

## **Hydrogen Cyanide Poisoning from Inhalation of Smoke Produced in Fires**

Much warning has been given on the dangers of carbon monoxide poisoning resulting from fires. But there is another danger to firefighters and victims in structural fires which is less recognized, and that is acute cyanide poisoning. The dangerous hydrogen cyanide fumes can be given off even after the fire is out but the material is still smoldering. Very mild cases might be shrugged off as a headache, but concentrations of a couple of hundred parts per million in air can kill within a few minutes. Antidotes are available which are effective if administered quickly, but the wrong diagnosis can also result in death. It is important to recognize the difference between hydrogen cyanide and carbon monoxide poisoning.

The Providence Journal carried an article [see <http://www.firerescue1.com/print.asp?act=print&vid=102408> ] about a 50-year-old firefighter who had collapsed while fighting two house fires in Providence R.I. on 24 March 2006. Fortunately, the correct diagnosis of cyanide poisoning was made at the local hospital, and the firefighter was given the correct antidote. Other firefighters at the house fires also had elevated cyanide levels in their blood stream. But there have been many other instances where people have died as the result of inhalation of hydrogen cyanide produced during fires. Even with administration of an antidote, survivors can still suffer long-term damage to the nervous system.

The First Responder published a similar article in October 2003, titled "Fires: What's in That Smoke".

### Where Does the Hydrogen Cyanide Come From?

No, we are not talking about a release from a cylinder of hydrogen cyanide or someone adding acid or water to cyanide salts stored somewhere. We are talking about ordinary materials of everyday life (e.g. insulation, furniture coverings, carpets, even some clothing, etc.) which can release cyanide if they catch fire.

The culprit is nitrogen which makes up the combustible material. Even the nitrogen gas which makes up the major part of the air can contribute under the right circumstances to form a minute amount of cyanide during burning of combustibles. High temperatures and low oxygen concentrations favor the formation of cyanide gas. Smoke from the combustion of grass clippings, green wood, tobacco, cotton, paper, wool, silk, weeds, and animal carcasses will likely contain some hydrogen cyanide gas. But the real offender is from the combustion of man-made plastics and resins containing nitrogen, especially if the fire is hot and occurs in an enclosed space. Common man-made materials which generate cyanide gas during combustion include nylon, polyurethane, melamine, and acrylonitrile. These materials are present everywhere in building

furnishings and our vehicles, foam insulation, furniture, carpets, draperies, appliances, many plastics, and articles of clothing.

### How Much Hydrogen Cyanide Gas Can Kill?

The Occupational Safety and Health Administration (OSHA) website [see <http://www.osha.gov>] lists the threshold odor concentration for detection of hydrogen cyanide as 0.58 parts per million (ppm) by the most sensitive individuals, but firefighters and other exposed to smoke from burning materials will not be able to smell the gas. Also possibly 40% of the human population are unable to smell hydrogen cyanide because of genetic and other factors.

Hydrogen cyanide causes rapid death by metabolic asphyxiation. The Lethal Concentration in air (LC50, concentration estimated to kill 50% of people) require to kill humans (cited in the same OSHA website) depends upon the duration of exposure, as shown in table 1:

Table 1. LC50 in Air Estimated for Humans [source: Hathaway et al. 1991. Proctor and Hughes' Chemical Hazards of the Workplace. 3<sup>rd</sup> ed Van Nostrand Reinold, N.Y., N.Y.]

<b>LC50, ppm, estimated</b>	<b>Exposure Duration</b>
3404 ppm	1 minute
270 ppm	6 to 8 minutes
181 ppm	10 minutes
135 ppm	30 minutes

The numbers are a little misleading when applied to unprotected emergency responders because other chemicals in smoke such as carbon monoxide can have synergistic effects with hydrogen cyanide. Also, emergency responders will be breathing more heavily.

