Chemicals exposure

Bader Alyahya

Simple asphyxiants Vs Pulmonary irritants

- Two mechanistically distinct groups of xenobiotics are capable of interfering with gas exchange:
  - Simple asphyxiants
  - Pulmonary irritants

Simple asphyxiants

- Generally speaking, have No pharmacological activity
- displace oxygen from ambient air
- $Fio_2 < 21\%$
- Decrease partial pressure of O_2
- Asphyxiation requires high concentration in a closed space

Simple asphyxiants

- Clinical features: mainly symptoms of hypoxia

TABLE 119–1. Clinical Findings Associated with Reduction of Inspired Oxygen

FiO_2[a]	Signs/Symptoms
21	None
16–12	Tachypnea, hyperpnea, (resultant hypocapnia), tachycardia, reduced attention and alertness, euphoria, headache, mild incoordination
14–10	Altered judgment, incoordination, muscular fatigue, cyanosis
10–6	Nausea, vomiting, lethargy, air hunger, severe incoordination, coma
<6	Gasping respiration, seizure, coma, death

[a]At sea-level barometric pressure appropriate adjustments must be made for altitude and depth exposures.

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Simple asphyxiants

Class	Gas	Effect, use
Noble gasses	Helium	SA
	Neon	SA
	Argon	SA
	Xenon	SA, anesthetic properties
Short chain aliphatic hydrocarbon gases	Methane (CH4)	SA, natural gas (fuel)
	Ethane (C2H6)	SA, natural gas (fuel), refrigerant
	Propane (C3H8)	SA, fuel, solvent
	Butane(C4H10)	SA, Fuel, solvent
Nitrogen	SA, nitrogen narcosis (similar to anesthetic gases)	
Carbon dioxide	SA, but also causes systemic toxicity	

SA: simple asphyxiant

Simple asphyxiants

- **Treatment**:
  - Immediate removal from exposure
  - Ventilator assistance
  - Supplemental oxygen
  - Supportive care as needed

Pulmonary irritants

- The irritant gases are a heterogeneous group of chemicals that produce toxic effects via a final common pathway: the destruction of the integrity of the mucosal barrier of the respiratory tract

- Damage of Pneumocytes → Inflammatory reaction → Acute lung injury **(ALI)** [cellular debris and plasma exudate in the alveolar sacs]

Pulmonary irritants

- **High water-solubility: Ammonia, Hydrogen fluoride, sulfur dioxide**
  - affect upper A/W (Oral, nasal, pharyngeal, conjunctival mucosa) and skin
  - irritation within seconds
- **Intermediate Water Solubility: Chlorine, Hydrogen sulfide** (rotten eggs smell)
  - Upper and lower respiratory symptoms
  - Symptoms develop after several hours
  - H_2S inhibits mitochondrial respiration (similar to cyanide)

Pulmonary irritants

- **Poor Water Solubility: phosgene (used in WWI), oxides of nitrogen, Ozone**
  - Delayed onset of symptoms
  - Affect lower A/W more (although in large concentrations they produce significant upper A/W symptoms

Pulmonary irritants

- **Management:**
  - A,B,C,D
  - Protect the A/W
  - Limit secretions
  - Oxygen supplementation, bronchodilators
  - ?Corticosteroids: may improve oxygenation, no specific benefit, small risk of harm
  - PEEP, Prone ventilation, inverse ratio ventilation, low tidal volume (for ALI)
  - Neutralization Therapy: nebulized 2% sodium bicarbonate may be beneficial in patients poisoned by acid-forming irritant gases

Pulmonary irritants

- **Management:**
  - Antioxidants: Ascorbic acid, NAC (negligible benefit)
  - Perfluorocarbon Partial Liquid Ventilation: improve oxygenation and may have anti-inflammatory effect
  - Exogenous Surfactant: no benefit in RCTs

Simple asphyxiants Vs Pulmonary irritants

TABLE 123–2. Toxic Combustion Products

Simple Asphyxiants	**Irritants**
Carbon dioxide	High water solubility (upper airway injury)
	Acrolein
	Sulfur dioxide
	Ammonia
	Hydrogen chloride
Chemical Asphyxiants	Intermediate water solubility (upper and lower respiratory tract injury)
Carbon monoxide	Chlorine
Hydrogen cyanide	Isocyanates
Hydrogen sulfide	Low water solubility (pulmonary parenchymal injury)
Oxides of nitrogen (methemoglobinemia)	Oxides of nitrogen
	Phosgene

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Case 1

- 25 year-old healthy male. Presented to the ED with history of syncope, H/A, SOB, cough and dizziness.
- 2 of his brothers have similar symptoms
- VS: HR=110 beat/min, RR=20, O2 sat= 100% in RA, temp= 37.0
- ECG: sinus tachycardia, Glucose= normal

Carbon monoxide (CO)

- The leading cause of poisoning morbidity and mortality in the United States
- HGB has 200-250 times greater affinity to CO than O_2

Carbon Monoxide (CO)

MW	=	28.01 daltons
Gas density	=	0.968 (air = 1.0)
Blood carboxyhemoglobin level		
Nonsmokers	=	1–2%
Smokers	=	5–10%
Action level	>	10%

Sources of CO

TABLE 125–1. Sources of Carbon Monoxide Implicated in Poisonings[168]

- Anesthetic absorbents[82]
- Banked blood
- Boats[19]
- Camp stoves and lanterns
- Charcoal grills[50]
- Coffee roasting[114]
- Gasoline-powered equipment (eg, generators, power washers)[17,18]
- Ice resurfacing machines[16]
- Methylene bromide
- Methylene chloride
- Natural gas combustion furnaces (water heaters, ranges and ovens)
- Propane-powered forklifts[46]
- Underground mine explosions[98]
- Wood pellet storage

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Half-life of CO

Room air	**300 minutes (5H)**
100 % O_2	60 minutes
HBO	30 minutes

Pathophysiology

- CO binds HGB rendering it incapable of delivering O_2 to the cells

  leftward shift of the oxyhemoglobin dissociation curve decreases offloading of O_2 to tissues (decrease 2,3-BPG)
- Interferes with cellular respiration by binding to mitochondrial cytochrome oxidase
- lipid peroxidation, particularly in the hippocampus and corpus striatum

CO poisoning

TABLE 125–2. Clinical Manifestations of CO Poisoning

Ataxia	Myocardial ischemia
Cardiac dysrhythmias	Nausea
Chest pain	Syncope
Confusion	Tachypnea
Dizziness	Visual blurring
Dyspnea	Vomiting
Headache	Weakness

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Investigations in CO poisoning

- COHb level (Most useful)
- ECG, monitor,
- VBG, Lactate, CK, Troponin, BNP, +/- Echo
- Neurologic exam and mini mental state exam
- CT as needed

