The fellowshipexam.com toxicology notes.

‘T’ is for TOX

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Beta Blockers Overdose

Rapid Absorption: peak clinical effects 1-4 hours
Propranolol- high lipid solubility – crosses blood brain barrier
B_1 receptors are in myocardium (chronotropy, inotropy) kidney and eye
B_2 receptors are in smooth and skeletal muscle (relaxes smooth muscle in blood vessels, bronchial tree) adipose tissue , pancreas and liver.
Toxicity develops within 6 hours of ingestion.

Different beta blockers have different properties: Atenolol , esmolol , metoprolol- B_1 selective.
Propranolol and Sotalol are not. Most mortality is due to Propranolol or Sotalol.

Propranolol may impede Na entry and affect phase O, resulting in a prolonged QRS similar to tricyclic antidepressants.

Toxic Dose

>1.5g of Propranolol is associated with severe toxicity.

How do they present?

Cardiac
Sinus node suppression
Conduction abnormalities- AV block, AV dissociation.
Decreased contractility

Propranolol

Na Channel blocking effect
QRS Prolongation
Ventricular arrhythmias

Sotalol

Beta Blockers and class 3 antiarrhythmic
QT Prolongation
Torsades

2. decreased loc and seizures.

Treatment

Catecholamines- isoprenaline or adrenaline
Hyperinsulinemia Euglycemia-
Actrapid 1V/KG IV then infusion +50 ml of 50% DEXT then infusion

SODIUM BICARBONATE
1-2mmol/KG 3-5Mn to a ph of > 7.3

Calcium Channel Blockers Overdose

Rapid absorption

Beware slow release preparation of verapamil

They affect myocardial contractility and slow conduction through SAN and AVN.

- Antagonize extracellular Ca^{2+} Into cardiac muscle
  Affect O phase depolarization in SAN, AVN.
- Antagonize extracellular Ca^{2+} Into smooth muscle
  Decreased smooth muscle contraction = vasodilation

The most toxic are verapamil and diltiazem. Symptoms and toxicity can occur with 2-3 times normal dose especially in elderly.

How do they present?

CNS	GIT	Metabolic	Cardiovascular
Confusion	N+V	Increase BSL	Hypotension
Coma		Lactic Acidosis	arrhythmia
Slurred Speech			Bradycardia
Respiratory Arrest			2°/3° AV Block
			Sinus Arrest asystole

Treatment

Charcoal
Supportive Treatment

Calcium- calcium gluconate 10% IV over 10 minutes (0.6ml/kg child)
calcium chloride 10% IV over 10 minutes (0.2ml/kg child)
It is an inotropic agent (can be used for beta blockers also)

Catecholamines- Adrenaline (1mg/kg/min)
Hyperinsulinemia euglycemia
Actrapid 1u/kg IV then infusion +50 ml of 50% dext then infusion
Sodium Bicarbonate: 1-2 mmol/kg 3-5 min to PH >7.3

Colchicine Overdose

Colchicine is a very prevalent drug. It's been used for the treatment of gout for some time. It's also used for scleroderma and now for the treatment of pericarditis.

Poisoning is rare except in cases of deliberate self-harm. Therapeutic overdose can occur especially in elderly with hepatic or renal disease.

Peak levels occur 0.5 to 2 hours post ingestion.

Elimination is by renal excretion, hepatic metabolism, and enterohepatic circulation with elimination of t ½ of 10.6-31.7 hours.

Binds to tubulin preventing formation of microtubules, affecting cell shape, secretion.

Toxic doses

<.5 mg/kg – GITS and zero mortality (some fatalities)

0.5-0.8mg/kg – bone marrow aplasia + 10 % mortality

>.8mg/kg – cardiovascular collapse 100% mortality.

How do they present?

There are 3 clinical stages which overlap.

