Antidotes

Atropine

Indications
AV conduction impairment: Cardiac glycosides, β-blockers, calcium channel blockers (CCBs).
Anticholinesterase inhibitors/Cholinergics: Organophosphates, carbamates

Contraindications
Relative: closed angle glaucoma, GIT obstruction, urinary obstruction

Mechanism
Competitive antagonist for ACh at muscarinic receptors.

Pharmacokinetics
Poor oral bioavailability, liver met, $T_{\frac{1}{2}}$=2-4hrs. Crosses BBB & placenta. 50% excreted unaltered.

Administration
AV conduction impairment: 0.6mg (20mcg/kg) IV repeated up to 3x
Cholinergics: 1.2mg IV bolus, double dose q5mins until chest clear [also sBP>80mmHg, HR>80, dry axillae & no miosis]. Then infusion starting at ~10-20% of total loading dose (max 3-5mg/hr)

Adverse Reactions
Excessive dosage → Anticholinergic toxidrome.

Calcium

Indications
CCB OD, HF exposure, hypocalcaemia, hyperkalaemia, iatrogenic hypermagnesaemia

Contraindications
Hypercalcaemia, ?digoxin toxicity - (contrary to traditional teaching, recently some evidence that Ca^{2+} is **not CI** if on digoxin or even if digoxin toxic – however **digoxin immune Fab** & **$MgSO_4$** 10mmol might be preferred initially in the latter case)

Mechanisms
Restore low $Ca2^{+}$ levels, binds F- ions, antagonises effects of high K^{+} & Mg^{2+} on heart.

Administration
Cardiac monitoring mandatory.
CCBs: 20ml $CaCl_2$ IV (central line) or 60ml (1ml/kg) Ca gluconate IV (peripheral) over 5-10mins
HF on skin: 2.5% Ca gel TOP OR local inj of 10% calcium gluconate (not fingers) OR Bier's block with 2% Ca gluconate (i.e. 10ml of 10% in 40ml NS) for 20mins & release cuff OR same dose intra-arterially over 4 hrs & rpt prn.
HF inhaled: Nebulised 2.5% Ca gluconate solution.
HypoCa/HypoMg/HyperK: 5-10ml $CaCl_2$ or 10-20ml (1ml/kg) Ca gluconate IV over 5-10mins

Adverse Reactions
Transient hyperCa., vasodilatation, hypoBP, dysrhythmias, tissue damage from extravasated $CaCl_2$. Don't irrigate eyes with Ca solution.

Notes
To get 2.5% Ca gel: add 10ml of 10% Ca gluconate to 30g/30ml KY jelly.

Cyanide Poisoning Antidotes

Options

Hydroxocobalamin (Vitamin B12a)
Sodium Thiosulfate
Dicobalt Edetate (cobalt EDTA)
Amyl or Sodium Nitrite

Contraindications

Known hypersensitivity
Dicobalt Edetate: Equivocal cyanide poisoning (as significant SEs).
Nitrites: Smoke inhalation (as if COHb already present, will add to poor O_2 carriage).

Mechanism

Hydroxocobalamin & Dicobalt Edetate: Forms stable less toxic cobalt complexes with CN.
Na Thiosulfate: enhances endogenous CN conversion to non-toxic thiocyanate by supplying S.
Amyl or Na Nitrite: Form metHb which binds CN better than mitochondrial cytochromes.

Pharmacokinetics

Hydroxocobalamin: small VD <0.5L/Kg. Renal excretion.
Na Thiosulfate: Rel. slow onset of action. Mainly renal excretion, small amount hepatic met.
Dicobalt Edetate: Crosses BBB. Renal excretion.