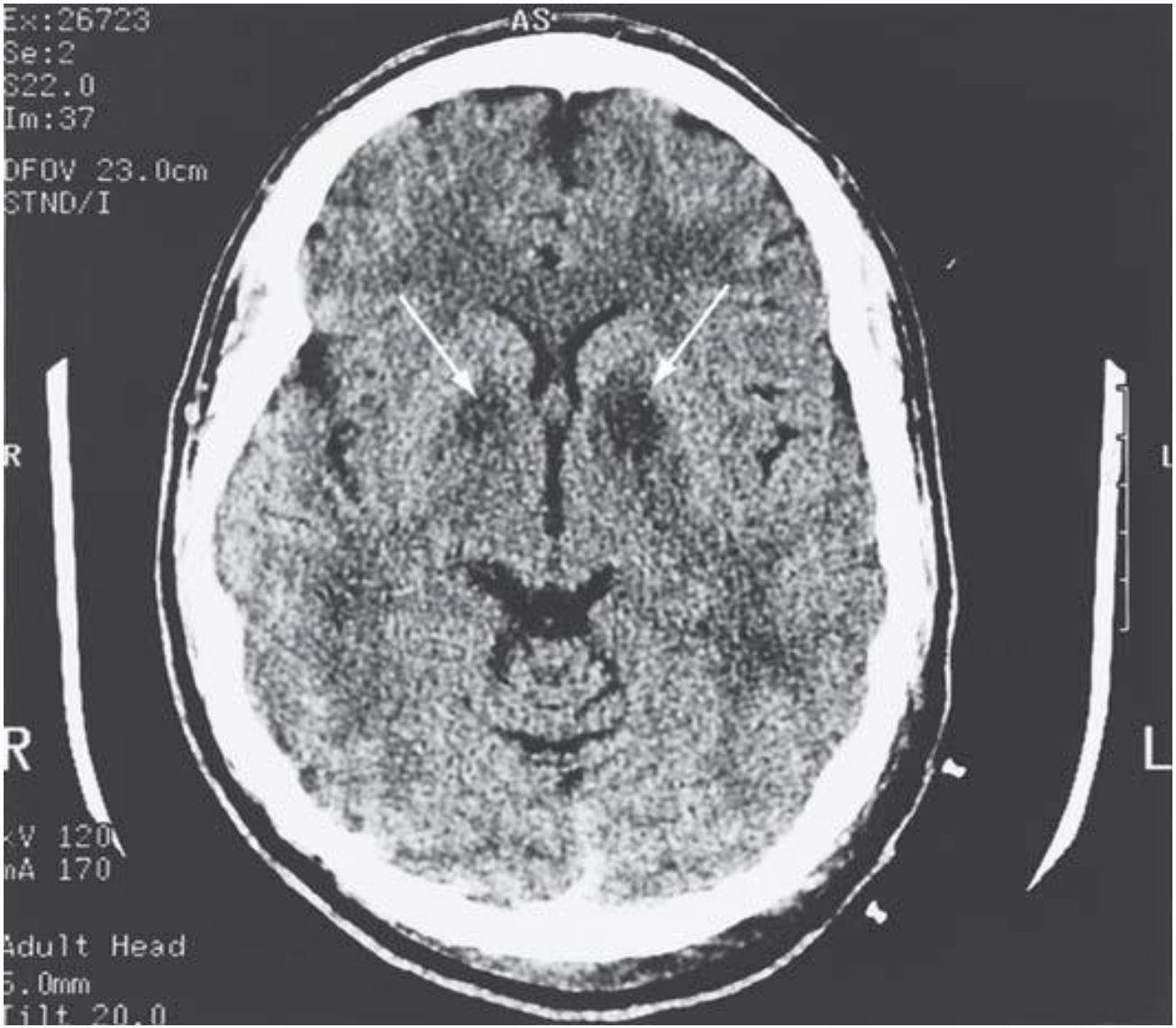

FIGURE 125–1. Computed tomography of the brain showing bilateral lesions of the globus pallidus (arrows) in a patient with poor recovery from severe carbon monoxide poisoning. *(Image contributed by New York City Poison Center Fellowship in Medical Toxicology.)*

(CO poisoning)Treatment

- Removal from site of exposure
- ABCD
- O_2 (100% ASAP) Mainstay of treatment
- Supportive care (IV fluid for hypotension, standard ACLS PRN)
- HBO

(CO poisoning)Treatment

TABLE 125–4. Suggested Indications for Hyperbaric Oxygen[a]

Syncope (loss of consciousness)
Coma
Seizure
Altered mental status (GCS<15) or confusion
Carboxyhemoglobin >25%
Abnormal cerebellar function
Age ≥36 years
Prolonged CO exposure (≥24 hours)
Fetal distress in pregnancy

[a] These are criteria that are potential risk factors for cognitive sequelae, suggesting that such patients have the most to benefit from HBO treatment)[174] GCS, Glasgow Coma Score.

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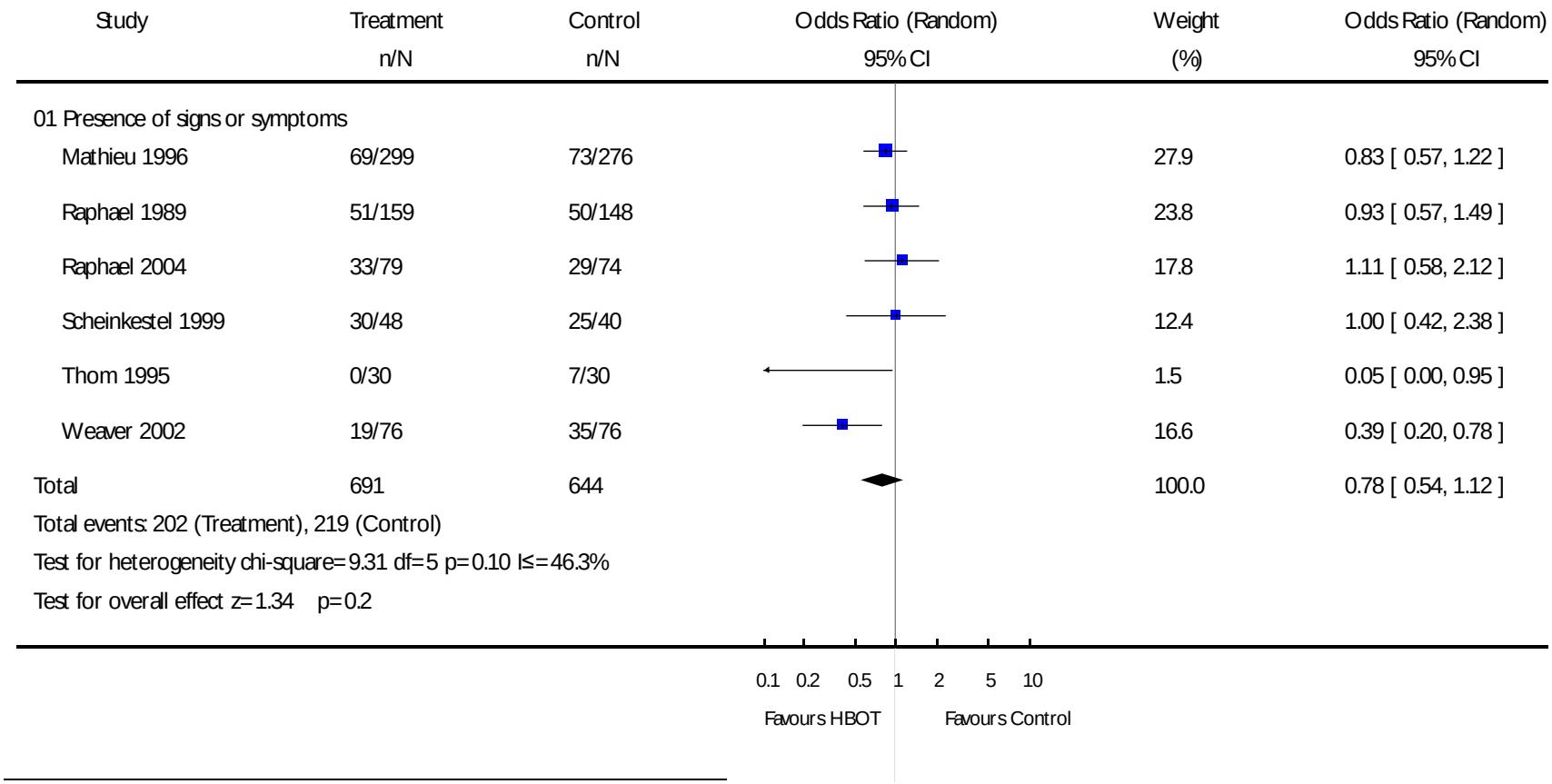
HYPERBARIC OXYGEN FOR ACUTE CARBON MONOXIDE POISONING

