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Diagnosis And Management Of Carbon Monoxide Poisoning In The Emergency Department

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CME Objectives

Upon completion of this article, you should be able to:

1. Recognize that presentation of CO toxicity is often non-specific, especially in children.
2. Understand how to obtain and interpret a COHb level.
3. Determine the appropriate treatment for CO-poisoned patients.
4. Assess for contraindications to hyperbaric oxygen therapy.

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Abstract

Carbon monoxide (CO) poisoning has a case-fatality rate as high as 30%. CO impairs oxygen delivery and peripheral utilization causing cellular hypoxia secondary to its 200-fold affinity for hemoglobin compared with oxygen. The acute neurologic effects of CO poisoning are the result of cellular hypoxia. Up to half of patients with CO exposure develop delayed neuropsychological sequelae. Headache is the most common presenting complaint, although severely poisoned patients may develop acute neuropsychological symptoms such as ataxia and cognitive disturbances. Standard pulse oximetry is incapable of distinguishing between carboxyhemoglobin (COHb) and oxyhemoglobin. Non-invasive pulse co-oximetry, which uses multiple wavelengths of light specifically absorbed by oxyhemoglobin, deoxyhemoglobin, COHb, and methemoglobin, can be useful at triage to rapidly identify patients with significant exposure. All patients with suspected CO exposure should undergo COHb-level testing in addition to an ECG and cardiac monitoring due to potential for myocardial ischemia or dysrhythmias. There is no clinically relevant difference between arterial and venous COHb samples. The mainstay of treatment in CO poisoning is oxygen therapy as it competitively displaces CO from hemoglobin. Use of hyperbaric oxygen (HBO) therapy in CO poisoning remains controversial. A systematic review of the literature did not find sufficient evidence

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that HBO reduces the incidence of delayed neurological sequelae.

Case Presentation

An 89-year-old female is found by her family, lying unconscious on her kitchen floor after they had been unable to reach her by phone for several hours. EMS is activated and when the paramedics arrive, they note that the gas oven is on, and there is thin, gray smoke coming from around the door. The house gas supply is turned off, windows are opened, and the family and the patient are immediately evacuated from the home. En route to the hospital, the patient is placed on high-flow oxygen at 15 liters per minute by non-rebreather mask. Her bedside glucose determination is 229 mg/dL. Vital signs are within normal limits during transport. She opens her eyes to sternal rub, and makes spontaneous movements of all extremities. Upon arrival to the ED, the patient becomes more alert and is able to respond to your questions. She tells you that she remembers putting a tray of calzones into the oven, after which she has no recall of the day's events. She has a past medical history of "well-controlled" hypertension, hyperlipidemia, and non-insulin-dependent diabetes. Her medications include hydrochlorothiazide 25 mg daily, lisinopril 10 mg daily, simvastatin 20 mg daily, and metformin 1000 mg twice daily. On physical examination, weight is 65 kg, blood pressure is 97/50 mm Hg, heart rate is 113 beats per minute, respiratory rate is 22 breaths per minute, temperature is 37.1°C (98.8°F), and oxygen saturation is 99% on 15 liters per minute via non-rebreather mask. She appears her stated age. Cardiopulmonary examination is remarkable only for tachycardia. Her abdomen is soft and non-tender with normal bowel sounds. Her skin is warm and dry, and there is no peripheral edema. Her cranial nerves are intact, with briskly reactive, symmetric pupils. Motor and sensory examination is non-focal, and cerebellar testing is notable only for an intention tremor on finger-nose-finger test. Gait is normal and speech is fluent and without errors. Laboratory testing shows a hemoglobin of 10.3 g/dL and a leukocyte count of 11.7 x10^9/L. Electrolyte results fall within the normal range, and her serum creatinine is 1.7 mg/dL. Qualitative CK-MB and troponin I tests are positive, and the sample has been sent to the STAT lab for quantitative testing. Serum carboxyhemoglobin level is 15% with normal serum pH on an arterial blood gas. An ECG reveals deep, down-sloping inferior and lateral ST-segment depressions which were not present on a routine cardiogram 1 month prior. You have many questions about this patient's care. What symptoms and physical signs need to be addressed and treated? What additional diagnostic testing should be performed? What treatment regimen is appropriate and what should be avoided? What are the risks or delayed complications from her illness? Are there special considerations for this or other patient populations?

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Available Online At No Charge To Subscribers

EM Practice Guidelines Update: "Current Guidelines For Management Of Acute Bacterial Meningitis In The Emergency Department," www.ebmedicine.net/meningitis

Introduction

Carbon monoxide (CO) poisoning is a frequently considered emergency department (ED) diagnosis.[1-3] Annual United States (US) ED visits related to CO poisoning are estimated at 50,000 per year.[4] It is one of the leading causes of accidental poisoning death in the US, although the majority of fatalities are intentional.[3,5,6] Non-specific and highly variable presentations make this a difficult diagnosis, especially if the exposure history is not clear.[1]

Patients with CO poisoning are at very high risk for morbidity and mortality. Unlike many other disease entities, emergent treatment for this toxin is aimed not only at treating immediate threats to life but also at preventing delayed and sometimes permanent neuropsychological morbidity. Special considerations must be made for populations with preexisting morbid conditions and for pregnant women. Treatment is based on reducing the duration of cellular exposure to the toxin. This can be accomplished by treating the patient with high-concentration oxygen or with hyperbaric oxygen (HBO). Deciding which patient requires which treatment falls under the scope of the emergency clinician's practice.

This issue of *Emergency Medicine Practice* covers the epidemiology, pathophysiology, diagnosis, and

management of CO poisoning in both the general population and special populations.

Abbreviations And Acronyms

ABG: Arterial blood gas
ACEP: American College of Emergency Physicians
CO: Carbon monoxide
COHb: Carboxyhemoglobin
CT: Computed tomography
DNS: Delayed neurological sequelae
ECG: Electrocardiogram
ED: Emergency department
EMS: Emergency medical services
HBO: Hyperbaric oxygen
HCG: Human chorionic gonadotropin
IV: Intravenous
NBO: Normobaric oxygen
RCT: Randomized controlled trial
US: United States
VBG: Venous blood gas

Critical Appraisal Of The Literature

An Ovid MEDLINE® search for randomized controlled trials (RCTs) was performed, using the search term *carbon monoxide,* to review trials published since 2004. Ovid MEDLINE® was also queried, using the search terms *carbon monoxide* and *(therapy* or *treatment),* to identify investigations that have not yet reached the RCT stage. The Cochrane Review of HBO for CO poisoning was used to identify and analyze the RCTs available as of its update in November 2004.