Administration

Need resus care available.
Hydroxocobalamin & Na thiosulfate: Give sequentially (not mixed). Hydroxocobalamin 5g (child 50-70mg/kg) in 200ml 5%Dex over 15-30min then if not improving give Na thiosulfate 200mg/kg (child: 400mg/kg) max 12.5g over 10min, or (if avail) repeat hydroxocobalamin.
Dicobalt Edetate: 300mg (child 7.5mg/kg) IV over 1min followed immediately by 50ml 50% dextrose (5ml/kg 10% dextrose). May be repeated 1-2 times.
Amyl Nitrite: 1-2 ampoules crushed in gauze Inh for 30s/min for 2-3min until Na nitrite avail.
Na Nitrite: 300mg (child 6mg/kg) in 100ml NS IV over 20min. Usually then give Na thiosulfate.
With nitrite admin, keep metHb level <20%.

Adverse Reactions

Hydroxocobalamin: orange-red discolouration of skin, mucous membranes & body fluids may interfere with lab tests).
Thiosulfate: N & V, rate-related ↓BP.
Dicobalt Edetate: convulsions, facial/neck oedema, chest pain, SOB, ↓BP, vomiting, urticaria.
Nitrites: headache, flushing, tachycardia. Severe metHb.

Notes

Hydroxocobalamin v. expensive & needs to be special conc preparation. Preferred for sev tox.
Sodium Thiosulfate can be used as adjunct in sev toxicity or alone for mild-mod cyanide toxicity or for chlorate, bromate, Br_2/I_2, cisplatin, mustard gas or nitrogen mustard poisoning.
Amyl nitrate may be used pre-hospital.
Dicobalt Edtate only used in critically ill patients with definite toxicity due to SE profile.
N.B. Potential confusion with sodium calcium edetate used in lead poisoning.

Cyproheptadine

Indications
Mild-mod serotonin syndrome.

Contraindications
Asthma, closed angle glaucoma, bladder neck obstruction (incl. prostatism)

Mechanism
H_1, $5HT_{1a}$ and $5HT_2$ blocker. Also blocks ACTH and has peripheral anticholinergic action.

Pharmacokinetics
Well abs PO. Peak level 1-3hrs. Liver met. + urinary excretion of metabolites.

Administration
12mg PO init. If effective 8mg PO q8h for 24h. Paed. dose 4mg (>6yrs)

Adverse Reactions
Nil significant.

Desferrioxamine (DFO)

Indications
Severe acute or chronic iron poisoning.

Contraindications
None

Mechanism
Binds to free Fe^{3+} (also in plasma transferrin/haemosiderin) to form water soluble complex (ferrioxamine) that is excreted in urine (vin rosé colour).

Pharmacokinetics
VD is 1L/kg. Remains mainly intravascular so best given early. Steady-state conc @ 6-12h IV. Hepatic met. Elim $T_{\frac{1}{2}}$=3h.

Administration
15-40mg/kg/hr IV infusion until patient stable and serum Fe<60µmol/L (usually ≤6h infusion). Mandatory cardiac monitoring.

Adverse Reactions
Hypersensitivity, hypoBP, ARDS (>24h infusion), toxic retinopathy, Yersinia sepsis.

Digoxin Immune Fab

Indications

Acute digoxin overdose – cardiac dysrhythmia/arrest, dose>10mg (4mg child), K+>5.0mmol/L, digoxin level>15nmol/L (12ng/ml).
Chronic digoxin poisoning – significant cardiac/GIT symptoms or if symptomatic & has RF.
Other cardiac glycoside poisonings – Oleander, cane toad (bufotoxin).

Contraindications

None.

Mechanism

Ovine IgG fragments against digoxin have affinity>>Na/K ATPase receptor. Bind intravascular and interstitial digoxin.

Pharmacokinetics

1 amp (38mg) binds 0.5mg digoxin, however digoxin load is reduced by bioavailability being 80%.
Elim of unused Fab has $T_{\frac{1}{2}}$=12h (non-renal). Dig-Fab Elim $T_{\frac{1}{2}}$=16-30h.

