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The Toxic Twins: An Advance Perspective On Cyanide and Carbon Monoxide Poisoning





The Toxic Twins: Hydrogen Cyanide and Carbon Monoxide - A Brief Review

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Cyanide (CN)

Cyanide and carbon monoxide (CO) are properly studied in the discipline of toxicology, the study of poisons, i.e. substances that have deleterious effects on the body. Cyanide is probably the most famous poison of murder mysteries and of legend. It is extremely poisonous to all aerobic organisms, and certainly to all mammals including man. As you will see, it has similar acute and long term physiologic effects to that of CO, but when present is usually more poisonous and elusive than its toxic twin.

Physical Properties

Cyanide is encountered by humans in a number of different forms. These include solids, liquids and gases. Hydrogen cyanide (HCN) is also known as hydrocyanic acid or prussic acid. It is a pale blue liquid or colorless gas, with a characteristic odor of bitter almonds. The molecular weight is 27.03 (44.44% carbon, 3.73% hydrogen, 51.83% nitrogen). It burns in air with a blue flame. The density of the gas is 0.941 (relative to air), i.e. is slightly lighter. The melting point is -13.4° C; the boiling point is 25.6° C. Thus, HCN is usually a gas at the temperatures we would encounter it. It is soluble in water and slightly soluble in ether. Cyanide is chemically unstable, but can be stabilized by the addition of sulfuric or phosphoric acids.

Sources of Cyanide

Both industrial and natural products are sources of human CN poisoning. In industrial settings, CN can be encountered during fumigation of structures and agricultural crops, in metal treatment operations, blast furnace and coke oven operations, metal ore processing, printing and photoengraving operations, in electronics manufacture, and in the production of acrylic plastics, nylon, chelating agents, dyes and pharmaceuticals. The thermal decomposition of polyurethane foam, nylon, asphalt, synthetic rubber, and natural fabrics such as wool and silk result in HCN release. It is also found in cigarette smoke, metal polishes, magnesium cyanide ("Cymag"), and nail glue remover (i.e. acetonitrile). Cyanide is naturally found in the leaves, fruit, flowers, bark and seeds of cherry laurel, chokecherry, wild black cherry, plums, peaches and apricots, the seeds of apples, pears and cranapples, in Johnson, Sorghum, Sudan and Arrow grasses, in flax and yellow pine flax, in elderberry, hydrangea, bamboo and cycad, and in lima beans and linseeds. Cyanide occurs in the medicinal drugs Laetrile, nitriles, succinonitrile and nitroprusside.

Cyanide In Fire Products

Clark and collaborators in 1981 studied blood CN and carboxyhemoglobin (COHb) concentrations in 53 fire survivors presenting at a hospital emergency department, 36 of whom had clinical evidence of smoke inhalation. Mean COHb saturation was 14.5%, which was greater ($P<0.005$) than in patients with no evidence of smoke inhalation. Mean CN level was 25.8 umol/L (range 2.0-126), which was greater ($p<0.05$) than in the non-smoke-inhalation group. Three patients with raised COHb levels showed normal CN levels. No patients with normal COHb concentrations had above-normal CN levels. The blood samples were taken 2-3 hours after exposure. The close relationship between CN and COHb levels was used to identify patients in need of immediate treatment for CN poisoning. Of 24 patients with minor smoke inhalation, only two showed a COHb level above the upper limit of normal for

their respective smoking categories. Several of the patients with high CN levels in this study were apneic (not breathing) and moribund (not moving, dying) on arrival, requiring emergency resuscitation, which involved assisted ventilation, intensive care, and treatment of their metabolic acidosis. Several patients were also found to have cardiac dysrhythmias, renal failure, neurological sequelae, and subsequent psychiatric sequelae. Five died from severe smoke inhalation after hospital admission.

Cyanide levels have been found to be significantly elevated in fatalities and in non-fatal cases in firefighters and civilians exposed to smoke. Seventy-eight percent of fatalities had elevated CN levels, 31% with levels that would have caused toxic effects, and, of these, 12% were likely to have symptoms of severe CN poisoning. No additive or synergistic effects were observed in the fatalities between CN and other factors such as CO, ethanol, victim age, or the presence of heart disease. More recently, it was found that 50% of people killed in building fires had been exposed to toxic levels of HCN, and 90% to toxic levels of CO. Lethal concentrations of CO were found in 83% of the victims. They concluded that while CO may be more important than HCN as a toxic fire agent, CN poisoning without CO poisoning may, in certain situations, cause death in fire victims.

