Carbon Monoxide Poisoning

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Carbon monoxide

- Carbon monoxide (CO) is a colorless, odorless and tasteless gas.
- The atmospheric concentration of CO is generally very low
    - Below 0.001%
    - 10 ppm
- It may be higher in urban areas

Carbon monoxide

- CO binds to hemoglobin in plasma forming carboxyhemoglobin (COHb)
- COHb level in blood;
  - Nonsmokers = 1-2 %
  - Smokers = 5-10 %

Epidemiology

- 16449 hospital admission with CO poisoning was stated in America in 2005
- 66 of them was resulted with death*
- Unintended poisoning is most common during the winter months

*Lai MW, Klein-Schwartz W, Rodgers GC, et al: 2005 Annual Report of the American Association of Poison Control Centers' national poisoning and exposure database. *Clin Toxicol (Phila) 44: 803, 2006.*

Epidemiology

- The most common causes of CO poisoning;
  - Smoke inhalation
  - Poorly functioning heating systems
  - Charcoal grills, camping stoves
  - Improperly vented fuel-burning devices
  - Gasoline-powered electrical generators
  - Motor vehicles operating in poorly ventilated areas
  - Exposure to exhaust
    - Living near the roads
  - Cigarette smoke

Epidemiology

- Methylene chloride (dichloromethane) is an industrial solvent
  - Metabolized to CO by the liver

Pathophysiology

- Carbon monoxide (CO) diffuses rapidly across the pulmonary capillary membrane
- CO binds to the hemoglobin (COHb)
    - 240 times the affinity of oxygen
- Once CO binds to the “heme” moiety of hemoglobin, an allosteric change occurs that greatly reduces oxygen binding
    - Diminishes the ability of the other three oxygen binding sites
- This results in an impairment in tissue oxygen delivery

Pathophysiology

- CO interferes with peripheral oxygen utilization.
- In extravascular area, CO bound to molecules such as myoglobin, cytochromes, and NADPH reductase.
- CO is bound to these molecules longer than that of COHb.
- As a result, oxidative phosphorylation is impaired at the mitochondrial level.

Pathophysiology

- CO also interferes with peripheral oxygen utilization by inactivating cytochrome oxidase in a manner similar to, but clinically less important than, cyanide.
- Combined effects of CO and cyanide on oxygen transport and utilization appear to be synergistic.

Pathophysiology

- Delayed neurologic sequelaes (DNS),
  - It cause lipid peroxidation
  - Perivascular oxidative stress in the brain leads to neuronal cell loss
  - It is thought that, during recovery from CO exposure, events analogous to ischemia-reperfusion injury and exposure to hyperoxia may exacerbate the initial oxidative damage
  - Glutamate increases in brain after CO poisoning resulting in intracellular calcium release and delayed neuronal cell death

Kinetics

- The half-life of CO,
  - While patient is breathing room air is approximately 300 minutes
  - While breathing high-flow oxygen via a nonrebreathing face mask is about 90 minutes
  - With 100% hyperbaric oxygen is 30 minutes.

Clinical Presentation

- The clinical findings of carbon monoxide (CO) poisoning are highly variable
- The most commmon symptom is headache
- Other signs and symptoms
  - Nausea
  - Vomitting
  - Visual blurred
  - Ataxia
  - Dizziness

Clinical Presentation

- May be misdiagnosed with acute viral syndromes
- CO poisoning may imitate food poisoning in the presence of vomitting

- Nausea
- Vomiting
- Ataxia
- Dizziness
- Confusion
- Syncope

- Chest pain
- Dyspnea
- Seizure
- ECG changes
- Visual blurred
- Focal neurologic deficit

