AIRBORN POISON
Toxic gases

Prof. Dr. Benay Can Eke

- Chemical substances;

- They are in our environment and workplace air
- Enter the organism by inhalation mainly

Exposure Routes

- Inhalation
- Skin
- Inhalation+Skin

- Oral

- Occupational Toxicology
- It is the sub-branch of toxicology which examines the unwanted effects of chemical, biological and physical factors encountered in the workplace.
- ??????????
- To prevent undesirable health effects caused by workplace environment
- To protect workers' health

To accept that chemicals are industrial/occupatinal poison or /not**.....**

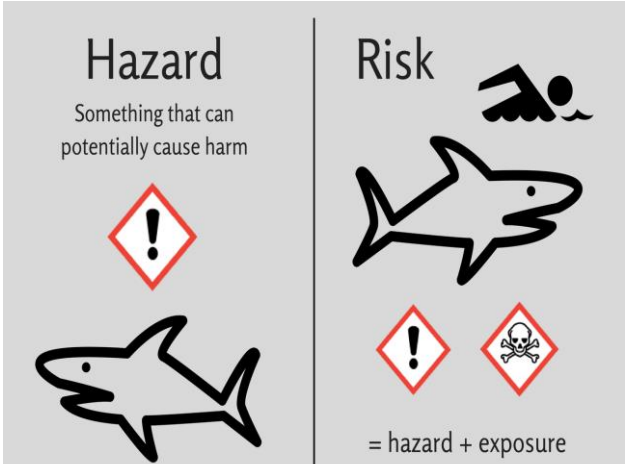
- The fact that the chemical substance is considered as an industrial poison causes the occupational disease.

- Continuous exposure to the substance (dose and duration time , individual factors)

- **Exposure –**someone is subjected to hazard

- **Hazard** — capability of a substance to cause an adverse effect.

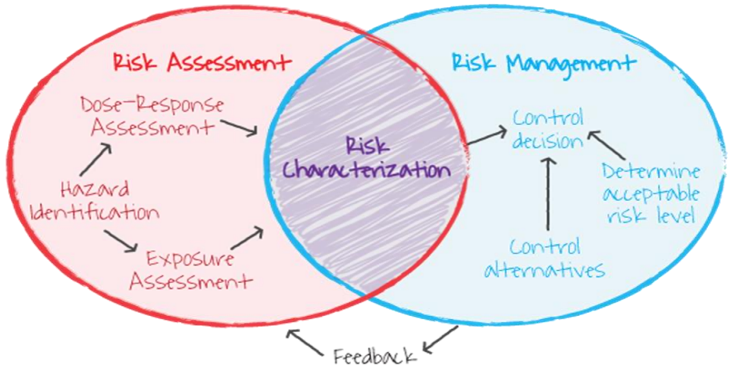
  - **Risk** — probability that the hazard will occur under specific exposure conditions.



Risk Assessment Steps

- **Hazard identification** — characterization of innate adverse toxic effects of agents.
- **Dose-response assessment** — characterization of the relation between doses and incidences of adverse effects in exposed populations.
- **Exposure assessment** — measurement or estimation of the intensity, frequency, and duration of human exposures to agents.
- **Risk characterization** — estimation of the incidence of health effects under the various conditions of human exposure./the process by which hazard, exposure, and risk are determined.

- THEN the process of risk management begins
- **Risk management** — the process of weighing policy alternatives and selecting the most appropriate regulatory action based on the results of risk assessment and social, economic, and political concerns/Regulatory process



- Each chemical may be toxic / dose????
- What is the maximum concentration of chemicals in the workplace air?
- Workers' health should not be adversely affected.
- Toxicity tests?

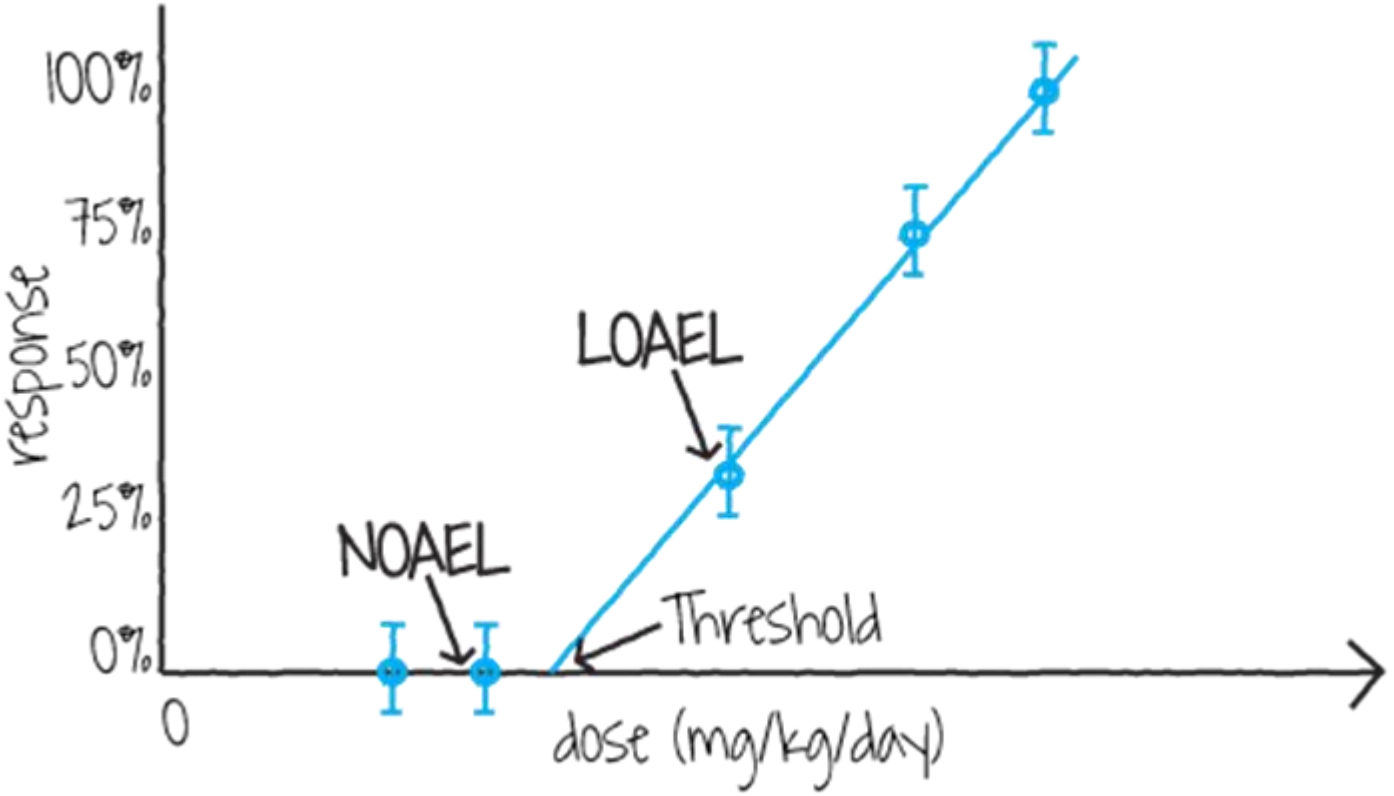
- LC50 (Median lethal concentration)
- It is a measure of acute toxicity of gaseous chemical compounds that enter the organism by inhalation.

