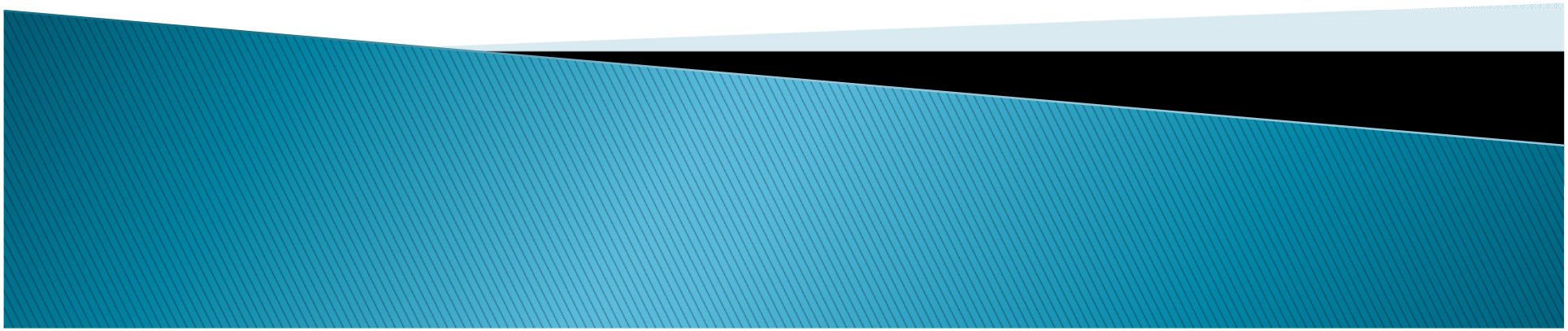
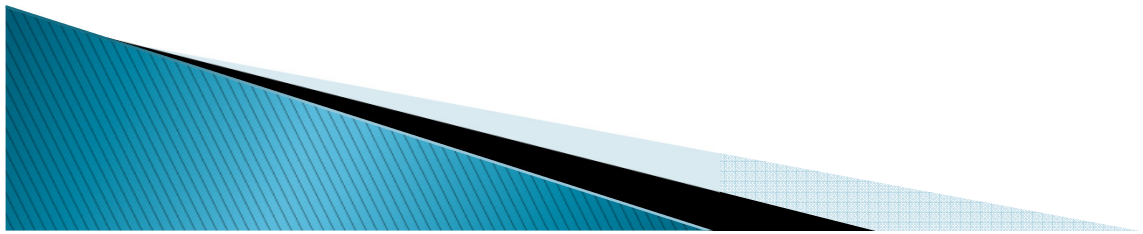
Poisoning

Dr Noluthando Nematswerani
Department of Pharmacology



"All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy."

Paracelsus (1493– 1541)



Types of poisoning

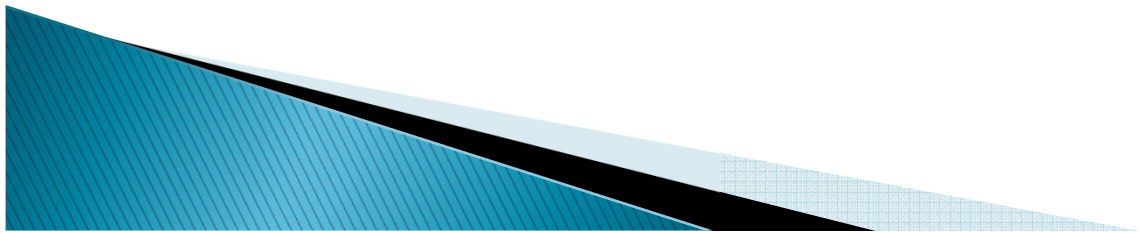
- Intentional self-poisoning
- Accidental poisoning
- Criminal poisoning

Intentional self-poisoning

- 30% of self poisonings involve multiple drugs
- 50% of patients will have taken alcohol as well
- Around 75% of deaths from overdose occur outside hospital
- Hospital treated cases have a mortality of < 1%
- Most cases fall into the psychological classification of suicidal gestures (cry for help)

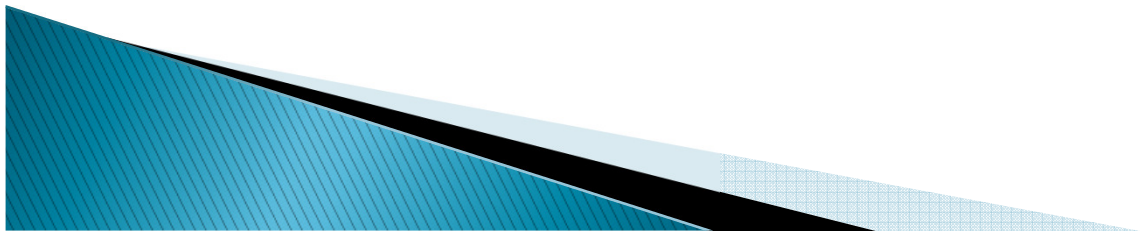
Predisposing risk factors

- Psychiatric diagnosis
- Personality trait
- Family history
- Society
- Environment



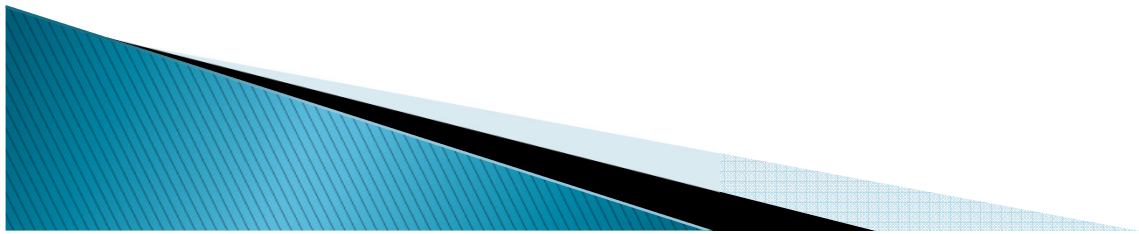
Severity

- Potency of poison
- Quantity ingested
- Duration of exposure
- Presence of other ingredients



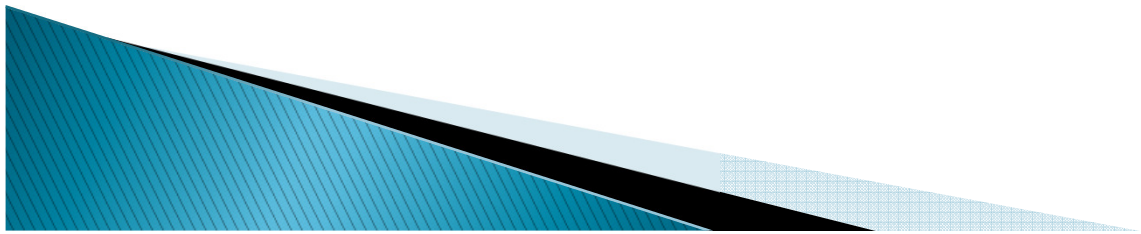
History

- When, What, How much?
- Why?
- Drug history
- Psychiatric history
- Past medical history
- Get history from paramedics, friends, relatives etc



Examination

- Pupils
- Salivation or dry mouth
- Ileus
- Muscle paralysis/ fasciculations
- Extrapyramidal signs
- Pyramidal signs
- Flushing of skin
- Sweating
- Tinnitus
- Local effects: erythema, blisters

