Chapter 28

TOXICOLOGY
ROBERT DUNN

EPIDEMIOLOGY OF POISONING
(T-H)

EXPOSURE TO TOXIC SUBSTANCES

• 80-90% of exposures occur in the home
• estimated yearly incidence of human poison exposures is 2%
• only 12.5% of patients calling poison centres report signs of toxic effects
• 60% of poisoning exposures are managed without presentation to hospital
• poisonings comprise approximately 1% of ED presentations
• > 10% of poisonings presenting to an ED result in hospital admission

Epidemiology of poisoning

• accidental 90%
  - failure to appreciate toxicity
  - recreational misadventure
  - drug errors
  - predominantly in children
• intentional 10%
  - deliberate self harm
  - malicious act by third party
  - predominantly adolescents and adults
• there is much higher incidence of intentional ingestions in patients that present to the ED compared to all poisonings

Route of exposure

<table>
<thead>
<tr>
<th>Route</th>
<th>%</th>
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<tbody>
<tr>
<td>Oral ingestion</td>
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<tr>
<td>Dermal</td>
<td>6</td>
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<tr>
<td>Ophthalmic</td>
<td>5</td>
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<td>Inhalation</td>
<td>5</td>
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<td>Bites and stings</td>
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<td>Parenteral</td>
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Poisoning in children

• children < 5 years of age account for 60% of poisoning exposures
  - 2 - 3 years of age is the peak incidence of poisoning
• accidental ingestion is unusual

after 5 years of age
- usually reflects the mistaken consumption of a substance from a mis-labelled container
• toxic exposures in children 5 - 9 years of age may reflect intra-family stress or suicidal intent
• toxic exposures in children > 9 years of age are usually non accidental
• the mortality from poisoning is lowest in patients between 5 -14 years of age

Common poisons

Number of agents taken in adults
• approximately 60% of poisonings involve more than one agent
• 5% involve > 3 agents

In adults presenting to the ED
• ethanol
• paracetamol
• benzodiazepines
• amphetamines
• marijuana
• antidepressants
• antihistamines
• opioids
• antipsychotics
• other stimulants
• hydrocarbons
• anticonvulsants
• NSAIDS

In children presenting to the ED
• paracetamol
• antihistamines
• rodenticides
• eucalyptus and other essential oils
• bleach
• detergents and other chemicals
• benzodiazepines
• noxious plants / mushrooms
• painting chemicals
• iron tablets

Poisoning mortality

• paediatric fatalities are rare
• 90% of deaths occur prior to any medical treatment
• 50% of all deaths are suicides
• 1/3 of all in hospital deaths are due to pulmonary embolism
• in hospital mortality for admitted patients is < 1% of admitted patients
• total mortality from poisoning is probably < 0.05% of all exposures

Poisons most commonly associated with mortality
• significant variation between countries
• ethanol present in approximately 40% of deaths in Australia
• carbon monoxide
• drugs of abuse
• analgesics
• antidepressants - mostly TCADs
• sedatives
• antipsychotics
• stimulants
• cleaning substances

Repeated poisoning

• 6-30% of patients admitted to hospital following poisoning will have a repeat episode within 12 months
• 15% will have multiple admissions
  - median time to readmission is approximately 72 hours
• repeat poisoners are mostly
  - males with antisocial personality disorder
  - females with borderline personality disorder

Suicide rate

• cumulative, following an episode of non fatal poisoning

<table>
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<th>Year</th>
<th>Rate</th>
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<tr>
<td>1</td>
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<td>1-5</td>
<td>3%</td>
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<tr>
<td>5-10</td>
<td>3%</td>
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<tr>
<td>&gt; 10</td>
<td>7%</td>
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Poisoning prevention

Strategies to prevent poisoning
• child proof containers
• proper medication storage
• drop off centres for no longer used medication
• reduction in the size of OTC preparations (e.g. paracetamol)
Strategies to prevent repeat poisoning
• none proven
• problem solving
• an emergency contact card
• flupenthixol may have a role
• dialectical behaviour therapy
  - most effective in borderline personality disorder

