanide in sublethal amounts can indirectly contribute to smoke-related death and injury.[5] Depending on the dose, cyanide has the ability to incapacitate a victim. Incapacitation can prevent escape from the fire environment and increase the likelihood of burns as well as increase the exposure to cyanide, carbon monoxide, and other toxic byproducts of combustion. The knockdown potential of cyanide is illustrated by research conducted in the mid-1980s.[5] Monkeys exposed to the fumes of heated polyacrylonitrile, which liberates cyanide when broken down by pyrolysis, first hyperventilated and

Cyanide exposure can be fatal even in the presence of normal oxygen levels.

then rapidly lost consciousness. The greater the concentration of cyanide exposure, the faster the monkeys lost consciousness. The degree to which these findings apply to humans is not known, but the results suggest that cyanide could also render firefighters and civilians incapable of self-rescue when exposed to smoke.

CYANIDE: MECHANISM OF ACTION

Cyanide disrupts the body's ability to perform aerobic (oxygen-utilizing) metabolism even in the presence of normal oxygen levels.

To appreciate cyanide's mechanism of action, it is first necessary to understand the process of oxygen transportation and utilization in the body and the basic idea of aerobic metabolism. The circulatory system transports life-sustaining oxygen to the cells of the body on hemoglobin affixed to red blood cells (Figure 1). The destination of the oxygen is the mitochondria (Figure 2)—intracellular power stations that are responsible for converting nutrients into energy-yielding molecules of adenosine triphosphate (ATP) to fuel cellular activities. ATP production is highly dependent on oxygen. Without it, normal aerobic metabolism is impossible. If this process is seriously compromised, death is imminent.

During normal cellular respiration, the mitochondrion's use of oxygen is made possible by the action of the enzyme cytochrome oxidase. Cyanide compounds, once absorbed in the body, poison the cytochrome oxidase and prevent oxygen use by the mitochondria. Cyanide effectively
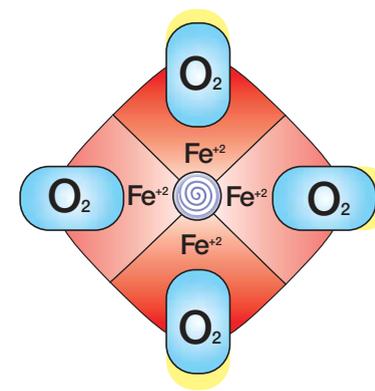

Figure 1. Oxygen affixed to hemoglobin on a red blood cell.

Figure 2. Mitochondria in a cell.

shuts down aerobic metabolism. Without oxygen, the cells switch to anaerobic metabolism, which produces toxic byproducts, such as lactic acid, that ultimately kill the cell. Thus, cyanide toxicity does not result from lack of oxygen in the body but rather from the inability of the body to use the oxygen that is present for aerobic (life-sustaining) metabolism.

The signs and symptoms of acute cyanide toxicity mimic the nonspecific signs and symptoms of oxygen deprivation. Headache, dizziness, stupor, anxiety, rapid breathing, and increased heart rate can all suggest cyanide poisoning. In severe cases of cyanide poisoning, patients may present with seizures, a significantly altered level of consciousness including coma, severe respiratory depression or respiratory arrest, and cardiovascular collapse.

TREATING SMOKE INHALATION IN THE PREHOSPITAL SETTING—IS THERE A BETTER WAY?

Treating a victim of smoke inhalation is one of the greatest challenges a health care provider can face. Patient outcomes vary greatly and are influenced by such factors as the extent and duration of the smoke exposure, amount and nature of toxicants in the
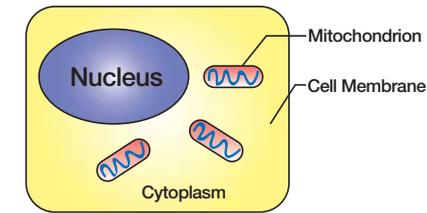
smoke, degree of thermal burns to the skin and lungs, quantity/size of inhaled particulates (soot), and the patient's age and underlying medical condition. The lack of established protocols for treating smoke inhalation leaves paramedics and other prehospital care providers with limited tools and/or training to care properly

Cyanide toxicity should be suspected in smoke-inhalation patients with soot in the nose or mouth and altered level of consciousness or significant hypotension.

for smoke-inhalation victims. In most cases, treating smoke inhalation outside the hospital is limited to supportive care including regaining or maintaining vital signs; administering high-flow oxygen; establishing intravenous (IV) lines; and performing advanced airway man-

agement techniques such as endotracheal intubation, cardiac monitoring, and rapid transport.