Baud (1991) found a significant correlation between the concentrations of plasma lactate and CN in victims of smoke inhalation. Blood samples were obtained from 109 victims of residential fires. The metabolic effect of smoke inhalation was assessed in 39 patients without severe burns, on the basis of plasma lactate at the time of hospital admission. They found that 66 surviving and 43 non-surviving fire victims had significantly higher CN levels than controls. Among the 43 non-survivors, the blood CN concentrations were above 40 umol/L in 32 victims, and above 100 umol/L in 20. The correlation of plasma lactate with blood CN level was better ($r=0.55$, $P<0.001$) than with CO concentration ($r=0.38$, $P<0.001$). They concluded that a plasma lactate concentration above 10 mmol/L is a good indicator of CN intoxication. In rat studies conducted by this author in 1993, a similar relationship between the severity of CN poisoning and blood lactic acid concentration was found.

Physiological Effects

Cyanide can affect the body if inhaled (as HCN or another gas or vapor), contacts the eyes, skin, or is swallowed. It is one of the quickest acting poisons, inhibiting vital mitochondrial oxidation-reduction reactions, resulting in loss of cellular energy generation. The effects are most strongly felt by the central nervous system, often producing respiratory paralysis. Cardiac irregularities are commonly observed, but pulmonary failure usually precedes cardiac failure. Because oxygen cannot be utilized by the tissues in the presence of CN, venous PO_2 rises and the blood appears red in color (i.e. becomes arterialized). Two to four out of ten people are incapable of smelling HCN.

Most human acute CN poisonings, many involving ingestion of a CN solid, result from accidents, suicides or homicides. Four fatal CN poisonings occurred in the state of Washington in 1991 as the result of product tampering with over-the-counter cold medication. During the period 1986 through 1992, the average reported fatalities from acute CN poisoning annually in the USA was 8.3. These data do not include individuals dying of CN poisoning as the result of fire. Many other cases probably go unreported or are undiagnosed. You will note that the number of fatalities caused by CN is only a tiny fraction of the number of people dying each year from CO poisoning (>2000).

One natural source of CN is plants that contain amygdalin, a substance that is hydrolyzed to CN in the gastrointestinal tract. The increased usage of Laetrile as an anti-cancer drug, and sodium nitroprusside as a vasodilator, has led to more reports of toxicity and death from the prolonged use and administration of large doses. Physicians have recently become aware once again of the potential for CN poisoning and the litigation resulting from over-prescribing or the accidental or willful overdosing with nitroprusside. There are estimates of as many as 1,000 excess deaths per year due to nitroprusside-induced CN poisoning, and 3,000 cases of CN toxicity in patients undergoing bypass.

The co-administration of sodium thiosulfate may eliminate the possibility of CN intoxication without altering the efficacy of nitroprusside. This approach is used in Europe. A review suggests hydroxycobalamin as the agent of choice in the treatment of nitroprusside-induced CN toxicity. Although one study concludes that the overall incidence of nitroprusside-induced CN poisoning is low, risk factors such as hypoalbuminemia, cardiopulmonary bypass procedures, hepatic or renal dysfunction, or the use of moderate to high

doses of nitroprusside should be recognized.

Cyanide produces histotoxic cellular hypoxia by initially binding to the protein portion of cytochrome oxidase and then to the ferric form of iron. This reaction forms a relatively stable but reversible complex. In the human body over 40 enzyme systems are potentially inactivated by CN. The most important of these are the cytochrome oxidases. This intramitochondrial system consists of the cytochrome a-a3 complex of the electron transport chain. Through binding to this enzyme complex, CN inhibits electron transfer to molecular oxygen, thus blocking ATP generation (i.e. the cellular energy currency). This results in the reduced cellular utilization of oxygen and increased venous PO_2. The impairment of cellular oxygen utilization reduces aerobic respiration with a decrease in pyruvate conversion in the Krebs citrate cycle. Lactic acid formation then increases, producing metabolic acidosis.

