Poisoning management

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Disclosure

I have no financial or academic conflicts to disclose.

Learning objectives

- Trainees will be able to undertake a basic assessment of a poisoned patient
- Trainees will be able to identify various methods of prevention of absorption
- Trainees will be familiar with common pharmaceutical products used in overdose and self harm
- Trainees will develop an understanding of the epidemiology of poisoning

Poisoning

- Timing
  - Acute
  - Chronic
  - Immediate
  - Delayed
- Intent or origin
  - Deliberate
  - Accidental
  - Occupational
  - Iatrogenic

Epidemiology of poisoning

This can be examined from different angles:

✓Overall mortality
✓Hospital admission rates
✓Enquiries to poison information services

- Data sources

  i.e. mortality data, hospital admissions, discharge data, enquiries to centres. Some countries collect on chemical exposures

Some statistics to think about…

- Highest incidence 15-35 years.
- 41% drug-related deaths in females in 2013 defined as suicide- 9% lower than year before.
- 29% drug-related deaths in males; 12% increase from year before.
- Largest proportion in UK accidental.

Causes of poisoning

- What common causes/presentations do we see in the Sudan?
- Are there any variations between rural and urban areas?
- Name some common chemical exposures

Useful definitions

- **Suicide** – an intentional act resulting in death
- **Accidental poisoning** – an exposure to a poison resulting in symptoms that arises by an accidental action. It is common in young children but can occur in adults in the home, in the workplace or as a result of fire or transport accident
- **Deliberate poisoning** – forms part of the spectrum of disorders now classified as deliberate self-harm. It has also in the past been referred to as parasuicide, although this term is now outdated
- **Occupational poisoning** – occurs in the context of employment
- **Environmental poisoning** – refers to exposure resulting from presence of a chemical in air, food or water

MEDICINE 44:2 (2016)

Deaths from poisoning, England & Wales (2009-2013)

Numbers of deaths from drug poisoning overall and in terms of selected substances being mentioned, England and Wales, 2009–2013[a]

	2009	2010	2011	2012	2013
All deaths from drug poisoning	2878	2747	2652	2597	2955
Heroin and morphine	880	791	596	579	765
Methadone	408	355	486	414	429
All amphetamines	76	56	62	97	120
MDMA/ecstasy	27	8	13	31	43
Para-methoxyamphetamine/paramethoxymetamphetamine (PMA/PMMA)	0	0	1	20	29
Novel psychoactive substances	26	22	29	52	60
Cathinones	0	6	6	18	26
Mephedrone	0	6	5	12	18
All benzodiazepines	261	307	293	284	342
Diazepam	160	186	179	207	228
Zopiclone/zolpidem	79	67	71	83	86
All antidepressants	406	381	393	468	466
Tricyclic antidepressants (BNF 4.3.1)	219	194	200	233	235
Selective serotonin reuptake inhibitors (BNF 4.3.3)	113	136	127	158	150
Other antidepressants (BNF 4.3.4)	81	74	84	104	123
Paracetamol	255	199	207	182	226
Tramadol	87	132	154	175	220
Other opiates (including codeine and dihydrocodeine)	418	418	418	348	469
Helium	21	33	42	58	62

Data from UK statistics for England and Wales.[1]
[a] Figures are for deaths registered in each calendar year.

MEDICINE 44:2 (2016)

Deaths by suicide in England & Wales (2000-2006)

Deaths by suicide and undetermined intent related to antidepressants in England and Wales for people aged 10 years and over, 2000–2006. Rates corrected by population and prescription volume to derive a fatal toxicity ratio