Supportive care alone does not correct the underlying cause of death in many smoke-inhalation patients. Until the underlying cause of asphyxia is reversed at the cellular level, normal oxygenation is often not possible. Chemical intervention—an antidote—may be required to restore the body's ability to use oxygen.

In the United States, the currently available cyanide antidote—known synonymously as the Cyanide Antidote Package, the Cyanide Antidote Kit, the Lilly kit, the Taylor kit, and the Pasadena kit—contains amyl nitrite, sodium nitrite, and sodium thiosulfate. Amyl nitrite is administered as an inhalant; sodium nitrite and sodi-

um thiosulfate are given intravenously. The nitrites are given to convert hemoglobin in the red blood cell to methemoglobin. Methemoglobin attracts

cyanide away from the cytochrome oxidase to form cyanomethemoglobin and restores the cell's ability to take in oxygen and continue the process of aerobic metabolism. Thiosulfate is administered to facilitate detoxification of cyanide by the body's own cyanide clearance system.

One downside of this treatment method is that methemoglobin does not transport oxygen. While methemoglobin does draw cyanide away from the cytochrome oxidase, it also eliminates the oxygen-carrying capacity of the red blood cell—a suboptimal tradeoff in smoke-inhalation patients. Since smoke-inhalation patients are commonly exposed to carbon monoxide, which also reduces the ability of red blood cells to transport oxygen, the oxygen-carrying capacity of the red blood cell may already be severely compromised, possibly to fatal levels. Additionally, nitrites, which can cause precipitous drops in blood pressure, may worsen the hypotension commonly found in smoke-inhalation victims. Because of the potential for these adverse effects, administering the currently available cyanide antidote kit can be a risky proposition for some smoke-inhalation patients.

Hydroxocobalamin, an antidote that is being developed for possible use in the United States, is currently approved (with the trade name of Cyanokit®, made by Merck Santé s.a.s.) in France. It has been used successfully since mid-1996 in the prehospital and hospital settings as an antidote for cyanide poisoning (Figure 3). Hydroxocobalamin is a precursor to vitamin B12. Its mechanism of action and apparently favorable side effect profile make possible

its use in the prehospital setting.

Hydroxocobalamin has no known adverse effects on the oxygen-carrying capacity of red blood cells and does not decrease blood pressure—potentially significant benefits when treating victims of smoke inhalation. The mechanism of action is simple: hydroxocobalamin binds to cyanide to form vitamin B12 (cyanocobalamin), a

Figure 3. Cyanokit® (hydroxocobalamin) as packaged in France.

compound ultimately excreted in the urine. Hydroxocobalamin can be administered to a smoke-inhalation patient with a presumptive diagnosis of cyanide poisoning with little fear of making the patient worse in part because it does not impair the oxygen-carrying capacity of red blood cells.

Hydroxocobalamin is used by the Paris (France) Fire Brigade as a prehospital antidote for cyanide poisoning associated with smoke inhalation as well as other routes of exposure. In a study of 81 victims (41 males and 40 females) treated for smoke inhalation by the Paris Fire Brigade from 1995 through 2003, 29 patients were in cardiac arrest and 15 were hemodynamically unstable (defined as having a systolic blood pressure <90 mmHg).[6] All patients were administered hydroxocobalamin for cyanide poisoning. Of the 29 patients in cardiac arrest before supportive care, 18 recovered

spontaneous cardiac activity with cardiac resuscitation, epinephrine, and hydroxocobalamin administration (typically a 5-gram initial infusion). The average time between administration of antidote and recovery of spontaneous cardiac activity was 19.3 minutes. Of the 15 hemodynamically unstable patients, 12 (80%) recovered normal blood pressure after infusion of hydroxocobalamin. The average time to hemodynamic improvement was 49.2 minutes from the beginning of antidote infusion. Ongoing analyses of additional cases of hydroxocobalamin treatment of smoke inhalation–associated cyanide poisoning by the Paris Fire Brigade will provide data to supplement these findings.

