Chapter 222: Carbon Monoxide

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**FIGURE 222-1.**

**INTRODUCTION**

Carbon monoxide is one of the most common toxic exposures that emergency physicians will encounter. It is the most common cause of fatal poisoning, via either intentional (suicidal) or accidental exposure in the United States, and may be the most common worldwide cause of fatal poisoning.\(^1\) Despite much clinical experience and several randomized trials, there is a great deal of controversy about the ideal approach for management.

**EPIDEMIOLOGY**

Exact statistics for carbon monoxide poisoning are difficult to determine, mainly due to incomplete reporting. Data from the American Association of Poison Control Centers Toxic Exposure Surveillance System in 2012\(^2\) reported 13,038 exposures, with 54 deaths. However, this information is limited, as many exposures and some deaths are not reported to the local poison control center. It is also unclear how often patients with mild carbon monoxide poisoning are misdiagnosed and thus are not included in the database. Data from the Centers for Disease Control and Prevention paint a much broader picture of exposures than the Toxic Exposure Surveillance System database. The most recent large epidemiologic report from the Centers for Disease Control and Prevention on the subject, which reviewed data on non–fire-related carbon monoxide exposures, revealed 5149 deaths, for an average of 430 deaths per year.\(^3\) Interestingly, the incidence of carbon monoxide exposure has not decreased despite more widespread use of carbon monoxide detectors.\(^3\)

In the past, vehicular emissions were the major source of carbon monoxide poisoning in adults. Currently, nonvehicular sources have become more common as use of catalytic converters has reduced carbon monoxide in vehicular exhaust emissions\(^4\) (**Table 222-1**)
TABLE 222-1
Sources of Carbon Monoxide

- Automotive exhaust
- Motorboat exhaust
- Propane-fueled heaters
- Wood- or coal-burning stoves or heaters
- Structure fires
- Gasoline-powered generators or motors
- Natural gas–powered heaters/furnaces/generators
- Methylene chloride
- Forklifts

Peak incidence occurs in the fall and winter months, generally due to increased use of space heaters, wood-burning stoves, charcoal burning for heat, or portable generators without adequate ventilation. Additional sources of carbon monoxide exposure include air conditioners, portable generators in camping tents, exhaust on motorboats, and Zamboni machines used in ice rinks. Exposures have been reported in persons riding in the back of pickup trucks, as well as in vehicles with an exhaust pipe occluded by snow.

It is believed that carbon monoxide poisoning is probably the most pressing danger from smoke inhalation and is a major contributor to fire-related deaths. Although carbon monoxide poisoning most commonly affects adults in the third to fifth decades, it may be seen across age groups, and it is not uncommon for entire families to be affected.

Another source for carbon monoxide poisoning is methylene chloride, which is found in varnishes and paint strippers, and in Christmas ornaments as a bubbling fluid. Routes of exposure are inhalation or ingestion, and the methylene chloride is metabolized in the liver to carbon monoxide. As a result of ongoing production, persistent elevation of carboxyhemoglobin occurs despite oxygen therapy. Time to peak carbon monoxide levels may be 8 hours or longer.

**PATHOPHYSIOLOGY**

Carbon monoxide is typically described as a colorless, odorless gas. It is normally present in air at 10 ppm or less, perhaps higher in urban areas. There are multiple industries in which there may be occupational exposure to carbon monoxide. The Occupational Safety and Health Administration set a permissible exposure level of carbon monoxide of 50 ppm averaged over an 8-hour shift. Toxicity generally begins at levels of 100 ppm.
Carbon monoxide is also an endogenous substance, with production occurring in the body during the normal breakdown of heme. Normal physiologic carbon monoxide levels from this process are ~1% in healthy nonsmokers. This physiologic production can be increased in hemolysis or sepsis. Baseline levels in smokers of up to 10% have been reported.

