



## Chapter 159 – Inhaled Toxins

### Episode Overview:

- 1) Define simple asphyxiants and list 5 examples
- 2) What are pulmonary irritants? Describe their management.
- 3) Describe the mechanism of cyanide toxicity
- 4) List 4 methods of exposure to CN
- 5) Describe features of presentation (Hx, PEX, Labs) suggestive of CN toxicity
- 6) List 4 specific antidotal therapeutic options for CN toxicity
- 7) List 3 situations when Lily kit may be contraindicated
- 8) List 4 pathophysiologic mechanisms of CO toxicity
- 9) What are the primary therapeutic goals for CO toxicity?
- 10) What are indications for hyperbarics?
- 11) List 8 DDx for hyperlactatemia

### Wisecracks

- 1) Describe the management of a fire victim
- 2) List inhaled toxins that are typically upper vs lower airway irritants

### Key Points:

- An asphyxiant is any gas that displaces sufficient oxygen from the breathable air. Treatment consists of removal from exposure, supplemental oxygen, and supportive care.
- Highly water-soluble gases produce rapid irritation and predominantly upper respiratory tract symptoms, such as airway irritation. Poorly water-soluble gases often produce delayed lower respiratory tract findings, such as bronchospasm or acute respiratory distress syndrome (ARDS).
- CO poisoning is confirmed by co-oximetry measurement. Cyanide poisoning is treated empirically when cardiovascular instability (eg, hypotension), altered mental status, or a serum lactate greater than 10 mmol/L are present in a fire victim.
- Hydroxocobalamin is the preferred antidote for most cyanide poisoned patients due to its efficacy, ease of use, and safety in patient with concomitant CO poisoning. Sodium thiosulfate may be administered concomitantly and may provide additional benefit.
- Patients with hydrogen sulfide poisoning generally respond to removal from exposure and ventilatory support.
- Normobaric oxygen therapy is sufficient for many patients with CO poisoning, but we recommend consultation with a hyperbaric oxygen (HBO) facility, poison control center, or medical toxicologist for consideration of HBO therapy for patients with a COHb greater than 25% or any new neurologic or cardiovascular abnormality.



## Rosen's in Perspective

The respiratory tract can be affected by local, noxious toxins and irritants.

Some systemic poisons can also enter through the lungs - leading to fulminant toxicity (cyanide, CO) or indolent, delayed toxicity (asbestos).

Therapy targets clinical manifestations of the inhaled toxins.

See [Table 153-1] for a long list of common inhaled toxins.

They can fall into different classifications:

- Irritants
- Simple asphyxiants
- Chemical asphyxiants (carbon monoxide; hydrogen cyanide; phosphine)

5 recognized categories:

- Simple asphyxiants
  - (CO<sub>2</sub>; methane; nitrogen gas; nitrous oxide; noble gases)
  - Displace oxygen
- Pulmonary irritants
  - (e.g pharmacologic CS or chloroacetophenone gas - tear gas; ammonia; phosgene ozone)
  - Direct pulmonary irritation
- Smoke/soot Inhalation
  - Irritation & O<sub>2</sub> displacement
- Cyanide & Hydrogen Sulfide
  - Cellular toxicity
  - Inhibits oxidative phosphorylation
- Carbon Monoxide
  - hypoxia

All these agents have varying solubility and some may have profound systemic effects (hydrofluoric acid for example: very irritating, highly soluble and profound systemic effects).

- Toxic Progression goes a little something like this:
  - Airway edema
  - Bronchoconstriction
  - Pneumonitis
  - ARDS
  - Resp Failure
  - Death
- OR
  - Inhalation of cellular poison → hypoxemia → death



## 1) Define simple asphyxiants and list 5 examples

Most are workplace related - where a worker is breathing a liquified gas while wearing an airline respirator in a confined space.

Because most cars have catalytic converters, intentional inhalation deaths from automotive exhaust result from simple asphyxiants (e.g. All the oxygen is used up). Not from CO poisoning.