Hydroxocobalamin appears to be generally well tolerated at the doses required for antidotal efficacy. Side effects, all of which are transient, include reddening of the skin, urine, and mucous membranes and interference with some colorimetric laboratory values such as bilirubin, blood glucose, and creatinine. These effects arise from the red color of the hydroxocobalamin molecule and do not appear to be clinically significant. Occasional allergic reactions to hydroxocobalamin have been observed.

CONCLUSIONS

In 1736, Benjamin Franklin formed the Union Hose Company to create the nation's first organized fire brigade. Franklin and his group of hearty Pennsylvanians were dedicated men who strived to improve their skills through training and innovative ideas. Franklin prided himself on being a firefighter and, throughout his life, continued to refine the service of firefighting.

Conceptually, the modern fire service is much as it was in Franklin's era. Fires occur every day, and firefighters put them out. Civilians are trapped in burning buildings, and firefighters attempt to save them. Frequently, rescuers and/or victims breathe toxic smoke and require medical attention. Firefighters and emergency medical personnel must dedicate themselves to understanding the injuries caused by structural fires and smoke inhalation.

There is a need to better address the prehospital treatment of smoke-inhalation victims. Because of the mechanism of cyanide poisoning, supportive care alone may not successfully resuscitate a smoke-inhalation patient. The experience of the Paris Fire Brigade with the use of hydroxocobalamin as a cyanide antidote suggests that improvement is possible and underscores the need to reevaluate the prehospital management of smoke-inhalation

cyanide poisoning in the United States. ◆

References
1. Karter, MJ Jr. Fire Loss in the United States During 2003. Fire Analysis Research Division, National Fire Protection Association. October 2004; Quincy, MA.
2. Alarie Y. Toxicity of fire smoke. *Crit Rev Toxicol.* 2002;32:259-289.
3. Baud FJ, Barriot P, Toffis V, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med.* 1991;325:1761-1776.
4. Silverman SH, Purdue GF, Hunt JL, et al. Cyanide toxicity in burned patients. *J Trauma.* 1988;28:171-176.
5. Purser DA, Grimshaw P, Berril KR. Intoxication by cyanide in fires: a study in monkeys using polyacrylonitrile. *Arch Environ Health.* 1984; 39:394-400.
6. Fortin J-L. Use of hydroxocobalamin in fire victims by the Brigade De Sapeurs Pompiers De Paris from 1998-2003. Presentation at The Second World Congress on Chemical, Biological and Radiological Terrorism. September 2003; Dubrovnik, Croatia.

Smoke and Fire:

RECOGNIZING CYANIDE AS A TOXIC AGENT

James J. Augustine, MD, FACEP
EMP, Ltd., the Atlanta Fire Department, and the
Department of Emergency Medicine, Emory University
Atlanta, Georgia

December 15, afternoon. The fire started in the kitchen in the home of a 70-year-old male, who was asleep on the living-room couch. His barking dog did not arouse him but did alert the neighbors, who activated the 911 system. First-arriving crews found the man quickly and pulled him out into the snow. His steaming body was turned over to the first arriving EMS crew. He was responsive to painful stimuli, had no thermal burns, and had soot in his mouth but clear lungs. His condition rapidly deteriorated. His pulse became weak and irregular; blood pressure became nearly unmeasurable; and respiratory arrest occurred. He was transported to the local hospital, which had a hyperbaric chamber, but treatment did not stabilize him. Within 24 hours of arrival at the hospital, he expired.

Emergency responders have been taught to suspect carbon monoxide poisoning in smoke-inhalation victims such as this one; however, features of this case do not resemble those of carbon monoxide poisoning. Emergency responders know that victims of carbon monoxide poisoning do not typically show these signs of respiratory depression and that circulatory collapse is unusual.

What happened, and what can be done to improve the care of patients with similar presentations?

