Acute Poisoning Emergencies and Responses

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Learning Objectives

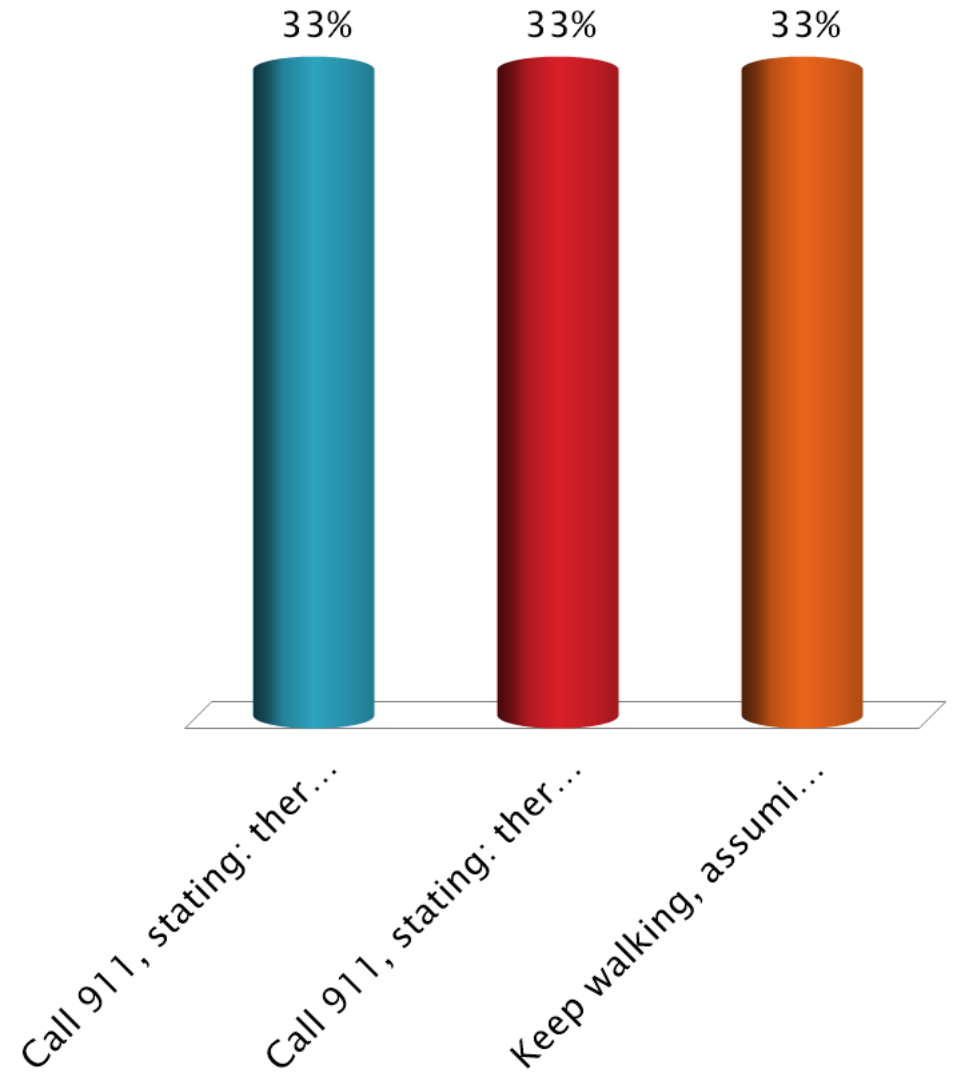
1. Describe key collection of signs and symptoms that suggest the identity of an underlying toxicological exposure
2. Describe the characteristic settings and circumstances associated with some poisonings, and what could be some preventive strategies
3. Describe emergency responses for some suspected poisonings