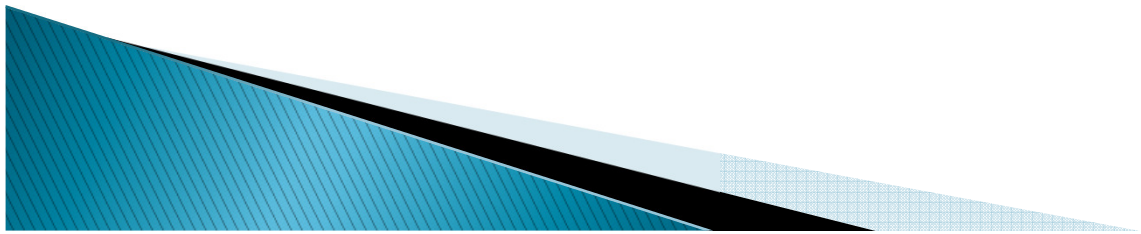


Clinical manifestations of some common poisons

Symptoms / Signs of acute overdose	Common poisons
Coma, hypotension, flaccidity	Benzodiazepines and other hypnosedatives, alcohol
Coma, pinpoint pupils, hypoventilation	Opioids
Coma, dilated pupils, hyper-reflexia, tachycardia	Tricyclic antidepressants, Phenothiazines, other drugs with anticholinergic properties
Restlessness, hypertonia, hyper-reflexia, pyrexia	Amphetamines, MDMA, anticholinergic agents
Convulsions	Tricyclic antidepressants, phenothiazines, carbon monoxide, MAOI,mefenamic acid, theophylline, hypoglycaemic agents, lithium, cynanide
Tinnitus, hyperventilation, pyrexia, sweating, flushing, usually alert	Salicylates
Burns in mouth, dysphagia, abdominal pain	Corrosives, caustics, paraquat

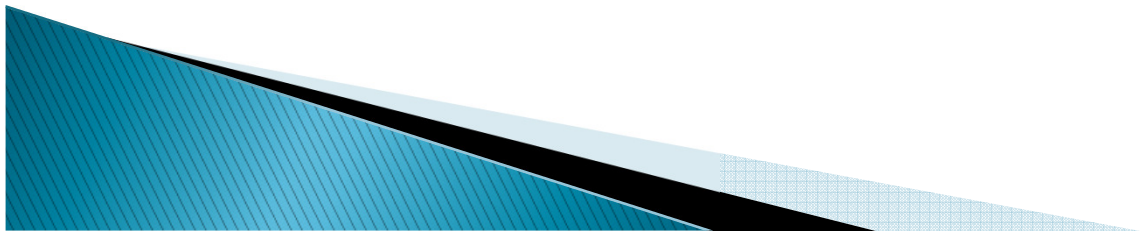
Blood tests

- Blood glucose
- Urea and electrolytes
- Arterial blood gases and O_2 saturation
- Toxicological screening



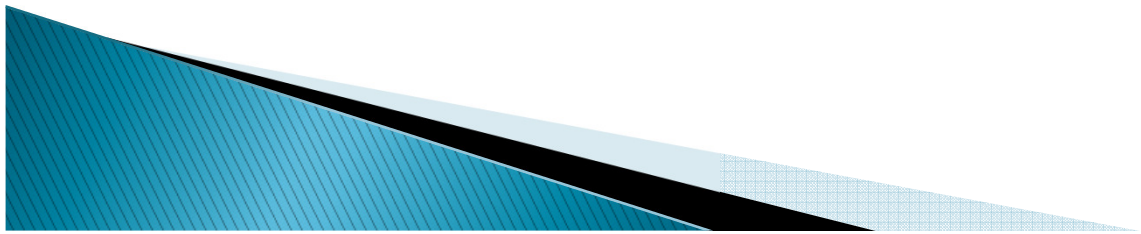
Plasma drug levels

- Emergency measurement is important for these drugs (clinical state of patient unhelpful)
  - Paracetamol
  - Iron
  - Salicylates
  - Lithium
  - Theophylline
  - Methanol/Ethylene glycol



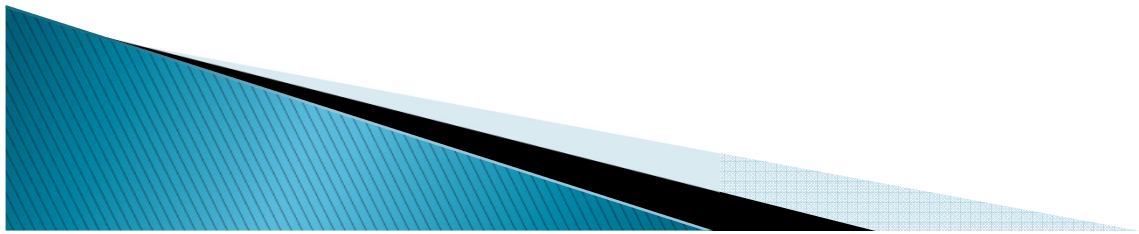
Basic Management

- Airway
- Breathing
- Circulation



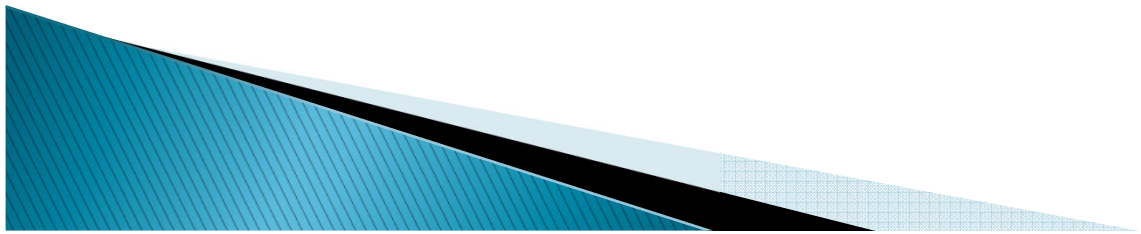
Management

- Prevent further absorption
- Supportive therapy
- Enhance elimination
- Administer specific antidotes



Prevent further absorption

- Decontamination
- Gastric aspiration and lavage
- Activated charcoal
- Ipecacuanha (no longer recommended)
- Laxatives



Decontamination

Skin:

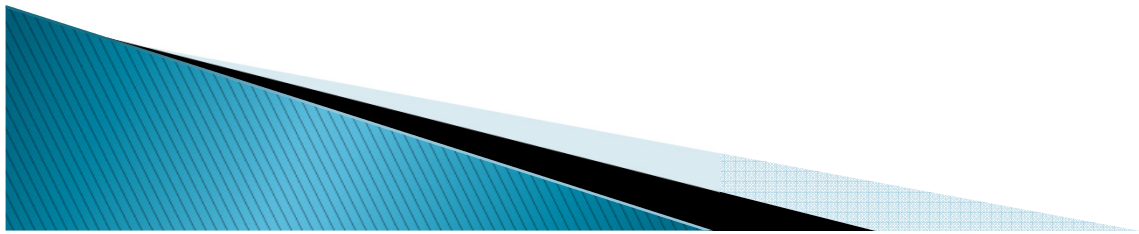
- In case of poison that is topically absorbed, remove all contaminated clothing
  - E.g. Organophosphates
- Wash soap with soap and water
- Protect yourself !!

Eyes:

- Rinse with water
- Alkali burns an emergency
- Must be seen by ophthalmologist

Lips/ mouth:

- Rinse
- Alkali: liquifying necrosis in esophagus
- Acid: coagulation necrosis in stomach



Gastric aspiration and lavage

- Unpleasant and potentially dangerous
- Can only be performed by experienced personnel
- Risks: laryngospasm, aspiration, hypoxia, perforation of GI tract or pharynx, fluid and electrolyte abnormalities
- CI = volatile hydrocarbons (paraffin) – risk of aspiration pneumonia
- CI = corrosives and acids –risk of oesophageal perforation
- May attempt if pt is fully awake, presenting within an hour of ingestion
- Airway must be intact

Gastric aspiration and lavage

Can be used with poisoning with:

- Salicylates
- TCA
- Toxic plant seeds
- Large quantity of tablets or capsules

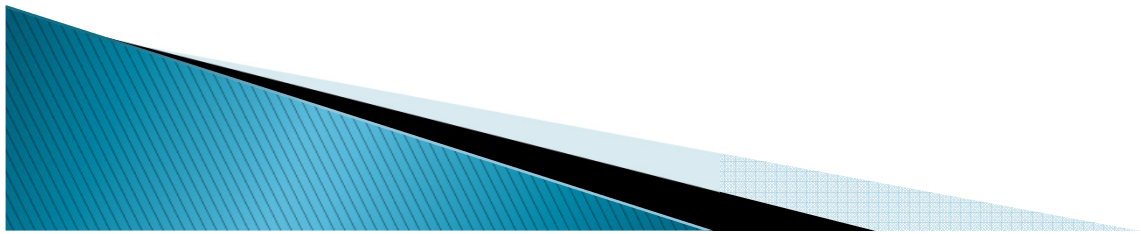
NB!! Protect the airway!!!

