# TOXICOLOGY
# CARDIAC POISON

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# CARDIAC POISON

These are the poison having an action mainly on heart, either **directly** or **through the nerves**.

Example:

- Cyanide
- Nicotine
- Digitalis
- Oleander
- Aconite

# CYANIDE

- A **cyanide** is a chemical compound that contains the **cyano group**, -C≡N, which consists of a carbon atom triple-bonded to a nitrogen atom.
- Cyanides most commonly refer to salts of the anion $CN^-$, which is isoelectronic with carbon monoxide and with molecular nitrogen.
- Most cyanides are highly toxic.

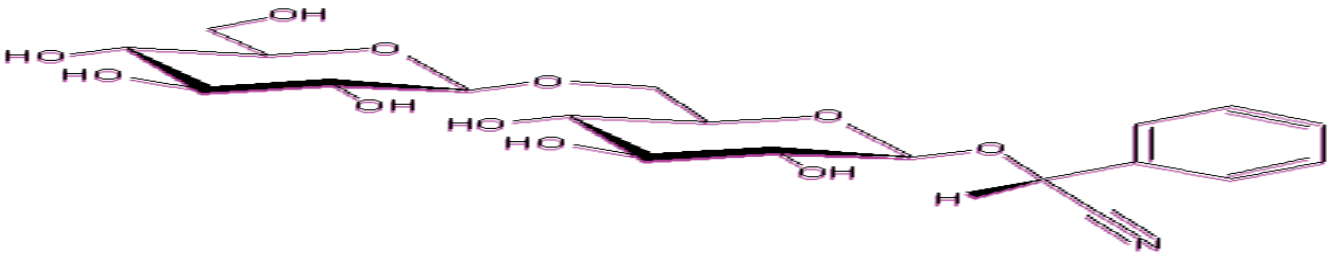
# CYANIDE PLANTS

250 mg CN/100g plant tissue

104 mg CN/ 100 g plant tissue

140-370 mg CN/ 100 g plant material

# CYANIDE PLANTS




# ABSORPTION

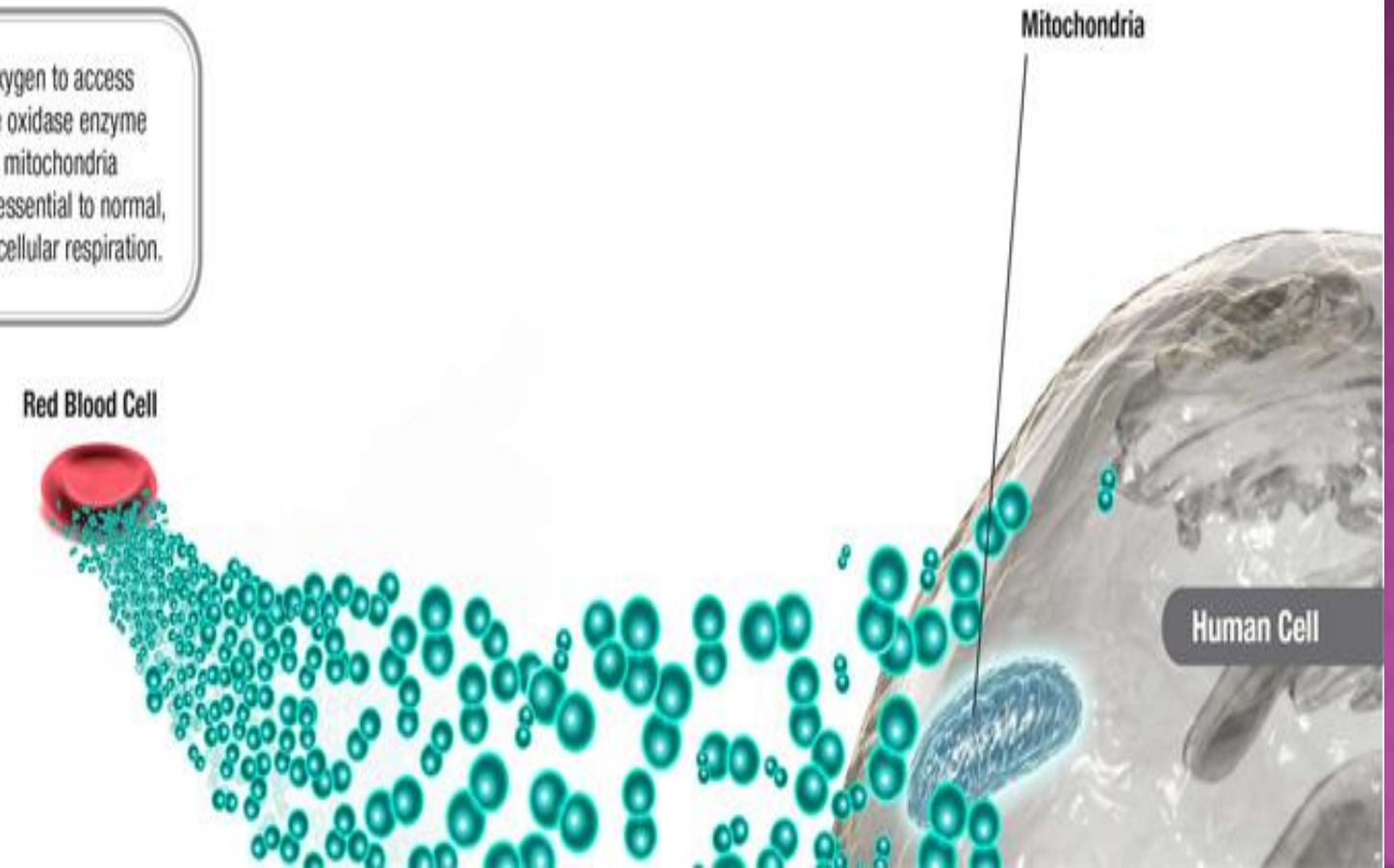
- Absorption rapidly from all route.
- Absorption delay due to
  1. full stomach
  2. large quantity of wine
- Cyanide Less effective when…….
  Kept for long time achlorhydria

