CARBON MONOXIDE AND CYANIDE POISONING

**CO Measurement**
- **Mechanics:** measured in blood & expired air
- **Gold Standard:** carboxyhemoglobin (COHb)
- **COHb Level:** inconsistent with degree of toxicity

**COHb Blood Stability**
recently questioned due to a study showing a significant and progressive decline in COHb blood samples in closed tubes.

**CO Poisoning**
- **New Recognition:** more complex than previously recognized
- **Intoxication by 3 Mechanisms:**
  - **Smoke Inhalation:** O2, CO, CO2, CN & Irritant Gases
  - **Auto Exhausts:** CO2, CO, NO & Organic Volatiles
  - **Pure CO Poisoning:** water heaters supplied by methane, butane or propane yield only CO, CO2 & H2O

**Mechanism of CO Poisoning**
Binds Cytochrome C Oxidase - inhibits mitochondrial respiration

**Carbon Monoxide Toxicity**
- **Scope of the Problem:** > 40,000 annually in US; 0.5 – 1.0 / 1,000,000 people fatality rates may be responsible for 50% of all fatal poisonings
- **CO Toxicity:** MCC of death in fire victims
- **Affinity:** combines with Hg 220 X than O2
- **Only Adequate Treatment:** removal & HBO
- **Relapses:** common unless HBO is repeated
- **Poor Record:** 5% - 6% ED patients receive HBO

**Carbon Monoxide Poisonings**
- **Speeds COHb Dissociation**
  - **Room Air:** CO ½ life – 320 min
  - **100% O2:** CO ½ life - 90 min
  - **HBO (3 ATA):** CO ½ life - 23 min

**Most important event in CO pathophysiology is Hb binding**
**VARIABLES IN CO UPTAKE / ELIMINATION**
- [CO] in breathing gas & relation to other partial pressures
- Density, Temperature & Humidity of Gas Mixture
- Alveolar Ventilation
- CO Alveolar - Pulmonary Gradient
- Cardiac Output
- Pulmonary CO Diffusing Capacity
- Speed of Reaction of CO with Hemoglobin
- Quantity & Speed of Lung Capillary Blood Flow
- Hemoglobin & Hematocrit Values
- Rate of Endogenous CO Production / Consumption
- Rate of CO Elimination

**PERIVASCULAR OXIDATIVE CHANGES**
1. CO competes with nitric oxide ([NO]) for binding sites & ↑ [NO]
2. [NO] interacts with superoxide anions (O2-) made by neutrophils to produce peroxynitrite (ONOO-) which activates platelet adhesion molecules
3. This leads to platelet-neutrophil aggregates
4. An oxidative burst then occurs & additional reactive [NO] derived species are made which degranulates more neutrophils
5. Neutrophils adhere to vascular lining & the vicious cycle repeats

**CO POISONING CNS TOXICITY**
- COHb Level does NOT correlate with the Development of Neurological or Cognitive Sequelae
- Permanent Brain Damage: 14% of survivors
- Delayed Neurological Sequelae (DNS): 3 - 21 days (21%)

**EFFECT ON HIGHER BRAIN FUNCTIONS**
- Dysfunctions: memory, perception, attention and concentration
- Decline in: new learning ability, tracking skills, visual-motor skills, abstract thinking & visual-spatial planning
- Other Abnormalities: personality changes and a Parkinsonian-like syndrome, occurs 2 weeks later with bradykinesia but without a tremor

**CO POISONING NEUROPATHOLOGY**
- Basal Ganglia Lesions: 70%
- Gray Matter Lesions: 30%
- White Matter Lesions: 30%
- Spongy Leukoencephalopathy
- Symmetric Myelinopathy: deep central white matter and periventricular zones
- Cerebral Edema
- Cell Death: necrosis & apoptosis

**CO POISONING NEUROPSYCHOMETRIC TESTING**
- Sensitive in detecting subtle dysfunctions
- PHYSICAL EFFECTS
  - Incontinence - Gait Disturbance - Tremor
  - Speech Impairment - Frontal Lobe & Cerebellar Signs
- "LATE SYNDROME" (2 – 3 weeks post-insult)
  - Oligodendrocyte loss 2* white matter myelin loss.
  - Ammon’s Horn destroyed (short term memory)
- NEUROLOGICAL SEQUELAE
  - 10% - 20% without HBO; 0% - 4% with HBO

**CO POISONING TREATMENT**
- 100% Oxygen: tight-fitting mask or ETT
- Labs: COHb, Lactate, CXR, EKG, drug screen, ABG
- Awake Pts: use lactate & neuropsychometric tests to determine condition & guide treatment
- Lactate & CK Levels: check serially in the CSF
- Comatose Pts: lactate predicts outcome
- If Victims Don’t Waken Quickly: use CSF rather than serum levels for prognostication

Supplemental Oxygen is the Cornerstone of Treatment However no Trials Demonstrate Improved Outcomes
Anginal Pain or Ischemic Changes on EKG
Measurable Neurologic Impairment
Any Unconsciousness, Transient or Prolonged