Oral activated charcoal

- Potent absorbent of wide spectrum of poisons
- Reduces absorption of toxin in GIT
- Administer as soon as possible
- Large quantities required, 10 times the amount of the poison
- No value in poisoning with strong acids/alkali/corrosives
- Adsorptive capacity too low for poisoning with iron/cyanide/lithium/organophosphates/petroleum products and organic solvents
- 50-100g in 400-800 mL water,orally or via ng tube
- May induce vomiting, constipation or diarrhea

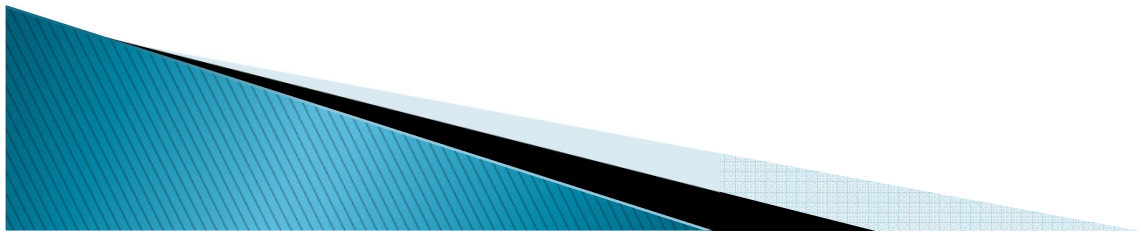
Oral activated charcoal

- May also inactivate antidotes (e.g. methionine)
- Indicated in poisoning due to:
  - Salicylates
  - Quinine
  - Dasponse
  - Carbamazepine barbiturates
  - Theophyllines



Ipecacuanha

- Stimulates CTZ
- Local irritant effect on GIT mucosa
- No clinical evidence



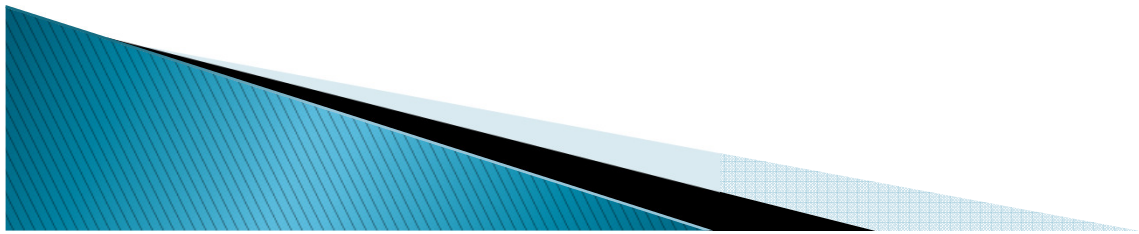
Enhancement of elimination

- Appropriate in < 5 % of patients
- Haemodialysis
- Haemoperfusion
- Serial activated charcoal (gastrointestinal dialysis)
- Alteration of urine PH
- Forced diuresis (no longer recommended)

Haemodialysis/ Haemoperfusion

- Use if pt deteriorates progressively besides treatment
- Use if complications develop: pneumonia, renal, hepatic and cardiac failure
- No value for poisons with large volume of distribution
- Haemodialysis effective for salicylates, lithium, methanol, ethylene glycol and ethanol
- Haemoperfusion effective if poison has small volume of distribution.

  e.g. Barbiturates, carbamazepine, theophylline



Gastrointestinal dialysis

- Repeated oral dose of activated charcoal
- Give charcoal in 1st 2 hours following ingestion
- 50 g every 4 hours for 4-6 additional doses is recommended for repeat administration
- Use for poisons with sustained -release preparations or poisons undergoing enterohepatic recycling
- CI: ileus, reduced bowel sounds, bowel obstruction

  e.g. Amitryptiline, carbamazepine,diazepam, digoxin, phenytoin, quinine, sotalol, theophylline

Alteration of urine PH

- Alkalinisation of urine by administering sodium bicarbonate, increases elimination of phenobarbital and salicylates
- Common complication is hypokalaemia
- 225 mL of 8,4% solution IVI over 1 hour
- Acidification of urine with ammonium chloride increases elimination of amphetamines, phencyclidine and strychnine. This is not recommended especially in pt with rhabdomyolysis. Myoglobin can precipitate.

Antidotes

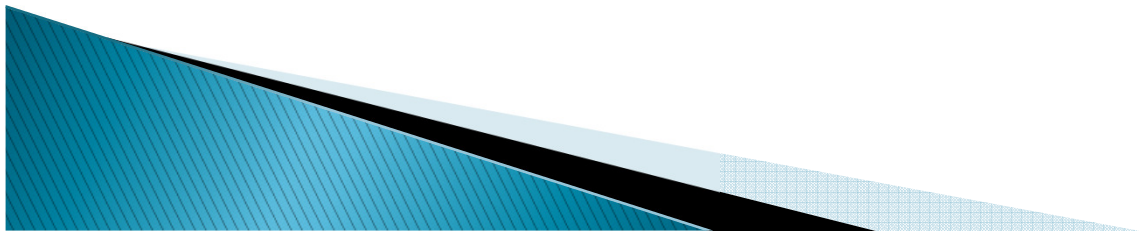
Overdose drug	Antidote
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Digoxin	Digoxin specific antibodies
Ethylene glycol/ Methanol	Ethanol
Iron	Desferrioxamine
Opioids	Naloxone
Organophosphates	Atropine Cholinesterase reactivators
Paracetamol	N-acetyl cysteine, Methionine
Warfarin	Vitamin K
Carbon Monoxide	Oxygen

Salicylates overdose

- Acute ingestion of less than 150 mg/kg with
- no symptoms of toxicity can be treated at
- home with fluids
- > 150 mg/kg must be referred to hospital
- Fatal dose: 0,2-0,5 g/kg
- Elimination is dose dependent

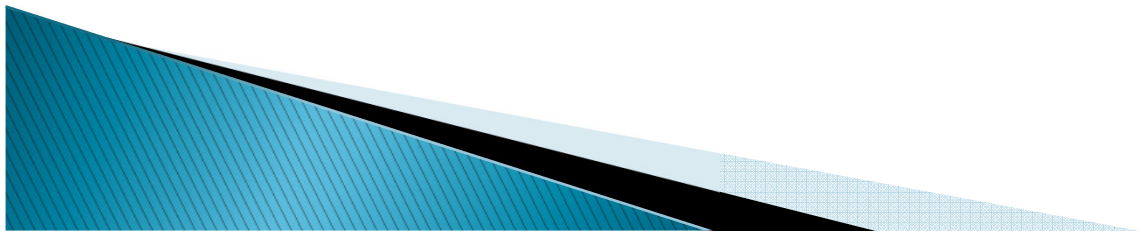
Salicylates overdose

- Hyperventialtion
- Metabolic acidosis
- Tinnitus
- Restlessness
- N+V
- Tachycardia
- Hyperthermia
- Dehydration



Investigations

- Arterial blood gases
- Electrolytes
- Renal function
- Blood glucose
- Plasma salicylate concentration



Management

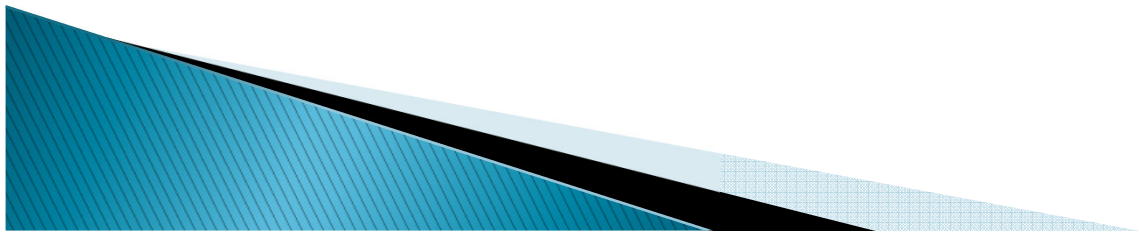
- ABC
- Gastric lavage
- Multiple dose activated charcoal
- Symptomatic treatment
- Treat electrolyte imbalance, dehydration and acidosis
- Cool pt down
- Alkaline diuresis (iv sodium bicarbonate)- not in the elderly
- If severe: Haemodialysis / haemoperfusion