While some RCTs of quality were identified, the results were varied, with a pooled analysis showing the odds ratio confidence interval including 1. However, the trials exhibit a high degree of variance in quality, degree of poisoning, time to HBO therapy, and methodology, making meta-analysis difficult. The most rigorous RCT does show a statistically significant benefit in neurologic outcome from the use of HBO although as discussed in this article, it too was criticized for its methodology. Further study is required, perhaps via multicenter RCT.

The American College of Emergency Physicians (ACEP) has an evidence-based clinical policy on critical issues in the management of adult patients presenting to the ED with acute CO poisoning. The ACEP commitee reviewed the English language literature between January 1980 and January 2006 via MEDLINE® searches. The review was further extended via bibliographic review of articles cited and from articles from the files of the clinical policy subcommittee members. Expert reviewers then commented on and graded the articles on their evidentiary strength into 3 classes. Studies with fatal flaws were excluded from the process of formulating recommendations. After completion of their review, only Level C recommendations could be offered. This class of evidence offers strategies for patient management that are "based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus."[7] The final recommendations of the ACEP clinical policy are:

1. Hyperbaric oxygen therapy is a therapeutic option for CO-poisoned patients; however, its use cannot be mandated.
2. No clinical variables, including carboxyhemoglobin levels, identify a subgroup of CO-poisoned patients for whom hyperbaric oxygen therapy is most likely to provide benefit or cause harm.[7]

The quality of evidentiary review in the formulation of the ACEP clinical policy is high. The ACEP policy tells the emergency clinician that he or she cannot depend on a specific clinical variable for knowing when to use HBO therapy. It also tells the emergency clinician that he or she is not bound to use HBO therapy due to best clinical practice imperatives or any binding guidelines or policies. Both are quite useful in guiding the activities in the care of patients in the ED.

Epidemiology And Etiology

Carbon monoxide poisoning has its peak incidence during the winter months in colder climates and is often a seasonal diagnosis.[8] Intentional exposure for purposes of self-harm, as well as various other unintentional exposures, can occur at any time of year and in any climate. Sources of exposure include use of fuel-burning devices without adequate ventilation, gasoline-powered vehicles or generators operating in enclosed spaces, heating systems, and open-air exposure to motorboat exhaust fumes.[9] Carbon monoxide poisoning must never be taken lightly, as it has a case-fatality rate as high as 30%.[3,5]

Pathophysiology

At room temperature, CO is a gas that is odorless, tasteless, and not irritating. Its density is similar to that of air, being approximately 97% as dense.[10] It is formed by the incomplete combustion of hydrocarbons, or formed endogenously from liver metabolism of methylene chloride, which is commonly found in paint stripper and aerosol propellants.[1]

Carbon monoxide impairs oxygen delivery and peripheral utilization, causing cellular hypoxia. Carbon monoxide binds to hemoglobin with an affinity more than 200 times that of oxygen after rapidly diffusing across the pulmonary capillary

membrane, forming carboxyhemoglobin (COHb). The conformation of the COHb moiety results in leftward shift of the normal oxyhemoglobin dissociation curve, which reduces tissue oxygen delivery. In addition, CO generates reactive oxygen species (leading to cellular apoptosis) and interferes with the cytochrome oxidase pathway in cellular respiration (impairing oxidative metabolism).[2] These effects are thought to be similar to ischemia-reperfusion injury, and they are potentiated by hypotension and hypoxemia. The acute neurologic effects of CO poisoning are the result of this cellular hypoxia. Certain tissues that are more sensitive to ischemic injury, such as the hippocampus and basal ganglia, are most commonly injured.

Much of the mortality in CO poisoning results from dysfunction of the cardiovascular system.[11] Carbon monoxide binds to myoglobin, altering its function. It also displaces nitric oxide from platelets, resulting in nitric-oxide-mediated smooth muscle relaxation and decreased systemic vascular resistance. Acute coronary syndrome, cardiogenic shock, and dysrhythmia can result. Patients with underlying coronary disease and/or history of prior myocardial infarction are therefore at increased risk for adverse outcomes.

Pulmonary edema may occur in the CO-poisoned patient; however, this occurs due to cardiac toxicity resulting in congestive heart failure, and not to direct pulmonary toxicity.

Patients with CO exposures are also at high risk (up to 46% of patients) for morbidity in the form of delayed neuropsychological sequelae, which may be persistent, disabling, or even permanent.[12-14] These effects include cognitive and affective changes, gait and motor disturbances, peripheral and cranial neuropathies, psychosis, and dementia and can arise days or weeks after exposure and apparent recovery.[13] Counterintuitively, this is believed to be due not to impaired cerebral oxygen delivery, but is more likely due to reactive oxygen species, lipid peroxidation in the central nervous system, and neuronal apoptosis.[15]

Table 1. Symptoms Reported In Carbon Monoxide Exposure By Frequency (n=1144)[16]

Symptom	Percentage of Patients
Headache	85
Dizziness	69
Fatigue or generalized weakness	67
Nausea or vomiting	52
Trouble thinking or confusion	37
Loss of consciousness	35
Dyspnea	7
Chest pain	2

This table was published in "Carbon Monoxide Poisoning" in *Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose*, by Eric Lavonas, page 1299, Copyright Elsevier, 2007. Used with permission.

Differential Diagnosis

The most common presenting complaint in mild to moderate CO poisoning is headache.[16] Other symptoms at presentation may include myalgias, malaise, nausea, vomiting, and dizziness. (**See Table 1.**) It is easy to see how the exposure history is critical in mild-to-moderate cases that can easily be mistaken for tension or other benign types of headache, such as migraine. Mild presentations may also mimic gastroenteritis, influenza, or other viral syndromes, especially in children.[15] In a convenience sample of 55 patients presenting in winter with flu-like symptoms to an urban ED, 13 patients (23.6%) had COHb levels greater than or equal to 10%. None of those patients was diagnosed by the treating physician as having subacute CO poisoning.[17] Carbon monoxide poisoning should always be considered when groups of patients present to the ED from a single event, household, or location with similar symptoms.

