Carbon Monoxide Lurking within: The Danger of Carboxyhemoglobinemia in Acute Care

Summary

Much is known about the causes, symptoms and detection of exogenous carbon monoxide (CO) poisoning and the treatment of the resultant carboxyhemoglobinemia seen in patients after CO exposure. However, it may be surprising to learn that CO poisoning can occur in the hospital and not just outside the hospital. In most cases, these patients present in the emergency department (ED) with equivocal, flu-like symptoms. Because the clearance of CO from the blood begins to occur immediately after the etiologic agent is removed, patients may begin to feel better in the ED and suffer a missed diagnosis as the symptoms abate. In many reported cases, these poisoned patients are sent back to the source of the odorless, colorless toxin, and poisoning continues, sometimes with lethal consequences. Others will find themselves admitted for acute care as the symptoms of CO poisoning mimic cardiac, pulmonary, and neurologic disorders that demand emergent care. Whether in the ED or other places in the hospital such as the OR, if and when carboxyhemoglobinema detection occurs, it is often after costly diagnostic procedures and protocols have been attempted with negative results.

Table I: Carbon Monoxide Poisoning in the Acute Care Setting

Clinical Area	CO Induction	Physiologic Impact	Compromised Outcomes
Emergency Department (ED)	Outside etiologies (Fires, exhaust, wood burning stoves, heaters, generators, boat ramps, etc.)*	Chronic Tissue Hypoxemia with elevated SpCO - carboxyhemoglobin	Immediate, delayed, and long term neurocognitive sequelae and cardiac damage Increased morbidity and mortality
Surgery/OR/ Anesthesia	Monday Morning Phenomena. The "Fluranes" Smokers and Outpatient surgery	Carboxyhemoglobinemia induced by desiccated soda lime, poisons during surgery (7-36% COHb) Smokers reporting for surgery with high SpCO values. Interaction with anesthesia	Increased SpCO compromises healing and may lead to death. Smokers with residual elevated COHb at the time of anesthesia are at cardiac ischemic risk
Neonatal Care	Inhaled Nitric Oxide (iNO) for Pulmonary Hypertension	Hemolytic activity produces endogenous carbon monoxide. Anemia/functional anemia. Activation of heme oxygenase-1 enzyme	Anemia and hemolysis consequences increase morbidity and mortality
Critical Care	iNO, Sodium Nitroprusside, Packed RBC infusions	Hemolytic activity produces endogenous carbon monoxide. Anemia/functional anemia. Activation of heme oxygenase-1 enzyme	Anemia and hemolysis consequences increase morbidity and mortality
Cardiac Care	Nitroglycerin, Transplant, Sodium Nitroprisside	Hemolytic activity produces endogenous carbon monoxide. Anemia/functional anemia	Anemia and hemolysis consequences increase morbidity and mortality
Pulmonary Care	iNO for ARDS	Hemolytic activity produces endogenous carbon monoxide. Anemia/functional anemia Diseases that produce inflammation of respiratory membranes produce CO Activation of heme oxygenase-1 enzyme	Anemia and hemolysis consequences increase morbidity and mortality

* See Masimo Whitepaper entitled: "Detecting Carbon Monoxide Poisoning in the Emergency Department."

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However, CO poisoning may be quickly caught within the acute care setting using a state-of-the-art Masimo Rainbow SET Pulse CO-Oximetry device. Expeditious diagnosis ensures proper treatment may ensue to minimize the known long-term cardiac and neuropsychiatric damage of CO exposure. In the case of a CO poisoned patient that presents in the ED and then transitions into the acute care environment, Pulse CO-Oximetry provides clinicians with immediate detection and subsequent continuous monitoring of carboxyhemoglobin (COHb) levels as feedback to the efficacy of treatment decisions. However, CO poisoning also occurs within the acute care setting – both endogenously and exogenously - contributing to severe tissue hypoxemia, ischemia, and death. Therefore, Pulse CO-Oximetry serves an additional role in detection and monitoring of nosocomial CO poisoning.

This paper explores a sampling of several areas in which nosocomial CO exposure is possible. Several disease processes produce endogenous CO through their natural progression as in the development of systemic inflammatory response syndrome (SIRS), sepsis, pulmonary inflammation, and hemolysis. In these events, the detection and measurement of endogenously produced CO may prove to be a valuable marker of disease severity. There are also reports of CO poisoning by the Monday Morning Phenomena where carboxyhemoglobinemia is induced within the closed circuit anesthesia system during surgery, inhaled nitric oxide therapy, and anti-hypertension treatment with sodium nitroprusside. Though these acute care sources of CO may not raise blood COHb to life-threatening levels for many patients, even slight increases in CO concentrations can be life-threatening to those patients compromised by cardiac disease, anemia, loss of pulmonary reserve and a host of other diseases.

In all cases, the clinical importance of continually and accurately measuring COHb within the hospital is established in the medical literature. New Pulse CO-Oximetry technology platforms, available as handheld and bedside devices, provide immediate and continuous results through non-invasive monitoring and enhance the clinical workflow by eliminating the need for a physician order, painful blood sampling, and the attendant high costs and likely delays associated with a laboratory CO-Oximeter analysis. In addition, they allow trended presentations of COHb which quickly illustrate significant changes that occur over time, changes that might be lost in visual or tabular displays of invasive COHb measurements.

I. Emergency Department/ER

Study shows prevalence of carbon monoxide toxicity in the ED may be higher than previously recognized

In a study led by Dr. Robert Partridge and Dr. Gregory Jay of Rhode Island Hospital at Brown University Medical School, a team of researchers performed a study to assess baseline CO levels of nearly 5,000 patients presenting to the emergency room. To accomplish this, all pulse oximeters in the ED were replaced with Masimo Rainbow SET Pulse CO-Oximeters and the ED staff began assessing baseline COHb levels of all adult patients as part of the standard triage process. In addition to confirming suspected cases of CO toxicity (COT) from smoke inhalation, there were nine unsuspected cases of COT discovered, in just three months, in patients who presented with non-specific symptoms or unrelated complaints. Toxic COHb levels ranged from 16-33% and were confirmed with an invasive laboratory blood test. If this rate were indicative of all US hospitals, it would equate to as many as 50,000 cases of unsuspected CO toxicity annually.

The study concluded that the use of Masimo Rainbow SET as a noninvasive test for COT can effectively and efficiently be performed at ED triage, and that "unsuspected COT may be identified using noninvasive COHb screening and the prevalence of COT may be higher than previously recognized."[1]

The team from Brown University also presented a case report of a previously healthy 52-year old non-smoking female who was brought to the ED complaining of nausea, headache, dizziness, and feeling cold. The patient had no history of carbon monoxide exposure. The Masimo Rainbow SET device recorded an SpCO level of 33%, which was later confirmed with an invasive laboratory measurement. After interviewing the woman, clinicians learned that her utilities had been shut off and she was running a gas-powered generator in her basement.

