To: Rep. Kelly Moller, Chair
Minnesota House of Representatives
Committee on Public Safety, Finance and Policy

From: Leslie L. Lienemann
351 Sophia Ave. E.
Maplewood, MN 55117
612-597-2024

Re: Committee Hearing on HF406 (Berg)
Tuesday, February 28, 2023 at 10:30 a.m.
Room 200 SOB

I am an advocate who will be testifying in favor of HF406, a bill to require hotels to install carbon monoxide detectors in each guest room used for sleeping. I will testify about carbon monoxide poisoning injuries my son and I suffered while sleeping in a hotel and our continued health issues. I would like to provide the committee with background materials relative to understanding the scope of the existing threat, cause of the threat, status of the law and number of past injuries.

Problem:

Carbon Monoxide is a deadly gas that causes immediate injuries ranging from headaches, dizziness and vomiting to unconsciousness and death, with potential long-term injuries including headache, fatigue, dizziness, and varying degrees of brain injury. See, CDC Clinical Guidance for Carbon Monoxide Poisoning, attached hereto. Carbon Monoxide is a particular risk during sleeping hours, as people can become incapacitated while sleeping. For this reason, hotel facilities are frequent sites of carbon monoxide injuries.

No CO detector requirement: No states require installation of carbon monoxide detectors in each individual hotel sleeping room. A few states require CO detectors in hallways or in areas near gas burning appliances. These provisions are inadequate to prevent injury, as demonstrated by the frequency of carbon monoxide injuries detailed in the attached materials. In addition, carbon monoxide gas can be introduced by motor vehicles running outside the hotel or in attached parking structures, can permeate drywall and can travel across hallways and in ceiling, floor, and other spaces, making CO detectors localized to maintenance areas inadequate to alert sleeping guests.

No reporting requirement: Hotels are not required to report carbon monoxide leaks or injuries. Fire departments may voluntarily report leaks to the National Fire Incident Reporting System (NFIRS), https://nfirs.fema.gov, but are not required to do so, and are not required to report injuries. As an example, my injuries were not reported to the NFIRS by the Warren, Michigan police and fire departments, despite each agency responding to the scene and generating reports documenting the CO leak.

Data on carbon monoxide poisoning is often not made public. See, Jenkins Foundation Data, submitted herewith, for a compilation of data generated by that foundation based upon publicly available information.

According to data compiled by REM Consultants and published on their website www.remrisk.com (see below), there were at least 15 carbon monoxide leaks at Minnesota hotels in the years 2019-2020, with injuries identified as "unknown."

Who is at risk:

Hotel guests: Every individual sleeping in a hotel room without a carbon monoxide detector

Hotel employees: Every employee of a hotel without carbon monoxide detector

Emergency Personnel: Emergency personnel are often called to the scene after report of an ill guest, without knowing the cause of the injury, subjecting them to dangerous levels of carbon monoxide poisoning.

My Personal Story:

In July of 2019, I traveled to Michigan with my then-eighteen-year-old son so that he could compete in a NAHL junior hockey tryout camp. We checked into a hotel on a Wednesday afternoon, and that night woke up with extreme headaches. We remained in the room. The next day, my son struggled in his hockey tryout with headaches and his feet feeling numb and I continued to feel ill. The second night, we again woke up with extreme headaches. There was no carbon monoxide detector in the room. We stayed. On the third night, we again awoke with extreme headaches. This time, we felt dizzy and nauseated. I began to vomit, and we decided to go to the emergency room. In the emergency room, the doctor struggled to find the source of our illness, until he decided to take blood samples, nearly an hour after we had left the hotel. The blood sample taken an hour after we left the hotel room showed my carboxyhemoglobin (COHgB) level to be nearly 27%. My son's level was 22%. According to the CDC, a COHgB level of above 2% for a non-smoker is considered "elevated." Carboxyhemoglobin levels of greater than 20%-30% cause shortness of breath, headache, fatigue, disturbed judgment, dizziness and other symptoms. See, information attached hereto printed from acutecaretesting.org. Higher levels cause unconsciousness and death.

The emergency room doctor notified 911 to evacuate the hotel. The fire department measured our room to have CO level of 260ppm. For context, safe CO exposure limits have been identified by various agencies as being no more than 8ppm (parts per million) to 50ppm. (see Jenkins Foundation data attached). Levels above 150 ppm become life threatening within 3 hours. See, GASLAB.COM, Carbon Monoxide Levels, attached.

We were given oxygen treatment at the emergency room, and we traveled back to Minnesota. In the weeks that followed, we suffered sleeplessness, fatigue, "brain fog," headaches, dizziness and other physical and emotional symptoms, some of which persist nearly two years later. My son has now been

diagnosed with brain injuries that will require him to take medication and receive medical care for the rest of his life, in addition to being at risk for more severe heart and neurological conditions.