Patients who present to the ED saying that they inhaled smoke, fumes, or gases may have been exposed to other harmful products of combustion in addition to CO. These compounds, their sources, and their effects are summarized in **Table 2**.

Because severely poisoned patients present with symptoms of major end-organ dysfunction such as coma, altered mental status, and angina pectoris, the differential diagnosis is broad. The history of exposure is critical to avoid missing this time-sensitive diagnosis by pursuing a broad evaluation (such as for coma). The prehospital care provider report is essential in this regard.

Prehospital Care

It is important for prehospital providers to recognize the potential for CO poisoning in a wide variety of clinical scenarios. A careful examination of the scene may reveal clues to potential CO exposure. Evidence of combustion or abnormal odors or fumes should alert the providers to the possibility of hazardous products of combustion. Any carbon-containing fuel, such as wood, charcoal, natural gas, diesel, or heating oil can generate CO when burned. The fire department can provide expertise and equipment to safely enter such an environment, test for hazards such as CO, and ventilate the area. Persons affected by the toxic byproducts of combustion may be in close proximity to the source or they may be distant, since they do not need to have been in direct contact with smoke to be exposed. If a single person was exposed, others in the vicinity may have been simi-

larly affected, and they should also be assessed and brought to the hospital for evaluation.

An intravenous (IV) catheter should be established, a rapid assessment for signs of cardiovascular or neurologic dysfunction should be performed, and the patient should be transported to the ED without delay. In cases where CO exposure is confirmed or suspected, empiric treatment with oxygen during transport is recommended. A prehospital electrocardiogram (ECG) is helpful in early diagnosis of myocardial ischemia.

Emergency Department Evaluation

Initial Stabilization

Patients with confirmed or strongly suspected CO poisoning may be triaged according to their clinical status. Special attention must be paid to airway management. As discussed above, co-inhalants from fires may lead to impending airway compromise. Patients with thermal or chemical injury to the pulmonary system or upper airways may require urgent intubation on the basis of their expected clinical course. Non-invasive co-oximetry may be useful at triage to rapidly identify patients with significant CO exposure. Patients should receive high-flow oxygen. Vital signs and a directed neurologic examination should be done frequently, and the patient should have continuous cardiac monitoring. An IV catheter should be inserted. Laboratory studies, including a COHb level by co-oximetry, should be ordered. This may be obtained from an arterial blood gas if acid-base disturbance is suspected. Patients with alteration in mental status or complaints consistent with myocardial ischemia should have an ECG.

History

Clinical signs and symptoms of CO poisoning are non-specific and vary widely.[1] Vague systemic symptoms such as fatigue, nausea or vomiting, or weakness may be the only indicators.

More severely poisoned patients may develop acute neuropsychological symptoms such as ataxia, seizure, syncope, coma, disorientation, and cognitive difficulties. Loss of consciousness is a marker of poisoning severity.[16,19]

Patient evaluation in suspected CO poisoning is directed at making the diagnosis, estimating the severity of poisoning, and identifying end-organ damage. Questions to ask include:

- Where was the patient found, and under what circumstances?
- Was there clear evidence of CO exposure?
- Was there loss of consciousness?
- Was there evidence of trauma?
- Was a fingerstick glucose determination performed?
- Was noninvasive co-oximetry performed?
- Was prehospital ECG performed?
- Was there evidence of attempted self-harm or suicidal intent?

In addition to performing a standard medical history, patients should be asked about symptoms consistent with end-organ dysfunction or damage. These include headaches, alterations in mentation or

Table 2. Combustion Products Complicating Smoke Inhalation[22]

Combustion Product	Source	Mechanism of Harm
Carbon monoxide	All combustible materials	Loss of oxygen-carrying capacity of hemoglobin, inhibition of cellular respiration, direct cytotoxicity
Hydrogen cyanide	Animal products, wool, acrylics, acrylonitrile-butadiene-styrene plastics, urea-formaldehyde foam insulation, nylons	Inhibition of cellular respiration
Carbon dioxide	All combustible materials	Simple asphyxia
Methemoglobin inducers	Unknown	Loss of oxygen-carrying capacity of hemoglobin
Phosgene, halogen acids	Fire extinguishers, flame retardants, acrylics, polyvinylchloride plastics, films, resins	Corrosive airway and/or pulmonary injury
Acrolein, organic acids, nitrogen oxides	Most combustible materials	Corrosive airway and/or pulmonary injury
Ammonia, isocyanates	Animal products, wool, acrylics, acrylonitrile-butadiene-styrene plastics, urea-formaldehyde foam insulation, nylons	Corrosive airway and/or pulmonary injury
Carbonyl fluoride	Fluorocarbons	Corrosive airway and/or pulmonary injury
Sulfur oxides	Animal and petroleum products, rubber, wool	Corrosive airway and/or pulmonary injury
Soot	All combustible materials	Mechanical airway obstruction

Adapted from O'Malley GF. Non-invasive carbon monoxide measurement is not accurate. *Ann Emerg Med.* 2006;48:477-478.

difficulty performing simple mathematical tasks, visual changes, syncope, other focal neurologic symptoms, or seizure. All patients, regardless of age or health status, should be asked about the presence of chest pain, shortness of breath, dyspnea on exertion, palpitations, or lightheadedness. Female patients should be asked about the possibility of pregnancy. Finally, all patients with CO poisoning should be questioned directly regarding suicidal intent.[6]

Physical Examination

The key components of the physical examination in CO poisoning are the trauma, neurologic, and cardiovascular examinations. The former is focused on identifying concomitant injuries, especially in patients who are coming from the scene of a fire or in those who had syncope secondary to CO exposure. The latter 2 components of the examination are focused on identifying signs of end-organ toxicity due to acute CO poisoning.

A methodical approach to the evaluation of trauma is indicated, especially in patients with altered mental status. Several parts of the examination bear special attention in suspected CO poisoning. Patients coming from the scene of a fire are at risk for thermal injury and pursuant upper airway obstruction, so definitive airway management should be considered early in the patient's hospital course. The oropharynx should be visualized to evaluate for edema and soot, and the neck should be carefully examined for the presence of stridor. Although hypotension in most trauma patients is often initially presumed to be from loss of circulating blood volume, CO-poisoned patients may have vasodilatory shock due to acidosis. Co-inhalants, such as cyanide, may present in the same manner, and these should not be overlooked in the differential diagnosis of the hypotensive patient, even while simultaneously treating with volume expansion. A careful pulmonary examination may detect small airways obstruction as wheezing in patients who are exposed to smoke or have inhaled other irritants. Patients may also have "cardiac wheezing" or crackles in the lungs, signifying myocardial depression secondary to smoke inhalation.