LINDELL K. WEAVER, M.D., RAMONA O. HOPKINS, PH.D., KAREN J. CHAN, B.S., SUSAN CHURCHILL, N.P., C. GREGORY ELLIOTT, M.D., TERRY P. CLEMMER, M.D., JAMES F. ORME, JR., M.D., FRANK O. THOMAS, M.D., AND ALAN H. MORRIS, M.D.

TABLE 2. OUTCOMES AT 6 WEEKS, 6 MONTHS, AND 12 MONTHS AFTER ENROLLMENT.*

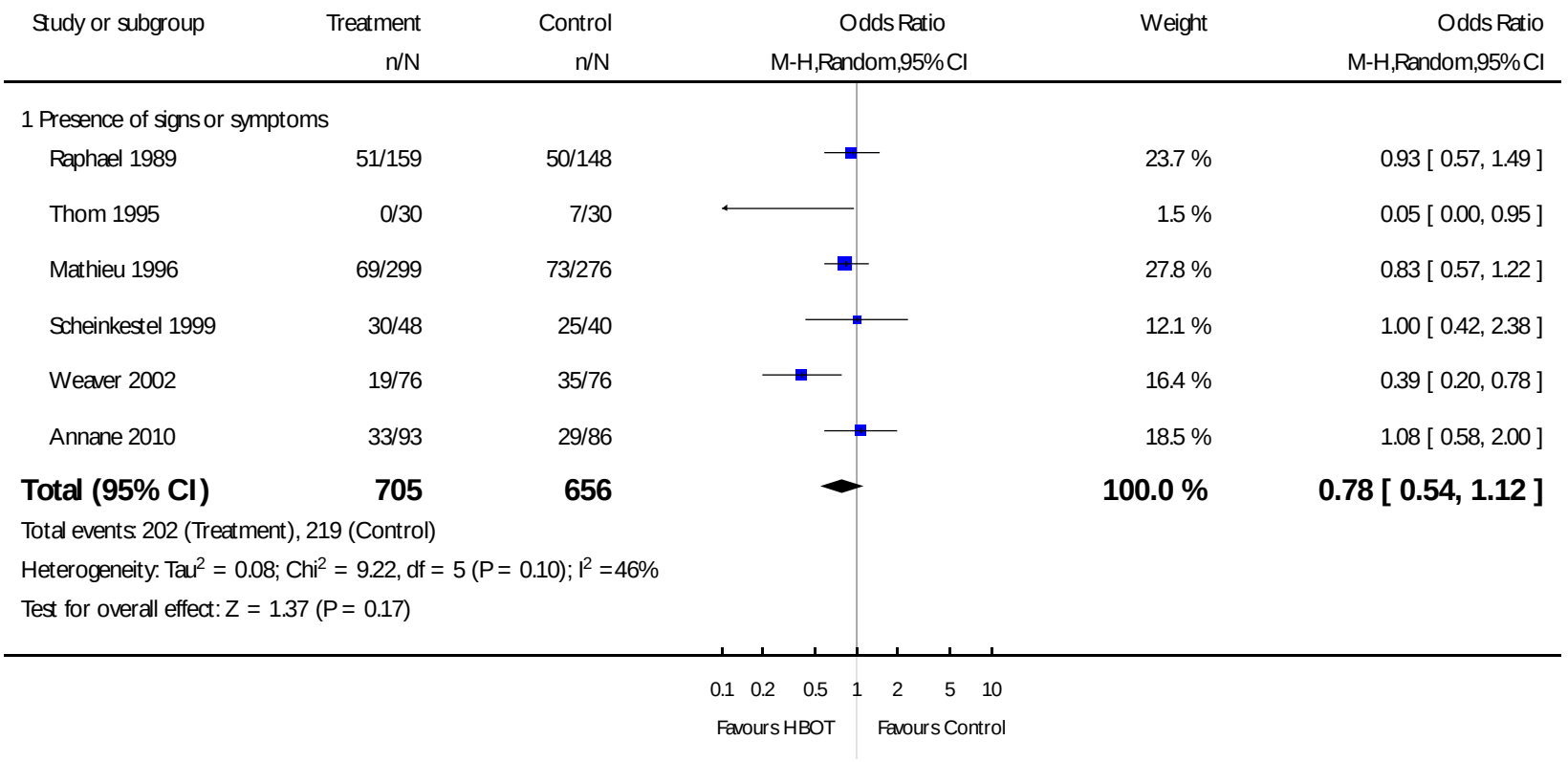
OUTCOME	HYPERBARIC-OXYGEN GROUP (N=76)	NORMOBARIC-OXYGEN GROUP (N=76)	UNADJUSTED ODDS RATIO (95% CI)†	P VALUE
	no./total no. (%)			
Cognitive sequelae				
At 6 wk				
Intention-to-treat population	19/76 (25.0)	35/76 (46.1)	0.39 (0.20–0.78)	0.007
Patients with complete data	18/75 (24.0)	31/72 (43.1)	0.42 (0.21–0.85)	0.01
Results on cerebellar testing before treatment				
Normal	16/69 (23.2)	23/59 (39.0)	0.47 (0.22–1.02)	0.05
Abnormal	1/3 (33.3)	9/11 (81.8)	0.11 (0.01–1.92)	0.18
At 6 mo				
Intention-to-treat population	16/76 (21.1)	29/76 (38.2)	0.43 (0.21–0.89)	0.02
Patients with complete data	10/58 (17.2)	21/59 (35.6)	0.38 (0.16–0.90)	0.03
At 12 mo				
Intention-to-treat population	14/76 (18.4)	25/76 (32.9)	0.46 (0.22–0.98)	0.04
Patients with complete data	9/62 (14.5)	18/66 (27.3)	0.45 (0.19–1.10)	0.08
Symptoms				
Reported by patient at 6 wk				
Difficulties with memory	21/75 (28.0)	37/72 (51.4)	0.37 (0.19–0.73)	0.004
Difficulties with attention or concentration	24/75 (32.0)	31/72 (43.1)	0.62 (0.32–1.22)	0.17