After we suffered carbon monoxide poisoning, I learned that three years prior to our stay, two guests of this same hotel were found unconscious due to carbon monoxide poisoning. Despite this prior incident, the hotel did not install carbon monoxide detectors in the guest rooms.

Solution: Installing inexpensive carbon monoxide detectors in individual guest rooms will save lives and prevent severe injuries like the ones my son and I suffered.

It has been suggested that requiring hotels to install carbon monoxide detectors in Minnesota would cost the hotels, in aggregate, $3.6M. I do not know the source of that estimate. However, according to the State of Minnesota Explore Minnesota web site, www.explore@state.mn.us, there are just under 1,000 hotels in Minnesota, averaging approximately 100 rooms per hotel. A compliant CO detector can be purchased at retail cost at any local hardware store or online for under $30, and they last for 5-7 years. At an average cost per hotel of $3,000, that cost spread over the life of the detector would be about $0.16 per day per room.

Common misconceptions: Many common misconceptions lead people to believe that carbon monoxide detectors are not needed in individual guestrooms. People assume that rooms that don't contain a gas appliance are safe from CO poisoning. That is not true. In our case, for example, the source of CO was an improperly vented gas water heater that was located in a utility room across an open air hallway from our room. Because CO can permeate building materials like drywall and travel through open spaces in ceilings, walls, elevator shafts and the like, CO harms many guests who are in rooms without a CO source. Commons sources include boilers, pool heaters, water heaters, gas fireplaces, attached parking garages or cars running near the building. CO levels can also vary greatly from room to room. For example, in our case, the room containing the water heater tested at over 400 ppm, our room tested at 260ppm and the room next to ours was at 150ppm.

Who is Protected by HF406

Hotel guests: This bill would prevent death or injury to hotel guests, employees and emergency response personnel.

Had there been a CO detector installed the room in which my son and I stayed, I would have known on the first night that there was poison gas in our room. Because there was no alarm, I was unaware that my son and I were sleeping in a room filled with poisoned gas—for three nights. Had there been an alarm, I could have informed the emergency room personnel there was a CO detector alarming, which would have alerted them to begin oxygen treatments much sooner.

Hotel employees: Hotel employees will also be protected by this bill. Every hotel is a workplace. Because CO is colorless and odorless, without appropriate CO detection, hotel employees can sustain acute or chronic exposure to CO without understanding the cause of the symptoms.

Hotel businesses: Carbon monoxide injuries are extremely detrimental to the businesses in which they occur. Injuries to hotel guests are bad for business, both in terms of liability claims and in terms of public relations. Hotel employees can suffer carbon monoxide poisoning, as well, causing claims for worker's compensation benefits. Sparing businesses the cost of even one CO injury far outweighs the cost of installing CO detectors.

Attached materials:

Dale & Shirley Jenkins Foundation Data Compilation of hotel CO deaths and injuries since 1969, www.thejenkinsfoundation.com

Center for Disease Control and Prevention, Clinical Guidance for Carbon Monoxide (CO) Poisoning

GASLAB.com, Carbon Monoxide Levels Chart

Carboxyhemoglobin reference range, Printed from acutecaretesting.org

Causes and Clinical Significance of Increased Carboxyhemoglobin, Printed from acutecaretesting.org

Natural Disasters, Severe Weather, and COVID-19

Know how the COVID-19 pandemic can affect disaster preparedness and recovery, and what you can do to keep yourself and others safe.

Clinical Guidance for Carbon Monoxide (CO) Poisoning

Carbon monoxide (CO) is an odorless, colorless, poisonous gas that can cause sudden illness and death if present in sufficient concentration in the ambient air. When power outages occur during emergencies such as hurricanes or winter storms, the use of alternative sources of fuel or electricity for heating, cooling, or cooking can cause CO to build up in a home, garage, or camper and poison the people and animals inside. Generators, grills, camp stoves, or other gasoline, propane, natural gas, or charcoal-burning devices should never be used inside a home, basement, garage, or camper – or even outside near an open window or window air conditioner.

How to Recognize CO Poisoning: The symptoms and signs of carbon monoxide poisoning are variable and nonspecific. The most common symptoms of CO poisoning are headache, dizziness, weakness, nausea, vomiting, chest pain, and altered mental status.

The clinical presentation of CO poisoning is the result of its underlying systemic toxicity. Its effects are caused not only by impaired oxygen delivery but also by disrupting oxygen utilization and respiration at the cellular level, particularly in high-oxygen demand organs (i.e., heart and brain).

Symptoms of severe CO poisoning include malaise, shortness of breath, headache, nausea, chest pain, irritability, ataxia, altered mental status, other neurologic symptoms, loss of consciousness, coma, and death; signs include tachycardia, tachypnea, hypotension, various neurologic findings including impaired memory, cognitive and sensory disturbances; metabolic acidosis, arrhythmias, myocardial ischemia or infarction, and noncardiogenic pulmonary edema, although any organ system might be involved.