In the report, researchers said that since early CO toxicity shares symptoms with other more common illnesses, "physicians must maintain a high index of suspicion to avoid incorrect diagnosis, management and disposition. Unrecognized CO poisoned patients returned to the site of exposure may develop more serious CO toxicity." They added that the noninvasive testing provided by Masimo Rainbow SET technology "is a rapid, inexpensive method for screening large numbers of patients for CO toxicity and identifying unsuspected cases that might otherwise be missed."[2]

II. Surgery/Operating Room/Anesthesia

Monday Morning Phenomena and Anesthesia-Related COHb

There is increasing evidence that exposure of volatile anesthetics, i.e., desflurane, enflurane, and isoflurane (in descending order of magnitude) to desiccated carbon dioxide (CO_2) absorbents may result in reactions in anesthetic breathing circuits and production of toxic products (e.g., CO, methanol, formaldehyde).[3-6] CO_2 absorbents such as soda lime are mixtures of chemicals, used in closed breathing environments, such as general anesthesia to remove CO_2 from breathing gases to prevent CO_2 retention and poisoning. There is significant evidence that potentially toxic products can be produced upon exposure of volatile anesthetics to other desiccated absorbents containing strong bases, particularly potassium and sodium hydroxide. The clinical scenario has been called the "Monday Morning Phenomenon," as anesthesia breathing circuits may be left on and cycling through the weekend in preparation for the early morning procedures on Monday. Unfortunately, during the delivery of the anesthetic the desiccant becomes exhausted and loses its ability to properly "scrub" the anesthetic gases. CO may be produced in significant quantities to poison the patient under anesthesia (see Figure 2).

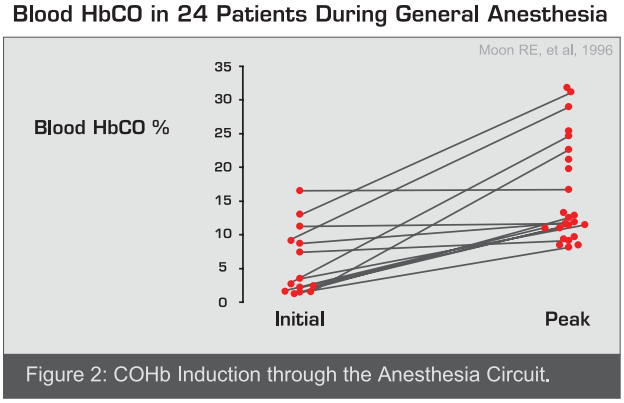

Figure 2: COHb Induction through the Anesthesia Circuit.

The desiccant does not transition from fully functional to suddenly consumed. The transition occurs over time, and thus, some patients may be exposed to low, but clinically significant levels of CO during a time when they can ill-afford a compromise to oxygen delivery, especially to the heart and brain. Case studies demonstrate this, and in spite of the general awareness and the adjustment of guidelines to thwart the possibility of this unfortunate preventable adverse event, it occurs even today. As concern has grown, the Anesthesia Patient Safety Foundation held a conference entitled Carbon Dioxide Absorbent Desiccation: *APSF Conference on Safety Considerations on April 27, 2005. From the proceedings: "There is increasing evidence that exposure of volatile anesthetics to desiccated carbon dioxide absorbents may result in exothermic reactions leading to fires in anesthetic breathing circuits and production of toxic products (e.g., carbon monoxide, compound A, methanol, formaldehyde)… In some cases this may lead to sub-clinical carbon monoxide exposure."*

The exact incidence of patient exposure to CO through CO_2 absorbent desiccation is unknown. The American Society of Anesthesia (ASA) estimates that 25 million anesthetic procedures are performed each year in the US. If as little as 33 percent of these anesthetics involve isoflurane, enflurane, or desflurane, and if four cases are performed in the average operating room each day so that 25 percent of cases will be first cases, i.e., the most likely to be impacted by desiccated absorbent, then up to 2 million patients may be at risk each year for intraoperative CO exposure.[7] If the published incidence of CO exposures can be extrapolated to other institutions and remains between 0.0005 and 0.005 first cases,[8] then approximately 1,000-10,000 patients may be exposed to CO annually in the US as a result of anesthetic breakdown. If these CO poisonings go undetected they can't be treated and injury and even death can occur.

Reports of elevated COHb concentrations detected intraoperatively in humans have ranged from 7 to 32 percent.[9-11] Berry et al. reported a patient who attained 36 percent COHb.[12] As a subject in a clinical study, the patient was a healthy female who did not appear to be adversely affected by her CO exposure. However, it may be possible that far lower CO exposure in the presence of concurrent disease may predispose patients to far greater risks. In patients with coronary artery disease, COHb levels as low as 2.9-4.5 percent can exacerbate myocardial ischemia.[13-14] Similarly, smoke inhalation with relatively mild CO exposure (COHb levels <30 percent) may produce various neuropsychiatric and neurocognitive abnormalities 3-21 days after exposure.[15]

ECRI and other investigators have published recommendations to minimize the risk of unintended desiccation of absorbents.[16] However, studies show that total cessation of CO production cannot be achieved despite implementation of anti-desiccation strategies. Other detection systems must be devised. Monitoring of CO gas in the circuit is currently possible with the most sophisticated and expensive detectors, and COHb monitoring is available through invasive CO-Oximetry, but is not routinely used. Monitoring of surgical patients intraoperatively generally involves continuous pulse oximetry (SpO_2) derived from a sensor placed on one of the fingers to allow for early detection of a fall in a patient's oxyhemoglobin saturation. However, CO cannot be detected by conventional two-wavelength pulse oximetry. As a result, the clinical effects of CO exposure may be concealed by post-anesthetic effects. Masimo Rainbow SET Pulse CO-Oximetry measures carboxyhemoglobin (SpCO) and methemoglobin (SpMet) noninvasively and continuously, thus providing a means to protect anesthetized patients from anaesthesia induced CO toxicity. Furthermore, expanded use of Rainbow monitors may become cost-effective if balanced against the potential cost of instituting a policy of replacing absorbent with each surgery.[17]

III. Neonatal/Critical Care

1. Hemolysis

It is possible that clinicians may suspect a case of CO poisoning due to desiccated CO absorbent when, in fact, the etiologic culprit may be an entirely different cause. As one clinical case illustrates hemolysis, although not usually a clinically significant event in routine delivery of anesthesia, has the potential to result in significant CO exposure.

Hemolysis is the breaking open of red blood cells and the release of hemoglobin into the surrounding fluid. A 39-year-old female with a history of hemolytic episodes was scheduled as the first surgical case on a Friday morning. Because of her continued hemolysis, intraoperative laboratory studies were obtained 20 minutes after induction of anesthesia. The test revealed a COHb of 7.3 percent. Desflurane breakdown was suspected and the absorbent was changed to fresh, unused normally hydrated absorbent. However, subsequent analysis of the initial absorbent revealed that it was not the source of CO production.

In this case, the CO exposure of the hemolytic patient imitated CO production from anesthetic breakdown. In reality, analysis of the patient's blood estimated CO production of 257 ml per 24 hours. Normal endogenous CO production is approximately 10 ml per day.[18] A mathematical model of CO uptake[19-21] predicts a COHb concentration between 5.6 percent and 7.3 percent using this rate of hemolysis. If this patient had received an anesthetic through a closed breathing circuit, the oxygen binding capacity of hemoglobin could have become an additional 23 percent saturated with CO during the 6-hour procedure because none of the endogenously produced CO would be removed. The model predicts that closed-circuit anesthesia during an episode of hemolysis may dangerously increase COHb concentrations.[22] As such, anesthesiologists should be aware of all sources of CO in the perioperative period and maintain constant awareness of the patient's COHb status.