Drug	Deaths in England and Wales (*n*)	Death rate per 100,000	UK prescriptions, (*n*)	Prescription rate per 100,000	Fatal toxicity ratio (95% confidence interval)	Relative toxicity index*
Tricyclic antidepressants						
Amitriptyline	395	0.1211	44,286,108	10,606	11.4 (10.3–12.6)	1.0
Clomipramine	39	0.0120	3,544,517	849	14.1 (10.0–19.3)	1.2
Dosulepin	589	0.1807	20,812,372	4984	36.3 (33.4–39.3)	3.2
Doxepin	22	0.0067	1,001,373	240	28.1 (17.6–42.6)	2.5
Imipramine	25	0.0077	2,575,206	617	12.4 (8.1–18.4)	1.1
Nortriptyline	5	0.0015	645,175	155	9.9 (3.2–23.2)	0.9
Trimipramine	13	0.0040	1,113,166	267	15.0 (8.0–25.6)	1.3
Selective serotonin reuptake inhibitors						
Citalopram	50	0.0154	37,371,364	8950	1.7 (1.3–2.3)	0.15
Fluoxetine	17	0.0052	39,818,056	9536	0.5 (0.3–0.9)	0.05
Fluvoxamine	0	0	195,897	47	0	0
Paroxetine	10	0.0031	25,980,311	6222	0.5 (0.2–0.9)	0.04
Sertraline	8	0.0025	15,374,325	3682	0.7 (0.3–1.3)	0.06
Other antidepressant drugs						
Mirtazepine	18	0.0055	6,386,479	1529	3.6 (2.1–5.7)	0.32
Venlafaxine	83	0.0255	20,100,751	4814	5.3 (4.2–6.6)	0.46

The fatal toxicity index represents drug-specific poisoning mortality relative to prescribing rates and is calculated from the mortality rate (numerator) and the prescribing rate (denominator).
Adapted from Hawton et al.[10]
* Index of toxicity relative to amitriptyline.

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Implications?

- Do these figures have any implications?
- Do we have figures for the Sudan?
- Discuss

So is the cause toxicological?

- Good history:
  - ✓Patient
  - ✓Parent
  - ✓Friends
  - ✓Family
  - ✓Facebook

Situations to think about… 1

- Unexplained coma
- Acute confusional state
- Hypoglycaemia
- Abnormal liver function
- Unexplained convulsions

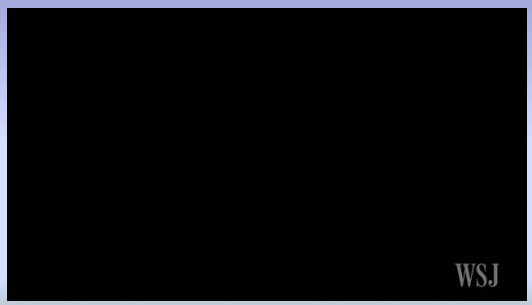
MEDICINE 44:2 (2016)

Situations to think about… 2

- Unexplained metabolic acidosis
- Abnormal bleeding
- Several individuals with similar presentations
- Recurrent or chronic unexplained symptoms in children

MEDICINE 44:2 (2016)

Other situations!



Initial management

What do you want to do?

Management strategies

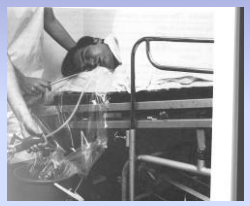
1. Prevent absorption
2. Enhance elimination
3. Specific antidote
4. Chelation
5. Support physiology

Gastric decontamination methods

- Aim to reduce absorption of poisons taken by mouth when ingested poison carries significant risk
- Little evidence for benefit unless used within 1 hr of poisoning
- Cannot be used in unconcious or drowsy patients unless the airway is protected because of aspiration risk
- Methods available
  - Activated charcoal
  - Gastric aspiration / lavage - avoid
  - Induced emesis (Ipecacuanha) - no longer used

Gastric Lavage / Aspiration

- Suitable for
  - very large and life -threatening overdoses
  - poisons not absorbed by activated charcoal
- More difficult and hazardous in children
- In drowsy patients with inadequate gag reflexes, airway should be protected with a cuffed endotracheal tub
- Now very rarely used