Ansell and Lewis (1970) reviewed body levels of CN in non-fatal and fatal cases of CN poisoning. They mention that the minimum human lethal dose is approximately 150 mg for sodium CN, 200 mg for KCN, and 100 mg/150 lbs for HCN. Nevertheless, factors such as age, body mass, state of health, and mode of ingestion alter these values. On this point, 37 mg of HCN has proved fatal, while recovery has been made from as much as 300 mg. Survival was reported without sequelae in a man exposed to HCN at 500 mg/m^3 over 6 minutes. Cyanide acts very quickly – faster than CO (see below).

As noted above, CN attacks the energy generating machinery in cells, preventing further operation. It also binds to myoglobin in muscle and hemoglobin in the blood, especially the methemoglobin form. Elimination of CN from the body involves the very rapid washout of gaseous HCN via the lungs, and excretion of small amounts in the urine, its incorporation into cyanocobalamin (vitamin B12), its oxidation to formate and carbon dioxide, and its incorporation into cysteine. Eighty percent of the detoxification takes place by conversion of CN to the SCN (thiocyanate) ion by an enzymatic reaction involving rhodanase and mercaptopyruvate sulfur transferase. The resulting thiocyanate is then excreted by the kidneys. This reaction is accelerated by sulfur, which can be supplied in the form of sodium thiosulfate. As stated, the washout process for HCN is very rapid, with a half-life of less than one hour. This is one-fourth to one-fifth that for CO. This means that accurate measurement of HCN in the blood of victims by hospitals is virtually impossible unless blood is drawn on-site, or monitored there electronically.



Symptoms of Cyanide Poisoning

The rapid and early recognition of CN poisoning is usually difficult because most of the clinical manifestations are non-specific. Potentially valuable CN blood levels are often not available for confirmation of a diagnosis. Arteriolization of the venous blood is considered to be a significant symptom in CN poisoning. Symptoms begin with headache, ataxia and nausea followed by dyspnea, palpitations, convulsions and unconsciousness as seen in **Table 1**. The symptoms are similar, but not identical to those of CO poisoning. The burning taste and odor, throat discomfort, salivation, giddiness, etc. with CN are not present with CO. Carbon Monoxide, unlike CN, does not stimulate hyperventilation, so there is no hyperpnea or tachypnea. Due to the presence of other irritant substances, smoke particulates, heat, increased work level, etc. in firefighter situations, it is virtually impossible to differentiate CN from CO poisoning in the field.

Table 1: Symptoms of cyanide poisoning

■ LOW LEVELS	Bitter almond odor on breath Burning taste Feeling of constriction or numbness in throat Salivation, nausea and vomiting Anxiety, confusion, vertigo, ataxia and giddiness Stiffness in lower jaw Weakness and headache
■ MODERATE LEVELS	Hypernea, dyspnea Rapid then slow irregular respiration Short inspiration with prolonged expiration Tachycardia, tachypnea
■ HIGH LEVELS	Loss of consciousness Venous oxygen saturation elevated Lactic acidosis often present Prolonged expiratory phase Transient respiratory stimulation, then respiratory failure Coma Cardiac arrhythmias Convulsions Hypotension Opisthotonos Involuntary micturition Defecation Paralysis Sweating Protruding eyeballs Pupils dilated and unreactive Foam around mouth with blood Skin-color may be brick-red Bradycardia, respiratory arrest Death often occurs in <10 min

Table 2: Range of cyanide toxicity in terms of blood cyanide concentration

ug/dl	umol/liter	Symptoms
0-30	0-11	Normal
0.05-0.50	5-50	Smokers
0.5-1.0	50-100	Hyperventilation, tachycardia
1.0-3.0	100-300	Decreased mental state which may be fatal
>3.0	>300	Fatal unless treated

Cyanide is a very fast acting poison. The inhalation of HCN produces reactions within a few seconds and death within minutes. Oral CN poisoning may be rapidly lethal. The mortality rate is high, but in non-fatal cases, recovery may be complete. The range of CN toxicity in terms of blood CN concentration is seen in Table 2. Ingestion of plants containing amygdalin, which is converted to CN in the gastrointestinal tract, may require as long as 12 hours before symptoms develop. Skin exposure to CN is rare and usually requires large surface areas. The reaction involving skin absorption is usually delayed.