- The concentration of a chemical in an environment (generally air or water) which produces death in 50% of an exposed population of test animals (in a specified time frame)

- In a certain period of time, the amount of substance that kills half of the experimental animals when given by inhalation is expressed by LCt50.

- unit is ppm or mg / m3 or mg/L

The **NOAEL** (**No Observed Adverse Effect Level)** is the highest level of a test substance to which organisms can be exposed without causing any observed and statistically significant adverse effects on the organism compared with the controls.
The **LOAEL** (**Lowest Observed Adverse Effect Level)** is the lowest level of a test substance, to which organisms can be exposed causing an adverse alteration of morphology, functional capacity, growth, development, or life span of a target organism compared with the control organisms of the same species and strain under defined conditions of exposure.



MAK (Maximum Allowed Concentration)

- Maximum concentration that is permitted to contain a chemical substance in environmental or industrial air and does not cause harmful effects.(ppm or mg / L)

CHEMICAL EXPOSURE LIMITS

Recommend or mandotary occupational exposure limits (OELs) have been developed in many countries for airborne exposure to gases,vapours and particulates.The most widely used limits, called threshold limit values **(TLVs),**are those issued in the USA by the American Conference of Governmental Industrial Hygienists (ACGIH)

Occupational Exposure Limit Values: Protecting Workers Health Definitions

Threshold Limit Value (TLV): For gases and vapors,TLV is stated as parts per million (ppm) of surrounding air,and for fumes,mists,and dusts as milligrams per cubic meter (mg / m^3) of surrounding air.

TLV is classified in three ways:

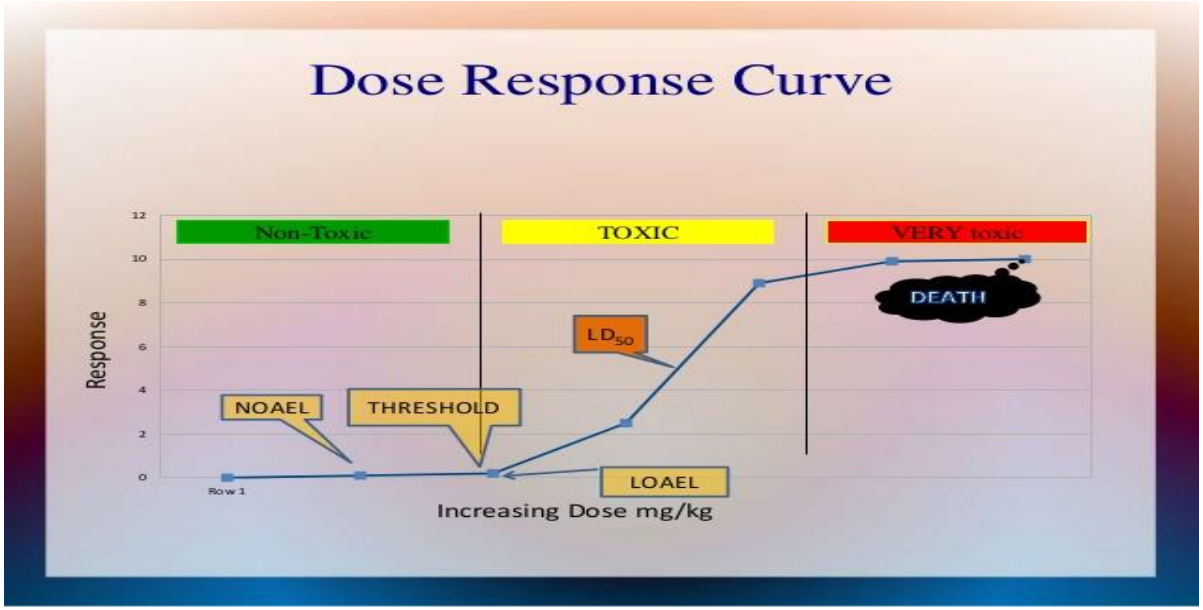
•Time-weighted average (TLV-TWA) exposure limit:The maximum average concentration of a chemical in air for a normal 8-hour working day and 40-hour week/daily concentration

Occupational Exposure Limit Values: Definitions

- Short term exposure limit(TLV-STEL); maximum concentration of a substance (a) for a continuous 15-minute exposure period,(b) for maximum of 4 such periods for day,(c) with at least one 60-minute exposure-free period between two exposure

Occupational Exposure Limit Values: Definitions

- Ceiling exposure limit (TLV-C) or maximum exposure concentration that should not be exceeded under any circumstance,



ACGIH (The American Conference of Govenmental Industrial Hygienists)

TLV- Treshold Limit Value

OSHA (Occupational Safety and Health Administration Air Pollutants Standarts)

PEL- Permissible Exposure Limit

NIOSH (National Institute for Occupational Safety and Health)

REL-Recommended Exposure Limit)

The difference between TLVs and PEL/REL is the agencies from which they come.

Biological Monitoring

- Urine
- Blood
- Environmental air

Evaluation of their effects

e.g.

- Determination of substance in urine/blood
- Determination of the metabolite of a substance in urine/blood….
- Measurement of cholinesterase enzyme inhibition
- Inhibition of enzymes in the synthesis pathway (such as ferrochelatase, levulinate dehydrate)
- Protoporphyrin levels in urine

- According to physical characteristics;

- Gases: They are gaseous at normal temperature and pressure. CO, H_2S, NxOx
- Vapors: Gaseous phase in air

  Benzene, CCl_4, CS_2
- Aerosol /particle

- According to the physiological effects of gases;

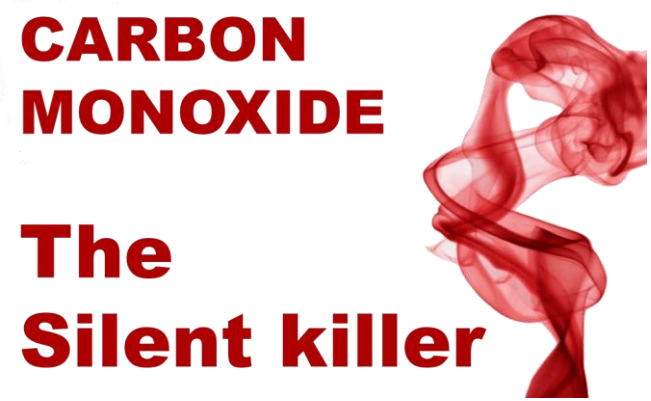
- **Causes of asphyxia**: Nitrogen, oxygen deficiency with its indirect effect, CO, direct oxygen-carrying capacity of the blood with the effect of blood, HCN, the oxygen utilization mechanism of tissues is damaged.