Any patient presenting with possible CO poisoning should undergo a formal assessment of mental status. In addition to typical orientation questions, it may be useful to perform a comprehensive mental status assessment. Carbon-monoxide-poisoned patients may present with cognitive changes, even in the acute phase of poisoning. Cranial nerves should be examined and a thorough motor and sensory examination performed to detect any focal neurologic deficits. Bedside tests of cerebellar function, such as finger-to-nose testing, heel-to-shin testing, or rapid alternating movements, may also detect abnormalities not evident on gross examination. Gait testing is a must, because ataxia can be a presenting sign of neurotoxicity and may be missed if the patient is not observed while ambulating.

The cardiac examination focuses on signs of myocardial ischemia and global hypoperfusion. Jugular venous pressure may be elevated, indicating acutely depressed cardiac function. A new gallop may represent acute diastolic dysfunction. Hypotension may indicate cardiogenic shock due to ischemia, or it may be related to acidosis and vasodilation.

Diagnostic Studies

Co-oximetry

Standard pulse oximetry uses 2 wavelengths of light that are absorbed by oxyhemoglobin and deoxyhemoglobin, respectively. A calculation is then done based on the relative absorption of these 2 wavelengths as they pass through the fingertip, which yields the oxyhemoglobin percentage. Because the wavelength utilized in this instrument for oxyhemoglobin is also absorbed by COHb, this tool will be incapable of distinguishing between them.

A more recent technological innovation—noninvasive pulse co-oximetry—uses multiple wavelengths of light which are specifically absorbed by oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin, and in some instruments, methemoglobin. Two small studies prospectively evaluated this technology. One, with 20 CO-intoxicated patients and 5 healthy controls, compared results obtained via the noninvasive pulse co-oximetry against the gold standard blood gas co-oximetry analysis. Results showed a mean absolute error of 3.15% for the noninvasive method. It is worth noting that comparison of COHb levels between the various blood gas analyzers used in the department revealed a mean absolute variation of 2.4%.[20] A second study, with 12 patients, compared pulse co-oximetry with blood gas co-oximetry. No difference was found between the 2 techniques ($P > 0.05$).[21] A third study, published as a letter, found 5 false positive readings in 328 patients, and the study was halted after a single false negative reading was found.[22] Although noninvasive pulse co-oximetry appears accurate on the basis of the small studies mentioned above, the equipment is relatively expensive and is not available in most EDs. It cannot be considered the standard of care.

Carboxyhemoglobin Testing

Any patient with known or suspected CO poisoning should undergo COHb-level testing. The relationship between COHb levels and poisoning severity is generally poor; accordingly, this should be obtained while initiating empiric treatment.[23] Carboxyhe-

moglobin levels may be determined from venous or arterial blood, in a heparinized tube (typically a "green-top" or arterial blood gas syringe). Arterial COHb levels are ideal. In addition to being an accurate measurement technique, the additional information obtained from blood gas testing is helpful in assessing the acid-base status of the critically poisoned patient, but in most circumstances, venous samples are more rapidly and readily obtained by non-physician personnel. In addition, there is no clinically relevant difference between arterial and venous COHb levels, with 95% of the samples falling in the range of between 2.4% and -2.1% of each other.[24] Therefore, venous COHb measurements are useful and accurate in the triage of multiple suspected poisonings, such as from a fire scene or industrial accident. If the clinical suspicion for acidosis is low, venous blood sampling causes less discomfort to patients than arterial blood sampling and may be preferable. Serial measurements of COHb are generally not helpful. An exception is in the case of CO poisoning via endogenous hepatic metabolism of methylene chloride to CO. In these patients, the apparent half-life of CO may be prolonged to 13 hours.[25]

A COHb level greater than 3% in non-smokers or greater than 10% in smokers suggests an abnormal CO exposure. Nonetheless, a patient may have toxicity with a normal or near-normal level, depending on the timing of exposure relative to sampling, length of exposure, degree of exposure, and any oxygen therapy initiated prior to sampling.

Electrocardiogram

All patients with a history suggestive of CO exposure should undergo ECG and cardiac monitoring because of the potential for myocardial ischemia or dysrhythmia. Ventricular dysrhythmias or ST-segment changes are sometimes seen.[26,27]

Cardiac Biomarkers

By consensus, most sources recommend cardiac biomarker testing be performed if patients have ECG changes or abnormalities suggestive of ischemia, symptoms consistent with myocardial ischemia, history of coronary artery disease, or age greater than 65.[9]

Pregnancy Testing

Qualitative urine or serum human chorionic gonadotropin (HCG) testing should be performed in female patients of childbearing age. Theoretically, elimination of CO from fetal hemoglobin takes over 3 times as long as it does for the mother; however, this is based on a sheep model.[28]

Pregnant women have been excluded from prospective trials of HBO therapy, so there is no evidence to suggest a difference in length of treatment or use of HBO therapy in the pregnant patient.

Chest Radiography

A chest x-ray is a useful diagnostic adjunct in the patient with abnormal lung findings, persistent hypoxia, or ventilatory failure. It may help distinguish between and guide treatment of pulmonary edema, aspiration, pneumonitis, pneumothorax, or an underlying preexisting condition such as chronic obstructive pulmonary disease (COPD).