Cardiac Effects

The effect of lethal doses of CN in humans was studied through the recording of the ECGs of four men executed by inhalation of HCN. Initially high heart rates (102-166 bpm) fell markedly, reaching a nadir between 1-3 minutes into the poisoning. This was accompanied by sinus irregularity and the complete loss of P waves. During the period of auricular arrest, the rhythm was A-V nodal in two subjects and idioventricular in the other two. Heart rate increased somewhat below control levels during the third and fourth minutes along with the irregular reappearance of P-waves, some of which were not conducted. All the men showed A-V dissociation with a secondary decrease in rate during the fifth minute. In the sixth and seventh minutes, heart rate tended to return to a normal sinus rhythm. Heart rate slowed progressively afterward. T-waves showed an early but transient increase in amplitude, and a progressive shortening of the ST-segment occurred to the point of disappearance. Near death, the T-waves

originated high on the R wave. The investigators suggest that the early changes are due to reflex (i.e. central, neurogenic) effects of CN, whereas the later changes are due to the toxic myocardial action of CN, plus the effect of hypoxia.

Longterm CNS Effects

A number of long-term effects of CN poisoning have been identified. These include alteration of brain metabolites, demyelinating lesions of the brain, encephalopathy such as a Parkinsonian-like syndrome, neuropsychological sequelae, ultrastructural changes of the myocardium, and goiter.

A severe Parkinsonian syndrome characterized primarily by akinesia and rigidity was reported in an 18-year-old man who ingested 975-1300 mg of KCN. At autopsy 19 months later, damage was evident in the globus pallidus and putamen (deep areas of the brain). Severe Parkinsonism and progressive dystonia (abnormal movement) were reported in a 39-year-old man following attempted suicide with sodium CN. Bilateral lucencies (i.e. brightness) in the putamen and external globus pallidus were seen with computed tomography (CT). In another case, a 46-year-old woman poisoned with CN survived, but showed progressive Parkinsonism, dystonia and apraxia of eye opening. CT and magnetic resonance imaging (MRI) showed lesions in the basal ganglia, cerebellum and cerebral cortex (outer layer of brain) consistent with reported pathological findings.

A 28-year-old man who survived CN poisoning only with intensive medical intervention, went on to develop severe Parkinsonian symptoms, including profound micrographia and hypersalivation. Bilateral, symmetrical basal ganglia alterations were observed using MRI. A 46-year-old man who ingested 1.5 g of KCN survived, but went on to develop severe Parkinsonian syndrome. MRI revealed damage in the globus pallidus and posterior putamen and a 6-fluorodopa positron emission tomographic study found bilateral decreased uptake in the basal ganglia. Damage to the putamen has also been reported in two other cases of CN poisoning suicide attempts, where one subject previously suffered from temporal lobe epilepsy. Not unlike acute severe CO poisoning, CN poisoning clearly impacts discrete brain regions (e.g. globus pallidus, putamen, basal ganglia, cerebral cortex).

Treatment

Artificial respiration is often used in the treatment of CN poisoning. Although useful, oxygen is not a specific antidote. It is theorized that oxygen therapy increases the rate of displacement of CN from cytochrome oxidase and the increased intracellular oxygen tension non-enzymatically converts the reduced cytochrome to the oxidized species, enabling the electron transport system to again function and generate energy.

Some studies report the successful use of hyperbaric oxygen (HBO) therapy. For example, KCN poisoning in a 43-year old chemist produced convulsions, cardiac arrest, massive lactic acidosis, and rhabdomyolysis. The use of 100% oxygen, vascular volume expansion, bicarbonate infusion and anticonvulsant drugs resulted in complete recovery.

A small fraction of the circulating hemoglobin is normally in the form of methemoglobin, where the iron is in the ferric rather than the ferrous state. As such, it competes with cytochrome oxidase for CN and acts to "mop up" available CN by forming the dissociable cyanmethemoglobin complex. While the therapeutic elevation of methemoglobin is one strategy, it also diminishes the oxygen carrying-capacity of the blood, which may act to compound tissue hypoxia. Therefore, it is recommended that methemoglobin be kept below 40-50%. Later, as CN is released from the complex in response to decreasing plasma concentration, it becomes available for metabolic detoxification. Methemoglobin is reconverted to ferrous hemoglobin by intra-erythrocytic enzymes.