CYANIDE POISONING: MECHANISMS AND MANIFESTATIONS

This victim shows symptoms and signs of poisoning with hydrogen cyanide, a toxic product of combustion of common nitrogen- and carbon-containing substances including plastics and other polymers, paper, cotton, wool, and silk.[1,2] Hydrogen cyanide is particularly likely to be generated under the conditions of high temperature and low oxygen that characterize closed-space fires. Given the ubiquity of sources of cyanide, it is reasonable to assume that cyanide is generated in any modern fire.[3] However, the concentration of cyanide, like that of other gaseous and particulate elements of fire smoke, can vary markedly from fire to fire as well as from location to location in a given fire depending on the materials burned and the ambient temperature and oxygen levels.[4]

Cyanide causes human toxicity by deactivating the mechanism that allows cells to utilize oxygen.[5,6] Oxygen is the substrate of aerobic (i.e., oxygen-dependent) metabolism, which produces adenosine triphosphate (ATP), the main source of cellular energy. The inability of cyanide-poisoned cells to use oxygen causes them to transition from aerobic metabolism to anaerobic (i.e., oxygen-independent) metabolism—a much less efficient process to power the cell and one that generates toxic byproducts such as lactic acid. Accumulation of toxic byproducts of anaerobic metabolism causes cell death.

The heart and brain—organs that typically rely on a substantial, continuous supply of oxygen—are most rapidly affected by cyanide poisoning. Accordingly, most signs and symptoms of acute cyanide poisoning reflect the nonspecific effects of oxygen deprivation on the heart and brain (Table).[1,7,8] Exposure to low concentrations can initially cause respiratory activation (manifested by hyperpnea and tachycardia) in an attempt to compensate for lack of oxygen. This activation is followed by respiratory and myocardial depression. Early neurologic manifestations that reflect the initial effects of brain oxygen deprivation include headache, anxiety, and loss of judgment. Later manifestations of exposure to smaller concentrations—which are also early manifestations of exposure to large concentrations—include cardiac arrhythmias, stupor, coma, and seizure that culminate in respiratory depression and death. The time between exposure and incapacitation or death varies depending on the concentration of exposure but is always relatively short. Exposure to substantial concentrations of cyanide can cause loss of consciousness within a minute, and respiratory depression and cardiac arrest can follow within minutes.

Table. MANIFESTATIONS OF ACUTE CYANIDE POISONING[1,7,8]

Early Manifestations of Exposure to Low Inhaled Concentrations	Later Manifestations of Exposure to Low Inhaled Concentrations or Early Manifestations of Exposure to Moderate to High Concentrations
• Faintness • Flushing • Anxiety • Excitement • Drowsiness • Vertigo • Headache • Dyspnea • Perspiration • Tachypnea • Tachycardia	• Altered consciousness • Tremulousness • Seizure • Respiratory depression • Noncardiogenic pulmonary edema • Respiratory arrest • Cardiac arrhythmia • Cardiovascular collapse

CYANIDE: A PRODUCT OF COMBUSTION

As a toxic product of combustion, cyanide has historically been over-shadowed by carbon monoxide, which many health care providers perceive as the primary clinically relevant toxin in smoke. While carbon monoxide is a potential cause of toxicity in any fire incident involving smoke inhalation, studies of blood cyanide concentrations in fire victims reveal that cyanide is also an important cause of toxicity.[3,9-13] The contribution of cyanide to smoke inhalation–associated death was assessed in a 2002 meta-analysis of smoke-inhalation casualties in fire incidents occurring over a span of two decades.[3] Data from fire incidents in which both carbon monoxide and cyanide were measured in victims' blood reveal that

- *Exposure to potentially lethal concentrations of cyanide commonly occurred in structural and other closed-space fires.* One third (33%) to 87% of individuals who died in these fires had potentially lethal blood concentrations of cyanide (Figure 1).[3]

- *Co-exposure to carbon monoxide and cyanide was frequent.* Elevated levels of both compounds were found in a proportion of victims in all of the fires. In other fires, it has been reported that carbon monoxide played a dominant role in fire deaths.[3]

- *In some fire incidents, cyanide may have played a more important role in causing death than carbon monoxide.* In the Dupont Plaza hotel fire and the Manchester aircraft fire, the majority of victims had potentially lethal levels of cyanide in their blood, and few victims had levels of carbon monoxide that are typically considered lethal (Figure 1).[3]

Additional evidence supporting a role of cyanide in smoke inhalation–associated death comes from the Paris fire study,[9] which was conducted with the aim of determining blood cyanide concentrations in victims exposed to fire smoke in residential fires in Paris. Efforts were made to obtain and analyze blood samples as quickly as possible after smoke exposure. Prompt attainment and analysis of blood samples was undertaken to overcome limitations of earlier studies having lag times between cyanide exposure and blood sampling and/or between obtaining and analyzing blood samples. Cyanide disappears quickly from the bloodstream and is unstable in blood samples; therefore, prompt sampling and assessment are necessary to enhance the probability of obtaining accurate readings.[14] (Improved assessment technology may assist in identifying cyanide in specimens more rapidly and with greater accuracy in the near future.[15])