Administration

Mandatory cardiac monitoring.
In cardiac arrest give 20 amps (acute OD) or 5 amps (chronic OD) stat (if available).
Acute OD: No. ampoules=Digoxin dose*2*0.8. Empiric dose 5 amps. Can rpt q30min.
Chronic OD: No. ampoules=Digoxin level (ng/ml)*wt/100 or Dig level (nmol/L)*0.8*wt/100.
Empiric dose 2 amps. Can rpt q30min.
For other cardiac glycosides give 5 amps every 30min until reversal of toxicity.

Adverse Reactions

Rare. HypoK+, loss of rate control of pre-existing AF, exacerbation of underlying CCF, allergy (very rare).

Notes

Dig level post-Fab may appear high as test assay doesn't distinguish free/bound.

Ethanol

Indications
Methanol, ethylene glycol or diethylene glycol poisoning. ?Other toxic alcohols.

Contraindications
Recent disulfiram ingestion.

Mechanism
Competetive inhibition as alcohol dehydrogenase has greater affinity for ethanol than methanol or ethylene glycol and can prevent production of toxic metabolites.

Pharmacokinetics
Rapidly absorbed by oral route. Crosses BBB & placenta. Hepatic met. saturated at low concs.

Administration
PO/NG: Loading - 1.8ml/kg 43% (~75 proof) EtOH or 3 x 40ml shots of vodka (alt: gin, whisky or brandy) in 70kg adult. Maintenance – 0.2-0.4ml/kg/hr 43% EtOH or a 40ml shot/hr.
IV: Loading - 8ml/kg of 10% EtOH. Maintenance – 1-2ml/kg/hr 10% EtOH.

Titrate maint dose to keep q2h blood EtOH levels 100-150mg/dL (0.1-0.15mg%, 22-33mmol/L).

Adverse Reactions
Intoxication, N&V, hypoglycaemia (esp children), thrombophlebitis (if IV), ↓Na with ↑tonicity.

Notes
May be used as a temporising measure before haemodialysis. Maintenance rate quite variable depending on patient (genetics, enzyme induction status)

Flumazenil

Indications
Rarely indicated for BDZ overdose (if compromised airway/breathing and skill/equipment not avail for intub/vent).

Contraindications
If seizures might be precipitated (epilepsy, pro-convulsant OD, TCA OD, BDZ dependence).

Mechanism
Competitive antagonist at BDZ site of GABA receptor.

Pharmacokinetics
VD 1L/kg. Rapid hepatic met. Elim $T_{\frac{1}{2}}$=40-80min.

Administration
Need to be able to treat any seizure that might result.
Aliquots of 100-200mcg (child 10-20mcg/kg) IV up to 2000mcg. Resedation expected around 90min. Occ. Infusion used.

Adverse Reactions
Seizures, BDZ withdrawal syndrome (agitation, tachycardia, seizures).

Folinic acid

Indications
Excessive methotrexate ingestion (dose too high e.g. >500mg [child 5mg/kg] or too frequent e.g. weekly dose given daily).
Adjunct for methanol poisoning.
Massive pyrimethamine and trimethoprim poisoning.

Contraindications
Hypersensitivity.

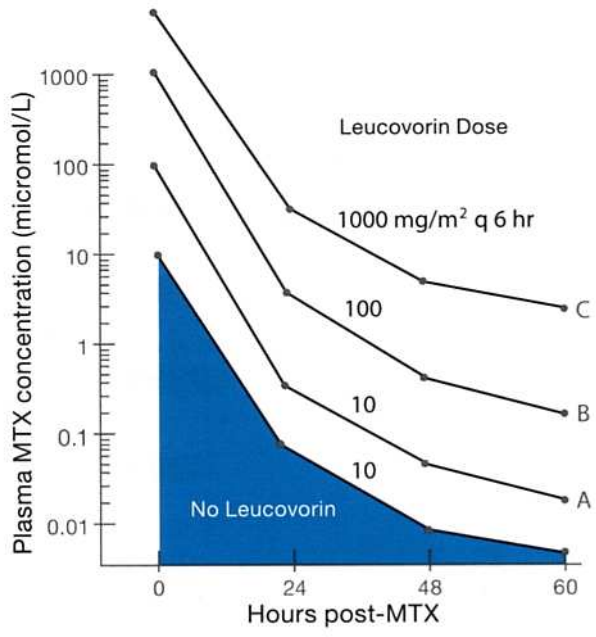
Mechanism
MTX inhibits DHF reductase conversion of folic acid to folinic acid required for DNA/RNA synthesis.

