Carbon Monoxide Poisoning: The Silent Killer

Daniel Mazzolini Jr., CHT, RRT-ACCS
Clinical Specialist – Adult Critical Care & Hyperbaric Oxygen

1

Objectives

- Discuss the prevalence of carbon monoxide (CO) poisoning
- List the various sources of CO exposure
- Review the pathophysiology of CO poisoning
- List the signs and symptoms of CO poisoning
- Discuss the diagnosis of CO poisoning
- Review appropriate treatment options
- Discuss CO poisoning in special populations
- Review the use of pulse oximetry in CO poisoning
- Discuss the importance of prevention

2

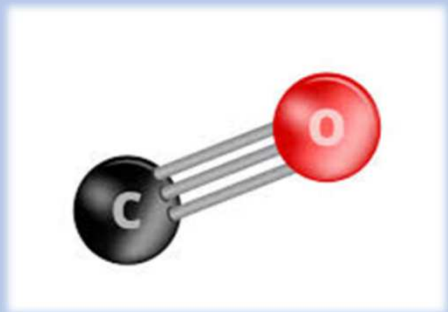
Discovery of Carbon Monoxide

Joseph Priestley, English chemist, is credited with the discovery of carbon monoxide in 1772.

3

Carbon Monoxide

- Molecule consisting of one carbon atom and one oxygen atom joined by a triple bond
- Colorless, odorless, tasteless gas
- Known as the “silent killer”



4

Prevalence

- A leading cause of poisoning deaths in the U.S.
- 1500 deaths per year in the U.S.
- Majority of deaths occur from November - February
- Approximately 50,000 ED visits per year (under reported)
- 15,000 intentional poisonings per year in U.S., accounting for 66% of CO poisoning deaths
- Males are 3X more likely to be poisoned and die
- Northern, high-altitude states have highest death rates (Wyoming, Montana, Alaska)
- Est. $1 billion/yr in societal costs (hospital costs & lost wages)

Source: Hampson NB. U.S. mortality due to carbon monoxide poisoning, 1999-2014 accidental and intentional deaths. Ann Amer Thorac Soc. 2016;13:1768-1774.

5

Prevalence

- Hospitalizations and deaths from accidental CO poisoning have been declining for many years in the U.S. due to:
  - Improved vehicle emissions policies
  - Use of catalytic converters
  - Use of carbon monoxide detectors
  - Improved public health education
  - Better product safety labeling

Source: Shin M, Bronstein AC, Glidden E, et al. Morbidity and mortality of unintentional carbon monoxide poisoning: United States 2005 to 2018. Ann of Emerg Med. 2023;81:309-317.

6

Sources of Exposure

Carbon monoxide is the result of incomplete combustion (burning) of carbon containing substances.





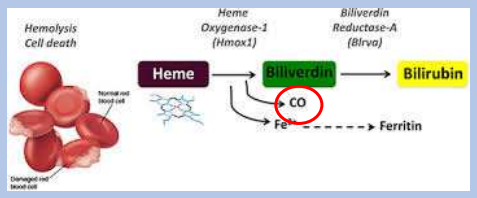

7

Sources of Exposure


8

Sources of Exposure

Methylene chloride (paint remover)
- Converted to CO primarily in the liver



Endogenous CO Production
- Heme catabolism in the liver

9

Pathophysiology

Carbon monoxide has 200 – 250 times the affinity for hemoglobin than that of oxygen

CO poisoning was originally thought to be caused by a simple anemic hypoxia.

10

Pathophysiology

- Some patients present with high COHb levels but have mild signs/symptoms.
- Some patients present with low COHb levels and have severe signs/symptoms.

Important Point

- Carboxyhemoglobin (COHb) levels do not correlate with the severity of poisoning!

CO poisoning is much more complex than first thought!

11

Pathophysiology

We now know that cellular toxicity plays a big part in CO poisoning.

Carbon monoxide:

- Binds to myoglobin
- Binds to cytochrome *c* oxidase
- Produces nitric oxide resulting in peroxynitrite
- Produces reactive oxygen species (free radicals)

These mechanisms result in the inhibition of mitochondrial function and disrupt cellular respiration and cause oxidative stress.

