CARBON MONOXIDE POISONING (COP)

The ‘silent killer’

- Carbon monoxide (CO) is a
  - COLORLESS
  - ODORLESS
  - TASTELESS
  - NON-IRRITATING GAS
  - READILY MIXES WITH AIR
- **Remarkably difficult to detect in the environment even when present at high ambient concentrations**

Introduction: epidemiology

- CO poisoning accounts for ~50,000 ER visits every year in US
- ~3,500 die of accidental or intentional exposure to CO each year
- **IN JORDAN:** *Trends of carbon monoxide fatalities in Jordan, Battah et al., 2009, Saudi Med J*
- Over 5-year period (2000-2004)
- 58% (n=107) were COP fatalities
- Accidentally during night between December and March

Sources

- **Non-vehicular sources** of CO such as **burning of wood or natural gas for heating and cooking…..**have increasingly accounted for most unintentional poisonings

- Using **gas stoves for supplemental heat** is predictive of CO poisoning in patients who present to the ED with headache and dizziness

- **Fires** another important source of CO exposure, contributing substantially to smoke inhalation deaths

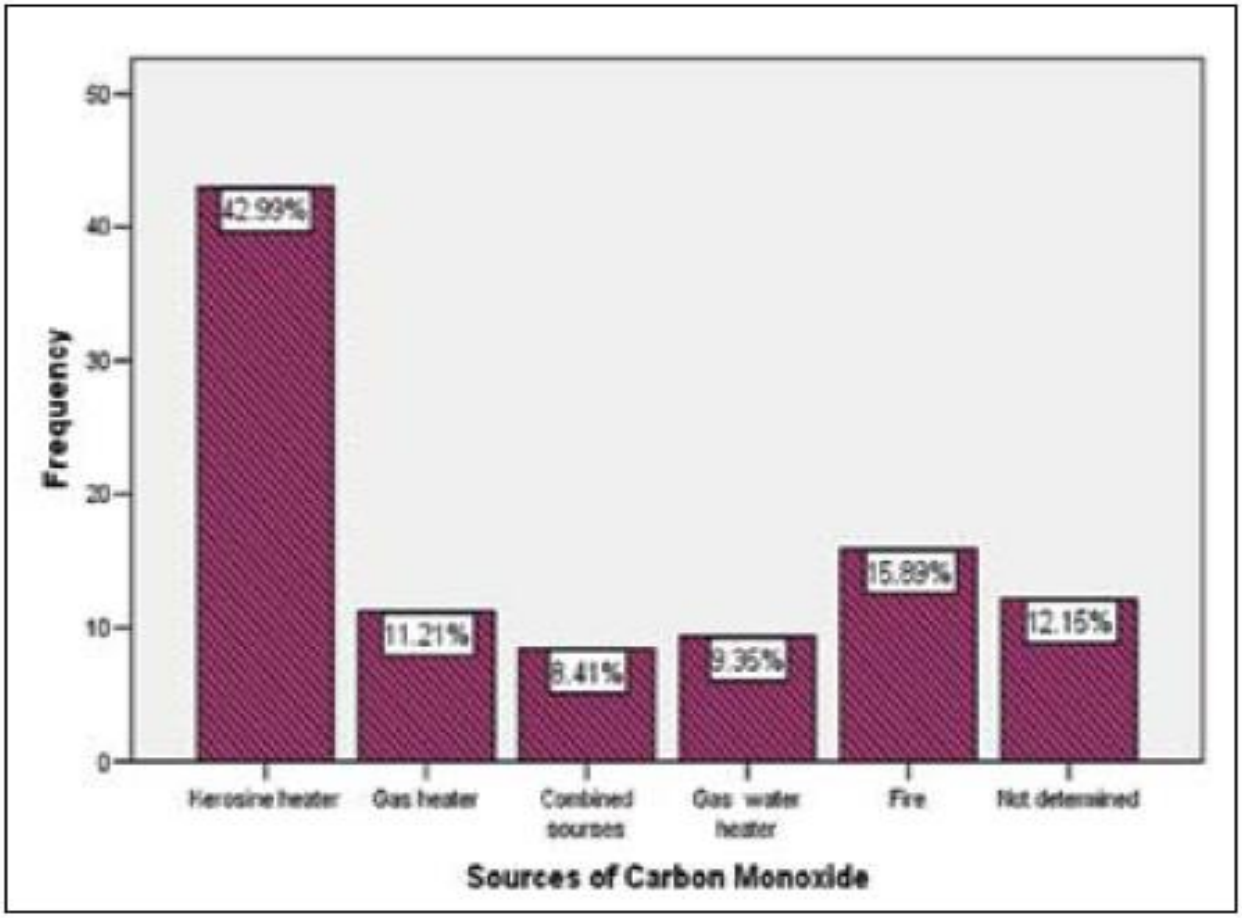


Figure 1 - Sources of CO that predisposed to COP fatalities and their percentage and frequencies. (Combined sources mean that more than one source was available at the scene of death, this category includes also central heating). COP - carbon monoxide poisoning, CO - carbon monoxide.

Sources

- Worldwide production is estimated to be in excess of 250 million tons a year

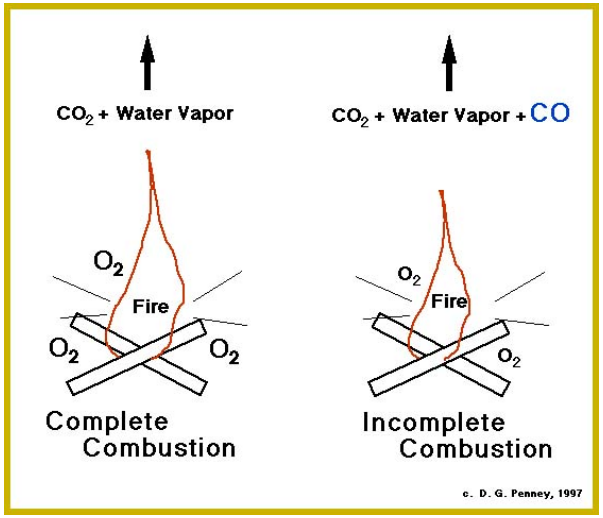
- The more significant problem with CO poisoning may be the **morbidity rather than mortality**….persistent or delayed neurologic or neurocognitive sequelae (up to 50% of patients with symptomatic acute poisonings)

Carbon Monoxide

- It is formed during:
  - INCOMPLETE COMBUSTION of virtually any carbon-containing compound
  - ENDOGENOUS PRODUCTION found naturally in the body as a byproduct of hemoglobin degradation by heme oxygenase found in the liver and spleen
  - METHYLENE CHLORIDE