Gastric Lavage / Aspiration

Complications
- gut perforation
- aspiration
- Laryngospasm
- Water intoxication (children)
- Dysrhythmias
- Pneumothorax
- Enhanced early drug absorption

Contraindications
- Hydrocarbon ingestion
- Caustic substance ingestion

(risk of aspiration pneumonitis and perforation)

Guidance

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informa healthcare

REVIEW ARTICLE

Position paper update: gastric lavage for gastrointestinal decontamination

B. E. BENSON[1], K. HOPPU[2], W. G. TROUTMAN[1], R. BEDRY[2], A. ERDMAN[1], J. HÖJER[2], B. MÉGARBANE[2], R. THANACOODY[2], and E. M. CARAVATI[1]

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Activated Charcoal

- Charcoal activated by heating in steam, air or carbon dioxide at 600-900ºC
- Adsorbs poison in GI tract by direct contact and reduces absorption
- Required charcoal to drug ratio is variable. In rat models 8:1 for >80% reduction in conc. (phenobarbitone, chloroquine, isoniazid)

Activated charcoal

- Preferred method (simple)
- 10 x dose of poison taken, up to 50G
- Unpalatable (suspend in flat cola)
- Can be administered by NG tube to unconcious patients but the airway should be protected by a cuffed endotracheal tube if the gag reflex is inadequate
- Ineffective for some poisons (see later)

Activated charcoal

Complications
- Aspiration pneumonitis
- Reduced absorption of therapeutic agents (e.g. ? methionine)
- Briquette formation / bowel obstruction

Contraindications
- Absent bowel sounds (ileus)
- Impaired gag reflex
- Unsafe swallow

Activated Charcoal-Ineffective

- Elemental metals/salts
  - Lithium, iron, boron salts
- Insecticides
  - Malathion
  - DDT
  - N-methyl carbamate
- Cyanide
- Strong acids/alkalis
- Alcohols
- Hydrocarbons


POISON PAPER

Position Paper: Single-Dose Activated Charcoal

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists

Increasing drug elimination

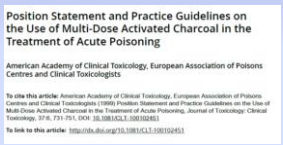
- Methods
  - Multiple dose activated charcoal [MDAC]
  - Haemodialysis [HD]
  - Haemoperfusion [CVVH]
  - Haemofiltration [CVVHDF]
  - Combined methods
    - haemodiafiltration
    - MARS

Multiple dose activated charcoal

- 50 g activated charcoal followed by further 25g every 2 hours
  - Laxative / stool softner to prevent constipation
- Reduces elimination half life by
  - 'Gastrointestinal dialysis'
  - Interfering with enterohepatic circulation

Multiple dose activated charcoal

- Good evidence of efficacy
  - Carbamazepine
  - Dapsone
  - Phenobarrbitone
  - Quinine
  - Theophylline
- Sometimes also used for
  - Salicylate
  - Phenytoin
- Complications
  - Intestinal obstruction



Position Statement and Practice Guidelines on the Use of Multi-Dose Activated Charcoal in the Treatment of Acute Poisoning

American Academy of Clinical Toxicology, European Association of Poisons Centres and Clinical Toxicologists

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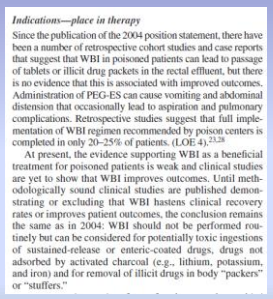
Whole bowel irrigation

informa
healthcare

REVIEW ARTICLE

Position paper update: Whole bowel irrigation for gastrointestinal decontamination of overdose patients



Indications—place in therapy

Since the publication of the 2004 position statement, there have been a number of retrospective cohort studies and case reports that suggest that WBI in poisoned patients can lead to passage of tablets or illicit drug packets in the rectal effluent, but there is no evidence that this is associated with improved outcomes. Administration of PEG-ES can cause vomiting and abdominal distension that occasionally lead to aspiration and pulmonary complications. Retrospective studies suggest that full implementation of WBI regimen recommended by poison centers is completed in only 20–25% of patients. (LOE 4).[23,28]