Stage	Time	Symptoms/ Signs
I	2-24 H	GIT Phase- N+V+D, Abdo Pain Peripheral leukocytosis
II	24-72	Multi Organ Failure Bone Marrow Suppression ARDS Arrhythmias, Cardiac Failure Arrest consumption coagulopathy Change in mental state Decrease in Ca/Na/Mg/P Oliguric renal failure Seizures, sepsis
III	6-8 DAYS	Recovery Phase

Treatment

Activated charcoal
Supportive therapy

- This will vary depending on the patient and may include
    - IV rehydration
    - Mechanical ventilation
    - Correction of coagulation disorder
    - Antibiotics

Note that activated charcoal in repeated doses , haemodialysis, will not be effective.

Corrosive Ingestion

Strong corrosives are those with PH of <2 or > 12
Alkalis- liquefactive necrosis – injure oesophagus
Acids- Coagulative necrosis- injure stomach
Tissue injury continues for several hours. Tissue remains friable until about 2nd week when collagen deposition begins.
Acute complications are: - haemorrhage, perforation, fistula formation

How do they present?

- Oropharyngeal Pain
- Drooling
- Abdominal Pain
- Pain on swallowing
- Vomiting
- Airway- Larynx- hoarse voice- stridor
- Fever
- Tachycardia
- Hypotension

Absence of burns to oropharynx does not exclude significant oesophageal burns.
Patients can present post oesophageal perforation and mediastinitis

- Chest pain , dysponea , fever , subcutaneous emphysema
- If abdominal oesophagus perforated – abdominal pain, fever, ileus

Systemic toxicity can result from large ingestions:

- Hypotension, metabolic acidosis, haemolysis, nephrotoxicity, haemoglobinuria, pulmonary oedema

Investigations

Bedside : ECG
Labs : ABG, FBC, Xmatch, EVC, BSL, LFT
RADIOL: CXR Upright
Upper GI endoscopy within 24 hours. Consider CT scanning (controversial)

How to treat

If evidence of airway compromise i.e. stridor , hypoxia – may need early intubation.
Rinse mouth with 250 ml water/ milk (controversial), Otherwise NBM
DO NOT- give charcoal, aspirate or try to neutralise.

What about

Broad spectrum antibiotics- ONLY if GIT perforation
Corticosteroids to prevent strictures – no evidence of efficacy
-Studies all post scope
-May increase risk of perforation

Who can be discharged?

Asymptomatic patients can be discharged – return if develop symptoms
Not likely to be cause by household bleaches and cleaners unless large amounts.

DIGOXIN OVERDOSE

It undergoes initial distribution then redistribution to a larger volume
Elimination t ½ = 36 hours
Excreted by kidney
Inhibits Na-K ATPase leading to intracellular depletion of K+ and hyperkalaemia.

How do they present?

N+V
Hyperkalaemia (indicates significant toxicity)
Arrhythmia – -Sinus Bradycardia

-SAN Arrest

-1° 2° 3° blocks

-VT VF

Overdoses can be acute or chronic. In chronic toxicity visual disturbance, weakness and fatigue occur along with nausea and vomiting.

Investigations

Bedside: ECG

Labs: EVC(looking for hyperkalaemia) + renal function

Digoxin level at 6 hours

0.6-1nmol/L- Therapeutic

- But may be chronic toxicity

Levels do not correlate with clinical picture.

Treatment

Indications for FAB Fragments

1. Hyperkalaemia (k>5.5mmo/L) in digoxin toxicity
2. > 10mg digoxin ingestion
3. Hemodynamically unstable cardiac arrhythmia
4. Cardiac arrest from digoxin toxicity.
5. Serum digoxin of > 15nmol/L

40mg fab Fragments (one vial) will bind 0.5 mg digoxin . In unknown dose give 2 vials and check response. In cardiac arrest give 5 vials. In chronic toxicity give 2 vials.

Who to send home

Those with only GIT Symptoms in chronic toxicity, cease digoxin, check electrolytes and renal function. Acute overdoses need 12 hours of observation.

GLYPHOSATE

A non-selective herbicide that inhibits the synthesis of an amino acid in plants. (not found in humans)

Toxicity is attributed to the surfactant co-formulates

HOW DO THEY PRESENT?