Carbon Monoxide

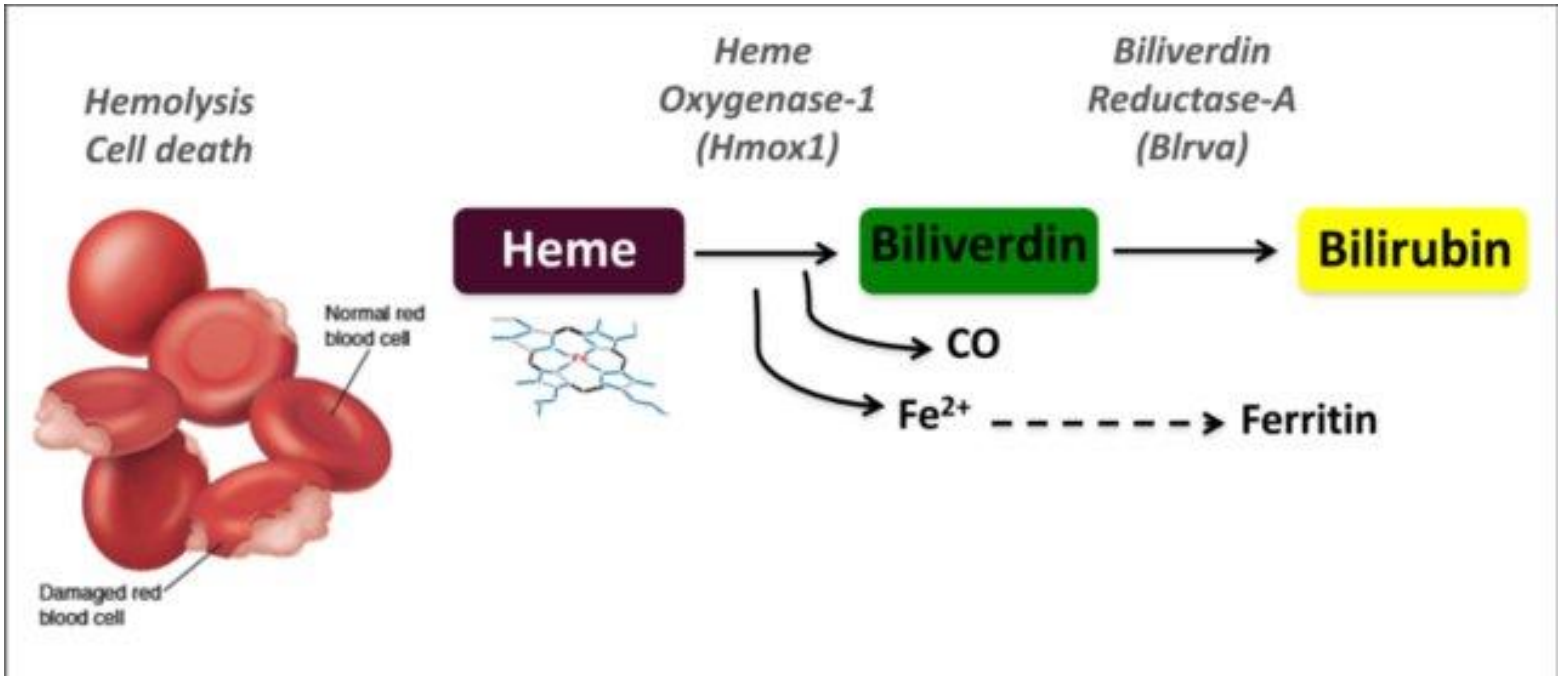
- INCOMPLETE COMBUSTION:
  - smoke inhalation in FIRES
  - AUTOMOBILE EXHAUST FUMES 7 TO 10 % CO
  - POORLY VENTILATED CHARCOAL
  - KEROSENE
  - GAS STOVES
  - CIGARETTES



Carbon Monoxide

- ENDOGENOUS PRODUCTION:
  - Heme catabolized to biliverdin with release of CO
  - **Contributes carboxyhemoglobin (COHb) levels** of less than **1% in healthy nonsmokers**
  - **Smokers may exhibit 5–10% saturation**
  - Increased in hemolytic anemia

Heme degradation pathway



Carbon Monoxide

- METHYLENE CHLORIDE [**Dichloromethane (CH_2CL_2)**]
  - Common industrial solvent and component of PAINTS VARNISH REMOVERS & SOLVENTS, METAL CLEANING, AND PLASTICS MANUFACTURING)
  - ABSORBED BY SKIN, GUT & LUNGS
  - MAY RESULT IN CO TOXICITY AFTER HEPATIC METABOLISM