At present, the evidence supporting WBI as a beneficial treatment for poisoned patients is weak and clinical studies are yet to show that WBI improves outcomes. Until methodologically sound clinical studies are published demonstrating or excluding that WBI hastens clinical recovery rates or improves patient outcomes, the conclusion remains the same as in 2004: WBI should not be performed routinely but can be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs, drugs not adsorbed by activated charcoal (e.g., lithium, potassium, and iron) and for removal of illicit drugs in body "packers" or "stuffers."

Haemodialysis and haemoperfusion

Useful when the poison

- Has a small volume of distribution
- Has a low inherent clearance rate
- Is sufficiently toxic
- Is
  - Small enough to cross the dialysis membrane (HD)
  - Bound to activated charcoal (HP)

Haemodialysis

- Considered for life-threatening overdoses of
  - ethylene glycol
  - isopropanol
  - methanol
  - salicylate
  - sodium valproate
  - lithium

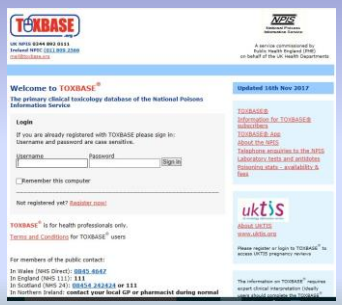
Charcoal Haemoperfusion

- Consider for life-threatening overdoses of
  - theophylline/aminophylline
  - phenytoin
  - carbamazepine
  - phenobarbitone/amylobarbitone
- Rarely available or used

Specific antidotes

MECHANISM	POISON	*ANTIDOTE*
Glutathione repleters	Paracetamol poisoning	*Acetylcysteine, Methionine*
Specific antagonists	Opiates	*Naloxone*
Specific antagonists	Benzodiazepines	*Flumazenil*
Alcohol dehydrogenase inhibitors	Ethylene glycol, methanol	*Ethanol, Fomepizole*
Chelating or fixing agents	Iron Heavy metals Cyanide	*Desferrioxamine,* *Dimercaprol,* *Edetate (dicobalt or sodium calcium), Hydroxocobalamin*
Reducing agents	Dapsone	*Methylene blue*
Cholinesterase reactivators	Organophosphates	*Pralidoxime*
Antibody fragments	Digoxin	*Digibind*
Antivenoms	Snake bites	*Zagreb antivenom*

TOXBASE



TOXBASE app

Other resources

TOXNET

http://www.toxinz.com

TOXINZ POISONS INFORMATION

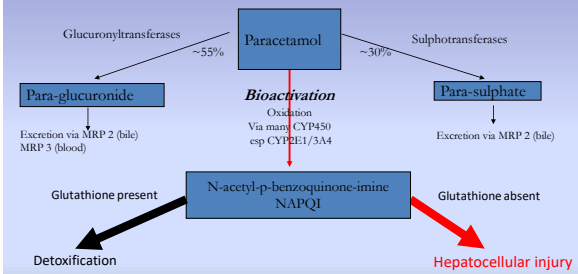
Specific poisons

- Covered here
  - Paracetamol
  - Salicylates / aspirin
  - Opioids
  - Tricyclic and other antidepressants
  - Benzodiazepines
  - Iron
- Why these substances?
  - Commonly used
  - Serious
- Also
  - Organophosphorus compounds
  - Common internationally

Paracetamol Poisoning

- Most popular analgesic in UK
- Almost half of overdoses presenting to hospital include paracetamol
- A leading cause of poisoning mortality in UK (100-200 deaths/year)
- Overall mortality of paracetamol o/d <1%

Mechanism of toxicity



Clinical Features - Early

- Warning! – may be none
- Non-specific
  - Nausea
  - Vomiting
  - Abdominal pain