Symptoms range depending on amount and concentration

- Abdominal pain
- N +V +- diarrhoea

TO

- Inflammation, ulceration, haemorrhage, infection of GIT

TO

Multi-organ dysfunction

- Kidney /liver dysfunction
- Hypotension
- Pulmonary oedema
- Pneumonitis
- Altered level of consciousness
- Metabolic acidosis

No Investigations that specifically assist

TREATMENT

All patients observed for 6 hours, there with GIT symptoms 2+ hours mostly supportive care – no antidote

PARAQUAT TOXCITY

It is one of the most toxic pesticides available. Mortality in acute poisoning is 50-90%
It works by mechanism of free oxygen radical generation which damages cell lipid membranes. It concentrates in pneumocystis and renal tubular cells.

TOXIC DOSE

> 20mL leads to

- Pneumonitis, hepatitis, renal injury
- Death within 48 hours

< 20ml leads to

- respiratory failure secondary to palm fibrosis
- Degrees of hepatic/renal damage
- Still a risk of death, but delayed weeks/months

HOW DO THEY PRESENT?

- GIT Toxicity V&D
- Oral mucosa neurosis within 12 hours
- Oesophageal perforation
- Pulmonary and renal and hepatic damage

INVESTIGATIONS

FBC

EUC – look at renal function – higher creatinine- worst outcome

ABG

CXR

Dithionite urine test

- Add sodium dithionite +Ig $NaHCO_3$ to 10mL urine
  - Blue + PARAQUART
  - Green + DIQUAT
- If negative at 6 hours = significant exposure unlikely

TREATMENT

Nothing works, but due to poor outlook try anything/everything
No great evidence that anything helps ;arge exposeure
Supportive care. IVF
Consider activated charcoal, hullers earth.
Anti-oxidants Vit C, E, acctyl-cystenine
Immune –suppression- cyclophosphamide, steroids, Haernperfusion.

Insulin Overdose

Insulin is eliminated by hepatic metabolism and renal clearance.

When used subcutaneously or intramuscularly it can form a depot and release insulin for several days.

Actions of Insulin

Intracellular movement of – glucose
Potassium
Magnesium
Phosphate

Decreases ketone production
Inhibits breakdown of fat and protein to release glucose.

How do they present?

Coma
Seizures
Diaphoresis
Tremor
Tachycardia

Investigations

Bedside : BSL to monitor and titrate dextrose administration.
LABS: EUC –especially potassium, Mg, P

Treatment

Dextrose- may need 50 % initially or a 10 % infusion at 100 ml/ hr. Replace potassium as needed.
All patients with insulin overdose should be admitted and watched for 8 hours. If asymptomatic at this time can go home.
In those with a dextrose infusion once hyperglycaemia begins to develop, the infusion can be halved every 2-4 hours. Watch 6 hours post dextrose to ensure euglycemic.

Malignant Hyperthermia

Caused by anaesthetic agents - inhalational anaesthetics
Habthane
Isoflurane
Enflurane
- Succinylcholine
- Ketamine???? Controversial

Untreated mortality= 70 %

How do they present?

- May simply present as postoperative fever
- May have failure of muscle relaxation post succinylcholine
- Tachycardia
- Tachypnoea
- May progress to hyperthermia , rhabdomyolysis , acidosis.

Investigations

No specific investigations
Aim at investigating alternative diagnosis

Treatment

Supportive care
Dantrolene – 2.5mg/kg IV then every 15 minutes to maximum of 30 mg/kg
- It inhibits release of calcium from sarcoplasmic reticulum

Beware as may occur post treatment.

How to differentiate between:

- Neuroleptic Malignant Syndrome (NMS)
- Serotonin Syndrome (SS)
- Malignant Hyperthermia (MH)

1. History is important
   Drugs they are on
   Have they had anaesthetic or sedation?
2. Altered Mental State
   Fever
   Muscle Rigidity
   Occur in all three- CK may be the one way to distinguish

METFORMIN OVERDOSE

- It is a biguanide
- Rapidly absorbed, minimally metabolized, excreted almost entirely by the kidneys.
- It inhibits gluconeogenesis

It does not tend to cause hypoglycaemia in both therapeutic doses and massive overdose.