Sodium nitrite has been used as a CN antidote, since it is a methemoglobin-forming agent; however, it acts slowly as seen in **Table 3**. Nitrites and sodium thiosulfate also sharply lower blood pressure by inducing vasodilation, and this may contribute to cardiovascular collapse.

One method of medical management of CN poisoning involves the inhalation of amyl nitrite for 15-30 sec of every minute, then the injection of sodium thiosulfate (adult, 10 ml of a 3% solution) over two to four minutes. Various drugs may also be given for blood pressure maintenance. Orally-ingested CN is treated by administering syrup of ipecac and/or using gastric lavage if the patient is asymptomatic.

When the nitrite-thiosulfate combination therapy is used as the antidote for CN poisoning in children, a body weight appropriate dose must be chosen lest lethal methemoglobinemia results. With a blood hemoglobin of 12 g/dL, an appropriate dose is 10 mg/kg immediately and 5 mg/kg repeated within 30 min,

Table 3: Antidotes for acute cyanide poisoning

■ Amyl nitrite	Used with thiosulfate; conversion of fraction of hemoglobin to methemoglobin
■ Sodium nitrite	Used with thiosulfate; conversion of fraction of hemoglobin to methemoglobin
■ Sodium thiosulfate	Used with nitrite; increases rate of conversion of cyanide to thiocyanate
■ Aminophenols	Have not been available in USA
■ Methylene blue	Inferior to nitrite
■ Sodium cobaltinitrite $Na3Co(NO_2)6$	Methemoglobin formation by dissociable nitrite
■ Cobalt gluconate, acetate, chloride	Successful in treating human CN poisoning
■ Hydroxocobalamin (aquacobalamin, vitamin B12a)	Reacts with CN to form Vitamin B12 or cyanocobalamin, does not impair oxygen-carrying capacity or cause hypotension; not available in USA
■ Oxygen	1 ATM used supportively with nitrite-thiosulfate antidotes

if necessary.

Cobalt EDTA has been used to treat three cases of HCN poisoning. Because of the possible side effects of cobalt itself (e.g. profuse diaphoresis, angina, nausea, vomiting, ectopic heart beats), it is suggested that this therapy be reserved only for patients with the most severe forms of CN poisoning, and that all others be treated with nitrite-thiosulfate.

Intravenous administration of hydroxycobalamin has been found to sharply decrease whole blood CN levels and to increase urinary CN excretion, whether used alone or with sodium thiosulfate. Its use was associated with a transient reddish discoloration of the skin, mucous membranes, and urine, and with modest hypertension and bradycardia. It did not produce the nausea, vomiting, or localized burning, muscle cramping or twitching at the infusion site, which occurs with sodium thiosulfate. Hydroxycobalamin was recently given in high doses to victims of residential fires and was well tolerated. It is recommended as an antidote for CN poisoning during the pre-hospital stage.

Carbon Monoxide (CO)

Carbon monoxide is a colorless, odorless, tasteless flammable gas that is exceptionally lethal to warm-blooded animals. It is totally undetectable by unaided humans. Electronic or chemical devices are necessary for people to be made aware of its presence. There are many common misconceptions about this gas, a few of which will be discussed here.

Physical Properties

Structurally, CO consists of a carbon atom triply bonded to an oxygen atom, resulting in a molecule roughly the shape and size of diatomic oxygen (O_2). The melting point of CO is -199°C and it boils at -191.5°C. Its density at 0°C, at 1 atmosphere, is 1.250 g/L and its specific gravity relative to air is 0.967. Carbon monoxide burns with a bright blue flame to produce carbon dioxide (CO_2). Under ordinary conditions, CO is quite inert, apart from its tenacious binding to heme in hemoglobin and myoglobin. However, it is a powerful reducing agent at higher temperatures or in the presence of catalysts, and is a valuable tool in many commercial applications.

Sources of Carbon Monoxide

Carbon monoxide is produced when carbonaceous materials are burned with insufficient oxygen, or in high-temperature reduction. Even what appear to be normally combusting fuels involve the production of some CO. Man-made CO accounts for most of that gas in the atmosphere

(motor vehicle exhaust, fumes from industrial plants, cigarette smoke, human caused fires and the burning of solid waste, defective household heating and cooking appliances, the detonation of explosives); natural sources also exist (volcanic gases, marsh gases, forest fires, breakdown of heme, vegetation during seed germination, marine brown algae) but they contribute very little to the overall atmospheric CO level.