- **Affecting Central nervous system** : Aliphatic hydrocarbons
- **Lung irritant**: Phosgene, ozone, nitrogen, chlorine
- **Vesicants** : Mustard gas
- **Nerve gases**: sarine, tabun
- **Irritants**: sternutators, lacrimators

CARBON MONOXIDE

Carbon Monoxide

- The most common form of poisoning
- Colorless, odorless, nonirritating gas- **silent killer**
- Produced by incomplete combustion of carbon containing compounds
- Combines with Hb to form carboxyhemoglobin
- CO-Hb will not transport O2



Carbon monoxide

- Sources:
  - propane powered engines
  - natural gas appliances - space heaters
  - automobile exhaust
  - Fireplaces
  - portable generators

Carbon monoxide

Mechanism of action:

- Competes with O_2 for active sites on Hb (220x the affinity for Hb as O_2)
- Interference with cellular respiration at the mitochondria level, binds to cytochrome oxidase
- After breathing through the lungs through the blood passes.
- Induces smooth muscle relaxation
- Hypoxemia, tissue hypoxia, CO-Hb is cherry red in color

Carbon monoxide

- Diagnosis based on patient ……
- Signs and symptoms vary widely
- Signs depend on % CO-Hb levels in the blood
- Presence of cherry red blood is important***

Carbon monoxide

- Normal serum carboxyhemoglobin (COHb) Level: 0.4-0.7%
- Serum COHb level in smokers: 5-10%

Carbon monoxide

Clinical grading of CO poisoning

- **Mild**
- headache, nausea, dizziness, vomiting, flu
- **Moderate**
- confusion, slow thinking, shortness of breath, blurred vision, tachycardia, tachypnea, ataxia, weakness
- **Severe**
- chest pain, palpitations, severe drowsiness, disorientation, hypotension, syncope, myocardial ischemia, pulmonary edema
- Generally, the severity of symptoms is related to the level of CO and the duration of exposure.

Carbon monoxide

- Occupational groups within the risk group
- Traffic cops,
- Fire brigade workers,
- Employees in underground garages,
- Steel industry employees,
- Central heating boiler
- Automobile repairers are those who are at risk.

- Carbon monoxide poisoning poses a **greater risk for pregnant women, children under the age of two, the elderly, anemia, respiratory system, and heart disease.**

- The % expression of the portion of the hemoglobin that can be combined with the CO is known as the% COHb saturation.

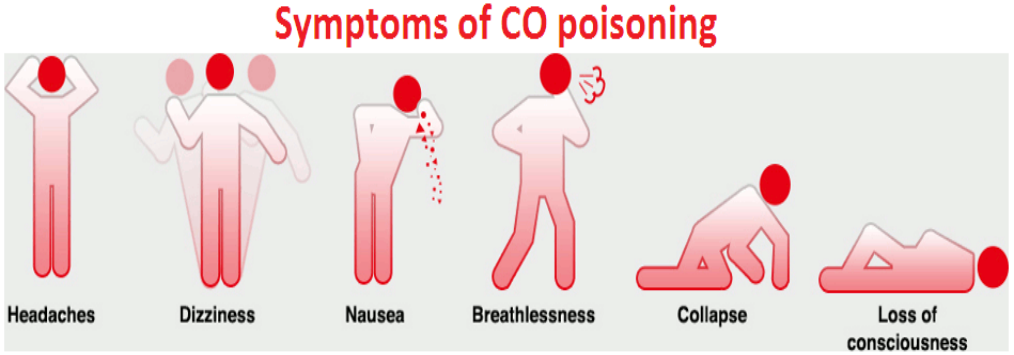
Carbon monoxide

- CLINICAL FINDINGS BY COHb LEVEL
- 10-20%: Nausea, fatigue, tachypnea, emotional instability, confusion, clumsiness
- 21-30%: Headache, dyspnea of effort, angina, changes in vision, inability to adapt to the environment, weakness in response to danger, slight power loss, slimming
- 31-40%: Dizziness, dizziness, nausea, vomiting, Visually impaired, insufficient decision-making
- 41-50%: Fainting, changes in consciousness, forgetfulness, tachycardia, tachypnea
- 51-60%: Seizures, coma, pronounced acidosis may result in death.
- Over 60%: Death

Carbon monoxide

- **Acute CO Poisoning Symptoms**

- Feeling of restlessness, tiredness and flu,
- Severe headache,
- Dizziness,
- Forgetfulness,
- Nausea - vomiting,
- Abdominal pain,
- Chest pain and palpitations,
- Drowsiness and drowsiness,
- Mind confusion,
- Attention disorder,
- Depression,
- Inactivity,
- hallucinations
- Agitation (extreme restlessness and tension),
- Loss of vision,
- Stool and urinary incontinence,
- Fainting and seizure,
- Coma,
- Respiratory arrest and death



Carbon monoxide

- **Chronic CO Symptoms of Poisoning;**
  Severe headache,
  Weakness,
  Nausea and vomiting,
  Abdominal pain,
  Reduction in cognitive functions,
  Drowsiness,
  Numbness,
  It's black,
  Retinal Hemorrhage,
  Forgetfulness,
  Unrest,
  Personality changes,
  Balance disorder.

Carbon monoxide

- TREATMENT
- In the treatment, rapid removal of the patient from the presence of CO and supportive oxygen should be prioritized.
- The patient's basic life support (airway, breathing, circulation)
- The antidote for CO poisoning is 100% oxygen

Carbon monoxide

- Normobaric Oxygen Therapy
- All patients with the possibility of CO intoxication begin.
- Continuous oxygen therapy; until the patient is asymptomatic or the COHb level is below 10%.
- Those with cardiovascular or lung symptoms should be reduced to less than 2%.