The American Conference of Governmental Industrial Hygienists reported (cited in same OSHA website) that workers exposed to hydrogen cyanide concentrations ranging from 4 to 12 ppm for 7 years reported increased headaches, weakness, changes in taste and smell, throat irritation, vomiting, effort dyspnea, lacrimation (tearing), abdominal colic, precordial pain, and nervous instability. Also workers exposed to low concentrations of hydrogen cyanide developed enlarged thyroid glands.

The OSHA permissible exposure limit (PEL) for hydrogen cyanide is 10 ppm as an 8-hour time-weighted average (TWA) concentration. The National Institute for Occupational Safety and Health (NIOSH) lists a lower limit of 4.7 ppm for worker short term exposure limit; the American Conference of Industrial Hygienists (ACGIH) has assigned 4.7 ppm as a worker ceiling limit. This is more conservative than OSHA. [the PEAC tool goes with the more conservative NIOSH/ACGIH listing of 4.7 ppm]. The word "SKIN" by the NIOSH and OSHA listing means that hydrogen cyanide can be absorbed also by the skin and eyes

in addition to inhalation. The NIOSH “Immediately Dangerous to Life and Health (IDLH)” listing for a 30-minute exposure is listed as 50 ppm for HCN. Recently, the IDLH level was lowered to 25 mg/m<sup>3</sup> as cyanide including inhaling salts. [reference <http://www.cdc.gov/niosh/idlh/cyanides.html>]. The lethal oral dose of cyanide salt for an adult (70 kg) is 50 to 100 mg as cyanide.

As mentioned before, hydrogen cyanide causes rapid death by metabolic asphyxiation. More precisely, cyanide prevents tissue utilization of oxygen by inhibiting the tissue enzyme cytochrome oxidase. Symptoms of acute exposure to cyanide include general weakness, headache, confusion, anxiety, and occasionally nausea and vomiting. Respiratory rate and depth may be initially increased but later become slow and gasping. Coma and convulsions may follow. Respiration may cease or become inadequate. If exposure is severe, collapse may be almost instantaneous followed by convulsions and unconsciousness and death.

### Symptoms of Exposure to Smoke Inhalation-associated Cyanide Poisoning

Firefighters and victims inhaling hydrogen cyanide associated with smoke as in the burning of plastic materials often experience cognitive dysfunction and drowsiness that can impair the ability to escape or to perform rescue operations. Exposure to low concentrations (or initial exposure to higher concentrations) may result in stupor, confusion, flushing, anxiety, perspiration, headache, drowsiness, tachypnea (rapid breathing), dyspnea (labored, uncomfortable breathing), and tachycardia (rapid heart rate, over 100 beats per minute in adult). Exposure to higher concentrations of hydrogen cyanide result in prostration, tremors, cardiac arrhythmia (irregular heartbeat), coma, respiratory depression, respiratory arrest, and cardiovascular collapse.

If the concentrations are high (>1,000 ppm), symptoms may occur 15 seconds after inhalation. Convulsions may occur in 15 to 30 seconds, and respiratory arrest in 2 or 3 minutes. Cardiac arrest follows within 6 to 8 minutes of exposure. If concentrations are lower, symptoms may not occur until after several minutes. Eventually respiratory and cardiac arrest occurs.

Other harmful chemicals may be in that smoke including carbon monoxide. Breathing the hot gas and smoke may cause thermal injury in the upper airway (mucosal damage, ethyema [abnormal redness due to inflammation], ulceration, and oedema [tissue swelling due to fluid buildup]). There may be blistering and soot deposits in the nose and mouth. There may be adsorption of other toxins. Upper airway oedema usually becomes apparent within 24 hours of injury and usually resolves itself within 3 to 5 days. Some toxins in the smoke irritate the bronchial mucosa causing airway inflammation, resulting in coughing, breathlessness, wheezing, and excess bronchial secretions. Pulmonary oedema (fluid buildup in lungs) may occur in severe cases.