# CYANIDE (HCN)

## Actions:

- Protoplasmic poison
- Inhibiting Cytochrome oxidase c
- Carbonic anhydrase
- Other cellular respiratory enzymes
- Corrosive for mucosa

1 The ability of oxygen to access the cytochrome oxidase enzyme (present on the mitochondria inside cells) is essential to normal, life-sustaining cellular respiration.

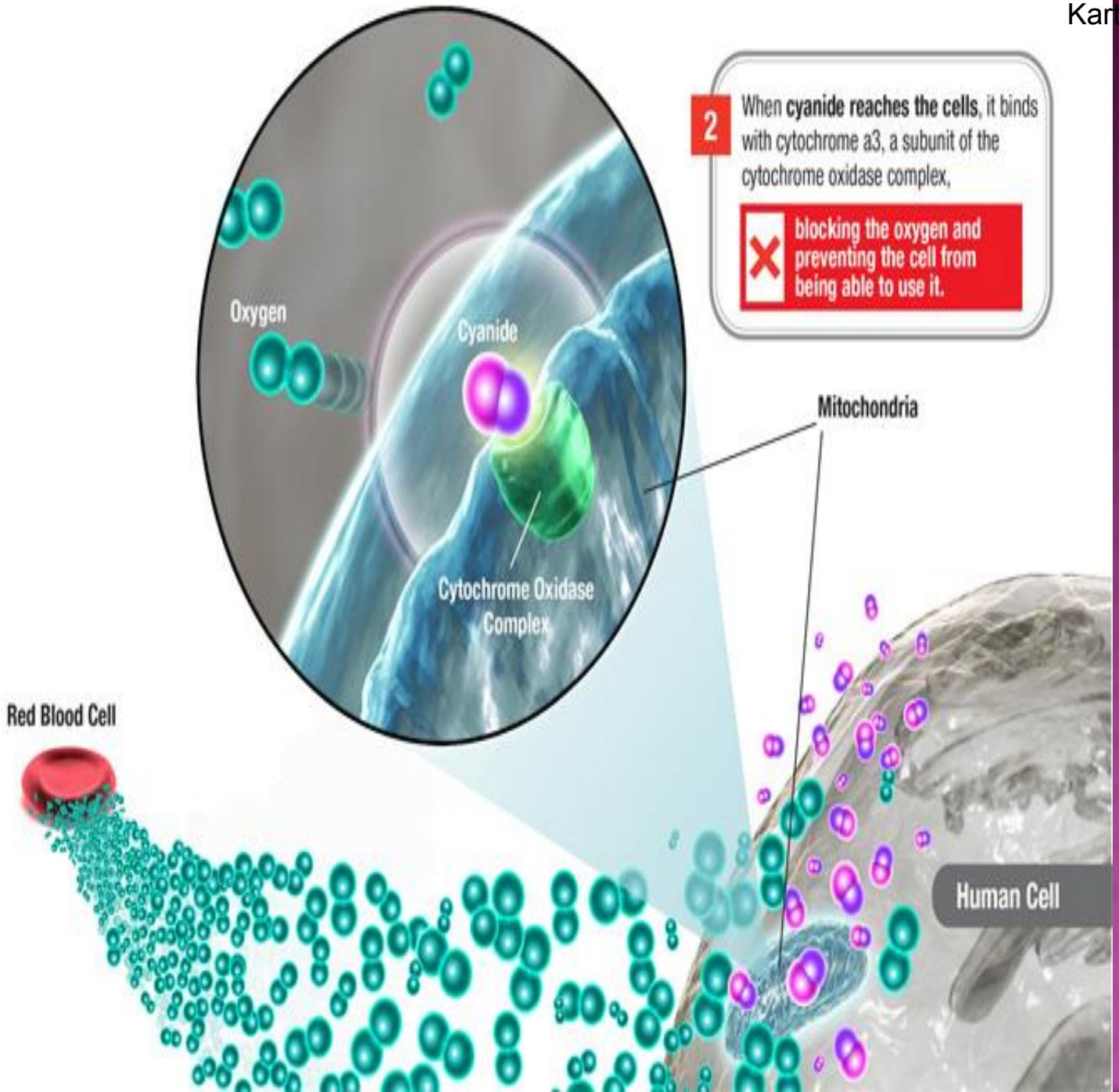


# TOXIC MECHANISM

- The cyanide anion is an inhibitor of the enzyme cytochrome c oxidase ($aa_3$) in the fourth complex of the electron transport chain (found in the membrane of the mitochondria of eukaryotic cells).