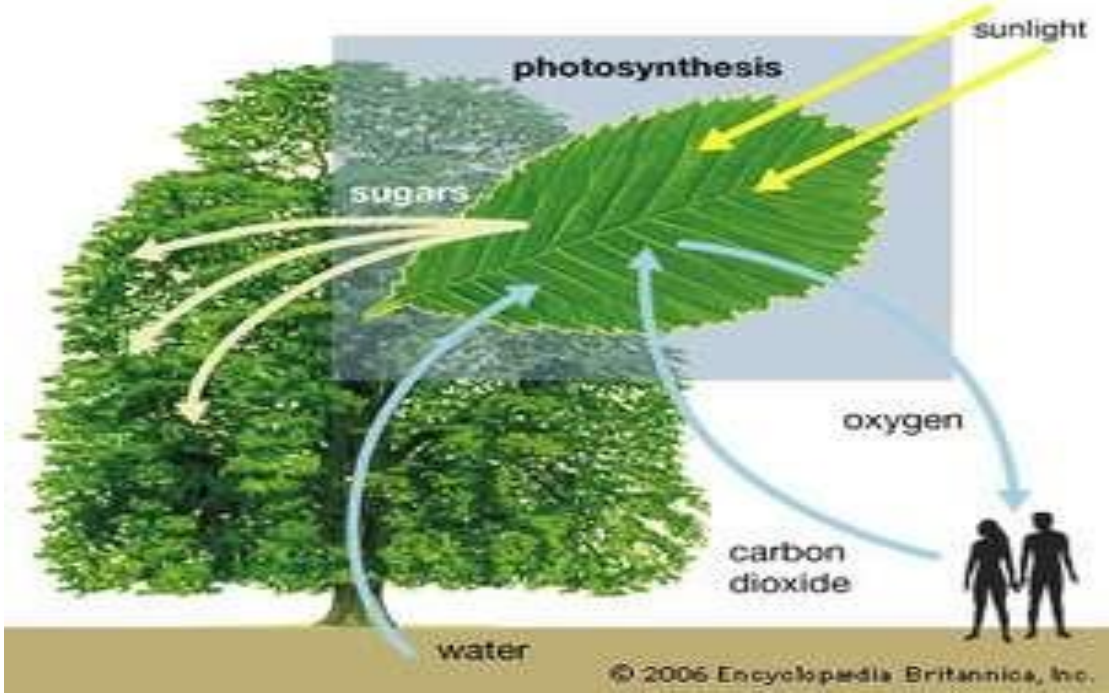
Carbon monoxide

- Hyperbaric Oxygen Therapy
- The patient is re-evaluated, symptoms persist, HBO is considered.

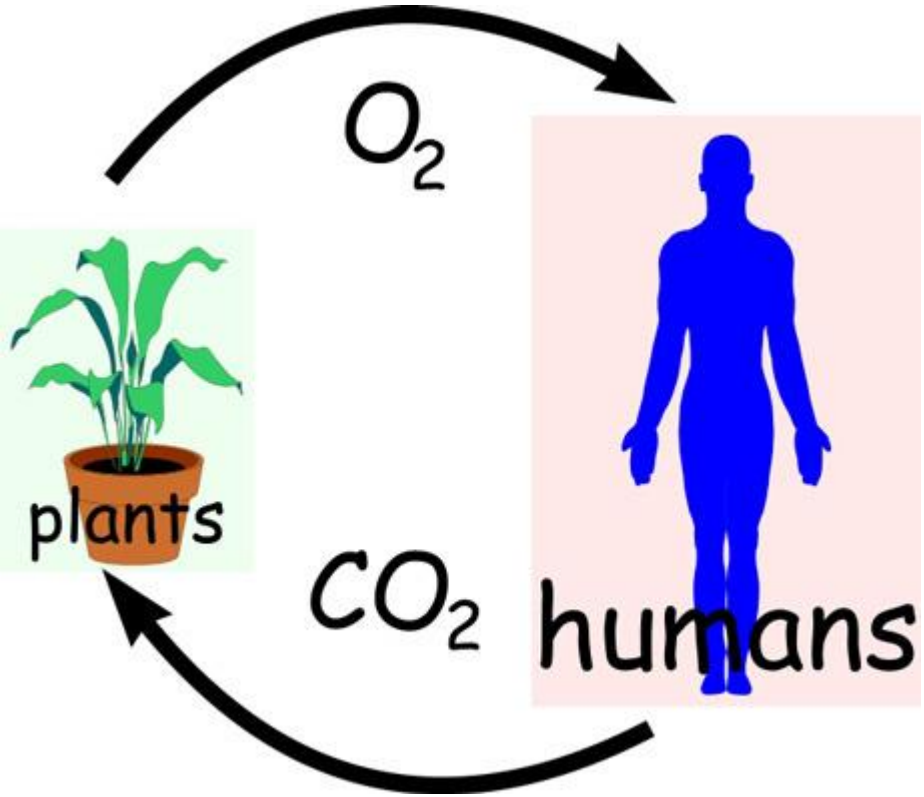
- Indications for HBO treatment:
- unconsciousness
- Coma

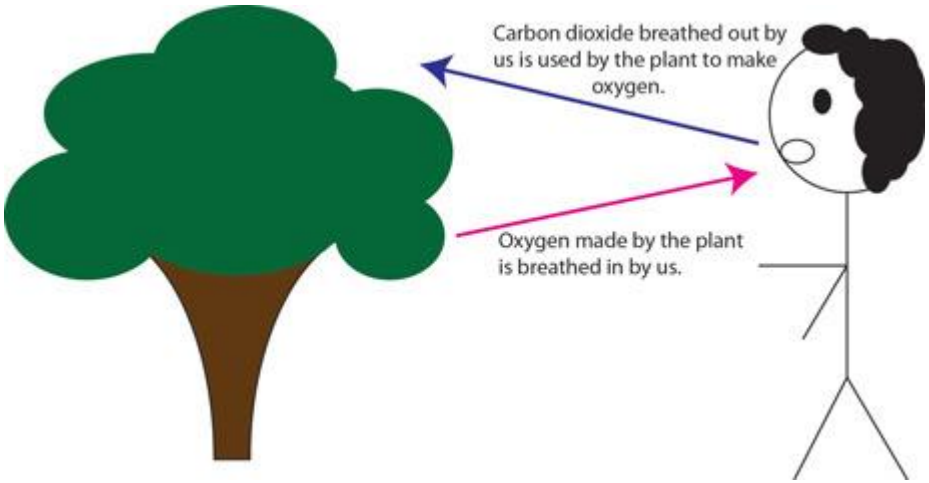
- Half-life of Carbon Monoxide
- Half-life – time required for half the quantity of a drug or other substance to be metabolized or eliminated
- CO half-life on 21% room air O2 – 4 - 6 hours
- CO half-life on 100% O2 – 80 minutes
- CO half-life with hyperbaric O2 – 22 minutes

CARBON DIOXIDE



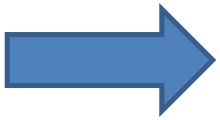
CARBON DIOXIDE





CARBON DIOXIDE

- It is a colorless, odorless,
- heavier than air gas
- produced by the complete combustion of carbon compounds in motor vehicles, heating vehicles and industry.
- It is found in the mines, in the lower part of the dumps because of the heavier than air.

- Dry ice  burn

- The absorbed CO2 causes stimulant until high concentration
- and at the high concentration, together with depression, cause unconsciousness and convulsion.
- Symptoms incresase between 2-30%

CARBON DIOXIDE

- **Treatment:**
- Remove/ Clean air
- O_2 treatment
- If necessary;
- Respiratory and blood pressure stimulants
- Symptomatic and supportive treatment

CARBON DIOXIDE

- Treatment:
- Removal / Clean air
- O2 treatment
- If necessary;
- Respiratory and blood pressure stimulants
- Symptomatic and supportive treatment

HCN

HCN

- Hydrogen cyanide / Hydrocyanic acid / also known as prussic acid, bitter almond fragrance is extremely toxic substance ..

- Everyone can not feel the smell 80% of the population can not genetically detect this smell.