HBO for CO poisoning



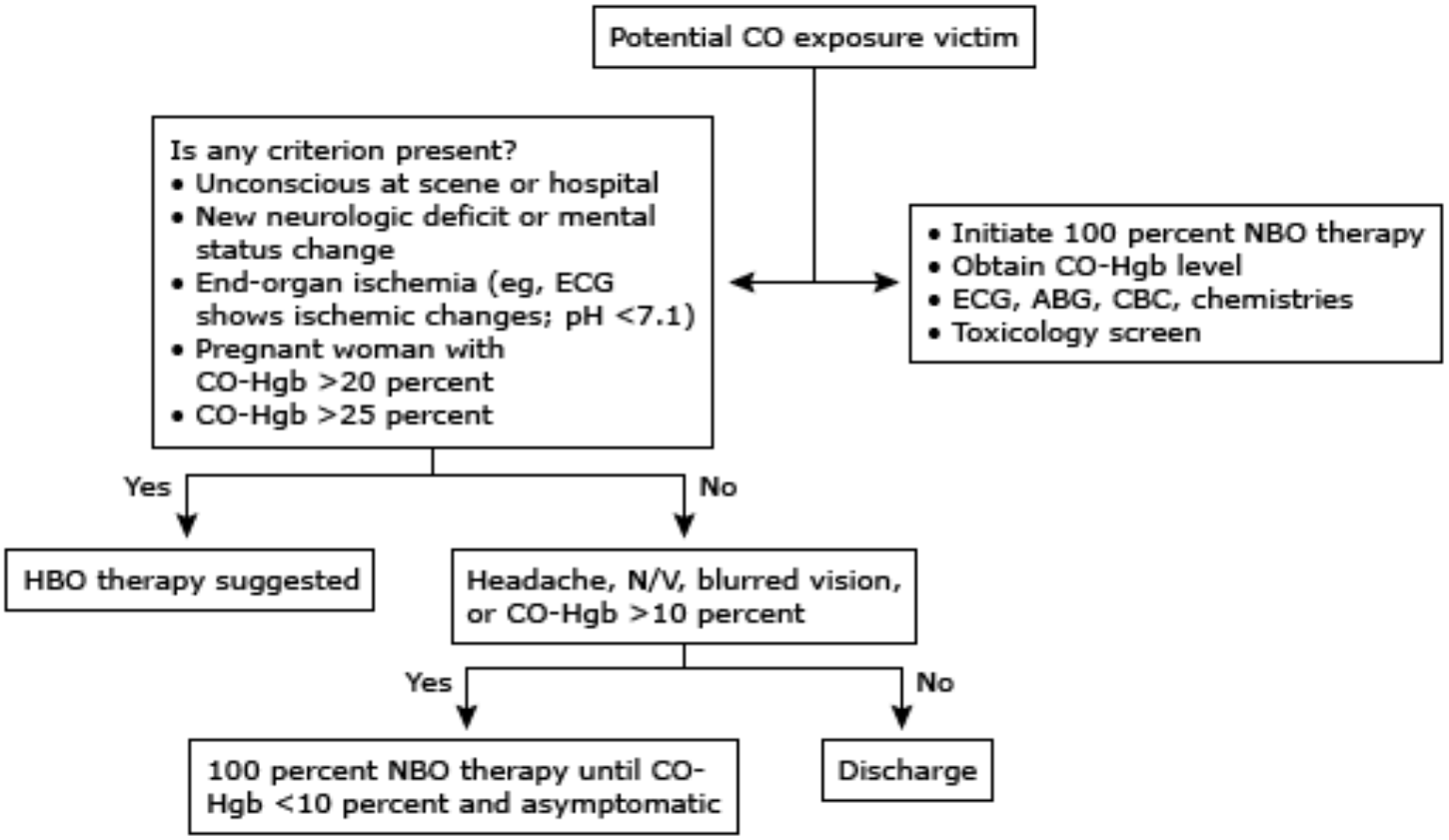
Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA

HBO for CO poisoning



Buckley NA, Juurlink DN, Isbister G, Bennett MH, Lavonas EJ

Algorithm for using normobaric and hyperbaric oxygen following carbon monoxide exposure



CO: carbon monoxide; ECG: electrocardiogram; CO-Hgb: carboxyhemoglobin; NBO: normobaric oxygen; HBO: hyperbaric oxygen; N/V: nausea and vomiting.

Adapted from: O'Brien C, Manaker S. Carbon monoxide and smoke inhalation. The Intensive Care Manual. Hanson, Lanken, Manaker (Eds), WB Saunders, Philadelphia, 2001.

Case 2

- 30-year-old male. Brought to the ED by EMS following a fire incident at a plastic factory. The patient is unresponsive. His BP= 80/40, HR= 130, RR= 30, O2 Sat is 90% on non-rebreather mask.
- He was intubated on arrival to the ED. Vital signs are unchanged.
- No obvious skin burn, Chest: few scattered wheezes

CVS: S1+S2+ no added sounds. Abdomen: normal

- Investigations: VBG: PH= 7.01, PCO2= 30, PO2=60,$HCO3^-$ = 5, lactate = 15, CO= 10%

Cyanide

Cyanide (CN)

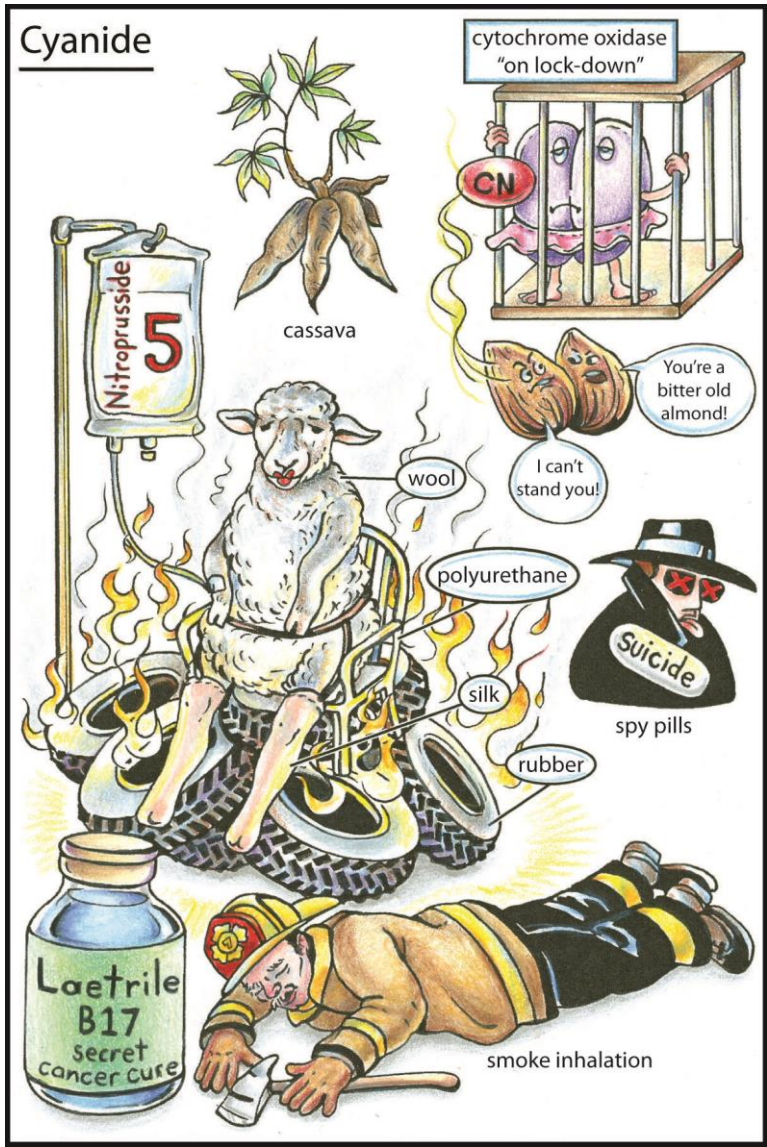
MW	=	26.02 daltons
Whole blood	<	1 µg/mL (38.5 µmol/L)

