

Principals of Management of Poisoning

Dr.Shaluka Jayamanne

Summary of Lecture

- General Principles in the Management of any Poisoning
- Specific management options with certain substances
 - Pesticides
 - Plant Poisoning
 - Drugs - Paracetamol

Accidental?



Deliberate?



The Case....

- Picture yourself in Polonnaruwa hospital – Intern
- Ward 6 , teaming with patients....
- nurse tells you there is a sick patient
 - 36yo F
 - Taken 100mls of Dimethoate after a domestic argument
- There's nowhere to run, or hide.... So you see the patient – what do you do?

Important Steps in the Management

- Resuscitation
- Gastric Decontamination
- Specific Management- antidotes
- Monitoring
- Management of Complications
- Psychiatric assessment

General Management -History

- Applies to ANY episode of Poisoning
- WHAT
- HOW MUCH (Ideally mg/Kg)
- WHEN
- WHAT ELSE (Including Alcohol)
- WHY
- Use Health care staff, friends, relatives, anyone!!

General Management -Resusitation

- A (Airway)
- B (Breathing)
- C (Circulation)
- D (Disability-AVPU/ Glasgow Coma Scale)
- DEFG (Don't ever forget the Glucose)
- GET A SET OF BASIC OBSERVATIONS

General Management –Identify the Poison Clinical Signs

- Use all your senses, search for the clues
- LOOK
 - Track Marks
 - Pupil Size
- FEEL
 - Temperature, Sweating
- SMELL
 - Alcohol

Specific Management Options- Decontamination

- DECREASING DRUG ABSORPTION
 - Gastric Lavage
 - Absorbents Activated Charcoal

Absorption

- Avoid forced emesis
- Gastric lavage
 - Only if within 1 hour & life-threatening amount
 - Never for corrosives
 - If ↓ LOC intubate
- Activated charcoal
 - 50 g single or repeated dose (\uparrow elimination)- effective in first 2 hours may be useful even later in certain poisons Kaneru
 - Doesn't bind heavy metals, ethanol, acids

Specific Management Options – Poison elimination

- INCREASING DRUG ELIMINATION
 - Alkaline Diuresis (Aspirin)
 - Haemodialysis (Aspirin)

Specific Management Options - Antidotes

- ANTAGONISING THE EFFECTS OF THE POISON
 - Desferrioxamine (IRON)
 - Naloxone (OPIATES)
 - N Acetylcysteine (PARACETAMOL)
 - Pralidoxime- OP

Investigations

- **Always** check blood glucose.
- Send blood & urine for toxicology screening.
- measure paracetamol & salicylate levels.
- U&Es, LFTs, glucose, ABG, clotting, bicarbonate
- ECG, CXR
- Specific blood levels

Organophosphate Pesticide Poisoning

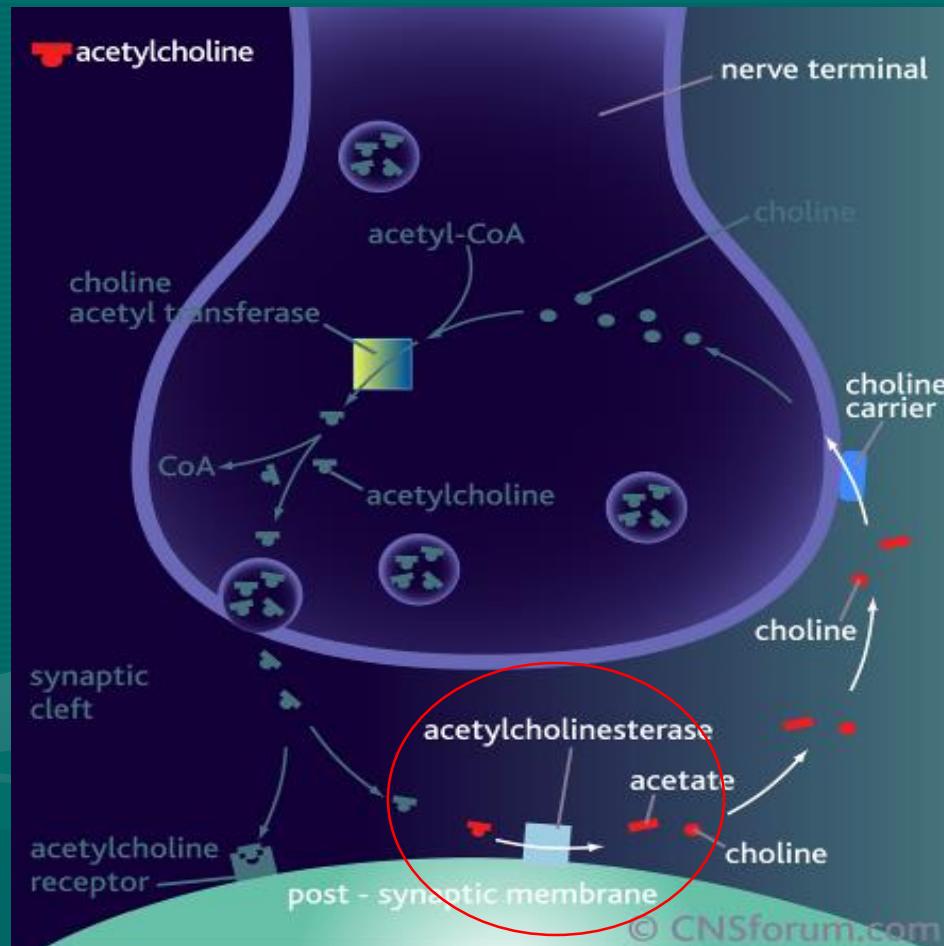


Organophosphate Poisoning in Sri Lanka

- Case Fatality rates (CFR)
 - 10-20% for most
 - 50-70% for some OP's
- In west CFR
 - 0.3% from all poisons
- Multifactorial
 - Toxicity of OP's
 - Patient transport
 - Lack of resources
 - Training