Pharmacokinetics
100% bioavail. At a dose of 15mg. VD 13.6L. $T_{\frac{1}{2}}$=35min. Long acting metabolite.

Administration
MTX OD – 15mg folinic acid PO/IM/IV q6h until below threshold for toxicity on nomogram if single ingestion or if chronic continued for at least 3 days and the level is <0.05µmol/L.
Methanol OD – 2mg/kg IV q6h.

Adverse Reactions
Rarely anaphylaxis or seizures. HyperCa if given rapidly (?160mg/min) IV.

Notes
MTX nomogram (NB. Leucovorin=folinic acid):



Plasma methotrexate Concentrations after Various Doses

Shaded area = MTX levels observed after doses of <60 mg/m²; leucovorin is usually not required. Up to curve B requires 10 mg/m² of LVR per dose every six hours until the MTX level is <0.1 micromol/L. Up to curve C requires 100mg/m² per dose.

Adapted from: Bleyer WA. Therapeutic drug monitoring of methotrexate and other antineo-plastic drugs. In: Baer DM ed. Interpretation in Therapeutic Drug Monitoring. Chicago: American Society for Clinical Pathology, 1981:174.

Fomepizole

Indications
Methanol, ethylene glycol poisoning.

Contraindications
Hypersensitivity. ?Pregnancy.

Mechanism
Alcohol dehydrogenase competitive inhibitor – prevents production of toxic metabolites.

Pharmacokinetics
Small VD 0.7L/kg. Hepatic met. Dialysable.

Administration
Loading dose: 15mg/kg in 100ml NS or 5%D IV over 30min
Maintenance: 10mg/kg in 100ml NS or 5%D IV over 30min q12h (or q4h if on dialysis) for 48h or until methanol/ethylene glycol level <8mmol/L.
Can give infusion (1mg/kg/hr) if haemodialysis.

Adverse Reactions
Mild headache, nausea, dizziness, metallic taste, mild infusion site irritation.

Notes
Not yet available in Australia/NZ.

Fuller's Earth

Indications
Paraquat poisoning

Mechanism
Clay soil adsorbant

Administration
PO

Notes
Traditional use, rarely available now and in any case no advantage over activated charcoal.

Glucagon

Indications
Second line Rx for BB or CCB OD if hypoBP.

Contraindications
None.

Mechanism
Increases cAMP and is ionotropic/chronotropic effects.

Pharmacokinetics
Small VD (0.25L/kg). Rapidly metabolised in plasma/liver/kidney. $T_{\frac{1}{2}}$=8-18min.

Administration
Initially 5mg IV repeat if no response after 5min. If effective start infusion 2-5mg/hr in 5%D until haemodynamically stable on withdrawal.

Adverse Reactions
N & V, hyperglycaemia, hypoK+.

Notes
Lack of human clinical trials. Difficult to source sufficient supplies.

(High dose) Insulin-Dextrose Euglycaemia

Indications
CCB (or ?BB) OD refractory to fluids & catecholamine infusion, or worsening acidosis.

Contraindications
None.

Mechanism
Insulin is inotropic & improves metabolic profile of heart. Dextrose maintains euglycaemia.

Pharmacokinetics
Because of mechanism, delay of 15-60min for onset of effect, so initiate early.

