Chapter 28

TOXICOLOGY

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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 poisoning

Route of exposure

Route	%
Oral ingestion	80
Dermal	6
Ophthalmic	5
Inhalation	5
Bites and stings	3
Parenteral	1

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

1 year	1%
1-5 years	3%
5-10 years	3%
> 10 years	7%

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 (eg 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

Carter G, Preventing self-poisoning and self harm re-presentations. Proceedings of 4th Australasian Clinical Toxicology Conference, Sydney December 1999

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

Carter GL, et al Repetition of deliberate self-poisoning in an Australian hospital treated population. MJA 1999;170:307-311.

Reith DM, Pitt WR, Hockey R. Childhood poisoning in Queensland: analysis of presentation and admission rates. J Paediatr Child Health 2001;37:446-450.

Bystrzycki A, Coleridge J. Drug and poison related deaths in Victoria during 1997. Emerg Med 2000;12:303-9.

Hawton K et al, UK legislation on analgesic packs: before and after study of long term effect on poisonings.BMJ 2004;329:1076.

RISK ASSESSMENT IN POISONING

(Dis-H)

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
  - Ca^{2+} channel blockers*
  - beta blockers*
  - antiarrhythmics*
- cyanide*
- colchicine*
- isoniazid*
- Amanita phalloides*
- theophylline*
- chloral hydrate*
- 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
  - benztropine
  - hyoscine
  - scopolamine
  - Trumpet lily / Angel's trumpet / (Brugmansia)
  - Jimsonweed (Datura stramonium)
- antihistamines
- tricyclic antidepressants
- amanita muscaria mushrooms

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

- tachycardia
- sweating
- mydriasis

Common sources
- amphetamines
- cocaine
- LSD
- caffeine
- theophylline
- phencyclidine
- methylphenidate

Opioid
(D-Ex)

Features
- CNS depression
- hypoventilation
- hypotension
- miosis

Common sources
- heroin
- codeine
- methadone
- dextropropoxyphene
- clonidine
- diphenoxylate
- dextromethorphan
  - opioid derivative of morphine
  - in some over the counter cold and flu medications
  - toxicity may be prolonged as 15% of the population are slow metabolisers

Drug withdrawal
(Dis - H)

Features
- diarrhoea
- mydriasis
- piloerection
  - "cold turkey"
- tachycardia
- lacrimation
- abdominal pain
- agitation
- hallucinations

Drugs with toxicity on withdrawal
- ethanol
- benzodiazepines / barbiturates
  - tremor
  - sleep disturbance
  - depression
  - seizures
- opioids
- amphetamines
- GHB
- beta blockers
  - hypertension
  - angina
- clonidine
  - hypertension
- SSRIs (short acting only)
- valarian
- steroids
  - adrenocorticoid deficiency

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

References

Dyer JE et al, Gamma-hydroxybutyrate withdrawal syndrome Ann Emerg Med 2001;37(2):147.

Schneider SM et al, Dextromethorphan poisoning reversed by naloxone. Am J Emerg Med 1991;9(3):237.

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
- paraldehyde

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

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.

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
- diuresis
- haemodialysis
- charcoal haemoperfusion

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)
  - chlorpropamide
  - diflunisal
  - fluoride
  - mecoprop
  - methotrexate
- indications
  - moderate severity salicylate poisoning not receiving dialysis
  - 2-4 dichlorophenoxyacetic acid (2,4-D) toxicity combined with diuresis > 600 mL/hour
  - phenobarbitone if toxicity continues despite multiple dose charcoal
  - unlikely to be of benefit in other poisonings

Urinary acidification
- there are no indications for urinary acidification
- acidic drugs have a large Vd
  - urine acidification alters elimination rates little
- may potentiate toxic effects of rhabdomyolysis

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

Proudfoot AT, Krenzelok EP, Vale JA. Position statement on urinary alkalinisation. J Tox Clin Tox.2004;42(1).

Hollander JE, McCraken G, Johnson S et al, Emergency department observation of poisoned patients: how long is necessary? Acad Emerg Med 1999;6(9):887-894.

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
- tranylcypramine

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
- lathyrism
  - 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

(M-Ex)

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 m^2 /g
  - CharcoAid - 2000 m^2 /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

- 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 adsorbed 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 alkalis

- 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!

Presentation

- aqueous suspension of: activated charcoal 50 g in 300 mL water

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 T ½
  - 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

- doxepin
- diltiazem
- imipramine
- chloroquine
- valproic acid
- tolbutamide, chlorpropamide and other sulphonylureas
- astemizole
- meprobamate
- methotrexate
- sodium valproate
- tobramycin, and vancomycin

Adverse effects

- as for single dose activated charcoal plus
  - constipation
  - bowel obstruction

References

Dorrington CL, Johnson CW, Brand R et al, The frequency of complications associated with the use of multiple-dose activated charcoal. Ann Emerg Med.2003;41:370-377.

AACT / EAPCCT. Position Paper: Single-Dose Activated Charcoal. Clin Tox 2005;43:61-87

Cooper GM, Le Couteur DG, Richardson D, Buckley NA.A randomized clinical trial of activated charcoal for the routine management of oral drug overdose. QJM 2005; 9: 655-60.

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

setting
- decreases absorption of ingested substances by 30% or less if emesis occurs within1 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**
  - < 1hour 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
- instil
  - 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 resonium
- 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

Linakis et al, Enhancement of lithium elimination by multiple dose sodium polystyrene sulfonate. Acad Emerg Med 1997;4:175-178.

AACT / EAPCCT. Position Paper: Cathartics J Tox Clin Tox. 2004;42(3):243–253.

AACT / EAPCCT. Position Paper: Whole bowel irrigation J Tox Clin Tox. 2004;42(6):843-854.

AACT / EAPCCT. Position Paper: Ipecac syrup J Tox Clin Tox. 2004;42(2):133-143.

AACT / EAPCCT. Position Paper: Gastric lavage J Tox Clin Tox. 2004;42(7):933-943.

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

- ethylene glycol
- methanol
- salicylates
- camphor
- carbamazepine

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
- problems with haemoperfusion
  - systemic heparinisation
  - thrombocytopaenia, neutropaenia
  - hypotension
  - blood loss
  - haematoma at vascular access sites
  - air emboli
  - hypocalcaemia

Haemodialysis
- perfusion across semipermeable membrane
- diasylate flows in the opposite direction to the perfusate
- 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 toxicity
- ethylene glycol
- amphetamines
- g-benzene hexachloride (lindane)
- camphor
- chloral hydrate
- heavy metals
  - arsenic
  - copper
  - iron
  - lead
  - magnesium
  - strontium
  - zinc
- salicylates
- theophylline
- thiocyanates

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

(I-H)

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
- involves the redistribution of drugs into blood from solid organs

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
  - 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

METHODS OF TESTING

Specific drug concentrations
- drugs where specific drug concentrations **may** guide therapy include
  - paracetamol
  - iron
  - lithium
  - carboxyhaemoglobin
  - methaemoglobin

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