References
Shannon M, Ingestion of Toxic Substances by Children. NEJM January 20, 2000;Vol. 342, No. 3

Risk assessment in poisoning

ASSESSMENT

History
May be unreliable due to
• altered mental state due to toxicity
• lack of patient compliance in self harm
• recreational drug users frequently have taken agents sold as another agent

Identify the substance
• determine the route of exposure
• establish the dose and formulation taken of each substance
• calculate the total amount of each substance taken
• determine the time when the substance(s) was taken

Risk of toxicity depends on
• the agent(s) taken
• the amount taken
  - toxic doses are usually > 10 times the normal therapeutic dose
• the effects of drug combinations
  - eg TCAD and BZD may be protective for seizures
  - alcohol and chloral hydrate potentiate toxicity
• drug interactions
• the degree of tolerance of the patient to the agents taken
• pre-existent health status

Evaluate the extent of toxicity
• determine what symptoms of toxicity are present

Establish the reason for the poisoning
• accidental
• suicidal
• recreational
• administration by a 3rd party

Other
• time of post ingestion emesis (if present)
• if other first aid measures

administered
  - emetic
  - charcoal
  - the source of supply of the agent taken

Dangerous poisons
ie poisons with markedly higher risk of significant toxicity
• paraquat *
• chloroquine *
• carbon monoxide
• organophosphates*
• strong alkalis and acids
• toxic alcohols
• cardiac medications
  - Ca²⁺ channel blockers*
  - beta blockers*
  - antiarrhythmics*
• cyanide*
• colchicine*
• isoniazid*
• Amanita phalloides*
• theophylline*
• tricyclic antidepressants
• dextropropoxyphene
• heavy metals
• cocaine
• hydrocarbons
  - toluene
  - vinyl chloride
  - trichloroethylene
  - carbon tetrachloride
  - benzene
  - toluene
  - xylene
  - camphor
  - phenol
  - lindane
  - DDT
  - camphor
  - eucalyptus oil
• strychnine
• many plants

NB
• this list is not exhaustive, however it includes the poisonings most likely encountered in emergency medicine practice in Australia
• poisonings with agents marked by an asterisk may result in fatality despite optimal treatment

As a general rule
• drugs used for the treatment of mental illness have a very high safety profile
• all cardiac medications that have an effect on heart rate or rhythm are potentially fatal when taken in large amounts
• chemicals and plants can be highly toxic when taken in relatively small amounts
• sustained release poisonings are particularly hazardous as onset of toxicity may be delayed, often after close observation has ceased

Examination
Examination to establish toxicological cause
• measure vital signs
• examine pupil size and reactivity
• check breath for diagnostic odours
• check for signs of recent IV drug use
• determine if features of a specific toxidrome are present

Search for associated potentially serious complications and conditions
• pulmonary aspiration
• trauma
• hypothermia
• rhabdomyolysis
• check for pregnancy

Poisons causing blindness

Hypotensive agents
• causing occipital cortical infarction
• usually in the elderly

Direct cortical toxicity
• carbon monoxide and hydrogen sulphide may produce cortical blindness
• pupillary reflexes should be normal despite complete loss of vision
Retinal toxicity
- methanol (most common)
- quinine

Blindness via retinal ischaemia
- cocaine
- ergots
- retinal changes of pallor or vasoconstriction should be seen
- phencyclidine is associated with sun-gazers retinopathy due to prolonged staring at the sun and UV damage to the retina

Poisons with delayed toxicity
- toxicity is usually apparent within 6 hours of exposure to most poisons
- serious toxicity is usually evident sooner

Mechanisms
- bezoar formation
- delayed gastric emptying
- drug effect eg antimuscarinic
- diabetic gastroparesis
- shock
- connective tissue diseases
- slow onset of action
- delay in reaching target organ
- sustained release preparations
- opioids
- calcium channel antagonists
- paracetamol

Common agents
- paracetamol
- theophylline
- calcium channel antagonists
- MS contin / oxycontin
- methadone / diphenoxylate
- iron
- lithium
- MAOI
- all anticonvulsants
- digoxin
- organophosphates
- amiodarone
- oral hypoglycaemic agents
- colchicine
- astemizole
- warfarin / superwarfarins
- thyroxine
- high volatility hydrocarbons

Investigations
- screening for paracetamol is commonly performed following self harm

ECG
- very important in detecting drugs with Na+ and K+ channel blocking action
- should be performed initially and repeated at 4-6 hours in patients with ingestion of potentially cardiotoxic agents or ingestions of unknown agents

References
Isbister GK et al, Presumed angel’s trumpet (brugmansia) poisoning: clinical effects and epidemiology. EMA 2003;15:376.