12

Pathophysiology Summary

- CO binds to hemoglobin with 200-250 times the affinity than that of oxygen resulting in tissue hypoxia
- CO binds to intracellular proteins (myoglobin, cytochrome *c* oxidase) which interferes with mitochondrial function impairing cellular respiration
- CO produces NO and ROS which cause oxidative stress

13

Signs and Symptoms

- Headache – 25%
- Nausea – 14%
- Dizziness – 12%
- Lethargy – 6%
- Vomiting – 6%
- Cough/choking – 3%
- Confusion – 2%
- Dyspnea – 2%
- Syncope – 2%
- Throat irritation – 2%
- Chest pain – 1.4%
- Tachycardia – 1%
- Muscle weakness – 1%
- Coma – 1%
- Eye pain/irritation – 1%

Source: Shin M, Bronstein AC, Glidden E, et al. Morbidity and mortality of unintentional carbon monoxide poisoning: United States 2005 to 2018. Ann of Emerg Med. 2023;81:309-317.

14

Signs and Symptoms

Mild/Moderate Poisoning
- Headache
- Nausea
- Dizziness
- Vomiting
- Lethargy

Severe Poisoning
- Syncope
- Neuro deficit
- Chest pain
- Arrythmias
- Increased troponin
- Lactic acidosis

Important Point
- CO poisoning is frequently misdiagnosed as viral illness in Emergency Departments.

15

Diagnosis

- Maintain a high level of suspicion especially during cold weather months
- Complete and thorough history
- Family members and pets are symptomatic
- Symptoms not specific and mimic viral illness
- COHb > 10% from co-oximetry confirms diagnosis
- Blood gas machines without co-oximeters will calculate the O_2Hb and not actually measure COHb

16

COHb Levels

Endogenous Production	< 0.5%
Non-Smoker	< 1.5%
Smoker	1.5 – 5%
Heavy Smoker	5 – 9%

Arterial or venous samples demonstrate same results.

17

Treatment

Oxygen accelerates the elimination of COHb and alleviates tissue hypoxia compared to air.

Normobaric Oxygen

- 100% oxygen by NRB mask

Hyperbaric Oxygen

- 100% oxygen under increased atmospheric pressure

18

Treatment

Normobaric Oxygen(NBO)

- Simple, well tolerated, and inexpensive
- For mild CO poisoning, normobaric 100% oxygen in the Emergency Department (ED) is the treatment of choice
- Until patient is asymptomatic and COHb < 3%
- Usually about 4 – 6 hrs
- Discharge patient with instructions to return to the ED if symptoms return, which is not typical
- Patient(s) should not return to contaminated environment (home, apt, etc) until cleared by Fire Dept, Utility Comp, etc.

19

Treatment

Hyperbaric Oxygen(HBO)

- Hyperbaric oxygen is more complex, not readily available, and expensive
- For moderate to severe CO poisoning, hyperbaric oxygen has been shown to be beneficial
- 90 minutes of 100% oxygen at 2.4 – 3 ATA
- Single tx is usually adequate but pt's with residual symptoms can be re-treated

20

Hyperbaric Oxygen

HBO is when a patient breathes 100% oxygen under increased atmospheric pressure and has been shown to:

- Significantly reduce the half-life of COHb
- Reverse mitochondrial dysfunction
- Reduce inflammation
- Stops cellular toxicity cascade
- Prevent delayed neurologic sequelae (DNS)

21

COHb Half-Life

Half-life: The time it takes for a substance in the body to decrease by half.

- Room Air = ≈5 ½ hours
- Breathing 100% Oxygen = ≈1 ½ hours
- Hyperbaric Oxygen = ≈½ hour

22

Thom, et al

Annals of Emergency Medicine, April 1995;25:474-480.

- prospective, randomized, comparative trial
- patients with mild to moderate poisoning, presenting within 6 hours, without loss of consciousness
- 30 patients received normobaric treatment with 100% oxygen by non-rebreather mask and 30 patients received HBO treatment
- neuropsychologic screening tests were used to assess cerebral dysfunction
- *results*: 7 of 30 patients (23%) receiving normobaric oxygen developed DNS, no sequelae developed in 30 hyperbaric treated patients
- *conclusions*: DNS after CO poisoning cannot be predicted on the basis of clinical history or CO level and HBO treatment reduces the incidence of DNS after CO poisoning

23

Lin, et al

Medicine, September 2018;97:39.