In the Paris study, blood cyanide levels from 66 fire victims who survived and 43 fire victims who died were compared with those from 114 control individuals who had not been exposed to cyanide (40 hospitalized patients with drug intoxication, 29 patients with carbon monoxide poisoning, and 45 patients with major trauma).[9] The results show that mean blood cyanide concentrations in both groups of fire victims substantially exceeded those in the control individuals. In addition, mean blood cyanide levels exceeded the threshold identified as potentially lethal (i.e., 1 mg/L) in the group of victims with fatal outcomes but not in the group that survived (Figure 2).[9] Mean blood cyanide concentrations in casualties exceeded by more than three times the concentrations in smoke-inhalation victims who survived (Figure 2). These data show a direct relationship between blood cyanide concentration and occurrence of fire-related death and suggest that cyanide contributed to many of these casualties.

These data are corroborated by findings in a mattress fire in Argentina that killed 35 inmates in 1990.[13] Carboxyhemoglobin saturation values in these victims ranged from 4% to 18% (generally considered to be within the nonlethal range) whereas blood cyanide levels, which ranged from 2.0 to 7.2 mg/L, exceeded the lethal range. The authors suggested that hydrogen cyanide generated by rapid thermal decomposition of polyurethane was the most likely cause of death in these 35 victims.

Considered in aggregate, data from studies in which blood cyanide levels were obtained in fire victims suggest that

(1) Cyanide exposure is highly probable in individuals who have inhaled products of combustion.

(2) Cyanide from smoke inhalation contributes significantly to fire-related deaths.

(3) In some victims, cyanide may have a greater role in causing death than carbon monoxide.

In fire emergencies, the fire service professional should consider seriously ill victims of smoke inhalation to have cyanide poisoning unless proven otherwise. Fire produces countless combustion products, including numerous toxins and asphyxiants; therefore, the probability of coexposure to other poisons—particularly carbon monoxide—should be borne in mind.