TOXIDROMES (E-Ex)

DEFINITION
- groups of examination findings that may suggest the pharmacological activity of a poison causing toxicity
- uncommon for all features of a particular toxidrome to be present simultaneously
- the greater the number of features present from a single toxidrome, the more likely the toxic substance possesses the suspected pharmacological activity
- toxidromes are most useful when no reliable information is available regarding the type of poisonous substance
- the diagnostic accuracy of toxidromes may be limited by ingestion of:
  - substances with opposite pharmacological effects eg mydriasis may occur if an anticholinergic is taken with an opioid
  - ingestion of multiple substances with different pharmacological actions

Muscarinic (D-H)
Features
- (DUMB BELS)
- defaecation
- urination
- miosis
- bradycardia
- emesis
- lacrimation
- salivation

Common sources
- inocybe and clitocybe mushrooms
- organophosphates
- funnel web venom
- betel nut
- pilocarpine

Nicotinic
Features
- tachycardia
- hypertension
- muscle fasciculation
- paralysis

Common sources
- insecticides (nicotinic)
- redback / funnel web (and associated species) spider venom
- tobacco
- nicotine replacement therapy

Antimuscarinic (D-Ex)
Features
- warm, dry skin
- mild hyperthermia
- dry mucous membranes
- mydriasis
- tachycardia
- urinary retention
- absent bowel sounds
- central anti cholinergic syndrome
  - confusion
  - hallucinations - usually visual

Common sources
- antimuscarinics
  - benztpoine
  - hyoscine
  - scopolamine
- Trumpet lily / Angel's trumpet / (Brugmansia)
- Jimsonweed (Datura stramonium)

Management
- supportive management only is usually required
- central anticholinergic syndrome may be treated with physostigmine
- sedation with benzodiazepines (avoid drugs with anticholinergic effects eg phenothiazines)

Sympathomimetic (D-Ex)
Features
- CNS excitation
  - agitation
  - tremor
  - seizures
  - hypertension
POISONING BY UNKNOWN SUBSTANCES

**EPIDEMIOLOGY**

When poisoning should be considered
- altered mental state
- psychosis
- aggressive behaviour
- seizures
- cardiac and vascular events in young patients
- unexplained abdominal pain, vomiting
- hepatitis

**ASSESSMENT**

Examination
- search for toxidromes
- search for diagnostic odours

Investigations
- may give clues to possible sources
- nearly always required to exclude other potential diagnoses

ECG
- essential to detect agents with Na⁺ or K⁺ channel blocking action
- needs to be repeated 4-6 hours later

Blood tests (in order of importance)
- bedside glucose
- blood gases
- electrolytes, creatinine
- LFTs
- FBC
- measured osmolality
- serum paracetamol
- blood ethanol
- clotting
- drug screen

Antidotes
- trial of naloxone appropriate if mental state depressed
- flumazenil potentially hazardous if agents ingested unknown
- thiamine 100 mg IV
  - low yield, but low risk

**DIAGNOSTIC ODOURS**

**Acetone**
- sweet, like apples
- alcohol
- isopropyl alcohol
- chloroform
- ketoacidosis
- acetone!

**Acrid**
- pear like
- chloral hydrate
- paraaldehyde

**Ammonia**
- uraemia
- sodium valproate toxicity

**Bitter almonds**
- cyanide

**Burnt rope**
- marijuana

**Disinfectants**
- phenol
- creosote

**Rotten eggs**
- hydrogen sulphide
- mercaptans
- disulfiram

**Garlic**
- organophosphates
- arsenic
- phosphorus
- selenium
- thallium
- arsine gas

**Mothballs**
- camphor
- naphthalene

**Tobacco**
- nicotine
- nicotinic insecticides

**Heavy metal poisoning**
- grey blue mucous membrane discoloration
- gastrointestinal features (like chloroquine)
- neurological
- cerebral
- renal impairment