It can cause life threatening lactic acidosis.

- It blocks intracellular oxidative pathways leading to increased metabolism
- Lactic acidosis can occur in normal dosing when renal impairment present causing drug accumulation

hypoglycaemia

How do patients present?

There are minor symptoms.
As lactic acidosis increases

- Tachypnoea
- Cardiovascular instability
- Altered mental state

Investigations

LABS: EUC, Renal function, lactate

Treatment

Supportive treatment with IV fluids

If lactate > 10 mmol/L with acidosis , renal dysfunction and worsening clinical condition then HAEMODIALYSIS is indicated. It removes metformin and corrects acid base disturbance.

Neuroleptic Malignant Syndrome

Occurs with Antipsychotics
Due to central dopamine blockade
Maybe difficult to distinguish from serotonin syndrome

How do they present?

1. Altered Mental Status- from delirium to coma
2. Hyperthermia T >38 degrees Celsius
3. Autonomic Dysfunction – Tachycardias
   - Arrhythmias
   - Respiratory irregularities
   - Hyper/Hypo tension
4. Muscular Rigidity- lead pipe + increased tone
   - Resistance to passive movement

Differential Diagnosis

- Heatstroke
- Thyrotoxicosis
- Drug Intoxication
- Serotonin toxicity
- Anticholinergic toxicity

Investigations- Findings

1. Increased Muscle Enzymes- CK,LDH, AST
2. Increased WCC

Treatment

-Dehydration- IVF
- Hyperthermia –Cooling of > 39.5 degree Celsius intubation and paralysis
- Thromboembolism prophylaxis
- Benzodiazepines- early
- Bromocriptine – 2.5mg PO tds to 40 mg daily for 1-2 weeks
- Dantrolene – if prominent hyperthermia and muscle rigidity
  - 2-3 mg/kg/day IV (controversial)

Serotonin Sydnrome

It is a clinical diagnosis. Most cases resolve within 24- 28 hours once agent withdrawn. Develops after a latent period (hours to days)

How do they present?

1. CNS Dysfunction
    - Agitation, anxiety
    - Confusion
    - Altered/ decreased level of consciousness
    - Seizures
2. Motor Dysfunction
    - Clonus, hyperreflexia , hypertonia
    - Incoordination
    - Tremor
3. Autonomic Dysfunction
    - Hyperthermia
    - Diaphoresis
    - Diarrohea
    - Hypertension
    - Tachycardia

The more serious cases develop hyperthermia and muscle rigidity resulting in rhabdomyolysis, DIC and renal failure.

Treatment

Benzodiazepines- in simple cases
Intubation and paralysis
Chlorpromazine 12.5-50 mg ?/iv
Cyproheptadine 4-8mg PO 8/24

PESTICIDES

ANTICHOLINESRASE COMPOUNDS – ORGANOPHOSPAHTES and CARBAMATE

HOW DO THESE PAITENTS PRESENT?

PAITENTS HAVE AN ACUTE CHOLINERGIC CRISIS- Symptoms develop within 6 hours

FEATURES	TREATMENTS
MUSCURINIC D-DIARRHOEA U-URINARY FREQUENCY M-MIOSIS B-BRACYCARDIA E-EMESIS L-LACRIMATION S-SALIVATION Bradycardia, broncorrhoea, bronchospasm and hypotension = significant toxicity	ATROPINE 1-3mg IV Endpoint is resolution of bronchorrhoea and HR > 80 bpm If endpoint not achieved in 3-5 minutes double atropine dose and continue to double. Signs of Atropine toxicity = delirium, hypertension
NICOTINIC Fasciculations and muscle weakness May progress to paralysis and respiratory failure.	Intubation and ventilation – AVOID SUX Give oxime- Parlidoxime - 2g loading dose - 24g/day for 48 hours
CENTRAL NERVOUS SYSTEM Altered level of consciousness Seizures Respiratory failure.	Intubation and ventilation – AVOID SUX BENZODIAEPINES – midazolam 5-10mg IV WAY TO AVOID SUXAMETHNZONE IN THESE CASES Suxamethonium is metabolised by butyrylcholinesterase. In toxicity is depressed within 6 hours. The result will be that the duration of paralysis will be prolonged.