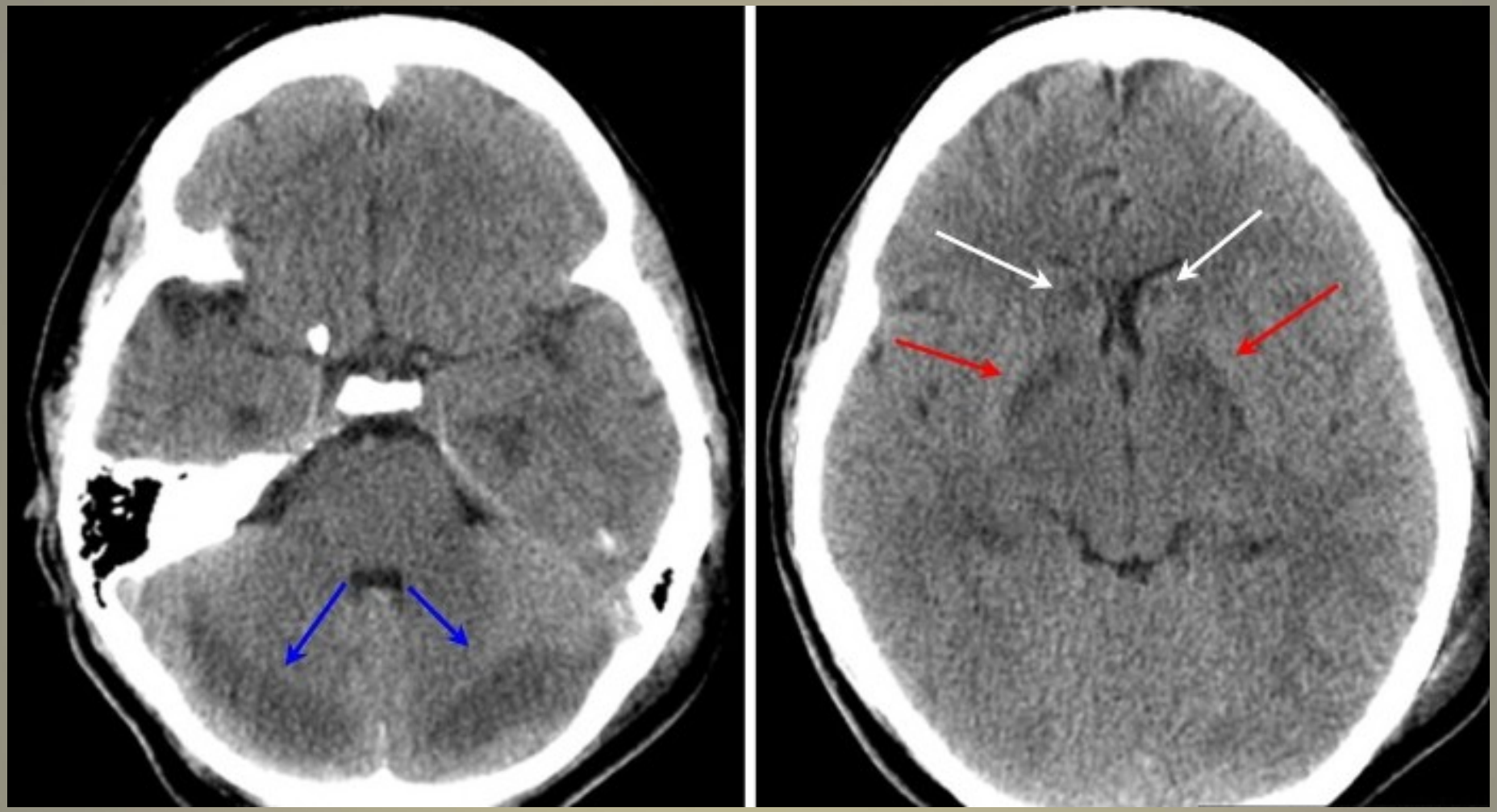
Web page: https://www.google.com/search?hl=en&site=imghp&tbm=isch&source=hp&biw=1280&bih=675&q=carbon+monoxide+poisoning&oq=carbon+mon&gs_l=img.1.2.0l10.2737.6138.0.8407.10.10.0.0.0.0.191.1211.2j8.10.0...0.0...1ac.1.7.img.Ab-A4fhJEms#imgrc=26Sn2DO3HLlScM%3A%3B6ojFs85kqC5IcM%3Bhttp%253A%252F%252Fwww.theaa.com%252Fresources%252Fimages%252Farticle-detail%252Finsurance%252Fcarbon-monoxide-gas-safety.gif%3Bhttp%253A%252F%252Fwww.theaa.com%252Finsurance%252Fcarbon-monoxide-gas-safety.html%3B440%3B200

Myocardial injury

- Acute myocardial injury is common among CO-poisoned patients
- In chronic exposure to CO a greater frequency of premature ventricular contractions is observed during exercise
- Acute exposure to CO usually results in ventricular dysrhythmias and ischemic symptoms

CNS injury

- The most sensitive organ to CO poisoning is CNS
- In low COHb levels headache, dizziness and ataxia are seen
- In chronic exposure to CO syncope, seizure and coma are seen
    - The EEG can show diffuse frontal slow-wave activity
    - The CT scan can show decreased density in the central white matter and globus pallidus



Web Page: http://www.learningradiology.com/caseofweek/caseoftheweekpix2006/cow232arr.jpg

Other clinical sign

- Cardiogenic pulmonary edema may occur
  - In severe cases
- Retinal hemorrhage
  - Exposure longer than 12 hours
- Cherry red skin
  - Rare in alive patients
- Development of cutaneous bullae
  - Thought to be caused by a combination of pressure necrosis and possibly direct CO effects in the epidermis