Study	CO poisoning time	Number of patients	Intervention	Comparison	Outcome measure time	Major outcome
Annane et al[12] (trial A)	<12 hours	I: 93 C: 86	HBO*1 (2.0 ATA, 2 hours) +NBO (4h)	NBO (6 hours)	1 mo.	Persistent and delay NPS
Annane et al[12] (trial B)	<12 hours	I: 105 C: 101	HBO*2 (2.0 ATA, 2 hours) +NBO (4h)	HBO*1 (2.0 ATA, 2 hours) +NBO (4 hours)	1 mo.	Persistent and delay NPS
Ducasse et al[8]	<12 hours	I: 13 C: 13	HBO (2.5 ATA, 2 hours) +NBO (100% O_2, 4 hours +50% O_2, 6 hours)	NBO (100% O_2, 6 hours +50% O_2, 6 hours)	2 hours, 12 hours and 21 days	NPS and EEG abnormalities
Raphael et al[7] (Trial A)	<12 hours	I: 173 C: 170	HBO*1 (2.0 ATA, 2 hours) +NBO (4 hours)	NBO (6 hours)	1 mo.	NPS
Raphael et al[7] (Trial B)	< 12 hours	I: 141 C: 145	HBO*2 (2.0 ATA, 2 hours) +NBO (4 hours)	HBO*1 (2.0 ATA, 2 hours) +NBO (4 hours)	1 mo.	NPS
Scheinkestel et al[10]	Not limited	I: 104 C: 87	HBO (2.8 ATA, 60 minutes)*	NBO (100 minutes)*	1 mo.	NPS
Thom et al[9]	< 6 hours	I: 33 C: 32	HBO (2.8 ATA, 30 minutes, then 2.0 ATA, 90 minutes)	NBO	4 weeks	Delayed NPS
Weaver et al[11]	< 24 hours	I: 76 C: 76	HBO*1 (3.0 ATA, 1 hours and 2.0 ATA, 1 hours) + HBO*2 (2.0 ATA, 2 hours)	NBO	6 weeks, 6 mos. and 12 mos.	Cognitive sequelae

ATA = atmosphere, HBO = Hyperbaric oxygen, mo (s) = month(s), NBO = normobaric oxygen, NPS = neuropsychological sequelae.
* plus daily 100-minute treatment with 100% O_2.

MEDICINE

Conclusions:
The meta-analysis indicated that compared with CO poisoning patients treated with NBO, HBO treated patients have a lower incidence of neuropsychological sequelae, including headache, memory impairment, difficulty concentrating, disturbed sleep, and delayed neurological sequelae. Taking into consideration the cost-effectiveness of one session of HBO, one session of HBO treatment could be an economical option for patients with CO poisoning with high severity.

24

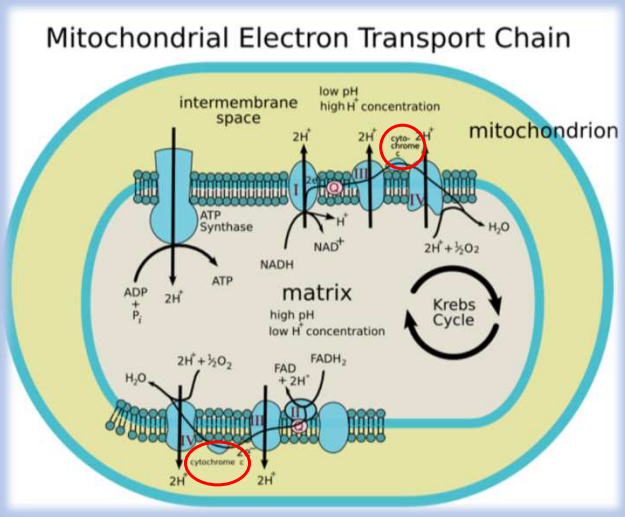
Is a PaO_2 of 2000 mm Hg physiologically possible?