Paracetamol

- Toxic dose after single ingestion of 150mg/kg, or 7 g in adults (20 tablets of 500mg)
- NAPQI (N-acetyl-P-Benzoquinone-imine), toxic metabolite conjugates with glutathion
- Increase in NAPQI, binds to proteins and lipid bilayer of hepatocyte membrane, leading to hepatocellular death and centrilobular liver necrosis

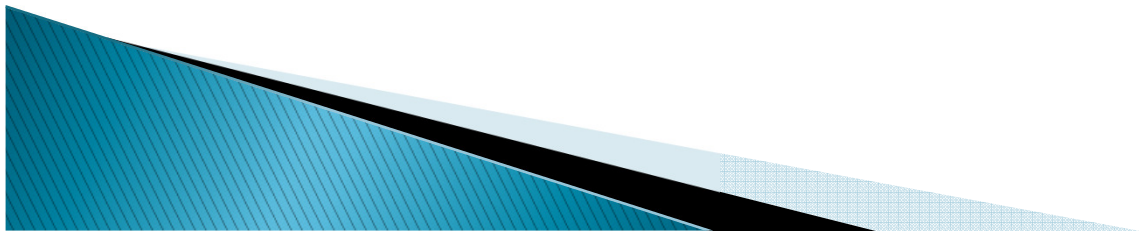
Presentation

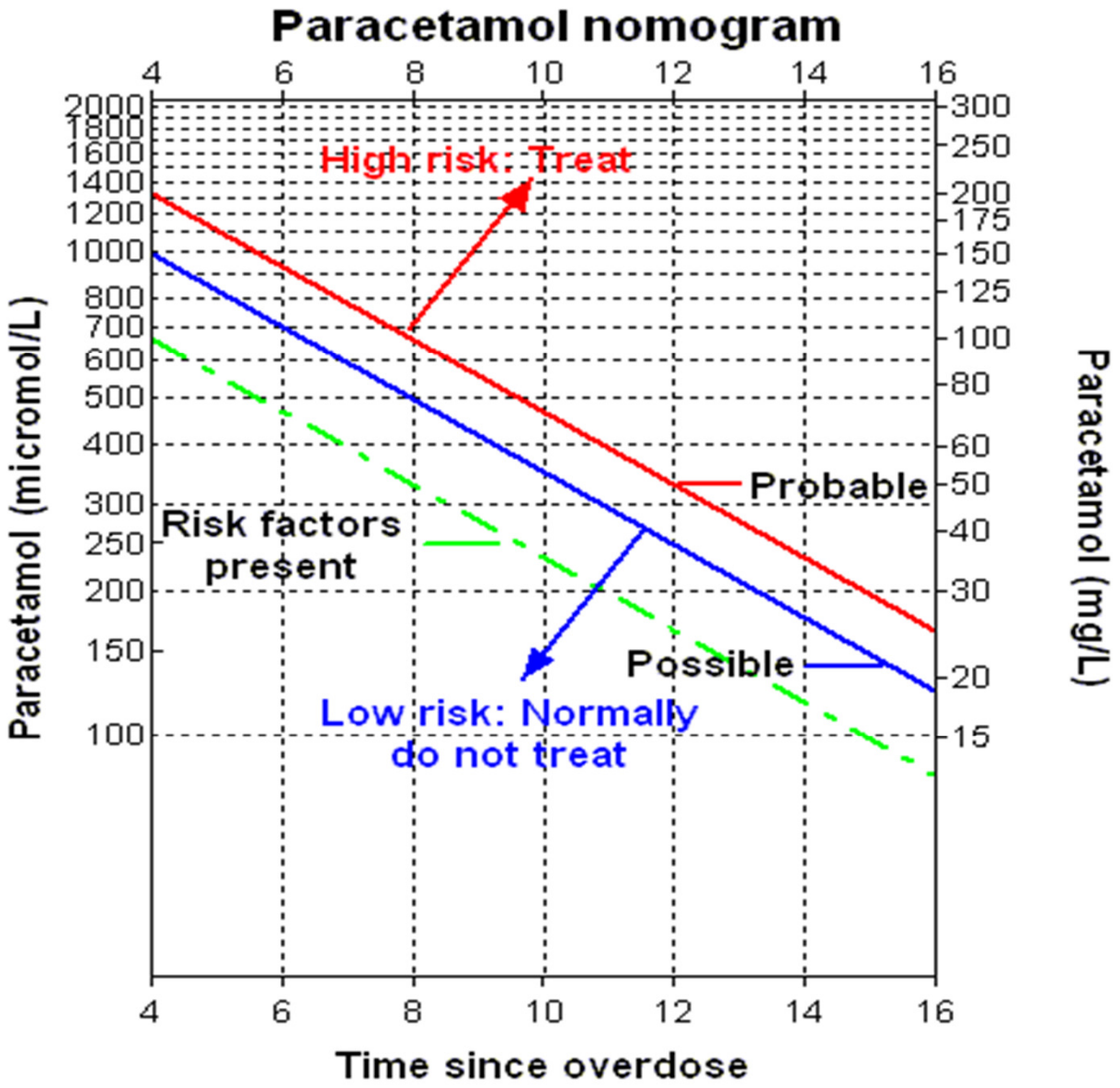
- Usually asymptomatic
- May complain of nausea and sweating
- Right hypochondrial pain and anorexia may precede hepatic failure
- Coma is rare



Investigations

- Paracetamol plasma levels
- Prothrombin time
- Creatinine and liver enzymes




Paracetamol nomogram
4
6
8
10
12
14
16
2000
1800
1600
1400
1200
1000
800
700
600
500
400
300
250
200
150
100
300
250
200
175
150
125
100
80
60
50
40
30
20
15
High risk: Treat
Probable
Risk factors present
Possible
Low risk: Normally do not treat
Paracetamol (micromol/L)
Paracetamol (mg/L)
Time since overdose

Management

- Potentially toxic overdose – Empty stomach within one hour
- Antidote – effective if given within 8 hours of ingestion, benefit obtained up to 24 hours afte ingestion
- Intravenous N-Acetyl cysteine (NAC) or oral methionine
- Give NAC in all cases of severe OD > 10g.

  Do not wait for plasma levels

Opioid overdose

- Opioids bind to opioid receptors. Resulting in inhibition of synaptic neurotransmission in CNS and peripheral nervous system
- Injected, snorted, smoked, taken orally
- Combined with amphetamines, cocaine, marijuana
- Abuse of opioids account for 1% of ED presentations

Presentation

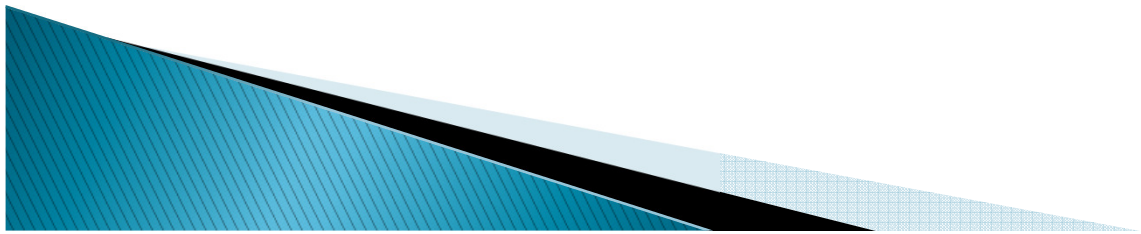
- Pin point pupils
- Respiratory depression
- Cyanosis
- Coma
- Seizures
- Hypotension, bradycardia
- Ventricular arrhythmias
- Severe OD: HT, pupil dilatation due to CNS hypoxia
- Look for needle tracks