Delayed neurologic effects

- A syndrome of delayed neurologic sequelae (DNS) can arise 3 to 40 days after apparent recovery
  - Dementia
  - Amnestic syndromes
  - Psychosis
  - Parkinsonism
  - Paralysis
  - Chorea
  - Cortical blindness
  - Peripheral neuropathy
  - Incontinence

Delayed neurologic effects

- 14% of severely poisoned survivors had permanent neurologic impairment.
- Most cases of delayed neurologic sequelae are associated with loss of consciousness in the acute phase of toxicity.
- In this patients have lesions of the cerebral white matter and basal ganglia.

Diagnosis

- The most useful diagnostic test for suspected CO poisoning is the COHb level
- Normal COHb levels range from 0-5%.
  - CO is a natural byproduct of the breakdown of protoporphyrin to bilirubin
    - In neonates
    - High levels may be seen in hemolytic anemia
  - COHb levels in 1-pack-per-day smokers can be 6-10%
  - COHb can be zero if the patient was treated with oxygen prior to the blood test

Diagnosis

- COHb level
  - Arterial or venous sample
  - Spectrophotometrically could be read from finger (pulse oximeter)
  - COHb level could be lower incorrectly on hydroxycobalamine treatment
- Directly blood CO level could be measured
  - Plasma CO level 1mmol/L → COHb level 11%

Diagnosis

- Arterial blood gas should be evaluated to detect **metabolic acidosis**
- **Plasma pH** isn't correlated with COHb level and neurologic examination
- Plasma pH isn't a criteria for oxygen therapy and neurologic sequele
- In severe poisoning **plasma lactate level** can increase

Diagnosis

- **ECG** should be performed to determine cardiac effects
    - Ischemia and dysrhytmia should be investigated
- Troponin levels can increase due to cardiac impairment
- Mild elevations of **creatine phosphokinase** usually result from rhabdomyolysis rather than cardiac sources

Diagnosis

- New markers are researched because COHb level isn't correlated with clinics and insufficient for results
  - Rats have early increases in glutathione release from erythrocytes*.
  - Serum S100B is increased due to hypoxic stress**.

*Thom SR, Kang M, Fisher D: Release of glutathione from erythrocytes and other markers of oxidative stress in carbon monoxide poisoning. J Appl Physiol 1997;82:1424-32.
**Bottiger BW, Mobes S, Glatzer R, et al: Astroglial protein S-100 is an early and sensitive marker of hypoxic brain damage and outcome after cardiac arrest in humans. Circulation 2001;103:2694-98.

Diagnosis

- Neuropsychological Testing;
  - A normal neurologic examination with a quick mini-mental status examination.
  - Mini-memory test can be applied
  - These test are usefull to specify the need to hyperbaric oxygen therapy

Neuroimaging

- Acute changes on CT scan of the brain occur within 12 hours of CO exposure that resulted in loss of consciousness
- In a series of 18 patients, a negative CT within 1 week of admission was associated with favorable outcome.*

* Zeiss J, Brinker R: Role of contrast enhancement in cerebral CT of carbon monoxide poisoning. J Comput Assist Tomogr 1988;12:341-43

Neuroimaging

- Assessing regional cerebral perfusion
  - SPECT (Single-photon emission computed tomography) showes hypoperfusion in patients with neurologic sequele*.
- PET (Positron emission tomography) can be used for assessing regional blood flow and oxygen metabolism
  - PET examination after HBO treatment showed increased oxygen extraction and decreased blood flow in the brain**

*Denays R, Makhoul E, Dachy B, et al: Electroencephalographic mapping and Tc HMPAO single-photon emission computed tomography in carbon monoxide poisoning. Ann Emerg Med 1994;24:947-52
**De Reuck J, Decoo D, Lemahieu I, et al: A positron emission tomography study of patients with acute carbon monoxide poisoning treated by hyperbaric oxygen. J Neurol 1993;240:430-4.