Carbon Monoxide

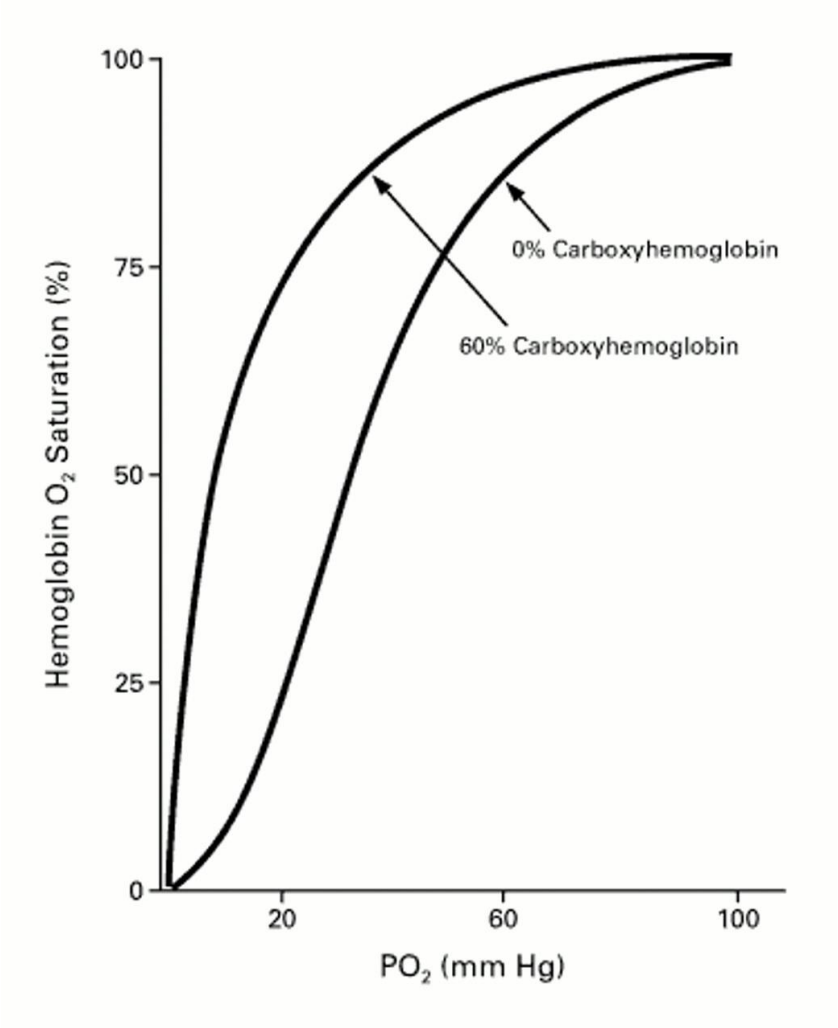
- The average concentration of CO in the atmosphere is about 0.1 ppm, (may exceed 100ppm in heavy traffic)
- Occupational Safety and Health Administration (OSHA) set a permissible exposure level of carbon monoxide of **25 ppm averaged over an 8-hour shift**…….**Threshold Limit Value (TLV)**
- The level considered **immediately dangerous to life or health (IDLH) is 1200 ppm (0.12%)**
- Exhaled CO concentration of a smoker ranges 10-50 ppm

CARBON MONOXIDE: pathophysiology

- **CO binds to hemoglobin with an affinity 250 times that of oxygen**, resulting in reduced oxyhemoglobin saturation and decreased blood oxygen-carrying capacity

  - Causes a **left shift** of the **oxyhemoglobin dissociation curve**, thus decreasing the offloading of oxygen from hemoglobin to tissue…..the net effect is decreased ability of oxygen to be delivered to tissue