Physiological Effects

In the third century B.C. Aristotle noted that "Coal fumes lead to heavy head and death." Today, CO is responsible for more deaths than any other single poison in our environment, over 2000 annually in the USA. Several hundred thousand people are exposed annually, and 20-40% of survivors suffer immediate or delayed neuropsychological deficits and other health damage. Its virulence is a result of the reversible reaction between CO and the heme moiety in blood hemoglobin. The affinity of CO for isolated heme is approximately 25,000 times that of oxygen. Hemoglobin and myoglobin, the major heme-carrying molecules in the body, have evolved such that the shape of the molecule forces CO and oxygen to bind at an angle. This reduces the affinity of CO to 250 times that of oxygen in these molecules. This prevents the small amount of CO produced endogenously in the body from displacing large quantities of oxygen in the blood. Still, relatively small quantities of CO can displace much of the oxygen carried by hemoglobin and myoglobin in the blood by the reversible reaction:

$HbO_2 + CO \ <---> \ HbCO + O_2$

It is this reaction upon which the famous Haldane equation is based. The reduction of the oxygen-carrying capacity of the blood leads to inadequate oxygenation of cells, tissues, and organs, i.e. "hypoxic stress". The brain is especially susceptible to hypoxia, but the subtle neurological effects of CO may prevent a victim from being aware of the danger. Eventually, brain function is depressed to the point where collapse and incapacitation occurs, followed by unconsciousness. If rescue does not occur, death will surely occur as pulmonary and cardiac functions fail due to lack of oxygen delivery. Recovery from CO poisoning, even with proper immediate therapy does not guarantee that irreversible brain damage will not have been done.

Passage through lung alveoli are virtually the only route of CO absorption into the body. The normal person has 0.4% to 1.4% COHb in his/her blood. A one-pack-per-day smoker may have up 5% COHb, enough to pose a serious threat to health. Recent epidemiologic studies show decreased cognitive ability in longtime smokers, possibly associated with cigarette-induced CO poisoning.



Symptoms of Carbon Monoxide

Recognizing the onset of CO poisoning is crucial, as it can be fatal in just a few minutes. The symptoms are usually non-specific and appear to involve many of the body systems. Common symptoms are headache, lethargy/fatigue, nausea, dizziness, confusion, etc. A victim may also suffer from shortness of breath, cardiac palpitations, convulsion, paralysis, loss of consciousness, coma and

eventually death. Table 4 lists many symptoms as they relate to blood HbCO levels, although this relationship in practice is quite poor. There is no hyperventilation, increased salivation, taste, odor, eye watering, or coughing, as HCN usually produces. Age, anemia, increased elevation, cardiopulmonary disease, and prior exposure to CO can increase the susceptibility to CO toxicity. The median level of COHb in people dying of uncomplicated CO poisoning is 53-55 percent.

An important key to identifying CO poisoning is the victim's environment and immediate past living or work situation. Was the victim exposed to sources of CO such as uncontrolled fires, motor vehicles, fuel-burning heaters or other internal combustion engines in a poorly ventilated room? Are others in that environment (e.g. family members living in the same house, pets) displaying similar symptoms? These facts are critical in accurately identifying CO poisoning.

Treatment

First and foremost, the victim must be moved out of the contaminated area and into fresh air. Eventually, the CO will be washed out of the blood through normal ventilation, although often serious health damage may be done before this can occur, so emergency measures should be started immediately.

In 1895, John Scott Haldane demonstrated that rats survive CO poisoning when placed in oxygen at two atmospheres pressure. In 1942 End and Long treated CO poisoning in experimental animals with HBO. The first human clinical use of HBO therapy in CO poisoning was by Smith and Sharp in 1960. This type of therapy is now strongly recommended for most seriously, acutely CO poisoned victims, but must be initiated immediately (<12 hrs.) upon reaching a healthcare facility.