With a focused history, exposure to a CO source may become apparent. Appropriate and prompt diagnostic testing and treatment is very important.

Red Flags: No fever associated with symptoms, history of exposure, multiple patients with similar complaints.

Sources of CO Poisoning

- Gas-powered generators
- Charcoal grills, propane stoves, and charcoal briquettes for both cooking and heating indoors
- Motor vehicles
- Fire
- Boats
- Power washers and other gas powered tools.

At-risk Populations include:

- Babies and infants
- Pregnant women
- The elderly
- People with chronic heart disease, anemia or respiratory illness.

Evaluation

- Diagnosis is based on a suggestive history and physical findings coupled with confirmatory testing. Patients should be examined for other conditions, including smoke inhalation, trauma, medical illness, or intoxication.
- Neurological exam should include an assessment of cognitive function such as a Mini-Mental Status Exam
- All women of childbearing age who are suspected of having CO poisoning should have a pregnancy test.

Confirmation of diagnosis

- The key to confirming the diagnosis is measuring the patient's carboxyhemoglobin (COHgb) level.
  - COHgb levels can be tested either in whole blood or pulse oximeter.
  - It is important to know how much time has elapsed since the patient has left the toxic environment, because that will impact the COHgb level. If the patient has been breathing normal room air for several hours, COHgb testing may be less useful.
- The most common technology available in hospital laboratories for analyzing the blood is the multiple wavelength spectrophotometer, also known as a CO-oximeter. Venous or arterial blood may be used for testing.
- A fingertip pulse CO-oximeter can be used to measure heart rate and oxygen saturation, and COHgb levels. The conventional two-wavelength pulse oximeter is not accurate when COHgb is present.
- COHgb levels do not correlate well with severity of illness, outcomes or response to therapy so it is important to assess clinical symptoms and history of exposure when determining type and intensity of treatment.
- Other testing, such as a fingerstick blood sugar, alcohol and toxicology screen, head CT scan or lumbar puncture may be needed to exclude other causes of altered mental status when the diagnosis of carbon monoxide poisoning is inconclusive.
- Note: carbon monoxide can be produced endogenously as a byproduct of heme metabolism. Patients with sickle cell disease can have an elevated COHgb level as a result of hemolytic anemia or hemolysis.

An elevated COHgb level of 2% for non-smokers and >9% COHgb level for smokers strongly supports a diagnosis of CO poisoning.

Guidance for Management of Confirmed or Suspected CO Poisoning

- Administer 100% oxygen until the patient is symptom-free, usually about 4-5 hours. Serial neurologic exams should be performed to assess progress, and to detect the signs of developing cerebral edema.
- Consider hyperbaric oxygen therapy (HBO) therapy when the patient has a COHgb level of more than 25- 30%, there is evidence of cardiac involvement, severe acidosis, transient or prolonged unconsciousness, neurological impairment, abnormal neuropsychiatric testing, or the patient is ≥36 years in age. HBO is also administered at lower COHgb(<25%) levels if suggested by clinical condition and/history of exposure.
- Hyperbaric oxygen is the treatment of choice for pregnant women, even if they are less severely poisoned. Hyperbaric oxygen is safe to administer and international consensus favors it as part of a more aggressive role in treating pregnant women.

Other Considerations

- Cardiac injury during poisoning increases risk of mortality over 10 years following poisoning, so in patients with severe CO poisoning, it may be important to perform an EKG and measurement of troponin and cardiac enzymes.
- Chest radiography is recommended for seriously poisoned patients, especially those with loss of consciousness or cardiopulmonary signs and symptoms. Brain computed tomography or MRI is also recommended in these cases; these tests may show signs of cerebral infarction secondary to hypoxia or ischemia.
- All discharged patients should be warned of possible delayed neurological complications and given instructions on what to do if these occur. Follow-up should include a repeat medical and neurological exam in 2 weeks.