Management

- The main treatment is giving 100% oxygen
  - With non-rebrating mask (90 min)
- Comatose patients, or those with severely impaired mental status, should be intubated
  - 100% oxygen
- For patients suffering from CO poisoning after smoke inhalation, it is important to consider concomitant cyanide toxicity

Management

- Most symptoms resolve with high-flow oxygen
- Non-rebreather mask delivers 70-90% oxygen
- A positive pressure mask or an endotracheal tube is necessary to achieve higher oxygen concentrations

Hyperbaric oxygen (HBO)

- HBO therapy appears to be the treatment of choice for patients with significant CO exposures.
- At 2.5 atmospheres absolute (ATA), the half-life of COHb is reduced to 20 minutes.
- Despite the uncertainty in benefit from HBO treatment, a broad set of recommendations has been established for therapy of CO poisoning

Hyperbaric oxygen (HBO)

- HBO therapy criteria;
  - COHb > 25%
  - Syncope
  - Coma
  - Altered mental status or confusion
  - Seizure
  - Neurologic deficit (Abnormal cerebellar examination)
  - Evidence of acute myocardial ischemia
  - Fetal distress in pregnancy

Hyperbaric oxygen (HBO)

- The COHb level at which HBO should be performed is controversial.
- Many toxicologists recommend HBO when the COHb level is greater than 25% whereas some societies use 40%

Hyperbaric oxygen (HBO)

- HBO should be initiated within 6 hours.
- Benefit for patients treated more than 12 hours after their CO exposure is unproven.
- Patients should have at least one session of HBO at 2.5 - 3.0 atm.
- Duration changes according to condition
    - 45-300 min
    - New sessions can be applied untill symptoms recruit

HBO and Delayed neurologic effects

- Hyperbaric oxygen therapy (HBO) may be beneficial in treating the late neurocognitive deficits associated with severe CO intoxication.*
- If applied in the first 6 hours, nearly all of the neurologic sequele recover.
- Also beneficial in the first 24 hours
- There are surveys that shows that HBO isn't beneficial.**

*Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002; 347:1057.
**Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. Med J Aust 1999; 170:203.

Hyperbaric oxygen

- Underwater and Hyperbaric Society Guide
  - HBO therapy is suggested in CO poisoning
  - The optimal number of HBO treatments for CO poisoning is unknown at this time
  - Multiple treatments should be reserved for patients who do not fully recover after one treatment

Isocapnic hyperpnea

- An intubated patient is hyperventilated with a normobaric mixture of oxygen and a small amount of CO2.
- Maintaining a PaCO2 of approximately 40 mmHg despite a sixfold increase in minute ventilation.
- Application of this technique in an animal model more than doubled the rate of CO elimination compared with conventional ventilation with 100% oxygen.*

*Fisher JA, Rucker J, Sommer LZ, et al. Isocapnic hyperpnea accelerates carbon monoxide elimination. Am J Respir Crit Care Med 1999; 159:1289.

Treatment of Pregnant Patients

- Fetal hemoglobin had a high affinity for CO
- COHb levels in the fetus exceeding the level and duration of that in the mother
- Elimination of CO from the fetus takes 3.5 times longer than maternal CO elimination
- After all, Intrauterine hypoxia and brain injuri may be develop

Treatment of Pregnant Patients

- Pregnant patients should be treated with HBO regardless of symptoms
  - COHb levels >15% (some authors)
  - COHb levels >20%
- Additional criteria include any signs of fetal distress

Treatment of Children

- Children are more sensitive to the effects of CO, because of their increased metabolic rate.
- Children can become symptomatic at COHb levels <10%
- They may have unusual presentations
- COHb levels in infants may be high
    - many cooximeters can give falsely elevated COHb levels due to fetal hemoglobin
    - CO is produced during breakdown of protoporphyrin to bilirubin. İt is may be high with precence of kernicterus

Treatment of Children

- Delayed neurologic sequela in children are observed less than in adults

Neuroprotective Treatments

- Hyperglycemia has been shown to exacerbate neuronal injury from stroke and during arrest situations.
- In rodent studies, Hyperglycemia increases neuronal injury.*
- In light of these findings, it may be benifical to treat hyperglycemia with insulin.

*White SR, Penney DG: Effects of insulin and glucose treatment on neurologic outcome after carbon monoxide poisoning. Ann Emerg Med 1994;23:606.

Neuroprotective Treatments

- Blockage of excitatory amino acids that are implicated in neuronal cell death
- Dizocilpine which blocks the action of glutamate at NMDA receptors
- In light of these findings, it ameliorates learning and memory.*

*Ishimaru H, Katoh A, Suzuki H, et al: Effects of *N-methyl-D-aspartate receptor* antagonists on carbon monoxide-induced brain damage in mice. J Pharmacol Exp Ther 1992;261:349-52.

Neuroprotective Treatments

- Ketamine, another glutamate antagonist and shown beneficial effects.*

*Penney DG, Chen K: NMDA receptor-blocker ketamine protects during acute carbon monoxide poisoning, while calcium channel-blocker verapamil does not. J Appl Toxicol 1996;16:297-304.

Prevention

- Home carbon monoxide (CO) dedectors with alarms may be life-saving.

Thanks