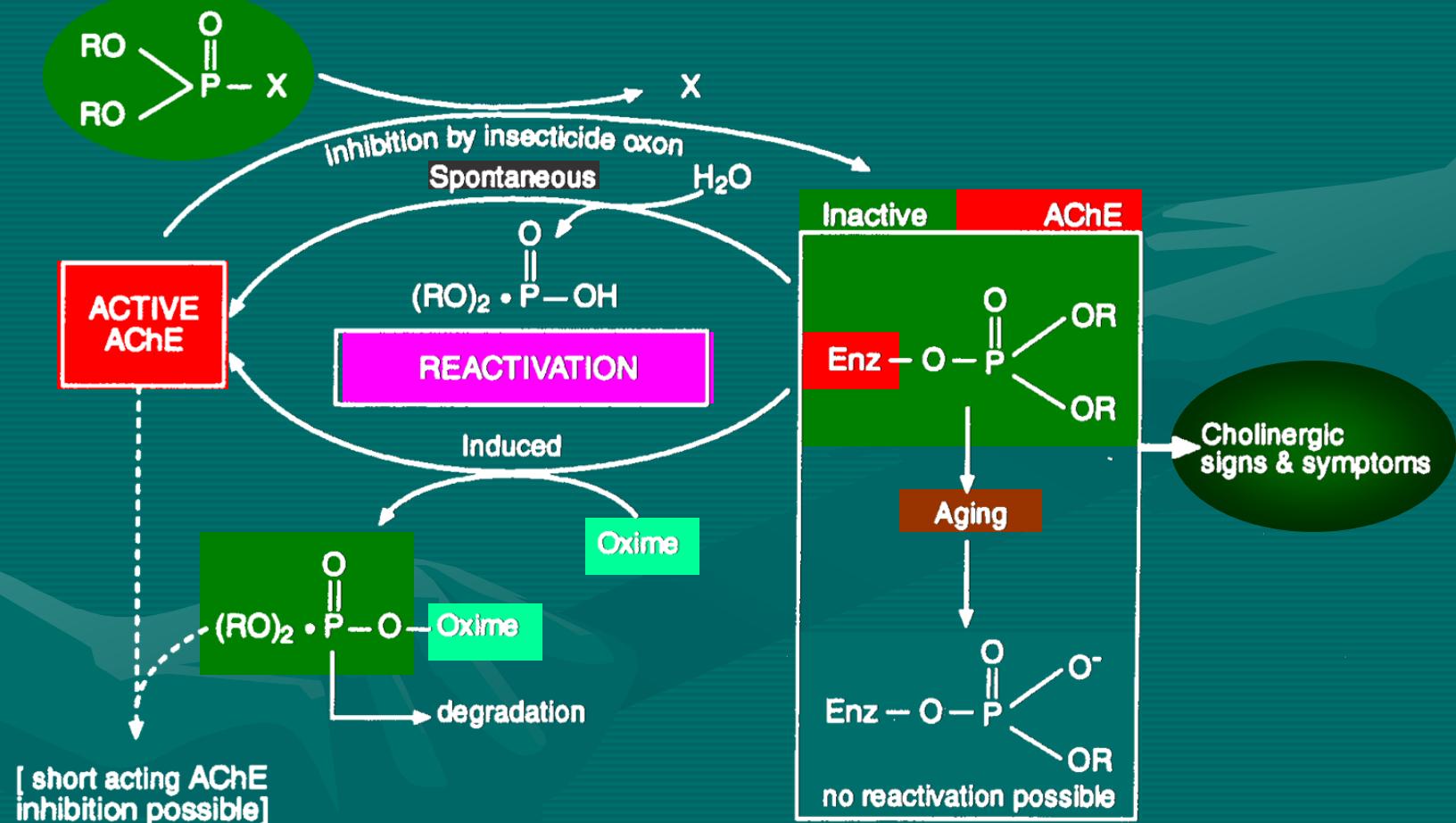
Mechanism of OP's



~~Simplified Acute OP Toxicity~~

- Inactivation of acetylcholinesterase enzyme

Organophosphate



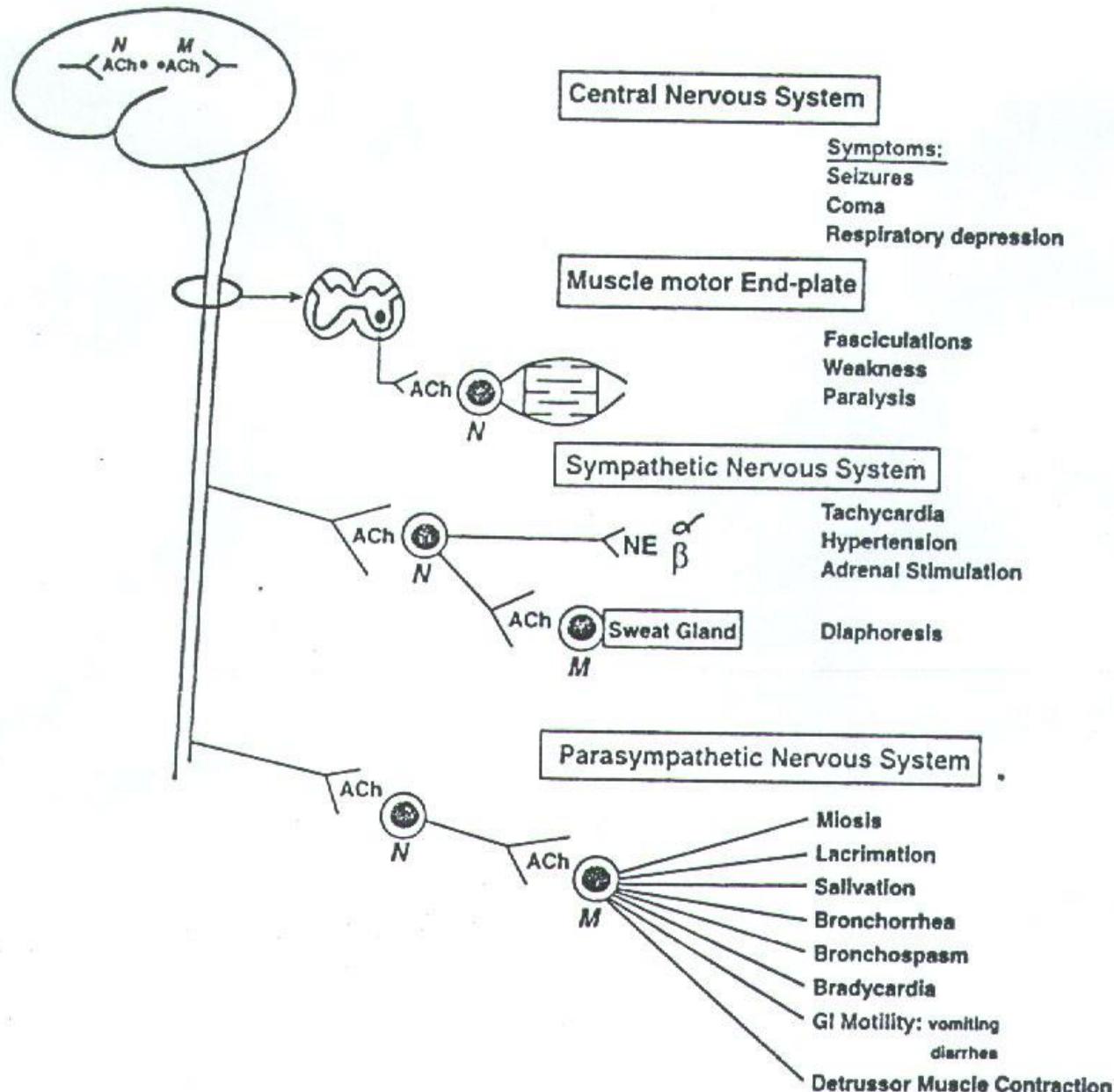
Clinical Syndrome

- Clinical Syndrome
- Acute Cholinergic:
 - Central
 - Peripheral Muscarinic
 - Peripheral Nicotinic
- Intermediate Syndrome
- OPIDN: Delayed peripheral neuropathy
- Neurocognitive dysfunction



