

# Therapeutic Drugs 1



Dr. Amodha Medagedara

# Objectives

- Principals of management of a patient with drug overdose/poisoning
- Specific management of paracetamol overdose

# Acute poisoning

- A medical emergency
- A common cause of morbidity and mortality



# Case 1

Mangala, a 17 year old girl is brought to the casualty ward by her parents claiming to have taken **25 tablets of paracetamol** after an argument with her parents.

- 1.What are the important aspects in history taking?
- 2.What are the important findings in examination you should elicit?
- 3.What are the useful investigations in managing a patient with poisoning ?
- 3.What would be the basic principals of management?

# History

- What agent? - single/multiple
- Amount
- What time?
- Circumstances – suicidal/ accidental  
/homicidal

# Examination-Poisoning

- Level of consciousness
- Respiratory rate/depth
- Temperature
- Pulse/Blood pressure
- Pupils
- Tone
- Reflexes

# Investigations

- Measurement of blood levels of specific substances
  - paracetamol
  - salicylate
  - lithium
- Toxicological screening of urine and blood

# Other investigations

- Arterial blood gas –acid base imbalance
- Prothrombin time- paracetamol/oral anticoagulants
- Transaminases
- Serum electrolytes
- Serum creatinine
- ECG
- FBC
- CXR (Ex: Paraquat poisoning-consolidation, pneumomediastinum+/- pneumothorax, cardiomegaly+ widening of mediastinum)



# Home work

- Name 2 drugs known to cause hypokalaemia in overdose
- What are the ECG changes expected in toxicity with
  - TCA
  - Digoxin

# Principals of management

- Resuscitation and assessment
- Specific measures
- Anticipate and manage complications
- Psychiatric assessment /support
- Medico legal duties

Majority will not need specific interventions

# Management- Resuscitation

- Airway
- Breathing
- Circulation
- GCS
- Blood sugar

# Management –Specific management

- **Decrease absorption -----  
gastrointestinal decontamination**

- Gastric lavage
- Adsorbents –activated charcoal/Fullers earth
- Whole bowel irrigation



- **Increasing elimination**

- Alkaline diuresis
- Haemodialysis/peritoneal dialysis

- **Antidotes**

# Decreasing absorption of toxic substance – gastrointestinal decontamination

- Consider once patient is stabilized
- Only in patients able to protect their airway and who have taken potentially dangerous amount of a poison
- *Avoid forced emesis*

# Gastric lavage

- Left lateral head down position
- Pass NG tube- check positioning
- 0.9 % NaCl in children/ adults – 0.9% NaCl or water

# Gastric lavage

- Only those who have
  - taken life threatening amount of a poison
  - presenting within 1 -2 hours of ingestion
  - protected airway –conscious or intubated
- Use with close monitoring by a doctor/by trained staff
- Risks of sudden death/aspiration pneumonia/ electrolyte imbalances

# Gastric lavage

- **Contraindications**

- Uncooperative patient
- Unable to protect airway
- Clinically unstable
- Corrosive ingestions –acids/alkali
- Petroleum products – kerosine
- Known oesophageal disease
- Taken harmless substance or small quantities





# Activated charcoal

- Adsorption of poisons to activated charcoal can reduce absorption
- Dose- 1g/kg suspended in 4ml per gram- adults 50g in 200ml –orally
- Most useful within 1-2 h of ingestion
- Not effective for – **alcohol/glycol/acid/alkali/iron/lithium**



# Multiple dose activated charcoal therapy

- >2 doses of activated charcoal
- Useful for certain agents by
  - interrupting enteroenteric, enterogastric & enterohepatic circulation of absorbed drugs
  - absorbing unabsorbed drugs
  - Ex- Mnemonic- *These People Drink Charcoal Quickly*
    - Theophyllin
    - Phenobarbitone
    - Dapasone
    - Carbamazepine
    - Colchicine
    - Quinine
- Also useful for *controlled release preparations* and *oleander seeds*.