Computed Tomography

Computed tomography (CT) scans of the head and cervical spine are useful in the patient with known or suspected trauma, such as those from the scene of a fire or explosion. Head CT is also helpful in the evaluation of the patient who presents with altered mental status and an unclear or unobtainable history in order to evaluate for traumatic intracranial injury, spontaneous intracranial hemorrhage, or structural abnormalities contributing to or causing the patient's symptoms. For patients who will be undergoing HBO therapy (and will thus be difficult to examine) this is more important. Changes on the CT scan due to CO poisoning appear acutely within 12 hours of CO exposure but may not be apparent if the CT scan is obtained upon presentation to the ED.[9] Therefore, neuroimaging is not useful and should not delay therapy in a patient with isolated CO poisoning and a well-established diagnosis. Hypodense lesions in the globus pallidus, caudate, and putamen are common findings.[49]

Toxicologic Testing

Toxicology screens, including assays for volatile alcohols, salicylates, acetaminophen, and drugs of abuse may be helpful in determining the cause of altered mental status. In patients who present after a suicide attempt or suicidal gesture, toxicol-

Figure 1. Hyperbaric Oxygen Chamber

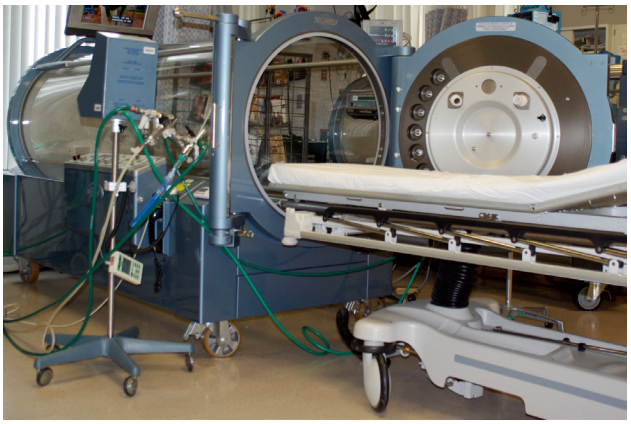
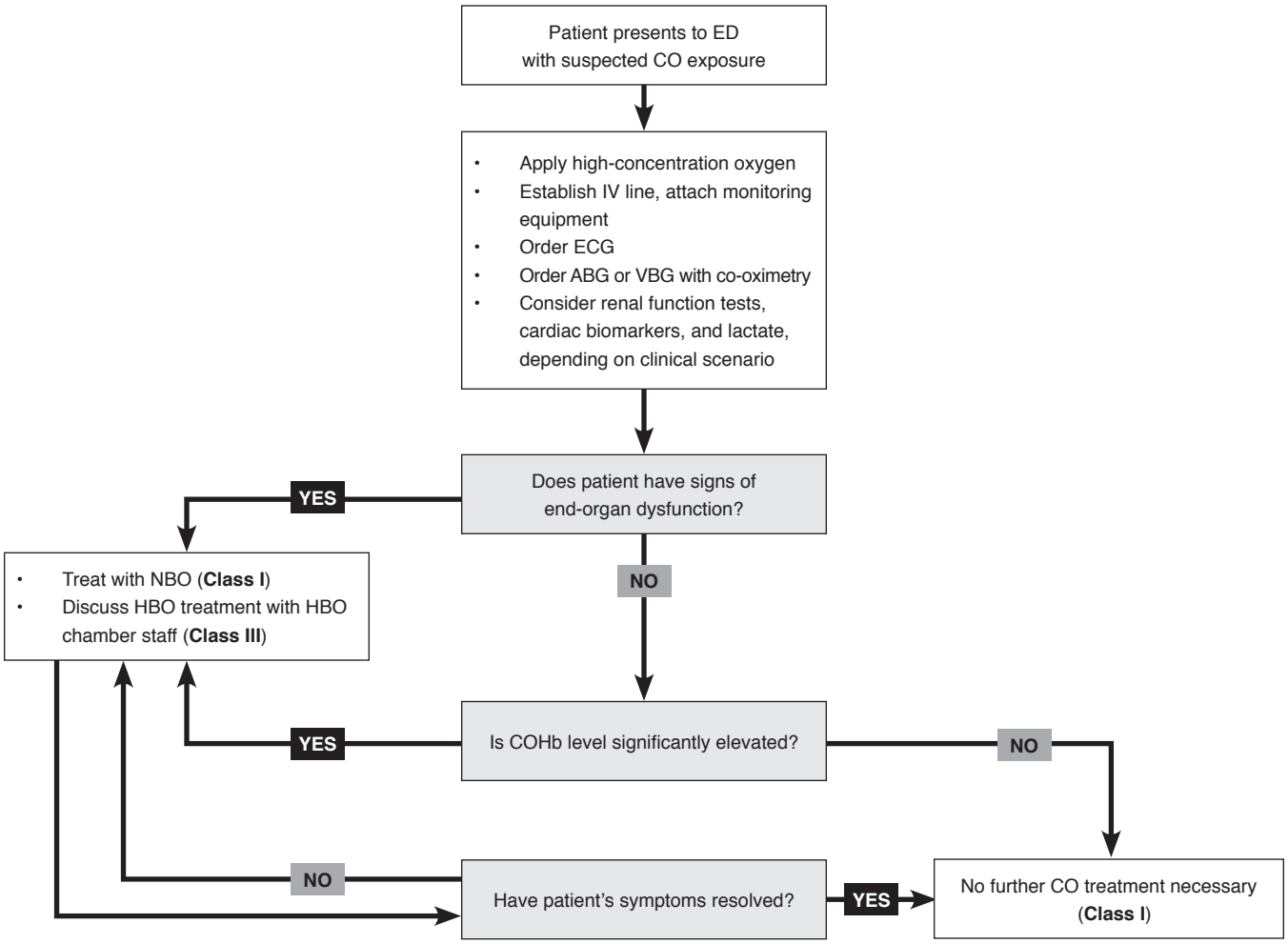


Photo courtesy of Norman Knight Hyperbaric Medicine Center, Massachusetts Eye and Ear Infirmary, Boston, MA. Used with permission, Heikki Nikkanen, MD.

Clinical Pathway For Diagnosis And Treatment Of Carbon Monoxide Poisoning



Abbreviations: ABG, arterial blood gas; CO, carbon monoxide; COHb, carboxyhemoglobin; ECG, electrocardiogram; ED, emergency department; HBO, hyperbaric oxygen; IV, intravenous; NBO, normobaric oxygen; VBG, venous blood gas.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

ogy screens may identify poisons that are treatable if identified early, such as acetylsalicylic acid and acetaminophen. The test characteristics and potential inadequacies of toxicologic assays and drugs of abuse screens are well-discussed in the medical literature, and care must be taken not to ascribe a patient's symptoms to toxic ingestion alone if other causes of altered mentation such as trauma, shock, and metabolic disturbance have not been thoroughly investigated.