2. Inhaled Nitric Oxide

Inhaled nitric oxide (iNO) is occasionally used to improve arterial oxygenation in patients with the acute respiratory distress syndrome (ARDS).[23] Inhaled NO induces selective vasodilation in pulmonary vessels to relieve hypertension. The use in ARDS cases has brought to light a potential pathophysiologic mechanism linking iNO, methemoglobin (MetHb), and carboxyhemoglobin (COHb). The withdrawal of iNO in this study resulted in a parallel decline in MetHb and COHb levels. Due to the negative influence of COHb on the oxygen-carrying capacity of the blood, its iNO-induced increase (through stimulants of hemoxygenase inductions) cancelled out the slight benefit of iNO on arterial oxygenation. A case report published in 2004 demonstrated a correlation between iNO and COHb.[24] The authors do propose that not only MetHb but also COHb levels be monitored if iNO is administered during the course of ARDS, since even low levels of COHb may potentially offset any benefit of iNO.

3. Sodium Nitroprusside

Sodium nitroprusside is the most widely used vasodilator drug in critically ill patients.[25-28] The drug is often administered intravenously to patients who are experiencing a hypertensive emergency and to produce controlled hypotension (low blood pressure) in anesthetized patients during surgery. Sodium nitroprusside breaks down in the blood and releases nitric oxide (NO) which enters the muscle cells in the walls of the blood vessels and causes them to relax. When the muscles relax, the vessels become wider and the blood pressure decreases. The most important toxic effects of sodium nitroprusside are cyanide poisoning, thiocyanate toxicity, and methemoglobinemia.[29] Like the reaction triggered by sepsis and pulmonary inflammation, research suggest that NO donors, such as sodium nitroprusside, can induce heme oxygenase-1, and produce CO by breakdown of heme molecules.[30-32]

One study examines the cases of four pediatric heart transplant cases.[33] The patients showed a moderate increase in COHb level after nitroprusside administration, and in three of these cases the withdrawal of the drug led to the normalization of COHb level. If in fact prolonged treatment with moderate or high doses of sodium nitroprusside can produce carboxyhemoglobinemia in children after heart transplant, specific medical management after pediatric heart transplant should include frequent measurement of COHb. Even low levels of carbon monoxide bound to hemoglobin in cardiac compromised patients can be lethal, starving the tissues of oxygen due to functional anemia, poor perfusion, cardiac output compromise, and suboptimal oxygen delivery mechanisms.

Accepted standards of patient monitoring associated with nitroprusside administration include analysis of MetHb concentrations.[34] Research suggests that COHb levels should be evaluated as well. Current blood analysis devices that measure CO-Oximetry in each blood gas sample permit diagnosis of moderate COHb elevations that probably would not have been discovered in the past. With noninvasive and continuous Pulse CO-Oximetry, results are faster and less resource-intensive than ever before. Of significant importance is the ability to trend the changes in COHb over time (see Figure 1), and view the trend at will. Days of trend data are saved for retrospective analysis of subtle changes in COHb (and when necessary, MetHb). Without the continuous assessment, the task of associating subtle changes in the dyshemoglobins is daunting, and impossible using traditional laboratory CO-Oximetry. As well, the trend value allows the patient to serve as their own baseline. At the beginning of the trend period, carboxyhemoglobin by Pusle CO-Oximetry (SpCO) may measure 1.0 percent, but with a course of sodium nitroprusside treatment, or following the transitions into SIRS, the clinician may note trends in elevation of COHb, and interact accordingly with the patient to achieve the desired outcome.

IV. COHb as a Marker

Endogenous production of CO was first reported in the mid 20th century, but it has been a known poison since Claude Bernard first noted its high affinity for hemoglobin a century earlier.[35] Moderate endogenous increases in COHb levels (0.8–2 percent) have been reported in critically ill patients[36] and clinical interest has grown rapidly as CO production has been proposed to induce excessive vascular relaxation, and hence a fall in blood pressure.[37] The mechanism behind this reaction is heme oxygenase (HO), the initial enzyme in heme metabolism.[38] HO produces CO during breakdown of heme molecules primarily in the liver and spleen. It is well established that metabolism of heme via heme oxidase results in production of one molecule of CO for each molecule of heme destroyed.[37] Recent data suggest that CO is also produced in the lungs. A number of stress-associated agents induce the expression of heme oxygenase, including heavy metals, hyperthermia, hyperoxia, hypoxia, heat shock, endotoxin, hydrogen peroxide, cytokines, ultraviolet radiation and nitric oxide, producing CO.[39-42]

To investigate whether critical illness results in increased CO production researchers have measured the CO concentration in exhaled air in critically ill patients and in healthy controls.[43] Sampling exhaled CO is only an approximation of COHb levels in the blood. In patients with pulmonary compromise, high dead space to tidal volume ratios, or ventilation to perfusion mismatch, exhaled CO will correlate poorly with CO bound to hemoglobin and induce tissue hypoxemia. In a study of 95 mechanically ventilated, critically ill patients, CO production was correlated with multiple organ dysfunction score. Patients suffering from cardiac disease and critically ill patients undergoing dialysis produced significantly higher amounts of CO compared to other critically ill controls. The findings suggest that endogenous CO production might reflect the severity of acute organ dysfunction and therefore may offer clinicians an effective, non-invasive gauge of patient condition. Two examples of this correlation exist in patients with sepsis and pulmonary inflammation.

1. Sepsis

Sepsis is among the top causes of death in the world today. It kills 210,000 people in the U.S. each year - more than lung and breast cancer combined. Nationally, sepsis is a complication in about 3.0 cases per 1,000 population, or 751,000 cases annually,[44] where related intravenous (IV) lines, surgical wounds or drains, and bedsores can be entry points for bacteria. Sepsis is caused most commonly by bacteria in the bloodstream, and is thought to be preceded by Systemic Inflammatory Response Syndrome (SIRS) with attendant hemolysis of red blood cells, producing CO. In adults, sepsis is most often a nosocomial infection seen after surgery or another invasive medical procedure in the hospital. Experts predict that sepsis will increase by 1.5 percent per year due to the high incidence of sepsis in the elderly and the overall aging of the population. They estimate that there will be 934,000 cases in the United States in the year 2010 and 1,110,000 cases in 2020.[45-46]

During the 1990s, CO was recognized as a new participant in the pathogenesis of sepsis syndrome. Products of the HO enzyme include COHb and bilirubin, which have protective effects in stressed states. The HO enzyme up-regulates during states of oxidative stress. The marked increase in HO activity stimulated by endotoxin suggests that overproduction of CO may contribute to the reduction in vascular tone during endotoxic shock. In support of this theory, research has demonstrated increased CO concentrations during stress, sepsis, and shock.[47-48]

Because early detection and intervention of patients who are sepsis/septic shock candidates has significant impact on morbidity and mortality, the clinical importance of measuring and trending CO concentrations as an ancillary marker of sepsis may prove highly valuable in treating this condition. To date, an evidence-base is being compiled to determine if monitoring subtle changes in CO production may prove to be a robust marker of sepsis or septic shock onset.

2. Pulmonary Disease

Exhaled CO is increased in patients with inflammatory pulmonary diseases such as bronchial asthma, bronchiectasis, upper respiratory tract infections, and seasonal allergic rhinitis.[49-53] Treatment with inhaled and oral corticosteroids, which have been shown to reduce airway inflammation, is associated with a reduction in the exhaled levels of CO in asthma.[54] Furthermore, exhaled CO is increased in exacerbations of bronchial asthma induced by respiratory virus infections.[55] Based on these findings, it has been proposed that measurements of exhaled CO may serve as an indirect marker of airway inflammation.[56-61]

Exhaled CO concentration is reported to correlate closely with blood COHb in smokers and non-smokers,[62] which suggests that the COHb levels may increase in patients with inflammatory pulmonary diseases. A study that was undertaken to determine whether arterial blood COHb increases in patients with inflammatory pulmonary diseases confirmed that COHb concentrations are increased in patients with bronchial asthma, pneumonia, and idiopathic pulmonary fibrosis (IPF).[63] Increased blood levels of COHb in patients with inflammatory pulmonary diseases may reflect lung inflammation. This finding was seen as a benefit for ventilatory limited patients, especially children, who cannot perform the vital capacity maneuver to measure exhaled CO. Also, patients with lung disease demonstrate poor correlations between COHb in the blood and exhaled values. The continuous measurement of blood levels of carboxyhemoglobin allows a trending presentation that graphically depicts subtle yet clinically significant elevations in COHb, providing a simple and valuable marker to indicate pulmonary inflammation.