Organophosphate – included delayed polyneuropathy

- Demyelination of long nerves
- Occurs 1-3 weeks post acute exposure
- Motor and sensory dysfunction
- It may be chronic or recurrent

The treatment is supportive care and rehabilitation.

INVESTIGATIONS

The diagnosis is essentially a clinical one

Base bloods should be done

If available or exposure questionable

Butyrylcholinesterase is a sensitive marker for exposure.

Sulphonylurea Overdose

Sulphonylurea – most common oral hypoglycaemic
Glibenclamide, gliclazine, glimemperide, glipizide
Hepatic metabolism renally excreted
Cause insulin release from cells, 2° to CA^{2+} influx
Overdose can lead to prolonged hypoglycemia

Treatment

Consider charcoal if early presentation
Correct Hypoglycemia

- Use 50 ml of 50% dextrose
- Then infusion of 10 % dextrose at 100 ml/ hour

Beware hypoglycemia is often refractory to dextrose and octreotide is needed.

OCTREOTIDE

Suppresses insulin release from cells by binding to and inhibiting CA^{2+} influx
It is first line treatment
It can remove the need for dextrose
Give 50 mg IV Bolus then infusion of 25 mg/ h. Continue for >= 24 hours
It can also be used in the non-acute overdose but in those patients where there is a therapeutic accumulation of sulphonylurea.

Admit all sulphonylurea overdose for up to 12 hours (slow release)

TOXIC ALCOHOLS

Methanol and Ethylene Glycol. Rare poisoning in Australia due to limited availability

METHANOL → FORMALDEHYDE → FORMIL ACID (affects cell respiration)
ETHYLENE GLYCOL → GLYCOALDEMDE → GLYCOLATE, GLYOXYLATE, OXYLATE

LEATHAL DOSE

Methanol is 0.5-1.0ml/kg of 100% solution
Ethylene Glycol 1ml/kg of 100% solution

INVESTIGATIONS

Serum levels of methanol or ethylene glycol > 50mg/dL = severe toxicity
ABG – raised anion gap metabolic acidosis raised osmolar gap.

HOW DO THEY PRESENT?

METHANOL

- Mild CNS depression
- A latent period of 6-24 hours where no symptoms
- Ophthalmic, GIT and CNS symptoms
- Coma and seizures indicate cerebral oedema and poor prognosis

ETHYLENE GLYCOL

Progression in three stages, although may overlap.

- Neurolgical - N +V, coma, seizures
- Cardiopulmonary
- Renal – rapid progression of renal failure.

TREATMENT

ADH (Alcohol Dehydrogenase Blockade)

Prevents metabolism of toxic alcohols to their metabolites.
Use ethanol (fomeprisole not available Australian)
8 mmL/kg of 10% IV ethanol or 3 X 40ml shots vodka

- Maintain 1-2mL/hr of 10% ethanol or 1 vodka/hour
- Half life of the toxic alcohols increases with methanol.

HAEMODALYSIS

Removes parent toxic alcohols and metabolites. Indications are:

1. 1 Metabolic Acidosts pH < 7.25
2. Toxic ingestion and Osmolar gap > 10 mmo/L
3. Levels $<$ 50mg/dL of either
4. Visual symptoms (methanol)
5. Renal Failure (ethylene glycol)

OTHER SUPPORTIVE TREATMENT

METHANOL –Folinic/Folic acid 2mg/kg IV QID. Bicarbonate to correct acidosis if pH < 7.3

ETHYLENE GLYCOL Ca^{2+} supplementation if hypocalcaemia or prolonged QT/seizures – controversial.