Management

- ABC
- Naloxone – pure opioid antagonist
- Onset of action – within 2 minutes
- Naloxone 0,8–1.2 mg IVI every 2–3 minutes until
  rousable, maximum 10 mg
- Reconsider diagnosis if no response after 2–3doses
- Be careful, can cause opioid withdrawal
- Other routes for naloxone: IMI, intralingually, ET tube

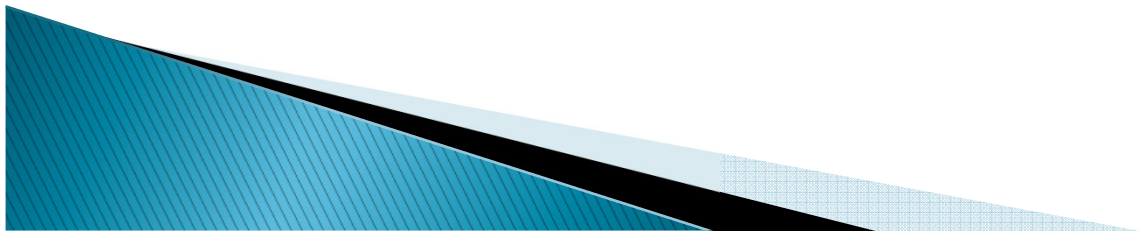
Tricyclic Antidepressants

- They cause death by
  - Dysrryhthmias
  - Myocardial depression
  - Convulsions or asphyxia



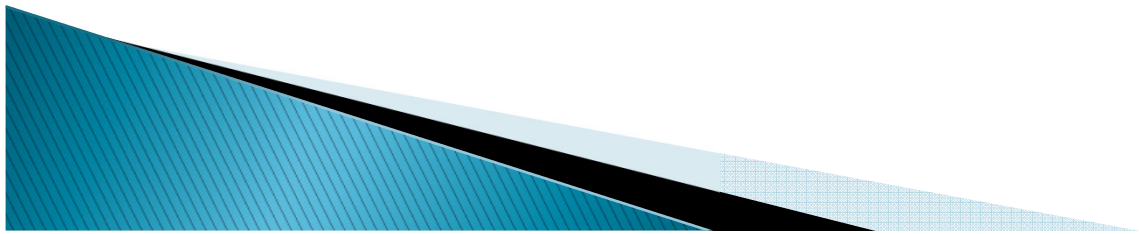
Presentation

- May be conscious, confused aggressive or in deep coma
- Dilated pupils
- Hyperreflexia
- Tachycardia



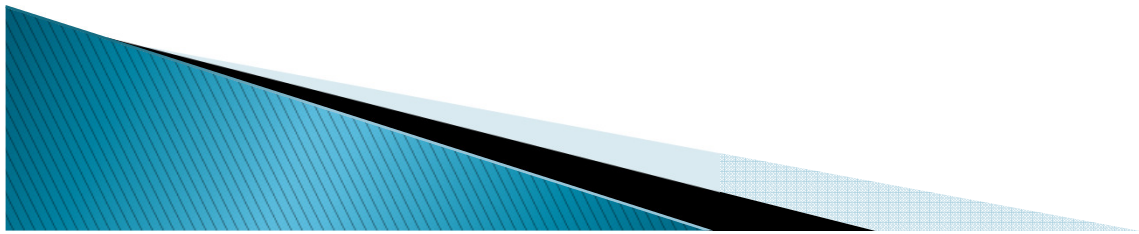
Evaluation

- ECG monitoring
- Bloods:
  - Arterial blood gases
  - Electrolytes



Management

- ABC
- Gastric lavage (up to 1 hour after ingestion in a fully conscious patient)
- Activated charcoal
- Control seizures with iv benzodiazepines
- Correct metabolic abnormalities: hypokalaemia, hypoxia and acidosis with IV sodium bicarbonate, 1–2 mmol/kg over 1–2 minutes
- Resistant ventricular tacchycardia (VT)iv magnesium
- VT with hypotesion – DC shock is indicated

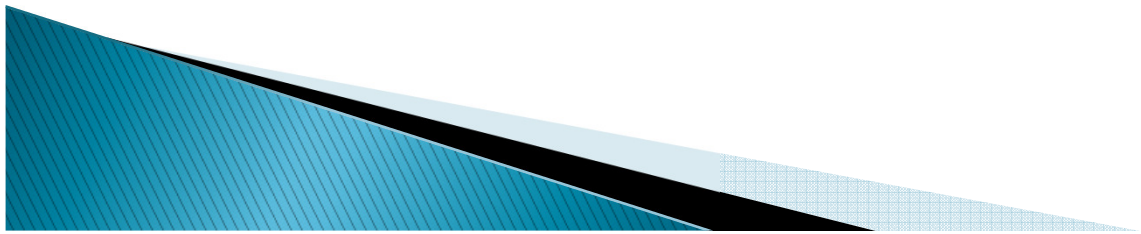


Organophosphates

- Irreversible inhibition of cholinesterase enzyme
- Accumulation of free unbound acetyl choline
- Symptoms within 5 minutes if massive ingestion
- Symptoms can occur several hours post exposure

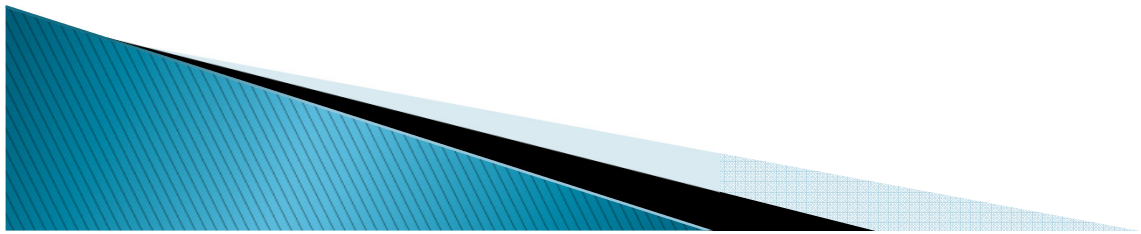
Presentation

- **Muscarinic effects:**
  - Bronchoconstriction
  - N+V, diarrhea, abdominal pain
  - Sweating, salivation, lacrimation
  - Hypotension, bradycardia
  - Miosis, blurred vision
  - Urinary frequency, incontinence
- **Nicotinic effects:**
  - Muscle twitching and fasciculation
  - Muscle paralysis



Presentation

- Sympathetic ganglia:
  - Tachycardia
  - Hypertension
  - Hyperglycaemia
- CNS:
  - Anxiety, apathy
  - Depression, drowsiness
  - Respiratory depression
  - Convulsions
  - Coma

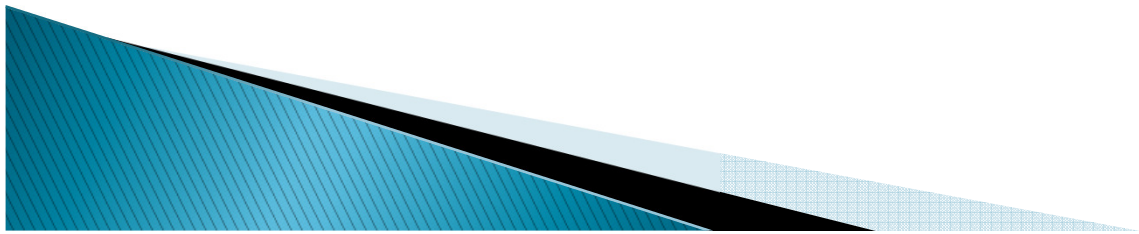


Management

- ABC
- Avoid scoline, morphine, theophylline, phenothiazines
- Activated charcoal
- Decontamination
- Atropine dose 1-2mg IVI (moderate cases) or (2-5 mg) for severe cases every 15 minutes until full atropinisation
- Infusion: 10-20mg/hour for severe poisoning
- Ach Esterase reactivators (less effective with malathion)
- Obidoxime / Pralidoxime
- Repeat once/twice at interval of 2 hours
- Use within 4 hours, latest 12 hours