# Management –Specific management

- **Decrease absorption ----- gastrointestinal decontamination**
  - Gastric lavage
  - Adsorbents –activated charcoal/Fullers earth
  - Whole bowel irrigation
- **Increasing elimination**
  - **Alkaline diuresis –aspirin**
  - **Haemodialysis – aspirin/lithium/methanol**
- Antidotes

# Antidotes

- Antidote is a substance that counteract the effects of a poison

Poison /drug	Antidote
Paracetamol	N-acetylcystine,Methionine
Beta blockers	Glucagon
Digoxin	Digoxin specific antibody fragments
Iron	Desferrioxamine
Warfarin	Vitamin K
Methanol	Ethanol
Heparin	Protamine sulfate
Organophospate	Pralidoxime
Cyanide	Amyl nitrate

# Case 1

- Mangala, a 17 year old girl is brought to the casualty ward by her parents claiming to have taken 25 tablets of paracetamol after an argument with her parents.
1. What are the important aspects in history taking?
  2. What are the important findings in examination you should elicit?
  3. What are the useful investigations in managing a patient with poisoning ?
  4. What would be the basic principals of management?

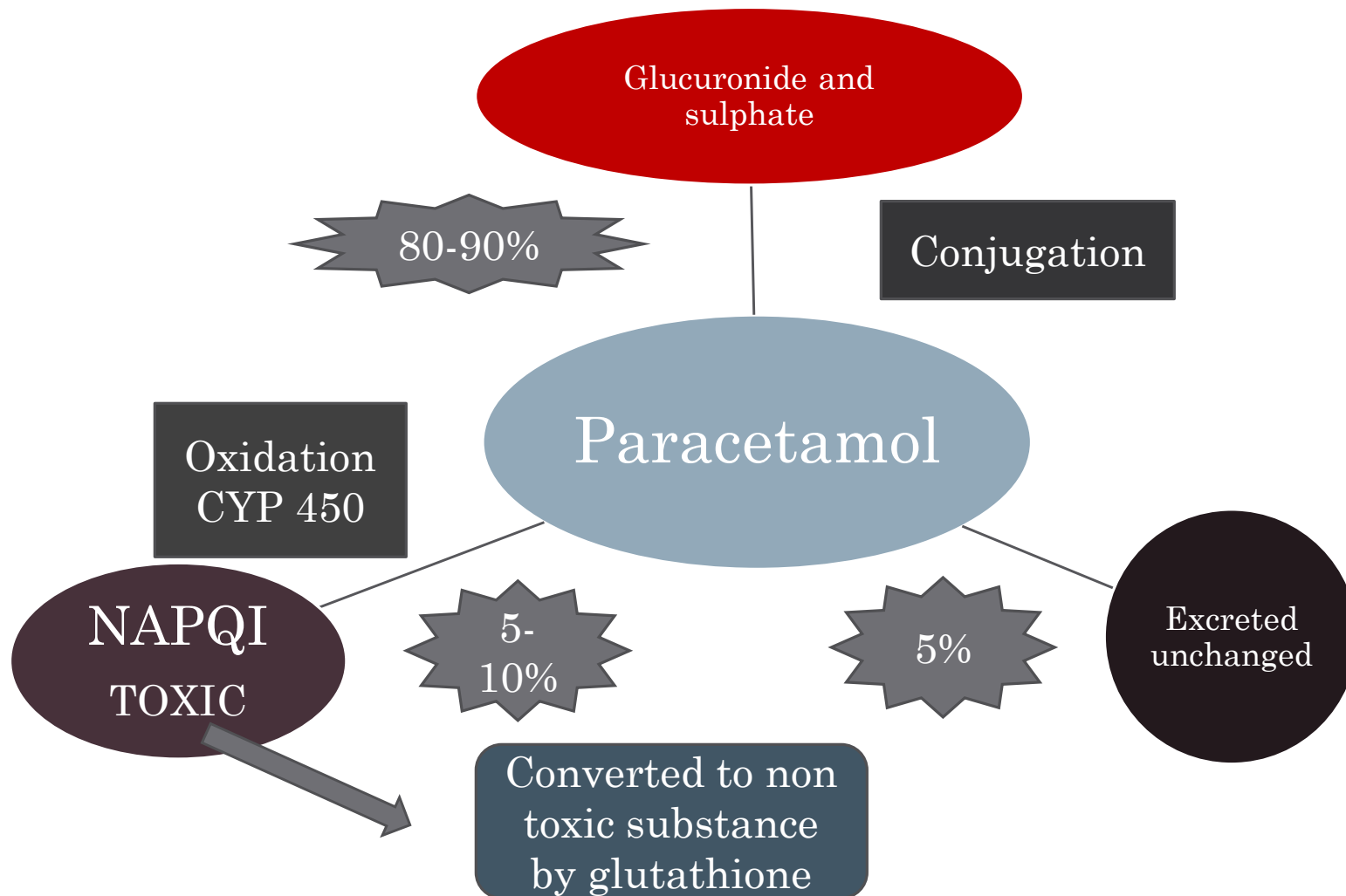
# Case 1 ctd

- On further questioning the patient reveals that the tablets were taken at 1 pm and the time when the doctor sees the patient is 7.30pm.
1. Will you consider gastric lavage for this patient?
  2. Will you consider activated charcoal for this patient?
  3. Does this patient need an antidote ?