Carbon monoxide binds to hemoglobin in the blood reducing the blood oxygen carrying capacity. The concentration of carboxyhemoglobin in the blood increases. The victim may suffer from both carbon monoxide and hydrogen cyanide poisoning.

### Distinguishing Between Hydrogen Cyanide and Carbon Monoxide Poisoning

Carbon monoxide poisoning is associated with malfunctioning furnaces, automobile exhaust, hot water heaters, kerosene heaters, and stoves, as well as fires. Carbon monoxide occurs when the combustion of fuel is incomplete. Hydrogen cyanide is associated with the burning of plastics, especially if the fire is hot and in a confined space. The burning of plastic materials in a confined space can also result in carbon monoxide.

Carbon monoxide concentrations of at least 1,500 ppm are associated with significant mortality. Ambient carbon monoxide concentrations can reach 1000 to 15,000 ppm during actual firefighting. Carbon monoxide poisoning is estimated to cause roughly 50% of all fire-related fatalities.

Many of the symptoms of exposure are the same for hydrogen cyanide and carbon monoxide: headache, nausea, vomiting, drowsiness, and poor coordination. In the case of mild carbon monoxide poisoning, the person recovers when moved to fresh air. Severe carbon monoxide poisoning will result in confusion, chest pain, shortness of breath, unconsciousness, and coma.

Differences between symptoms of hydrogen cyanide and carbon monoxide poisoning are subtle and difficult to characterize. Hydrogen cyanide inhalation will result in difficulty breathing, the person gasping for air even when he/she is brought out to fresh air whereas in the case of carbon monoxide poisoning he/she may simply feel sleepy but breath normally. A bright, red color of venous blood is a symptom of acute cyanide poisoning because of inability of tissue cells to utilize oxygen. Blood depleted in oxygen content will appear bluish or purple. Bright red skin and the absence of cyanosis (bluish or purple skin) have been described in patients with cyanide poisoning. Caution is indicated because cherry red skin may also be seen in some severe carbon monoxide poisoning cases [reference: Myers et al, "Cutaneous Blisters and Carbon Monoxide Poisoning, Ann. Emerg. Med. 14(6), 1985, pages 603-6]. Also, a firefighter may experience both hydrogen cyanide and carbon monoxide poisoning.

The eye pupils may be normal or slightly dilated in cyanide poisoning. There may be diaphoresis (excessive sweating).

Sometimes carbon monoxide poisoning is misdiagnosed as influenza. But influenza is accompanied with a fever, and carbon monoxide poisoning is not accompanied with a high temperature as the flu does. Caution here is still

required for diagnosis in the case of firefighters because the firefighting effort can still elevate the body temperature somewhat.

Blood tests can conclusively distinguish between carbon monoxide and hydrogen cyanide poisoning, but tests take time. The blood tests include:

- Measurement of blood oxygen concentration (hospitals and some responders have a device that attaches to the end of a finger) gives useful information but may be misleading. Pulse oximetry alone cannot distinguish between COHb and oxyhemoglobin and is not a reliable measurement of oxyhemoglobin saturation.
- Measurement of blood cyanide concentrations. Nonsmokers: < 0.02 µg/ml; smokers typically 0.04 to 0.05 µg/ml; toxic > 0.2 µg/ml; tachycardia and flushing 0.5 to 1 µg/ml; coma 1 to 2.5 µg/ml; death >3 µg/ml.
- Measurement of carboxyhaemoglobin (COHb) concentration. Normal COHb levels for non-smokers breathing clean air are 0.3% to 0.7% (e.g. 0.3% to 0.7% of hemoglobin is bound with carbon monoxide forming COGb). Smokers may be as high as 8%. COHb levels above 25% are considered toxic (symptoms: throbbing headache, slight confusion). COHb readings above 50% could result in unconsciousness. CoHb readings above 60% could result in death. Caution is indicated because patients receiving 100% oxygen treatment might have a normal COHb reading even though the carbon monoxide is not completely flushed out. Again, pulse oximetry is not a reliable estimate of oxyhemoglobin saturation.
- Measurement of carbon monoxide in the blood. If the person is breathing, some carbon monoxide may be detected in the gases exhaled.
- Measurement of plasma lactate concentration. A high plasma lactate (>10 mmol/L) in the absence of severe burns or hypotension is an indicator of cyanide toxicity.
- An increased mixed venous PO<sub>2</sub> and a decreased difference in arteriovenous oxygen content suggests concurrent carbon monoxide and hydrogen cyanide poisoning.

