CYANIDE TOXICITY

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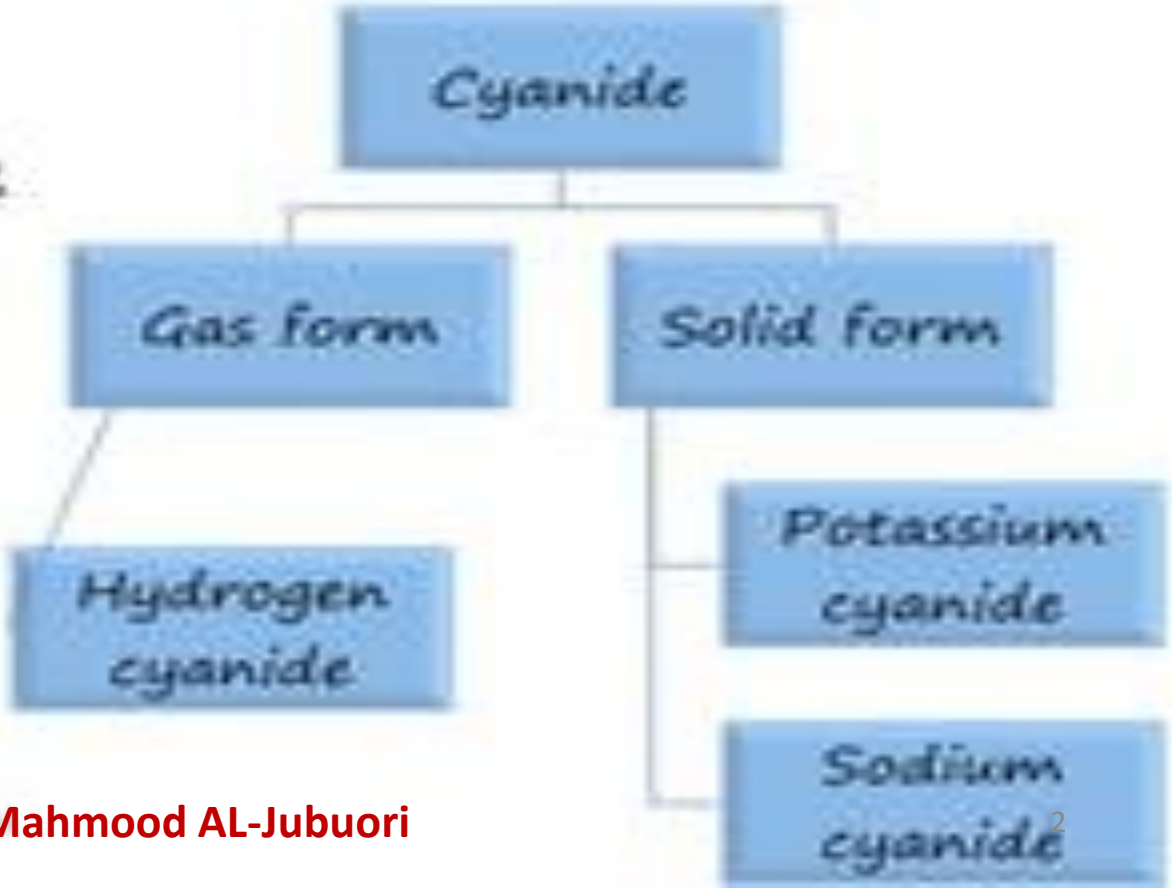
What is cyanide?

- Highly lethal systemic poison causing rapid death
- Derivatives of cyanide



CN FORMS

- The most common forms are

1. **HCN** (liquid at room temp. & gas at higher temp.). HCN is a common combustion byproduct of burning plastics, wool, & many other natural & synthetic products. HCN is important cause of death from fire.
2. **NaCN & KCN** (white crystals)

- these forms have bitter almond like odor.

CN SOURCES

➢Cyanide sources include

1. **Cigarette** smoke
2. **Combustion products** of plastics (aliphatic nitriles like acrylonitrile & propionitrile that used in plastics manufacturing are metabolized to cyanide)
3. Prolonged use of **high doses of cyanogens** (cpds librate CN) like laetrile (anticancer drug), Na-nitroprusside (vasodilator), & cyanocobalamine (vit. B12)
4. **Natural source** of CN in plants containing amygdaline (glycoside hydrolyzed to CN in GIT) such as apricot & peach pits.