- It attaches to the iron within this protein.

- The binding of cyanide to this cytochrome prevents transport of electrons from cytochrome c oxidase to oxygen.



# TOXIC MECHANISM

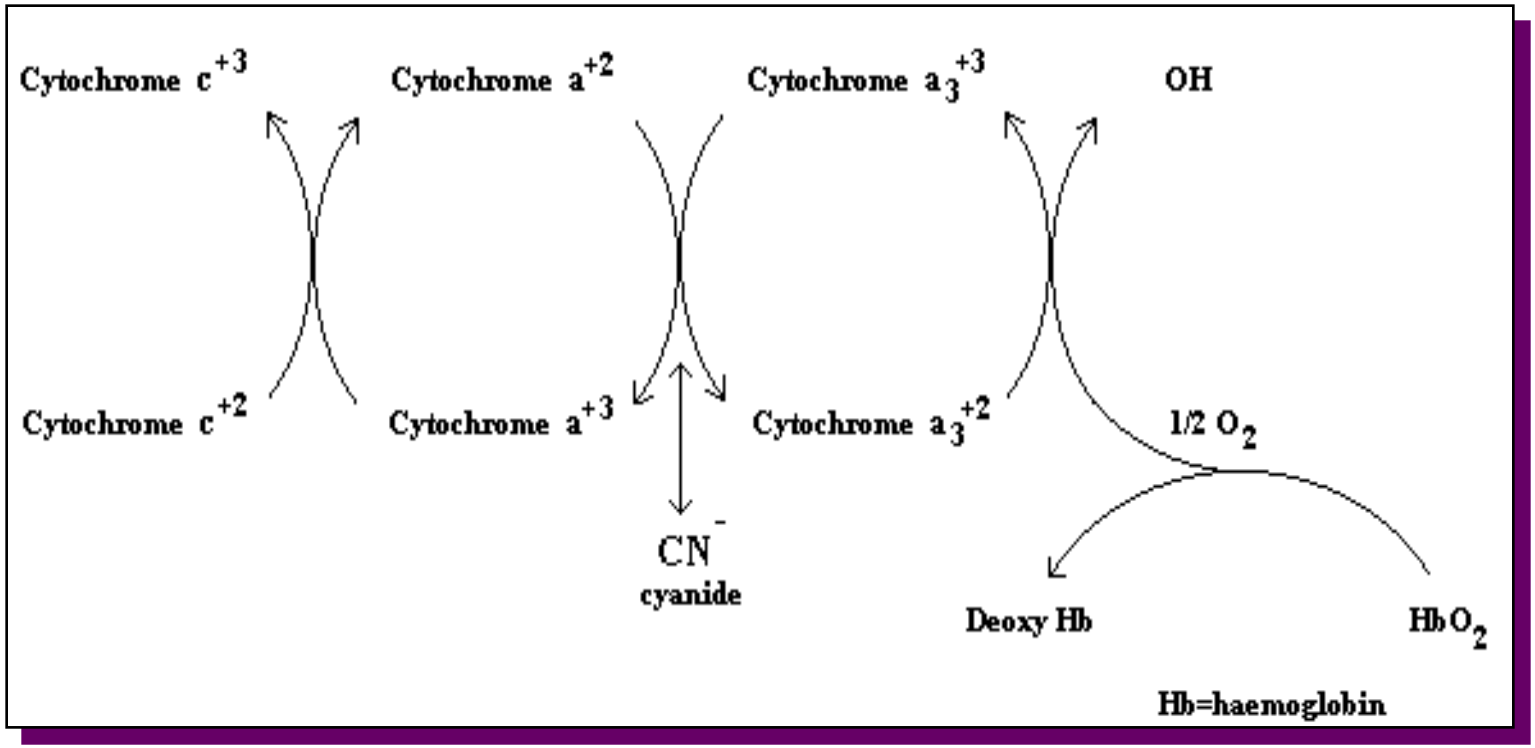
- As a result,

  The electron transport chain is disrupted, meaning that the cell can no longer aerobically produce ATP for energy.

  Tissues that depend highly on aerobic respiration, such as the central nervous system and the heart are particularly affected.

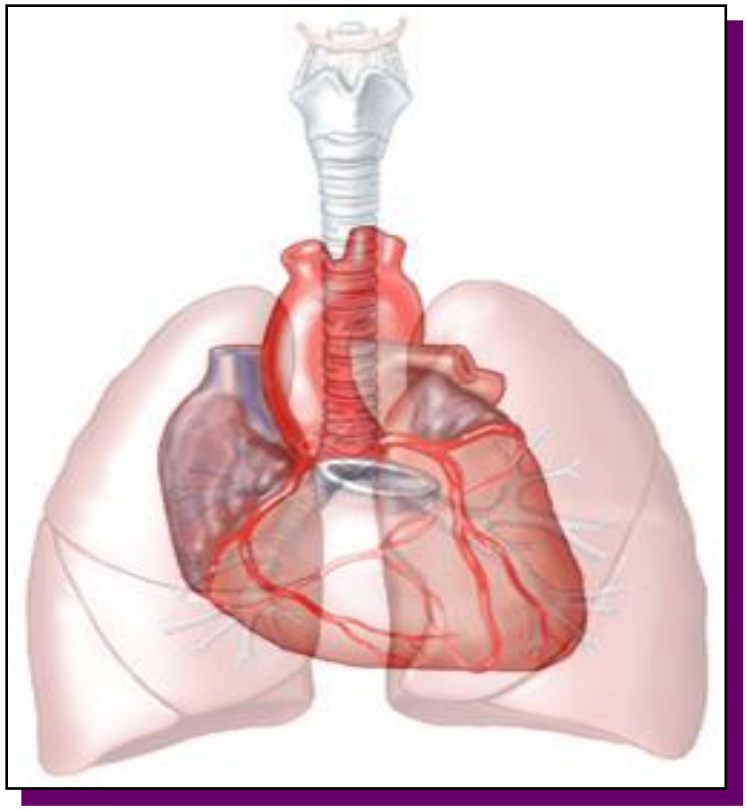
  This is an example of histotoxic hypoxia