Clinical Features - Delayed

- Hepatic necrosis (starts 2-3 days later)
  - Jaundice
  - Liver pain
  - Encephalopathy
  - Coagulopathy
  - Fulminant hepatic failure
  - Death (3-6 days after overdose)

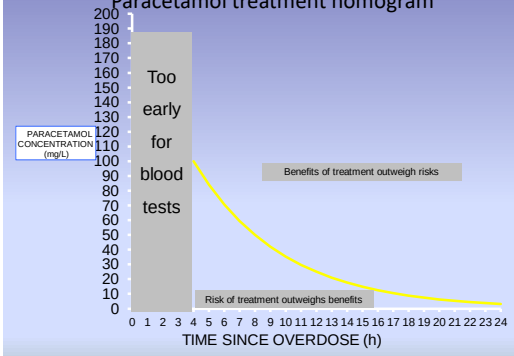
Clinical Features - Delayed

- Renal failure
  - Less common
    - 2-7 days after poisoning
    - Oliguria
    - Loin pain
- Others
  - Hypoglycaemia
  - Metabolic Acidosis

Investigations

- Paracetamol level
  - Best early predictor of prognosis
  - Determines need for antidotes
- Clotting esp. PT or INR
  - Increased due to reduced clotting factor production (II,V,VII)
- Urea, electrolytes and creatinine
  - elevated if renal damage
  - NB urea may remain low due to reduced hepatic urea production

Paracetamol treatment nomogram



Investigations

- Blood gases
  - may show metabolic acidosis
    - indicates very severe poisoning
- Liver function tests
  - INR or PT prolonged
  - Elevated transaminases common and poor prognosticator
  - Elevated bilirubin indicates significant hepatic necrosis

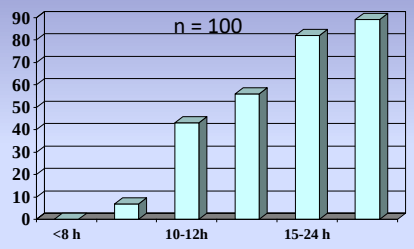
Poor Prognostic Features

- PT or INR rising after day 3
- PT >180 s at any time
- Bilirubin > 70 umol/l
- Metabolic acidosis
- Encephalopathy [III or IV]
- Raised Lactate
- Creatinine > 300 micmol/L

Treatment 1

- Prevent absorption
  - Activated charcoal in large dose
  - Within 1 hour
- Specific antidote
  - Provide glutathione for detoxification of NAPQI as IV N-acetyl cysteine
  - Warning! Value of antidotes decreases with time

Proportion of patients above '200 line' developing severe hepatic dysfunction after i.v. acetylcysteine



Interval to treatment

Prescott et al, 1979

Treatment 2 : N-Acetylcysteine

- Intravenous over 21 hours (UK)
  - Oral over 72 hours (USA) appears equally effective
- Highly effective up to 8 hours
  - Value decreases thereafter
  - Probably some effect up to 24 hours
  - Value after that unknown
- Beneficial in patients with fulminant hepatic failure
- Current opinion supports use at any time after severe poisoning

Treatment 3 : N-Acetylcysteine

- Complications
  - Anaphylac*toid* reactions
    - urticaria
    - wheeze
    - hypotension
- These are not true allergic reactions but rather caused by dose-related histamine release
- Reduce infusion rate and give antihistamines
- Steroids not indicated

Treatment 4 : Supportive therapy

- Vitamin K
- Fresh frozen plasma (for active bleeding only)
- Hepatic intensive care
  - Fluid balance
  - Inotropic support
  - Intracranial pressure monitoring
- Dialysis for renal failure
- Orthotopic liver transplantation

Aspirin (salicylate) poisoning

- Less common o/d than paracetamol in UK
- Clinical Features
  - Dizziness
  - Sweating
  - Tinnitus
  - Vomiting
  - Vasodilatation
  - Hyperventilation
  - Agitation
  - Delirium
  - Coma (esp' children)