Cystic fibrosis treatment stands to benefit in particular. Inflammation, oxidative stress, and recurrent pulmonary infections are major aggravating factors in cystic fibrosis. NO, a common marker of inflammation, is not increased in cystic fibrosis patients probably because it is metabolized to peroxynitrite,[64-65] making this measurement of little use for monitoring lung inflammation in cystic fibrosis. However, exhaled CO which is induced by inflammatory cytokines and oxidants, has been established as an effective noninvasive marker of airway inflammation and oxidative stress.[66] If CO measurement were simple and non-invasive it could be used to continuously monitor all patients with severe disease.

V. Detection Systems: Expired CO, CO-Oximetry and Pulse CO-Oximetry

Two methods have been widely studied for assessing CO concentrations in clinical practice: exhaled CO and COHb levels measured via CO-Oximetry. The differences between the readings obtained from the two methods have deemed exhaled CO to be clinically acceptable for the purposes of epidemiological studies, but only in those few patients who can perform a robust, repeatable vital capacity maneuver and in those patients without cardiopulmonary compromise.

While the end-expired method can be used to measure moderate and low COHb levels in individuals, patients admitted with CO poisoning or who are otherwise critically ill are not in a state to blow a sample of expired air into an analyzer sample reservoir. Therefore, taking a sample of blood is the primary method by which COHb level is measured in cases with high acuity.

In hospitals, the most common means of measuring CO exposure is a CO-Oximeter. A blood sample, under a physician order, is drawn from either venous or arterial vessel and injected into a laboratory CO-Oximeter. The laboratory device measures the invasive blood sample using a method called spectrophotometric blood gas analysis.[67] Because the CO-Oximeter can only yield a single, discrete reading for each aliquot of blood sampled, the reported value is a noncontinuous snapshot of the patient's condition at the particular moment that the sample was collected. Another issue that profoundly affects the clinical usefulness of invasive CO-Oximetry relates to the relative paucity of devices currently purchased by and installed in acute care hospitals. One recent study indicates that fewer than half of hospitals in the U.S. have the necessary equipment on site to diagnose CO poisoning.[68] For those that did not have the testing equipment, the average time to receive results of a blood sample sent to another facility was over 15 hours.

Conventional two-wavelength pulse oximeters are incapable of isolating the carbon monoxide contaminated hemoglobin from oxyhemoglobin.[69] Of greater potential confusion and negative consequence, two-wavelength oximeters will report carboxyhemoglobin as oxygenated hemoglobin, a false negative with potentially fatal results.

The latest technology in CO poisoning detection in the acute care setting is Masimo Rainbow SET Pulse CO-Oximetry [Masimo Corporation, Irvine, CA]. This is the first technology that allows clinicians to non-invasively detect and continuously monitor CO levels in the bloodstream. Using one sensor with more than 7 wavelengths of light to distinguish the various forms of hemoglobin (oxy-, deoxy-, carboxy- and met-) the device is capable of measuring blood SpCO levels, in addition to pulse rate, arterial hemoglobin oxygen saturation during motion and low perfusion, perfusion index, plethysmograph variation index (PVI) and SpMet. The device's accuracy has been demonstrated to 40 percent SpCO, with a range of ±3 percent (at 1 Standard Deviation) around the measurement.[70] The trending feature benefit of the Rainbow technology platform allows for the real-time monitoring of the critical dyshemoglobins COHb and MetHb, permitting prophylactic and/or early interventions to elevations of the critical dyshemoglobins. Since these dyshemoglobins can change their profile and effect dynamically during the course of therapy, trend monitoring through continuous evaluations is considered a significant breakthrough.

Non-invasive monitoring reduces the opportunity for hospital acquired infection, sepsis and overall patient discomfort. Needle-free testing means a safer environment for patients and caregivers alike. In addition, the immediacy of results available at the point of care represents a less resource intensive, streamlined workflow. As opposed to conventional CO-Oximetry which requires a new blood sample for each time a status of dyshemoglobins is required, the continuous nature of the Masimo Rainbow SET Pulse CO-Oximeter platform enables the ability to non-invasively trend data over time.

Conclusions

There are several conditions that cause dangerous elevations of carbon monoxide in the blood, and thus, CO poisoning, in the acute care environment. There are also many disease states that are accompanied by a more subtle rise of COHb in the blood. These subtle elevations may be significant or insignificant. However the ability to trend analyze these subtle increases is an important breakthrough to capture the dyshemoglobins potentially as disease markers. As these are recent breakthroughs, there may be more of which we are unaware. We are likely on the rise of a steep learning curve when it comes to fully understanding heme metabolism and its affect on COHb levels in the hospital. However, the medical literature does suggest that even low levels of COHb can have serious deleterious health effects on patients with pre-existing disease states including cardiac disease, anemia, and respiratory impairment. With 71 million American adults afflicted with one or more types of cardiovascular disease, with sepsis cases growing rapidly in our aging population, and considering the other disease states that induce hemolysis and endogenously produce CO, the accurate noninvasive detection of carboxyhemoglobin concentrations as well as methemogobin concentrations will become an increasing vital clinical tool for the diagnosis and treatment of hospitalized patients.

Due to the lack of onsite laboratory CO-Oximetry equipment at many hospitals, timely detection via blood draw and analysis is not practical given the severity of the conditions described in this paper. Periodic "spot-checks" do not provide enough useful clinical data to intervene. Real time measurements are important to track the COHb levels and insure that they are being adequately managed to low, innocuous levels. Access to an immediate and continuous gauge of COHb levels from the ED to the inpatient care unit and in the surgical suite is essential for optimal patient care.

"How Many People Are We Missing?"
Ann left New York in 2005 to retire in the warm Florida weather. She rented a condominium in a newly renovated building in the Tampa area. Within months she became increasingly ill, collapsed, and was rushed to a local hospital for a battery of tests over several days, all negative. Her condition improved, and she was sent home where her symptoms returned. After her headaches, fatigue, and flu-like symptoms progressed to convulsions, she was transported to a different hospital where she was properly diagnosed with carbon monoxide poisoning. Ann died from the exposure to the toxic CO gas that seeped into her condo via holes in her chimney flue. Because new technology is now available to instantly detect the blood levels of carbon monoxide without a blood sample, her mourning daughter wonders why every hospital does not have access to this test that could save so many lives. Mary Russell, EdD MSN, and a Research & Organizational Preparedness Specialist at Boca Raton Community Hospital, uses and trains on the new detection technology. She asks the question: "How many people are we missing?"