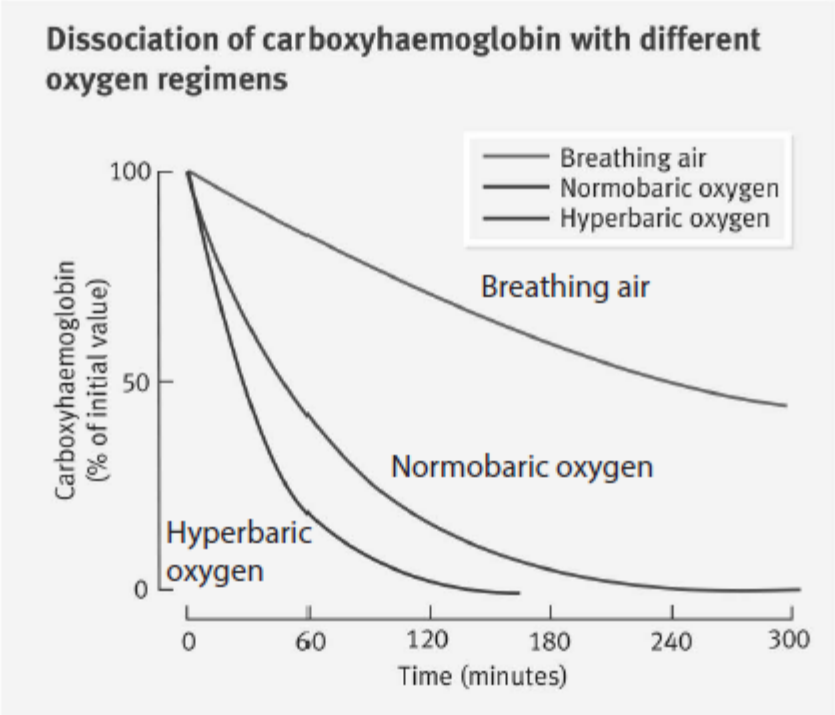
Oxygen-Hemoglobin Dissociation Curve



TOXICOCOKINETICS

- Approximately **85% of carbon monoxide** is bound to **hemoglobin** to form **COHb**, and the **rest is dissolved in plasma or bound** intracellularly, often **to myoglobin**
- **Fetal hemoglobin is more sensitive to binding by CO**, and **neonatal levels may be higher than maternal levels**
- The carboxyhemoglobin (CO-Hgb) **complex gradually dissociates** after removal from exposure