**References**
**Chapter 28 : Toxicology**

**Violets**
- turpentine in the urine

**Wintergreen**
- methyl salicylate

**DRINK SPIKING**
- increasingly commonly reported phenomenon
- associated with sexual assault in approximately 25% of cases
  - facilitated date rape

**Most common agents involved**
- ethanol 70%
- amphetamines 20%
- benzodiazepines 10%
- GHB 5%
- marijuana or cocaine also involved in approximately 10% of cases

**Assessment**
- hospital drug screening of no use in immediate management
- samples for forensic examination required for any potential police investigation
  - require chain of evidence to be maintained
  - no formal mechanism for this exists in most jurisdictions
- blood samples preferred to urine samples
- early sample taking important due to the short elimination T 1/2 of GHB and ethanol

**Management**
- as for other unknown poisoning
- encourage early police involvement
  - however the difficulty is proving that any substances detected were taken without the patients consent

**References**
Weir E, Drug-facilitated date rape. CMAJ 2001;165(1);80.

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**MANAGEMENT OF POISONING**

**IS ANY TREATMENT REQUIRED?**
- a large proportion of patients who present to the ED following poisoning require only symptomatic therapy for their poisoning
- especially patients
  - with poisonings predicted to have little or no toxic effects
  - who present many hours following poisoning who have no features of toxicity
- gastrointestinal decontamination is not required in patients with low likelihood of toxicity

**Principles of management**

**Reduce absorption**
- skin decontamination; important with:
  - organophosphates
  - organic metals
  - aniline
  - phenol
  - ethylene dibromide
- GIT decontamination options
  - oral activated charcoal
  - gastric lavage
  - ipecac
  - cathartics
  - whole bowel irrigation
  - ion binding resins

**Enhance elimination**
- repeated activated charcoal
  - effective in only a small number of poisoning types
- manipulation of urinary pH

**Use of specific antidotes**
- required in < 2% of poisonings

**Supportive**
- treat associated symptoms
- treat associated complications
- adequate observation prior to making disposition decision
  - 4 hours of observation will allow medical clearance in 75% of cases
  - longer periods of observation necessary following ingestion of slow release substances and toxins with known slow onset of action
- poison prevention education
- psychiatric counselling, if appropriate
- drug and alcohol service referral, if appropriate
- notification of relevant agencies if involving a child at risk

**Urinary pH manipulation**

**Urinary alkalinisation**
- enhances the elimination of
  - salicylates
  - phenobarbitone
  - 2-4 dichlorophenoxyacetic acid (2,4-D)
  - chloropropamide
  - diflunisal
  - fluoride
  - mecoprop
  - methotrexate

**Lipid partitioning**
- lipid soluble emulsions may be of benefit in treatment of high Vd drug toxicity
- intralipid 12 mL/kg 20% intralipid
- may act as a fluid compartment into which drug diffuses, therefore reducing tissue levels

**References**
**DRUG INDUCED SEIZURES**

**DRUGS THAT COMMONLY CAUSE SEIZURES**
- ethanol
- TCADs
- amphetamines
- cocaine
- antihistamines
- camphor
- theophylline
- caffeine
- bupropion
- anticholinergics
- phenothiazines
- organophosphates
- isoniazid
- chloroquine
- lithium
- lead
- nicotine
- cyanide
- carbamazepine

**PATHOPHYSIOLOGY OF DRUG INDUCED SEIZURES**

**GABA-A antagonism**

**Direct**
- penicillin (> 20 million units)
- cephalosporins
- imipenem
- fluoroquinolones

**Indirect**
- organochlorines (lindane)
- TCADs
- amoxapine
- isocarboxazid
- tranylcypromine

**Withdrawal**
- ethanol is a GABA agonist
- chronic ethanol use causes down regulation of the GABA receptor

**Adenosine**
- antagonised by
  - theophylline
  - caffeine
  - carbamazepine at high doses
- integral in the self-termination of the high frequency phase of seizures