# Paracetamol overdose

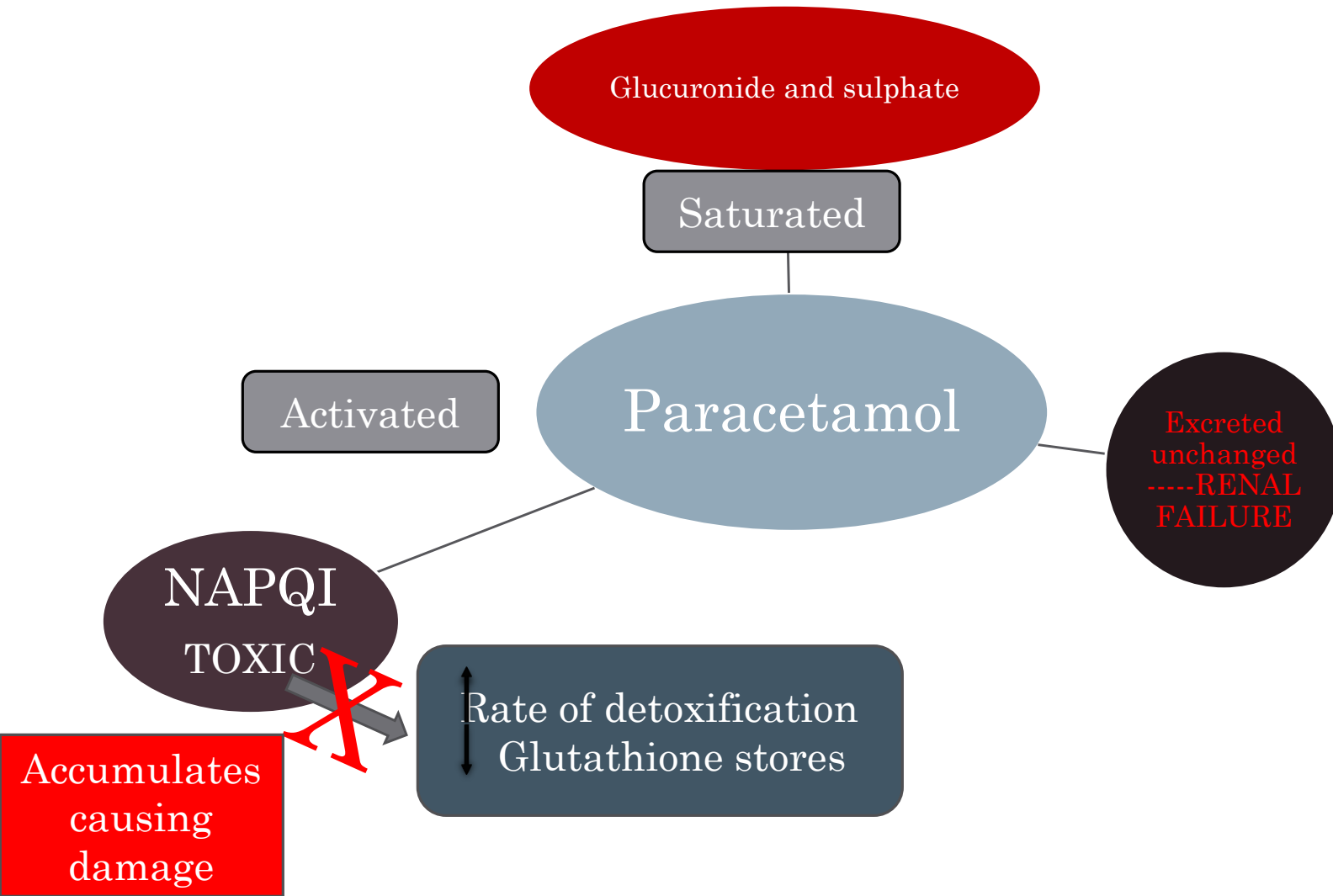
- Most widely used over the counter drug in Sri Lanka
- Responsible for most cases of drug induced deliberate self harm in the country.
- Toxicity is mainly by hepatic injury

# Pathophysiology-Normal metabolism





# Pathophysiology-Overdose



# What is the therapeutic dose of paracetamol?

- Adult dose -1g /6 hourly
- Pediatric dose – 15mg/kg /dose -----  
maximum recommended ---100mg /kg /d
- What are the different dosage forms of paracetamol available?