Respiratory
failure

+ Death



Cholinergic Effects

- Diarrhoea
- Urination
- Miosis
- Bradycardia, Bronchorrhoea, Bronchospasm
- Emesis
- Lacrimation
- Salivation

CNS effects

- Malaise
- Memory loss
- Confusion
- Disorientation
- Delirium
- Seizures
- Respiratory centre depression or dysfunction
- Coma

Intermediate Syndrome

- Delayed Respiratory Failure
 - Proximal muscle weakness and cranial nerve lesions
 - Typically 1-4 days after cholinergic crisis has resolved
- Prolonged Effects on Nicotinic receptors
- Primary motor end plate degeneration
- Clinical importance
 - Delayed respiratory failure leads to death if not aware of it or prepared for it

Chronic Effects

- Organophosphate induced delayed neuropathy (OPIDN)
 - 1-3 weeks
 - Peripheral neuropathy
 - Axonopathy due to Neuropathy Target Esterases (NTE)
- Chronic organophosphate induced neuropsychiatric disorder (COPIND)

Management

The priorities in management are to:



- Resuscitation
- Atropinisation of symptomatic patients
- Decontamination
- Other Treatments - Pralidoxim

Antidotes

- Atropine
- Pralidoxim
 - Expensive



? Dose
? Duration
?
Effectiveness

Does the patient need atropine?

- How much and for how long

Atropine

- Loading
 - Doubling dose regime e.g. 2 4 8 16 mgs every 5 minutes
- Maintenance
 - Continuous infusion < 3mg/hr
 - 10-20% of loading dose/hour
- Endpoints
 - Clear chest on auscultation with no wheeze
 - Heart rate >80 beats/min
- Withdrawal
 - Atropine toxicity
 - Clinical Improvement

What if you give too much Atropine ?

- Anticholinergic Syndrome:
 - Hot as hell
 - Blind as a bat
 - Red as a beet
 - Dry as a bone
 - Mad as a hatter



Pralidoxim

- Ineffective in some situations
 - Ageing
 - Variation between organophosphates
- Protocol
 - 1g 6 hourly

Summary

- OP's are Indirect Cholinomimetic
 - Block AChE, prolonged duration of ACh in synapse
- Effects
 - Muscarinic, Nicotinic, CNS
 - Respiratory failure and Death result from this
- Treatment
 - ABC's, Atropine, Decontaminate, Oximes
- Important also in West

Other Pesticides

- Carbamates
- Management and clinical presentation is same as OP
- PAM is not effective
- Same regimen of Atropin

Paraquat Formula

Paraquat

Diquat

2,4dichlorophenoxyacetic acid

**Color : Blue-green
emetic agent**

Paraquat

A leading cause of suicide



Paraquat in Sri Lankan agriculture



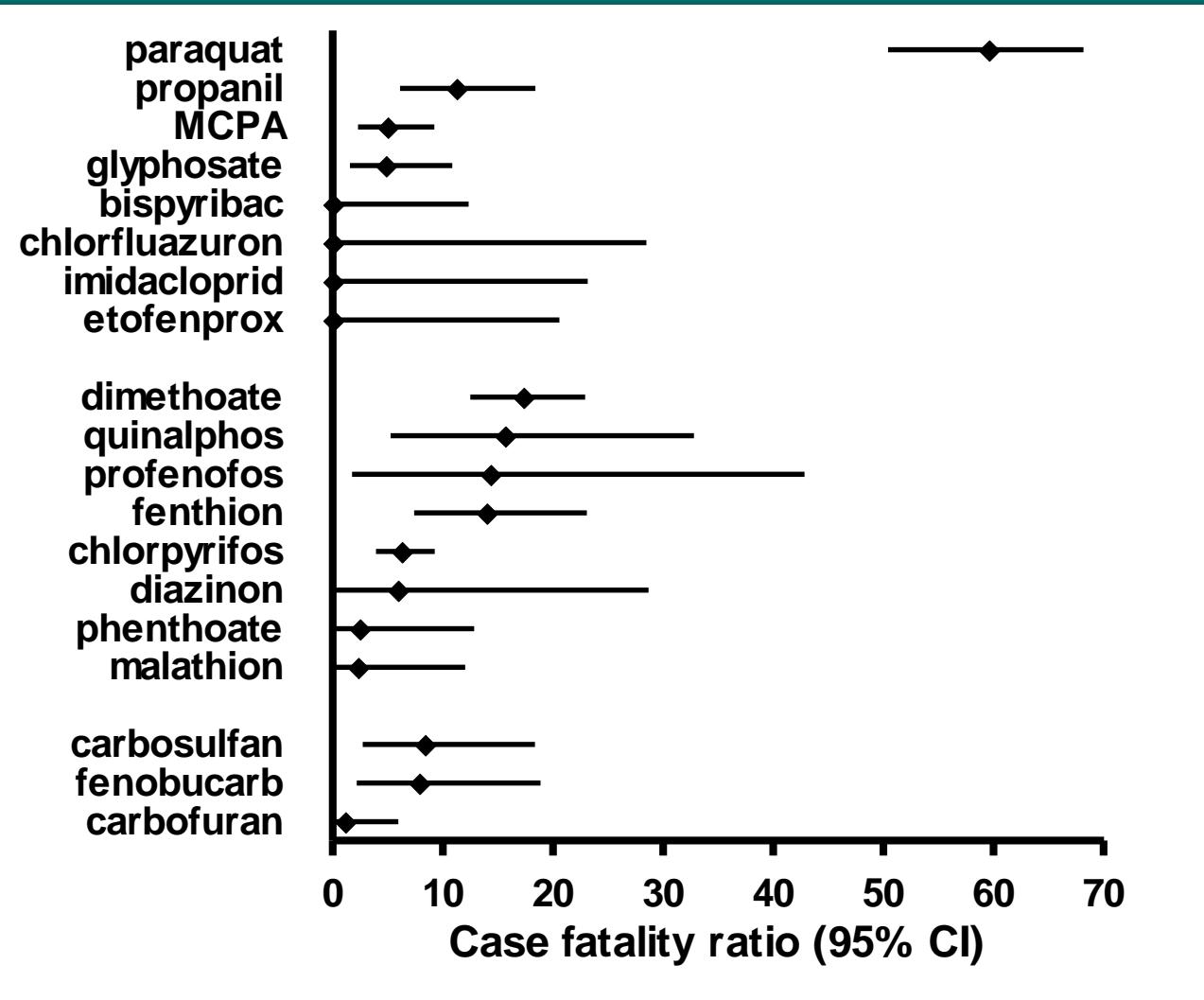
- No damage to surrounding crops
- Broad spectrum, no weed resistance
- Key crops in Sri Lanka are tea and rice

