Toxicology Summary

Sources:
Toxicology Handbook 2nd edition by Murray & Daly et al.
UpToDate

General Aproach

Resuscitation
- Airway
- Breathing
- Circulation
- Seizure control
- Correct hypoglycaemia
- Correct hyperthermia
- Resuscitation antidotes
- Consider ECMO
- Keep going!

Risk assessment

Supportive care and monitoring

Investigations — screening (ECG, BSL and paracetamol) and specific

Decontamination

Enhanced elimination

Antidotes

Disposition (inc psychiatric referral)

Dialysable Drugs

(an incomplete but useful list)

B — Barbituates
L — Lithium
A — Aspirin
S — Sotalol / Atenolol
T — Theophylline

'E — Ethelene glycol
M — Methanol

TOXIDROME	TOXICITY	DRUGS	RISK ASSESSMENT	INVESTIGATIONS	DECONTAMINATION	ENHANCED ELIMINATION	ANTIDOTE	NOTES
Aspirin	Inhibition of COX — ↓prostaglandins Respiratory centre stimulation Uncoupling of eTC — lactate Lipolysis — ketoacidosis **GI:** N&V **CNS:** tinnitus, hearing loss, vertigo, seizures, cerebral oedema, come and death **Metabolic:** RAGMA and resp alkalosis, ↓↑temp, ↓↑glucose		ingestion > 300mg/kg toxic > 500mg/kg potentially fatal	ABG Lactate Ketones Salicilate	**Activated charcoal** for ingestions > 150mg/kg indicated within 8hr repeat at 4hr if level still rising	**Urinary alkalisation** is highly effective 100mmol $NaHC0_3$ bolus 25mmol/hr thereafter Aim urinary pH >7.5 **Haemodialysis** usually not required with decontamination and urinary akalinisation but is highly effective	None available	Acidosis ionises salicilate and favours movement into brain where principal toxicity occurs hepatic metabolism becomes zero order in OD Half life increases from 3hr – 24hr+
Beta blockers	**CVS:** bradycardia, HB, hypotension, TCA like QRS widening with propanolol, QT prolongation with sotalol **CNS:** delirium, coma and seizures **Resp:** bronchospasm, pulmonary oedema **Metabolic:** ↓K, ↓↑glucose	*non-selective* **Propranalol** **Sotalol** carvedilol labetalol *Beta1 selective* atenolol metopralol esmolol	Dose less important Preexisting heart and lung disease Advanced age **Propranalol** (TCA like Na block) and **sotalol** (K block leading to long QT) are the main concerns Co-ingestion of other cardiotoxic drugs	ECG	**Activated charcoal** helpful within 2 hours (be aware of seizures in propranolol OD)	Atenolol and sotalol are renally cleared (and dialysable).	**Glucagon** 50-150 mcg/kg bolus followed by 50 mcg/kg/hr **High dose insulin therapy (HDIT)**: Bolus 1 U/kg short-acting insulin and 25 g/kg glucose Infuse 0.5 u/kg/hr short-acting insulin and 25 g/kg/hr glucose avoid K replacement **Adrenaline / isoprenaline** **Pacing** (capture can be a problem)	Glucagon supply will run out fast. HDIT is becoming the new standard.
Calcium channel blockers	L-type Ca channel blockade **CVS:** bradycardia, impaired contractility and vasodilation. Dihydropyridines predominantly cause the latter.	**Verapamil** **Diltiazem** Amlodopine Felodipine Lercanidipine Nifedipine Nimodopine	Dose less important Any deliberate self poisoning considered serious Preexisting heart disease Advanced age **Diltiazem / verapamil** Co-ingestion of other cardiotoxic drugs	EUC Ca lactate serial blood gasses	**Activated charcoal** helpful within 1 hour for standard preparations and 4 hours for XR preparations. **Whole bowel irrigation** after charcoal	Not helpful	60 ml **calcium gluconate** 10% or 20 ml **calcium chloride** 10% over 15 mins **Atropine** 600 mcg every 2 mins up to 3 mg **Catecholamines** **High dose insulin therapy (HDIT)**: Bolus 1 U/kg short-acting insulin and 25 g/kg glucose Infuse 0.5 u/kg/hr short-acting insulin and 25 g/kg/hr glucose and avoid K replacement **Pacing** (capture can be a problem) **Intravenous lipid emulsion** 100 mL of 20%	Intralipid experimental