Figure 3. Dissociation of Carboxyhaemoglobin with Different Oxygen Regimens

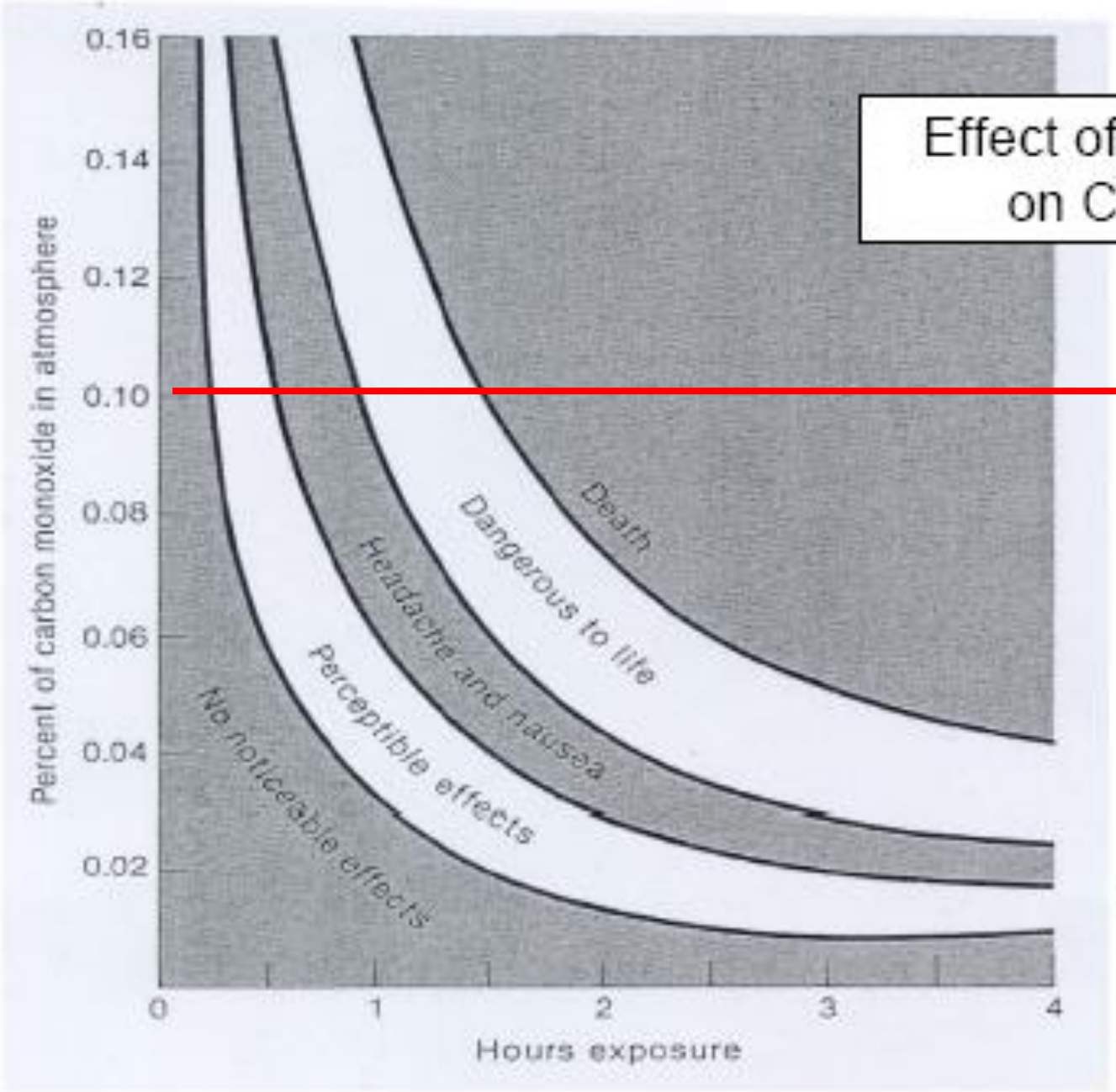


Increasing the partial pressure of inspired oxygen accelerates elimination of carbon monoxide.

Reprinted with permission from Bateman DN. Carbon monoxide. *Medicine* 2012;40:115-116.

Carbon Monoxide poisoning

- CO is readily absorbed after inhalation
- Abs. depend on **duration of exposure**, conc. in the environment, ventilation rate
- **CO toxicity cannot be attributed solely to COHb-mediated hypoxia….!!**
- Neither clinical effects nor the phenomena of delayed neurologic deficits are completely predicted by the extent of binding between hemoglobin and CO
- Heart & brain are most sensitive to O2 deprivation…worsen hypoxia


Effect of Dose & Time on CO Toxicity
Percent of carbon monoxide in atmosphere
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0
1
2
3
4
Hours exposure
Death
Dangerous to life
Headache and nausea
Perceptible effects
No noticeable effects
Exposure to 1000ppm results in 50% COHb…..take several hours to reach this level
Medical Toxicology (Elenhorn, Barceloux, Ed.), Elsevier 1988, p 821

CARBON MONOXIDE: pathophysiology

- **DISRUPTION OF CELLULAR FUNCTION:**
  - CO **interferes with cellular respiration** by binding to mitochondrial **cytochrome oxidase**….accompanied by **increased lipid peroxidation**
  - CO also bind to **myoglobin**…**impaired cardiac contractility**
  - This binding may partially **explain the myocardial impairment** that **occurs** in **low-level exposures** in **patients** with **ischemic heart disease**

CARBON MONOXIDE: pathophysiology

SYSTEMIC HYPOTENSION:

- In animal models of intoxication, dam**age is most severe in areas of the brain** that are highly sensitive to **ischemia**…….often correlates with the severity of **systemic hypotension**
- Endogenous **CO behaves like NO**, binding to **guanylyl cyclase** and thereby increasing **cGMP concentrations**……vascular smooth muscle **relaxation** …….**hypotension**
- Although low endogenous conc. are physiologic, excessive conc. of CO from exogenous sources may be problematic because CO persists much longer than NO