Normal PaO2 = 80 – 100 mm Hg

PAO2 = (2280 mm Hg – 47 mm Hg) x 1.0 – 40/0.8 = 2183 mm Hg

25

Reverse Mitochondrial Dysfunction



26

Hyperbaric Oxygen
Guidelines For Use

- Loss of consciousness
- Neurological deficit
- Ischemic cardiac changes
- Significant metabolic acidosis
- COHb > 25%

27

Treatment Summary

- High concentration oxygen competes for binding sites on hemoglobin
- Hyperbaric oxygen decreases CO half-life to ½ hour
- Hyperbaric oxygen reverses the cellular toxicity cascade resulting in reversal of mitochondrial disfunction and reduced inflammation
- Hyperbaric oxygen prevents delayed neurologic sequelae

28

CO Poisoning in Children

- Signs and symptoms of CO poisoning may be more subtle
- Infants can be very challenging to diagnose unless high level of suspicion
- Good history is key to diagnosis
- Children may develop signs/symptoms quicker and present more ill due to their higher oxygen utilization and minute ventilation
- Treatment is not different from adults

29

CO Poisoning During Pregnancy

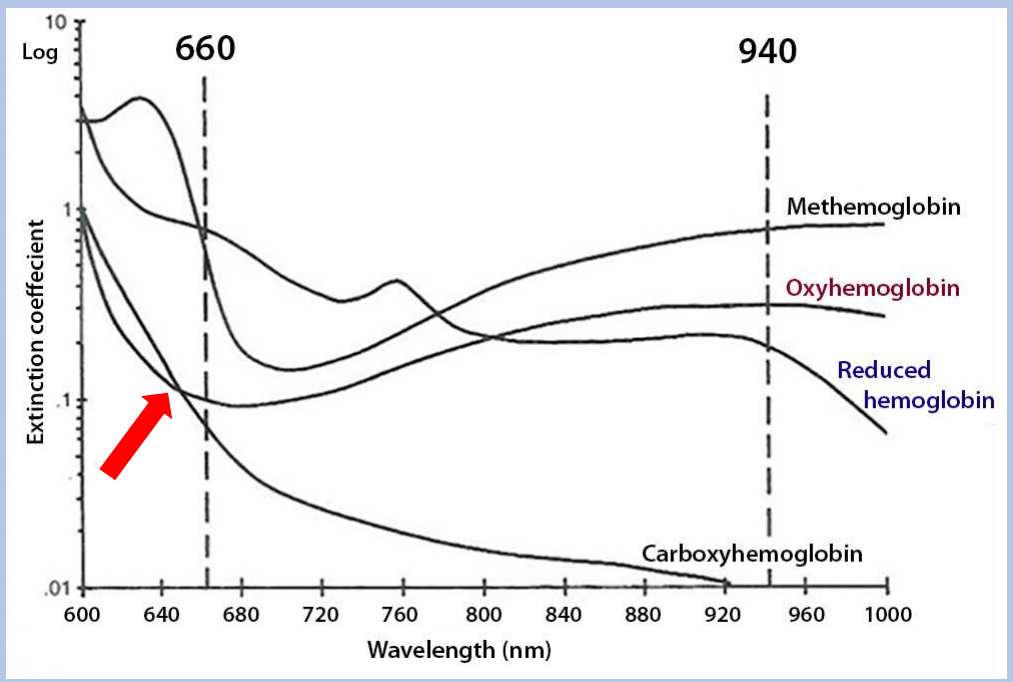
- CO poisoning early in pregnancy results in fetal anatomical malformations
- CO poisoning late in pregnancy is associated with low birth weights and neurologic sequelae
- Fetal hemoglobin has much greater affinity for CO
- CO diffuses across the placenta by passive diffusion
- Fetal COHb levels are 10 – 15% > than maternal levels
- Elimination of CO from fetus is slower due to slower dissociation from fetal hemoglobin resulting in longer half-life

30

Pulse Oximetry

- Conventional pulse oximeters use 2 wavelengths of light
  - Red (660 nm)
  - Infrared (940 nm)
- COHb and O_2Hb absorb light at 660 nm in a similar manner
- In other words, COHb is seen as O_2Hb by current generation pulse oximeters

31



32

Pulse Co-Oximetry

- One manufacturer of pulse co-oximeter in U.S.
- Uses 8 wavelengths of light
- Can read SpO_2, SpCO, SpMet, and SpHb
- Questionable accuracy
- Not recommended in clinical practice

33

REVIEWS

Accuracy of pulse CO-oximetry to evaluate blood carboxyhemoglobin level: a systematic review and meta-analysis of diagnostic test accuracy studies

Papin, Mathilde; Latour, Chloe; Leclere, Brice; Javaudin, Francois

European Journal of Emergency Medicine 30(4): August 2023, 233-243.