Acute care is now able to realize the untapped potential of non-invasive Pulse CO-Oximetry, a technology cleared for market by the FDA, readily available, fully validated and easy to use.[71] There is good reason to believe that this technology will have a positive impact on mortality and morbidity statistics in the hospital. With patient safety awareness issues elevated to unprecedented levels, the case for noninvasive and continuous monitoring of the critical dyshemoglobins COHb and MetHb has never been more compelling. Without monitoring COHb, patients remain vulnerable to known but preventable toxic episodes involving carbon monoxide.

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Instruments and sensors containing Masimo SET technology are identified with the Masimo SET logo. Look for the Masimo SET designation on both the sensors and monitors to ensure accurate pulse oximetry when needed most.

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Detecting Carbon Monoxide Posioning in the Emergency Department

Summary

Carbon Monoxide (CO) is a gas produced by the combustion of carbon-containing fuels or the inadequate ventilation of natural gas. Once in the bloodstream, CO prevents oxygen from reaching tissues. Undetectable by humans, exposure to CO is the leading cause of death by poisoning in industrialized countries. Still, the condition presents a constellation of symptoms that mimic other illnesses. As a result as many as half of all CO-poisoned patients may be misdiagnosed when presenting to emergency departments, delaying treatment and even returning vulnerable patients and their families to potentially lethal environments.

CO exposure may be detected by measuring the carboxyhemoglobin (COHb) levels in a person's blood. In hospitals, the most common means of measuring COHb is through the analysis of an invasive blood sample using a laboratory CO-Oximeter. However, according to one recently published study, only about half of all hospitals have the devices onsite. For hospitals with a CO-Oximeter, results may be obtained in about 10 minutes but in hospitals that must send the samples elsewhere for testing, results require an average of 15 hours. Each additional reading requires another blood draw and analysis. Conventional pulse oximeters are unable to detect COHb but a new device, the Masimo SET with Rainbow Technology monitor allows clinicians to detect and continuously monitor CO levels in the bloodstream noninvasively. Using multiple wavelengths of light to distinguish the various forms of hemoglobin (oxy-, deoxy-, carboxy- and met-) the device is capable of measuring blood CO saturation (SpCO™) levels and methemoglobin saturation (SpMet™) levels, in addition to the conventional variables of pulse rate, perfusion index and arterial oxygen saturation.

The stakes for properly diagnosing and treating CO poisoning are high. Assessment of a patient's COHb level first provides an accurate diagnosis of CO poisoning and then guides treatment especially in cases elevated to the range of 10 percent or greater. Some mistakenly believe that if a patient recovers from the initial CO poisoning, they have made a complete recovery. However, multiple studies show that patients with prolonged and untreated CO exposure have long-term side effects and increased risk. If untreated, CO exposure may damage the neurological, cardiac, metabolic, pulmonary and renal systems of the body. Organs with a high metabolic requirement for oxygen, such as the heart and brain, are most susceptible to injury from CO. Even at relatively low COHb levels, patients with underlying cardiovascular disease are especially at serious risk for cardiac complications including myocardial ischemia or infarction, and even cardiac arrest.

Fortunately, the effects of CO poisoning can be reversed if caught in time. The immediacy of results and ability to trend the results over time expedite efficacious treatment and may contribute to improved clinical outcomes. With lives and significant resources at stake, the speed at which suspicion evolves to diagnosis is critical. A quick noninvasive measurement of COHb using a new Rainbow Pulse CO-Oximeter™ device may contribute to better informed treatment decisions.

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The Guessing Game

CO poisoning is the leading cause of death by poisoning in industrialized countries[1] and may be responsible for more than half of all fatal poisonings worldwide.[2] It is estimated that approximately 43,000 emergency room visits are attributed to CO poisoning in the United States each year.[3] At least 3,800 people die annually in the U.S. from the effects of CO poisoning, and 1,400 of these deaths are accidental.[4-5] Unfortunately, for most patients poisoned by the colorless, odorless, tasteless gas, CO poisoning is not the immediate and obvious diagnosis. Variable symptoms, a wide range of patient sensitivity and unsophisticated detection systems often result in misdiagnosis and treatment delays.

Rapid Determination of Carbon Monoxide Poisoning (COHb)

- Emergency Departments
- Urgent Care Facilities
- Physicians Offices
- Inpatient / Outpatient Surgery Centers
- First – Responders/ Emergency Medical Services and Fire / Homeland Security
- Acute Care Hospitals
- Point of Care – Natural Disaster Zones
- Toll Booths / Parking Garages
- Airplanes
- Construction zone

Even in the case of Randal McCloy, the sole survivor of the Sago Mine tragedy, in which CO poisoning was the probable cause of illness (according to multiple published accounts of the incident), the first physician to attend to the miner reported that McCloy's carbon monoxide levels were negative. “That means that as best as we can tell with somewhat primitive equipment that we have here for measuring those, his carboxyhemoglobin levels were negative, indicating no carbon monoxide in his system, as far as we could tell,” she told reporters.

When pressed for more information, the clinician told the media, “When you put the oxygen saturation monitor on their finger, it's false [but] it doesn't give you a true reading in somebody with carbon monoxide poisoning. So you really have to be able to run the blood and check for carboxyhemoglobin.” In fact, tests run in the subsequent days show McCloy to be suffering from brain hemorrhaging and edema, muscle injury, liver failure and faulty heart function due to severe CO poisoning.

Later, physicians at Allegheny General Hospital stated that after receiving three hyperbaric oxygen (HBO) treatments, McCloy was showing signs of improved brain stem and organ function. MRI scans illustrated the evidence of neurological damage but the clinical consequences remain to be seen.

Some people are more susceptible to long-term harm from CO exposure than others. It is possible that the same physiology that enabled McCloy to survive generally lethal CO levels for more than forty hours may also afford him a better clinical outcome than would be expected. While there are populations known to be highly susceptible to the negative effects of CO: children, pregnant women, adults with cardiac disease, individuals with increased oxygen demand and patients with chronic respiratory problems; it is not possible to assess a person’s CO resilience.

Elevated COHb: Patients at High Risk for Negative Outcome

- Children; elderly
- Adults with cardiac disease;
- Pregnant women
- Patients with increased oxygen demand or decreased oxygen-carrying capacity;
- Patients with chronic respiratory insufficiency.

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Symptoms

CO poisoning is the single most common source of poisoning injury as treated in hospital emergency departments. While its presentation is not uncommon, the constellation of symptoms that manifest when a patient is poisoned with carbon monoxide do not prompt most clinicians to consider carboxyhemoglobinemia when attempting a diagnosis. The vague symptoms can be mistaken for those of many other illnesses including food poisoning, influenza, migraine headache, or substance abuse. In the attempt to find the causative agent for the symptoms, many unnecessary, potentially costly and sometime resource-intensive diagnostics may be ordered, to no avail. Because the symptoms of CO poisoning may mimic an intracranial bleed, time and cost for a negative result may precede proper diagnosis, unnecessarily increasing healthcare costs. During the delay associated with running unnecessary diagnostics, patients may find that their symptoms abate and their health improves as the hidden culprit, CO, is flushed from the blood during the normal ventilation patterns over time. Multiple reports have shown that the patients may be discharged and returned back to the environment where the poisoning occurred, only to once again be exposed to the silent killer, carbon monoxide.

There are two main types of CO poisoning: acute, which is caused by short exposure to a high level of carbon monoxide, and chronic or subacute, which results from long exposure to a low level of CO. Which symptoms appear depend on the level of CO in the environment and the length of exposure, as well as the patient's state of health.