The most easily quantified physiologic effect seen after carbon monoxide exposure is its binding to hemoglobin. The binding affinity of normal adult hemoglobin for carbon monoxide is approximately 200 times that of oxygen. Binding is higher for fetal hemoglobin, which may account for potentially more severe fetal toxicity. Approximately 85% of carbon monoxide is bound to hemoglobin; the remaining carbon monoxide is dissolved in plasma or bound intracellularly, often to myoglobin. Carbon monoxide binds to hemoglobin to form carboxyhemoglobin. There are mathematical models for predicting the half-life of carboxyhemoglobin; these have been evaluated in both volunteer human models and actual carbon monoxide–poisoned patients. Quoted half-lives of carboxyhemoglobin on room air at normal atmospheric pressure range from 249 to 320 minutes. On 100% oxygen at atmospheric pressure, this is reduced to an average of 74 to 80 minutes. The exception to this is carboxyhemoglobin generated by methylene chloride exposure, which can have a half-life of up to 13 hours due to ongoing metabolic production.

Carboxyhemoglobin does not participate in oxygen delivery to the cells, and as carboxyhemoglobin levels increase, relative anemia and hypoxia occur. Further, carbon monoxide shifts the oxyhemoglobin dissociation curve to the left, impairing oxygen release to the tissues. However, these features alone do not fully explain the physiologic effects of carbon monoxide or its delayed neurologic sequelae. Patients with corresponding levels of hypoxia, or anemia, who are not carbon monoxide poisoned, do not have similar short- and long-term effects seen with carbon monoxide poisoning. This indicates that there is a separate toxicity to carbon monoxide irrespective of the level of carboxyhemoglobin. Carboxyhemoglobin appears to be more a marker for the degree of poisoning than the primary cause of injury itself. The best experimental evidence of this involved dogs that were given carbon monoxide by inhalation to produce carboxyhemoglobin levels of 80%. Exchange transfusion of this blood into healthy dogs produced no symptoms, suggesting that something other than simply the carboxyhemoglobin level is at play in explaining the full range of toxic effects.

As carboxyhemoglobin level rises, there is an increase in body burden of carbon monoxide. Ten to 15% of the carbon monoxide is dissolved unbound into plasma, a large proportion of which ultimately moves into the intracellular compartment. Like hemoglobin, myoglobin has a greater affinity for carbon monoxide than it does for oxygen, and myoglobin will bind to carbon monoxide with approximately 60 times the affinity of oxygen. Carbon monoxide inhibits intracellular cytochrome oxidase, interfering with cellular respiration and adenosine triphosphate generation. This results in a relative uncoupling of oxidative phosphorylation and the generation of elevated lactate levels, resulting in a lactic acidosis. Carbon monoxide also causes endothelial dysfunction and vasodilatation through the release of guanylate cyclase and nitric oxide. Carbon monoxide–induced nitric oxide release may in fact be one of the key factors in the cytotoxic effects of carbon monoxide poisoning. The release of guanylate cyclase and nitric oxide can contribute to hypotension. The combination of relative hypoxia and hypotension can cause ischemia-reperfusion injury in cardiac myocytes,
as well as neuronal tissue. The damaged endothelium attracts neutrophils and triggers an inflammatory cascade, resulting in lipid peroxidation and ultimately neuronal cell death. This complex intracellular process explains many of the clinical effects of carbon monoxide. Rhabdomyolysis, acute myocardial infarction, and neuronal cell death are a result of this cellular toxicity. Cells in the basal ganglia are particularly sensitive to this neurotoxic effect, demonstrated by the globus pallidus lesions sometimes seen on cranial CT imaging.

**CLINICAL FEATURES**

The clinical presentation of carbon monoxide poisoning is protean, which likely leads to misdiagnosis in many cases (Table 222-2). An unconscious patient pulled from a house fire or from a running car in a closed garage does not present a diagnostic dilemma; the patient with "flu-like" symptoms or the elderly person presenting with syncope and ischemic changes on their ECG may be more difficult to diagnose. Given the lack of any predictable clinical toxidrome for carbon monoxide poisoning, a strong clinical suspicion remains the best initial method of detection.