Cholinergic syndrome	**CNS:** Agitation, respiratory depression, coma, confusion, lethargy, seizures **Neuromuscular:** fasciculations, weakness **Parasympathetic muscarinic effects:** cramping, bradycardia, bronchoconstriction, bronchorroea, diarrhoea, lacrimination, mitosis, salivation, urinary incontinance, vomiting **Sympathetic nicotinic effects:** hypertension, mydriasis, sweating, tachycardia	Organophosphate fertilizers carbamate insecticides warfare nerve agents pilocarpine	All GI exposures are potentially fatal Skin exposures usually mild early seizures are a bad sign	Cholinesterase (PChE) — duration of praldoxime 50-50 plasma mixing — dose adjustment of praladoxime ABG CXR ECG	**Activated charcoal** helpful within 2 hr Remove clothes and wash skin	Not helpful	**Atropine** 1-2 mg boluses repeated to maintain moderate airway secretions / ECG **Praladoxime** bolus 30 mg/kg then infuse 15 mg/kg/hr, infusion ceased after 24 hours if the patient is well **Benzodiazepines** reduce psychological complications	Praladoxime only works before irreversible binding ('aging') of OP to ACh-esterase.
Cyanide	CN binds to the Fe^{3+} portion of **cytochrome oxidase** and inhibits cytochrome oxidase leading to lactate acidosis Stimulates the release of **biogenic amines** — pulmonary and coronary vasoconstriction **NMDA** release in CNS causing seizures	SNP Cyanide salts Inhalation of HCN	Any exposure is serious Death likely to occur before arrival at hospital.	Lactate correlates well with severity Cyanide levels can be measured in plasma to confirm poisoning but do not correlate with severity and comes too late to guide antidote (> 100 micromol/L lethal)	Remove clothes and **wash** skin	Not helpful	Cyanokit (**hydroxocobalamin**) 5g IV if available **Sodium Thiosulphate** 12.5mg **Dicobalt EDTA** 300mg **Sodium Nitrite**	Hydroxocobalamin is safe even if there is no cyanide Dicobalt EDTA caries risk of AKI Nitrites induce MetHb which may not be tolerated
Digoxin	**GIT:** nausea, vomiting and abdo pain **CVS:** bradycardia due to SA block, tachycardia due to increased automaticity **Neuro:** lethargy and confusion K^+: hyperkalaemia (direct inhibition of NaK ATPase)		Potentially fatal: > 10g in adult (40 x 250mcg tabs) > 4g child	Potentially fatal: plasma > 15 nmol/L K^+ > 5.5 mmol/L ECG	**Activated charcoal** helpful within 1 hour	Not helpful	**Digoxin immune Fab** Each vial can bind 0.5mg of digoxin If ingested dose known: digibind ampules = Ingested dose x 0.8 x 2 empiric treatment: 5 ampules if stable, 10 if unstable	Digoxin level will continue to be high after digoxin immune Fab. Digoxin is renal cleared, t½ is 12 hours. Digoxin-Fab is renally cleared t½ 36 hours
Ethelene glycol	Oxalate, glycolate and lactate acidosis **Calcium oxalate** crystals deposit in the kidneys, muscles, brain and heart. **Renal failure** predominates Consumptive **hypocalcaemia** Intoxication — cardiopulmonary — renal Flank pain Late cranial **neuropathies** (5-20 days)	antifreeze	Ingestion > 1ml/Kg Ethylene glycol level > 8mmol/L	ABG Osmolar gap lactate Ca^{++} Urine microscopy Ethylene glycol level (if available) Ethanol level	Not helpful	Haemodialysis is the definitive management. Elimination half life is reduced to 2.5–3.5 hours depending on setup. Indications for CRRT: • Large ingestion > 1ml>kg • AKI • Ethylene glycol level > 8mmol/L • pH < 7.25	**Ethanol** (target level= 0.5–1mg/kg, 005–0.1%) **Fomepezole** (inhibits alcohol dehydrogenase) 15mg/kg loading then 10 mg/kg BD (Q4h if on dialysis)	Fomepizole not currently available in Australia