# TOXIC MECHANISM




**"HISTIOTOXIC ANOXIA"**

# TOXIC MECHANISM



**VASOSPASM**

# CYANIDE TOXICITY

## INGESTION

**LETHAL DOSES**

**60- 90 mg Hydrogen Cyanide (HCN)**

**200 mg Potassium Cyanide (KCN)**

# CYANIDE TOXICITY

## INHALATION

| Concentration ($mg.m^{-3}$) | Effect |
|---|---|
| 300 | immediately lethal |
| 200 | lethal after 10 minutes |
| 150 | lethal after 30 minutes |
| 120-150 | lethal after 30-60 minutes |
| 50-60 | 20 minutes to 1 hour without effect |
| 20-40 | light symptoms after several hours |

# SIGNS AND SYMPTOMS



- **Mild Toxicity**
  - Nausea
  - Dizziness
  - Drowsiness
- **Moderate Toxicity**
  - Loss of consciousness for a short period
  - Convulsion
  - Vomiting
  - Cyanosis
- **Severe Toxicity**
  - Deep coma
  - Dilated non-reactive pupils
  - Deteriorating cardio-respiratory function

# INVESTIGATIONS

- History
  - Occupation, access to cyanide
- Smell
  - Bitter almonds
- ECG
  - Sinus tachycardia
  - Sinus bradycardia
  - Ischaemic changes
- Pulse Oximetry
  - Normal

# INVESTIGATIONS

- **ABG**
  - **Metabolic acidosis**
  - **Normal oxygen**
- **Anion gap ($Na^+ – [Cl^- + HCO_3^-]$)**
  - **Elevated**
- **Serum lactate**
  - **Elevated**
- **Blood cyanide level**
  - **Elevated –**
  - **difficult to rapidly determine**

# MANAGEMENT

- HAZARD ASSESSMENT
- ABC's
- TOXICOKINETICS

  ABSORPTION DISTRIBUTION

  METABOLISM ELIMINATION
- TOXICODYNAMICS
- SUPPORTIVE CARE

# MANAGEMENT

## HAZARD ASSESSMENT

**Cyanide is hazardous by:**

- **Ingestion**
- **Respiratory exposure**
- **Dermal exposure**

# MANAGEMENT

## ABC's

- **Avoid:**
  - **mouth to mouth, or**
  - **mouth to nose artificial ventilation**

