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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° < 400°C into CO_2 (accelerated by catalysts such as platinum (Pt) ⇒ used in CO detectors)

Oxidizable: by O_2 and other oxides (MnO, CuO, I_2O_5…) ⇒ analytical interest

Reducing agent: converted into CH_4 by reduced Ni ⇒ (interest for CH_4 measurement by gas chromatography)

Absorbs in IR: 3 absorption bands (2.2 – 4.5 – 4.6 μm) ⇒ 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 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:

$$2C + O_2 \rightarrow 2CO$$
$$2CO + O_2 \rightarrow 2CO_2$$

- **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_2 pressure, cardiovascular/respiratory state, age, initial HbCO

Normal HbCO: 0.1–1.2%, Smokers: 3–10%

IV-2 Distribution

Binding to hemoproteins (Fe^{2+} affinity):

Hemoglobin (Hb):

- Rapid, reversible, saturable binding
- Affinity 220× greater than O_2
- Cooperative binding (sigmoid curve)
- Half-life: 3–5 h

Myoglobin (Mb):

- 40× affinity vs O_2
- Cardiac > skeletal muscle
- Reversible (symptom recurrence possible)

Cytochrome oxidase (mitochondria):

- High affinity (especially low PO_2)
- Also binds: P450, catalase, peroxidase
- Crosses BBB and placenta (fetal Hb affinity higher)

Metabolism

- <1% converted to CO_2

Elimination

- Mainly exhaled unchanged
- HbCO dissociation is slow

$$HbO_2 + CO \rightleftarrows HbCO + O_2$$

Half-life HbCO:

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

Depends on O_2 pressure ⇒ basis of hyperbaric therapy

- **V – Toxicodynamics**

Hemoglobin forms:

- **T form:** low O_2 affinity → BOHR effect → O_2 release
- **R form:** high O_2 affinity → HALDANE effect → ↓ tissue oxygenation

- **VI – Mechanisms of Toxic Action**

VI-1 Hypoxic Effect

- HbCO formation ⇒ impaired O_2 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_2):** HbCO t½ = 90 min
- **Hyperbaric (2.5 atm):** HbCO t½ = 20 min

Indications for hyperbaric O_2:

- 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:
HbCO (%) = 0.5 + [CO]/5

X-2 Atmospheric Analysis

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