Related Information

- CDC Carbon Monoxide Poisoning

CARB RT

0 ppm	**Recommended Safe Level**	
6 ppm	WHO 24 Hour Average	
9 ppm	ASHRA 8 Hour Average EPA 8 hour 8 Hour Average NAAQS 8 Hour Average WHO 8 Hour Average	**Physical Symptoms** physical symptoms may include headache, fatique, dizziness and/or nausia
25 ppm	ACGIH 8 Hour Average	
30 ppm	WHO 1 Hour Average	
35 ppm	NIOSH 8 Hour Average NAAQS 1 Hour Average	Physical symptoms after 6-8 hours.
50 ppm	OSHA 8 hour Average (PEL)	
30-69 ppm	UL 30 Day Alarm	
87 ppm	WHO 15 Minute Average	
70-149 ppm	UL 1-4 Hour Alarm	
200 ppm	NIOSH 15 minute STEL	Physical symptoms after 2-3 hours.
150-399 ppm	UL 10-50 Minute Alarm	
400+ ppm	UL 4 Minute Alarm	Physical symptoms in 1-2 hours. Life threatening 3 hours.
		Physical symptoms in 45 minutes. Unconscious in 2 hours. Fatal in 2-3 hours.
800 ppm		Physical symptoms in 20 minutes. Fatal within 1 hour.
1,600 ppm		Physical symptoms in 5-10 minutes. Fatal with in 25-30 minutes.
3,200 ppm		Physical symptoms in 1-2 minutes. Fatal in 10-15 minutes.
6.400 ppm		
12,800 ppm		Fatal within 1-3 minutes.

GASLAB.COM
SENSOR SPECIALISTS

April 2006

Carboxyhemoglobin reference range

Summarized from

Van Sickle D, Chertow D. Inappropriate reference intervals for carboxyhemoglobin at some Florida hospitals. Clin Chem 2006; 52(2): 338

Carboxyhemoglobin (COHb) is the product of the reaction between hemoglobin and carbon monoxide, and measurement of COHb is used in the diagnosis of carbon monoxide poisoning. Since carbon monoxide is a common pollutant present in cigarette smoke and car exhaust, it is difficult to be too dogmatic about what constitutes a normal COHb.

Clearly, a non-smoker living and working in the countryside will have a lower COHb than a cigarette-smoking city slicker, who spends much of his or her working day sitting in slow-moving car traffic. This difficulty has led to the adoption of COHb reference ranges that are frankly wrong; a problem that has been highlighted recently by two US experts in the letter pages of the journal Clinical Chemistry.

Best evidence quoted by the experts suggests that the upper limit of normal COHb should be set at between 2 and 3 % for non-smokers and between 7 and 9 % for non-smokers.

During an investigation of carbon monoxide poisoning in Florida they identified 2 of 10 hospitals where the upper limit of normal COHb for non-smokers was quoted as 20 %. Adoption of this reference range would result in failure to identify many people (those whose measured COHb is between 3 and 20 %) who might well be suffering carbon monoxide poisoning.

The experts cite a 1995 survey of 23 Boston hospitals that revealed a wide variation in COHb reference ranges, with 38 % of laboratories using inappropriately high concentrations for non-smokers. They suggest that all clinical laboratories should review their COHb reference range.

October 2005

Causes and clinical significance of increased carboxyhemoglobin

by Chris Higgins

Hemoglobin is the oxygen-carrying protein contained in red blood cells (erythrocytes). Although normally present in only trace amounts, there are three species of hemoglobin that cannot transport oxygen.

The three species, collectively called dyshemoglobins because of their functional redundancy, are methemoglobin, sulfhemoglobin and carboxyhemoglobin.

The last of these is the subject of this article. Carboxyhemoglobin (COHb), which normally comprises less than 1-2 % of total hemoglobin, is the product of reaction between carbon monoxide and hemoglobin.

Carbon monoxide is produced endogenously but is also a common environmental pollutant; both sources contribute to the amount of COHb in blood. The focus of this article is causes and clinical significance of an increased amount of COHb. Three illustrative case histories will be discussed.

It begins, however, with a brief review of some relevant physiology.

NORMAL PHYSIOLOGY

Normal cell function is crucially dependent on a continuous supply of oxygen, and a principle function of blood is delivery of oxygen in inspired air from lungs to every tissue cell.

This essential gas transport function depends on the protein hemoglobin (Hb) contained in red blood cells (erythrocytes).

Structure and function of hemoglobin

Each of the 5×10^{10} erythrocytes contained in every mL of blood contains 280 million Hb molecules. The Hb molecule comprises four polypeptide subunits (the globin portion) each of which has a heme group attached [1].

At the center of the four heme groups is an atom of iron in the ferrous state. Oxygen binds reversibly to these four iron atoms; the product is oxyhemoglobin (O_2Hb).

The oxygen transport function of hemoglobin, that is its ability to pick up oxygen in the lungs, transport it around the body as O_2Hb and then release it to tissue cells, is made possible by a change in the quaternary structure of the hemoglobin molecule, which alters the affinity of hemoglobin for oxygen.

The quaternary state and consequent affinity of hemoglobin for oxygen is governed principally by local partial pressure of oxygen (pO_2), although pH, pCO_2 and organic phosphate concentration are important modulating factors.

In the environment of the lungs, where conditions (high pO_2, low pCO_2) determine that hemoglobin has a relatively high affinity for oxygen, O_2Hb is readily formed.