Metabolic abnormalities

- Metabolic Acidosis
  - Salicylic acid
  - Uncouples oxidative phosphorylation
- Respiratory alkalosis
  - Direct CNS 'respiratory centre' stimulation
- Hypoglycaemia
- Hypokalaemia

Investigations

- Plasma salicylate concentration
- Urea, electrolytes, bicarbonate
- Blood glucose
- Arterial blood gases

Treatment 1

- Gastric decontamination
  - 50g activated charcoal
  - Within 1 hour
  - ? gastric lavage + activated charcoal if very large o/d (rarely used)
- Prevention of CNS penetration
  - Sodium bicarbonate
- Enhanced elimination
  - Urinary alkalinisation (sodium bicarbonate)
  - MDAC

Treatment 2

- Haemodialysis
  - Highly effective at removing salicylate
  - Also corrects metabolic abnormalities
- Consider with
  - pH < 7.3
  - salicylate level > 700 mg/l (600 mg/l in children)
  - patients in renal failure

Treatment 3

- Airway
- I.V fluids
- Ventilation
- Glucose for hypoglycaemia
- KCl for hypokalaemia

Opiates/Opioids

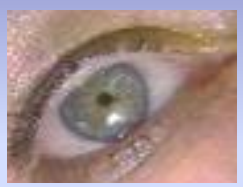
- Heroin
- Morphine
- Methadone
- Dihydrocodeine
- Codeine
- Pethidine
- Dipipanone
- Dextropropoxyphene
- Tramadol
- Buprenorphine

Opiates - Common methods of administration

- Oral
- Smoked
- Intravenous
- Inhaled

Opiates - effects

- CNS and respiratory depression
- 'Pin-point' pupils
- Hypotension, tachycardia
- Hallucinations
- Rhabdomyolysis
- Non-cardiac pulmonary oedema



Opiates - Management

- Airway management if reduced GCS or respiratory rate
- Breathing
  - Consider Opioid receptor antagonist
    - Naloxone
  - Ventilation
- Circulation
- Disability – reduced GCS
  - Consider Opioid receptor antagonist
- Hepatitis B,C and HIV precautions (IV users)

Naloxone - rational use

- Use in suspected opiate intoxication for
  - Diagnosis & Treatment
- Indications
  - Reduced respiratory rate <10/min
  - Reduced conscious level <10/15
- Use adequate doses
  - Adults: 400microgram up to 2.0 mg or more
  - Children: titrate up from 0.1 mg/kg
- Repeat as necessary or use a continuous infusion
  - 2/3 of initial dose required to rouse patient by IVI per hour

Naloxone - dangers

- Danger! – Shorter ½ life than most opioids
- Acute withdrawal syndrome
  - muscle aches, diarrhoea, palpitations, rhinorrhoea, yawning, irritability, nausea, fever, tremor, cramps
- Self-discharge during alert phase with subsequent coma / death
- Unmasking of pain
- Hypertension
- Behavioural disturbances (high doses)
- Rarely fits, arrhythmias, pulmonary oedema

Tricyclic antidepressant poisoning

- About 6% of overdoses
- High case fatality.
- 100-200 deaths/year in UK

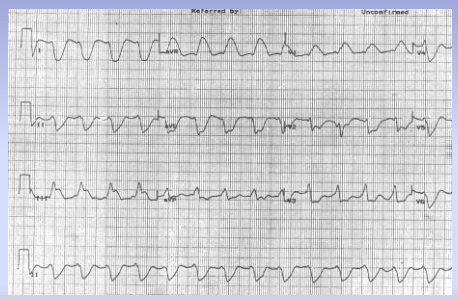
Clinical Features by pharmacodynamic action