Case 1

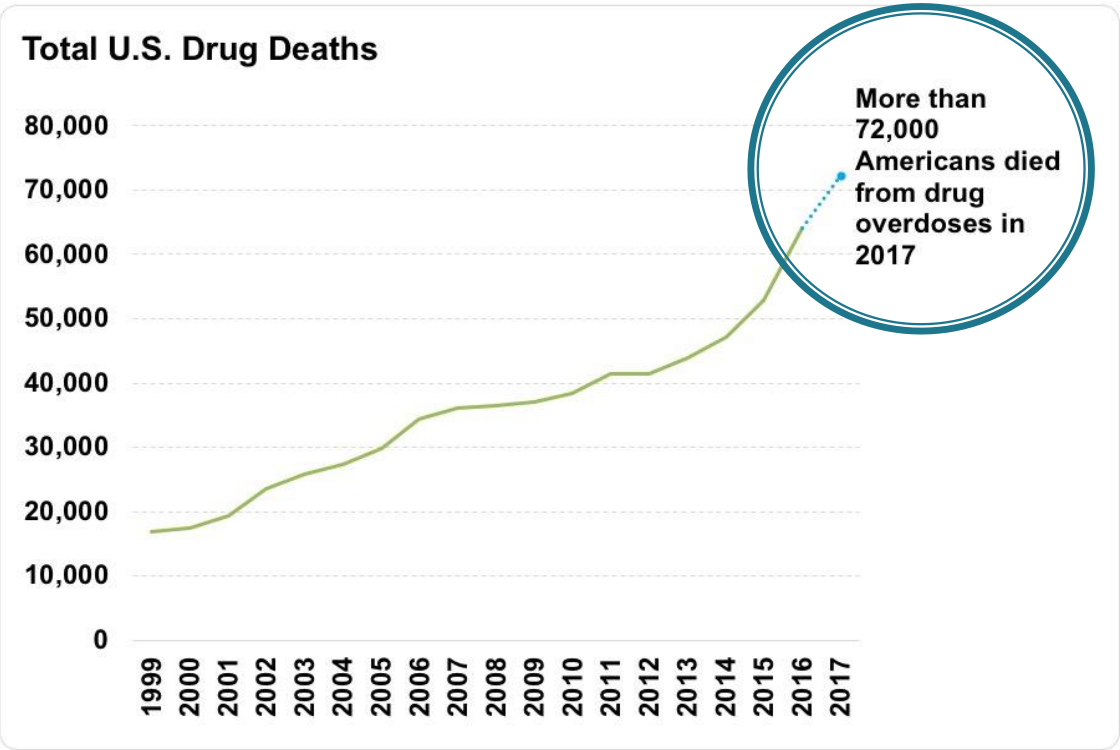
As you are walking toward your work entrance, you notice a man slumped over on a bench. You touch him to try to arouse him, and see he has pinpoint pupils, slow breathing, marked sedation.

Case 1: Your response to seeing man slumped on the bench is to:

A. Call 911, stating: there may be someone unconscious due to opiate overdose
B. Call 911, stating: there may be someone poisoned by nerve gas
C. Keep walking, assuming this is someone intoxicated with alcohol and sleeping it off on the bench

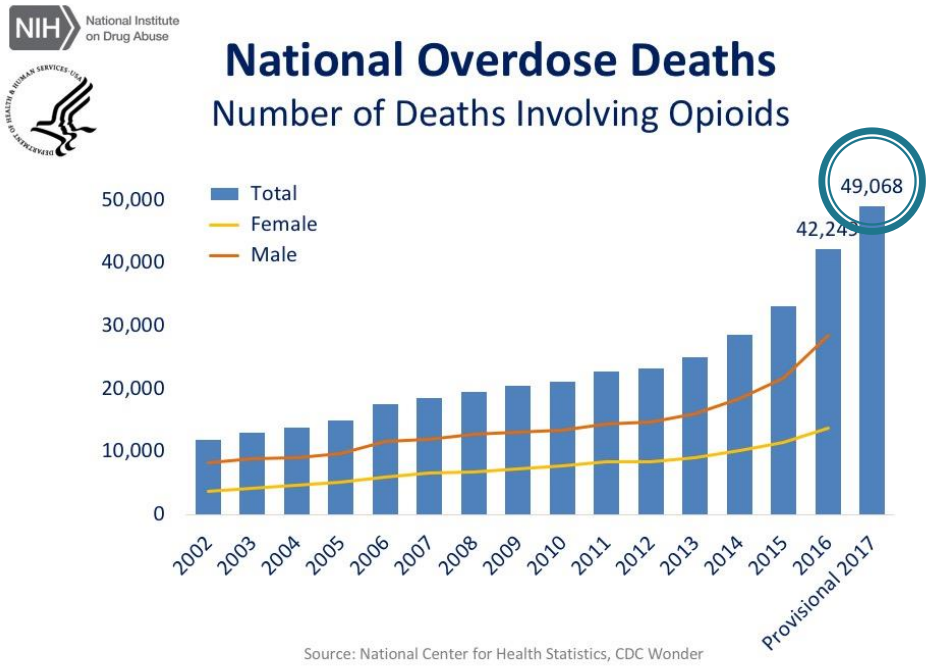


Opiate overdose (choice #1)



Total U.S. Drug Deaths* - More than 72,000 Americans died from drug overdoses in 2017, including illicit drugs and prescription opioids—a 2-fold increase in a decade. Source: CDC WONDER, National Institute on Drug Abuse

