

## CARBON MONOXIDE TOXICOLOGY

### • I – Physicochemical Properties

Toxic asphyxiating gas, non-irritating, colorless, odorless, tasteless ⇒ **insidious nature** (“**silent killer**”), hence the danger of poisoning

Density = 0.97 ⇒ highly diffusible in air

Liposoluble ⇒ good absorption (easily crosses cell membranes)

Thermal stability: dissociation at  $T^\circ < 400^\circ\text{C}$  into  $\text{CO}_2$  (accelerated by catalysts such as platinum (Pt) ⇒ used in CO detectors)

Oxidizable: by  $\text{O}_2$  and other oxides ( $\text{MnO}$ ,  $\text{CuO}$ ,  $\text{I}_2\text{O}_5$ ...) ⇒ analytical interest

Reducing agent: converted into  $\text{CH}_4$  by reduced Ni ⇒ (interest for  $\text{CH}_4$  measurement by gas chromatography)

Absorbs in IR: 3 absorption bands (2.2 – 4.5 – 4.6  $\mu\text{m}$ ) ⇒ analytical interest

Does not adsorb on activated charcoal ⇒ charcoal masks are ineffective

### • II – Origin and Formation

#### II-1 Biological

##### Exogenous CO formation:

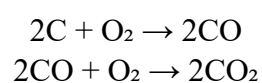
- Metabolism of microorganisms, plants
- Photodegradation of atmospheric  $\text{CO}_2$

##### Endogenous CO formation:

- Heme degradation (hemoproteins), increased in hemolytic anemia
- Higher levels in pregnancy and some metabolic diseases

#### II-2 Chemical

Incomplete combustion of carbon in insufficient oxygen:



- **III – Sources of Exposure and Poisoning**

### **III-1 Natural**

- Environmental (biological and non-biological, volcanoes)

### **III-2 Anthropogenic**

- **Industrial/professional:** mines, parking workers, combustion
- **Automobile:** vehicles running in enclosed/urban spaces
- **Domestic:** main cause of acute poisoning (heaters, water heaters, poorly ventilated areas)
- **Other:** tobacco, fires (CO + cyanides + toxic gases)

- **IV – Toxicokinetics**

### **IV-1 Absorption**

- Exclusively pulmonary
- Follows pressure gradient
- Depends on: CO concentration, duration, ventilation, O<sub>2</sub> pressure, cardiovascular/respiratory state, age, initial HbCO

Normal HbCO: 0.1–1.2%, Smokers: 3–10%

### **IV-2 Distribution**

#### **Binding to hemoproteins (Fe<sup>2+</sup> affinity):**

##### **Hemoglobin (Hb):**

- Rapid, reversible, saturable binding
- Affinity 220× greater than O<sub>2</sub>
- Cooperative binding (sigmoid curve)
- Half-life: 3–5 h

##### **Myoglobin (Mb):**

- 40× affinity vs O<sub>2</sub>
- Cardiac > skeletal muscle
- Reversible (symptom recurrence possible)

##### **Cytochrome oxidase (mitochondria):**

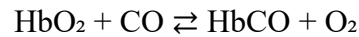
- High affinity (especially low PO<sub>2</sub>)
- Also binds: P450, catalase, peroxidase
- Crosses BBB and placenta (fetal Hb affinity higher)

## Metabolism

- <1% converted to CO<sub>2</sub>

## Elimination

- Mainly exhaled unchanged
- HbCO dissociation is slow



## Half-life HbCO:

- 3–5 h (awake)
- 6–8 h (sleeping)
- Fetus: ~7 h

Depends on O<sub>2</sub> pressure ⇒ basis of hyperbaric therapy

- **V – Toxicodynamics**

## Hemoglobin forms:

- **T form:** low O<sub>2</sub> affinity → BOHR effect → O<sub>2</sub> release
- **R form:** high O<sub>2</sub> affinity → HALDANE effect → ↓ tissue oxygenation

- **VI – Mechanisms of Toxic Action**

## VI-1 Hypoxic Effect

- HbCO formation ⇒ impaired O<sub>2</sub> transport ⇒ hypoxia
- Also binds myoglobin ⇒ ↓ cardiac output
- Binds cytochrome oxidase ⇒ cellular anoxia

→ metabolic acidosis, ↓ ATP, ROS formation

## VI-2 Oxidative Stress

- Lipid peroxidation
- Protein & DNA oxidation
- Apoptosis
- NO release ⇒ vasodilation, hypotension
- Inflammation (cytokines, platelet activation)

### VI-3 Reoxygenation Injury

- Excess ROS after oxygen therapy
- Ischemia-reperfusion syndrome
- Prevented by hyperbaric oxygen

- **VII – Acute CO Poisoning**

#### Clinical Features (non-specific)

##### Phases

Phase	Symptoms	HbCO
Asymptomatic	None	5–15%
Impregnation	Headache, dizziness, nausea, dyspnea	15–25%
State	Cardiac + neurological signs	>25%
Severe	Convulsions, coma	~30%
Death	—	>60%

##### Diagnosis

- HbCO (specific marker)
- Skin: pink/red coloration (rare)
- Biology: acidosis, ↑CPK

- **VIII – Treatment**


- Remove patient from exposure
- **Oxygen therapy (antidote)**

##### Types:

- **Normobaric (100% O<sub>2</sub>):** HbCO t<sub>1/2</sub> = 90 min
- **Hyperbaric (2.5 atm):** HbCO t<sub>1/2</sub> = 20 min

##### Indications for hyperbaric O<sub>2</sub>:

- Pregnancy
- Loss of consciousness
- Severe neurological/cardiac signs
- HbCO > 40%

 Sequelae may still occur

- **IX – Chronic CO Poisoning**

**Causes**

- Occupational exposure
- Smoking

**Symptoms (non-specific)**

- Headache, fatigue
- Memory & concentration issues
- Atherosclerosis

**Values**

- Urban population: HbCO = 1–2%
- Smokers: up to 15%

- **X – Toxicological Analysis**

**X-1 Biological**

**Blood:**

- Sample in full tubes (avoid air)
- Use NaF, EDTA

**HbCO measurement:**

- Spectrophotometry
- CO-oximeter
- Gas chromatography (reference method)

**Expired air**

- CO measurement (smoking studies)
- Electrochemical sensors
- Colorimetric tubes

**Ringold formula:**

$$\text{HbCO (\%)} = 0.5 + [\text{CO}]/5$$

**X-2 Atmospheric Analysis**

- Chemical methods (palladium, iodine pentoxide)
- Physical methods: IR detection (reference)