Concentrations: Airborne

Immediately fatal	=	270 ppm
Life threatening	=	110 ppm (>30 min)

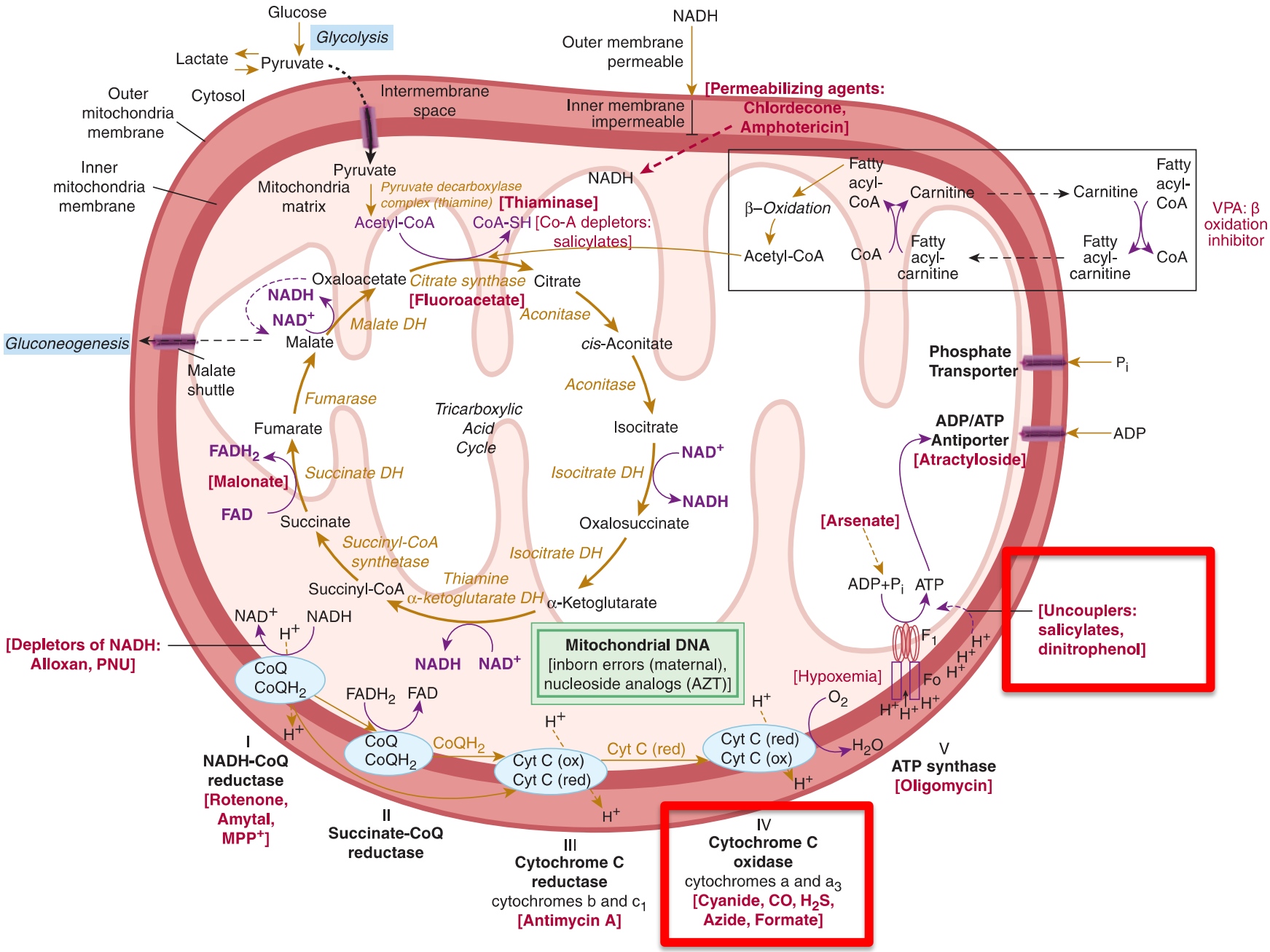
Cyanide exposure

- Fire in closed space (plastic burn)
- Chemistry labs
- Plants (cassava, apricot seeds)
- Iatrogenic (nitroprusside)
- photographic industries
- Jewelry manufacturing



Cyanide

- Cyanide is an inhibitor of multiple enzymes, including succinic acid dehydrogenase, superoxide dismutase, carbonic anhydrase, and **cytochrome oxidase**


Glucose
Glycolysis
Lactate
Pyruvate
Outer mitochondria membrane
Cytosol
Intermembrane space
Inner mitochondria membrane
Pyruvate
Mitochondria matrix
Pyruvate decarboxylase complex (thiamine)
[Thiaminase]
Acetyl-CoA
CoA-SH [Co-A depletors: salicylates]
NADH
Outer membrane permeable
Inner membrane impermeable
[Permeabilizing agents: Chlordecone, Amphotericin]
β–Oxidation
Fatty acyl-CoA
Carnitine
Acetyl-CoA
CoA
Fatty acyl-carnitine
VPA: β oxidation inhibitor
Oxaloacetate
Citrate synthase
[Fluoroacetate]
Citrate
NADH
NAD+
Malate DH
Malate
Aconitase
cis-Aconitate
Gluconeogenesis
Malate shuttle
Fumarase
Fumarate
Tricarboxylic Acid Cycle
Isocitrate
Aconitase
FADH2
[Malonate]
FAD
Succinate DH
Succinate
Isocitrate DH
NAD+
NADH
Oxalosuccinate
Succinyl-CoA synthetase
Succinyl-CoA
Thiamine α-ketoglutarate DH
Isocitrate DH
α-Ketoglutarate
Phosphate Transporter
Pi
ADP/ATP Antiporter [Atractyloside]
ADP
[Arsenate]
ADP+Pi
ATP
[Uncouplers: salicylates, dinitrophenol]
[Depletors of NADH: Alloxan, PNU]
NAD+
H+
NADH
CoQ
CoQH2
Mitochondrial DNA
[inborn errors (maternal), nucleoside analogs (AZT)]
F1
Fo
H+
[Hypoxemia]
O2
FADH2
FAD
CoQ
CoQH2
Cyt C (ox)
Cyt C (red)
Cyt C (red)
Cyt C (ox)
H2O
I
NADH-CoQ reductase
[Rotenone, Amytal, MPP+]
II
Succinate-CoQ reductase
III
Cytochrome C reductase
cytochromes b and c1
[Antimycin A]
IV
Cytochrome C oxidase
cytochromes a and a3
[Cyanide, CO, H2S, Azide, Formate]
V
ATP synthase
[Oligomycin]