# MANAGEMENT

## DECONTAMINATION (absorption)

1. Nasogastric aspiration
2. Activated charcoal
3. Gastric lavage
4. Emesis

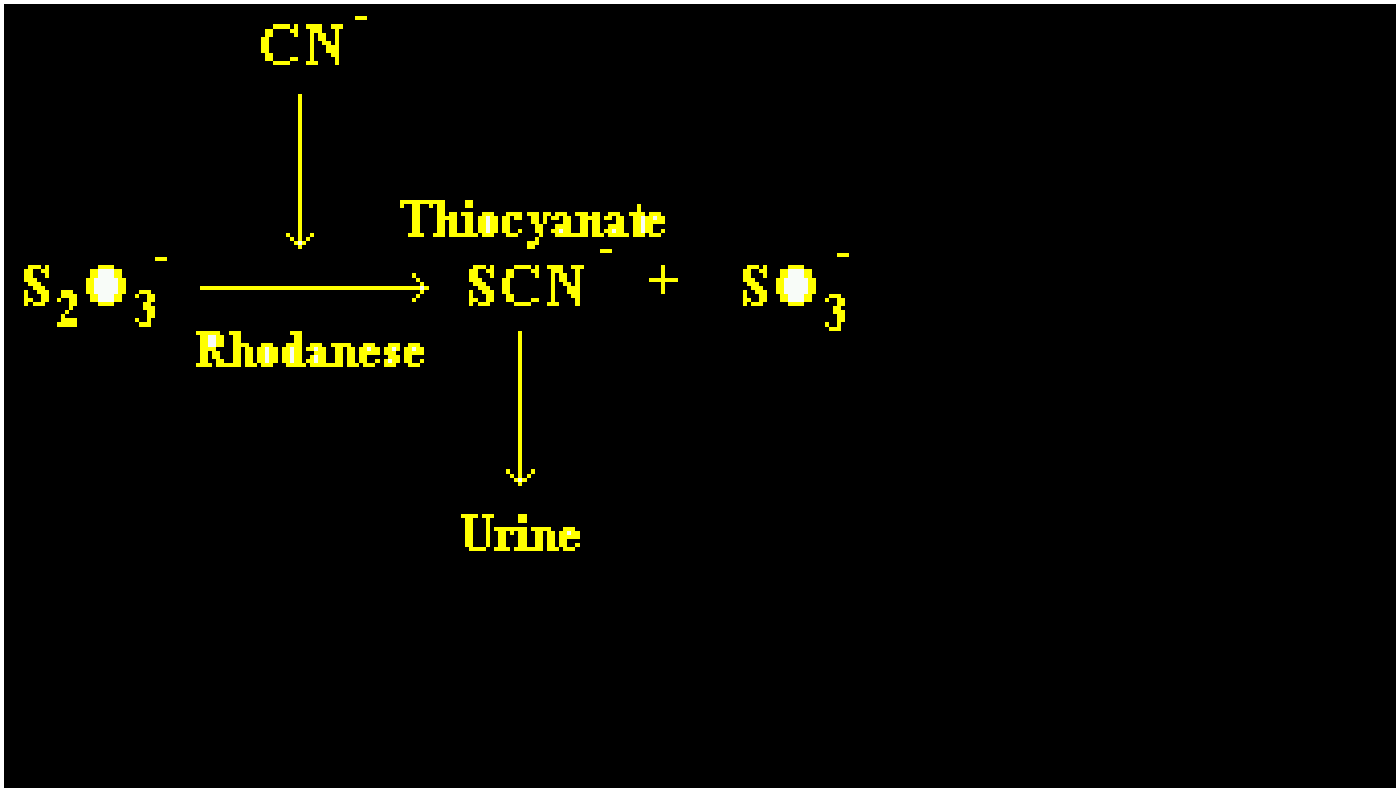
# MANAGEMENT

## ANTIDOTES (distribution/metabolism)

### Enhanced cyanide metabolism

- Enhancement of body's natural mechanisms for dealing with cyanide:
  i. oxygen
  ii. Sodium thiosulphate