**Glutamate**
- main excitatory neurotransmitter in the brain
- involved in propagating neuronal damage from a wide variety of causes
- glutamate induced intracellular calcium accumulation causes cellular damage

**Receptor types**
- kainate
- AMPA
- N-methyl-D-aspartate (NMDA)

**Agonists**
- domoic acid
- excessive domoic acid and NMDA receptor stimulation
- mussel toxins
- lathyrisim
- excessive ingestion of chick peas
- contains BOAA and AMPA agonist
- causes degenerative CNS changes
- alcohol withdrawal
- alcohol prevents glycine binding to NMDA causing upregulation
- withdrawal leads to increased NMDA activity

**Glycine**
- post synaptic inhibitory neurotransmitter
- inhibits reflex arcs
- suppresses firing from lower motor neurones
- strychnine acts as an antagonist at spinal cord receptors

**Pyridoxine kinase inhibition**
- inhibition of GABA formation
- anticonvulsants that work through GABA are less effective (ie benzodiazepines)

**References**
Kerr F, Drug induced seizures.
Proceedings of Australasian Toxicology Conference, Sydney December 1999

**ACTIVATED CHARCOAL**

**SINGLE DOSE**
- treatment of choice for the vast majority of poisonings when gastrointestinal decontamination is necessary
- should not be administered routinely in the management of poisoned patients
  - not required in most cases of mild poisoning
  - there are no satisfactorily designed clinical studies that have shown clinical benefit from single-dose activated charcoal
  - does not reduce patient length of stay for most patients

**Mechanism of action**
- charcoal adsorbs substances onto its surface by weak electrostatic forces
- is activated by cooking in a supra oxygenated atmosphere to increase its surface area
- liquichar - 1000 m²/g
- CharcoAid - 2000 m²/g
- higher surface area charcoals appears to decrease serum levels of ingested poisons

**Reduction in absorption**
- reduces absorption more than ipecac or gastric lavage for charcoal responsive substances
- most effective at binding agents with a MW of 100 - 1000
- 50 g of activated charcoal will cause a mean reduction in absorption of
  - 45% when administered at 30 minutes
  - 40% at 60 minutes
  - 15% at 120 minutes

**Charcoal sensitive substances**
- paracetamol
- benzodiazepines
- barbiturates
- tricyclic antidepressants
- phenothiazines
- most anticonvulsants
- aspirin
- theophylline
- digoxin
- dextropropoxyphene
- amphetamines
Chapter 28: Toxicology

Activated charcoal

- quinine
- morphine
- ciclosporin
- most NSAIDs
- beta blockers

Charcoal resistant substances
- charcoal resistant toxins do not include cyanide in lethal doses (1-200 mg)

Alcohols
- ethanol
  - is absorbed by activated charcoal but there is no reduction in bioavailability
  - may interfere with the binding of aspirin, quinidine and amitriptyline to charcoal
- methanol
- ethylene glycol

 Ionic compounds
- iron salts
- lithium
- KCl
- gold salts
- arsenic
- thallium is adsorbed by charcoal

Strong acids and alkalies
- boric acid
  - relatively charcoal resistant

Pesticides
- organophosphates / malathion
  - relative resistance
- DDT
- methyl carbamate
- dicophane

Contraindications
- isolated strong acid and alkali ingestion and upper GI haemorrhage
  - makes assessment by early endoscopy more difficult
  - ineffective in isolated alkali ingestions
  - not contraindicated if high risk from co-ingestion of charcoal sensitive poison
- bowel obstruction
- bowel perforation

Pregnancy
- appears to be safe in pregnancy as there is no systemic absorption

Complications
- no reports of gastrointestinal obstruction, constipation or haemorrhagic rectal ulceration associated with single dose activated charcoal therapy
- black stools