Examples: (all are toxic at a high partial pressure)

- Carbon dioxide
- Nitrogen (scuba diving)
- Methane
- Helium (and other noble gases)
- Nitrous oxide (whipping cream cans)

These cause acute effects - due to their displacement of O<sub>2</sub> - causing hypoxia and ischemia.

Symptoms: tachycardia, tachypnea, dyspnea, cerebral hypoxia (ataxia, dizziness, incoordination, confusion, syncope). Lethargy (cerebral edema) occurs as the FIO<sub>2</sub> is < 10%.

When removed from the environment, symptoms usually resolve. If they persist: ischemic complications are the cause: seizures, coma due to cerebral edema, or cardiac arrest.

Diagnosis is made based on history and rapid resolution of symptoms after victim is removed from the environment. Determining the exact gas is of limited value in the ER workup (public health does care though).

Management is supportive (remove pt. from that environment!), supplemental O<sub>2</sub>. Hypoxic cardiac or brain damage is managed as per the normal resuscitative sequence. Anyone with more than mild symptoms should get ABGs, CXR, ECG, possible CT head.

## 2) What are pulmonary irritants? Describe their management.

A class of gases that cause pulmonary irritation/inflammation after inhalation. Usually exacerbate chronic lung disease and can cause direct cellular toxicity.

Examples:

- Products of combustion
  - Sulfur dioxide (smog from fossil fuels)
  - Oxygen, hydrogen fluoride
  - Chlorine from pools
  - Smoke inhalation
  - Tear gas
  - Ammonia
  - Phosgene



They act on the mucous membranes, eyes and upper airways = lacrimation, nasal burning, coughing, dyspnea, progressing to ARDS.

*The low solubility gases may cause a delay in presentation - at 24-36 hrs, whereas the high solubility gases present immediately and severely.*

The specific irritant may not be known, but the workup and management is supportive based on the degree of illness.

Management: Intubate those patients with hoarseness and stridor - due to the risk for progression. Treat bronchospasm with beta-2 agonists and ipratropium. Steroids may assist those with underlying asthma/COPD.

2% NaHCO<sub>3</sub> may help people who have had chlorine/hydrogen chloride gas exposure. Exogenous surfactant and NO may help this toxin-induced ARDS.

Special note on decontamination: remember the chemical exposures podcast:

- PPE
- Remove Clothing and place in plastic bags
- BRUSH OFF DRY CHEMICALS before hydrotherapy
- Use gentle irrigation with low pressure water

### 3) Describe the mechanism of cyanide toxicity

Cyanide

- This is a tricky gas, because it doesn't cause lung or airway injury directly....
  - Cyanide (gas form) is liberated from burning plastic-containing compounds and in some fumigation applications. As a salt - it has low solubility.
    - It is a cellular toxin - and inactivates cytochrome oxidase
      - The electron transport chain and inhibits **oxidative phosphorylation / metabolism by binding to complex IV in the ETC.**
        - This binding takes milliseconds, and the poisoned cells run out of ATP rapidly.
        - Leading to cellular hypoxia and death
    - **\*\*\*the oxygen-binding hemoglobin complex is unaffected by cyanide\*\*\*\***

Interesting note that hydrogen sulfide - works in a similar way, but doesn't permanently bind to cytochrome complex IV in the mitochondria.

### 4) List 4 methods of exposure to CN

- Cyanide gas from fumigation
- Gas from burning plastic/synthetic fibers
- Cyanide salts (jewelry or photography industries) exposed to acidic conditions



- Released in vivo from apricot pits or other prunus species pits (plums, cherries, nectarines, peaches).
- KGB/spies assassinations

## 5) Describe features of presentation (Hx, PEX, Labs) suggestive of CN toxicity

- CNS:
  - Mild vague cns symptoms
  - Coma
  - Seizures
  - Can develop persistent or delayed neurologic-psychiatric syndromes similar to CO or sulfur poisoning
- CV:
  - Chest pain
  - Hypotension
  - Bradycardia
  - Dysrhythmias
  - Cardiac arrest / shock

If the salts/acid are ingested (metal cleaners, photographic production) usually results in sudden CV collapse, coma and acidosis.