The general symptoms of CO poisoning, including headache, dizziness, nausea, fatigue, and weakness, are vague. See Table 1. Patients with acute CO poisoning are more likely to present with more serious symptoms, such as cardiopulmonary problems, confusion, syncope, coma, and seizure. Chronic poisoning is generally associated with the less severe symptoms.[14] Low-level exposure can exacerbate angina and chronic obstructive pulmonary disease, and patients with coronary artery disease are at risk for ischemia and myocardial infarction even at low levels of CO.[15-16]

Patients that present with low COHb levels correlate well with mild symptoms described in Table 2 as do cases that register levels of 50-70%,[17] which are generally fatal. However, intermediate levels show little correlation with symptoms or with prognosis. It seems that the severity of clinical condition is not only related to CO concentration but also the duration of exposure and the prevailing clinical disposition of the patient. Some patients presenting with a carboxyhemoglobin level of 20% may be remarkably symptomatic, while others experiencing the same level of COHb% may exhibit only mild, equivocal symptoms. A patient exposed to high concentrations for a short time may be less symptomatic than a patient who reaches the same COHb level after a prolonged exposure.

Table 1: Clinical Signs & Symptoms associated with CO Poisoning and correlated COHb levels[18-19]

Severity	COHb Level	Signs & Symptoms
Mild	<15 - 20%	Headache, Nausea, Vomiting, Dizziness, Blurred Vision.
Moderate	21 - 40%*	Confusion, Syncope, Chest Pain, Dyspnea, Weakness, Tachycardia, Tachypnea, Rhabdomyolysis
Severe	41 - 59%*	Palpitations, Dysrhythmias, Hypotension, Myocardial ischemia, Cardiac arrest, Respiratory arrest, Pulmonary edema, Seizures; Coma
Fatal	60+%	Death

* At moderate to severe levels of COHb posioning the correlation between blood levels and symptomatology is poor.

Detection

Table 2: COHb Levels in Persons 3 - 74 Years of Age[20]		
Smoking Status	**Percent COHb (mean + SD)**	**Percent COHb (98th percentile)**
Nonsmokers	0.83 ± 0.67	< 2.50
Current smokers	4.30 ± 2.55	≤ 10.00
All statuses combined	1.94 ± 2.24	≤ 9.00

One thing that is certain about COHb levels is that smokers present with higher levels than do non-smokers. As can be seen in Table 2,[20] the COHb level in non-smokers is approximately one to two percent. In patients who smoke, a baseline level of nearly five percent is considered normal, although it can be as high as 13 percent. Although COHb concentrations between 11 percent and 30 percent can produce symptoms, it is important to consider the patient's smoking status.

CO poisoning is known as the *great imitator* for its ability to present with equivocal signs and symptoms, many of which closely resemble other diseases. In particular, patients may be misdiagnosed with viral illness, acute myocardial infarction, and migraine. It is estimated that CO poisoning misdiagnosis may occur in up to 30-50 percent of CO-exposed patients presenting to emergency departments.[21-23] As described below, failing to assess COHb levels early may return vulnerable patients and their families to potentially lethal environments.

Missing the Signs

A 67-year-old man sought medical help after three days of light-headedness, vertigo, stabbing chest pain, cough, chills and headache. His wife had experienced similar ailments over the past week. He was admitted, evaluated and discharged with a diagnosis of viral syndrome. Ten days later he returned to the ER with vertigo, palpitations and nausea but was sent home for outpatient follow-up. Four days later he again returned to the ER with diarrhea and severe chest pain, collapsing to the floor. He was admitted to the Coronary Care Unit with acute myocardial infarction. Among the results of a routine arterial blood gas analysis, it was found that his COHb levels were 15.6%. A COHb level then obtained on his wife was 18.1%. A rusted furnace was found to be the source.[15]

A 69-year-old man came to the ER after days of confusion, nausea, vomiting, intermittent syncope, hallucinations and shortness of breath. An arterial blood gas measurement found an oxygen saturation of 89%. He was admitted to the coronary care unit with a diagnosis of acute myocardial infarction. The next day a COHb level was measured and normal. While the patient was hospitalized he invited his sister and daughter-in-law to stay in his home. They both arrived at the ER the next morning with headaches, vomiting, and vertigo. Their COHb levels on initial observation were 28% and 32%. The man's gas water heater was faulty.[15]

A 47-year-old male urologist and his wife attended a medical conference in Jackson, Wyoming. Both reported to a local emergency department with symptoms including headache, malaise, and metabolic acidosis. The husband and wife were sent back to the conference resort hotel with a diagnosis of gastroenteritis. The following day, they were both found unresponsive in their hotel. He died 3 hours later, and his wife has severe long-term neurocognitive sequelae. The cause of death and long-term morbidity was carbon monoxide poisoning due to a faulty boiler. A $17,000,000 verdict was awarded to the afflicted family against the resort hotel owners.

Regardless of the means of detection used in emergency department care, several factors make assessing the severity of the CO poisoning difficult. The length of time since CO exposure is one such factor. The half-life of CO is four to six hours when the patient is breathing room air, and 40–60 minutes when the patient is breathing 100 percent oxygen. If a patient is given oxygen during their transport to the emergency department, it will be difficult to know when the COHb level peaked.[15]

In addition, COHb levels may not fully correlate with the clinical condition of CO-poisoned patients because the COHb level in the blood is not an absolute index of compromised oxygen delivery at the tissue level. Furthermore, levels may not match up to specific signs and symptoms; patients with moderate levels will not necessarily appear sicker than patients with lower levels.[31]

In hospitals, the most common means of measuring CO exposure is through the use of a laboratory CO-Oximeter. A blood sample, under a physician order, is drawn from either venous or arterial vessel and injected into a lab CO-Oximeter. The laboratory device measures the invasive blood sample using a method called spectrophotometric blood gas analysis.[24] Because the CO-Oximeter can only yield a single, discrete reading for each aliquot of blood sampled, the reported value is a noncontinuous snapshot of the patient's condition at the particular moment that the sample was collected. To compound the difficulty of detecting CO exposure, when the laboratory calculates the patient's oxygen saturation levels from the oxygen partial pressure (PO_2), the arterial SaO_2 may appear normal. The clinical usefulness of CO-Oximetry is inhibited further by the relative deficiency of devices currently installed in acute care hospitals. One recent study found that fewer than half of hospitals in the U.S. have the necessary equipment on site to diagnose CO poisoning.[25] For those that did not have the testing equipment, the average time to receive results of a blood sample sent to another facility was over 15 hours. In hospitals that have CO-Oximetry equipment, results may be returned in an average of 10 minutes (see Table 4.)

Unfortunately, standard pulse oximeters are incapable of isolating the carbon monoxide contaminated hemoglobin from the oxyhemoglobin.[26] Thus, pulse oximeters artificially overestimate arterial oxygen saturation in the presence of elevated blood carbon monoxide. Therefore, the readings will be falsely high when carbon monoxide is occupying binding sites on the heme molecule.