RECOGNIZING AND TREATING ACUTE CYANIDE POISONING

In the prehospital setting, acute cyanide poisoning must be diagnosed presumptively as no diagnostic test can confirm the presence of cyanide poisoning within the short time available for initiating potentially life-saving intervention. Cyanide poisoning should be suspected in any person exposed to smoke in a closed-space fire regardless of whether burns have been sustained.[3,6] Soot in the mouth and altered level of consciousness suggest a high probability of cyanide toxicity. The concurrent presence of hypotension increases confidence
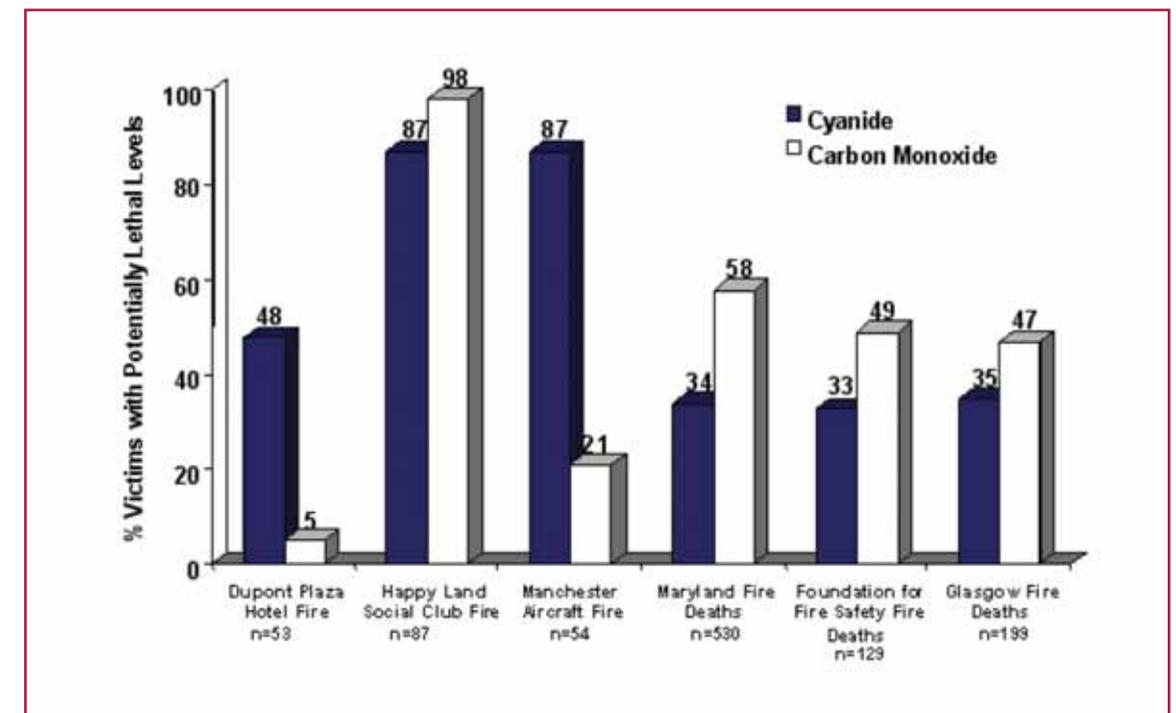
Figure 1. Percentage of smoke-inhalation deaths with potentially lethal blood cyanide and carbon monoxide levels in various fires, 1971 to 1990.[3] Potentially lethal blood levels were defined as ≥1 mg/L for cyanide and >50% carboxyhemoglobin for carbon monoxide.
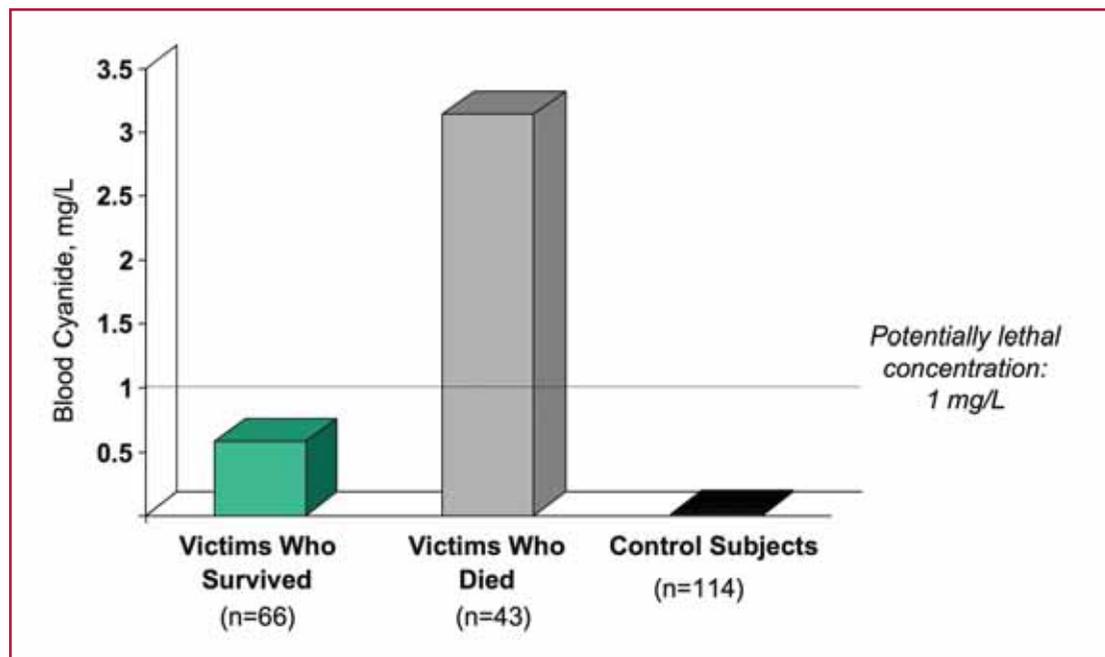
Figure 2. Mean blood cyanide concentrations in the Paris fire study.[9]

in the diagnosis. Some cyanide-poisoned victims have a pinkish to cherry-red complexion caused by the (abnormal) high oxygenation of venous blood. Also, the victim's breath may have an almond-like odor attributed to excretion of small amounts of cyanide in the breath. Many people lack the ability to smell this odor; therefore, the failure to detect an almond odor does not suggest the absence of cyanide poisoning.