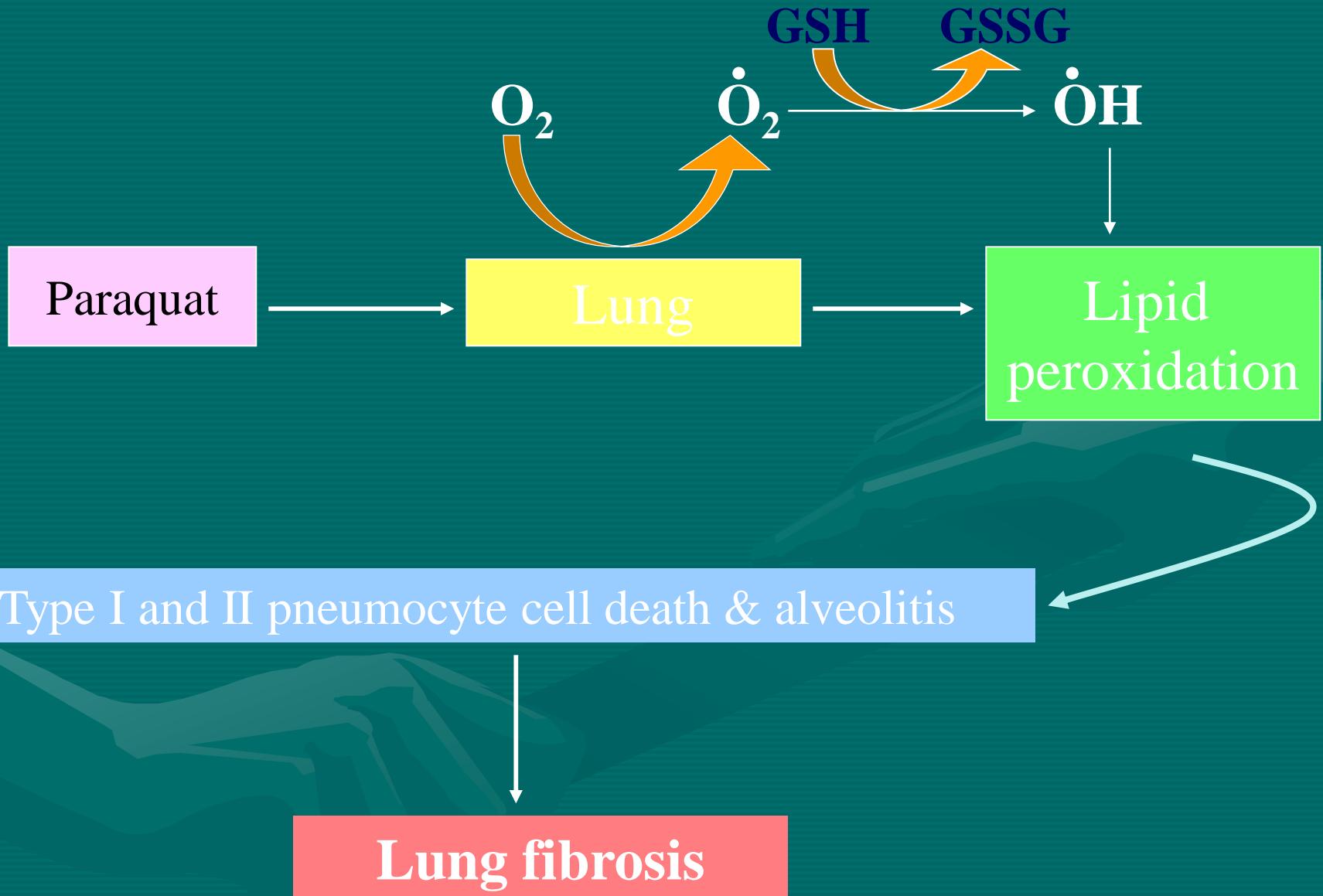
- Non-systemic, fast acting
- Rain-fast, quickly deactivated in soil
- No tillage preserves soil structure



Predictors of Death

Case Fatality Rates of pesticides in self-poisoning





Paraquat

- Cause oxidative damage– Oxygen free radicals
- Early--- Hypotension and multi organ failure– Death
- Late-- up to 2-4-weeks – Pulmonary fibrosis Liver failure
- Only effective treatment – Gastric decontamination – Activated charcoal / Fullers earth

Other Pestisides

- Propanil- 3-4 DPA
- Causes Methaemoglobinaemia
- Antidote- Methelin Blue IV Oral
- Exchange Transfusions

GLYPHOSATE

- Glyphosate is a non-selective herbicide : of 41% Glyphosate
15% Surfactant
- Glyphosate is an organophosphate but it does not act as an acetylcholinesterase inhibitor in man.
- The surfactant is approximately three times as toxic as glyphosate