Administration
0.5g/kg (as 25%-50% soln) dextrose IV and then 1 IU/kg short acting insulin IV bolus.
Continue with dextrose 0.5g/kg/h IV infusion and insulin 0.5-10.0 IU/kg/h.
Monitor BSL & [K^+] & titrate glucose infusion accordingly to maintain euglycaemia.

Adverse Reactions
Hypo/hyperglycaemia, hypoK+.

Heavy Metal Chelators

Indications

Dimercaprol (BAL – British Antilewisite) – Arsenic, inorganic mercury, gold, lead, & others
Sodium Calcium Edetate – Lead, ?other heavy metals
Succimer (DMSA) – Lead, other heavy metals (mercury, arsenic, bismuth, antimony, copper)
Penicillamine – Copper, second line for arsenic, iron, lead, mercury & zinc

Contraindications

Known hypersensitivity.
Dimercaprol: Peanut allergy, G6PD Def.
Sodium Calcium Edetate: anuric renal failure.
Penicillamine: penicillin allergy, pregnancy, renal failure.

Mechanism

Chelation.

Pharmacokinetics

Dimercaprol: not absorbed orally. Given IM in peanut oil. Hepatic met. BAL-complexes removed in urine or by dialysis.
Sodium Calcium Edetate: small VD, renal excretion.
Succimer: water soluble analogue of dimercaprol. Complexes renally excreted.

Administration

In ICU.
Dimercaprol: Hg/As: 3mg/kg IM q4h initially. Pb: 4mg/kg q4h x 5d commenced 4h before EDTA.
Sodium Calcium Edetate: 4h after starting dimercaprol, 25-50mg/kg (50-75mg/kg if encephalopathy) in 500ml NS or 5%D over 24h x5d, 4d rest (Pb redistribution) & repeat x5d.
Succimer: 10mg/kg PO tds x 5d then bd x 14d.
Penicillamine: 4-7mg/kg (max 2g) PO qid

Adverse Reactions

Dimercaprol: >50% have pain, fever, HT, ↑HR, headache, N&V, burning lips/mouth, lacrimation, rhinorrhoea, salivation, haemolysis with G6PD def, nephrotoxicity.
Sodium Calcium Edetate: thrombophlebitis, malaise, fever, dermatitis, headache, urinary frequency, hypoBP, lacrimation, glycosuria, LFT derangement, ECG changes, nephrotoxicity.
Succimer: Foul-smelling, GI upset, rarely reversible neutropaenia
Penicillamine: hypersensitivity, marrow depression, myasthenia gravis, peripheral neuropathy, GN, Goodpasture's, hepatotoxicity, pancreatitis.

Notes

Threshold blood level for succimer Rx in children is controversial and may not improve outcome. Probably should use succimer in mild poisoning (or child OD if possible), or as adjuvant to EDTA in severe poisoning. Dimercaprol less used and only in severe cases as common & significant SE. EDTA may cause redistribution of lead from soft tissues to CNS so if high Pb levels use with other Rx. Potential confusion with dicobalt edetate used in cyanide poisoning.

IV Lipid Emulsion (Intralipid®)

Indications

Local anaesthetic or other highly lipid soluble poisonings, e.g. BB (propranolol), CCB (verapamil), TCA, with refractory hypotension/cardiac arrest. Role outside LA toxicity is controversial.

Contraindications

Inadequate standard resuscitative efforts.

Mechanism

In addition to sequestering lipophilic drug molecules ("lipid sink"), may ↑ mitochondrial FFA delivery producing ↑myocardial ATP, activate myocyte Ca^{2+} & K^{+} channels, and ↑intracellular Ca^{2+}.

Administration

Continue standard resuscitation protocols.
1-1.5mg/kg 20% lipid emulsion bolus IV over 1min. Repeat 1-2x @ q3-5min if required.
Then 0.25-0.5ml/kg/min infusion until haemodynamically stable.
E.g. Using 500ml bags of 20% lipid emulsion for 70kg adult: Give 100ml bolus, then 400ml over 20min while giving adrenaline etc. If no response, rpt 100ml bolus and infuse 400ml over 10mins.