CN SOURCES OF EXPOSURE AND ROUTE OF INTOXICATION

- Most cyanide ingestions occur from

1. accidental exposure
2. intentional ingestion of a cyanide-containing compound

- Intoxication can occur also from:

1. Inhalation or
2. ingestions or
3. Absorption through the skin

CYANIDE USES

- Is highly toxic chemical with a variety of uses, including:

1. chemicals industry
2. laboratory analysis.
3. metal plating

TOXIC DOSE

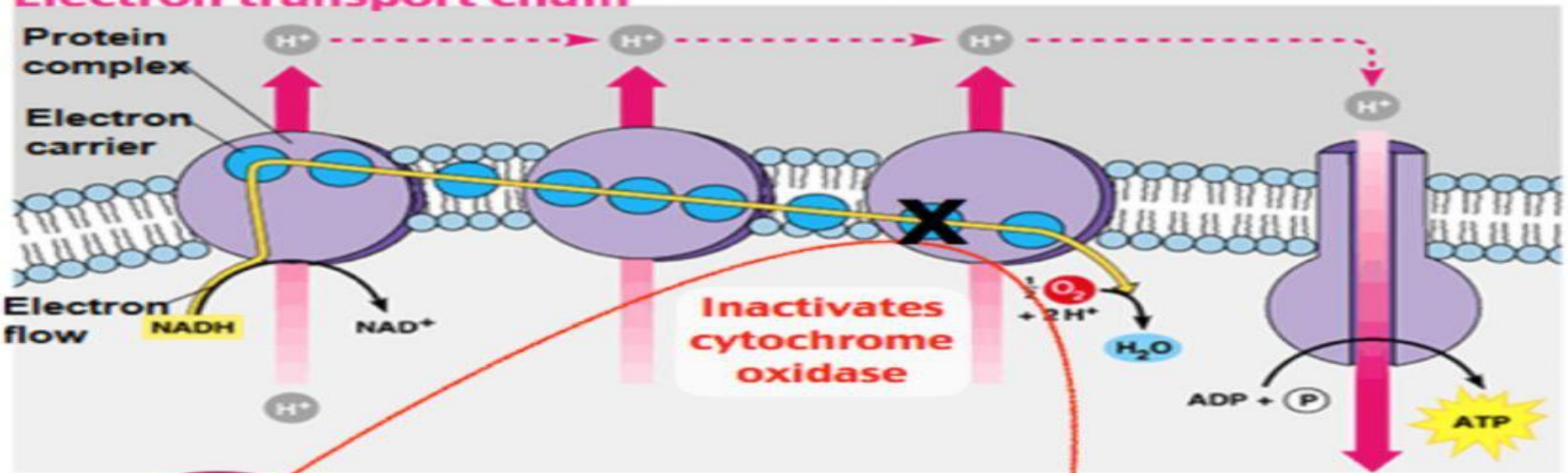
- Adult ingestion of as little as 200mg of NaCN or KCN may be fatal (Solutions of cyanide salts can be absorbed through intact skin), & 100mg/150Ibs for HCN
- The LD50 for these salts is approximately 2 mg/kg, with ingestion of 50 to 75 mg of any one of them usually resulting in syncope and respiratory difficulty within a few minutes

MECHANISM OF TOXICITY

- Cyanide inhibit mitochondrial cytochrome oxidase system (cytochrome AA3 complex) thus blocking ATP generation resulting in reduced cellular utilization of O2 & increased venous PO2 that reduce aerobic respiration with decreased pyruvate conversion in Krebs cycle leading to increased lactic acid formation & metabolic acidosis.
- CN produce histotoxic cellular hypoxia by initially binding to protein portion of cytochrome oxidase & then to ferric form of iron. Also binds to myoglobin in muscle & hemoglobin in blood especially the methemoglobin form.