Funduscopy examination of eyes may reveal erythematous (reddish) retinal veins in the case of cyanide poisoning.

A portable carboxyhemoglobin oximeter (the RAD-57) is manufactured by Masimo Corporation in Irvine, California ([www.masimo.com](http://www.masimo.com)). It is also a pulse oximeter.

Technical details on Carbon monoxide poisoning and treatment can be obtained at the government website at <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~MCvzk8:1>. See also Postgraduate Medicine on line, vol 105(1), Jan. 1999, Carbon Monoxide Poisoning, at <http://www.postgradmed.com>.

Technical details on Hydrogen cyanide poisoning and treatment can be obtained at the government website at <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~k0AwBW:1>. See also Postgraduate Medicine on line, vol 105(2), Feb. 1999, Smoke Inhalation Injury, at <http://www.postgradmed.com>.

### Treatment

Remove the incapacitated person from the fire scene. If the person is wearing an air pack or other respiratory protection it should not be removed until after he/she is brought to clean air. Implement appropriate emergency treatment, including treatment of trauma.

Give high flow humidified oxygen to smoke inhalation victims. Consider early intubation if there is respiratory distress or coma. Consider early intubation if there are facial or neck burns, erythema (reddening of skin), blistering, or oedema (fluid buildup) in the oropharynx (airway).

Richard Alcortaf, MD, FACEP, and EMS director for Maryland Institute for Emergency Medical Systems, writes [see <http://www.fireresque1.com/hazards/articles/102410/>]:

“Prehospital management of acute cyanide poisoning in the smoke inhalation victim involves moving the victim from the source of exposure (while maintaining appropriate provider respiratory protection, SCBA), restoring or maintaining airway patency, administering 100% oxygen via non-rebreather mask or bag-valve mask technique, aggressive advanced airway management, including early intubation, providing cardiopulmonary support and stabilizing vital signs, including the use of trauma and burn management (Parkland formula). When clinically indicated, anticonvulsants (benzodiazepines) should be given for seizures, epinephrine and antiarrhythmics to stabilize cardiovascular function, and sodium bicarbonate to correct metabolic acidosis if known.”

These instructions are also similar to those recommended at the government TOXNET website for Emergency Medical Treatment for Carbon Monoxide {see <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./etemp/~MCvzk8:1:emt> }.

Teofilo L. Lee-Chiong Jr., MD, writes in the Feb. 1999 issue of Postgraduate Medicine [see [http://www.postgradmed.com/issues/1999/02\\_99/chiong.htm](http://www.postgradmed.com/issues/1999/02_99/chiong.htm)]:

“Most fatalities resulting from burn injuries can be attributed to smoke inhalation. Patients who were trapped in an enclosed space or lost consciousness during a fire are at increased risk for significant smoke inhalation. Prompt evaluation is important and can include chest films, pulmonary function testing, arterial blood gas analysis, and bronchoscopy. Positive findings require aggressive treatment with adequate oxygenation, ventilation, pulmonary toilet, and fluid resuscitation. “

The treatments for carbon monoxide poisoning and hydrogen cyanide poisoning are different after these initial steps described above. Treatment for cyanide requires administration of an antidote. Treatment for carbon monoxide requires

administration of oxygen until the carbon monoxide is flushed out of the system. The danger is that the standard treatment for cyanide (administration of amyl nitrite, thiosulfate, sodium nitrate) used in the United States has certain risks, among them being that it can worsen or be even fatal to a victim suffering from carbon monoxide poisoning. A safer antidote (hydroxocobalamin) has been used in France and other European countries. The decision is compounded because antidote administration must be started before all laboratory tests are available.