Cyanide

- Clinical features:
- CNS: altered level of consciousness, SZ, Anxiety, H/A, agitation
- CVS: Hypotension, tachycardia, arrhythmia (may have transient HTN and tachycardia)
- Respiratory: SOB, tachypnea, (later hypoventilation and pulmonary edema) Metabolic: lactic acidosis (classically lactate more than 10) (needs VBG with Carboxyhemoglobin)

[Unconscious, hypotensive, and high lactate]

Cyanide treatment

- ABCDE
- Antidote: almost always empirical
  - Hydroxocobalamin (5 g IV during 15 minutes for adults and 70 mg/kg IV for children, up to an adult dose)

  Cyanide + hydroxycobolamine = Cyanocobalamin

  - cyanide antidote kit:
    - Amyl nitrite
    - Sodium nitrite
    - Sodium thiosulfate
- Supportive care

Cyanide kit

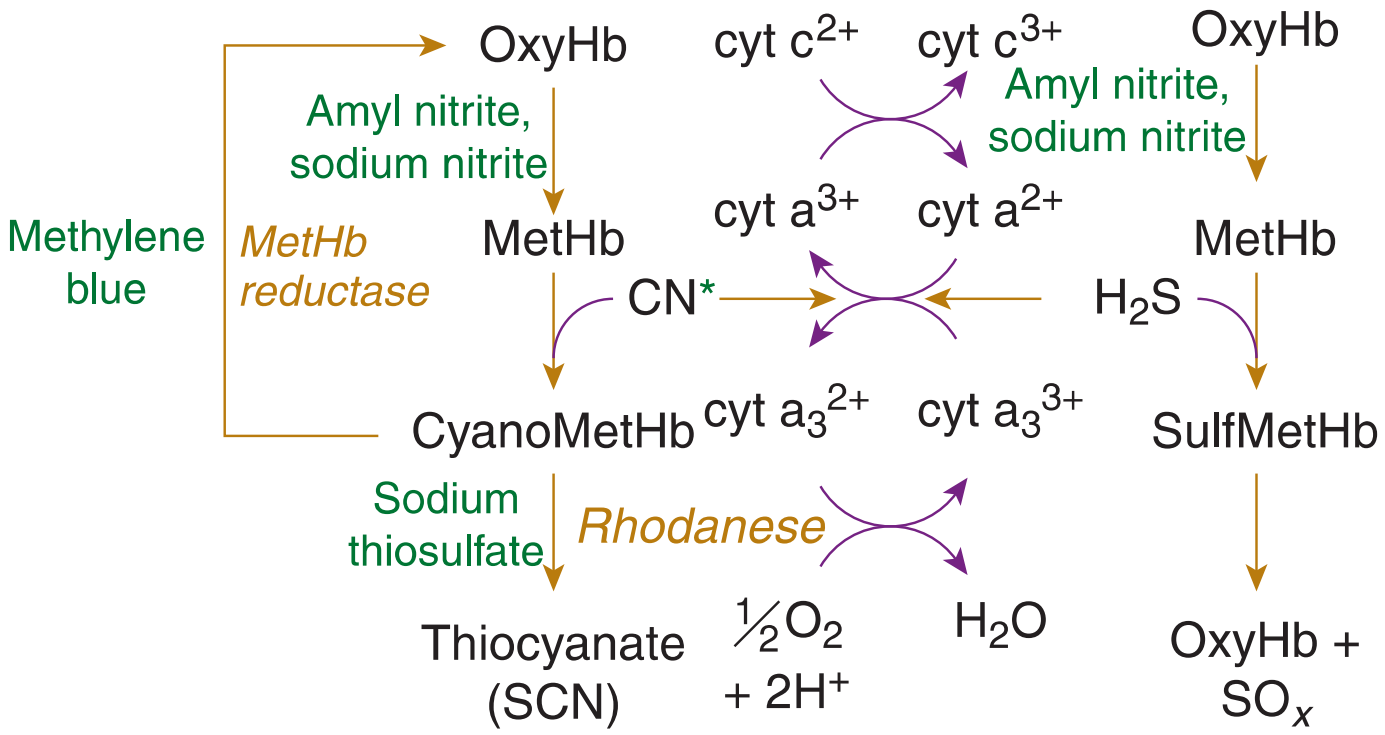
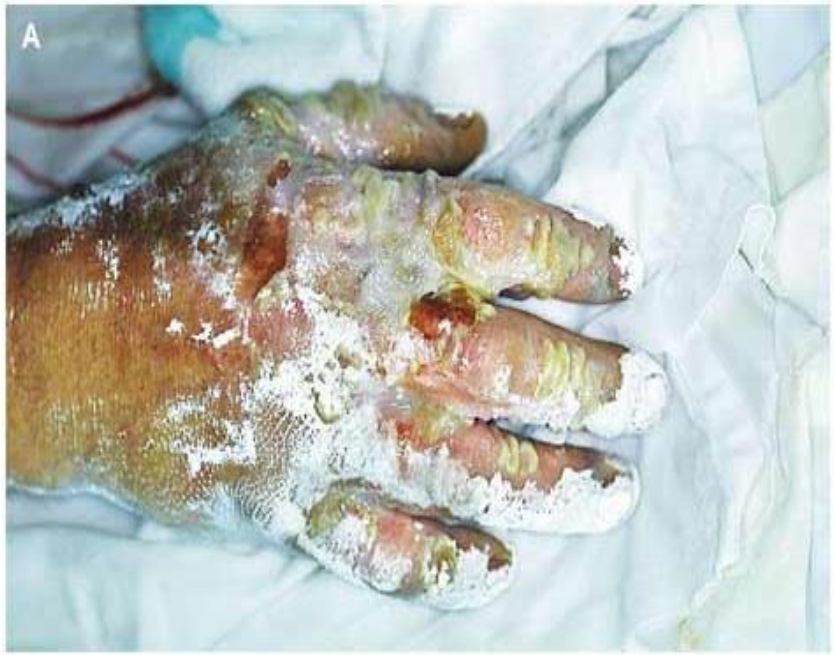
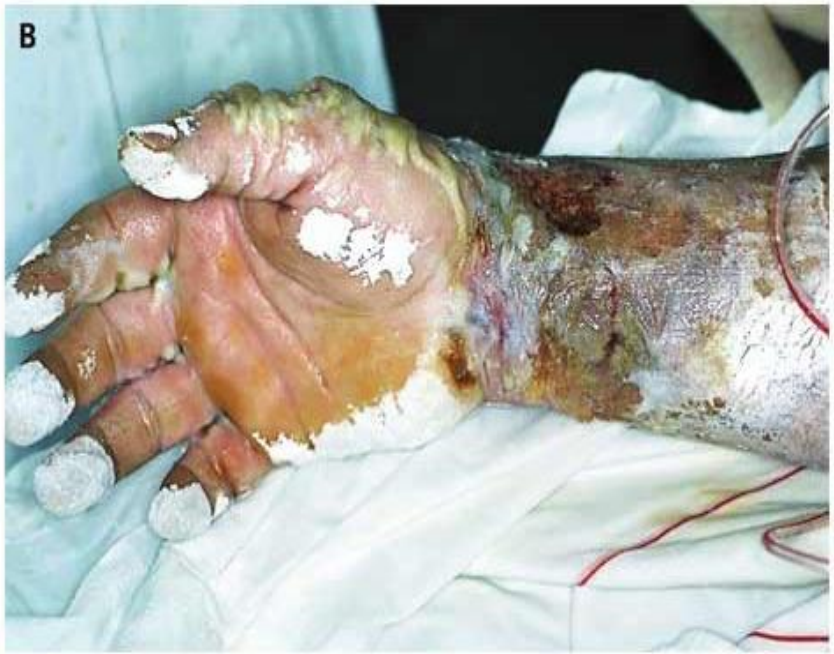
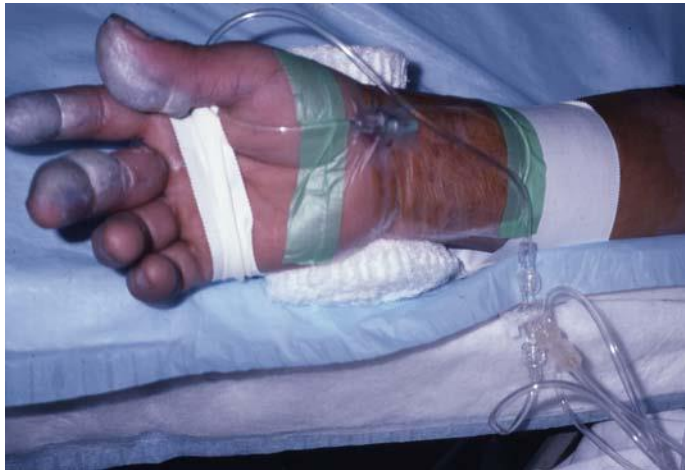