<table>
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<tr>
<th>Signs and Symptoms of Acute Carbon Monoxide Poisoning</th>
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<td>Headache</td>
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<tr>
<td>Vomiting</td>
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<tr>
<td>Ataxia</td>
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<tr>
<td>Seizure</td>
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<tr>
<td>Syncope</td>
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<td>Chest pain</td>
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<td>Focal neurologic deficit</td>
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<td>Visual disturbances</td>
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<td>Confusion</td>
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<tr>
<td>Dyspnea/tachypnea</td>
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<td>ECG changes/dysrhythmias</td>
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<td>Retinal hemorrhage</td>
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<td>Bullous skin lesions</td>
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History may be strongly suggestive, such as use of a propane heater in an apartment associated with a headache at home but relieved with exit from the home. Symptoms such as a new-onset seizure, syncope, myocardial infarction, or cardiac arrest may not be helpful. Sometimes, concurrent symptoms in other members of the household, or even pets, can be a clue. However, even within a household, different persons may manifest different symptoms, depending on age, comorbid disease, and proximity to the source of carbon monoxide. Occupational history may help, particularly in cases due to less common causes such as methylene chloride exposure. Exposure to any gas- or propane-powered motors, especially if working inside enclosed facilities, or fumes from methylene chloride, which is used as a varnish or paint stripper, may serve as a clue in patients with nonspecific symptoms. **Carbon monoxide poisoning should be in the differential diagnosis for comatose patients, patients with mental status changes, and those with an unexplained elevated anion gap metabolic acidosis or lactic acidosis.**
Physical exam findings are diverse. The classically touted finding of cherry red oral mucosa is rarely seen in living patients. Vital signs may demonstrate mild fever, tachycardia, tachypnea, hypertension, or hypotension. Severe poisoning may present with respiratory or cardiac arrest. Neurologic findings, which are generally thought of as being one of the hallmark signs for this poisoning, are also variable, ranging from mild headache and confusion to irritability, seizures, focal neurologic deficits, and coma. Retinal hemorrhages have been reported with severe poisoning. Skin findings include bullous lesions, generally seen in patients with prolonged immobility from pressure necrosis, although a direct toxic effect of carbon monoxide on epidermal tissue is also possible. Carbon monoxide poisoning may be obscured by other findings, such as trauma or severe burns. A comatose patient removed from a fire scene should be assumed to have carbon monoxide poisoning until proven otherwise, even in the absence of cutaneous or airway burns.

Although most discussions of carbon monoxide poisoning focus on acute exposure, chronic carbon monoxide poisoning, generally from occupational sources, must also be considered. Symptoms are usually more insidious, such as trouble concentrating, personality changes, or memory loss, and can be difficult to diagnose. Patients with chronic carbon monoxide poisoning are at risk of carbon monoxide–related neurotoxicity and may have long-term neuropsychiatric issues.

**DIAGNOSIS**

The diagnosis is best made by measuring carboxyhemoglobin levels. Although carboxyhemoglobin in and of itself may not be the most significant factor in carbon monoxide–mediated injury, obtaining free plasma carbon monoxide is rarely feasible. Thus, carboxyhemoglobin serves as a marker of severity of exposure and can help to stratify patients at risk for delayed sequelae. **Co-oximetry, which measures total hemoglobin as well as oxyhemoglobin, methemoglobin, and carboxyhemoglobin saturation, is the only accurate measurement tool.** Routine arterial blood gas analyzers without co-oximetry calculate, rather than measure, saturation, and will not differentiate the contribution of dyshemoglobinemias to total saturation. As a result, the oxygen saturation may appear artificially high. There is excellent correlation between arterial and venous carboxyhemoglobin levels, and thus, a venous blood gas with co-oximetry is sufficient in most cases.\(^{12}\)

Interpreting carboxyhemoglobin levels can be challenging and needs to take into consideration time and duration of exposure, time from exposure to presentation, treatment (such as high-flow oxygen) rendered en route, and clinical symptoms. Although a markedly elevated level, such as 50%, is a clear indicator of severe intoxication, a level of 10% in a patient who experienced serious symptoms a few hours earlier presents a dilemma in terms of diagnosis and appropriate disposition. Symptomatology and carboxyhemoglobin levels do not always correlate well: levels as high as 47% have been reported in minimally symptomatic patients, whereas levels as low as 10% have been reported in comatose patients in whom the diagnosis of carbon monoxide poisoning was ultimately confirmed.\(^{13}\)

**Standard pulse oximetry is unreliable in the diagnosis of carbon monoxide poisoning.** The wavelengths for carboxyhemoglobin fall into the same range of those for oxyhemoglobin, and standard pulse oximetry does
not differentiate the two. As a result, the oxyhemoglobin saturation by pulse oximetry reading will appear artificially high \(^{14}\) (Figure 222-1). The **pulse oximetry gap** is a measure of this discordance. When the pulse oximetry values are compared to the oxygen saturation on an arterial blood gas, the oxygen saturation on the pulse oximeter will be higher than the saturation on the arterial blood gas.