CARBON MONOXIDE: pathophysiology

TOXIC PRODUCT FORMATION:

- Postanoxic injury appears to be complicated by **inflammatory changes**, **excessive release of ROS and lipid peroxidation**
- Simultaneously there is **activation** of **excitatory amino acids** (**GLUTAMATE**), which **increase intracellular calcium release** and may be responsible for the subsequent neuronal cell loss
- Ultimately rats show histologic evidence of neuronal **necrosis and apoptosis** in the brain, accompanied by deficits in learning and memory

Clinical Presentation

- The symptoms of CO poisoning are those of any type of **hypoxia**….the **most prominent early symptom** is **headache** (91%) associated usually with **dizziness**, and **nausea**
- **Patients with coronary disease** may experience **angina** or **MI**
- The **severity of symptoms** usually **correlates** with **carboxyhemoglobin** levels
- **Low COHb levels 10–20%**
  - Headache
  - Dizziness
  - Abdominal pain
  - Nausea

Clinical Presentation

- **Significant levels (COHb 20–50%)**
  - Confusion, impaired thinking
  - Dyspnea
  - Syncope
- **With high levels (COHb > 50–60%)**
  - Hypotension
  - Coma
  - Seizures
- Death results when about **70–80%** of the circulating hemoglobin is converted to **COHb**

Clinical Presentation

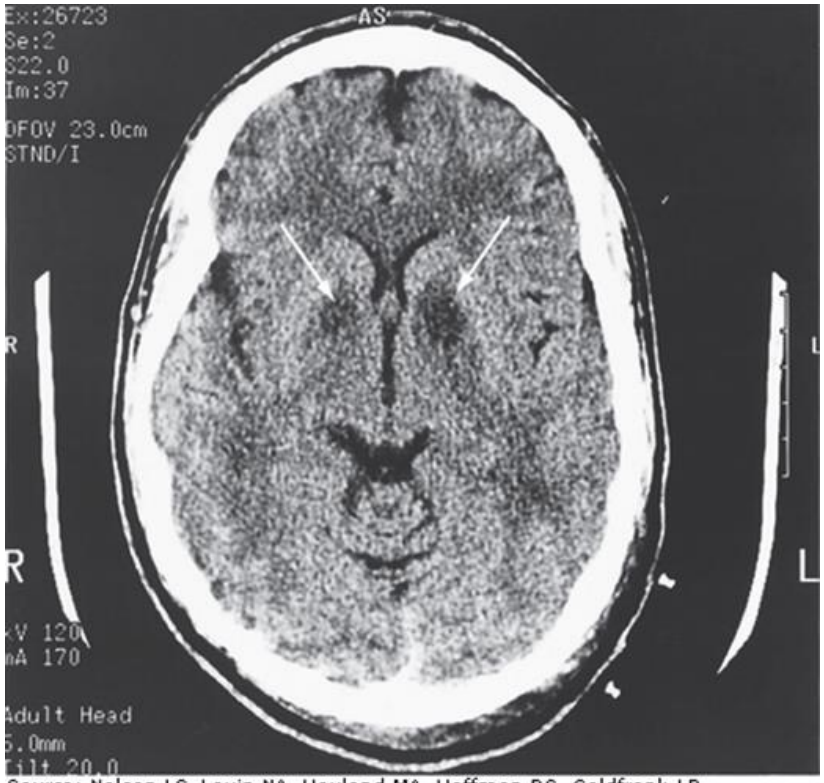
- Signs of hypoxia without cyanosis: **'cherry-red' skin coloration!!** Occurs after excessive exposure representing combination of **CO-induced vasodilation, tissue ischemia, and failure to extract oxygen from arterial blood**

- **MI & dysrhythmias** are described in victims of CO poisoning, and **acute mortality** from CO is usually a result of **ventricular dysrhythmias**