Table 3: Comparison of Testing Methods Time to Results[25]

Testing Method	Average Time to Result
Pulse CO-Oximeter	Seconds
Onsite CO-Oximeter	10 Minutes
Off-Site CO-Oximeter	15 Hours

The latest technology in CO poisoning detection employs a noninvasive and continuous platform. The Masimo SET® with Rainbow Technology Pulse CO-Oximeter Monitor [Masimo, Irvine, CA] is the first device that allows clinicians to detect and continuously monitor CO levels in the bloodstream noninvasively. Using 7+ wavelengths of light to distinguish the various forms of hemoglobin (oxy-, deoxy-,carboxy- and met-) the device is capable of measuring blood CO saturation (SpCO™) levels, methemoglobin saturation (SpMet™) levels, in addition to pulse rate, arterial oxygen saturation, and perfusion index. The device's accuracy has been demonstrated accurate to 40 percent SpCO, with a range of ± 3 percent around the measurement.[27]

Noninvasive monitoring reduces the opportunity for hospital acquired infection and overall patient discomfort. Needle-free testing means a safer environment for patients and caregivers alike. In addition, the immediacy of results available at the point-of-care results in less drain on resources while expediting efficacious treatment and better outcomes. The continuous nature of the noninvasive Rainbow Pulse CO-Oximeter device enables the ability to trend data over time while conventional CO-Oximetry requires a new blood sample each time the status of the dyshemoglobins is required.

Because clinicians traditionally order blood measurement of COHb only when the condition is suspected, there has been a tendency to diagnose only the most symptomatic patient whose exposure history is known. With noninvasive Pulse CO-Oximeter technology now available, one might expect that many instances of elevated COHb will be discovered among patients without a classic history of recognized exposure to CO.[28]

Treatment

Due to the challenges of traditional COHb detection and the lack of correlation between levels and symptoms, most experts recommend using COHb level only as confirmation of the diagnosis in a patient with suspected CO exposure. Treatment is then based on the patient's history and the severity of symptoms. Still, COHb levels are recommended to guide management especially in cases elevated to the range of 25 percent or greater.[29] Because noninvasive and continuous Pulse CO-Oximetry allows real-time trend evaluation of the CO-poisoned patient, efficacious treatment protocols can be quickly identified and implemented. Carbon monoxide toxicity is traditionally treated with either 100% oxygen therapy by mask or high flow device, or by hyperbaric medicine (HBO). A significant relationship exists between the delay between efficacious treatment, the severity of the CO toxicity, and the potential for delayed neuropsychiatric and/or abnormal cardiac sequelae.

Table 4: Carbon Monoxide: Half-life Elimination from Blood

Room Air	240 - 360 minutes
Oxygen (100%)	80 minutes
Hyperbaric Oxygen (HBO)	22 minutes

With the half-life of COHb at four to six hours, a COHb level should be obtained soon after exposure is suspected. Noninvasive and continuous COHb measurements employing Rainbow technology provide an increasingly valued diagnostic methodology without delays and potentially costly missed diagnosis.

Noninvasive Pulse CO-Oximeters capable of immediately and accurately detecting COHb in patients presenting with a host of symptoms are likely to drastically reduce misdiagnosis and aid rapid treatment. However, emergency department clinicians will need a guidance protocol for patient management when they uncover patients suffering from CO poisoning. One such triage protocol was developed for first-responders[28] but applies well for emergency department care. See Figure 1 (next page).

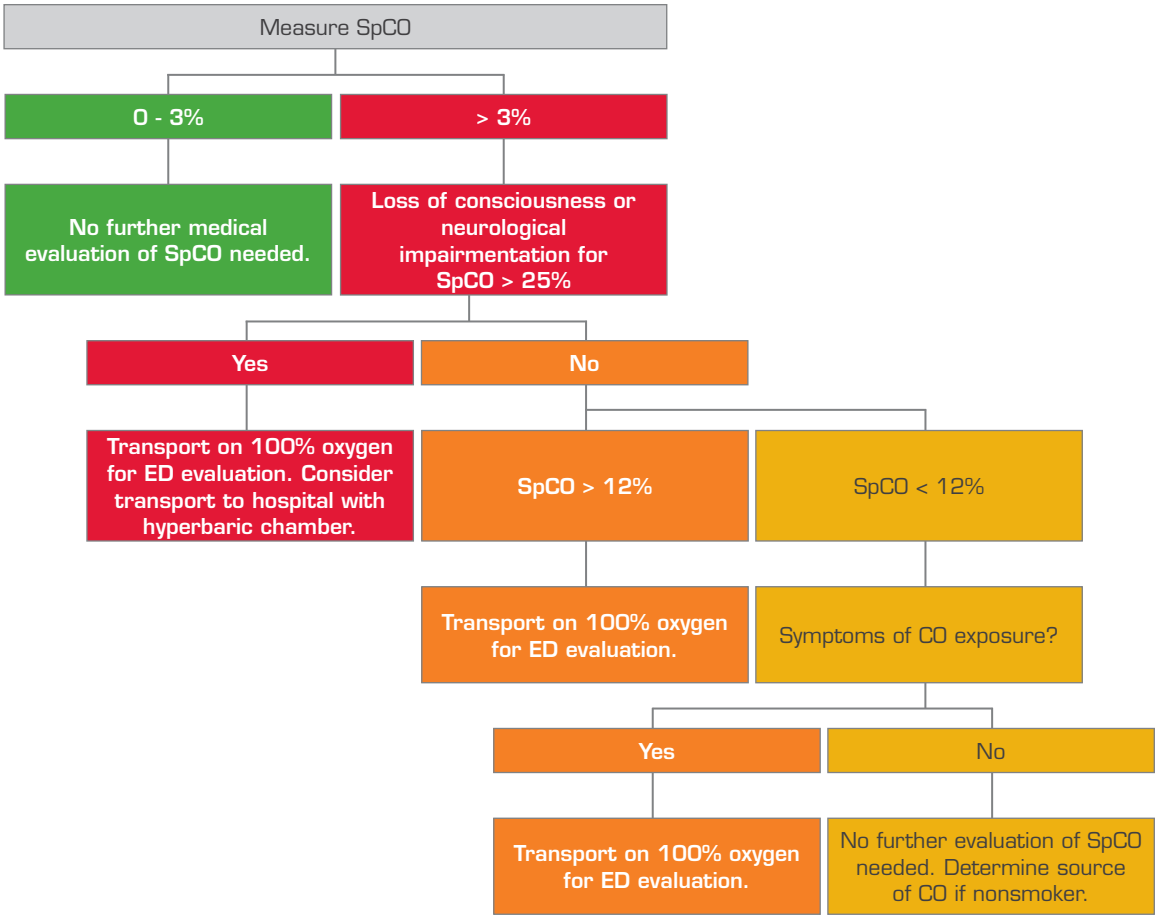

Figure 1: Hampson SpCO Triage Algorithm[28]

If the SpCO level is 3–12 percent, the elevation could be due either to smoking or another source. If the patient is experiencing such symptoms as headache, nausea or vomiting, they should receive 100 percent oxygen and undergo further evaluation and treatment as needed. If the SpCO level is 3–12 percent and the individual is asymptomatic, no further medical evaluation of the SpCO level is necessary (although the source of the exposure should be identified and fully understood such that it can be eliminated as a future etiologic agent of CO poisoning). Without this understanding a patient may be inadvertantly sent from the ED back to the environment where the poisoning likely occurred.

Hyperbaric Oxygen Therapy (HBO) can decrease the half-life of CO to 22 minutes, induce cerebral vasoconstriction to reducing intracranial pressure and cerebral edema, and reduce the risk of long-term disability. In particular, HBO treatment is appropriate for patients who experience unconsciousness, neurological signs, cardiovascular dysfunction or severe metabolic acidosis, irrespective of their COHb levels.[30]

Clinical Effects

The stakes for diagnosing and treating CO poisoning are high. Fast, effective treatment can do much to improve clinical outcomes and contain damage to the neurologic, cardiac, metabolic, pulmonary and renal systems of the body as described in Table 5.