- “May smell a note of bitter almonds on their breath” -- not often clinically noted though

Unfortunately no rapid cyanide / hydrogen sulfide serum test is readily available in the ER - so consider giving empirical therapy

- Most telling laboratory findings is:
  - **\*\*\*Profound lactic acidosis\*\*\* Lactate > 10 mmol/L**
    - **ABG will show metabolic acidosis with an AG**
  - **Elevated mixed venous O2 saturation** (cellular utilization of O2 is blocked)
    - “Arterialization of the venous blood”
  - **Shortened QT interval**
  - **Normal pulse oximeter reading** - despite cellular hypoxia

ALL these symptoms, signs, history and lab findings can also occur with concomitant carbon monoxide poisoning. So don't wait for the carboxyhemoglobin level in a patient with critical illness following a possible exposure.

## 6) List 4 specific antidotal therapeutic options for CN toxicity

Goal is to “re-activate” the cytochrome oxidase system, required to reduce NAD+.

- Treatment:
  - PPE and decontamination



- ABC's
- Antiarrhythmics
- Vasopressors
- **Antidotes:**
- These provide a “high affinity source” of ferric ions for cyanide to bind.
  - 1) tripecta of pimping:
    - Amyl nitrite, sodium nitrite, sodium thiosulfate
      - Amyl nitrite: pearls are broken open and breathed for 30 seconds on 30 sec. Off. until an IV is established
        - Can be dangerous to hospital staff - causing syncope, dizziness, hypotension.
      - Sodium nitrite: 300 mg IV dose over 5 minutes
        - Often causes hypotension
      - Sodium thiosulfate: 12.5 g IV dose
    - The Nitrites induce methemoglobinemia. Cyanide has a high affinity for the MetHb unit and leaves the cytochrome oxidase unit to form cyanmethemoglobin (which requires sodium thiosulfate for excretion).
    - The thiosulfate causes transsulfuration of cyanide - so it can be renally excreted as thiocyanate
      - \*\*\*\*if coexisting carbon monoxide inhalation toxicity is suspected (smoke inhalation) the nitrites should be avoided!\*\*\* because BOTH CO and MetHb reduce oxygen delivery to tissues
  - Some argue that the sodium thiosulfate portion combined with oxygen and bicarbonate may be sufficiently protective in mass exposures.
- 2) hydroxocobalamin (Cyanokit) - IM / IV
  - The cobalt binds cyanide to form cyanocobalamin (vitamin B12)
    - This is then renally excreted
    - administer 5g hydroxocobalamin diluted in 200 mL of 5% dextrose IV over 30 minutes
    - Causes serum laboratory measurements to be unreadable - so draw all labs before giving it!
  - May safely be used with the “trifecta kit”, but usually only thiosulfate is given due to the risks associated with the nitrites.
  - Can be safely used even if no cyanide poisoning has occurred; it only causes a mild hypertension and can cause reddening of the skin

According to Rosen’s “there is insufficient clinical data to support the use of one cyanide antidote kit over another. *Hyperbaric oxygen therapy has been advocated but is of no proven benefit and not routinely indicated for cyanide poisoning.*” If it is readily available it may “super-oxygenate the plasma and tissues which prevents further methemoglobinemia”



### **Hydrogen sulfide poisoning:**

- Remove from exposure
- Supportive care
- Consider using the nitrite portion of the CN kit to create MetHb.
  - But no defined role for thiosulfate, hyperbarics or cyanocobalamin.