Mild

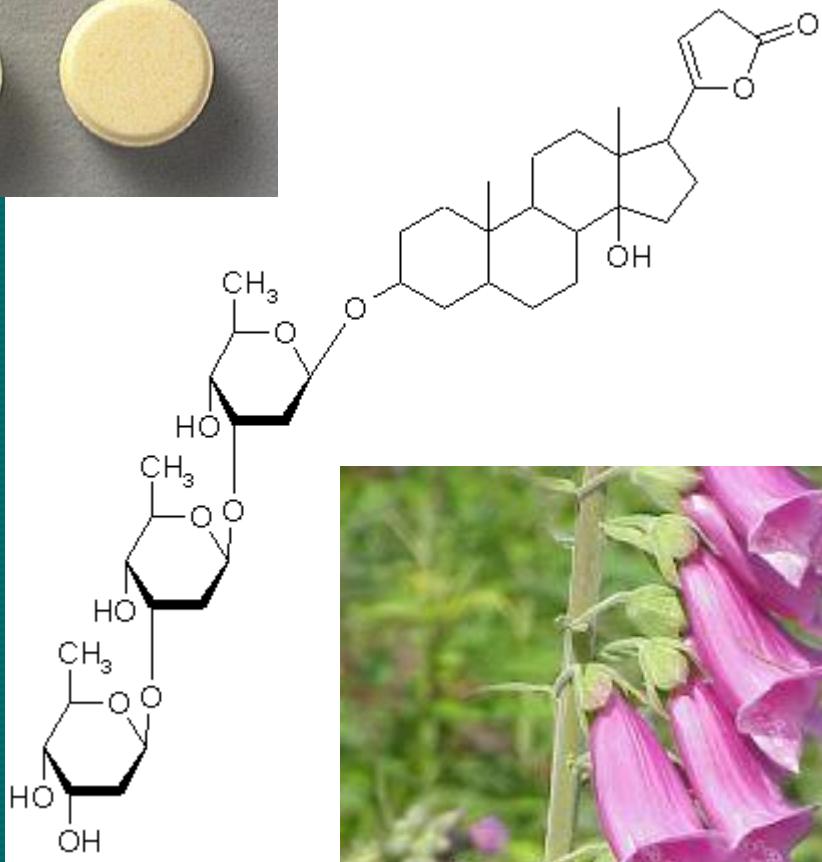
Predominantly
gastrointestinal symptoms

Moderate

Gastrointestinal symptoms
lasting longer than 24 hours
Hypotension Pulmonary
dysfunction. oliguria

Severe

Pulmonary dysfunction requiring
intubation Renal failure requiring
dialysis Hypotension requiring
pressor amines Cardiac arrest Coma
Repeated seizures Death



Plant Poisons

- Kaneru
- Niyangala
- Enderu
- Divi Kaduru
- Diya Kaduru
- Goda Kaduru
- Olinda
- Habarala
- Attana



P. Schönfelder

Symptoms of substantial oleander poisoning

Cardiac dysrhythmias

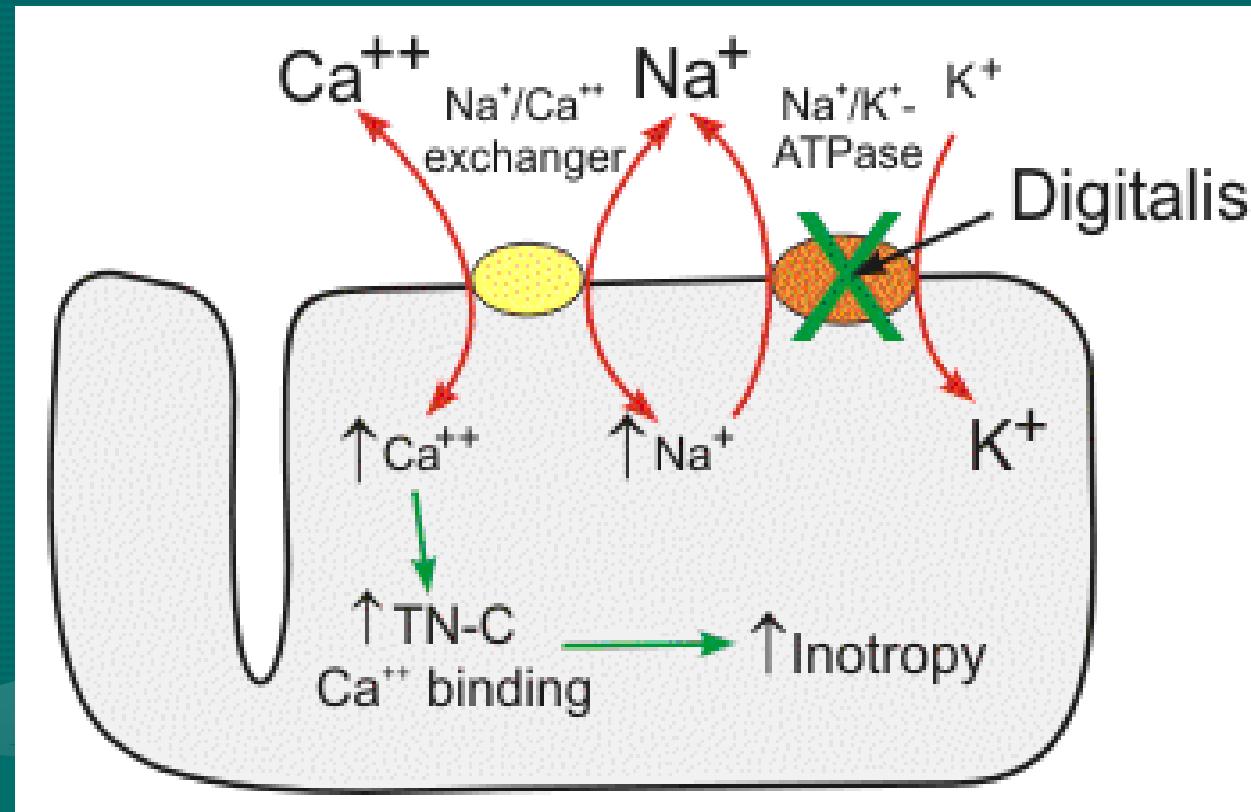
- Nausea
- Vomiting
- Weakness
- Fatigue
- Diarrhoea
- Dizziness
- Abdominal Pain
- Visual Symptoms

Mode of Action

inhibit sodium-potassium ATPase

- increased intracellular sodium and serum potassium
- negative chronotropic, positive inotropic effects

Effect of cardiac glycosides



Consequences of cardiac glycoside binding 1

- Rises in intracellular Ca^{2+} and Na^+ concentrations
- Partial membrane depolarisation and increased automaticity
- Generation u waves that may trigger dysrhythmias

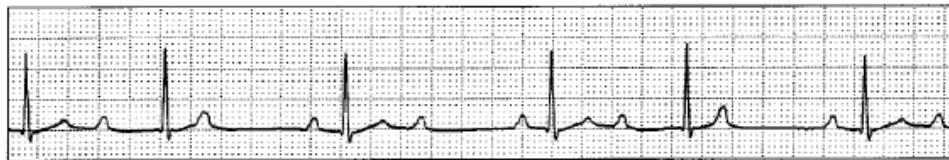
Consequences of cardiac glycoside binding 2

- Decrease in conduction through the SA and AV nodes
- Due to increase in vagal parasympathetic tone and by direct depression of this tissue