Treatment for carbon monoxide requires administration of oxygen. An increase in oxygen tension in the blood promotes the disassociation of carbon monoxide and hemoglobin. The carbon monoxide is excreted by the lungs. The half-life of carbon monoxide in the blood is 3 to 4 hours in room air, 30 to 40 minutes with 100% oxygen therapy, and 22 minutes with 2.5 atm hyperbaric oxygen therapy. There may also be complications in administering hyperbaric oxygen, and some physicians feel there is no distinct advantage over 100% oxygen. More details are at Postgraduate Medicine on line, vol 105(2), Feb. 1999, Smoke Inhalation Injury, at <http://www.postgradmed.com>.

Supportive oxygen treatment may benefit cyanide poisoning victims as well. Theoretically, oxygen will not rid or flush out cyanide from the body, and oxygen therapy should not help. In practice, oxygen treatment has helped in a number of cases with cyanide poisoning, especially with smoke inhalation situations where there is also some carbon monoxide poisoning.

#### Antidotes for Hydrogen Cyanide Poisoning

- Taylor Kit; Lilly Kit; Pasadena Kit: Amyl nitrate, thiosulfate, and sodium nitrite. The amyl nitrite is first administered via a mechanical ventilation device or by a gauze sponge for inhalation. This is followed by intravenous administration of sodium nitrite and thiosulfate. The nitrites supplied in the kit reduces the blood's oxygen-carrying capacity by binding with hemoglobin to form methemoglobin, which in turn binds and neutralizes cyanide. The problem is that the nitrite treatment also reduces the blood's capacity to carry oxygen which could be fatal to a victim with carbon monoxide poisoning. Another risk is that the antidote may cause severe hypotension (low blood pressure) leading to shock. Vomiting may occur. Amyl nitrite is also a controlled substance in the United States.
- Hydroxocobalamin (available in Europe as Cyanokit<sup>tm</sup>, Hydro Cobrex, Merck-Santé s.a.s). The Cyanokit<sup>tm</sup> kit contains two vials of 2.5 grams of hydroxocobalamin lyophilizate for reconstitution with 100 mL saline per vial and two sterile transfer kits which are injected intravenously. The usual dose in Europe is 70 mg of hydroxocobalamin per kg of body weight. The hydroxocobalamin neutralizes cyanide by fixing it to form cyanocobalamin (vitamin B12) which is excreted in the urine. It does not have the problem of reducing the blood's capacity to carry oxygen as in the case of nitrite administration. Hydroxocobalamin is red in color and

will turn the mucous membranes, skin, and urine red, which could interfere with clinical laboratory tests which depend on color.

- Dicobalt-EDTA (Kelocyanor) and 4-dimethylaminophenyl: Available in Europe and used prior to development of hydroxocobalamin treatment but has safety concerns similar to use of the Taylor kit.

Should the Taylor Kit be used for treatment of smoke inhalation victims if this is the only antidote available? Richard Alcortaf, MD, cited above, writes:

- Consider antidotal therapy if [cyanide poisoning] diagnosis is strongly suspected.
- Begin antidotal therapy without waiting for laboratory confirmation.
- Avoid the sodium nitrate portion of the Taylor cyanide antidote kit in patients with smoke inhalation unless the carboxyhemoglobin (COHb) concentration is very low (<10%).

Dr. Alcortaf further writes that injection of sodium nitrite portion of the Taylor kit involves online medical control. Anticonvulsants may be needed for general seizures. Vasopressors (e.g. epinephrine) are indicated for hypotension not responsive to a fluid challenge.