Heart Disease
Renal Dysfunction
> 60 years old
Severe Metabolic Acidosis
Pregnant (> 15% COHb)
COHb > 25%
Persistent Symptoms

↑COGNITIVE SEQUELAE
Age > 36 years
CO Exposure > 24 hrs
Pre-Existing Cerebellar Dysfunction

Cardiac Arrest Predicts a Dismal Outcome
with or without HBOT

Heart Disease
Respiratory Failure
> 60 years old
Severe Metabolic Acidosis
Pregnant (> 15% COHb)
COHb > 25%
Persistent Symptoms

MATERNAL SYMPTOMS
Severe CO Poisoning
Mom Mortality = 19% - 24%
Fetal Mortality = 36% - 67%
Fetal Morbidities
Malformed Limbs
Hypotonia/Areflexia
Persistent Seizures
Microcephaly
Mental & Motor Disabilities

CO POISONING LAB STUDIES
- COHb: heparinized blood tube (art or ven) at beginning of O2 therapy for later analysis (CO elimination curve)
- Psychometric Tests: more sensitive indicator of exposure
- Lab Abnormalities: ↑ CPK, MB, troponin, BUN, & Cr
- Serum Lactate: may be only abnormal lab finding after a period of surface O2
- Myoglobinuria: significant rhabdomyolysis
- EEG: non-specific diffuse changes (encephalopathy)

HBO CHAMBER SESSIONS
1st Treatment
2nd & 3rd Treatments
100% O2: at 3.0 ATA for minimally 30 minutes, followed by treatment at 1.9 to 2.5 for 90 min – 3 hrs
Thom: lipid peroxidation blocked by HBO at 3 ATA (only moderate effect at 2 ATA); same for inhibition of leukocyte adherence
Table Treatment 6: has been used with success
Repeat Treatments: Gorman found that at one year flu, pts who received 2 HBO treatments were better off than those who received just one.

A 50 y/o man presents to the ED with carbon monoxide poisoning. Which of the following chemicals in his garage is the most likely to lead to carbon monoxide poisoning?
A. Acetone
B. Methylene Chloride
C. Methylene Blue
D. Isopropyl Alcohol
E. Wood Glue

Methylene Chloride, a paint stripper, is a relatively common source of CO poisoning

TREAT AGGRESSIVELY
a single treatment is frequently not enough
BENEFITS OF HBOT
- Reduces Cerebral Edema & ICP: vasoconstriction
- Halts Ischemic-Reperfusion Injury: by inhibiting leukocyte B2 integrins & decreasing leukostasis (benefit unmatched by other txs - ↓ neuro sequelae)
- Prevents Brain Lipid Peroxidation: animal studies
- Restores (Mitochondrial) Cytochrome Redox State, pH & Energy: surface O2 may result in energy failure & cellular acidosis despite eliminating CO
- Maintains Tissue Oxygenation & Dissociates COHb
- Animal & Human Studies: show a ↓ mortality, ↓ neurological sequelae + ↑ cardiovascular status

CO VERSUS CYANIDE TOXICITY

CO VERSUS CYANIDE TOXICITY

EMS presents with a presumed gas exposure patient. No obvious trauma, but comatose with dilated pupils. Dilated pupils often seen with cyanide-induced coma but rare in CO victims (at presentation).

EMS transports a fire victim, GCS 3, intubated with soot at nares & mouth. Transitory LOC is consistently reported in pure CO poisonings with improvement upon removal & O2. Intubation is rarely required. With cyanide, LOC is sustained & requires intubation.

Severe lactic acidosis occurs in severe CO cases. However cyanide levels were not documented. Pure CO toxicity may ↑ plasma lactate, however there is a poor / no correlation between lactate levels & COHb levels unless a sustained exposure or LOC. There is a strong positive correlation between blood cyanide & and either an anion gap or elevated plasma lactate.

You are evaluating a fire victim. Your intern reports a lactate level of 10 mmol / L.
EMS reports fire victim, initially tachycardic & hypertensive, but then became hypotensive, and is now bradycardic.

This is the presentation for cyanide toxicity. The bradycardia immediately precedes cardiac arrest. Hypotension is the hallmark of significant cyanide poisoning. There is a decrease in SBP in CO poisonings with a low incidence. Bradycardia is rare in pure CO poisonings.

Seizures are listed as common in CO, however a prospective study showed a 2.9% incidence. Convulsions common with cyanide poisonings.

Bystanders report a fire victim seizing at the scene, no obvious trauma.

TRIVIA BONUS

• IN WHAT FOODS DOES CYANIDE NATURALLY OCCUR?

CO VERSUS CYANIDE TOXICITY

Fire victim with nausea, vomiting, dizziness, and a headache. The symptoms remain stable with removal from source and supplemental oxygenation.

This is Mild Cyanide Poisoning if there are no further Cardiovascular or Neurological Symptoms

OTHER CYANIDE ANTIDOTES

- 4-Dimethylaminophenol
- Dicolbalt Edetate (Kelocyanor)
- Stroma-Free Methemoglobin
- Alpha-Ketoglutarate
- Dihydroxyacetone
- Nitric Oxide
- Hemodialysis
- Hyperbaric Oxygen Therapy