By contrast in the tissues, local conditions (low pO_2, raised pCO_2) result in reduced hemoglobin affinity for oxygen, thus favoring release of oxygen from hemoglobin to tissue cells. The relationship between pO_2 and the relative affinity of Hb for oxygen is described in the oxygen saturation curve (Figure I).

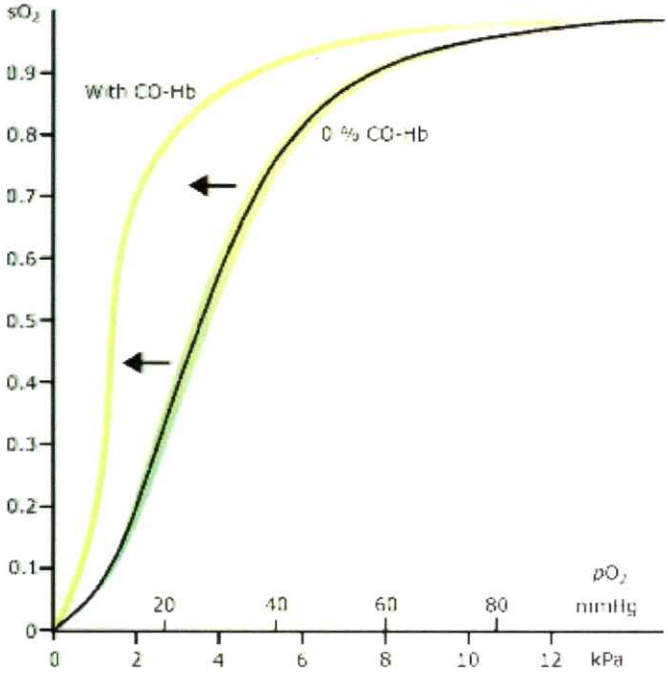

FIGURE I

Oxygen has to compete with other hemoglobin-binding ligands that may be present in blood for occupation of hemoglobin binding sites; among these is carbon monoxide, a colorless odorless gas produced during normal metabolism.

Endogenous production of carbon monoxide

It is more than 50 years since Sjostrand first demonstrated that carbon monoxide (CO) is produced during normal metabolism [2]. In fact, around 0.4 mL CO is produced every hour almost exclusively from the catabolism of heme-containing proteins [3].

The most abundant heme-containing protein and therefore the source of most endogenous CO is hemoglobin. At the end of their 120-day life, erythrocytes are sequestered from the circulation by the reticuloendothelial system.

Hemoglobin released from senescent erythrocytes is degraded to its constituent parts: heme and protein polypeptide. The protein is recycled but heme is metabolized further.

In a reaction catalyzed by the rate-limiting enzyme heme oxygenase, heme is converted to equimolar quantities of biliverdin, iron and CO. Biliverdin is subsequently converted to the yellow pigment bilirubin, which is excreted by the liver in bile, and iron is recycled.

Catabolism of heme derived from other heme-containing proteins, e.g. myoglobin and the cytochromes, contribute to endogenous production of CO by the same heme-oxygenase-mediated route.

There is evidence that CO is also derived from non-heme sources, e.g. lipid peroxidation [4], but compared to that derived from catabolism of heme, this is of very minor significance, indeed may only occur in pathological situations.

The biological effect of endogenous CO is due largely to the high affinity that heme has for CO and the resulting binding of CO by heme-containing proteins. By a curious quirk of nature then, heme is both the source of CO and the mediator of its biological effect.

The modulation in function of some heme-containing proteins that results from CO binding has important physiological effects.

Thus endogenously produced carbon monoxide is not, as was once supposed, simply a potentially toxic waste product of metabolism but is involved in many physiological functions, including regulation of respiration [5], neuronal signaling [6], regulation of blood pressure [7] and uterine contraction during pregnancy [8].

Of all heme-containing proteins, Hb is not only the most abundant but also exhibits the highest affinity for carbon monoxide, so that most CO in blood is bound to Hb.

Reversible binding occurs at the same iron atom on the heme site where oxygen binds; the product of this binding is carboxyhemoglobin (COHb).

This provides the means by which endogenous carbon monoxide can be transported, prior to elimination from the body by the lungs in expired air. A minimum of 0.5-1.0 % COHb is inevitably present in blood as a result of endogenously produced CO [9].

Environmental sources of carbon monoxide

In addition to the CO produced endogenously, the air we breathe contains CO, partly the result of natural processes but mostly from the incomplete combustion of hydrocarbons.

The most significant unnatural source of environmental CO is motor-vehicle exhaust. Although normally present at concentrations of less than 10 parts per million (ppm) [10], carbon monoxide in inspired air has an important additive effect on the amount of COHb in blood due to the high affinity that Hb exhibits for CO.