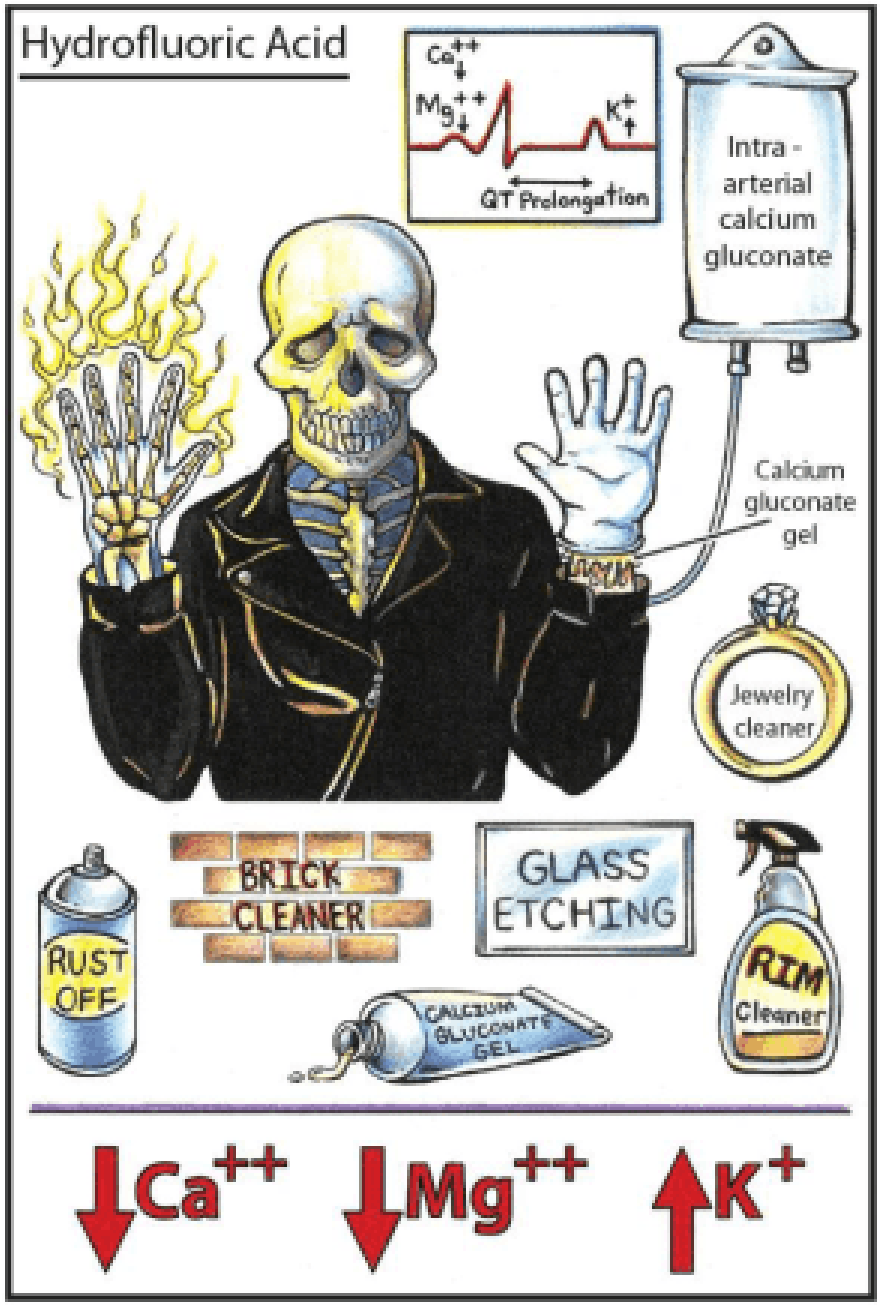
FIGURE 126–2. Pathway of cyanide and hydrogen sulfide toxicity and detoxification. * = hydroxocobalamin.