- **Troponin may be elevated in the absence of any coronary artery disease**…these patients have an **increased propensity for cardiac mortality**; **one-third die within 8 years after serious CO poisoning**

Clinical Presentation

- ✓ Patients may present with **focal neurologic symptoms suggestive of a cerebrovascular accident**
- ✓ **Survivors** of **serious poisoning may experience neurologic sequelae ranging from** gross deficits such as **parkinsonism** and a **persistent vegetative state** to subtler personality and **memory disorders** (may have a delayed onset of hours to days after exposure
- □ **Exposure during pregnancy may result in fetal death**



Source: Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE: *Goldfrank's Toxicologic Emergencies, 9th Edition*: http://www.accessemergencymedicine.com

Computed tomography of the brain **showing bilateral lesions of the globus pallidus** (arrows) in a patient with poor recovery from severe carbon monoxide poisoning. *(Image contributed by New York City Poison Center Fellowship in Medical Toxicology.)*

Clinical Presentation

- ✓ **Symptoms of chronic exposure to sublethal concentrations** of CO are **often nonspecific** although the hallmark is **headache**....usually described as **dull, frontal, and continuous**
- □ **Toxicity may be misdiagnosed as an acute viral syndrome**, in part because of increased frequency in **winter months**

- □ **Objective** deficits improve with **elimination of the exposure or HBO Tx.**
- □ Progressive brain damage, including mental changes and, sometimes, a parkinsonism-like state

Aggravating factors

- **Anemia**, **increased metabolic rate** (e.g. children) and **underlying ischaemic heart disease** all increase susceptibility to CO

- **Neurological recovery depends on the *duration of hypoxic coma***: complete recovery has been reported in young subjects (under 50) after up to 21 hrs versus 11 hrs in older ones

Diagnostic Testing

- The most useful diagnostic test obtainable in a suspected CO poisoning is a COHb level:
  - **NORMAL = ~ 1 % COHb**
  - **SMOKERS = 5 - 10 %**
  - **LETHAL = 60 %**
- The usual method for measuring COHb is with a **co-oximeter**, a device that **spectrophotometrically reads the percentage of total hemoglobin saturated with CO**

Diagnostic Testing

- **glutathione released from erythrocytes**, a potential **marker** for **CO oxidative stress** that could ultimately **lead to brain injury**
- **serum S100B**, a **structural protein in astroglia** that is **released** from the **brain after hypoxic stress**
- The extent of neurologic insult from CO can be assessed by tests such as mental status examination
- **Other useful laboratory studies** include electrolytes, glucose, BUN, creatinine, ECG, neuroimaging

Management

- The mainstay of treatment is initial attention to the airway
  1. **Remove from area (decontamination)**
  2. **ABC**
  3. **100% O2??**
- The immediate effect of oxygen is to **enhance the dissociation of COHb (decrease half life)**
- A **valid end point being the resolution of symptoms, usually accompanied by a COHb below 5%**

Management

- Consider **hyperbaric oxygen** in **severe cases**
- **Hyperbaric oxygen provides 100% oxygen under 2–3 atm of pressure and can enhance elimination of CO (half-life reduced to 20–30 minutes).**
- In animal models, it **reduces lipid peroxidation**

Management

INDICATIONS OF HYPERBARIC O2

- Hb carboxy > 25% or prolonged exposure >24hrs?
- Altered mental status
- Myocardial ischemia
- Unconsciousness
- Pregnancy with carboxy Hb ≥ 10%
- Metabolic acidosis PH <7.2

Management

- **Hypotension** can initially be **treated with IV fluids**
- **Patients** with a **depressed mental status** should have a **rapid blood glucose checked**
- **Cardiac dysrhythmia** should be treated with appropriate **anti-arrhythmic agent**
- **Dexamethasone** (0.1 mg/kg IV or IM every 4–6 hours) should be added if **cerebral edema** develops
- Because smoke often contains other toxic gases, consider the possibility of **cyanide poisoning**, or **methemoglobinemia**