$t = -5\text{min}$



$t = 30\text{min}$



$t = 60\text{min}$



$t = 2\text{hrs}$



$t = 8\text{hrs}$



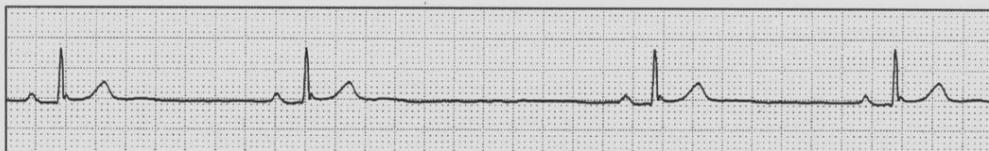
$t = 48\text{hrs}$



Yellow oleander cardiotoxicity



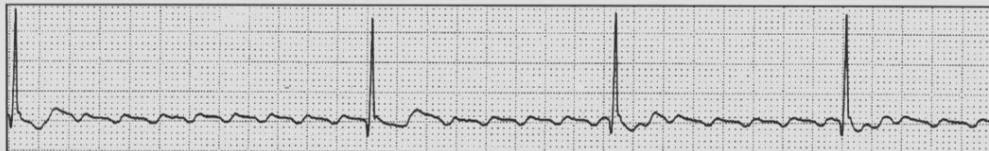
A



B



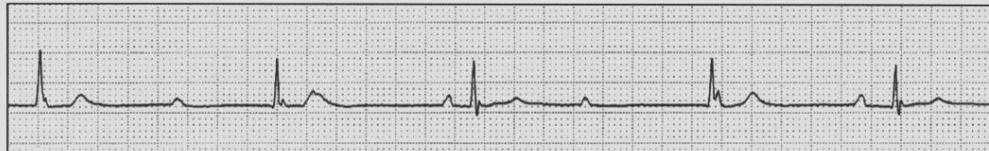
C



D



E



F



Standard treatment

Only two interventions have been carefully studied

- **Anti-digoxin/digitoxin Fab**
- Activated charcoal

Both these treatments work by affecting the pharmacokinetics of the cardiac glycoside, by:

- speeding elimination and/or
- reducing absorption

Gloriosa superba

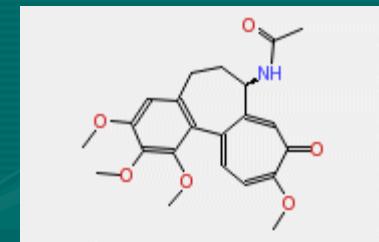
NIYAGALA





Main toxic constituents:

colchicine



Mode of action:

- Colchicine has an antimitotic effect

Niyagala

Clinical features of poisoning:

- **Initial symptoms**
 - develop within 6-12 hours of ingestion
 - burning pain, numbness, itching and tingling around the mouth and throat with thirst
 - nausea, intense vomiting
 - abdominal pain, severe diarrhea with blood and mucus
- **These lead to**
 - electrolyte imbalance, dehydration, hypovolaemic shock manifested hypotension and tachycardia

- **After 24 hours** patients develop
 - Muscle weakness, myoglobinuria, bronchial constriction, leucopenia, thrombocytopenia, clotting defects with bleeding, polyneuropathy cardiac arrhythmias, hepatic insufficiency, acute renal failure
- **In severe cases** there may be
 - Respiratory depression, confusion, delirium, convulsions,
 - **Death** occurs due to shock or respiratory failure



Management

- Aggressive early gastrointestinal decontamination - Charcoal
- Intensive supportive care
 - Fluid and electrolyte replacement
 - Ventilatory and vasopressor support
 - Blood and coagulation products
 - Antibiotic treatment
 - □ G-CSF
 - □ Immunotherapy with anti-colchicine antibodies

Paracetamol

- Commonest drug poisoning
- DANGEROUS AND PEOPLE DON'T KNOW IT. YOU FEEL WELL AND THEN THE LIVER FAILURE SETS IN..