- Cyanide is a highly volatile substance in hot dry air.
- Low M.W./ diffuse / fumigant in the past

HCN

- Nazis in World War II,
- In 1980s in Iraq and Syria,
- Terrorism in 1995 in the massacre of the Tokyo subway
- World Trade Center: Suspected of cyanide in attack

HCN

- Sources:
  - electroplating, jewelry and metal cleaners
  - photographic processing
  - X-Ray film recovery
  - fumigant rodenticide

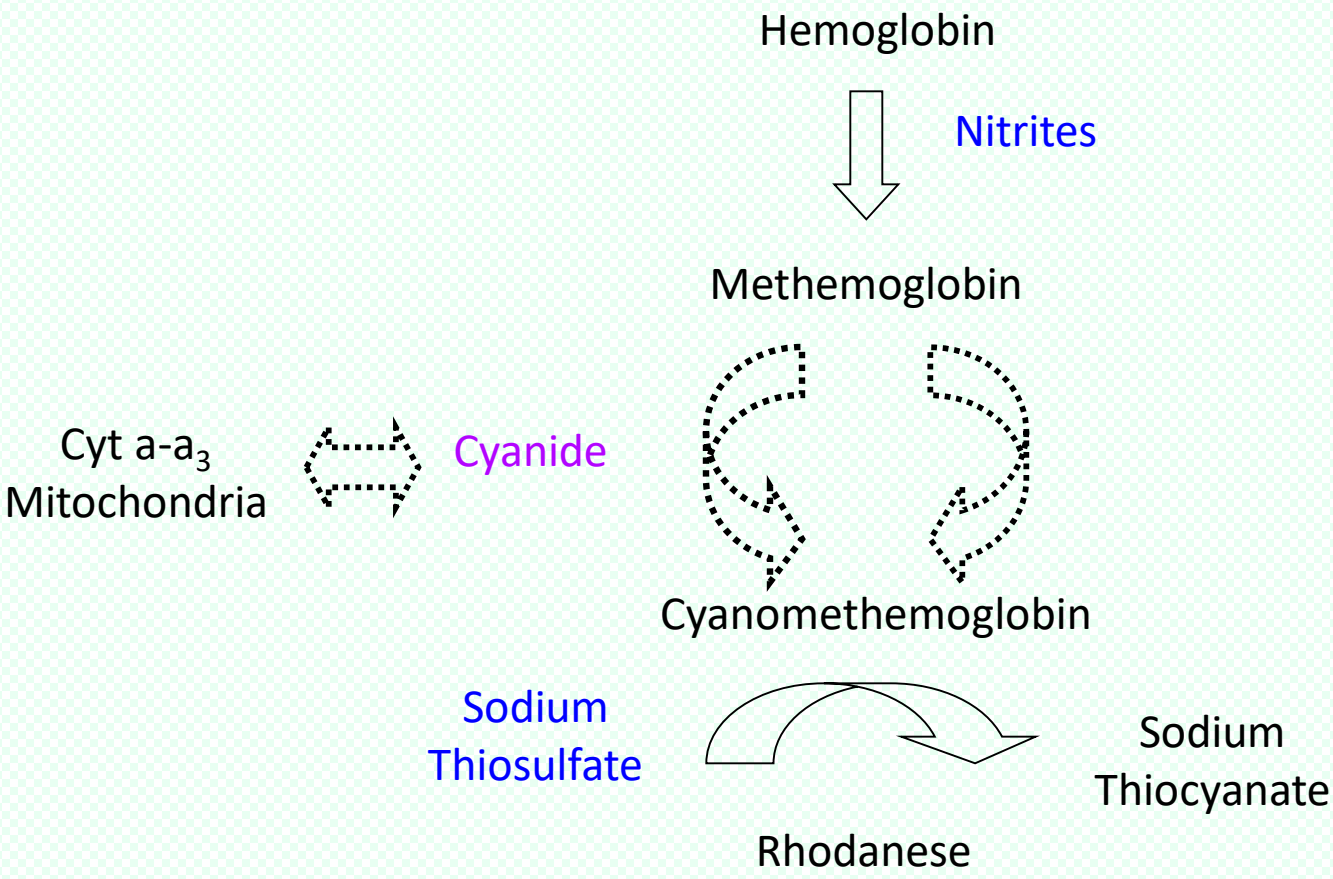
HCN

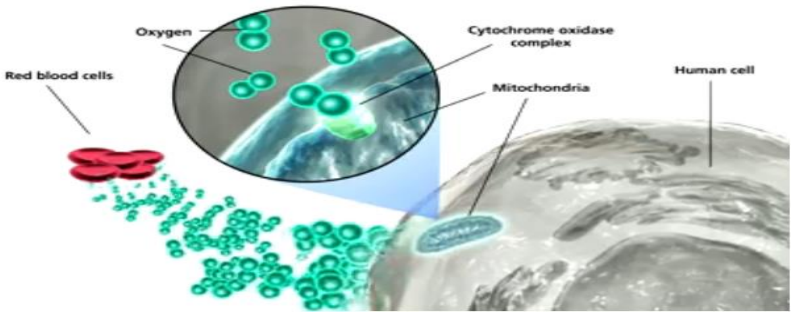
- In nature;
- peach seed, apple, pear kernel; cyanogenic glycosides such as amygdalin
- glycosides in the gastrointestinal tract

HCN

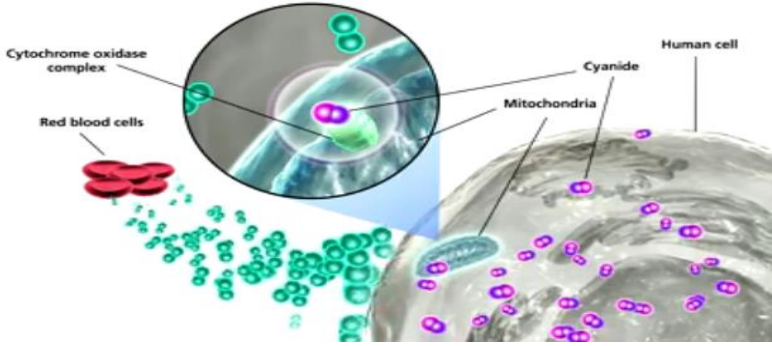
- The compounds formed in this way or taken orally are less likely to be poisoned than are gaseous because they are enzymatically detoxified.
- (Cyanide is oxidized to cyanate and thiocyanate in the organism. At low doses, it is converted into thiocyanate (SCN) by the action of sulfur transferase (rodenase) and excreted in urine.