Opiate overdose deaths – USA



Also a world wide problem: W.H.O.: 27 million people world wide with opiate use disorder in 2016

http://www.who.int/substance_abuse/information-sheet/en/

Opiate overdose – Signs

- Pinpoint pupils
- Slowed breathing
- Decreased responsiveness or unconsciousness
- Limp body
- Slow pulse

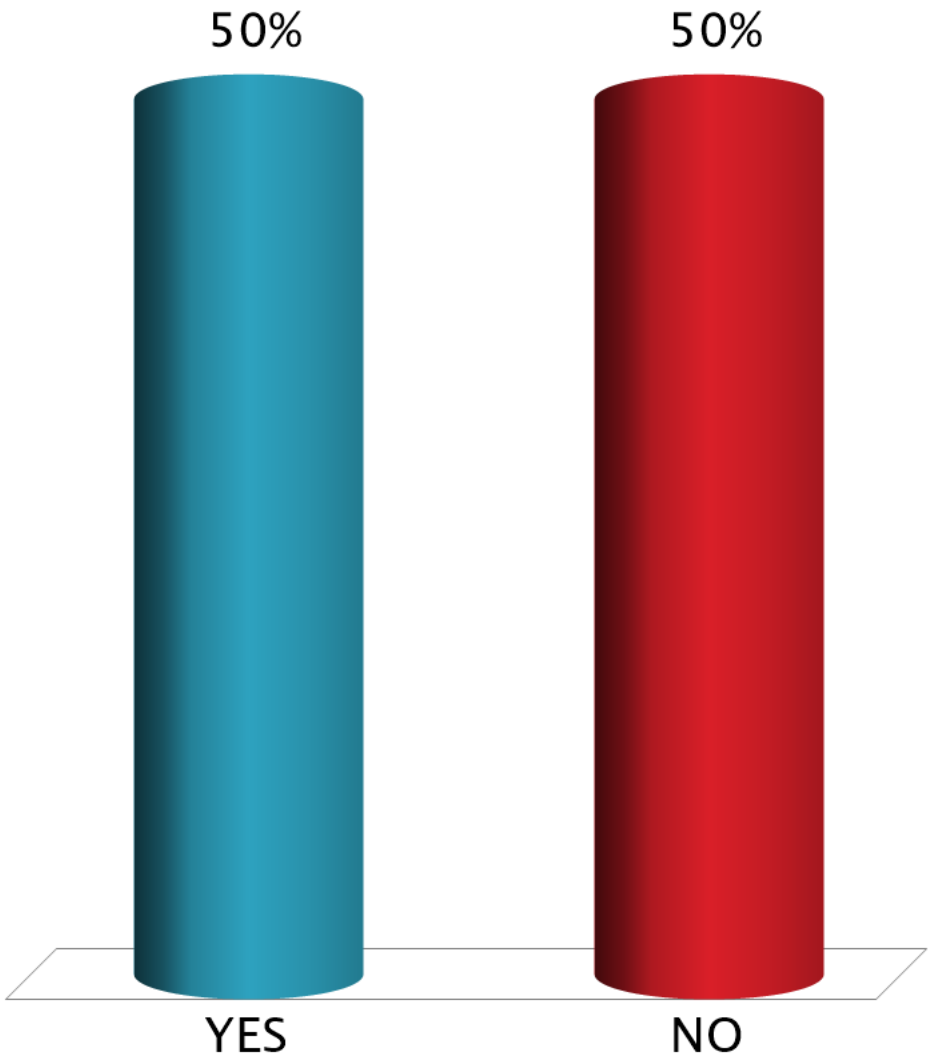
Opiate overdose: treatment

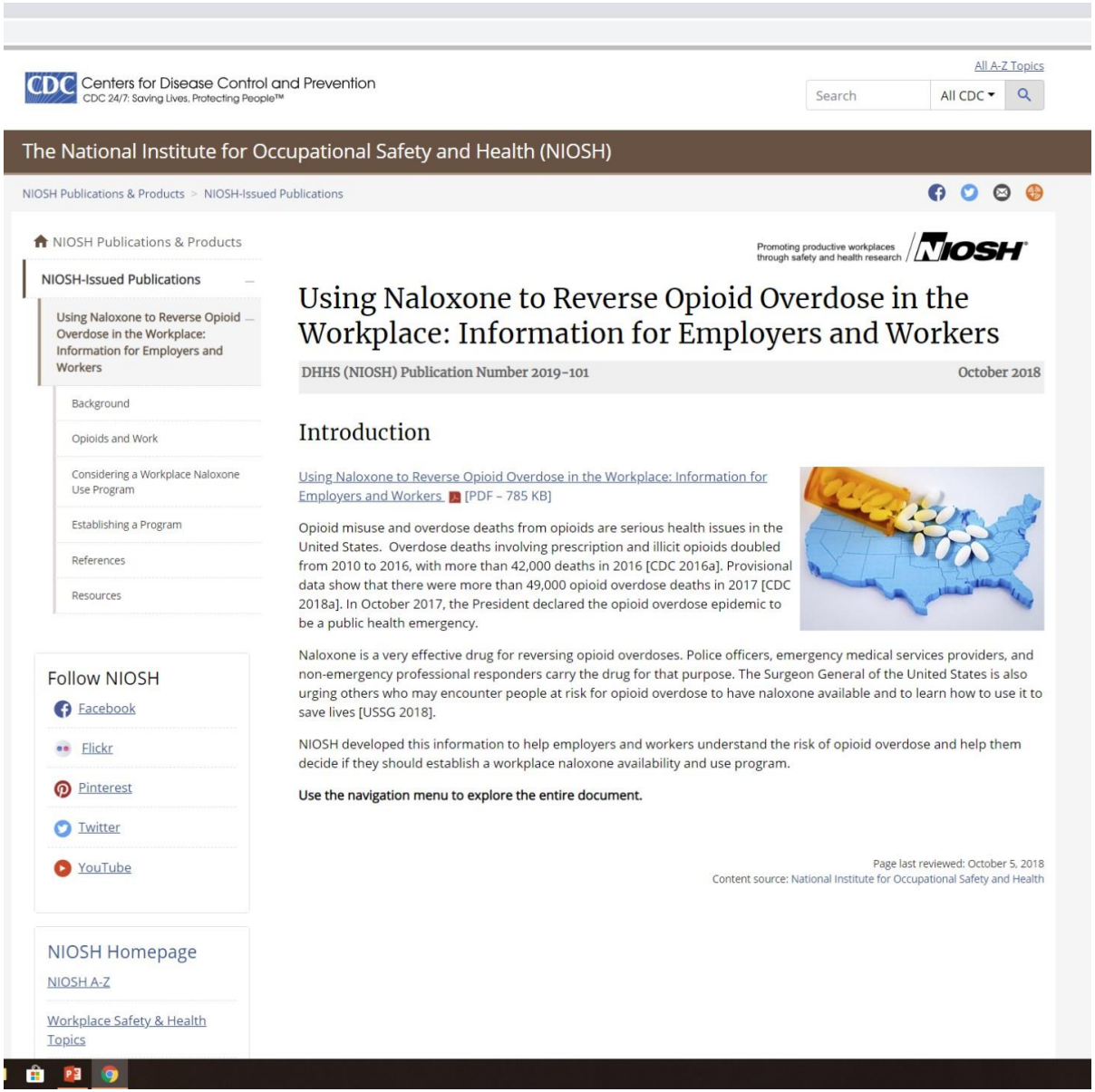
- Call 911 – immediate resuscitation
- Naloxone (“Narcan”)
  - Opioid antagonist
  - Nasal spray
  - I.V, sub q, IM

- Follow up: ideally to get into a treatment and rehab program

Your institution have an emergency response for opiate OD, like available naloxone spray?

A. YES
B. NO





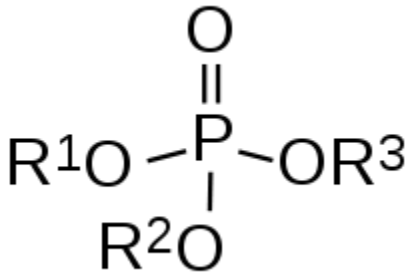
https://www.cdc.gov/niosh/docs/2019-101/default.html

“Nerve Gas” (choice #2)

- Potent organophosphates inhibit cholinesterase -> cholinergic crisis.
- Actual case: 3/2018 Sergei Skripal (ex-Soviet spy, double agent) and daughter Yulia Skripal found unconscious, “foaming at mouth” on park bench in Salisbury, England.
  - Agent: Novichok;
  - Eventually found on the door knob of their house (police officer became ill who went to the house)
  - Others exposed: two others several months later (accidental—perfume bottle containing agent, sprayed on herself-she died, partner hospitalized)

