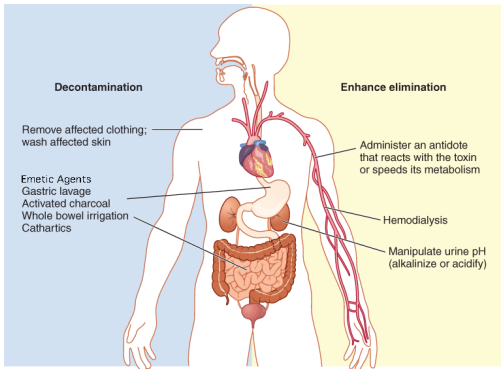
PHARMACOLOGICAL BASIS OF POISONING



Decontamination

Activated Charcoal (AC) is the preferred means of gastric decontamination for ingested poisoning. It is inert, insoluble and has a very extensive network of pores created when organic matter is treated with pyrolysis then acid and steam The resultant binding surface of area 950-2000m2 per gram. The amount of drug absorbed is dependent on the time since the poison was ingested, the dose of charcoal (usually 1g/kg) and the type of charcoal. It is not particularly effective with small ionised molecules (metals, electrolytes, highly ionised acids and alkali, and alcohol). The main contraindications are similar for all the ingested decominators; perforation or obstuction, decreased GCS without definitive airway, uncooperative concious patient and significant risk of GI bleed. Specific contraindications (relative) are likelyhood of gastroscopy (makes the procedure redundant).

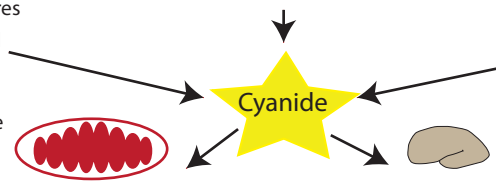
Gastric Lavage (GL) May be useful for drugs that are not effectively absorbed by activated charcoal. Typically it is given via a wide bore OG or NG tube. The lavage fluid is usually around five litres of warmed saline. Of note it is associated with an increased risk of ICU admission and aspiration.
Ipecac very limited indications for this emetic agent, it may be useful in witnessed out of hospital ingestion of poison.
Whole Bowel Irrigation enteral administration of polyethylene glycol balanced electrolyte solution (PEG-ELS). Despite volumes of 5 to 50 litres typically being used it does not normally result in electrolyte disturbances. Like GL it may be useful when AC is not effective, particularly with enteric coated and slow release medications.
Cathartics Cathartics are intended to decrease poison absorption by osmotically enhancing rectal evacuation of the poison-activated charcoal complex. The most common of these is sorbitol. They are only used as an adjunct therapy.

Cyanide

Fires - most common cause, the combustion of carbon and nitrogen in domestic fires liberate cyanide which is then inhaled

Industrial byproduct in mining and engineering

Medical sodium nitroprusside contains five units of cyanide per molecule and may develop into toxic levels folloing prolonged admission. (this is why it is stored and delivered in a covered bag and silver foil covered tubing.



Mitochondria - Cyanide binds to the ferric (3+) ion of the Cytochrome Oxidase a3 enzyme which is required for the final step in oxidative phophorylation OP in the mitochondrial. The result is the body must use anaerobic metabolism, resulting in increased lactatic acidosis with the associated HCO3 decrease. Despite ample O2 the body cannot utilise it due to the blocked OP which results in 'functional or histotoxic hypoxia'. The high O2 demand organs (CNS and Heart) are usually the worse affected.

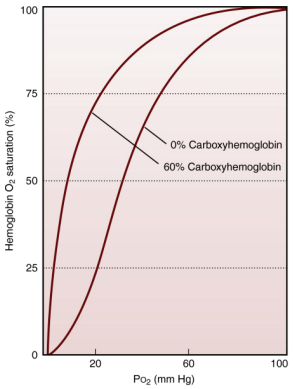
Brain A number of other mechanisms may exacerbate brain injury. Cyanide's nonspecific inhibition of antioxidants results in the accumulation of toxic oxygen free-radicals. Cyanide causes the release of glutamate, and also inhibits glutamic acid decarboxylase (GAD), the enzyme responsible for the formation of the inhibitory neurotransmitter gamma–aminobutyric acid (GABA) from glutamic acid. Consequently, cyanide reduces the seizure threshold as GABA levels fall.