# MANAGEMENT



# MANAGEMENT

## ANTIDOTES

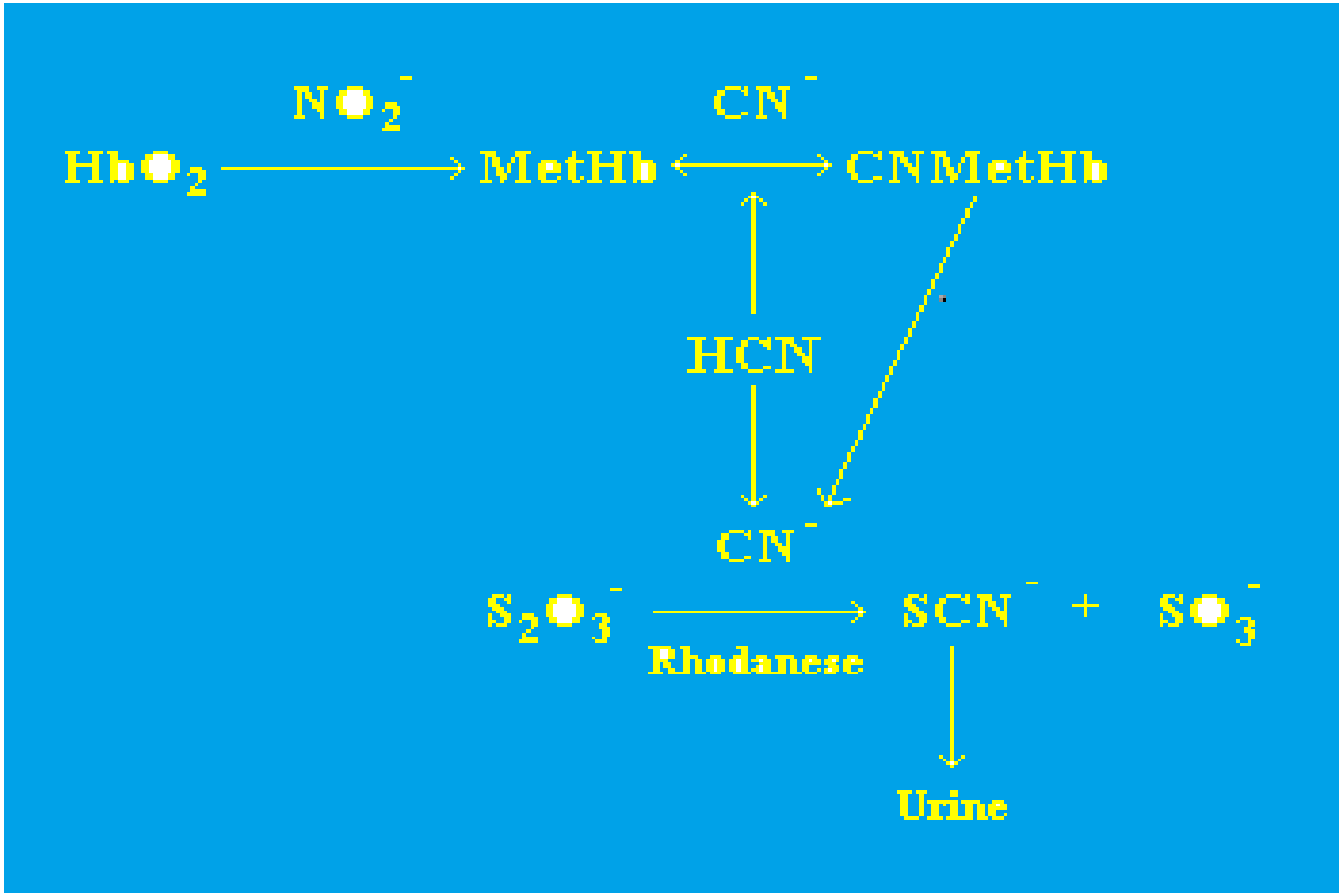
**(Distribution/metabolism)**

### Cyanide ion binding

1. **Cobalt containing drugs**

2. **Methaemoglobin forming drugs**

# MANAGEMENT
# ANTIDOTES : CYANIDE IRON BINDING



# MANAGEMENT

## 1. Cobalt containing drugs

- Cyanide ions will bind to cobalt which can be supplied in the form of either;

  i. Hydroxocobalamin

  ii. Dicobalt edetate.

# MANAGEMENT

## 2. Methaemoglobin forming drugs

- Cyanide will also bind to methaemoglobin formed after administration of:

  i Amyl nitrite
  ii. Sodium nitrite
  iii. 4-dimethylaminophenol (4-DMAP)

# TREATMENT

- Antidote kit
  - Amyl nitrate ampule (for inhalation)
  - Sodium nitrite 3%

    10mL (300mg)
  - Sodium thiosulfate 25%

    50mL (12.5g)

# MANAGEMENT
# FIRST AID

- **If the patient is unconscious:**
- **Commence forced artificial ventilation with 100% oxygen using a mask and bag with a “non-return” valve (to prevent inspiration of inhaled gases)**
- **Amyl nitrite may be administered via the ambu bag 0.2 - 0.4 ml for adults and 0.1 ml for children**
- **NOTE:**

  **Amyl nitrite forms a flammable mixture when combined with oxygen. It must therefore not be used in situations where it may be ignited.**

# MANAGEMENT MILD POISONING

- In those circumstances where an individual exposed to hydrogen cyanide by inhalation is conscious five minutes after exposure has ceased, and complains only of nausea, dizziness, drowsiness or other mild symptoms:
- Oxygen
- Reassurance
- Bed rest

# MANAGEMENT
# MODERATE POISONING

Those patients who have been observed to have lost consciousness for a short period, or are suffering convulsions, vomiting and/or cyanosis

# MANAGEMENT MODERATE POISONING

- **Oxygen 100%:** but for no longer than 12-24 hours
- **Amyl nitrite:** 0.2 - 0.4 ml for adults and 0.1 ml for children via “ambu bag” (if there is delay in administering sodium thiosulphate)

**Then**

- **Sodium thiosulphate:** 50 mL of 25% solution (12.5g) IV over 10 minutes. In children the dose is 300 to 500 mg/kg

# MANAGEMENT SEVERE POISONING

- Hydroxocobalamin: 5 g (70 mg/kg for children) by rapid IV infusion. This dose may be repeated once or twice, depending upon response, with IV infusions over 30 minutes to 2 hours
- Sodium nitrite: 10 ml of 3% solution (300mg) IV for 5 - 20 minutes. May be repeated at half initial dose
- Dicobalt edetate: 20 ml of 1.5% solution (300mg) IV over 1 minute followed immediately by 50 ml of hypertonic glucose solution. May be repeated twice
- Sodium thiosulphate: 50 ml of 25% solution (12.5g) IV over 10 minutes. In children the dose is 300 to 500 mg/kg

# POSTMORTEM FINDINGS

External :

- Smell
- Cyanosis
- Fine froth
- Rm : early

Internal :

- Cranial cavity open first
- Corrosion
- Signs like asphyxia

# MEDICOLEGAL IMPORTANCE

- Ideal suicidal poisoning
- Accidental
- Homicidal rarely
- Judicial execution

# DIGITALIS PURPUREA

- This is a poisonous plant.
- Its root, leaves, & seeds contains several glycosides

- ✓ Digitoxin,
- ✓ Digitalin,
- ✓ Digitalein,
- ✓ Digitonin

# DIGITALIS PURPUREA

- **Cumulative action.**

- **<u>Main toxic effects are</u>:**

  - Irritation of stomach,
  - Slowing of heart rate leading to heart block,
  - Extra systoles
  - Ventricular fibrillation.

# SIGNS & SYMPTOMS

Nausea, Vomiting, Abdominal pain, Diarrhoea, Depression, Headache & Giddiness.

Toxic effect on heart includes Bradycardia (rate may fall to 20 per minute), heart block, extra systole & fibrillation

There is feeling of faintness & precordial oppression.

The respiration become slow & sighing.

The patient becomes drowsy & the condition may deepen into coma.

Convulsions may precede death

# FATAL DOSE & FATAL PERIOD



**Fatal dose :**

Digitalin 15-30mg

Digitoxin 4mg

**Fatal period:**

Varies from ½ hrs to 24 hrs

# TREATMENT



- Stomach wash with solution of tannic acid.
- If parts of plant is taken then bowels should be evacuated.
- Atropine in dose of 0.6 mg should be given hypodermically to combat bradycardia.
- Potassium salts may be given to reduce extrasystoles provided the kidney function is normal.
- Specific antidotes such as Novocaine or Propanolol for digitalis induced arrhythmias are helpful.
- Trisodium EDTA may help to lower serum calcium.
- The rest of the treatment is symptomatic.
- ECG monitoring is necessary as a guide to treatment.