WHERE ARE TOXIC ALCOHOLS FOUND?

METHANOL: Model aeroplane fuel, laboratory solvents

Ethylene Glycol: radiator antifreeze, or coolant, hydraulic fluids or solvents

<u>Paracetamol Overdose</u> – Acetaminophine

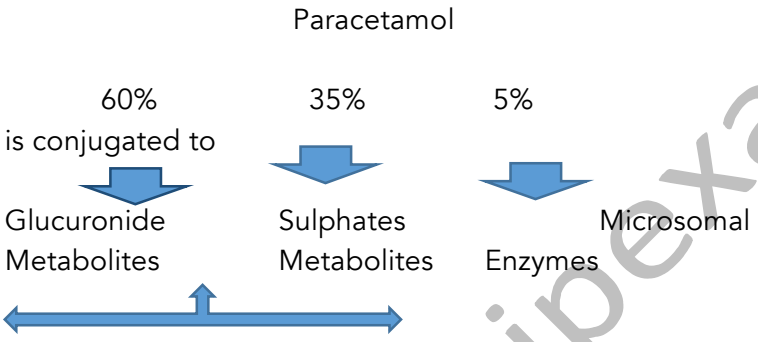
Peak Plasma Concentrations: 30-60 min (tablet), < 30min (syrup)

Bioavailability: Increases with size of dose: 60% with 500 mg
90% with 1-2 g

Volume of distribution: 1L/KG: 50% is plasma protein bound
Where does metabolism occur? Primarily Liver + Small Amounts Kidney

Elimination Half Life: 1.5-2.5 hours. Same for adults and children.

Metabolism of Paracetamol



In overdose these 2 pathways are rapidly saturated ? metabolism results in production of NAPQI(N-acetyl-p-benzo-quinone imine.
Conjugated with glutathione to produce non toxic metabolites excreted by the kidney. When gluthathione stores are depleted by 70% HAPQI accumulates in the liver, binds to hepatocytes and causes centrilobular hepatil necrosis.

<u>Microsomal Metabolism</u>

Inhibited (i.e less NAPQI) in -acute alcohol ingestion

- Administration of 4 methylpyrazole

Enhanced by

- Chronic alcohol ingestion
- Starvation
- barbiturates
- Carbamazepine
- Oral Contraceptives

Variants to the single dose overdose

1. Sustained release formulations (Panadol Osteo)
    - 665 mg –one third immediate release: the rest sustained
    - Aims to maintain therapeutic levels for up to 8 hours
    - Result in reduction in peak paracetamol concentration under the curve? > 50%
    - There is also a delay in peak concentration in 1-3 h
    - A peak level may be missed by a? measure.

2. Repeated sub therapeutic dosing
    - There is a risk of hepatotoxicity especially in those with hepatic risk factors.
    - Nomogram can't be used
    - If LFts are up its due to toxins
      In the alcohol/ viral ? Patient aminotransferase is? ? 1000 IU/L

3. Staggered acute overdose: ie > 1 overdose over several hours.
   Assume that the paracetamol has been ingested as a total dose at the earlier overdose time.

The stages of paracetamol poisoning

Paracetamol toxicity presents with non-specific features. If left untreated it would progress thru 4 stages.

Stage 1
Lasts 24 hours
Subclinical apart for mild nausea, vomiting and malaise.
During this period toxic metabolites develop 24-48 hours

Stage2
Nausea and vomiting resolve
Right upper quadrant tenderness develop at 24-48 hours
LFT's deteriorate . Bilirubin ↑ AST ↑ PT ↑

Stage 3
72-96 hours
Deterioration hepatic function
Jaundice,?
Peak aminotransferase occur

Stage 4
Resolution or less commonly fulminant hepatic failure.

Most patients recover with untreated mortality < 1 %

And in untreated patients with hepatoxicity 3.5%

Other clinical presentations of paracetamol poisoning

Coma- due to massive ingestion and independent of hepatic damage- levels needed are > 6500 mol/L
Lactic academia
Cardiac damage
ECG abnormalities – ST-T wave changes
Bundle branch block
Sinus bradycardia
Renal failure- independent of hepatotoxicity or as hepatorenal syndrome

How do we assess the risk of hepatotoxicity?