- vomiting in 20-30%
  - occurs in 70% of females, 20% of males
  - higher incidence if administered with sorbitol
  - not related to rate of administration
  - incidence may be decreased by antiemetics
- aspiration pneumonia
  - incidence of approximately 0.5% with multiple dosing
  - more severe if povidone is included in the charcoal mixture
  - decreases absorption of other medication
  - any concurrent medication should be given parenterally
  - increased risk of subsequent pregnancy if patient is on the oral contraceptive pill
- some formulations contain propylene glycol
  - may elevate the serum osmolality by up to 7 mosmol/L
  - hypernatraemia in 5%
  - not usually clinically significant
  - hypermagnesaemia in 3%
  - not usually clinically significant
  - corneal abrasions may occur upon direct ocular contact

Administration
- should be administered as soon as possible after ingestion of the poison
- may be more effective if the stomach is empty
- administration options
  - drunk by the co-operative patient in liquid form
  - administered as a mousse
  - given via NGT
- palatability may be increased by
  - chilling
  - addition of saccharin or flavouring
- yoghurt decreases binding capacity by 10%
- if given via a nasogastric tube then a minimum gauge of 16G should be used
  - necessary to squeeze the bag gently to maintain flow
  - ensure connections between NGT and bag are tight!

Dosage
- 0.5-1 g/kg in children < 1 year of age
- 25-50 g in children 1-12 years of age
- 25-100 g in adults
- ideally should use > 10 times weight of toxin ingested
  - a massive ingestion (eg 20 g of salicylate) would theoretically require 200 g for adsorption
  - this would need to be given 50 g/hour for 1-2 hours
  - in practice, repeated dosing is rarely required

MULTIPLE DOSE
- repeated administration of 50 g every 4 hours (12.5 g/hour) until improvement in the patient’s condition and laboratory parameters
- cathartics should not be used routinely

Gastrointestinal dialysis
- binds free drug in the lumen of the gut, lowering its free concentration
- free drug in circulation passes down its concentration gradient into the lumen of the gut where it is then bound to charcoal
- may enhance the elimination of many substances even after their absorption is complete
  - especially useful if administered during the distribution phase of the substance
- more likely to be useful when the substance has the following properties
  - enterohepatic circulation
  - long elimination T½
  - low endogenous clearance
  - low non restrictive protein binding
  - Vd < 1 L/kg

Indications
- life threatening poisonings
- charcoal sensitive poisoning
- no contraindications

Definitely indicated
- theophylline
- carbamazepine
- phenobarbitone
  - superior to haemodialysis or haemoperfusion
- quinine
- dapsone

Probably effective
- aspirin
- amitriptyline / nortriptyline
- dextropropoxyphene
- digoxin
- verapamil
- piroxicam
- sotalol
- phenytoin

Not effective
- amiodarone
OTHER METHODS OF GIT DECONTAMINATION

AGENTS THAT DECREASE GIT TRANSIT TIME

Sorbitol (M-Ex)

Pharmacology
- polyhydric alcohol
- poorly absorbed from the GIT
- small amount reaches the circulation and metabolised in the liver to fructose

Uses
- osmotic laxative
- commonly administered with charcoal
  - no evidence of added efficacy
  - there are no definite indications for the use of cathartics in the management of the poisoned patient
  - not recommended for routine use
  - no indications for the treatment of poisoning if used alone

- may:
  - increase palatability of charcoal
  - prevent unbinding of toxins when prolonged GIT transit time present

Contraindications
- fructose intolerant patients
- pregnancy
- absent bowel sounds
- intestinal obstruction or perforation
- ingestion of a corrosive substance
- volume depletion
- significant electrolyte imbalance

Special precautions
- children < 1 year old and the elderly
- severe diarrhoea and electrolyte disturbances may occur
- reduced dose in older children

Adverse effects
- increased gastrointestinal fluid load may
  - increase systemic absorption of some toxic substances
  - increase hypotension and intravascular volume depletion
  - pulmonary toxicity if aspirated
  - abdominal pain and bloating
  - nausea
  - diarrhoea
  - associated with lactic acidosis

Dose
- laxative dose for adults is 20-40 mL of 70% solution
- recommended dose with charcoal
  - 1-2 mL/Kg of 70% sorbitol in adults
  - 2-4 mL/Kg of 35% sorbitol in children
- a single dose only should be used in poisoning
- some charcoal solutions contain 150 mL of 70% solution