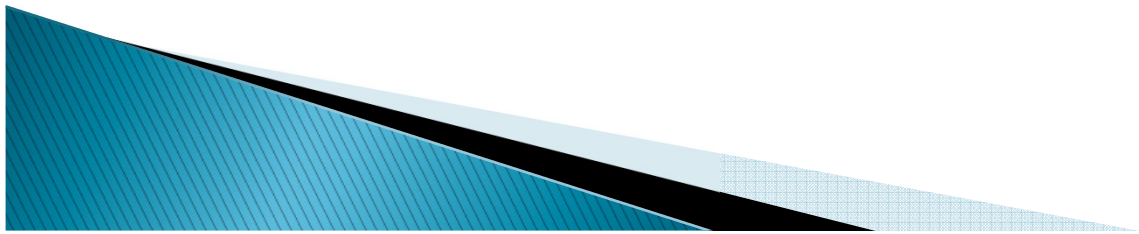
Benzodiazepine

- Drowsiness
- Slurry speech
- Nystagmus, ataxia
- Hypotension
- Coma
- Respiratory depression
- Cardiorespiratory arrest



Management

- ABC
- Activated charcoal
- Mild – moderate overdose, no further intervention
- Severe OD: BZD antagonist, Flumazenil 0,2 mg IVI followed by 0,1 mg every 2-3 minutes until rousable
- BZD have longer duration of action than flumazenil
- Avoid excess flumazenil to completely reverse effect of BZD. In chronic abusers can lead to agitation and seizures



Carbon Monoxide

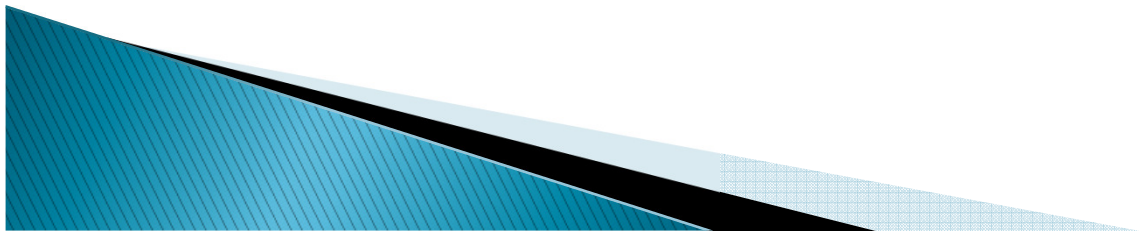
- Carbon monoxide generated from exhaust fumes (suicide)
- Accidental – ineffective heaters with inadequate ventilation

Presentation

- N+V (50%), headache (90%), vertigo (30%) confusion, dyspnoea, palpitations, convulsions, coma, clonus,hyperreflexia
- Carboxyhaemoglobin levels confirm exposure and severity

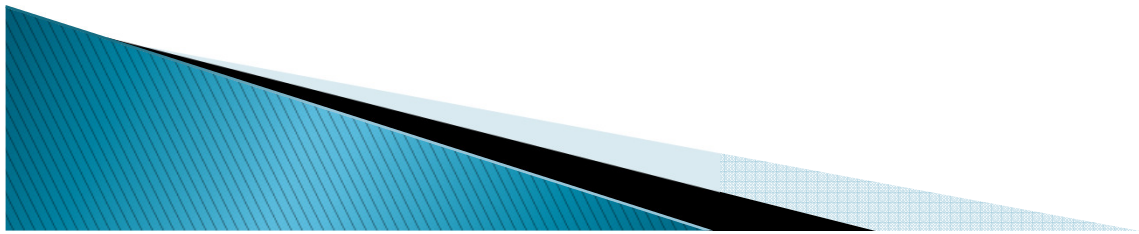
Management

- Removal from exposure
- 100% Oxygen
- Hyperbaric oxygen
- Dantrolene if muscle tone is increased
- Treat rhabdomyolysis
- Mannitol and Dexamethasone if cerebral oedema



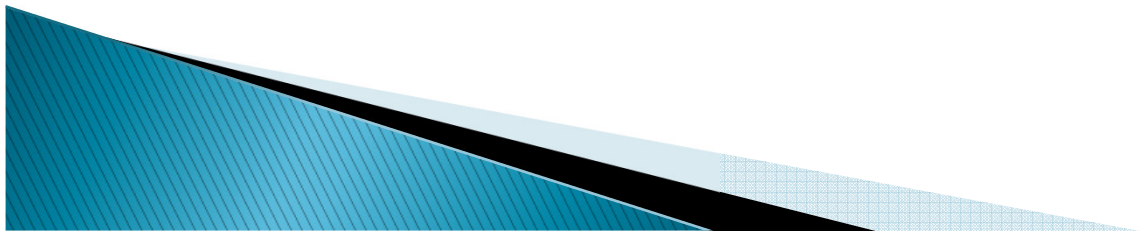
Paraffin poisoning

- Stored in cool drink bottles
- Burning sensation in mouth
- Aspiration pneumonitis



Paraffin poisoning

- CXR 5-6 hours after ingestion
- Observe for 8 hours
- Gastric lavage, emesis, activated charcoal contra-indicated
- Oxygen
- Steroids have no benefit
- Prophylactic antibiotics not advocated
- Treat secondary infections



Cyanide

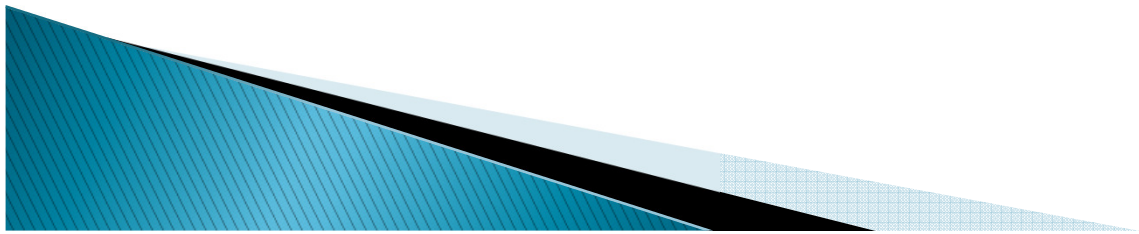
- Forms stable complex with Fe^{3+} ® inhibits cellular respiration
- Symptoms within seconds to minutes
- Headache, confusion, delirium, convulsions, coma, dyspnoea, hypotension, heart block, arrhythmia, asystole
- ABC
- Avoid skin contact
- Dicobalt Edetate – 300mg over 1 minute
- Nitrite / sodium thiosulphate regimen (Kit)

Irritants and corrosives

- Irritants: Household soaps, shampoos, liquid dishwashing detergents, bleach, surface cleaning agents
- Do not cause vomiting
- If asymptomatic observe at home
- Corrosives: Drain cleaners, battery acid, swimming pool/toilet cleaners
- Chemical burns, oesophageal and stomach injury
- Avoid gastric lavage
- Endoscopy

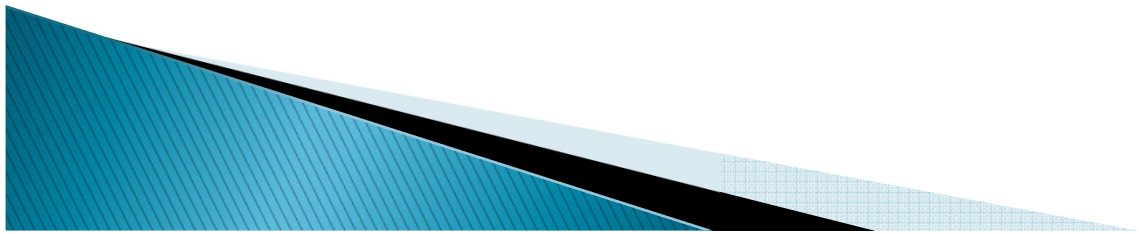
Barbiturates

- Intoxication resembles that of alcohol
- Hypoxia
- Hypercapnoea
- Respiratory acidosis
- Coma
- Hypoglycaemia
- Shock due to medullary depression