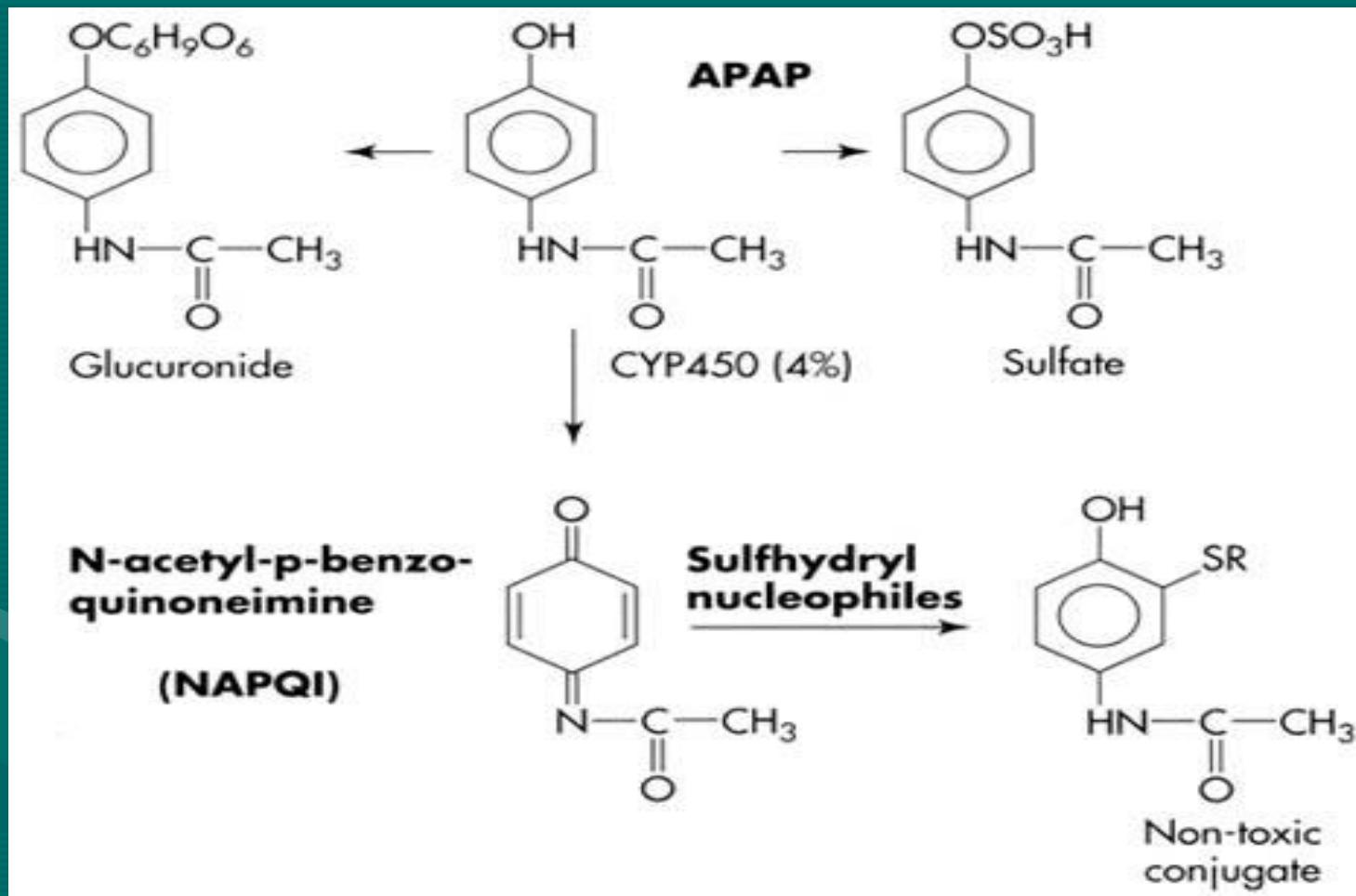
Paracetamol-Normal Metabolism

- Paracetamol converted to:
- N-Acetyl-p-benzoquinonamine (TOXIC)
- This is conjugated with Glutathione
- Glutathione stored in the body
- Produces a NON TOXIC metabolite

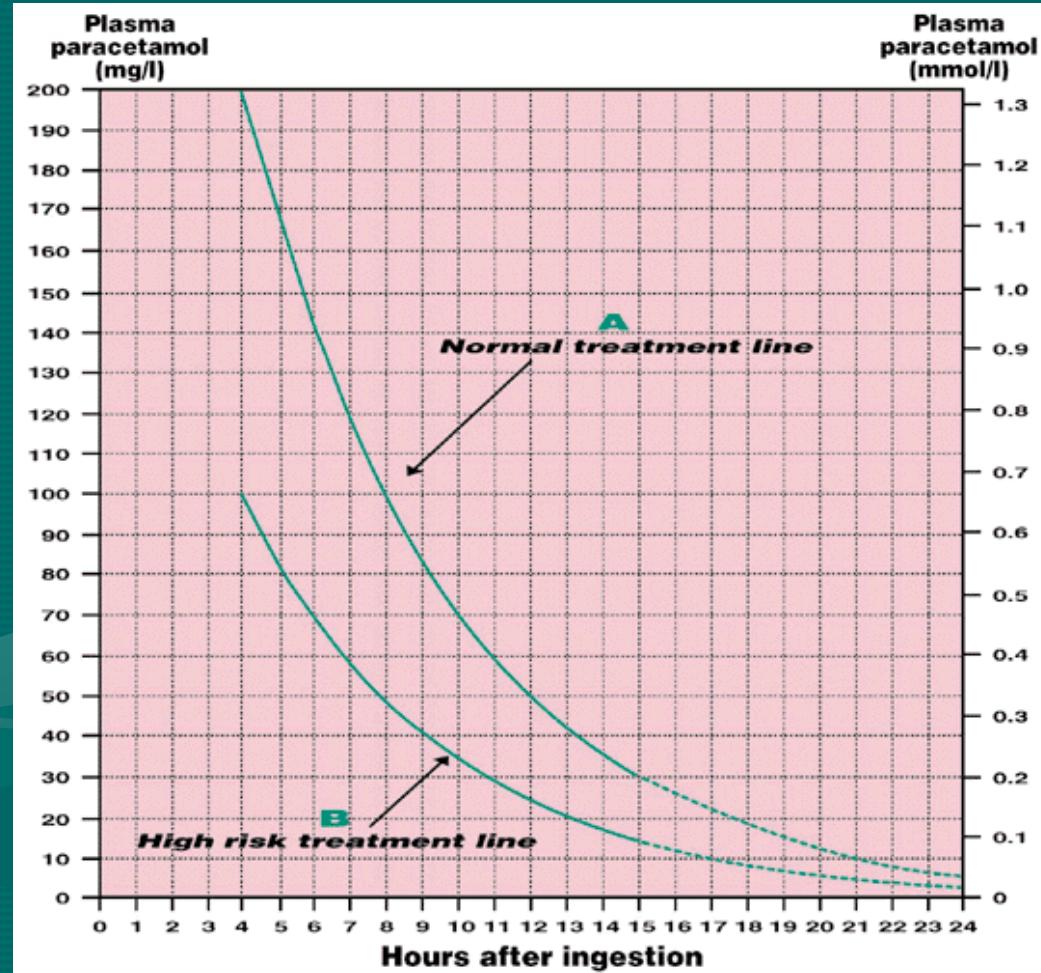
Paracetamol Metabolism in Overdose

- Glutathione stores are used up by the excess Paracetamol
- Toxic Metabolite build up
- Binds IRREVERSIBLY to Hepatic Cell membranes
- Resulting in LIVER NECROSIS

Paracetamol Metabolism



Treatment Graph



Paracetamol Overdose- management

- Initial ABC (usually well systemically)
- Get a good history
 - TIME TAKEN, AMOUNT –10g in adults
 - Any other medication
 - History of Liver disease
- N-Acetylcysteine. Shown to be advantageous if given in the first 10 hours
- Methionine effective in first 6 hours

N - Acetylcysteine

- Specific antidote used for Paracetamol
- Provides the Sulphydryl groups needed to increase the availability of Glutathione
- So that Body can turn the TOXIC metabolite into the non toxic form and prevent Liver Cell Damage and NECROSIS

Aspirin Overdose

- Early features
 - hyperventilation, sweating, tremor, tinnitus, nausea / vomiting, or hyperpyrexia
- Metabolic features
 - Hypo- or hyper-glycaemia, hypokalaemia, respiratory alkalosis, metabolic acidosis
- Others
 - renal failure, pulmonary oedema, seizures, coma, death

Aspirin

- Activated Charcoal
 - 1 hour
- Gastric Lavage
 - less than 1 hour .

Aspirin-Increasing Drug Elimination

- Urinary Alkalinisation
 - If you increase urinary pH from 5 to 8 there is a 10-20 fold increase in the renal salicylate clearance
 - This is done by giving an infusion of Sodium Bicarbonate.