The Combined Effects of CN and CO

Because CN and CO inhibit cellular energy generation, albeit by somewhat different mechanisms (CN inside cells, CO primarily in blood), it would not be expected that much of an additive or synergistic interaction would occur. This is because one or the other poison would determine the rate-limiting step. However, animal studies show some degree of additivity. In primates, time to incapacitation by HCN is reduced by the presence of high CO concentrations. One reason is that the CN-induced hyperventilation increases the rate of uptake of both CN and CO. This is likely also why the uptake-effects plot for CN is quite different from that of CO alone, which does not cause hyperventilation (either tachypnea or hyperpnea). At low CN concentrations (<100 ppm) time to incapacitation is >20 minutes, but at higher CN concentrations (e.g. 200 ppm), the time to incapacitation is very short, around two minutes. Therefore, HCN is a very rapid "knock-down" gas in fires unlike CO which usually acts over the longer term (see Chapt. 7, Penney, 2000). Once you are incapacitated by CN, you will continue to take up CO as long as you are alive. This is why it is thought that the majority of deaths occur due to CO, while CN is right behind it.

Other components of fire smoke also influence the uptake of CN and CO, thus may have other additive toxic effects. Carbon dioxide and reduced oxygen in the air stimulate ventilation, both rate and depth, thus increasing uptake of all smoke components. Physical work and heat do the same. The toxic effects of CO have been shown to be greater in humans working in heat. These factors do two things with regard to CO: 1) increase the uptake rate into the blood, and 2) produce a higher final COHb level. Irritant gases such as HCl, the sulfur oxides, the nitrogen oxides, acrolein, etc. on the other hand tend to dampen hyperventilation, i.e. decrease air flow through of the unprotected lung, and thus my reduce rate of uptake of CN and CO.



Table 4: Symptoms of carbon monoxide poisoning as related to carboxyhemoglobin levels in the blood

Blood HbCO	Symptoms
■ <5%	Usually no obvious symptoms Decreased birth weight after chronic exposure of pregnant women Many abnormalities seen in adults / children in epidemiologic studies
■ 5%-10%	Decreased tolerance for exercise in persons with pulmonary disease Decreased angina threshold Decreased ability to use oxygen at high work rates in normal people
■ 10%-20%	Headache Nausea Dizziness Lethargy / fatigue Confusion Decreased visual acuity Death can occur at COHb levels in this range
■ 20%-30%	Severe headache Shortness of breath Vomiting, diarrhea Vertigo Irritability Impaired judgment Other visual disturbances Hearing problems Incapacitation at high physical work levels
■ 30%-40%	Decreased awareness of environment Cardiac irregularities Muscular weakness Incapacitation / collapse (death is virtually certain unless rescue occurs) Paralysis
■ 40%-50%	Loss of consciousness Altered breathing Convulsions Pulmonary congestion
■ 50%-60%	COHb range most frequently found at death Continued coma Suppression of pulmonary and heart function
■ 60%-70%	Continued coma Usually death occurs in a few minutes
■ >70%	Almost immediately fatal COHb values may reach 85%

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Dr. Penney's published works on carbon monoxide include more than 65 peer-reviewed research articles, several dozen other articles and abstracts, a number of review articles, book chapters, and four books in print. He is the leading author of published research articles and books on the topic of CO toxicology.

Currently, Dr. Penney assists Underwriters Laboratory (UL) as a medical expert on CO and in establishing standards for CO alarms and other gas monitoring equipment. He is also currently working with the World Health Organization (WHO) to evaluate indoor air quality and produce world-wide standards.

Dr. Penney's professional interests have been focused on carbon monoxide for more than 39 years, in both animal models and humans. His special interests focus on chronic CO poisoning, education of the public about the dangers of CO poisoning, the diagnosis and management of CO poisoning victims, and the medico-legal aspects of carbon monoxide toxicology.

Dr. Penney has assisted many national and international government and non-government agencies in matters involving carbon monoxide. He was among the earliest consultants to the U.S. Environmental Protection Agency (EPA) in 1975 in setting CO standards for outside air and evaluating the effects of CO on humans under various conditions. He assisted the WHO in the late 1990s in setting similar standards for the world. He has worked with the Australian Medical Association (AMA) and with other concerned groups in Australia to attempt to stem the tide of suicides involving CO.

Dr. Penney obtained his Bachelor of Science degree from Wayne State University in 1963 and his Master of Science and Ph.D. degrees from the University of California, Los Angeles, in 1966 and 1969, respectively. Before going to Wayne State University in 1977, he was a faculty member at the University of Illinois, Chicago. With his wife, Linda Mae Penney, the couple has six children.

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