Adverse Reactions

Allergy/anaphylaxis. Pulm HT, acute lung injury & haematuria have been described, but ?cause.

Methylene blue

Indications

Methaemoglobinaemia – if symptomatic or MetHb>20%

Contraindications

G6PD Def, methaemoglobinaemia reductase deficiency, nitrite-induced methaemoglobinaemia following Rx for cyanide poisoning, hypersensitivity. Reduce dose in RF.

Mechanism

Methylene blue is rapidly reduced by methaemoglobinaemia reductase in presence of NADPH to leucomethylene blue which reduces MetHb to Hb.

Pharmacokinetics

Leucomethylene blue excreted in urine.

Administration

1-2mg/kg IV over 5mins. Flush with NS. Rarely need repeat doses unless dapsone OD.

Adverse Reactions

Local pain/irritation. Malaise. Blue staining of mucosae & urine. MetHb if given in high doses (>7mg/kg).

N-Acetylcysteine (NAC)

Indications

Potentially toxic paracetamol overdose, prevention of contrast-induced nephrotoxicity, ?other (chemoRx, paraquat, CCl_4, chloroform, acrlyonitrile, cyclophosphamide, and amanita mushrooms)

Contraindications

None.

Mechanism

Prevents NAPQI-hepatotoxicity if given <8hrs of OD. Reduces toxicity if given after that time. Mechanisms may include ↑glutathione availability, direct binding to NAPQI, provision of inorganic sulphate, reduction of NAPQI back to paracetamol. Also ↑blood flow to brain, heart, kidneys.

Pharmacokinetics

$T_{\frac{1}{2}}$=6h and 30% excreted unchanged in urine.

Administration

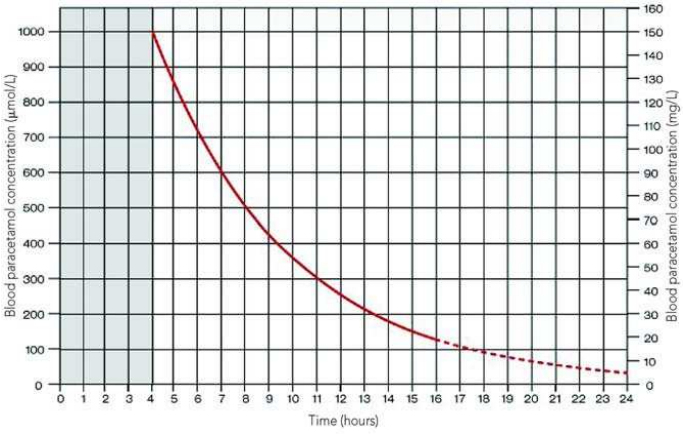
150mg/kg in 200ml 5% Dextrose (>20kg:100ml,<20kg:3ml/kg) over 15min-1hr
50mg/kg in 500ml 5% Dextrose (>20kg:250ml,<20kg:7ml/kg) over 4hr
100mg/kg in 1L 5% Dextrose (>20kg:500ml,<20kg:14ml/kg) over 16hr
Extended dose: Advised if paracetamol still detectable, LFT's still sig abnormal or not improving, INR<2, or encephalopathy. Dosage: Repeat last bag dose (i.e. 6.25mg/kg/hr)

Adverse Reactions

Anaphylactoid reaction – stop/slow infusion, give antihistamine. Restart when settled at half rate and slowly increase to full rate.

Notes

Paracetamol Nomogram:



Naloxone

Indications
Opioid OD causing CNS/respiratory depression.

Contraindications
Relatively CI in opioid dependency.

Mechanism
Competitive inhibition at mu, kappa & delta opioid receptors.