Table 5: Impact of CO Poisoning on the Body Systems

Neurologic	CO poisoning causes central nervous system depression presenting in a host of impairments. In mild cases, patients report headaches, dizziness and confusion. In severe cases, patients may be comatose or develop seizures. Long-term neurocognitive and neuropsychiatric sequelae are reported even after moderate to severe single exposures.
Cardiac	CO poisoning causes decreased myocardial function and vasodilatation and a decreased oxygen delivery to, and utilization of, oxygen by the myocardium. As a result, the patients may present hypotensive or with tachycardia, chest pain, arrhythmias or myocardial ischemia. Most deaths from CO poisoning ultimately result from ventricular dysrhythmias.[7] Long-term cardiac sequelae are reported even after moderate to severe single exposures, increasing the odds ratio of premature cardiac death.
Metabolic	Respiratory alkalosis (hyperventilation) is possible in mild cases. With severe exposure, metabolic acidosis may result in elevated levels of acid throughout the body.
Pulmonary	Pulmonary edema occurs in 10 – 30 percent of acute CO exposures.[7] This may be due to a direct effect on the alveolar membrane, left ventricular failure, aspiration or neurogenic pulmonary edema.
Multiple Organ Failure	At high levels, multiple organ failures are expected, with a lethal outcome likely without immediate treatment to remove the CO.

The effects of CO are not confined to the period immediately after exposure. Persistent or delayed effects have been reported. In particular, a syndrome of delayed neurological effects, often referred to as DNS may manifest in a myriad of forms. DNS is experienced by 11 percent to 30 percent of patients who have had CO poisoning.[12,19] The resultant sequelae—confusion, seizures, hallucinations, persistent vegetative state, parkinsonism, short-term memory loss, psychosis, and behavioral changes— may appear anywhere from three to 240 days after carbon monoxide exposure, even in patients in whom neurologic impairment isn't initially recognized, and may be chronic.[31] There is no way of predicting which patients will suffer such sequelae. In general, those with more severe initial symptoms are at highest risk. Most mild cases resolve within two months, although patients with severe exposure may never make a full recovery from delayed neuropsychiatric sequelae.[20]

Lasting Effects of CO

Catherine Mormile was competing in her third Iditarod race in Alaska when she stopped at a tent along the route to change her wet socks. Minutes later, she felt nauseous. Hours later, she would be unconscious from the carbon monoxide from a propane heater in an unventilated tent. With no medical evaluation or oxygen treatment, she was put back on her sled to continue for another 4 days by the Iditarod race officials.

The 51-year-old physical therapist breathed the odorless gas for three hours. She said it took her years to recover. Her IQ plunged from 140 to 76. She had to relearn skills such as reading and writing.

Patients with underlying cardiovascular disease are at risk for cardiac complications. Risk of sudden cardiac death increases with CO poisoning. Hypotension and inadequate oxygenation can cause myocardial ischemia or infarction, and even cardiac arrest.[15,16,31] Even years after being treated for moderate to severe CO poisoning, patients who sustained myocardial injury as a result of exposure had an increased risk of death.[32]

Metabolic disturbances such as respiratory alkalosis and metabolic acidosis, as well as pulmonary and renal maladies may also arise from CO exposure. Pulmonary edema which occurs in 10–30 percent of acute CO exposures. The build up of COHb in the blood stream may also cause rhabdomyolysis - the breakdown of muscle fibers resulting in the release of muscle fiber contents into the circulation. Some of these are toxic to the kidney and frequently result in kidney damage and renal failure.

Causes of CO Poisoning

Carbon monoxide is a gas produced by the combustion of carbon-containing fuels (oil, kerosene, gasoline, coal, wood) or the inadequate ventilation of natural gas. It is undetectable by humans. Faulty furnaces, motor vehicles, motor boat docks with swimming platforms, portable generators, stoves, gas ranges, and gas heaters are the most common sources of carbon monoxide poisoning. At one time, it was estimated that 29 percent of unintentional CO-related deaths were due to motor vehicles exhaust.[4] This rate has declined significantly since 1979, likely owing to improved emissions standards. Before catalytic converters, closed environment exposure to car exhaust could produce death within 30 minutes.[6] CO poisoning occurs most often in the fall and winter months, when the use of gas furnaces and alternative heat sources increases.[1] It also occurs when generators, which provide power to residences and businesses, are used in poorly ventilated areas. Portable generators are commonly used in situations where power interruptions are expected (hurricane zones, ice storms, flood regions). A lesser known source of carbon monoxide is the vapors from methylene chloride[7], a compound commonly found in paint strippers. When the fumes are inhaled, it is converted *in vivo* to carbon monoxide.

Pathophysiology

Once in the bloodstream, CO has a multi-prong deleterious effect on the body. But despite the many adverse mechanisms outlined in Table 6 [8-11] each produces the same result: preventing oxygen from reaching tissues thus causing tissue hypoxia:

Table 6: Oxygen-limiting mechanisms of CO

Limits oxygen transport	The affinity between carbon monoxide and hemoglobin is more than 200 times greater than that between oxygen and hemoglobin. As a result, CO more readily binds to hemoglobin, forming carboxyhemoglobin (COHb).[12]
Inhibits oxygen transfer	CO further changes the structure of the hemoglobin molecule, which inhibits the already limited oxygen that has attached to be prematurely released into tissues.
Tissue inflammation	The tissue damage caused by poor perfusion and lack of oxygen attracts leukocytes to the damaged area. This initiates and sustains an inflammatory response, causing further tissue damage with increased capillary leakage and edema.[12] This process results in a tissue reperfusion injury, similar to what is seen in patients who have suffered a myocardial infarction.
Poor cardiac function	Decreased oxygen delivery to, and utilization of, oxygen by the myocardium may cause tachycardia, arrhythmias or myocardial ischemia.[7] Long-term damage to the heart has been demonstrated even after a single moderate to severe CO exposure.
Increased activation of nitric oxide	CO increases the production of nitric oxide, an important component in peripheral vasodilatation. In systemic inflammatory response syndrome (SIRS), nitric oxide can increase secondary to CO, or induce CO secondary to hemolysis.
Vasodilatation	CO increases the production of nitric oxide. Nitric oxide causes vasodilation. Vasodilatation is responsible for decreased cerebral blood flow and systemic hypotension.[13] Nitric oxide is largely converted to methemoglobin in the body.
Free radical formation	Nitric oxide also accelerates free radical formation. Free radical formation causes endothelial damage and oxidative damage to the brain.[13]

Conclusion

The effects of CO poisoning can be reversed if caught in time. Detection and diagnosis of CO poisoning is currently based upon clinical suspicion and confirmed by invasive blood sampling for COHb analyzed by CO-Oximetry. While many hospitals have blood gas machines with CO-Oximetry, many smaller hospitals do not, which makes timely confirmed diagnosis of CO poisoning in these situations impossible. Organs with a high metabolic requirement for oxygen, such as the heart and brain, are particularly susceptible to injury from CO. The resulting tissue ischemia can lead to organ failure, permanent changes in cognition, or death. Those that survive the initial poisoning may experience serious long-term neurological, cardiac, metabolic, pulmonary and renal impairment as a result of their CO exposure.

With lives and significant resources at stake, the speed at which suspicion evolves to diagnosis is critical. A quick noninvasive measurement of COHb using the new Masimo Pulse CO-Oximeter device may contribute to better informed treatment decisions ending the guessing game.

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Instruments and sensors containing Masimo SET technology are identified with the Masimo SET logo. Look for the Masimo SET designation on both the sensors and monitors to ensure accurate pulse oximetry when needed most. 

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