Cyanide toxicity

Electron transport chain



CN- Cyanide

Inactivates mitochondrial **oxidative phosphorylation**

→ Inhibits cellular respiration

→ Aerobic → Anaerobic metabolism

→ ↑ Lactic acid

1. **Hydroxocobalamin** + Cyanide = Cyanocobalamin (nontoxic)

Or

2. **Amyl nitrite** causes methemoglobinemia
   Methemoglobin binds cyanide
   Sodium thiosulfate enhances conversion of cyanide to thiocyanate (renally excreted)

CLINICAL MANIFESTATIONS

- bitter almond odor on breath
- GI upset(nausea and vomiting)
- stiffness in lower jaw, weakness & headache
- dyspnea, rapid then slow irregular respiration (short inspiration & prolonged expiration);
- then loss of consciousness, convulsions, coma, transient respiratory stimulation followed by respiratory failure, & cardiovascular collapse ensure rapidly after heavy exposure.
- Also red skin, unreactive dilated pupils, & bloody foam around mouth.
- Death often occurs in < 10 min.

CLINICAL MANIFESTATIONS

- Delayed in onset of symptoms (mins or hrs) may also occur after ingestion nitriles & plants derived cyanogenic glycosides, because metabolism to cyanide is required.
- Survivors from severe CN poisoning may suffer from chronic neurological consequences.

DIAGNOSIS

- :Is based on:
- History of exposure to cyanogens or other CN sources & presence of rapidly progressive signs & symptoms.
- Severe lactic acidosis is usually present with significant exposure.
- Specific diagnosis in peripheral blood by measuring venous O2 saturation that may be elevated owing to block cellular O2 consumption.

TREATMENT

➢ **Supportive measures**

1. Maintain open airway & assist ventilation.
2. Treat hypotension & seizure if occur.
3. Start IV fluid & monitor vital signs & ECG closely.
4. Note: hyperbaric oxygen has no proven role in CN poisoning.

TREATMENT

➢ **Decontamination**

1. ***Inhalation***: remove victims from HCN exposure site & give supplemental O2.
2. ***Skin***: remove & isolate contaminated clothing & wash contaminated area with soap & water.
3. ***Ingestion:***

- Prehospital: immediately administer activated charcoal
- Hospital: immediately place gastric tube & administer activated charcoal.

CYANIDE ANTIDOTES

- Methemoglobin Generators {usually nitrites such as sodium nitrite (IV), amyl nitrite (Inhaled); also dimethyl aminophenol (IV, IM)}:
- these oxidizing agent converting ferrous ion (Fe 2+) of Hb to ferric ion (Fe 3+), the resultant methemoglobin binds strongly with CN as cyanomethemoglobin {cyanide scavenging methemoglobinemia (reversible met-Hb)}.
- Note: sodium nitrite can induce methemoglobinemia that extremely dangerous (if > 10-15% of total Hb since low O2 amount in met-Hb) & even lethal; therefore sodium nitrite should not be given if the symptoms are mild or if the diagnosis is uncertain, especially if concomitant CO poisoning is suspected.