Pharmacokinetics
Well abs IM/SC/ET admin. Poor oral bioavail. Rapid distribution & onset of effect. Extensive 1st pass hepatic metab. Elim $T_{\frac{1}{2}}$=30-90min.

Administration
Full monitoring. Variable dosing. Initially 50-100mcg IV or 400mcg IM/SC. Repeat IV dose every 30-60s (or double dose q1-2min) until adequate spontaneous respiration. If opioid dependent do not fully reverse as may get withdrawal & become aggressive or abscond. If re-sedation/long acting opioid consider infusion at 2/3 of initial effective dose/hour. Observe for 2hrs post last dose.

Adverse Reactions
Withdrawal syndrome in opioid-dependent patients.

Notes
IN or neb naloxone routes not yet validated. Usefulness in EtOH/BDZ/clonidine/valproate OD unproven.
In buprenorphine (partial μ-agonist) bell shaped response curve so although effective doses often larger, but if too large then less effective.

Octreotide

Indications
Sulphonylurea OD or quinine-induced hypoglycaemia not responsive to initial glucose Rx.

Contraindications
None.

Mechanism
Suppresses pancreatic islet cell insulin release (synthetic somatostatin analogue).

Pharmacokinetics
Excellent bioavail. (~100%). Peak levels <30min. 30% excreted unchanged in urine, $T_{\frac{1}{2}}$=90min.

Administration
Initial bolus of 50mcg IV (child 1mcg/kg IV/SC), then 25 mcg/hr (child 1mcg/kg/hr) for 24h. Alternatively 100mcg SC/IM q6h. Should not need dextrose supplementation unless breakthrough hypoglycaemia in which case give 50% dextrose & double infusion rate. Need to maintain BSL for 6hrs off octreotide on normal diet before d/c.

Adverse Reactions
Minor nausea.

Physostigmine

Indications
Central antimuscarinic manifestations (agitated delirium) or isolated anticholinergic poisoning.

Contraindications
Bradyarrhythmias, intraventricular block, AV block, bronchospasm. Avoid I pregnancy.

Mechanism
Reversible acetylcholinesterase inhibitor.

Pharmacokinetics
Poor oral absorption. Crosses BBB. Elim. $T_{\frac{1}{2}}$=20min.

Administration
If ECG shows no conduction defects or bradycardia, 0.5-1mg (child 0.02mg/kg) IV over 5min rpt q10min until response. Rarely need >4mg. Delirium may recur 1-4hrs later as physostigmine effect wanes.

Adverse Reactions
Cholinergic stimulation (seizures, bradycardia, bronchospasm, bronchorrhoea, N & V & D).

Pralidoxime

Indications
Organophosphate (OP) poisoning. May also be used in carbamate or nerve agent poisoning.

Contraindications
Hypersensitiviy.

Mechanism
Can reactivate acetylcholinesterase inhibited by OP binding if given before 'ageing' occurs.

Pharmacokinetics
VD 0.8L/kg. >80% excreted unchanged in urine. Elim $T_{\frac{1}{2}}$=75min. VD & $T_{\frac{1}{2}}$ prolonged in poisoning & with IV infusion.

Administration
WHO protocol: Initially 2g (child 25-50mg/kg) in 100ml NS IV over 15min. Then infuse 500mg/hr (child 10-20mg/kg/hr) and continued for at least 24 hrs or longer until asymptomatic (no weakness, no drop in serial red cell cholinesterase activity assays).

Adverse Reactions
Usually minor. Non-specific (N, headache, dizziness, drowsiness, blurred vision, ↑RR). Rapid admin can cause ↑HR, Laryngospasm, muscle rigidity, ↑BP & transient neuromuscular blockade.

Notes
Use is currently unclear/controversial as some studies show no, or negative, mortality benefit using WHO protocol despite evidence for reactivation of AChE. More studies required to see if other dosing regimens have better outcomes. In theory benefit most likely if given early in diethyl OP OD, least likely benefit in late dimethyl OP ODs.