Aspirin- Increasing Drug Elimination

- HAEMODIALYSIS
 - Used in severe life threatening overdose

Management

- General measures
- Activated charcoal
- Rehydrate, monitor glucose, correct acidosis and K⁺
- If levels >500mg/L alkalanize urine (HCO_3^-)
- Levels > 700 mg/L before rehydration, renal failure or pulmonary oedema consider haemodialysis

TCAs -Introduction

- Potentially fatal (2.5 to 3.5g of amitriptyline)
- Neurological and cardiac problems common
- Serious toxicity results from:-
 - Ventricular dysrhythmias
 - Seizures
 - Hypotension
 - Respiratory depression

TCAs-Features of poisoning

- Peripheral
 - Sinus tachycardia, hot dry skin, dry mouth, urinary retention, hypotension and hypothermia may occur
- CNS
 - Dilated pupils, ataxia, nystagmus, squint, ↓LOC, coma, seizures, respiratory depression, ↑tone, ↑ ↓reflexes, ↑ plantars
- ECG
 - prolonged PR and QRS interval, ↑ QT
 - ventricular dysrhythmias

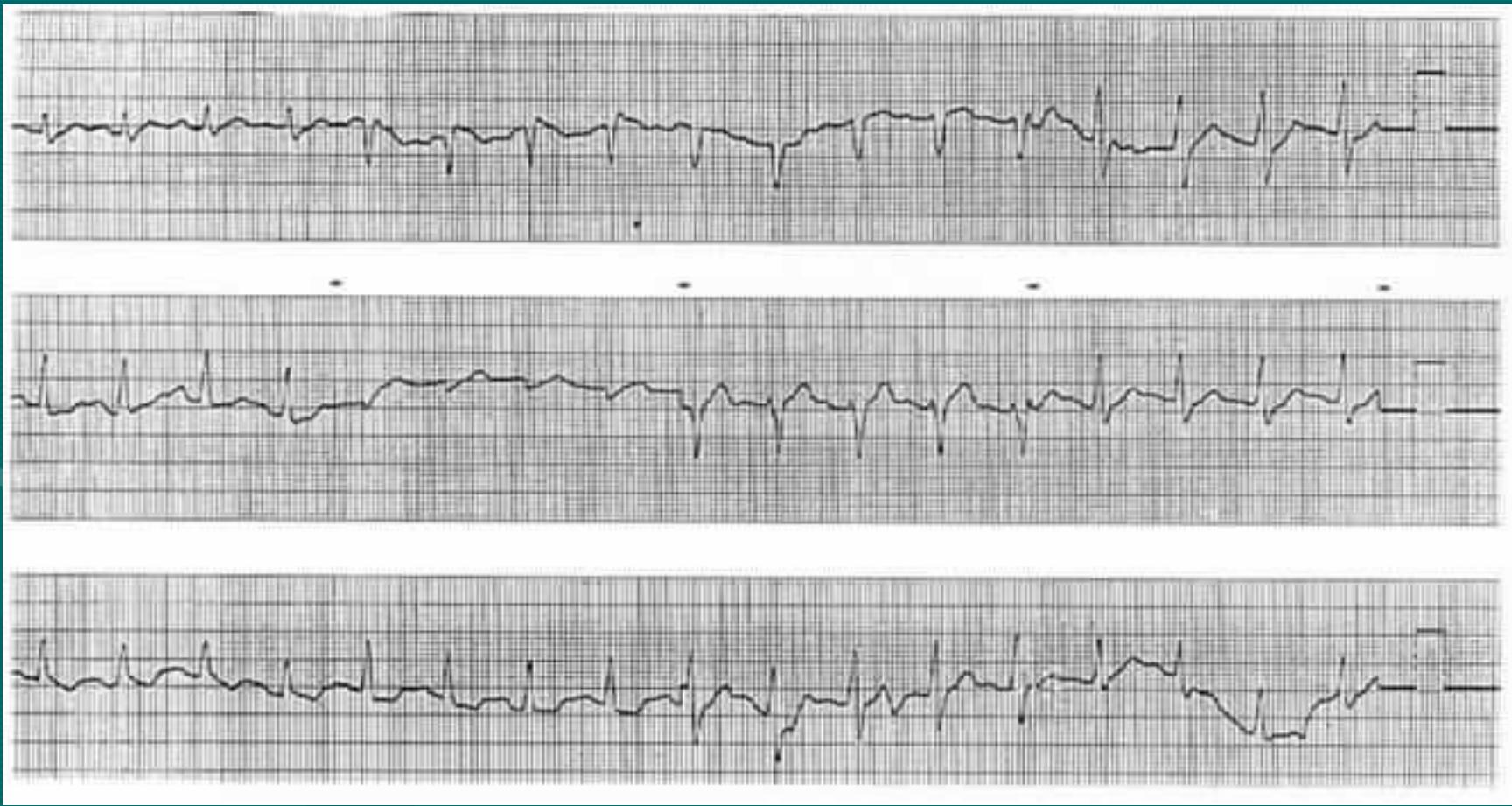
TCA_s -Management

- GCS and QRS, best indicators of toxicity
- Supportive
- Check airway, maintain ventilation, correct hypoxia
- Correct hypotension (crystalloids)
- Gastric lavage if within 1 hr, and activated charcoal
- Rx fits and agitation with diazepam
- Rewarm slowly if hypothermic

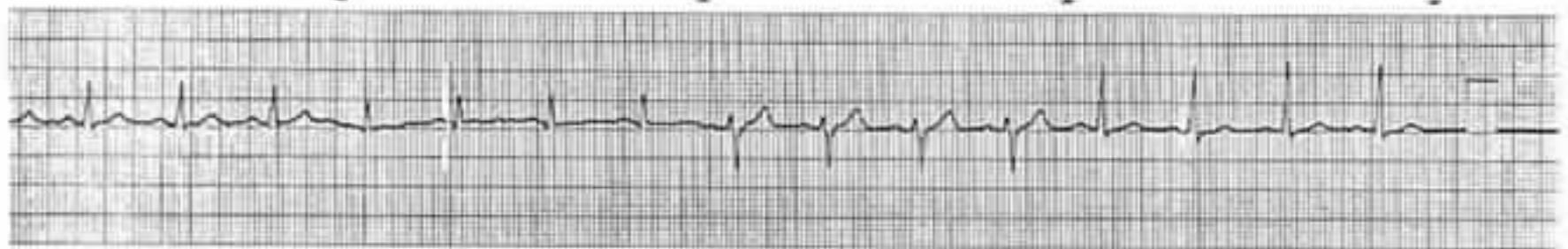
TCA_s- Dysrhythmias

- Careful ECG monitoring is required
 - QRS interval is a guide to cardiac toxicity (>100ms)
- Correct hypoxia and acidosis. Aim for a pH of 7.45-7.50 (no higher)
 - use iv boluses of sodium bicarbonate

Tricyclic OD – Initial ECG



Tricyclic OD – Recovery ECG



Other agents

- Opiates Naloxone
- Iron Desferrioxamine
- Lead Sodium EDTA
- Digoxin FAB
- Calcium blockers Calcium
- Ethylene glycol Ethanol
- Lithium Dialysis

The Case....

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