Exposure to Organophosphates

- "Nerve Gas": Novchok, Vx, Sarin, Tabum
- Organophosphate (carbamate) pesticides
  - examples: parathion, malathion, chlorpyrifos, diazinon, dichlorvos, phosmet
  - Aerial spraying of Naled (breaks down to chemical dichlorvos) –mosquitoes carrying Zika virus
- Inhibit cholinesterase, more acetylcholine neurotransmitter at receptors ->
  - Increased nicotinic and muscarinic effects



Organophosphates: symptoms and signs

- Muscarinic:
  - Pinpoint pupils (miosis) frequently
  - Increased secretions (sweating, salivation, bronchorrhea, rhinorrhea)
  - Bronchospasm
  - Bradycardia
  - HA, poor vision
  - GI: abdominal cramps, nausea, vomiting, diarrhea
- Nicotinic – AChE excess in skeletal muscles
  - Weakness of skeletal muscles
  - Fasciculations, tremors
  - Cardiac: tachycardia, hypertension
- Respiratory failure
- CNS: agitation, seizures, eventually coma

Emergency Response

- Avoid contamination of emergency personnel (can be absorbed from skin, inhalation, ingestion)
- Decontamination of victim
- Cannot await results of testing to treat: must recognize the “toxidrome” and note history
- Administration of atropine and pralidoxime immediately (sometimes in Nerve agent antidote kit)
- Emergency supportive care
- References: Kales, Christiani NEJM 2004:350; Ciottone, NEJM 2018: 378:1611

Case 1: take away

- Opiate overdose: pinpoint pupils, slow breathing, sedation
- Organophosphate overdose: usually pinpoint pupils, sedation; other signs--increased secretions, fasciculations, weakness, paralysis
- Both cases: Need for immediate intervention

Case 2

Several people working in a warehouse, including people in the administrative offices in the same building, call to the medical department because they developed headache and nausea in the afternoon. They are worried about the diesel fumes given off from the new noisy forklifts brought in to move the heavier boxes at the warehouse.

Case 2: HA, nausea in warehouse

- Your response in this situation:

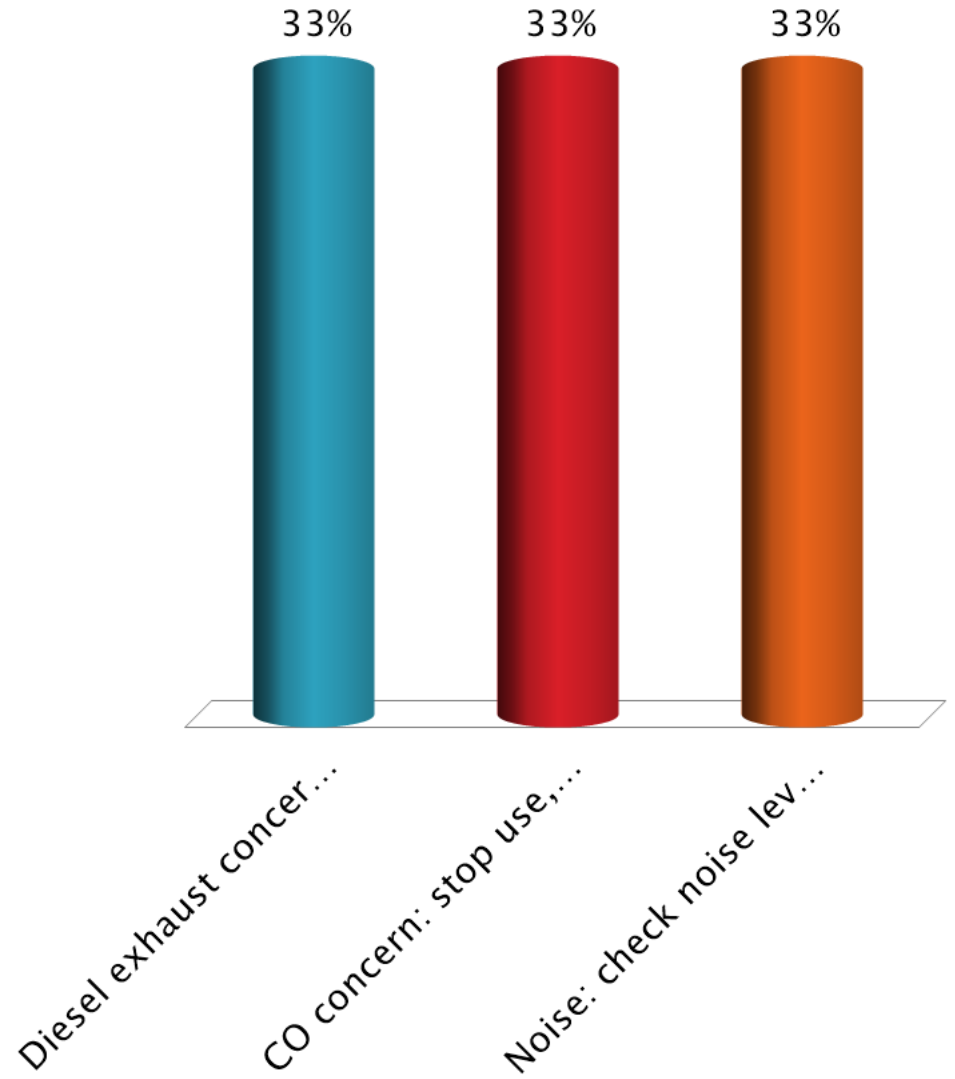
A. Because of concerns of exposure to diesel exhaust overexposure, immediate effects (HA, irritation) and future risk of cancer, you advise to increase the ventilation in the ware house, put air purifiers in offices, and arrange for IH evaluation.