Cyanide Antidote Kit





HCN



- This enzymatic metabolism is not sufficient when taken in toxic doses and in particular by inhalation.
- Cyanide inhibits cytochrome-c oxidase by binding with high affinity to the ferric iron of mitochondrial cytochrome aa 3.
- Adequate O2 / cells cannot use O2.
- Histotoxic hypoxia
- Death / respiratory arrest

HCN

- **Other effects**
- Antioxidant enzyme inhibition
- Lipid peroxidation increases
- Degradation of lipid metabolism
- Disruption of glycogen metabolism

HCN

- **Inhalation of toxic amounts of HCN**;
- Respiratory failure
- Headache
- Weakness
- Mental confusion
- Convulsion
- Out of demand defecation
- Frequent urination
- Pulse alter
- Vomiting (smell of HCN in the breath)
- Apoptotic paralysis

Symptoms of CN poisoning

HCN

- **Chronic poisoning;**
- Goiter and hyperthyroidism
- Flutter in the heart
- Red bubbles in the skin
- Ear whining

HCN

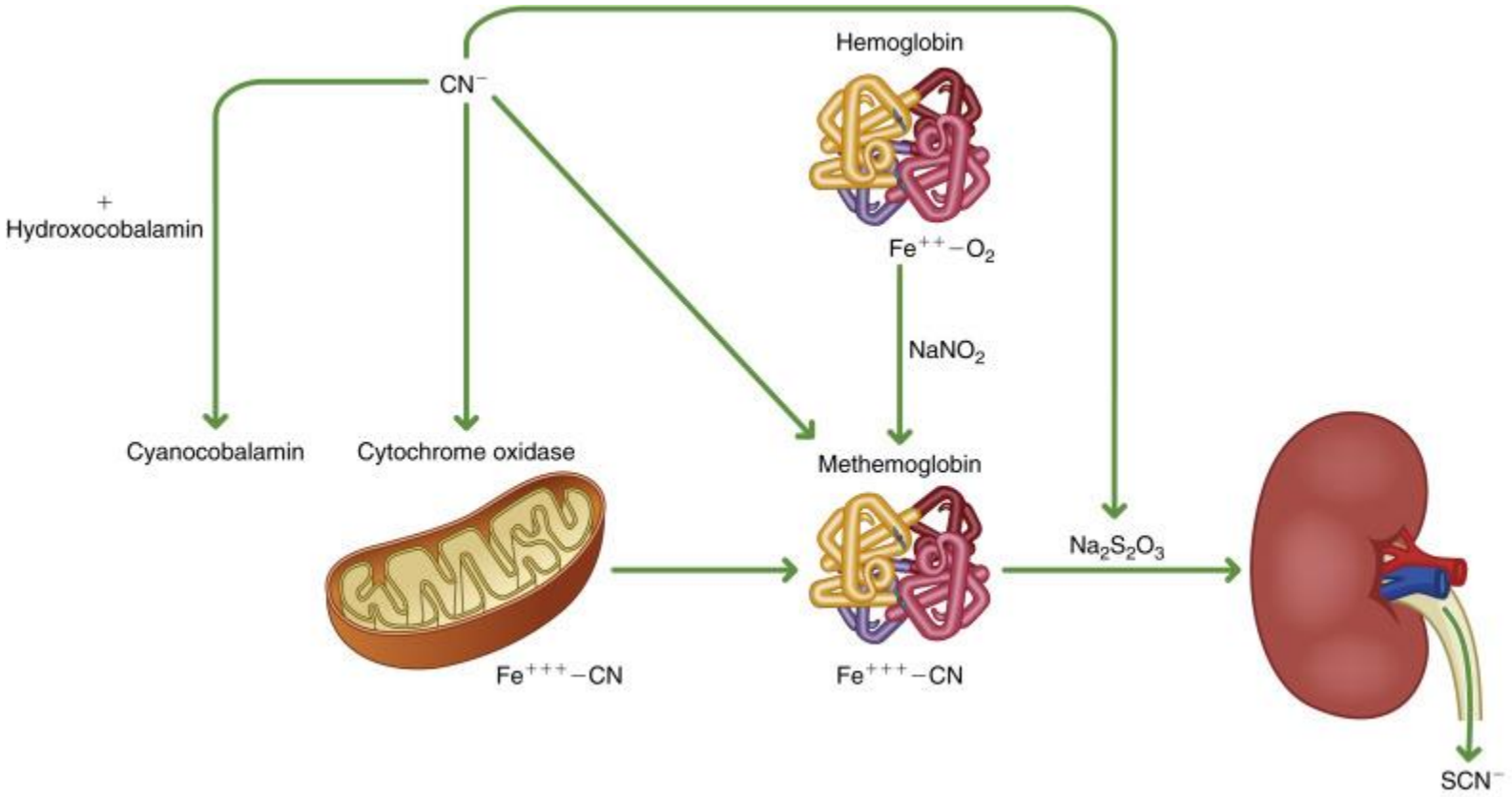
- Supportive (symptomatic) treatment (time????)
- Specific antidote therapy
- Inhalation poisoning: rapidly remove from the scene,
- Exposure - Decontamination
- The basis of treatment is to convert hemoglobin into methemoglobin by nitrites.
- The affinity of cyanide to methemoglobin is more than hemoglobin.
- Methemoglobin acts as a scavenger an by capturing and binding cyanide.

HCN

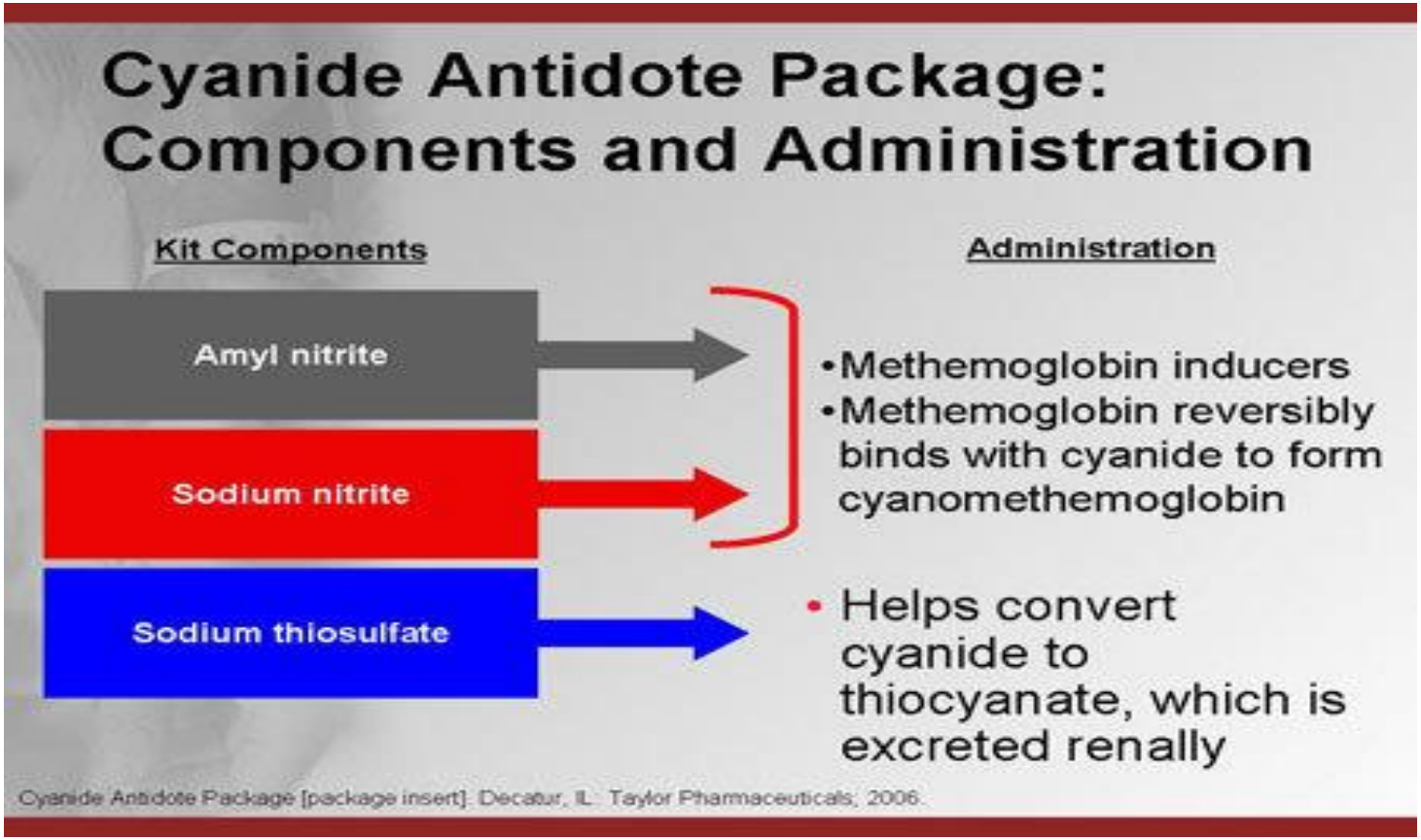
- **Treatment/**Nitrite derivatives used:

- Amyl nitrite inhalation
- Rapid injection of IV sodium nitrite
- It forms a methemoglobinemia up to 5%.

- Another component of the treatment: IV sodium thiosulfate
- the conversion of cyanide to thiocyanate


Hemoglobin
CN^-
+
Hydroxocobalamin
$Fe^{++}-O_2$
$NaNO_2$
Cyanocobalamin
Cytochrome oxidase
Methemoglobin
$Na_2S_2O_3$
$Fe^{+++}-CN$
$Fe^{+++}-CN$
SCN^-

Cyanide Antidote Package: Components and Administration



Cyanide Antidote Package [package insert]. Decatur, IL: Taylor Pharmaceuticals; 2006.

HCN

- 100% oxygen against respiratory failure
- It both reduces cyanide binding to cytochrome oxidase and has a synergistic effect with nitrites and thiocyanate.
- It is emphasized that it is not beneficial or even harmful.
- Hyperbaric oxygen is recommended when standard treatments are unsuccessful or if CO poisoning is present.

HCN

- Respiratory breathing is mouth-to-mouth is not recommended
- People who breathe can be poisoned.

- Following the symptoms, cardiovascular disorders are monitered with drugs such as dopamine, vasopressin and , if it is necesarry ,alpha sympathomimetics and antiarrhythmics are used.
-
- Blood gases are monitored.
- Na-bicarbonate is for acidosis

HCN

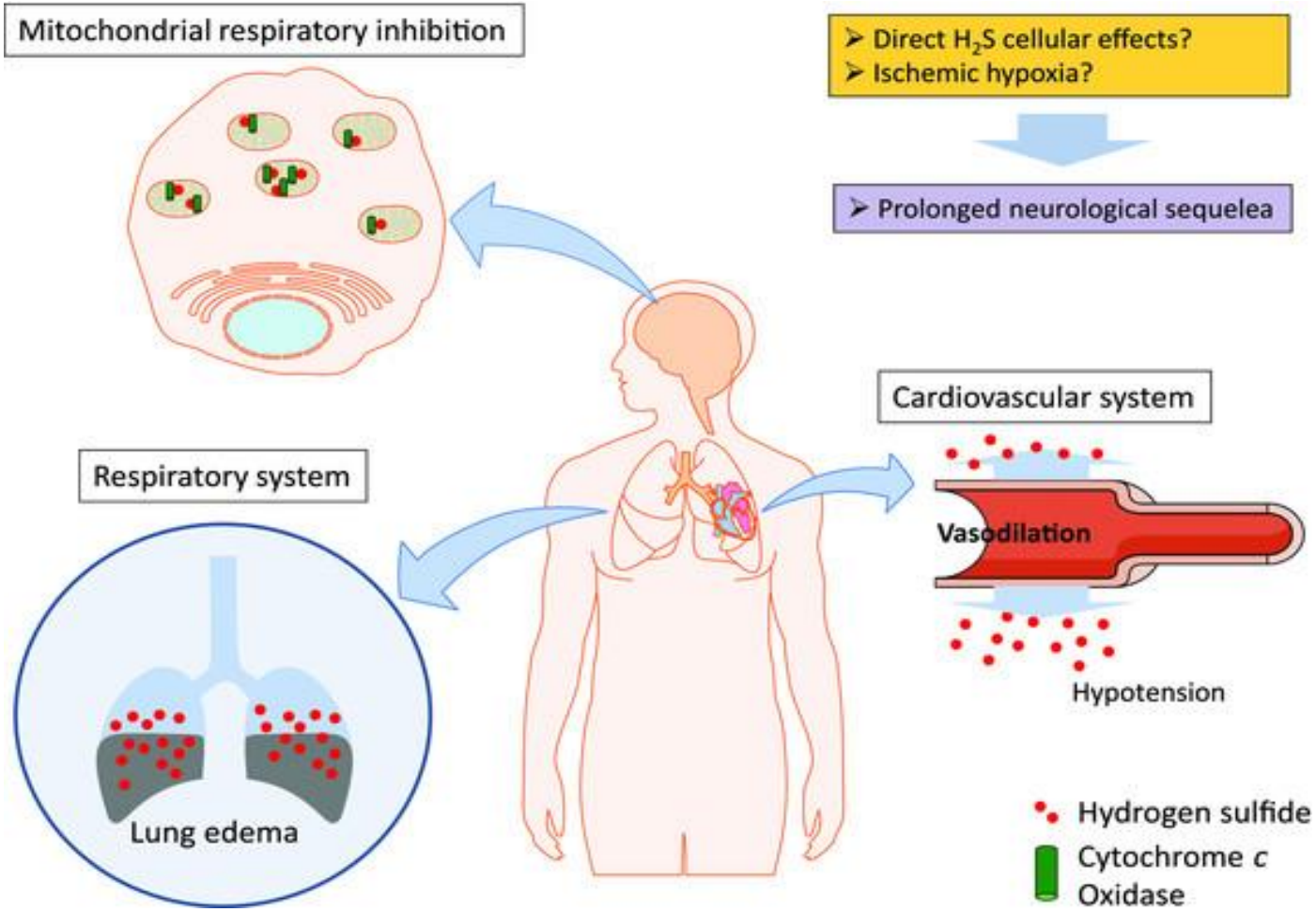
- Get into to body by orally, active charcoal can be used
- Emesis is not recommended due to aspiration possibility
- Hemodialysis or hemoperfusion (except for thiocyanate) ,no use.