### **7) List 3 situations when Lily kit may be contraindicated**

1. Concomitant smoke inhalation in fire victims
  - a. Nitrite induces methemoglobinemia which further reduces tissue oxygen delivery
2. Patient in hypotensive, shock where further hypoxemia and hypotension would cause harm
3. inability to administer the inhaled amyl nitrite safely (risk of exposure to health care workers)

### **8) List 4 pathophysiologic mechanisms of CO toxicity**

“The most common cause of acute poisoning death in developed nations and the most common cause of fire related death.”

- CO is generated through incomplete combustion of any carbon-containing products - structure fires, methane gas from clogged vents in home heaters, gas-powered generators.

#### **Mechanisms of toxicity:**

- 1) CO interacts with deoxyhemoglobin to form COHb - which CANNOT CARRY OXYGEN.
  - This is a slowly reversible bond - which allows CO to accumulate on Hgb even in low ambient conditions.
  - ...there's probably more to the CO toxicity than just preventing oxygen binding on to Hgb...because anemia doesn't kill in the same way.
    - \*\*\*super toxic to the unborn human in utero\*\*\*\*
- 2) In the muscle, CO binds myoglobin, which is what leads to atraumatic rhabdomyolysis.
- 3) CO affects oxygen use in tissues - by inhibiting cytochrome oxidase IV - similar to cyanide
- 4) Delayed onset neurologic complications - due to reperfusion injury, lipid peroxidation, alteration of the platelet-associated nitric oxide cycle;
  - This leads to “free-radical” injury → inflammation and dysfunction
  - \*\*\*loss of consciousness is a huge risk factor for developing delayed neuro. injury\*\*\*\*



**Clinical features:**

- Similar to cyanide poisoning and anyone with altered mental status (use the DIMES approach!):
  - CNS: AMS, coma, seizures,
  - CV: abnormal vitals, hypotension, arrest
  - Labs: metabolic acidosis
- But **mild symptoms may occur, so should be thought of with anyone with a benign headache syndrome or viral illness or multiple family members.**
  - Headache, N/V
  - Dizziness
  - Myalgia
  - Confusion
  - Normal neuro exam, with perceptual changes.
    - Cherry red skin finding is a myth-unless you work in the morgue

**Lab features:**

- Use your history and physical!
- Co-oximetry with an arterial blood gas is the standard of care
- Remember that pulse oximetry will be falsely normal!

**Side note on delayed neuropsychiatric symptoms:**

- Frequency 12-50%
  - Usually asymptomatic for 2-40 days before symptoms develop.
- Symptoms:
  - Focal deficits, seizures
  - Cognitive apathy, memory deficits,
  - Mood changes
- Risk factors:
  - Older age
  - Loss of consciousness

Remember, that high-level CO poisoning can occur with low-level exposure due to a “soaking” phenomenon - where the tissues are soaked with CO, but the serum level is low.

**9) What are the primary therapeutic goals for CO toxicity?**

**To prevent delayed neurologic and neuropsychiatric sequelae.**

**The first ER treatment is** high flow oxygen with a non-rebreather, because the half life of COHb is inversely related to to the PO<sub>2</sub>. On room air the ½ life is 5 hrs, but on 100% O<sub>2</sub> it is 1 hr (with HBO it is ½ an hr).

Ideally treated for 6 hrs, or until symptom free *and* their levels have dropped sufficiently.



## 10) What are indications\* for hyperbarics?

**Any evidence of poor tissue oxygenation or risk for serious permanent neurologic damage**

\*=discuss with an expert!

- Neurologic abnormalities: altered mental status, coma
- Cardiovascular instability:
  - syncope, myocardial ischemia, dysrhythmias
- COHb > 20-40%
  - \*\*\*"the decision about HBO therapy should not be strictly based on COHb level, because this correlates poorly with toxicity"\*\*\*
  - There is a range in levels because it is centre specific; the decision is significantly impacted by travel time and the patient condition.
- Pregnant women with a COHb > 15%

Goal: to prevent delayed neuro-psych. Sequelae

- Decrease from 12% to 1% in one study, but this was not found in some other studies when compared with extensive normoxic therapy.