Hydrofluoric acid








Hydrofluoric Acid
Ca++
Mg++
K+
QT Prolongation
Intra - arterial calcium gluconate
Calcium gluconate gel
Jewelry cleaner
BRICK CLEANER
GLASS ETCHING
RUST OFF
CALCIUM GLUCONATE GEL
RIM Cleaner
↓Ca++ ↓Mg++ ↑K+

Chemical	Clinical manifestations	Treatment
Hydrofluoric acid (etching glass, removing rust, and cleaning cement and bricks)	Severe painful burn, decrease Ca+, Mg+, arrhythmia	irrigation with water at least 15-30 min, remove blisters, Calcium gluconate (2.5%) gel, SC Ca, IV /IA Ca, regional anesthesia
Formic acid (used in industry and agriculture)	coagulative necrosis, acidosis, hemolysis, and hemoglobinuria.	Copious wound lavage, sodium bicarbonate for PH<7.30, exchange transfusion, HD
Anhydrous ammonia (Fertilizers, manufacture of explosives, petroleum, plastics, and synthetic fibers), Meth dry cook	Can freeze any tissue, chemical burns by liquefaction necrosis	prompt irrigation of the eyes and skin with water and management of inhalation injury
Cement	three types of cement burns. The most common is a chemically abrasive form, heat-related or blast burns can occur	copious irrigation after all clothes have been removed. Early excision and grafting are often necessary

Chemical	Clinical manifestations	Treatment
Phenol and derivatives (widely used in the agri-cultural, cosmetic, and medical fields)	Coagulative necrosis, stimulation, lethargy, seizures, or coma. Tachycardia/bradycardia	irrigated with large volumes of water delivered under low pressure. ACLS PRN
White Phosphorus (munitions manufacturing, in fireworks, methamphetamine production, fertilizers, rodenticide)	profound thermal injury, hypocalcemia and hyperphosphatemia, ECG changes Three stages: GI, latent, multi-organ failure	Copious water irrigation, decontamination, treatment of electrolyte disturbances, management of the skin burns is as with any other burn wound
Hydrocarbons (fuels, solvents, paints, paint and spot removers, dry cleaning solutions, lamp oil, rubber cement, lubricants)	aspiration (e.g., coughing, gagging, vomiting, wheezing, tachypnea, or hypoxia). Inhalation (headache, dizziness, nausea, or wheezing). Cardiac sensitization	Removal from exposure site. Supportive care (O2, B-agonists)

Chemical	Clinical manifestations	Treatment
Nitrate and Nitrites	Symptoms depend on methemoglobin conc: 20%: headache, anxiety, dyspnea, and tachycardia 40-50%:Confusion, lethargy, and acidosis. 70%: SZ, hypotension, dysrhythmias and death	Supportive care, Methylene blue
Tar	Burn	Immediate cooling with cold water then removal in the ED using Solvents. Sunflower oil can be used. Antibiotic ointment if in cornea
Elemental metals (lithium, sodium, and potassium)	harmless unless they come in contact with water when violent exothermic reaction occurs	Use **mineral oil** if available before water. If using water use large amount to limit the reaction

Table 1: An overview of chemical warfare agents (CWAs)

CWA type	Chemical agents	Method of exposure	Clinical symptoms
Nerve agents	G-agents (sarin, cyclosarin, tabun, soman)	Inhalation	SLUDGE, miotic pupils, bradycardia, bronchospasm, bronchorrea, muscle spasms/fasciculations, weakness, flaccid paralysis, tachycardia, seizures, respiratory failure
	V-agents (VE, VG, VM, VR, VX)		
Blistering agents	Nitrogen mustard & sulfur mustard (mustard gas)	Inhalation	Acute: Skin, eye and lung damage (pulmonary edema and pulmonary hemmorhage), erythematous rash, skin blistering
			Chronic: Lung damage (chronic obstructive pulmonary disease, asthma, bronchiolitis obliterans), neutropenia, pancytopenia
Asphyxiants	Carbon monoxide, chlorine, phosgene, hydrogen sulfide gases	Inhalation	Upper airway distress, skin and eye irritation, fatal pulmonary edema and acute respiratory distress syndrome
Blood agents	Cyanide	Skin absorption, inhalation and ingestion	Severe distress, tachycardia, cyanosis, hypotension, severe metabolic acidosis, seizures, cardiac arrest
Hydrofluoric acid	—	Skin absorption, inhalation and ingestion	Severe pain in exposed area, gastrointestinal distress, vomiting, cardiac arrhythmias, hypocalcemia, hyperkalemia

Table 64-1 Common Gases That Can Be Encountered as Weapons of Mass Destruction

CLASS	EXAMPLE*	TREATMENT
Nerve agents	Tabun (GA) Sarin (GB) Soman (GD) Cyclosarin (GF) VX	Atropine and pralidoxime
Vesicants	Mustard agents Mustard, sulfur mustard (H) Distilled mustard, sulfur mustard (HD) Nitrogen mustard (HN1, HN2, HN3) Organic arsenical agents (e.g., lewisite; L) Halogenated oxime agents (e.g., phosgene oxime; CX)	Hydrotherapy Moist dressing on blisters Supportive care
Choking agents	Phosgene (CG) Chlorine (CL) Military smoke (HC) Chloropicrin (PS)	Supportive care
Cyanide agents	Hydrogen cyanide	Cyanide kit Amyl nitrite Sodium nitrite Sodium thiosulfate Hydroxocobalamin

*Chemical or common name (military chemical symbol).

KEY CONCEPTS

- For chemical injury, the degree of skin destruction is determined mainly by the properties of the toxic agent, its concentration, and the duration of its contact.
- Chemical injuries are commonly encountered after exposures to acids and alkalis.
- Hazmats are substances that can cause physical injury and can damage the environment if improperly handled.
- In dealing with hazmat incidents, two distinct goals must be achieved: (1) The hazmat must be contained, fire and explosions should eventually be extinguished, and the site must eventually be cleaned, and (2) people exposed to the hazmat must be treated.
- Alkali burns tend to penetrate deeper than acidic burns; as a result, alkali burns tend to be associated with greater morbidity.
- HF burns can be associated with significant hypocalcemia.
- Exposure to various toxic gases can occur from routine industrial settings, and knowledge of these agents is necessary for proper treatment by the emergency physician.
- Unconventional chemical weapons may be categorized into four major classifications: nerve agents, vesicants, choking agents, and cyanide agents.

- Thank you!
- Questions?

TABLE 123–1. Common Materials and Their Combustion Products

Products	Combustion Products
Wool	Carbon monoxide, hydrogen chloride, phosgene, chlorine, cyanide
Silk	Sulfur dioxide, hydrogen sulfide, ammonia, cyanide
Nylon	Ammonia, cyanide
Wood, cotton, paper	Carbon monoxide, acrolein, acetaldehyde, formaldehyde, acetic acid, formic acid, methane
Petroleum products	Carbon monoxide, acrolein, acetic acid, formic acid
Polystyrene	Styrene
Acrylic	Acrolein, hydrogen chloride, carbon monoxide
Plastics	Cyanide, hydrogen chloride, aldehydes, ammonia, nitrogen oxides, phosgene, chlorine
Polyvinyl chloride	Carbon monoxide, hydrogen chloride, phosgene, chlorine
Polyurethane	Cyanide, isocyanates
Melamine resins	Ammonia, cyanide
Rubber	Hydrogen sulfide, sulfur dioxide
Sulfur-containing material	Sulfur dioxide
Nitrogen-containing material	Cyanide, isocyanates, oxides of nitrogen
Fluorinated resins	Hydrogen fluoride
Fire-retardant materials	Hydrogen chloride, hydrogen bromide