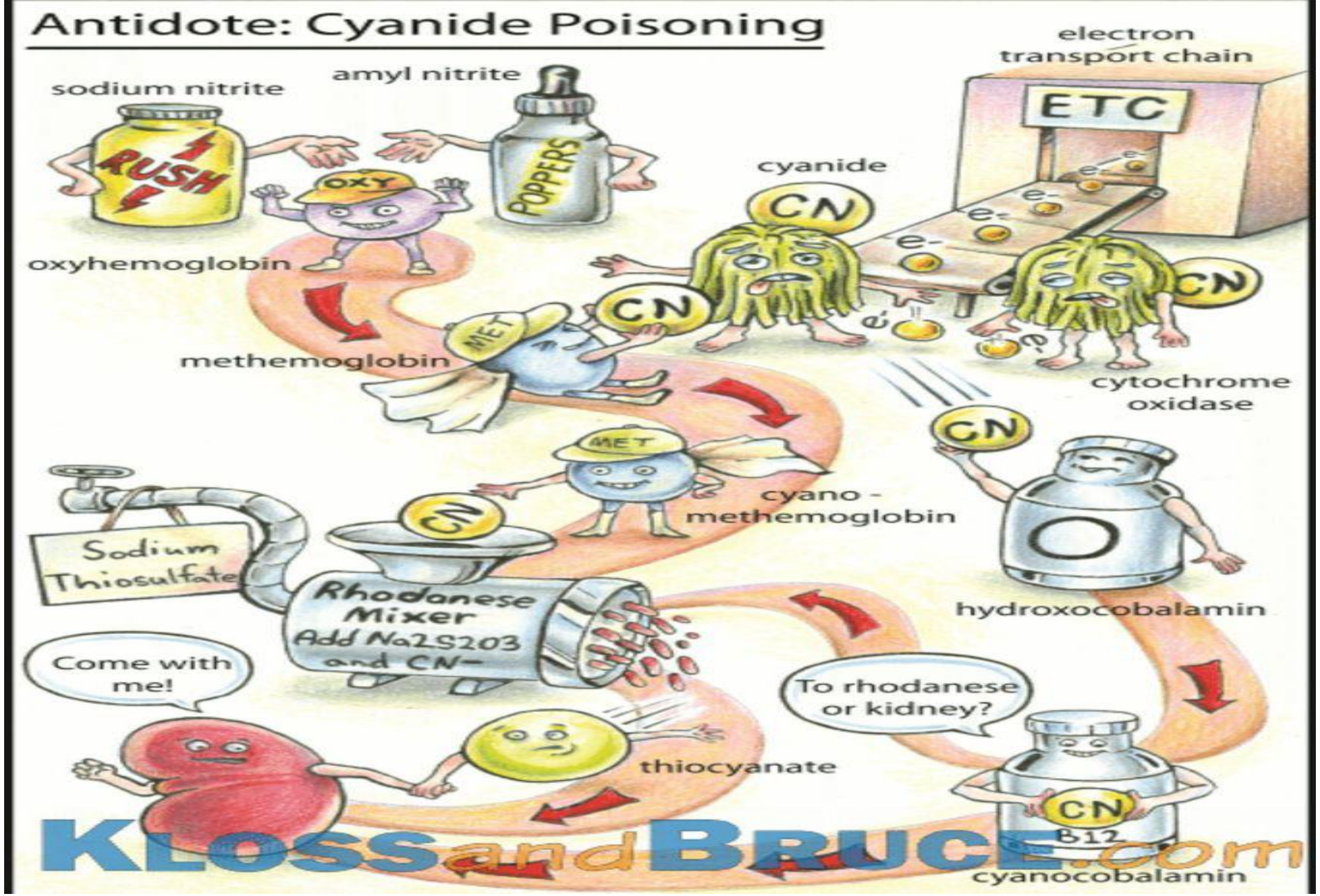
CYANIDE ANTIDOTES

- Sulpher Donors {usually sodium thiosulfate (IV)}:
- the normal route of detoxification is conversion of CN to thiocyanate that eliminated outside the body (irreversible process normally done by glutathione, but when saturated, the toxicity occurs); so the use of sodium thiosulfate (substrate for enzyme rhodanase) will accelerate conversion of CN to thiocyanate.
- Note: sodium thiosulfate is too slow in its action, therefore should be regarded as adjuvant therapy (2nd line therapy).

CYANIDE ANTIDOTES

- Direct Binding Agents {usually hydroxocobalamine (Cyanokit IV), dicobalt edetate (Kelocyanor IV)}:
- these agents chelate CN ion directly forming complex easily eliminated, & considered as alternative or adjuvant therapy.

- Note: hydroxocobalamine is more specific antidote since it enters the cells & pulls CN from IC sites & increase its elimination from vascular sites, in addition to its safety since it doesn't induce methemoglobinemia.


Antidote: Cyanide Poisoning
sodium nitrite
amyl nitrite
RUSH
POPPERS
OXY
oxyhemoglobin
methemoglobin
MET
cyanide
CN
electron transport chain
ETC
e-
cytochrome oxidase
cyano - methemoglobin
hydroxocobalamin
O
Sodium Thiosulfate
Rhodanese Mixer
Add Na2S2O3 and CN-
Come with me!
To rhodanese or kidney?
thiocyanate
B12
cyanocobalamin
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