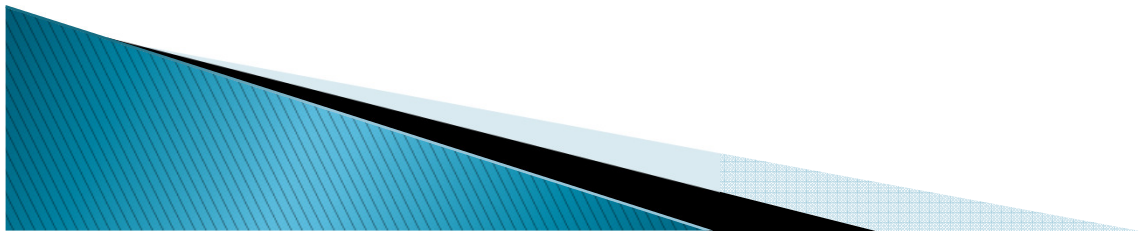
Management

- ABC
- Gastric lavage
- Activated charcoal
- Alkaline diuresis used for phenobarbitone
- Symptomatic treatment



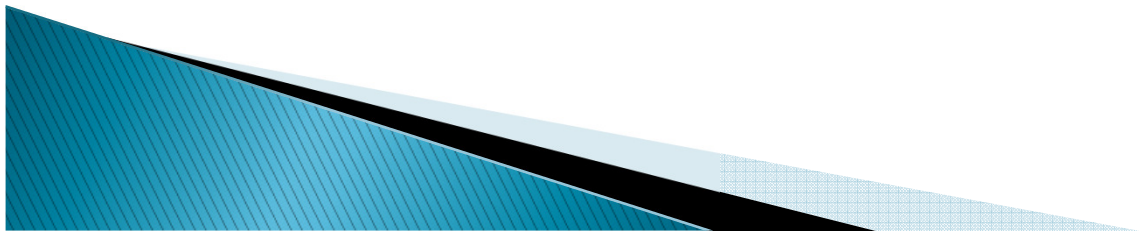
Phenytoin

- Acute toxicity: irritability, tremor and confusion
- Mental status varies
- Movement abnormalities
- N+V
- Diplopia, nystagmus, opthalmoplegia
- Arrhythmias (associated with IVI infusion)



Management

- ABC
- Serial activated charcoal
- Serum levels
- Symptomatic treatment
- Extracorporeal elimination ineffective



Cocaine

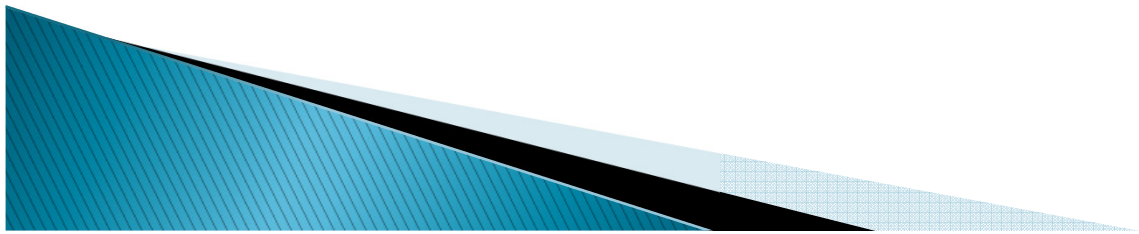
- Stimulates release and blocks reuptake of noradrenaline, adrenaline, dopamine and serotonin
- Taken orally, snorted, applied to mucous membranes and injected IVI
- Free base form “crack”, smoked
- Combined with heroin: “speedballing”
- 30-60 % of individuals take it with alcohol
- In 74% of cocaine related fatalities in
- USA, another drug was ingested

Presentation

- Lethal dose: 1200 mg
- Hypertension, tachycardia
- Mydriasis
- Ventricular arrhythmias
- Seizures
- “Crack lung”
- CNS depression
- Cardiorespiratory failure
- Rhabdomyolysis, hyperpyrexia, renal failure, liver dysfunction and DIC have been reported. These indicate a poor prognosis
- Cx: MI, stroke, subarachnoid haemorrhage

Management

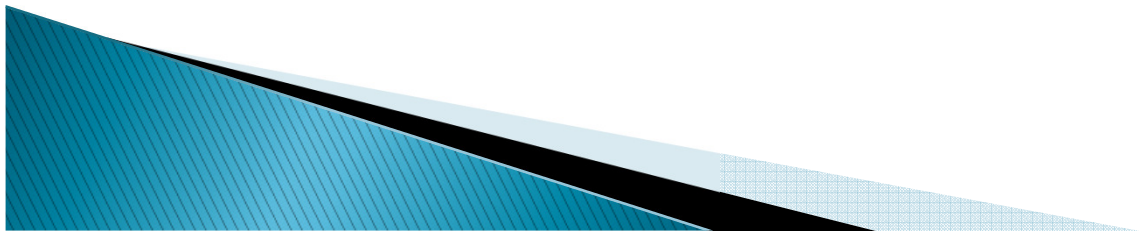
- Adequate ventilation
- Rx hyperpyrexia with cooling down pt
- Rx agitation, seizures, tachycardia and hypertension with BZD
- Specific antihypertensive therapy (e.g., intravenous nitrates or calcium-channel blockers) can be given
- Avoid beta blockers



Amphetamines

- Active ingredients:
  - Amphetamine, Dextra amphetamphetamine, Met amphetamphetamine
- Release CA from presynaptic vesicles
- Taken orally, sniffed, injected
- Combined with cocaine, heroin, LSD, PCP
- Tik: Metamphetamine. Inhaled from light bulbs, heated from below, producing a rush, giving its name speed
- MDMA = 3,4 methylene dioxy methamphetamine (ecstasy)

  Selective serotonergic neurotoxin, causing massive release of serotonin and inhibits
- its uptake.



Amphetamines

- Ecstasy tablets contain 50-100mg MDMA
- Severe hyperthermia reported at doses of 4-
- 5mg/kg
- 31% of people 16-25 yrs admitted to using
- MDMA
- 500 000- 1 million people in Britain use MDMA
- every weekend
- Misconception that it is a “safe” drug
- Effects unpredictable and potentially fatal

Presentation

CVS

- Chest pain, palpitations, tachydysrhythmias, HT crisis

Musculoskeletal

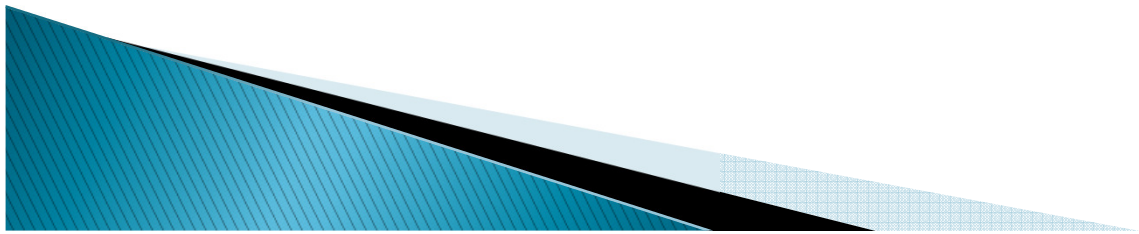
- Tremors, hyperreflexia, spasms, trismus

GIT

- N+V, dry mouth, cramps, loss of appetite

Urogenital

- Urinary retention, sexual dysfunction



Presentation

Skin

- Sweating, hyperthermia

Psychiatric

- Paranoid delusions, anxiety, hallucinations

CNS

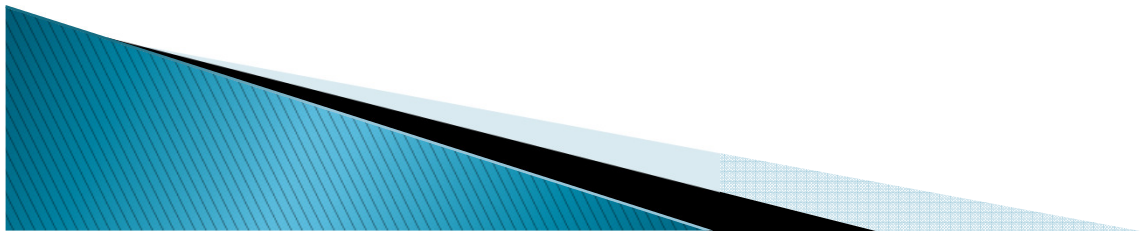
- Syncope, ataxia, diplopia, headache, seizures,parasthesias