The combined effect of endogenous and environmental CO results in a COHb of less than 3 % for most non-smoking urban dwellers and may be just 1-2 % for those living in rural areas where air is less polluted with CO.

Cigarette smoke contains a high concentration of CO and smokers are exposed to an estimated 400-500 ppm CO while smoking and consequently have much higher COHb. A necessary consensus, given the variability level of COHb due to environmental CO, suggests an absolute upper limit of normal COHb of 3 % for non-smokers and 10 % for heavy smokers [11].

CAUSES OF RAISED COHb

The amount of COHb in blood is determined principally by the amount of CO in blood. The source of the CO in blood is both endogenous (heme catabolism) and environmental (CO content of inspired air) so that the causes of raised COHb can be addressed under two main headings:

- Increased endogenous production of CO
- Breathing air polluted with high CO content – carbon-monoxide poisoning

Increased endogenous production of CO

Increased endogenous production of CO is a feature of any condition associated with increased heme catabolism. The hemolytic anemias are a group of conditions of variable etiology whose common pathological feature is increased rate of red-cell destruction (hemolysis).

Increased red-cell destruction results in increased heme catabolism and therefore increased production of CO. The severity of hemolysis correlates closely to CO production and measured COHb [12, 13].

In general, COHb increases due to hemolysis are of the order of only 2-3 %, but they can be higher. In one series of 75 neonates suffering hemolytic jaundice [14], five had COHb values in excess of 4 % and one baby with severe hemolysis had a level of 8.3 %. (The normal neonatal COHb range determined for this study was 0.15-0.75 %.)

It is rare for COHb to exceed 10 % in non-smokers, even in the most severe hemolytic episodes.

Slight increase in COHb – so slight to be of little clinical significance per se – is often a feature of severe inflammatory disease, e.g. sepsis, pneumonia [15]. It is thus a relatively common finding in critically ill patients [16].

The mechanism of this increase is thought to be increased expression of heme oxygenase (the enzyme responsible for CO production) induced by inflammatory cytokines [17].

Increased endogenous production of CO can arise independently of heme catabolism. Methylene chloride (dichloromethane) is a toxic organic solvent with wide application, including paint remover, degreaser and aerosol propellant. The toxicity of methylene chloride is due in part to its *in vivo* metabolism in the liver to CO.

Subjects who inhale toxic amounts of methylene chloride vapor, usually a result of working in poorly ventilated conditions, have raised COHb caused by increased production of CO. COHb levels, which can be severe enough to threaten life, correlates well with methylene chloride exposure levels [18].

Breathing air polluted with high CO content – carbon-monoxide poisoning

This is clinically the most significant cause of increased COHb for two reasons. First it is a more common cause of increased COHb than endogenous production of CO, and secondly it can result in a much more severe increase in COHb.

Most clinical requests for measurement of COHb are made in the context of known or suspected acute or chronic carbon-monoxide poisoning.

Epidemiology of carbon-monoxide poisoning

Deliberate or accidental poisoning by carbon monoxide remains a significant problem. In the US, it accounts for an estimated 40,000 emergency room attendances and between 5,000 and 6,000 deaths each year [19].

Most of these are suicides, usually the result of deliberate exposure to motor-vehicle exhaust, but still 600 deaths a year result from accidental exposure to carbon monoxide from a wide variety of sources. In the UK, CO is responsible for 50 deaths and 200 serious injuries every year [20].

Internationally, CO may be responsible for more than half of all fatal poisonings worldwide [21]. Low-grade chronic CO poisoning is associated with non-specific symptoms and requires a high degree of suspicion for diagnosis, and most authorities believe many cases remain undiagnosed or misdiagnosed [22].

Sources of carbon monoxide

Carbon monoxide is a ubiquitous product of incomplete combustion of hydrocarbons. Common sources of CO in cases of poisoning include house fire, motor-vehicle exhaust and faulty domestic heating systems.

Less commonly, gas ovens, paraffin (kerosene) heaters and even charcoal briquettes, e.g. for use on barbeques, have been implicated.

Clearly a closed or poorly ventilated environment is an important contributory factor in most cases, but it remains possible to suffer severe, even fatal, CO poisoning in the outdoors if close enough to a rich source of CO, e.g. swimming near boat exhaust [23].

Effect of CO exposure on COHb levels

The amount of COHb in blood is a function of both inspired CO concentration (parts per million, ppm) and duration of exposure.

During exposure to a fixed CO concentration, COHb levels increase rapidly over the first 2 hours, then begin to plateau at around 3 hours, reaching an equilibrium steady state at 4-6 hours. Table I describes the relationship between CO exposure and equilibrium COHb.