Lactate

Protracted exposure to CO can cause an increase in the serum lactate due to increased anaerobic cellular metabolism in the setting of tissue hypoxia,[31] but the quantitative lactate level does not correlate with the severity of CO poisoning. A very high lactate level in a patient who has suffered smoke inhalation might prompt empiric treatment for cyanide toxicity, but there is insufficient evidence to guide the threshold for such therapy.

Treatment

The mainstay of treatment in CO poisoning is oxygen therapy. (**See Figure 1.**) Both normobaric oxygen (NBO) and HBO are used. One rationale for oxygen therapy is to reduce the duration of exposure to exogenous CO. Carbon monoxide is competitively displaced from hemoglobin and eliminated from the body via the pulmonary circulation. Its half-life is inversely proportional to the fraction of inspired oxygen. The elimination half-life of CO is approximately 300 minutes on room air, 90 minutes on reservoir "non-rebreather" facemask, and 30 minutes breathing HBO.[1]

The use of HBO therapy (defined as 100% inspired oxygen delivered at greater than 1.4 atm of pressure) in CO poisoning remains controversial.[7,32] Hyperbaric oxygen raises the amount of dissolved (non-hemoglobin-bound) oxygen in the blood and has been demonstrated to expedite elimination of CO, as well as to mitigate other effects of CO within the body. Hyperbaric oxygen treatment is also thought to remove CO from cytochrome oxidase, inhibit adherence of neutrophils on vascular endothelium, and prevent the downstream effects of lipid peroxidation.[33-35]

There are no objective scales or scoring systems to assess the severity of CO poisoning. Despite mixed outcome data of varying quality, the use of HBO therapy for patients who have loss of consciousness/syncope, coma, seizure, profound acidosis (pH < 7.1), neuropsychological abnormalities, fetal distress in pregnancy, or evidence of myocardial ischemia continues to be suggested as a treatment option.[10,15,36] In older literature and even in some current toxicology textbooks, a COHb level of 25% or greater (some authors suggest 40%) is often recommended as a threshold for therapy.[10,37] A lower threshold for HBO therapy is sometimes used in the pregnant patient. **(See the "Special Circumstances" section on Pregnancy, below.)** Neither of these recommendations is supported by sound evidence. One must remember that COHb levels in the ED will often be lower than peak levels if the patient has received prehospital oxygen therapy or been transferred from another facility. Further, neither peak nor ED COHb levels correlate well with severity of poisoning or patient outcomes.

General risks and relative contraindications to HBO therapy are available in other texts. Untreated pneumothorax is an absolute contraindication to hyperbaric therapy of any kind.

Special Circumstances

Pregnancy

Pregnant patients with CO poisoning require special consideration. Risk to mother and fetus must be managed, both from the toxin and the potential risks of therapy. Acute, severe CO poisoning is associated with high maternal and fetal mortality.[38] There is contradictory data on whether fetal hemoglobin has a greater affinity for CO than does hemoglobin A, with much of the data coming from animal models. It is, however, well-demonstrated that steady-state levels of COHb in the fetus are higher than in maternal blood. It takes longer to reach steady-state, and fetal elimination of CO is also prolonged.[37] For these reasons, many centers advocate hyperbaric treatment for pregnant females with a COHb level greater than 20% or signs of fetal distress (decreased or absent fetal movement or fetal bradycardia).

A rat model of CO poisoning has previously demonstrated reduction in the rate of spontaneous abortion among pregnant rats treated with HBO.[39] There are no human data from RCTs of HBO therapy for CO poisoning, as pregnant patients were excluded from these trials. Contradictory data exist on fetal risk from HBO therapy when it has been tested in pregnant patients for a variety of other conditions, with some studies showing no apparent risk.[38]

Delayed Effects Of CO Exposure

A syndrome of delayed neuropsychological sequelae (DNS) may develop in CO-poisoned patients, with symptoms that include disorientation; cognitive difficulties including judgment, memory, and concentration deficits; Parkinsonism; personality changes; and visual disturbances. These DNS may develop in up to 46% of presenting patients poisoned by CO, though reported rates vary across studies.[1,5,12,13,40] This typically occurs from 3 to 40 days after apparent recovery and may be long-lasting or permanent. Recent investigations in CO poisoning have focused on prevention of these late effects.

Controversies And Cutting Edge

There have been multiple RCTs comparing hyperbaric and normobaric oxygen for prevention of late neurological complications in CO poisoning.[12,40-43] These trials have been of varying quality, and the outcomes have been mixed. A double-blinded RCT of 191 patients found a significantly higher rate of neuropsychological test abnormalities among the patients treated with HBO at completion of treatment and no difference at 1-month follow-up.[43] Another double-blinded study measured the incidence of cognitive sequelae at 6 weeks in 152 patients randomized to hyperbaric versus normobaric 100% oxygen and room-air treatments. The study was halted early when interim data analysis detected less-frequent cognitive defects in the HBO group (25%) than in the NBO group (46%).[40] Both of these studies have been criticized for their methodologies. In the first study, only 46% of patients presented to 1-month follow-up. In addition, it is not clear how cognitive differences at completion of treatment relate to long-term function, which is the primary outcome of interest to patients and physicians. In the second study, the 2 groups had significant differences in baseline cerebellar dysfunction (4% vs 15%) as well as different lengths of exposure to CO at baseline (13 +/- 41 hours vs 22 +/- 64 hours), favoring the group randomized to hyperbaric treatment.

A Cochrane review of 6 RCTs of HBO for CO poisoning did not find sufficient evidence to establish that the administration of HBO reduced the incidence of delayed neurological sequelae. Further, the Cochrane group found that "design or analysis flaws were evident in all trials."[32]

The ACEP 2008 policy statement on the subject came to the conclusion that HBO therapy is a treatment option but that "its use cannot be mandated."[7] The Undersea and Hyperbaric Medical Society lists CO poisoning in its indications for the use of HBO but does not give criteria for its consideration.[44]

Hyperbaric oxygen therapy continues to be widely recommended for cases of severe poisoning, given the presence of some RCT data demonstrating a benefit and that the natural course of severe CO poisoning leads to high morbidity and mortality without treatment. At facilities that do not have a hyperbaric chamber, the clinician must make a risk-versus-benefit decision regarding transfer to another facility.