# POSTMORTEM APPEARANCE

- These are not characteristic Irritation of gastric mucosa & digitalis leaves or seeds may be found in the stomach.

- The seeds are reddish brown, remarkably small & somewhat angular in shape with peculiar markings

# MEDICO LEGAL ASPECTS

- **Accidental** from an overdose of medicinal preparation or from eating leaves by mistake.
- **Homicide** poisoning is recorded & it is interesting to note that *no suspicious* of poisoning may arise in such cases.
- Rarely it may be used to stimulate the heart & result in death.

# Oleander

# OLEANDER

- Three types ……

1. Nerium Odorum (White ,Pink)
2. Cerebra Thevetia (Yellow )
3. Cerbera Odollum (Dhakur, Dabur)

Toxic Parts :

All parts of plant mainly fruits and seeds

Toxic Principles :

Toxic Principles are glycosides.

# 1. NERIUM ODORUM (WHITE, PINK)

- **Neriodorin :**

  The principal action of neriodorin is similar to that of digitalis causing death from cardiac failure.

- **Neriodorein :**

  Picrotoxin like effect, i.e. it causes muscular twitching & tetanic spasms more powerful than those of **strychnine .**

- **Kerabin :**

  Acts on the heart like digitalis & on the spinal cord like strychnine

# 2. CEREBRA THEVETIA (YELLOW )

- **Thevetin** :
  Powerful cardiac poison.

- **Thevotoxin :**
  less toxic than thevetin & resembles the glycosides of digitalis inaction.

- **Cerberin**
  Action like strychnine.

# OLEANDER

- Action :

Act like Digitalis , leading to cardiac failure and convulsion with lethal dose.

- Route of administration

1. Skin
2. GIT

# *SYMPTOMS & SIGNS OF* NERIUM ODORUM

- Abdominal pain, vomiting, profuse frothy salivation, followed by restlessness.
- Ingestion causes difficulty in swallowing & often lock jaw
- Pulse is at first slow and weak, BP falls, respiratory rate increased, pupils dilated, muscular twitchings, tetanic spasm.
- This is followed by exhaustion, drowsiness, coma and death occurs from heart failure.

# *SYMPTOMS & SIGNS OF* CEREBRA THEVETIA

- Burning sensation in mouth with tingling
- Dryness of throat, Vomiting, Diarrhoea,
- Headache, Dizziness, Dilated pupils
- Irregular action of the heart.
- Somewhat resembling that due to digitalis,
- Drowsiness, collapse, coma, & death.
- Tetanic convulsions are occasionally observed

# FATAL DOSE & FATAL PERIOD

| Nerium Odorum | Cerebra Thevetia |
| --- | --- |
| About 15 grams of the root can kill an adult. | 8-10 seeds or 15-20 gms of the root prove fatal to an adult. |
| About 24 hours | Death ensuing within 24 hours |

# TREATMENT

- Washing out the stomach & treating the symptoms.
- Administration of anaesthetic is usually necessary.
- Morphine injection seems to be beneficial.

# POSTMORTEM APPEARANCE

## Nerium Odorum

- These are not specific.
- Petechial haemorrhages on the heart are characteristic feature.
- Nerium odorum resists heat & can be detected even from burnt remains of the dead body.

## Cerebra Thevetia

- Signs of gastrointestinal irritation, congestion of various organs, generalized engorgement of veins & subendocardial ecchymosed.
- Yellow oleander resists putrefaction & can be detected even years after death in exhumed putrefied bodies

# MEDICOLEGAL ASPECTS

- **Suicide** with decoction from root, leaves, or fruit of nerium odorum is common among village girls, in certain part of India on account of dowry problems or matrimonial mishaps.

- **Accidental** poisoning is sometimes met with when
  (1) Any part is used as love philter
  (2) Decoction of leaves is applied externally to reduce swelling
  (3) Root is used internally as remedy for venereal diseases or
  (4) Root in the form of a paste is used in treatment of cancerous conditions & other growths.

- **Cattle poison**

- **Abortifacient**

# TREATMENT

- Stomach wash.
- Intravenous administration of molar solution of sodium lactate to combat acidosis.
- 5% glucose solution with102 mg of atropine, 2 ml of adrenaline 1:1000 & 2 mg of noradrenalin (if blood pressure is low) to counteract heart block.

# ACONITE

Kartiknhlmmc

## Monks hood

## Mitha bish

## Blue Rocket


# ACONITE

- Grows in Himalaya ranges.
- All parts are poisonous, the root is most potent.
- The dry root is tapering, slightly arched, usually shrivelled & with longitudinal wrinkles.

# ACONITE

**Chief active principles are:**

**Picraconitine,**
**Peudoaconitine**
**Aconine.**


**Action:**

It stimulates & then depresses the myocardial muscles, Smooth muscles, skeletal muscles, Central nervous system & Peripheral nerves

# SYMPTOMS & SIGNS

- Contact : Tingling & Numbness.
- There is tingling & numbness in the lips, mouth, tongue & pharynx, followed by Salivation, Nausea, Vomiting & Diarrhoea.
- The patient feels giddy, his vision & speech are impaired, the limbs become weak & he is unable to stand or walk.
- Twitching of the muscles & convulsions may occur.
- The pulse is slow & irregular when collapse takes place.
- Hipus :The pupils alternately contract & dilate but remain fully dilated in later stage.
- Death ensues from cardiac arrhythmia or respiratory paralysis.