B. Because of concern about carbon monoxide exposure (CO), you advise to stop use of diesel forklifts, evacuate employees, and send any symptomatic employees to nearby hospital for evaluation and possible treatment.

C. You suspect employees are suffering headaches and increased tension because of noise from the forklifts. You call engineering to check the noise levels and provide employees with hearing protection (ear plugs).

Case 2: Headache, nausea in a warehouse

A. Diesel exhaust concern-increase ventilation, IH eval, air purifiers
B. CO concern: stop use, evacuate employees, symptomatic to hospital
C. Noise: check noise levels, consider ear plugs



Case 2: Don't Miss Dx of CO

- Non-specific symptoms of mild poisoning
  - Headache, nausea, dizziness, flu-like illness
  - Irritability, fatigue
  - Mild confusion
  - Cardiac: arrhythmia; ischemia in those with underlying heart disease
- More severe acute symptoms
  - Confusion, syncope
  - Seizure
  - Myocardial injury, Ventricular arrhythmias
  - Coma, death
- Long term effects
  - Persistent or delayed neurological sequelae

Excellent recent reference: Am J Respir Crit Care Med 2017; **195**(5): 596-606.

CO- Mechanisms of Effects

- CO binds to Hgb 200x O_2-> hypoxia
- Direct effects of CO: inhibition of mitochondrial respiration
- Generation of free radicals
- Inflammatory mechanisms (NO's, reactive oxygen species)
- Binds myoglobin
- Injury to nervous system, cardiovascular system

Diagnosis

- Think of this possibility
- Std pulse oximetry CANNOT screen for CO
- Carboxy hemoglobin (COHb)
  - Half life about 4 hours on room air
  - Shorter if get O_2
- COHb-imprecise correlation with degree of poisoning, not predictive of delayed to persistent neurological sequelae

Treatment

- Oxygen
- Check EKG, follow cardiac status
- Carboxyhemoglobin (interpret result accordingly)
- Toxicology consult for severe cases – may need hyperbaric oxygen
  - Co-HGB >25%; if pregnant, >20%
  - Unconscious
  - Ischemia on EKG
  - New neurological deficit