Figure 2. Sample Discharge Instructions Following Emergency Department Treatment For Carbon Monoxide Exposure

Diagnosis: Carbon Monoxide Exposure

About your diagnosis: You were exposed to carbon monoxide (CO) gas. Carbon monoxide is poisonous if you are exposed to a large enough amount. You cannot see or smell carbon monoxide gas. Carbon monoxide can reduce the amount of oxygen carried by your blood to vital organs, causing damage. It can also be directly toxic to your brain, heart, lungs, and other important tissues in your body.

Carbon monoxide is created by incomplete burning of various fuels. Exposure to carbon monoxide can cause headache, dizziness, fatigue, weakness, nausea, vomiting, confusion, shortness of breath, chest pain, and other symptoms. Patients exposed to carbon monoxide may have trouble with thinking or with other brain functions, which may not appear until weeks after exposure. Prompt treatment for carbon monoxide exposure helps to remove carbon monoxide more quickly from your body. Treatment may reduce the chance that you will experience delayed problems from your carbon monoxide exposure.

What to do:

Follow-up: Please follow up with your doctor within 2 weeks. Your doctor may ask you to undergo additional testing that could include blood tests, imaging tests to look at the structure of your brain, or testing to evaluate your brain function.

Prevention: Please do not return to the place where you were exposed to carbon monoxide until the fire department has declared it safe. This is true even if you were exposed in your own home. You should make sure that your fireplace, furnace, and gas appliances such as water heaters and stoves are inspected and are working properly. Certified home inspectors can check this. Check that the exhaust of your motor vehicles is not blocked or leaking. Never run a motor vehicle in an enclosed space. Avoid being near the exhaust fumes of running vehicles. Do not use propane stoves, grills, or open fires to cook in enclosed spaces. This includes inside tents and under awnings. Install at least one carbon monoxide detector in your home, near where you sleep. Carbon monoxide detectors can be purchased at home-improvement, hardware, and some department stores.

Smoking: If you smoke tobacco, you should try to quit. Smoking increases the levels of carbon monoxide in your blood as well as having many other harmful effects on your health. Talk to your doctor about medications and other therapies to help you quit smoking.

Medications: You can resume taking all your medications.

When to seek care: Call 911 and return to the emergency department immediately if you have chest pain, have shortness of breath, pass out or faint, have a seizure or convulsion, are weak, or have very dark-colored urine or are not passing any urine. Please contact your primary care doctor or return to the emergency department for any other new, worsening, or concerning symptoms.

Disposition

Consensus among leading sources is that patients who did not have loss of consciousness, who have complete recovery from any symptoms, whose COHb level has returned to normal, and who have no evidence of end-organ damage (ECG changes, elevated cardiac biomarkers, neurological deficits) may be safely discharged to home.[10,16,36] **(See Figure 2 for a Sample Discharge Instruction sheet.)**

An observation unit stay would be a useful option for stable patients requiring prolonged NBO therapy, for EDs that are so equipped. Only those patients showing signs of significant end-organ toxicity will require hospitalization, with or without HBO therapy.

Discussion Of Investigational Information

Some insurance companies have recently reclassified HBO therapy as an investigational therapy in the treatment of acute CO poisoning, which implies that they would withhold payment for its use.[45] However, Medicare continues to reimburse for its use, as do some private insurance companies.[46]

Tight regulation of glucose with insulin is another measure that can be undertaken in the CO-poisoned patient. Although there are some data that suggest the benefit may be independent of the glucose level and accrue directly to the use of insulin, its use in this manner would be off-label.[47,48]

Other agents (including ketamine, dimethyl sulfoxide, and allopurinol) have been proposed as beneficial, through blockade of excitatory amino acids, antioxidant properties, or prevention of free

Risk Management Pitfalls For Carbon Monoxide Poisoning
(Continued on page 12)

1. **"The hyperbaric fellow is reluctant to treat my patient who had syncope because his COHb level is normal. Can I send the patient home?"**
   All patients with CO poisoning must be questioned about syncope. There is no clear relationship between the severity of poisoning and the presenting COHb level. Syncope or loss of consciousness is a surrogate for more severe poisoning, and patients with syncope should be considered for advanced therapies and hospital admission.

2. **"My patient says he was just out working on his car in the garage with the engine running. This seems suspicious to me."**
   Intentional CO poisoning comprises a large share of fatal cases. All patients with CO poisoning should be questioned directly about suicidal ideation and plan.

3. **"The nurse is sending an arterial blood gas to assess the patient's degree of poisoning. Do I need to request any special testing?"**
   Carboxyhemoglobin level by co-oximetry is not part of routine blood gas analysis in most hospital laboratories and should be specifically requested by name. Arterial blood gas analysis with co-oximetry is the ideal means for obtaining COHb level because it also provides important information about the patient's acid-base status, which helps quantify the severity of poisoning.

4. **"My 18-year-old previously healthy patient with CO exposure has an abnormal ECG. Isn't this most likely a normal variant?"**
   Carbon monoxide impairs oxygen delivery and cellular respiration and can cause myocardial ischemia and infarction even in patients without native coronary artery disease. Those with symptoms such as syncope, chest pain, or shortness of breath and/or an abnormal ECG warrant cardiac biomarker testing.

5. **"My senior resident is telling me that there is no benefit from hyperbaric treatment in CO poisoning. What does the best available evidence tell us?"**
   Taking all RCTs into account, systematic reviews have found insufficient evidence to demonstrate improvement in delayed neuropsychological sequelae following CO poisoning in patients who receive hyperbaric therapy.[32]

6. **"My pregnant patient is asymptomatic and had a normal COHb level. She is asking me about the risks to her baby. What can I tell her?"**
   Multiple studies have shown that pregnant women with normal mental status and no history of loss of consciousness have good outcomes in terms of normal delivery and future development of their children.[52,53,54]

7. **"I have a pregnant patient who lost consciousness and has ongoing chest pain after a CO exposure. She is nervous about undergoing hy-**

radical formation. However, these agents are not approved for treatment of CO poisoning by the US Food and Drug Administration (FDA).[49,50,51]

Summary

Carbon monoxide poisoning is a potentially life-threatening or permanently disabling toxicity that is commonly encountered in the ED, with an increased incidence in the winter months. A clear exposure history and information from prehospital providers is essential to making the diagnosis, since CO poisoning may mimic multiple common conditions.