# FATAL DOSE & FATAL PERIOD

- One gram of the **root**
- 250 mg of the **extract**
- 25 drops of the **tincture**
- 4 mg of the **alkaloid** prove fatal.

- The average fatal period is about **six hours**

# ACONITE

## Treatment

- **Gastric lavage** with solution of tannic acid or strong tea or potassium permanganate to precipitate any remaining alkaloid.
- The **heart** may be supported by hypodermic injection of atropine 1 mg, or digitalin 0.25 mg.
- **Cardiac arrhythmias** may require 50 ml of 0.1 % novocaine given slowly intravenously.
- **Artificial respiration & oxygen** inhalation may be necessary.
- The rest of the treatment is symptomatic.

## Postmortem appearance

- Not characteristic.
- Remnants of the plant may be detected in contents of stomach.
- The odour of chloroform may be perceived when the liniment is swallowed.
- Aconite is largely destroyed in the body & also by alkalis. It is therefore difficult to detect it after death.

# MEDICOLEGAL ASPECTS

- Accidental poisoning occurs from

  (1) Eating root in mistake for horse-radish root

  (2) Quack remedies

  (3) Therapeutic application of liniment containing aconite or drinking it

  (4) When added to liquor for a greater kick.

- Homicidal cases are not uncommon.
- Arrow poison
- Cattle poison
- Abortifacient

Kartiknhlmmc

# Nicotine
# Tobacco

# NICOTINE

- **Tobacco**
- **Nicotiana tabacum.**
- **Toxic Part:**

  Dried Leaves

  All parts of the plant except the ripe seeds.
- **Toxic Principle:**

  **Nicotine** a pyridine derivative alkaloid

  Colourless liquid

# NICOTINE

## Actions:

Nicotine first stimulates then depresses & later paralyses autonomic ganglia, Midbrain, Spinal cord, Muscles

## Uses

Nicotine is used extensively in agricultural & horticultural work as fertilisers, fumigants & insecticide sprays.

## Route of Absorption

Absorbed via skin and oral

# MILD POISONING

## ***Symptoms & Signs:***

Chewed or smoked for the first time or when insecticide spray has been inhaled.

- Dizziness,
- Nausea, Vomiting,
- Headache,
- Perspiration,
- General weakness
- Mild rise in blood pressure with Increased pulse rate may occur.

- These symptoms subside in a few hours.

# MILD POISONING

Occurs when nicotine is *absorbed in poisonous* amounts.

There is burning in the mouth, Throat & Stomach followed by rapid progression of the symptoms of mild poisoning, passing into prostration, convulsions respiratory slowing, cardiac irregularity & coma

Death may occur from cardiac arrhythmia exhaustion or respiratory failure

# CHRONIC POISONING

***Symptoms & Signs:***

- Continued use of tobacco by chewing, smoking or from exposure to nicotine during processing, storage or insecticide spray.
- Chronic cough
- Laryngitis pharyngitis & Bronchitis
- Stains on teeth bad odour in breath
- Angiospasms & Muscular tremors may be found
- Amblyopia, blindness
- Cardiac arrhythmia with extrasystole & chest pain suggesting angina pectoris.
- Cancer of mouth, tongue, throat larynx & lungs is common

# FATAL DOSE & FATAL PERIOD

60 mg of Nicotine

2 gms of Tobacco.

One cigarette contains one gram of tobacco, about half the lethal dose.

A teaspoonful of insecticide is fatal.

- Death may occur rapidly in a few minutes when nicotine is swallowed.
- In some cases, it may be delayed for a few hours.

# TREATMENT



- If nicotine has contaminated the skin, it should be removed by flooding the skin with water & scrubbing it vigorously with soap.
- If it is ingested, stomach should be washed with warm water containing activated charcoal, tannic, potassium permanganate.
- A purgative such as sodium sulphate 15gms in 100 ml of water is useful.
- Artificial respiration & oxygen may be necessary.
- Rest of the treatment is symptomatic.
- Those with chronic nicotine poisoning should be removed from the risk of further exposure.
- Patients with leukoplakia, hyperacidity, peptic ulcer, respiratory problems, high blood pressure, angina, thromboangiitis obliterans & tobacco amblyopia should stop smoking permanently.

# POSTMORTEM APPEARANCE

- These are those of asphyxia.
- There may be characteristic smell in stomach with brown discolouration of its wall if nicotine has been swallowed or of the skin if it has been spilled.
- Depending on the strength of the poison, there may be gastric irritation & pulmonary oedema.
- Nicotine resists putrefaction

# MEDICOLEGAL ASPECT



- Nicotine is a drug of addiction & leads to psychological dependence.
- Its use lead to serious, oral, dental, respiratory & cardiac problems resulting in chronic disability & decreased life expectancy.
- Poisoning is mainly

**Accidental** from

(1) chewing large dose

(2) ingestion of the decoction

(3)absorption through the skin when applied as a poultice

(4) excessive smoking or

(5) exposure to fertilisers, insecticides & fumigants.

Tobacco has been used for **infanticide** in certain parts of India.