HYDROGEN SULFIDE

Hydrogen sulfide

- Hydrogen sulfide, colorless, heavy air, blue flame burning, rotten eggs in the smell of a gas, highly toxic, intensely irritating gas

- Sources:
  - decaying organic materials
  - natural gas
  - volcanic gas
  - petroleum
  - sulfur deposits
  - sulfur springs
- Most exposures are occupational


Mitochondrial respiratory inhibition
➢ Direct H_2S cellular effects?
➢ Ischemic hypoxia?
➢ Prolonged neurological sequelea
Cardiovascular system
Vasodilation
Hypotension
Respiratory system
Lung edema
Hydrogen sulfide
Cytochrome *c* Oxidase

Hydrogen sulfide

Mechanism of action:

- inhibits mitochondrial cytochrome oxidase
- paralyzes the electron transport system
- plenty of O2 in the bloodstream,
- cells can not utilize it.
- hypoxia

Hydrogen sulfide

Mechanism of action, cont.:

- more potent cytochrome oxidase inhibitor than cyanide
- rapidly absorbed through the inhalation route
- metabolized by the liver and excreted through the kidneys
- cause of death is respiratory paralysis due to toxic effects of H2S on respiratory centers in the brain

Hydrogen sulfide, cont.

Concentration (ppm)	Clinical effect
0.02	odor threshold
100-150	nose/eye irritation, olfactory nerve paralysis
250-500	sore throat, cough, keratoconjunctivits, chest tightness, pulmonary edema
500-1000	headache, disorientation, loss of reasoning, coma, convulsions
>1000	death

Hydrogen sulfide

- EXPOSURE LEVEL SYMPTOMS
- Low Level Exposure · Headache · Depression · Bronchitis

- High Level Exposure · Cough · Dyspnea · Dizziness · Confusion · Nausea, vomiting · Hemoptysis · Unconsciousness.

- Very High Exposure · Myocardial infarction · Sudden loss of consciousness · Seizure · Cardiopulmonary arrest

- Treatment????

Hydrogen sulfide

- Very low concentrations of hydrogen sulfide can also be felt. Combustible.
- In H_2S poisoning;

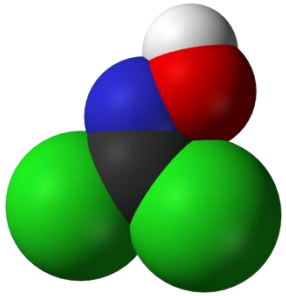
- Exposure time and quantity are important.

- Depending on these two factors, symptoms ranging from mild headache to seizure and cardiopulmonary arrest can be observed.

Hydrogen sulfide, cont.

Treatment:

- basic life support
- give O2,
- hyperbaric oxygenation may be beneficial



Phosgene

Phosgene

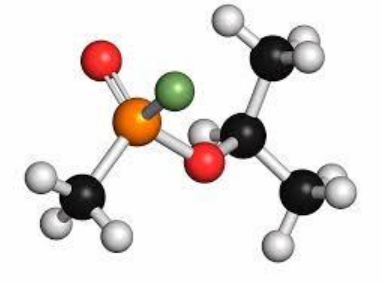
- Phosgene is a heavy, colorless and liquid at 80ºC.
- Low concentrations of freshly cut straw.
- Due to its low water solubility, it is particularly effective in distal airways.

Phosgene

- Today, as an intermediate in the synthesis of isocyanates, pesticide is formed during the production of plastic, paint and medicine. Firefighters, welders and painters, heating of substances containing chlorinated hydrocarbons (eg solvents, dry cleaning agents)

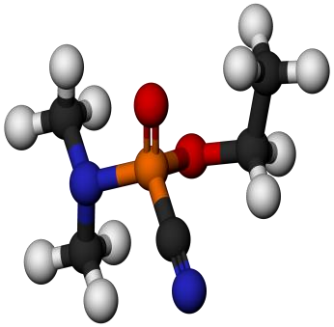
- In the lung phosgene is slowly hydrolyzed carbon dioxide and hydrochloric acid .....
- Very high concentrations of mucous membrane irritation, such as lingering eyes, sore throat and cough are evident.

- Treatment.....supportive care



- **Sarin**
- Sarin is a nerve gas. It was discovered by German chemist Gerhad Schrader in 1938. Sarin gas is an extreme poisonous agent, disrupts the balance of nervous systems in the body and causes paralysis (AcHE inhibitor). The production and storage of Sarin gas was prohibited in 1993 by the CWC (Chemical Weapons Convention). The specific antidote is Atropine.
- PAM -must be administered within minutes to a few hours

- **Tabun**



DUSTS

Dust ; The general name of solid particles suspended in the air!

Dimensions that are important for human health: Dusts between 0.5 and 100 microns!

Larger particles cannot enter the airways.

- Dusts are divided into three groups according to their physiological effects:
- Toxic dusts with systemic effect: Lead, cadmium.

- Toxications caused by poisoning by inhalation: Zinc oxide, aluminum hydroxide.

- Toxic dusts with allergic effect: Pollen powder, chalk powder, wood powder.

- Chemical and physical structure of …….
- **Size** of dust particles
- **Dust density** in inhaled air
- Exposure **time**
- **Individual sensitivity**

- **Pneumoconiosis (** Pneumoconiosis is major disease that are seen with dusts**)**
- Pneumoconiosis is a general term given to any lung disease caused by dusts that are breathed in and then deposited deep in the lungs causing damage. Pneumoconiosis is usually considered an occupational lung disease, and includes asbestosis, silicosis and coal workers' pneumoconiosis (CWP), also known as "Black Lung Disease."

- Pneumoconiosis can develop when airborne dusts, particularly mineral dusts, are inhaled at work. The dust particles remain in the lung where they can cause inflammation or fibrosis (scarring).

Major Pneumoconiosis

- Inhalation of some dusts results in “major fibrosis” of the lungs, which results in interference of lung architecture or lung function tests.

- As:
  - **Silica → silicosis**
  - **Asbestos → asbestosis**
  - Talc → talcosis
  - Coal → coal workers pneumoconiosis (anthracosis)

  - Bagassosis – from sugarcane dust
  - Berylliosis – from beryllium

- **Asbestos fibers** are very durable and resistant to heat, leading to their use in insulation and fireproofing, as well as in textile manufacturing. Examples of workers who might be exposed to asbestos include plumbers, roofers, mechanics and shipyard workers, including naval officers. People are at higher risk of developing asbestosis if they have higher levels of exposure to asbestos dust over longer periods of time. The disease typically does not develop for 10 or 20 years after first exposure.

- **Crystalline silica** is a main component of dust from sand and rock. Examples of workers who might be exposed to silica include miners, sandblasters, stonemasons and foundry workers. Risk factors for developing silicosis include higher levels of silica exposure and longer time of exposure.