# MCQ

- Which of the above would be a considered as toxic dose of paracetamol taken as a single ingestion by an adult?
  - a) ingestion of 2 500mg tablets of paracetamol
  - b) Ingestion of 20 500mg tablets of paracetamol
  - c) Ingestion of 100 500mg tablets of paracetamol

# Toxic dose of paracetamol

Single dose of

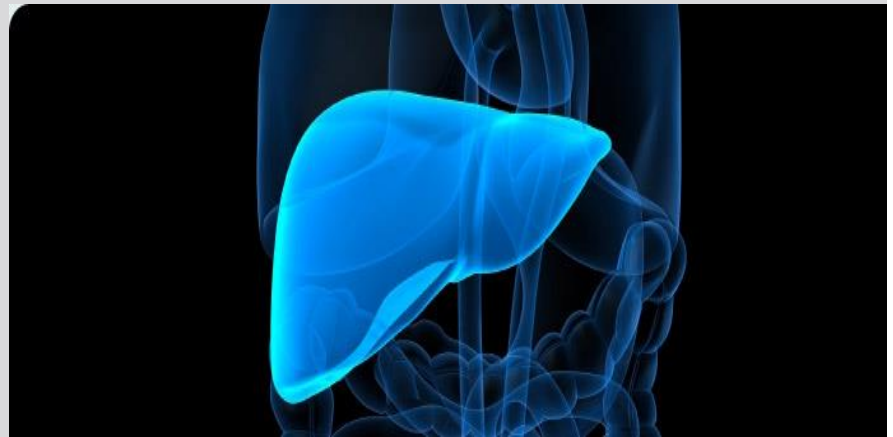
- 10g

OR

- $\geq 200$  mg/kg
  
- Repeated doses  $\geq 200$  mg/kg/d

# Paracetamol overdose – Clinical picture

- 0-24 h : mostly asymptomatic
- 24-72h : after a latent period hepatotoxicity develops
  - asymptomatic except RHC tenderness
  - elevated transaminases
- 72-96h: Liver failure- hypoglycaemia/GI bleeding/cerebral oedema/encephalopathy
  - ATN
  - Metabolic (lactic)acidosis
  - pancreatitis/myocarditis/DIC
- 96h-2 weeks : recovery /death