Probably not beneficial when time from exposure to HBO is > 6 hrs

## 12) List 8 DDx for hyperlactatemia

Copied from: <http://lifeinthefastlane.com/ccclactic-acidosis/>

Type A: Inadequate Oxygen Delivery

- Anaerobic muscular activity (sprinting, generalised convulsions)
- Tissue hypoperfusion (shock, cardiac arrest, regional hypoperfusion -> mesenteric ischaemia)
- Reduced tissue oxygen delivery (hypoxaemia, anaemia) or utilisation (CO poisoning)

Type B – No Evidence of Inadequate Tissue Oxygen Delivery

B1: associated with underlying diseases

- LUKE: leukaemia, lymphoma
- TIPS: thiamine deficiency, infection, pancreatitis, short bowel syndrome
- FAILURES: hepatic, renal, diabetic failures



B2: associated with drugs & toxins

- phenformin
- cyanide
- beta-agonists
- methanol
- adrenaline
- salicylates
- nitroprusside infusion
- ethanol intoxication in chronic alcoholics
- anti-retroviral drugs
- paracetamol
- salbutamol
- biguanides
- fructose
- sorbitol
- xylitol
- isoniazid
- lactate-based dialysate in RRT

B3: associated with inborn errors of metabolism

- Congenital forms of lactic acidosis with various enzyme defects (e.g. pyruvate carboxylase deficiency, glucose-6-phosphatase and fructose-1,6-bisphosphatase deficiencies, oxidative phosphorylation enzyme defects)

## Wisecracks

### 1) Describe the management of a fire victim

Smoke inhalation kills. The inhalation of heated particulate matter and absorbed toxins damage the deep respiratory mucosa.

Normally dry air - has a low heat capacity and doesn't cause damage even when very hot (>300 deg. C), but the addition of steam and soot transfers thermal energy to the respiratory tract.

This “double-whammy” of thermal and irritant damage causes a spark of cascading respiratory tract inflammation: cough, dyspnea, bronchospasm, and alveolar disruption.

\*\*standard assessment of singed nasal hairs, soot in the sputum are non-sensitive/specific\*\*

In addition, must be aware that victims may be distant - the “triple whammy”: inhaled chemical toxins such as CO and Cyanide - may have inhaled “smokeless” metabolic poisoning effects.



The key decision points:

1. Is there immediate or impending airway compromise?
  - a. Hoarse voice
  - b. Progressive dyspnea
  - c. Hypoxia
  - d. Altered LOC / coma
  - e. Carbonaceous sputum / closed space exposure
2. Is there concomitant metabolic acidosis?
  - a. Must assess for co-oximetry and lactic acidosis

**Management:**

- Airway assessment -- possible intubation
- \*\*\*\*all smoke inhalation victims with coma, hypotension, severe acidosis, cardiogenic shock\*\*\*\*
  - **Should receive hydroxocobalamin +/- sodium thiosulfate**
- High flow oxygenation (via ventilator or non-invasive means)
- Consider transfer to a hyperbaric facility (or call them ASAP)
- Inhaled beta-adrenergic agonists (little known evidence for this)
- Pulmonary toileting
  - ? role for bronchoalveolar lavage
- Don't give corticosteroids
- Uncertain efficacy for:
  - Ibuprofen
  - Exogenous surfactant
  - Antibiotics

**2) List inhaled toxins that are typically upper vs lower airway irritants**

Upper = High water solubility

Think CASHH

- Chloramine
- Ammonia
- Sulfur Dioxide
- Hydrogen Chloride
- Hydrogen Fluoride

Lower = Poorly Water soluble

Think COOOP

- Chlorine
- Oxygen
- Ozone
- Oxides of Nitrogen
- Phosgene