Besides these physical findings in the field or the Emergency Department, hospital laboratory tests that may indicate a strong possibility of cyanide poisoning include

- *Elevated plasma lactate concentrations* caused by the accumulation of lactic acid, a byproduct of anaerobic metabolism; and

- *Elevated oxygen content of venous blood* caused by the failure of cyanide-poisoned cells to extract oxygen from arterial blood.[1,8]

Measures of whole-blood cyanide

concentrations can be useful in hospital confirmation of cyanide poisoning. However, this testing is not timely in most institutions, and initial therapy needs to occur based on clinical findings.

Prehospital management of acute cyanide poisoning in the smoke-inhalation victim involves moving the victim from the source of exposure, administering 100% oxygen, providing cardiopulmonary support, and restoring organ and cellular perfusion.[1,2,6,8] When clinically indicated, anti-convulsants should be given for treatment or prevention of seizures; antiarrhythmics to stabilize cardiovascular function; and sodium bicarbonate to correct metabolic acidosis.

Although cyanide antidotes exist, the only one currently available in the United States should not be used outside of a hospital in smoke-inhalation victims because of the problems associated with concomitant inhalation of carbon monoxide and other products of

combustion. (On the other hand, the currently available kit can be useful for victims of cyanide poisoning occurring because of a laboratory or industrial accident or for victims of a terrorist event not involving fire smoke.) The currently available cyanide antidote kit includes amyl nitrite and sodium nitrite, both of which reduce the oxygen-carrying capacity of the blood by binding with hemoglobin to form methemoglobin, which binds and neutralizes cyanide. In most smoke-inhalation victims with cyanide poisoning, the oxygen-carrying capacity of the blood is compromised by concurrent carbon monoxide poisoning. Superimposition of additional reductions in oxygen-carrying capacity of the blood from antidote-induced methemoglobinemia is dangerous and potentially fatal.[4,16,17] The currently available cyanide antidote also can cause severe hypotension, an effect that counteracts efforts to achieve hemodynamic stability in fire victims.[16,17]

Hydroxocobalamin, a cyanide antidote that can be administered safely to smoke-inhalation victims, has been available for nearly a decade in France and is being evaluated for potential introduction in the United States. It has been used and studied globally as described by Captain Rob Schepp in the paper *Where There's Fire, There's Smoke!* on Pages 12 to 17 of this supplement. A precursor of vitamin B12, hydroxocobalamin detoxifies cyanide by binding with it to form cyanocobalamin, which is excreted in the urine.[18] Hydroxocobalamin does not cause methemoglobinemia or hypotension. Hydroxocobalamin has been used safely in the prehospital treatment of victims of smoke inhalation–associated cyanide poisoning—including those with concurrent carbon monoxide poisoning.[19] Should it become available in the United States, hydroxocobalamin potentially will enable prehospital antidote treatment of cyanide poisoning in smoke-inhalation victims. The ability to administer antidote in the prehospital setting should increase the speed of intervention and, hopefully, its effectiveness. The dosage used in most countries around the world is a single, 5-gram intravenous dose administered when cyanide poisoning is suspected on a clinical basis. Additional doses may be indicated for the severely poisoned patient.[20]

CASE DISCUSSION AND CONCLUSION

As many as 10,000 deaths per year in the United States are attributed to inhalation of products of combustion from fire.[17] On the basis of studies measuring blood cyanide concentrations in smoke-inhalation victims, it is reasonable to conclude that hydrogen cyanide may contribute to the majority of these deaths. Studies also show that smoke inhalation–associated cyanide poisoning can be treated effectively provided that

intervention is initiated shortly after exposure. Supportive measures currently constitute the mainstay of prehospital intervention for smoke-inhalation victims. The currently available cyanide antidote kit may pose safety hazards in victims with concurrent carbon monoxide poisoning. Hydroxocobalamin, a cyanide antidote that can be administered safely at the fire scene to smoke-inhalation victims, has been studied and used extensively in other countries and is currently being evaluated for introduction in the United States.