CO concentration of inspired air (ppm)	COHb %
70	10
120	20
220	30
350-520	40-50
800-1200	60-70
1950	80
To maintain COHb below 2.5 % all the time CO exposure cannot exceed 10 ppm	

CO concentration in specific environments:

- Global background: 0.05-0.12 ppm
- Urban taffic environment: 17 ppm overall with peaks of up to 53 ppm
- Underground carparks, road tunnels: up to 100 ppm may peak even higher
- Environmental tobacco smoke (offices, restaurants): 20-40 ppm (8-hour average)
- Workplace safety limit: 50 ppm (8-hour average)

TABLE I: Data relating CO exposure to % COHb and CO concentration in specific environments

CONSEQUENCES OF RAISED COHb

Toxicity of carbon monoxide

The toxicity of CO is due in part to the effect that hemoglobin binding of CO has on the oxygen-carrying capacity of blood. Affinity of hemoglobin for CO is 200-250 times greater than that for oxygen [9, 20, 23, 24].

CO displaces oxygen from hemoglobin and thus COHb effectively reduces the oxygen-carrying capacity in a dose-dependant manner. In addition, binding of CO by Hb at the first of the four heme sites has an effect on its quaternary structure that results in decreased affinity for oxygen at the remaining three sites.

This effect is evident in a shift of the hemoglobin dissociation curve to the left (Figure I) and results in reduced release of oxygen from hemoglobin at the tissues. The combined effect of a reduced oxygen-carrying capacity and reduced release of oxygen to tissue leaves tissues effectively starved of oxygen (hypoxic).

Organs like the brain and heart, whose normal oxygen consumption is by comparison with other organs relatively high, are particularly sensitive to the relative anoxia induced by increased COHb.

Fetal Hb exhibits an even higher affinity for CO than adult Hb, so that since CO diffuses readily across the placental membrane, the developing fetus is particularly vulnerable to tissue anoxia in cases of maternal CO exposure [26].

If increased production of COHb were, as was once supposed, the only mechanism involved in CO toxicity, then the severity of symptoms would be accurately predicted by the level of COHb, but this is not always the case.

It is now clear that "free" CO dissolved in blood plasma enters tissues and competes with oxygen for sites on tissue-cell heme proteins such as myoglobin, peroxidase and the cytochrome enzymes with a variety of pathological effects independent of hemoglobin CO binding [20].

Clinical sign and symptoms of carbon-monoxide poisoning

A high index of suspicion is required to entertain a diagnosis of carbon-monoxide poisoning unless CO exposure is certain, because all symptoms of mild-to-moderate poisoning are non-specific. The classic "cherry-red" skin color of carbon-monoxide poisoning is in fact not usually evident.

The most common symptoms: headache, dizziness and confusion reflect the marked sensitivity of the brain to relative anoxia. Nausea and vomiting are also common.

Affected patients may be breathless, particularly on exertion, and have clinical signs (tachycardia, tachypnea) indicating compensation for the oxygen deficit.

In more severe cases there are frank signs and symptoms of cardiac involvement, including palpitations, hypotension, ischemic chest pain (angina) and even myocardial infarction. Convulsions and coma occur in severe toxicity.

Exposure to carbon monoxide at concentrations greater than 1,900 ppm is immediately fatal.

A raised COHb in the absence of a disease process associated with the hemolytic process is diagnostic of carbon-monoxide poisoning; the actual level correlates with the severity of symptoms in the majority of cases (Table II).

Carboxyhemoglobin in blood %	**Symptoms**

10	No appreciable effect except shortness of breath on vigorous exertion, possible tightness across forehead
20	Shortness of breath on moderate exertion, occasional headache
30	Headache, easily fatigued, judgement disturbed, dizziness, dimness of vision
40-50	Headache, confusion, fainting, collaps
60-70	Unconsciousness, convulsions, respiratory failure, death if exposure continues
80	Immediately fatal

TABLE II: Relationship between % CO-Hb and symptoms

SOME ILLUSTRATIVE CASE HISTORIES

Case history 1: Severe CO poisoning with only marginally raised COHb

This case [27] concerns a 13-year-old boy who started his motorbike in the family garage. Before he could get to the garage door he was overcome by the exhaust fumes and collapsed. He was found unconscious around 9 hours after he was last seen, wedged between the family car and the unopened garage door.

Although by now there was no evidence of CO exposure, e.g. running motor or smell of exhaust, the moribund boy was suffering the effects of severe CO inhalation. After initial assessment at the local hospital, his respiration, already "rapid and labored" on admission, deteriorated and he was intubated and transferred to a tertiary referral center, some 13 hours after he was found.

The cause of his continuing unconscious state remained a mystery at this time. On admission to the second hospital, blood was sampled for COHb estimation. The laboratory reported a COHb of 4.9 %.

The boy remained deeply comatose for 10 days and was dependent on mechanical ventilation for 11 days. During this time, convulsions were frequent. Other significant complications included acute renal failure and severe muscle necrosis. Neurological recovery was gradual.