Poisoned patients should undergo blood COHb measurement, electrocardiography, and pregnancy testing. Cardiac biomarkers should be sent in those with symptoms of cardiac ischemia, ECG changes, a history of coronary disease, or age over 65. High-flow oxygen should be given to all patients with known or suspected CO poisoning. Hyperbaric oxygen therapy should be considered in cases of severe poisoning based on contradictory data regarding decreases in delayed neurological sequelae. There is insufficient evidence in the medical literature to support HBO treatment on the basis of COHb level alone.

Case Conclusion

The local Poison Control Center was promptly contacted and the controversies, risks, and benefits of HBO treatment were discussed. The local HBO center was contacted and because of its close proximity and because the patient had evidence of end-organ damage, the decision was made to transfer the patient for treatment. She received an aspirin for her ECG changes and was transferred with

Risk Management Pitfalls For Carbon Monoxide Poisoning
(Continued from page 11)

perbaric therapy and wants to know the risks to her fetus associated with this treatment."
Pregnant patients were, unfortunately, excluded from all RCTs testing hyperbaric therapy. Animal and human studies on hyperbaric therapy in pregnant subjects show conflicting results in terms of fetal risk. Results range from no apparent effects of HBO therapy on the fetus to adverse effects on fetal development; however, case series and a literature review of severely poisoned pregnant patients who did not receive HBO therapy demonstrated poor fetal outcomes, including stillbirth, limb and cranial malformations, mental retardation, and cerebral palsy.[54] Current consensus among major texts in the field of toxicology is to treat pregnant patients the same as other patients meeting clinical criteria for HBO therapy, as well as considering HBO therapy for signs of fetal distress.[10,16,36] Further, pregnant patients treated with NBO should be treated for longer times due to prolonged elimination of CO from the fetal circulation.[45]

8. **"My pregnant patient has no symptoms, but her COHb level is 22%. Is the threshold level for HBO treatment different in pregnancy?"**
The widely held belief that pregnant patients with CO poisoning should have a lower threshold to undergo HBO therapy is not supported by current evidence. Levels of COHb recommended as treatment thresholds vary and have been arbitrarily chosen. As above, clinical markers of poisoning severity should guide therapy for all patients, regardless of pregnancy status.

9. **"My patient was stripping furniture in his basement and has an unexplained COHb level of 15%."**
Methylene chloride, a common ingredient in commercial paint removers, is metabolized to CO in the liver. Exposure to this agent via ingestion or inhalation can cause CO poisoning. Remember that the endogenous production of CO in this case continues long after removal from the source, and therefore treatment should be prolonged.

10. **"I won't bother calling the hyperbaric chamber about this patient; he's intubated."**
Most chambers are capable of handling patients who are endotracheally intubated. This alone should not disqualify your patient. Ventilators have been adapted to function in the hyperbaric chamber. The endotracheal tube's cuff, interestingly, will have to be filled with saline instead of air to avoid its deflation under the higher pressure. The only absolute contraindication to hyperbaric therapy is untreated pneumothorax, although previous exposure to bleomycin is a strong relative contraindication, because it sensitizes the lung to the toxic effect of oxygen at higher concentrations.

ongoing NBO therapy. The HBO treatment was provided without complication. The patient was admitted to the medical service, after which she underwent 2 additional "dives" during her hospitalization. Her 6-hour troponin I level peaked at 2.1 mg/L, and an ECG obtained at that time had returned to her baseline. Subsequent cardiac biomarkers were obtained 12 hours after presentation and were normal. She remained hemodynamically stable and free of symptoms during her hospitalization. After undergoing stress echocardiography testing on hospital day 2, which did not reveal evidence of reversible myocardial ischemia, she was discharged on hospital day 3. At a 6-week clinic follow-up appointment, she denied any symptoms and had a normal examination. However, she said she had sold her apartment and moved in with her son's family.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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1. Which of the following items is not likely to cause an exposure to CO?
a. Propane-powered saw
b. Compressed-air-powered nail gun
c. Gasoline-powered electric generator
d. Space heater

2. Which of the following fuels is not capable of producing CO?
a. Diesel
b. Propane
c. Hydrogen gas
d. Charcoal

3. Which of these chemicals can cause CO toxicity without combustion?
a. Methylene chloride
b. Methyl ethyl ketone
c. Ethylene glycol
d. Glycolic acid

4. What sign or symptom of CO poisoning is more often seen in children than in adults?
a. Headache
b. Ataxia
c. Vomiting and diarrhea
d. Obtundation

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In This Month's *Pediatric Emergency Medicine Practice*

An Evidence-Based Review Of Pediatric Pneumonia In The ED

by Taj Jadavji, MD, FRCPC, FAAP
Professor, Departments of Microbiology and Infectious Diseases and Paediatrics; Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada

Pneumonia occurs more often in early childhood than at any other age and causes significant morbidity and mortality.[1] Over the past decade, a large number of studies have addressed the problems of diagnosis and management of childhood pneumonia. Many of these studies have been conducted in developing countries where acute respiratory infection is now the leading killer of young children. Definitions of pneumonia vary widely. Some require only the presence of infiltration on a chest radiograph,[2] whereas others require only certain respiratory symptoms or signs.[3] The World Health Organization (WHO) defines pneumonia solely on the basis of clinical findings obtained by visual inspection and timing of the respiratory rate.[4] Identifying the cause of pneumonia in children is difficult due to a lack of rapid, accurate, commercially available laboratory tests for most pathogens. Thus, empirical therapy is the common course in most cases. Pneumonia in children has previously been excluded from treatment guidelines because adults and children differ in the frequency and type of underlying illness and causative pathogens.[5,6] Many guidelines give little direction for diagnosing viral pneumonia, for which antibiotics are not indicated. Antibiotic selection is important, and the emergency clinician should consider prevalent organisms, the child's age, and the presence of risk factors or atypical or resistant organisms when choosing appropriate therapy.[7] This article of Pediatric Emergency Medicine Practice will help you:

1. *Recognize children with pneumonia who need to be admitted for intravenous therapy.*
2. *Describe the major pathogens of childhood pneumonia in different age groups.*
3. *Identify the antibiotic regimens used to treat pneumonia for both inpatients and outpatients.*
4. *Recognize the findings that distinguish bacterial pneumonia from viral pneumonia.*
5. *Identify preventive measures that will reduce the risk of pneumonia.*

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Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this article, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

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