Potential work settings in which CO exposure could occur

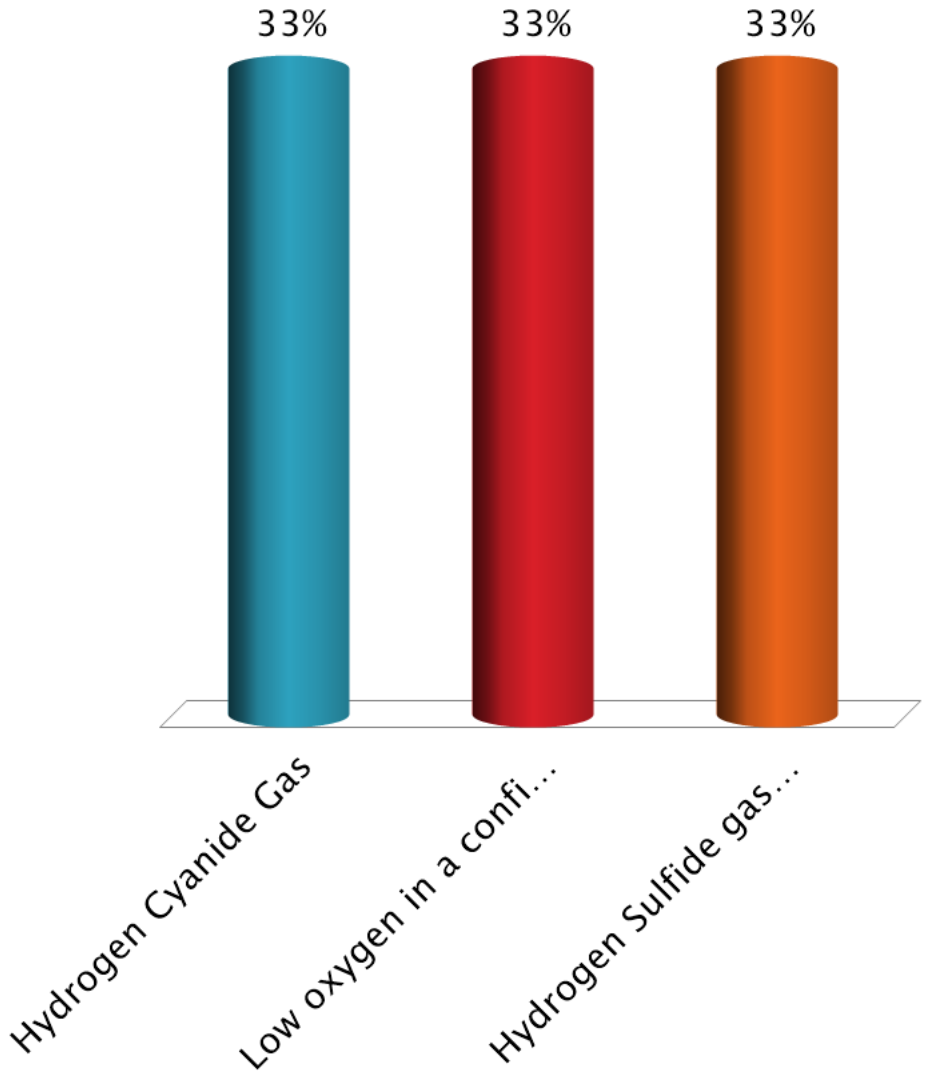
- Running gasoline or diesel/gasoline powered motor vehicles in poorly ventilated space (auto repair garage, ice rinks (Zamboni), warehouses, parking garages; use of gas powered electrical generator inside; improperly vented furnace
- Use of **methylene chloride** (dichloromethane)
  - industrial solvent (in paint thinner, other mixed solvents)
  - metabolized in the liver giving off CO as a metabolite;
  - longer half life of CO

Case 3

- 16 year old boy working for an aquaculture research facility went down into a 16-foot-deep drained tank to clean out some sludge at the bottom
- Soon after, he collapsed
- His adult supervisor climbed down to rescue him, and he lost consciousness

Case 3: Collapse in drained tank Result of exposure to…

A. Hydrogen Cyanide Gas
B. Low oxygen in a confined space
C. Hydrogen Sulfide gas (H_2S)



Hydrogen Sulfide (H_2S)

- Flammable, colorless, heavier than air gas- smells like rotten eggs
- Settings and sources: natural and man made
  - Volcanic gases, hot sulfur springs, swamps, stagnant water, crude petroleum, natural gas (natural sources)
  - By product of decay of organic matter
  - Swine containment, manure handling
  - Sewage and sewage treatment plants
  - Pulp and paper operations, petroleum refineries, petrochemical plants, tanneries, etc

CDC-ATSDR Tox Profile Hydrogen Sulfide

Hydrogen Sulfide: toxic mechanisms

- H_2S can be produced by bacteria action on organic matter
- Rapidly absorbed from respiratory tract
- Distributed throughout body
- Contact with mucous membranes, water -> sodium sulfate-irritant eyes and lungs
- Metabolized three pathways
  - Oxidation to thiosulfate – excreted in urine
  - Methylation
  - Reaction with metalloproteins
    - Mitochondria, inhibits cytochrome oxidase, impairs oxidative metabolism -> cellular hypoxia
    - Contrast to cyanide: H_2S more rapidly disassociates from mitochondria

Pediatrics **113**(4): 927-929;
Toxicol Lett **231**(3): 374-377.