Although apparently alert by day 12, at first he was unable to recognize family members, unable to speak, had no memory and his control of movement was greatly restricted.

At six weeks, his memory had improved sufficiently to recall the events of the day of the accident, and he was able to confirm exposure to motorbike exhaust fumes. Eight weeks after admission he was eventually discharged to a rehabilitation unit, still with some restriction of movement of his lower limbs.

The CO exposure had left him with some impairment of short- and long-term memory, reduced ability to concentrate and a probable IQ deficit.

This is a case history of severe, near-fatal CO exposure with typically severe neurological sequelae. Such severe exposure would normally be associated with very high COHb, possibly in the range of 40-50 %, certainly greater than 20 %. Why then was the COHb only 4.9 %? After all, most smokers endure a COHb > 5 %.

The answer lies in the temporal relationship between exposure and blood sampling and highlights an important limitation of COHb measurement for diagnosis of CO poisoning.

COHb has a half-life of only 4 hours when breathing room air; this is reduced to 90 minutes when breathing 100 % oxygen and less than 30 minutes if hyperbaric oxygen is instituted [10]. This is the rationale for the use of 100 % oxygen or hyperbaric oxygen in the treatment of CO poisoning.

However, it also means that if there is more than a few hours delay between exposure and sampling of blood, COHb will not accurately reflect exposure. In this case, 13 hours elapsed between the time the boy was found and the time blood was sampled.

Given a half-life of 4 hours, this is time enough for COHb to drop from a peak of say 40 % to 5 %. Whilst a raised COHb always indicates CO poisoning, a normal COHb is not sufficient to exclude a diagnosis of CO poisoning if there has been delay between exposure and blood sampling, especially if oxygen therapy has been administered.

Case history 2: An unusual cause of raised COHb

The patient was a critically ill 41-year-old non-smoking male who had been transferred from his local intensive care unit to a tertiary referral center for continued management of large bilateral spontaneous adrenal hemorrhage [28].

On day 6 after referral, blood gas analysis revealed a COHb of 3.9 %, which increased to a maximum of 6.4 % three days later and fluctuated between 1.7 % and 5.6 % for the following two weeks.

Despite repeated transfusion of fresh frozen plasma to correct the presumed causative coagulopathy, internal bleeding continued and on day 14 at exploratory laparotomy, a 4,000 mL hematoma was removed. Biopsy of the adrenal gland revealed a benign tumor (pheochromocytoma) as the cause of bleeding.

Both before referral and for the following 14 days, repeated transfusion of packed red cells were needed to maintain hemodynamic stability. Despite continued intensive care and several further surgical interventions, including adrenalectomy, the patient's condition deteriorated and he died 58 days after referral.

The principle cause of raised COHb in this case was increased endogenous production of carbon monoxide. This was due to the ongoing degradation of hemoglobin within the retroperitoneal hematoma formed as a result of accumulating blood.

An additional contributory factor may have been the repeated red-cell transfusions. There is evidence that some packed red cells for transfusion may have COHb levels as high as 12 % [29].

Case history 3: COHb does not always correlate well with symptoms [30]

After traveling in a poorly maintained family car for nearly an hour, one of the five passengers, a normally boisterous two-year-old girl fell asleep and was sufficiently unresponsive to raise concern.

She was driven direct to a nearby pediatric emergency room where she was found to be flaccid and responded only to deep painful stimulation with a cry and sluggish opening of her eyes (Glasgow Coma Score 8).

Apart from this reduced level of consciousness, physical examination revealed no abnormalities and a presumptive diagnosis of carbon-monoxide poisoning was made. Within 15 minutes of starting 100 % oxygen therapy the girl was awake. COHb of blood sampled before therapy was 35 %.

After two hours of oxygen therapy, COHb was 7 % and the little girl was fully alert. (GCS 15).

Blood was also sampled for COHb from four other occupants of the car; two children aged two and seven years and two female adults. COHb of the two children was 33.6 % and 34.7 % and the adults had COHb of 18.4 % and 16.1 %. Both children were asymptomatic, one of the adults complained of slight headache and the other of light-headedness.

This case study demonstrates that simultaneous exposure to the same CO source does not necessarily result in the same measured level of COHb, and symptoms manifested by individuals exposed to the same CO source may be dissimilar, despite almost identical COHb results.

SUMMARY

It is difficult to establish a normal range for COHb because the amount of COHb in blood is crucially dependent on variable levels of environmental carbon-monoxide pollution.

Unequivocal increase in COHb indicates either a hemolytic process or more commonly carbon-monoxide poisoning. Increased COHb reduces tissue oxygenation but this is not the only mechanism of CO toxicity. Laboratory measurement of COHb is the only routinely available blood test for diagnosis of CO poisoning.

It provides useful though limited prognostic information in such cases.

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