Risk is dose dependent. Adult 200mg/kg or 10 g whichever is least
Children < 6 yo 200 mg/kg= toxic
The nomogram begins at 4 hours post ingestion. Levels taken earlier than 4 hours are unreliable.
The treatment line in Australia is 1000 u Mol/L (150mg/L) at 4 hours post ingestion and 125 u MOl/L (16mg/l) at 16 hours. These values have shown to result in no deaths.
There are some higher risk group's i.e.

- Chronic alcohol liver disease
- Chronic active hepatitis

The treatment nomogram capture these

What antidote do we use?

n-acetylcysteine (NAC) prevents hepatotoxicity which is defined as ACT >1000 IU/L
Administered by a 20 hour protocol
Incidence of hepatotoxicity if commenced within 8 hours of ingestion is 1-6%
Incidence of hepatotoxicity increases to 40% if delayed 10-16 hours (20%)
Adverse reactions to NACare anaphylactoid i.e not IgE mediated but due to direct histamine release from mast cells. They respond to slowing or stopping the infusion for a short time.
Occasionally antihistamines or adrenaline maybe used.
Previous adverse reaction with NAC does not preclude its use.
Life threatening reactions have reported in patients with asthma.

How we treat overdose patients

The overdose can be acute and within time frames.

- Acute and delayed
- Chronic
- Repeated

What about the pregnant patient?

As per other patients

Acute overdose- paracetamol toxicity increases

-the risk of spontaneous abortion.

1. Within 8 hours

   In patients presenting within 1-2 hours consider activated charcoal.

   Give NAC as per protocol over 20 hours

   - 150 mg/kg over 15 mins
   - 50 mg/kg over 4 hours
   - 100 mg/kg over 16 hours

2. Within 8-24 hours.

   Commence NAC on presentation

   Take bloods for paracetamol level and LFT

   If LFTs show rising aminotransferases prior to the end of 20 hours , prolonged NAC infusion maybe needed.

3. At greater than 24 hours post ingestion.

   Commence if - detectable paracetamol level.

   Evidence of aminotransferases elevation

   Clinical evidence of hepatotoxicity

   Nausea, vomting , RUQ pain

May need prolonged NAC ie at rate of 100mg/kg/12h until PT/ INR and liver function normalizes or the patient requires liver transplantation.

What if the time of ingestion is unknown?

Commence NAC as per the 20 hour protocol. Take paracetamol level, LFTs and PT/INR.

Can cease treatment with a more accurate history or if aminotransferases are normal at 20 hours.

What if there is more than one dose?

Assume that the total dose is ingested at an earlier time. Assume if > 200 mg/kg to treat.

What if there are repeated small doses?

In adults and children > 6 yo if

- > 200 mg/kg or 10 g ingested over 24 hours or
- >150mg/kg or 6 g per 24 hours for preceding 48 hours.

If liver impairment > 100 mg/kg or 4 g per 24 hours

In all the patients if -serum paracetamol < 70 u mol/L and

-serum aminotransferases are < 50 IU/L

-NO TREATMENT

If either raised treat with NAC and retake with LFTs in 8 hours. If LFTs are not rising within 8 hours can stop NAC otherwise can continue for full 20 hour course.

What about sustained release paracetamol?

The peak paracetamol concentration may be delayed.
Give if present > 20 hours
Give if dose is >200mg/kg or 10 g
Take paracetamol levels at 4 or more hours post ingestion. The 4 hours after this- if both fall below the line, cease treatment otherwise continue for 20 hour protocol.

What if the patient has taken a massive ingestion?

This can be defines as >500 mg/kg or > 50 or paracetamol levels > 3000umol/L

In these cases consult with toxicology, but there need to be a doubling of the 16 hour infusion dose to 200mg/kg/16 hours