- Anticholinergic effects
  - Hot dry skin
  - Dilated pupils
  - Tachycardia
  - Urinary retention
  - Agitation
  - Delirium
  - Fits
  - Coma
  - Hypertonia
  - Hyperreflexia
- Sodium channel blocking effects
  - Cardiac Arrhythmias
  - Conduction block
  - Prolonged QRS and QT intervals
- Alpha adrenoceptor antagonism
  - Hypotension

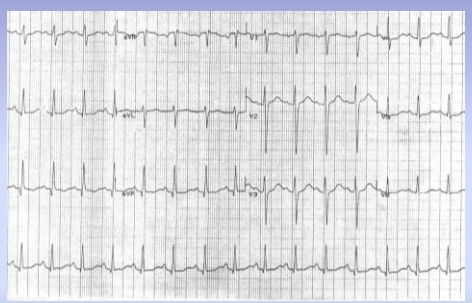
Investigations

- Urea & electrolytes
- Blood glucose
- Arterial blood gases
- ECG
  - QRS duration
    - > 160 ms (4 small squares) = very high risk of arrhythmia
    - > 120 ms (3 small squares) = specific urgent action
- Constant cardiovascular monitoring
  - CCU or ITU if large overdose or initial ECG abnormal

Tricyclic antidepressant Cardiac toxicity



Tricyclic antidepressant toxicity - following sodium bicarbonate



Treatment 1 - General

- Gastric decontamination
  - Activated charcoal if within 1 h
- Enhance elimination
  - MDAC: Further doses of activated charcoal every 2 hours may enhances elimination of some tricyclics (amitryptiline, nortryptiline)

Treatment 2 - Arrhythmias

- More likely if pH < 7.4
- Give Sodium Bicarbonate for
  - Acidosis
  - Wide QRS complex [120ms]
  - Arrhythmias
- Correct K^+
- If bicarbonate fails consider DC cardioversion or overdrive pacing
- Danger DO NOT USE ANTI-ARRHYTHMICS (may worsen arrhythmias)

Treatment 3 - Fits

- Use DIAZEPAM or LORAZEPAM
- If fails, consider paralysis and mechanical ventilation

Iron Poisoning

Warning - Corrosive!

- Uncommon
- May be serious [esp children]

- Early (0-6 hours)
  - Nausea and vomiting
  - Abdo pain
  - Diarrhoea [bloody]
  - Massive GI fluid loss
- Delayed (2-72 hours)
  - Black offensive stools
  - Drowsiness/coma
  - Fits
  - Circulatory collapse
- Late (2-4 days)
  - Acute liver necrosis
  - Renal Failure
- Very late (2-5 weeks)
  - Gastric strictures

Investigations in iron toxicity

- History - establish amount of elemental iron taken (serious overdose >10mg/kg)
- Iron level
  - After at least 4 hours
  - Repeat after 2-3 hours
- Blood count [usually see leucocytosis]
- U&E's
- Bicarbonate - monitor daily
- Glucose [usually see hyperglycaemia]
- Clotting - monitor daily
- LFT's

Treatment 1

- Gastric decontamination if large OD
  - Gastric lavage
- Danger - Activated Charcoal ineffective
- Induced emesis has been used in small children but vomiting may mask symptoms - not generally recommended

Treatment 2 : Desferrioxamine

- Chelates iron and reduces toxicity
- Chelate (ferrioxamine) is water soluble and excreted in urine (red discolouration)
- Can cause adverse effects, e.g.
  - hypotension and pulmonary oedema
- Contraindicated in renal failure
- Used for patients with severe toxicity
  - Fits, coma, circulatory collapse
  - GI symptoms, leucocytosis, or hyperglycaemia and high iron concentration (>3 mg/l)

Treatment 3 : Supportive

- Hypotension - I.V fluids
- Vomiting - Antiemetics
- Fits - Diazepam / Lorazepam
- Acidosis - Correct with bicarbonate
- Renal failure - Dialysis

Poisons Information

- **TOXBASE - database of National Poisons Information Service (NPIS)** www.toxbase.org