# Investigations

- **Paracetamol levels**

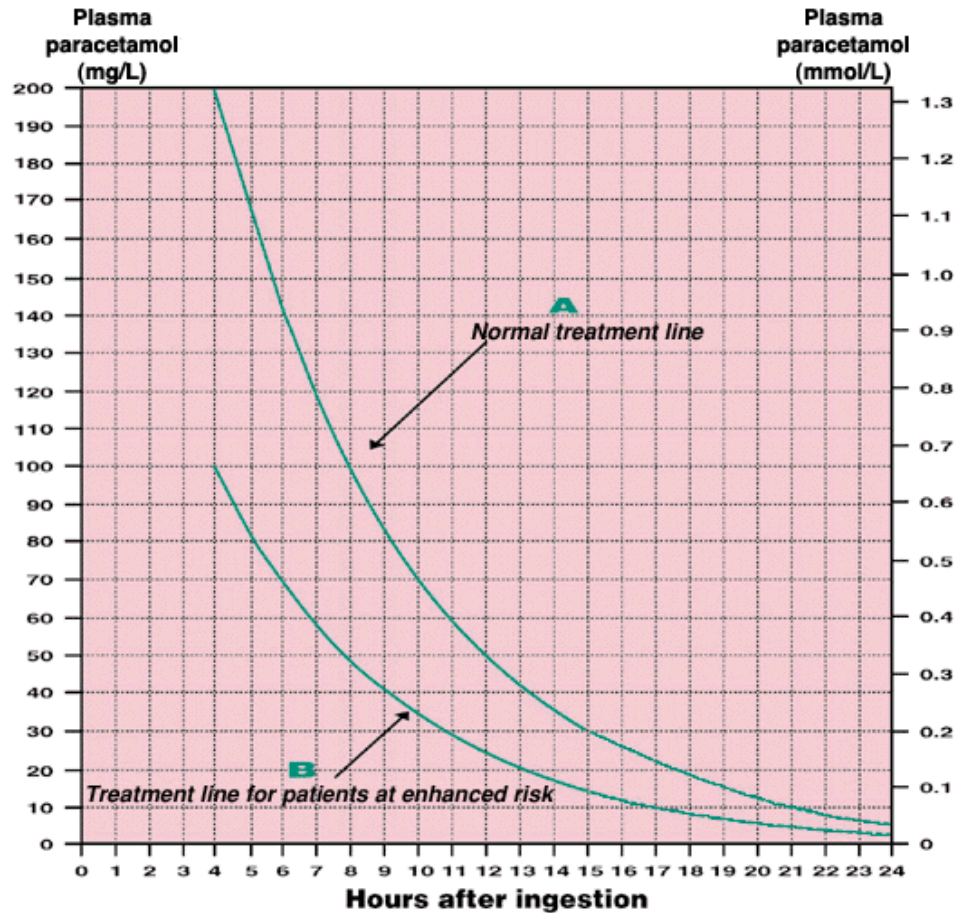
- Useful guide to therapy

- Useful only if done within 4-16h of ingestion.

- Rumack-Mathew normogram is used for interpretation of results

- Limitation: in local setting not readily available

# Normogram



# High risk categories

- Regular excess alcohol usage
- Enzyme inducing drugs- Carbamazepine, Phenytoin, Rifampicin, Phenobarbitone, Primidone
- Glutathione depletion- Malnutrition, Eating disorders, Malabsorption, HIV



# Investigations

- Other investigations –
- Glucose
- LFT-Transaminases/PT/INR
- RFT-Electrolytes
- ABG
- FBC (severe thrombocytopenia in severe overdose)