The use for hydroxocobalamin is expected to get fast track approval by the U.S. Food and Drug Administration for use in the United States for treatment of smoke inhalation victims, with possible approval by January 2007. The drug is already used to treat other medical conditions, but the doses required to treat cyanide are large. It is even available as a vitamin supplement (vitamin B12a). Dosages and adverse side effects are being studied with reference to cyanide poisoning. A treatment reported by Evanston Northwestern Healthcare [see <http://www.enh.org/healthandwellness/bioterrorism/hf065250.aspx?lid=1093>] under study in the United States uses a combination of hydroxocobalamin (4 grams) and sodium thiosulfate (8 grams) injected intravenously as a solution; a 5 gram dose of hydroxocobalamin appears to bind all cyanide ions in patients with initial cyanide levels up to 40  $\mu\text{mol/L}$  (= 1  $\mu\text{g/ml}$ ). Co-administration of folic acid may be required. Possible adverse side effects with patients using certain other medications need to be better defined. The study notes reddening of the skin, stools, and urine as side effects along with possible pulmonary edema, diarrhea, and anaphylactoid reactions (adverse immunologic response) in some patients.

A French study examined the results of prehospital use of hydroxocobalamin by the Paris Fire Brigade during the period Jan. 1998 to Dec. 2002 [reported in <http://www.jems.com/data/pdf/smoke-poisoning.pdf>]. Over this period, hydroxocobalamin (usually a 5 gram dose) was administered to 81 smoke inhalation patients in structural or closed space fires; of these patients, 70 recovered cardiac and/or respiratory function at the fire scene and 11 patients died. Of the 81 patients, 29 were in cardiac arrest before hydroxocobalamin administration, and of the 29 patients, 18 spontaneously recovered following hydroxocobalamin (plus adrenalin and supportive care) administration in an

average time of 19.3 minutes. Twelve (12) of 15 patients were hemodynamically unstable (systolic blood pressure < 90 mm Hg) recovered systolic blood pressure in an average of 29 minutes after hydroxocobalamin infusion.

Additional reading: see <http://emedicine.com/emerg/topic118.htm>

### Respiratory Protection Required

Firefighters and other emergency response personnel must wear airpacks / SCBA when entering a building or any confined area where a fire is taking place. The danger of hydrogen cyanide and/or carbon monoxide poisoning is very real even after the fire is out but the structure and contents are still smoldering. Theoretically, 10 pounds of furnishings based on acrylonitrile-type polymer could under air-starved conditions form as much 5 pounds of hydrogen cyanide. In a room measuring say 20 by 30 feet and 9 feet high, the concentration of hydrogen cyanide might reach in the ballpark of 14,000 ppm (more or less depending upon what the temperature is in the room). Considering that a concentration of 3,400 ppm can kill in one minute and a concentration of 180 ppm can kill in 10 minutes, air packs are required when entering structures or other confined spaces. Concentrations of carbon monoxide might also be high, in excess of 1,000 ppm.

Occupational Safety and Health Administration regulations (see 29 CFR 1910.1000) require the use of a full-facepiece, pressure demand self-contained breathing apparatus (SCBA) meeting the requirement of the National Fire Protection Association Standard 1981 (see rules for Open-Circuit Self-Contained Breathing Apparatus for Fire Fighters available at <http://www.nfpa.org>) when entering structures in firefighting efforts.

Even if firefighters do not enter the structure and remains outside, there have been instances of hydrogen cyanide poisoning when SCBA is not used.

An air-purifying respirator using a cartridge will not provide adequate protection against either carbon monoxide or hydrogen cyanide. Some may provide limited protection against hydrogen cyanide, but none are certified for firefighting use.

Dr. Richard Alcorta, referenced earlier, estimated that smoke inhalation causes between 5,000 and 10,000 deaths annually in the United States, plus more than 23,000 injuries including 5,000 firefighters. Hydrogen cyanide poisoning or the combination of hydrogen cyanide and carbon monoxide poisoning is believed to play a significant role in these deaths.