Occular

- Mydriasis, nystagmus

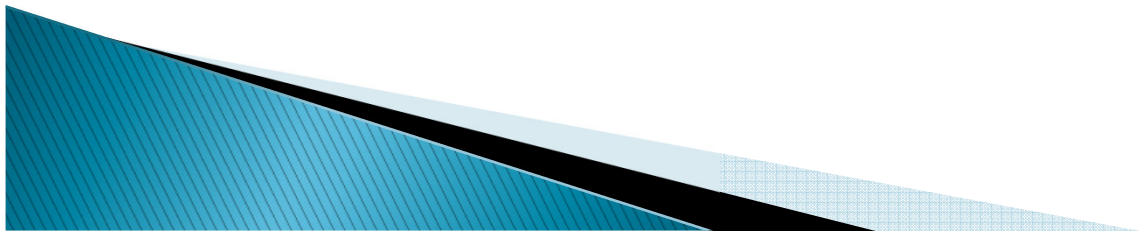
Complications

- Hyperpyrexia > 40–42 ^{0}C
- Rhabdomyolysis
- DIC
- Acute renal failure
- Cardiac failure
- Acute hepatic failure
- Hyponatraemia
- Cerebral oedema and coma
- Intracranial and subarachnoidal haemorrhage



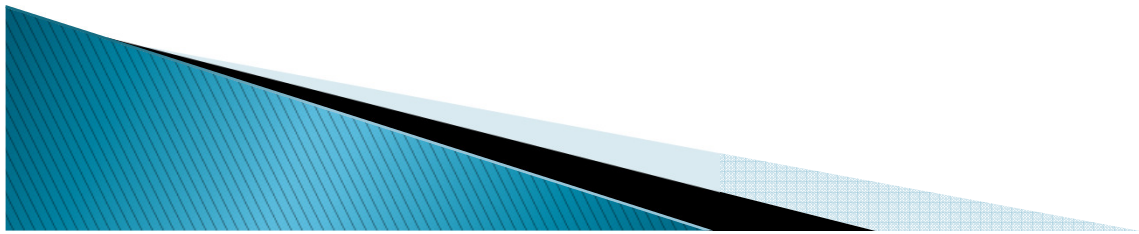
Management

- Sedate patient if agitated
- Control seizures with BZD
- Rx HT with BZD, Nifedipine, Sodium Nitroprusside
- Rx Serotonin syndrome with Cyproheptadine
- Rx hyperthermia:
  - Cool pt down, Replace fluids
  - Ice packs, Iced gastric lavage
  - BZD for agitation
  - Intubate and ventilate prn
  - Dantrolene if temp >39°C



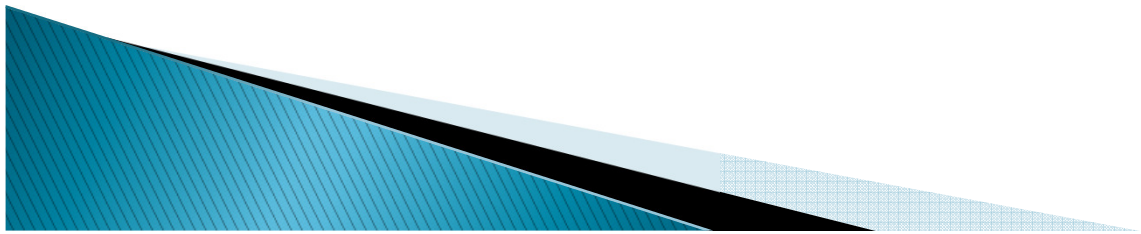
Management

- Rx hyponatraemia
- NB!! Fluid restriction vs administration of fluids (CVP)
- Rx rhabdomyolysis – hydration and forced diuresis
- Alkalization of urine can slow down MDMA excretion
- Acidification of urine can cause myoglobin to precipitate



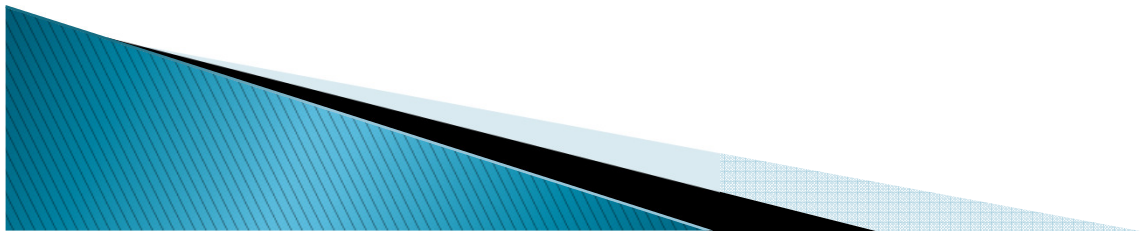
Phenothiazines

- Cardiotoxic: anticholinergic effects, depression of myocardial contractility and conduction, blockade
- Neurotoxic: depressant effect, dystonias, seizures
- Neuroleptic malignant syndrome
- ABC
- Gastric lavage
- Serial activated charcoal
- AXR: radio-opaque
- Supportive treatment
- Acute dystonia responds to diphenhydramine



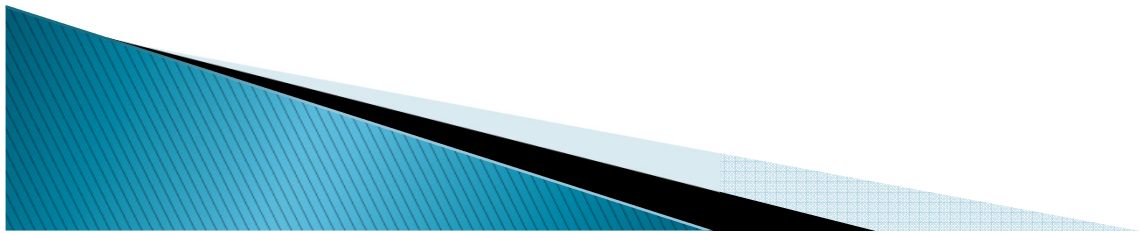
Lithium

- Early: N+V, abdominal pain
- Slowing of cognitive functions
- Confusion, stupor and coma
- Difficult to distinguish from organic delirium
- Acute renal failure
- Conduction abnormalities, dysrhythmias
- Respiratory failure and CVS collapse



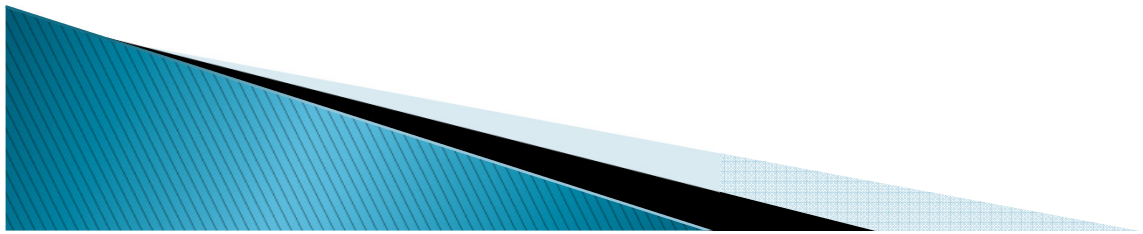
Management

- ABC
- Supportive management
- Activated charcoal ineffective
- Gastric lavage
- Rehydrate pt with normal saline
- Avoid diuretics
- Alkalinisation of urine
- Haemodialysis



Iron salts

- Dose above 20mg/kg potentially toxic
- Lethal dose 180-300 mg/kg
- Corrosive action in GIT
- Free iron is a vasodilator



Management

- Gastric lavage
- AXR
- Treat shock and acidosis
- If levels are <54 mcmol/L, pt is asymptomatic 6 hours after ingestion, no active treatment needed
- Levels > 90 mcmol/L need chelation Rx
- Desferrioxamine forms a complex ferrioxamine which is excreted. Need normal urine output.
- 15 mg/kg /hour IVI as continuous infusion