Polyethylene glycol (M-Ex)

- commonly used in preparation for colonic surgery
- isotonic solution

Actions
- when administered orally, it cleanses the bowel rapidly by inducing diarrhoea
- acts as an osmotic agent
- little net ion absorption or loss
- rarely changes water and electrolyte balance

Indications
- only used for serious or potentially serious poisoning
- iron toxicity
- pharmacobezoars
- sustained release preparations
  - lithium
  - verapamil
  - potassium formulations
- to remove packets of illicit drugs

Contraindications
- all ingested substances are charcoal sensitive
- intestinal obstruction or perforation
- GI haemorrhage
- ileus

Precautions
- in infants and the elderly
- causes desorption from charcoal of some agents when it is used following charcoal administration
  - fluoxetine
  - cocaine
  - theophylline
  - salicylates
  - chlorpromazine

Administration
- orally or by NGT
  - NGT preferred
  - 12F is sufficient size
- patient should be seated or the head of the bed elevated to at least 45 degrees
  - decreases the likelihood of vomiting
- treat vomiting with maxolon
  - if persistent, reduce infusion rate by 50% for 30 minutes then return to the original rate
- have commode handy

Dose
- children
  - 9 months - 6 years: 500 mL/hour
  - 6–12 years: 1000 mL/hour
- adults: 1500–2000 mL/hour
- continue until clear faecal return

GASTRIC EMPTYING TECHNIQUES

- gastric emptying techniques have no advantage over activated charcoal in charcoal responsive poisonings
- gastric emptying techniques should never be used as punitive measures

Ipecac (M-Ex)
- used to promote emesis
- rarely indicated in the hospital

References
setting
- decreases absorption of ingested substances by 30% or less if emesis occurs within 1 hour of ingestion

Pharmacology
- comprised of emetine and other alkaloids

Contraindications
- children < 6 months of age
- rapidly deteriorating conscious state
- corrosive ingestion
- high volatility hydrocarbon ingestion

Indications
- very limited (approximately 0.5% poison centre cases)
- cases remote from other health care providers
  - serious risk of toxicity and < 1 hour following ingestion or charcoal resistant poison
- in the ED
  - charcoal resistant poison and
  - serious risk of toxicity and
  - large fragments still in stomach
  - however whole bowel irrigation is preferable in these situations
- may remove large poison fragments
  - Fe^{2+}
  - sustained released lithium
  - enteric coated tablets
  - poisonous mushrooms

Adverse effects
- minimal risk of oesophageal rupture
- contraindicated in rapid onset poisonings
  - TCADs
  - camphor
  - cocaine
  - strychnine
- delays charcoal administration

Dose
- administered with 100-200 mL water
- adults - 30 mL followed by 240 mL water
- children
  - < 6 months of age - contraindicated
  - 6 months - 1 year of age: 5-10 mL followed by 120-240 mL of water
  - 1-12 years of age: 15 mL followed by 120-240 mL of water
- a second dose may be administered after 30 min if emesis has not occurred

Gastric lavage (M-Ex)
- recovery rate of ingested substances
  - 25% if performed at 30 minutes
  - 10% if performed at 60 minutes
- cannot remove large tablet fragments in children as smaller orogastric tubes must be used

Contraindications
- poisoning with charcoal responsive poison
- corrosive ingestions
- depressed airway reflexes (unless intubated)
- any suspicion of oesophageal perforation
- infants

Indications
- extremely rare in the hospital setting
  - the minimal benefits of this technique are nearly always offset by its significant risks
  - potentially very serious poisonings that present < 1 hour following poisoning when other gastroenteric decontamination techniques and specific antidotes are unavailable
  - non elemental mercury ingestion
  - arsenic ingestion
  - some hydrocarbon ingestions

Complications
- oesophageal or stomach injury
- pulmonary aspiration
- laryngospasm