**FIGURE 222-1.**
Carboxyhemoglobin "shift to the left" reshaping of the oxyhemoglobin (HbO\(_2\)) dissociation curve. (A) Carbon monoxide (CO)–affected HbO\(_2\) dissociation curve (asymptotic) and (B) normal HbO\(_2\) dissociation curve (sigmoid).

Data on currently available pulse co-oximeters are mixed. Until a large, randomized, and well-designed study looking at the accuracy of these devices in an ED setting can be performed, it is not recommended to rely solely on pulse co-oximeters to exclude carbon monoxide poisoning. \(^{15,16,17}\)

Other laboratory and diagnostic testing can be also be informative. Elevated lactate from the interference in the electron transport chain, an unexplained elevated anion gap metabolic acidosis, elevated creatine phosphokinase, or elevated troponin may trigger an investigation for carbon monoxide poisoning. Concomitant cyanide poisoning may be seen in patients rescued from structure fires. Neuron-specific enolase or S100B, \(^{18}\) CNS proteins that are released in greater quantities into the plasma when neuronal injury has occurred, and cerebrospinal fluid myelin basic protein are markers for carbon monoxide neurotoxicity. However, these tests may be more useful in determining prognosis than diagnosis and are rarely available for use in ED clinical decision making.

Electrocardiographic findings may range from entirely normal to acute injury patterns, such as ST elevation myocardial infarction. There does not appear to be any classic carbon Monoxide ECG pattern. Few patients
with acute myocardial infarction due to carbon monoxide poisoning have occlusive lesions identified at cardiac catheterization.\textsuperscript{19}

Radiographic imaging is generally of limited utility and is usually more helpful in establishing an alternative diagnosis. There is, however, one radiographic finding that has been specifically associated with carbon monoxide poisoning, and that is lesions in the globus pallidus. Lesions are generally bilateral and symmetric and are usually noted in severely poisoned patients.\textsuperscript{7}

**TREATMENT**

Initial resuscitation of the carbon monoxide–poisoned patient does not differ from initial resuscitation of any other critically ill patient. If carbon monoxide poisoning is strongly suspected based on history, immediately provide supplemental oxygen in the highest concentrations available.

Conditions for the application of hyperbaric oxygen treatment have not been clearly identified. Despite years of experience using hyperbaric oxygen and several clinical trials, identifying individuals who can benefit from HBO is challenging. The most recent comprehensive review on the subject is a Cochrane review from 2011.\textsuperscript{20} Six clinical trials were reviewed. Two of the six demonstrated a benefit in terms of decreased neurologic sequelae; the remaining four trials failed to demonstrate a benefit. All studies had various methodologic flaws. The only trials to include sham dives (diving but at room air instead of high-concentration oxygen) were the two positive trials (Weaver and Scheinkestel). These two positive trials were stopped early due to reported clear benefit; however, they did not test multiple hypotheses and had significant heterogeneity in their treatment protocols. The four negative trials were smaller, methodologically heterogeneous, and suffered from problems with long-term follow-up. Given the lack of conclusive evidence-based data, the best guidance comes from consensus recommendations from multiple professional groups (Table 222-3). Recommendations consider multiple factors such as carboxyhemoglobin level, comorbid conditions (including pregnancy), stability of the patient, and location of the nearest center with emergency hyperbaric capabilities.
The rationale behind hyperbaric oxygen therapy stems from early studies demonstrating its effectiveness in decreasing carboxyhemoglobin levels. Initial studies on both volunteers and poisoned patients in the 1940s demonstrated that use of hyperbaric oxygen at 2.5 atmospheres of pressure lowered the effective half-life of carboxyhemoglobin to an average of 24 minutes due to a competitive displacement of carbon monoxide from its binding sites by the increased concentration of oxygen. The clinical logic that led to recommendations for routine use centered on the premise that rapid reduction in carboxyhemoglobin levels meant that carbon monoxide was being cleared from the system and that toxicity could be reversed. Neurotoxicity is the endpoint most commonly studied; however, not all studies use the same assessment tools or follow-up periods. Scheinkestel et al were unable to demonstrate any conclusive prevention of delayed neurologic sequelae with use of hyperbaric oxygen, whereas Weaver et al saw a significant reduction in neurologic sequelae (cerebellar dysfunction and cognitive sequelae).