# Management

- Depends on
  - ☐ amount ingested
  - ☐ timing



# Management

- Reduce absorption
  - Gastric lavage
  - Activated charcoal

Only useful within  
2 hours

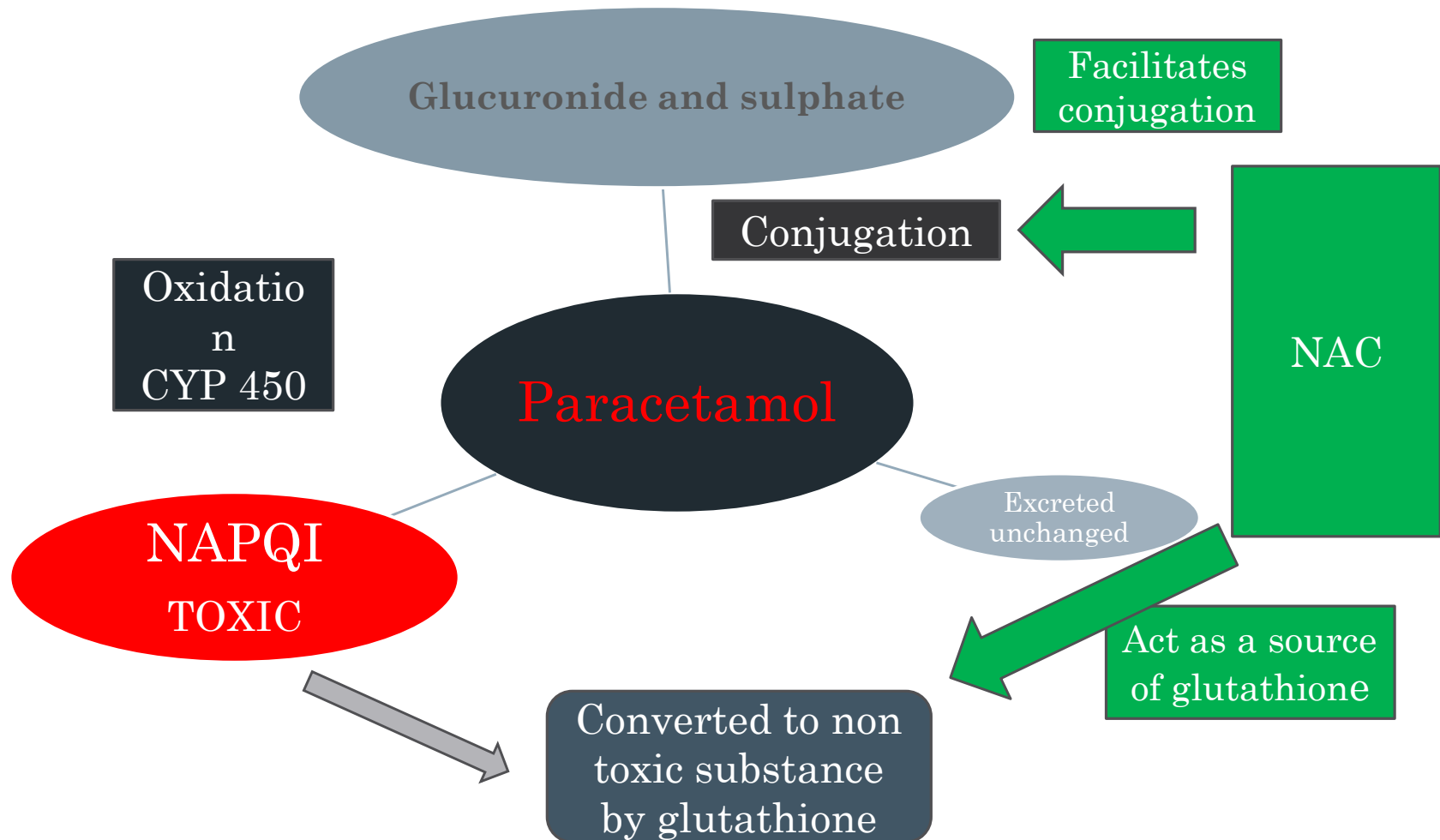
# Management

- Antidote –N- acetylcysteine (NAC)  
Methionine

**NAC-**

- Helps to replenish glutathione;  
which converts NABQI to a less  
toxic form**
- Acts as a source of sulphate and  
facilitates the conjugation pathway  
of metabolism**

# Mechanism of action of NAC



# Management

- **When to give NAC?**

- ingested >toxic dose

- or paracetamol levels above the treatment line when plotted in normogram

- Ideally should start within 8h of ingestion
- Treatment started between 8-24h- Lowers mortality/incomplete protection from hepatotoxicity

# Case 1 ctd

- On further questioning the patient reveals that the 25 tablets were taken at 1 pm and the time when the doctor sees the patient is 7.30pm.
- Does this patient need an antidote ?
- What will be the other important aspects in management ?

# Case 2

- Ajith, a 34 year old driver is brought to the casualty ward of a Base hospital by his wife.

He has consumed 35 tablets of paracetamol 12 hours prior to admission.

He is a regular alcoholic but has not taken alcohol on the day of admission.

1. Would you consider gastric decontamination?
2. What are the investigations you would order on admission?
3. What is the importance of the patient being a chronic alcoholic?
4. Would you consider treating with an antidote? How will you give it?



# NAC dosing

- 150 mg/kg over the first hour (200ml)
  - 50 mg/kg over the next 4 hours(500ml)
  - 100mg/kg over the next 16 hours(1000ml)
- 
- NAC may be diluted in 5% dextrose or 0.9% saline

# Case 3

- A 25 year old female is admitted 48 hours after ingestion of 35 tablets of paracetamol. She complains of abdominal pain

1.What are the important aspects in management?

# Management of patients presenting >24h after

- Paracetamol levels of no use
- NAC is not routinely indicated and less effective
- Start if derangement of liver functions(INR/AST) +/- clinical evidence of liver failure or elevated serum creatinine

# Case 3 ctd...

- On examination she has RHC tenderness and AST -1200u/l

ALT-1450 u/l

What is the possible complication?

How will you manage this patient ?

# Paracetamol induced liver failure

- Conventional management /Supportive care
- NAC infusion
- Liver transplant in acute fulminant liver failure

# Poor Prognostic indicators/ Indications for liver transplantation after Paracetamol overdose

- pH <7.30
- INR >6.5 (PT >100 seconds)
- Serum creatinine >300 micromol/L (>3.4 mg/dL)
- Grade 3 or 4 hepatic encephalopathy.

# Methionine

- Only for patients who are allergic to NAC and do not respond to antihistamines
- Less effective unless given within 8hrs of over dose
- 2.5mg-stat & 3 more doses 4hrly
- Acts by increasing Glutathione synthesis

Thank you....