Hydrogen Sulfide: Clinical Effects

- Depends of concentration and length of exposure
- Moderate concentrations:
  - Mucous membrane irritation (eye irritation, “halo’s”) rotten egg smell BUT olfactory extinction, sore throat and cough, skin burning
  - Headache
- Higher concentrations-rapid effects, “knock down gas” -> Systemic effects
  - Pulmonary edema
  - CNS: convulsions, loss of consciousness, respiratory center paralysis
  - DEATH

Hydrogen Sulfide – Emergency Response, treatment

- Think it could be H_2S– Setting, clue (exposed copper pipes, coins, jewelry turns black)
- Remove immediately from the environment, BUT have to protect the rescuer (proper protective gear)
- Oxygen – mainstay
- Supportive care in hospital–IV's, intubation/mechanical ventilation
- Biomarker: urine thiosulfate–result not in time to influence urgent treatment

Back to Case 3 report

- Halibut in hatchery tank died, water tested and was + H_2S, +odor in air
- Water drained, odor disappeared
- Boy went down 16-foot-deep tank to clean sludge at the bottom, soon collapsed
- Supervisor followed, collapsed, did not recover, died
- Boy received high flow O_2 at site, got out of tank, rushed to ED

Nikkanen, H. E. and M. M. Burns (2004). "Severe hydrogen sulfide exposure in a working adolescent." Pediatrics 113(4): 927-929.

Back to Case 3 Report

- ED: labored breathing, low O_2 sat, depressed mental status, jerking movements
- Intubated, transferred to tertiary hospital, pediatric ICU
- CXR: Bilateral hilar infiltrates
- Urine thiosulfate (day 1) was 0.7 µmol/mg Cr (ref <0.4 µmol/mg Cr)
- Hospital day 10: corticosteroids for noncardiogenic pulmonary edema
- Extubated day 13, discharged day 22 to rehab facility
- Eventually returned to school with normal function
- Preventive actions

What about cyanide?

- Hydrogen cyanide gas; potassium cyanide salt
- Also a “chemical asphyxiant”
- Also a mitochondrial toxin, inhibiting cytochrome oxidase, and production aerobic utilization of O_2 Tissue hypoxia; anaerobic metabolism--acidosis
- Inhibits antioxidants, so more free radicals
- Interferes with neurotransmitter gamma-aminobutyric acid (GABA) production, and decrease GABA -> increase seizures

Cyanide

- Rapidly absorbed, and quickly distributed throughout the body
- Metabolism, neutralization via enzyme rhodanese—converts cyanide to thiocyanate, excreted in the urine.
- Thiosulfate is a sulfur donor in the above reaction catalyzed by rhodanese

Cyanide: clinical effects

- CNS: HA, confusion, dizziness, seizures, coma
- CVS: early: tachycardia and increased BP, breathlessness; later bradycardia and hypotension; AV block; arrhythmias
- Tachypnea at first, pulmonary edema
- Renal failure
- Hepatic necrosis
- Labs: anion gap acidosis, high lactate; blood cyanide- not available in time for treatment; poor correlation with survival

Cyanide: settings and sources

- Industrial: electroplating, jewelry, laboratories (chemical synthesis, analysis) , photographic processes, plastics and rubber mfg, hair removal from hides.
- Release in fires: combustion of products with carbon and nitrogen—polyurethanes (insulation, upholstery), plastics, wool, silk, synthetic rubber, etc. {smoke inhalation: not just CO, but also cyanide}
- Dietary sources-cyanogenic glycosides-amygdalin Pits and seeds apricots, peaches, etc. Laetrile-derived from apricot and peach pits, alternative anti-cancer agent. Intestinal digestion of amygdalin releases hydrogen cyanide (HCN)

Cyanide- Emergency Response

- Consider: setting, clinical features-point to cyanide
- Remove from area, decontaminate
- Protect the rescuer (proper protective gear)
- Stabilize airway, breathing, circulation, no mouth to mouth
- High flow oxygen (regardless of pulse oximetry)
- Connect with toxicological expert

Cyanide – antidotes

- Supportive care, + antidotes
- Antidotes strategies: bind cyanide, induce methemoglobinemia, and use sulfur donors.
- If hydroxocobalamin available
  - Hydroxocobalamin IV
    - Contains cobalt, binds to intracellular cyanide stronger than cytochrome oxidase ->cyanocobalamin, excreted in the urine
  - Sodium thiosulfate-sulfurs for the rhodanese ->thiocyanate
- If no hydroxocobalamin, and no contraindication to nitrites, then (*FDA approved kit: Nithiodote Kit-does not have amyl nitrite)
  - Sodium nitrite IV
  - Sodium thiosulfate IV
  - *Amyl nitrite-held under patient's nose or via ET tube (present in other cyanide kits, may no longer be FDA approved—problem with abuse
- If contraindications to nitrites, then sodium thiosulfate IV

Reference: UpToDate: Cyanide Poisoning

Key points

- Treatment needs to be initiated before any confirming biological tests are available
- Use setting, clinical manifestations (toxidrome), to suggest potential poison
- Remove and decontaminate (if indicated) person, while also protecting rescue personnel
- Treat: oxygen, supportive care, antidotes when available