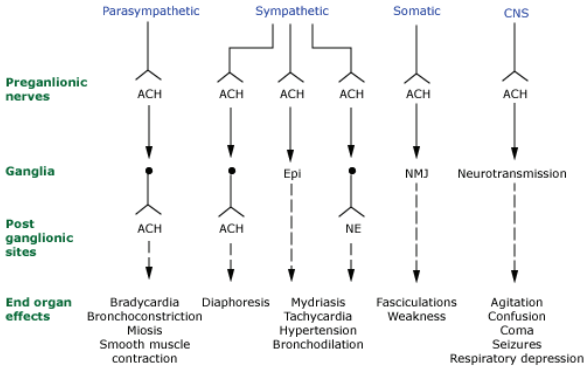
Management

Treat symptoms ABCs, reduce seizure risk, continue high flow O2
Reduce absorption if the cyanide has been ingested. AC binds cyanide poorly but is nevertheless recommended
Bind cyanide directly hydroxycoalbumin binds cyanide to form cyanocoalbumin which is excreted in urine
Produce Fe3+ to compete with mitocondrial binding sites by inducing methemoglobulin which oxidises Fe2+ in the blood
Provide sulphur donors to assist rhodanese - a ubiquitous enzyme that detoxifies cyanide by transforming it to thiocyanate

Carbon Monoxide

Poisoning usually due to inhalation but may be due to ingestion of methylene chloride which is metabolised in the liver to CO. CO binds to heme with an affinity 240 times that of O2. It causes an allosteric change in which greatly inhibits the three other heme binding sites from offloading O2. The result is a shift of the O2 dissociation curve to the left. CO also inhibits OP like cyanide but to a less extent which exacerbates the hypoxia. The mechanism of the delayed neurological sequelae is not well understood but may be related to toxic oxygen species generated by xanthine oxidase. Treatment is via high flow O2 and HBOT may be indicated.





Organophosphates

Acute toxicity from organophosphorous agents presents with manifestations of cholinergic excess. Primary toxic effects involve the autonomic nervous system, neuromuscular junction, and central nervous system. The parasympathetic nervous system is particularly dependent on acetylcholine regulation, since both the autonomic ganglia and end organs of the parasympathetic nervous system are regulated by nicotinic and muscarinic cholinergic receptors. Treatment is with atropine which competes with acetylcholine at muscarinic recpetors to reduce the deleterious affects (but not at nicotinic). Oximes such as pralidoxime reactivates cholinesterase therefore works at both musc/nict receptors. Benzos are useful for seizure reduction.

Methanol and Ethylene Glycol

The "parent alcohols" methanol and ethylene glycol are relatively nontoxic, and cause mainly central nervous system (CNS) sedation. However, profound toxicity can ensue when these parent alcohols are oxidized (primarily by alcohol dehydrogenase and aldehyde dehydrogenase). The methanol metabolite formate and the ethylene glycol metabolites glycolate, glyoxylate, and oxalate accumulate following large ingestions. Formate causes retinal injury with optic disc hyperemia, edema, and eventually permanent blindness, as well as ischemic or hemorrhagic injury to the basal ganglia. Ethylene glycol metabolites target the kidney and lead to reversible oliguric or anuric acute kidney injury (acute renal failure), which in turn slows elimination of ethylene glycol. The renal failure is primarily due to glycolate-induced damage to tubules, although tubule obstruction from precipitated oxalate crystals may contribute. Hypocalcemia in ethylene glycol overdose results from calcium oxalate formation. With ingestions of either parent alcohol, a profound anion gap metabolic acidosis develops, which directly correlates with the accumulation of toxic acid metabolites. Acidemia increases the ability of the toxic metabolites to penetrate cells, further depressing CNS function and causing a rapid downward spiral of hypoxia and acidemia. Treatment is ABCs, HCO3 for acidosis, and ADH inhibitor fomepezil or ethanol, and consider hemodyalisis if there is end organ damage.

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