TOXIDROME	TOXICITY	DRUGS	RISK ASSESSMENT	INVESTIGATIONS	DECONTAMINATION	ENHANCED ELIMINATION	ANTIDOTE	NOTES
Iron overload	**GI** oedema, diarrhoea, vomiting **Cardiac** and **hepatic** toxicity via cellular poisoning **CNS** secondary **Late**: cirrhotic liver and GI strictures	Fe tablets Fe infusion PRBC	> 60 mg/kg elemental iron dose systemic toxicity no systemic toxicity without GI upset	CXR / AXR to look for undigested tablets Fe > 90 micro mol/L Echo LFTs	Whole Bowel Irrigation Gastric lavage Endoscopic tablet retrieval	May be helpful to remove desferroxamine-Fe complex in patients with severe renal failure	**Desferroxamine** 15 – 40 mg/kg/hr for 6 – 24 hours	Desferroxamine works when iron is extracellular so needs to be early
Methaemaglobinaemia		metoclopromide dapsone nitrites (SNP, NO, GTN) chloroquine prilocaine sulphonamides benzene derivatives	>20%	Co-oximetry ABG Lactate	Not helpful	Not helpful	**Methelyne blue** 1-2 mg/kg CI in: • G6PD (no NADPH to activate drug and causes haemolysis). • Nitrite induced MetHb (to treat CN)	
Methanol	**Formate** inhibits cytochrome oxidase — lactate Retinal blindness Subcortical white matter haemorrhage Putamen oedema Demyelenation Intoxication headache, dizziness, blurred vision, photophobia, seizures		Ingestion > 0.5ml/Kg Deliberate self poisoning assumed to be potentially lethal	ABG Osmolar gap lactate Ethanol level	Not helpful	**Haemodialysis** is the definitive management. Elimination half life is reduced to 2.5–3.5 hours depending on setup. Indications for CRRT: • Any patient needing alcohol dehydrogenase blockade • Methanol level > 16mmol/L • pH <7.25 • Visual symptoms	**Ethanol** (target level = 0.5–1mg/kg, 005–0.1%) **Fomepezole** (inhibits alcohol dehydrogenase) 15mg/kg loading then 10 mg/kg BD (Q4h if on dialysis)	Fomepizole not currently available in Australia
Paracetamol	90% hepatic metabolism to glucuronide lade sulfate. 2% renal excreted unchanged. Remainder oxidised by cytochrome P450 to NAPQI. NAPQI is highly reactive and toxic. NAPQI is rapidly conjugated with glutathione to form non-toxic compounds that are renal excreted. In overdose glucuronidation and sulfation pathways are overwhelmed and greater proportion is oxidised by P450 system to NAPQI. When glutathione stores are diminished to 30% oxidative hepatocellular injury takes place with hallmark centrilobular necrosis. Secondary cytokine release may extend the area of injury.	Many preparations	• Life threatening hepatotoxicity rare. • Potentially fatal > 150mg/kg • Survival = 100% if NAC within 8 hr • Deranged LFT > 8 hr after ingestion assumed to serious • If >24 hr and no detectable paracetamol and normal LFTs has little risk	Paracetamol level LFTs INR and fibrinogen	**Activated charcoal** effective within 1 hour but risks considered in light of highly effective antidote	Not helpful	**N-acetylcysteine** 150 mg/kg over 1hr 50 mg/kg over 4hr 100 mg/kg over 16hr Prescott-Rumack-Mathew normogram covers 4-15 hours post ingestion Beyond 24 hr NAC if detectable paracetamol or LFT / INR derangement	NAC provides glutathione to conjugate NAPQI to non-toxic metabolites
Tricyclic antidepressants	Inhibition of: Noradrenaline and seritonin reuptake $GABA_A$ Na^+ Channels K^+ Channels M_1 H_1 $alpha_1$ CNS: Coma and seizure, especially with dothiapin, anticholiergic delirium obscured by coma CVS: Fast Na channel blockade	Amitriptyline Nortriptaline Trimipramine Clomipramine Dothiapin Doxepin Imipramine	>10 mg/kg ingestion Onset of toxicity is within 2 hours	**ECG** ↑R/S ratio (>0.7) in aVR QT prolongation indicates K^+ block QRS widening indicates Na^+ block QRS > 100ms predicts seizures QRS > 160ms predicts VT	**Activated charcoal** for ingestions > 10mg/kg indicated after airway secured	Not helpful	**NaHCO3** 100 mmol IV every 1-2 mins until ROSC Intubation and hyperventilation **Intravenous lipid emulsion** 100 mL of 20% **Lignocaine** 1.5mg/kg DO NOT give class Ia, Ii or III	