Abstract
Carbon monoxide (CO) poisoning is one of the most common causes of poisoning death and its diagnosis requires an elevated carboxyhemoglobin (COHb) level. Noninvasive CO saturation by pulse oximetry (SpCO) has been available since 2005 and has the advantage of being portable and easy to use, but its accuracy in determining blood COHb level is controversial. To evaluate the accuracy of SpCO (index test) to estimate COHb (reference test). Systematic review and meta-analysis of diagnostic test accuracy (DTA) studies. Four electronic databases were searched (Medline, Embase, Cochrane Central Register of Controlled Trials, and OpenGrey) on 2 August 2022. All studies of all designs published since the 2000s evaluating the accuracy and reliability of SpCO measurement compared to blood COHb levels in human volunteers or ill patients, including children, were included. The primary outcome was to assess the diagnostic accuracy of SpCO for estimating COHb by blood sampling by modeling receiver operating characteristic (ROC) curves and calculating sensitivity and specificity (primary measures). The secondary measures were to calculate the limits of agreement (LOA) and the mean bias. This systematic review was conducted according to the Preferred Reporting Items for a Systematic Review and Meta-analysis-DTA 2018 guidelines and has been registered on International Prospective Register of Systematic Reviews (PROSPERO, CRD42020177940). The risk of bias was evaluated using the Quality Assessment of Diagnostic Accuracy Studies-2 tool. Twenty-one studies were eligible for the systematic review; 11 could be included for the quantitative analysis of the primary measures and 18 for the secondary measures. No publication bias was found. The area under the summary ROC curve was equal to 86%. The mean sensitivity and specificity were 0.77, 95% confidence interval (CI, 0.66–0.85) and 0.83, 95% CI (0.74–0.89), respectively (2089 subjects and 3381 observations). The mean bias was 0.75% and the LOA was −7.08% to 8.57%, 95% CI (−8.89 to 10.38) (2794 subjects and 4646 observations). Noninvasive measurement of COHb (SpCO) using current pulse CO oximeters do not seem to be highly accurate to estimate blood COHb (moderate sensitivity and specificity, large LOA). They should probably not be used to confirm (rule-in) or exclude (rule-out) CO poisoning with certainty.

34

Prevention

- Prevention is key!
- Many accidental CO poisonings are preventable

35

Prevention

- Have your heating system, water heater and any other gas, oil, or coal burning appliances serviced by a qualified technician every year.
- Install battery-operated or battery back-up CO detectors in your home. Check or replace the battery when you change the time on your clocks each spring and fall. If the detector sounds leave your home immediately and call 911.
- **Do not** use a generator, charcoal grill, camp stove, or other gasoline or charcoal-burning device inside your home, basement, or garage or near a window.
- **Do not** run a car or truck inside a garage attached to your house, even if you leave the door open.
- **Do not** burn anything in a stove or fireplace that isn't vented.
- **Do not** heat your house with a gas oven.
- **Do not** use a generator, pressure washer, or any gasoline-powered engine less than 20 feet from any window, door, or vent.
- Seek prompt medical help if you suspect CO poisoning and are feeling dizzy, light-headed, or nauseated.

Source: U.S. Centers for Disease Control and Prevention (CDC): June 10, 2019.

36

Summary

- CO is a leading cause of poisoning deaths in the U. S. every year
- Hospitalizations and deaths have been decreasing for many years
- CO is produced by the incomplete burning of carbon containing substances
- CO has 200 – 250 times the affinity for hemoglobin than oxygen
- The pathophysiology of CO poisoning is quite complex and cellular toxicity plays an important role
- CO poisoning is frequently misdiagnosed as viral illness
- Normobaric 100% oxygen is treatment for mild/moderate poisoning

37

Summary

- Hyperbaric oxygen is used for more severe cases of CO poisoning and can prevent delayed neurologic sequelae
- Treat CO poisoning during pregnancy more aggressively because you may be treating fetus and not the mother
- Conventional pulse oximeters overestimate $O_2Hb\%$ and should not be used to gauge oxygenation in the ED
- Many accidental CO poisonings are preventable!

38