The consensus recommendations for consideration of hyperbaric oxygen therapy are listed in Table 222-3. The decision to initiate hyperbaric oxygen needs to occur in conjunction with a specialist in hyperbaric medicine. The Undersea and Hyperbaric Medicine Society maintains a list of chambers at the following Web site: www.hyperbariclink.com. For complete discussion of hyperbaric oxygen, see the chapter 21, "Hyperbaric Oxygen Therapy."

**DISPOSITION**

Three distinct categories of carbon monoxide–poisoned patients exist: (1) those with minimal intoxication, with mild or no symptoms throughout their clinical course; (2) those with symptoms attributable to carbon monoxide poisoning but without any high-risk features that suggest a need for hyperbaric oxygen referral; and (3) those with signs of serious toxicity for whom consultation with a specialist in hyperbaric medicine should be considered.

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<thead>
<tr>
<th>Commonly Used Indications for Referral for Hyperbaric Oxygen Treatment</th>
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<tr>
<td>Pregnancy with carboxyhemoglobin level &gt;15%</td>
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<tr>
<td>Carboxyhemoglobin &gt;25%</td>
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<tr>
<td>Syncope</td>
</tr>
<tr>
<td>Evidence of acute myocardial ischemia</td>
</tr>
<tr>
<td>Confusion/altered mental status</td>
</tr>
<tr>
<td>Seizure</td>
</tr>
<tr>
<td>Coma</td>
</tr>
<tr>
<td>Focal neurologic deficit</td>
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Those with minimal intoxication, who are asymptomatic initially or after a period of brief observation, may be sent home if the exposure is not a suicide attempt and discharge is to a safe environment. If there is a suspected source of carbon monoxide poisoning, contact other potentially exposed persons for ED evaluation, and notify the fire department to measure ambient levels of carbon monoxide at the source site. Once the safety of the discharge destination is established, the patient may be discharged.

Those with more serious symptoms, such as headache or vomiting, or those with an elevated carboxyhemoglobin level but no high-risk features (Table 222-3) should be treated with supplemental oxygen, have pertinent labs checked, and be observed for several hours. After 4 hours of observation, patients may be discharged home if symptoms have resolved, assessment is otherwise benign, and discharge is to a safe environment.

Patients who require referral for possible hyperbaric oxygen therapy need consultation with a hyperbaric specialist and stabilization as best as possible prior to transfer. Critically ill or unstable patients should continue to receive high-concentration normobaric oxygen and should be reassessed prior to transfer.

**SPECIAL POPULATIONS**

Children may be more susceptible to the effects of carbon monoxide due to a higher percentage of fetal hemoglobin as well as higher metabolic rates.\(^7\) The indications for referral of pediatric patients for HBO therapy are similar to those for adults. HBO has been used in children with a good safety profile.

Pregnant women should be referred to a hyperbaric center at carbon monoxide levels of 15% to 20% because fetal morbidity has been demonstrated at lower levels than usual due to the high affinity of carbon monoxide for fetal hemoglobin.\(^7\)

The elderly, particularly those with serious comorbid disease, are also at higher risk from carbon monoxide poisoning. In patients with known coronary artery disease, even low levels of carboxyhemoglobin (4% to 6%) can cause ECG changes and myocardial ischemia.\(^7\) Some of the elderly may also be at risk due to use of alternate heating sources, particularly during the winter.

**PREVENTION**

Preventive measures center on education. Educate the public about the dangers of using wood- or coal-burning appliances to heat their homes during the winter and about using adequate ventilation, and review warning signs and symptoms of carbon monoxide exposure. A relatively inexpensive preventative measure is the use of carbon monoxide detectors in the home; some municipalities have even given these away through the fire department. Local fire departments are generally willing to screen for elevated carbon monoxide levels in homes. Many educational resources are available on the Internet ([http://www.cdc.gov/co/guidelines.htm](http://www.cdc.gov/co/guidelines.htm); [http://www.carbonmonoxidekills.com](http://www.carbonmonoxidekills.com); [http://www.carbonmonoxidekills.com](http://www.carbonmonoxidekills.com); [http://www.usfa.dhs.gov/citizens/all_citizens/co/index.shtml](http://www.usfa.dhs.gov/citizens/all_citizens/co/index.shtml)).