Pyridoxine (Vitamin B6)

Indications
Seizures induced by hydrazine compounds (isoniazid, gyromitra mushrooms, jet/rocket fuels).
Adjunct in ethylene glycol toxicity.

Contraindications
Hypersensitivity.

Mechanism
Hydrazines inhibit/deplete endogenous activated Vit. B6 which is required to make GABA.

Pharmacokinetics
Oral bioavail of 50%. VD 0.6L/kg. Rapidly met. outside liver.

Administration
EEG monitoring essential if patient intubated & paralysed (to monitor cessation of seizures).
Isoniazid OD – 1g pyridoxine per gram isoniazid up to max 5g (child max 70mg/kg) as infusion at 0.5g/min until seizures cease. Remainder of dose infused over 4hrs. Give BDZ concomitantly.
Ethylene glycol poisoning – 50mg IV q6h.
Hydrazine poisoning – Initial bolus 25mg/kg IV.

Adverse Reactions
The peripheral neuropathy assoc with chronic high PO dosing not seen in this setting.

Sodium bicarbonate

Indications
Cardiotoxicity 2° to fast Na channel blockade (TCA, bupropion, venlafaxine, propranolol, quinine)
Ion trapping - to outside CNS (salicylates) or to within the urine (salicylates, phenobarbitone)
Correction of life-threatening metabolic acidosis (cyanide, isoniazid, toxic alcohols)
Increased urinary solubility (MTX, myoglobin in drug-induced rhabdomyolysis)

Contraindications
Severe hyperNa, RF, hypoK+, Met or resp alkalosis, poorly controlled CCF, APO.

Mechanism
Na load & bicarbonate raises serum & urinary pH → direct effects on fast Na-channels, mitigates the deleterious effects of acidosis on myocardium, also promotes H+ donation by weak acids & if then ionised will be less able to cross cell membranes.

Administration
Life-threatening cardiotoxicity: 2mmol/kg IV boluses
Serum alkalinisation for cardiotoxicity: 100mmol in 1L NS @ 250ml/hr IV. Keep pH 7.5-7.55
Prevention of redistribution of salicylate to CNS: If not intubated but unwell give 2mmol/kg IV bolus and intubate then hyperventilate±serum alkalinisation to keep pH>7.4 until haemodialysed.
Urinary alkalinisation: 1-2mmol/kg IV bolus then 100mmol in 1L 5%D + 20mmol KCL @ 250ml/hr IV titrate to maintain urine pH>7.50. Add separate fluid line to keep urine output 2ml/kg/hr.

Adverse Reactions
Alkalosis (serum pH>7.6 affects cardiac function), hyperNa, hyperOsm, fluid overload/APO, hypoK, local inflammation with extravasation.

Vitamin K

Indications

Coumadin-induced coagulopathy (warfarin, brodifacoum)
Hepatotoxicity

Contraindications

Hypersensitivity.

Mechanism

Vit K is an essential co-factor for synthesis of factors II, VII, IX & X.

Pharmacokinetics

Oral bioavail ~50%. Rapid hepatic met. Elim. $T_{\frac{1}{2}}$=2hr. Onset 3-6hr IV, 6-12hr if given PO.

Administration

Over warfarinisation:
Warfarin OD:

- Not on warfarin already, give Vit K 10-20mg (child 5-10mg) PO & check INR @ 48hrs.
- On warfarin, if INR>5 give rpt doses of Vit K 0.5-2mg IV. Heparinise if INR falls<2.

Long-acting rodenticide:

- May require very large oral doses (10-50mg) qds for weeks or months if INR rises.
- If INR>9 will also need blood products (**FFP**, **prothrombin complex concentrate**).

Adverse Reactions

Minor facial flushing, chest tightness, dyspnoea or dizziness if given IV. Anaphylaxis (rare).
Overcorrection in person requiring anticoagulation.

Notes

Don't give Vit K IM.