ACKNOWLEDGMENT

References

1. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. Cyanide toxicity. *Am Fam Phys.* 1993;48:107-114.
2. Lee-Chiong TL. Smoke inhalation injury. *Postgrad Med.* 1999;105:55-62.
3. Alarie Y. Toxicity of fire smoke. *Crit Rev Toxicol.* 2002;32:259-289.
4. Kulig K. Cyanide antidotes and fire toxicology. *N Engl J Med.* 1991;325:1801-1802.
5. Klaassen CD. Nonmetallic environmental toxicants. Air pollutants, solvents and vapors, pesticides. Chapter 28 in *Goodman and Gilman's The Pharmacologic Basis of Therapeutics.* 10th edition. Hardman JG, Limbird LE, eds. New York: McGraw-Hill; 2001: 1877-1902.
6. Koschel MJ. Where there's smoke, there may be cyanide. Am J Nurs. 2002;102:39-42.
7. Sauer SW, Keim ME. Hydroxocobalamin: improved public health readiness for cyanide disasters. *Ann Emerg Med.* 2001;37:635-641.
8. Chemical Casualty Care Division, Aberdeen Proving Ground, MD. Cyanide AC, CK. *United States Army Medical Research Institute of Chemical Defense: Medical Management of Chemical Casualties Handbook.* 3rd edition. The Virtual Naval Hospital Project, 1997-2004.
9. Baud F, Barriot P, Toffis V, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med.* 1991;325:1761-1766.
10. Silverman SH, Purdue GF, Hunt JL, et al. Cyanide toxicity in burned patients. *J Trauma.* 1988;28:171-176.
11. Jones J, McMullen MJ, Dougherty J. Toxic smoke inhalation: cyanide poisoning in fire victims. *Am J Emerg Med.* 1987;5:317-321.
12. Gill JR, Goldfeder LB, Stajic M. The happy land homicides: 87 deaths due to smoke inhalation. *J Forensic Sci.* 2003;48:161-163.
13. Ferrari LA, Arado MG, Giannuzzi L, et al. Hydrogen cyanide and carbon monoxide in blood of convicted dead in a polyurethane combustion: a proposition for the data analysis. *Forensic Sci Int.* 2001;121:140-143.
14. Moriya F, Hashimoto Y. Potential for error when assessing blood cyanide concentrations in fire victims. J Forensic Sci. 2001;46:1421-1425.
15. Calafat AM, Stanfill SB. Rapid quantitation of cyanide in whole blood by automated headspace gas chromatography. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2002; 772:131-137.
16. Hall A, Rumack BH. Clinical toxicology of cyanide. *Ann Emerg Med.* 1986;15:1067-1074.
17. Borron SW, Baud FJ. Toxicity, cyanide. February 2003. Available at: www.emedicine.com/emerg/topic118.htm. Accessed 13 January 2004.
18. Mégarbane B, Delahaye A, Goldgran-Tolédano D, et al. Antidotal treatment of cyanide poisoning. *J Chin Med Assoc.* 2003;66:193-203.
19. Borron SW, Vicaut E, Ruttimann M, et al. Biological tolerance of hydroxocobalamin in fire victims intoxicated by cyanide. *Intensive Care Medicine.* 1997;23:S181.
20. Houeto P, Hoffman JR, Imbert M, et al. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning. *Lancet.* 1995; 346:605-608.

One Team Together
Improving Capabilities In Emergency Response

The risk of acute cyanide poisoning related to smoke inhalation in structural fires or as a potential chemical terrorism weapon is underappreciated by most emergency response and emergency medicine professionals. This is due in large part to the fact that current treatment options have limitations.

EMD Pharmaceuticals, Inc., the North American Affiliate of Merck KGaA of Darmstadt, Germany, is developing a cyanide antidote in the United States. For more information on the use of cyanide antidotes in response to industrial accidents, smoke inhalation, or potential terrorist activities, please contact one of the following:

In North America:
Elizabeth Field, PhD, Senior Director, Medical Communications
EMD Pharmaceuticals, Inc.
3211 Shannon Road, Suite 500
Durham, NC 27707
Tel: 919-401-7238 Fax: 919-401-7180
Email: elizabeth.field@emdpharmaceuticals.com

In Europe:
Emmanuel Eumont, Senior Global Operations Manager
Global Special Projects
Merck S.A. - France
37, rue Saint-Romain
Lyon Cedex 08 - F 69379
Tel: 33-(0)-472-78-2813 Fax: 33-(0)-472-78-0939
Email: emmanuel.eumont@merck.fr