Technique
- airway protection as required
- ensure suction is available
- performed in left side and head down 20 degrees position
- pylorus of the stomach is uppermost
- may decrease passage of poison into the duodenum
- prevents pulmonary aspiration
- may use a bite block to prevent obstruction of the orogastric tube
- lubricate tube prior to insertion
- orogastric tube
  - must have a rounded end
  - adults 36-40 F
  - children 24- 28 F
- instill
  - adults: 200–300 mL boluses of water warmed to body temperature
  - children: Normal saline 10 mL/kg
- lower tube to below bed height to drain fluid into receptacle
- repeat instillation / drainage until clear return
- a negative return does not rule out a significant ingestion

SODIUM POLYSTYRATE
- also known as resinum
- ion exchange resin
- effectively binds potassium following ingestion
- may have limited effectiveness following ingestions of some other ions (all charcoal resistant) however affinity for K+ limits its usefulness
  - lithium
  - iron
  - technetium

References

EXTRACORPOREAL ELIMINATION OF TOXIC COMPOUNDS
(M-H)

INDICATIONS
- low inherent clearance
- small Vd (eg alcohols)
- severe toxicity present and clearance can be increased by >

30%
- deterioration despite full supportive care
- impaired method of excretion
  - eg ethylene glycol with acute renal failure

Drug toxicity where extracorporeal elimination may be of use
- atenolol
- theophylline
- lithium
Charcoal haemoperfusion
• blood flow of 200 mL/min across a charcoal filter
• only useful if agent is
  - adsorbed by charcoal
  - lipophilic
  - not significantly bound to protein
• useful in toxicity of
  - salicylates
  - theophylline
  - carbamazepine
• no use for toxicity of
  - alcohols
  - lithium
  - cyanide
  - Fe^{2+}
  - heavy metals
• the higher the blood flow tolerated through the perfusion column the greater the clearance

Haemodialysis
• perfusion across semipermeable membrane
• diasylate flows in the opposite direction to the perfusat
• effective if toxin is
  - water soluble
  - low molecular weight
  - non protein bound
• haemoperfusion usually superior if toxin adsorbs to charcoal

Increases elimination of
• alcohols
• lithium
• indicated if
  • > 6 mmol/L in acute toxicity
  • > 2.5 mmol/L in chronic

Haemofiltration
• membrane has pores
• size of filtered molecule varies on the size of the pores
  - usually molecular weight > 10,000 will not be filtered
• useful for
  - some metal - chelate complexes
  - carbamazepine
  - valproate

ANALYTICAL TOXICOLOGY

SAMPLE TYPES
• blood
  - usually only for specific drug levels
• urine
  - usually used for drug screening
• hair / skin
  - usually only to diagnose chronic toxicity (eg arsenic)
• saliva
  - concentrations of drugs are usually lower than in urine
  - may be able to estimate serum concentration if salivary concentration known
• meconium
  - represents the entire intestinal contents of the foetus before birth
  - used to detect intrauterine toxic exposure
• sweat
  - may be used to screen for common drugs of abuse

POST MORTEM TESTING

Postmortem redistribution
• changes that occur in drug concentrations after death

Drugs most likely to undergo postmortem redistribution
• basic compounds
• highly lipid soluble
• Vd > 3 L./kg
• examples
  - TCADS
  - digoxin
  - amphetamines
• anatomical location of blood sampling can influence the drug concentration
  - ideal site is a ligated femoral vein or aqueous humor of the eye

METHODS OF TESTING

Specific drug concentrations
• drugs where specific drug concentrations may guide therapy include
  - paracetamol
  - iron
  - lithium
  - carboxyhaemoglobin
  - methaemoglobin
  - carbamazepine
  - digoxin
  - phenytoin
  - methanol
  - theophylline
  - lead
  - mercury
  - arsenic
  - ethanol
  - salicylates
• the drug concentration for the specific compound should be determined at an appropriate time after a suspected ingestion of the compound
• with the exception of paracetamol (see below) these drug concentrations should not be used as screening tests for an unknown ingestion

Chemical spot tests
• used for quick detection of specific substances
• urine sample the most commonly used
• provides qualitative but not quantitative information
• can be performed in < 20 min
• usually low sensitivity and specificity