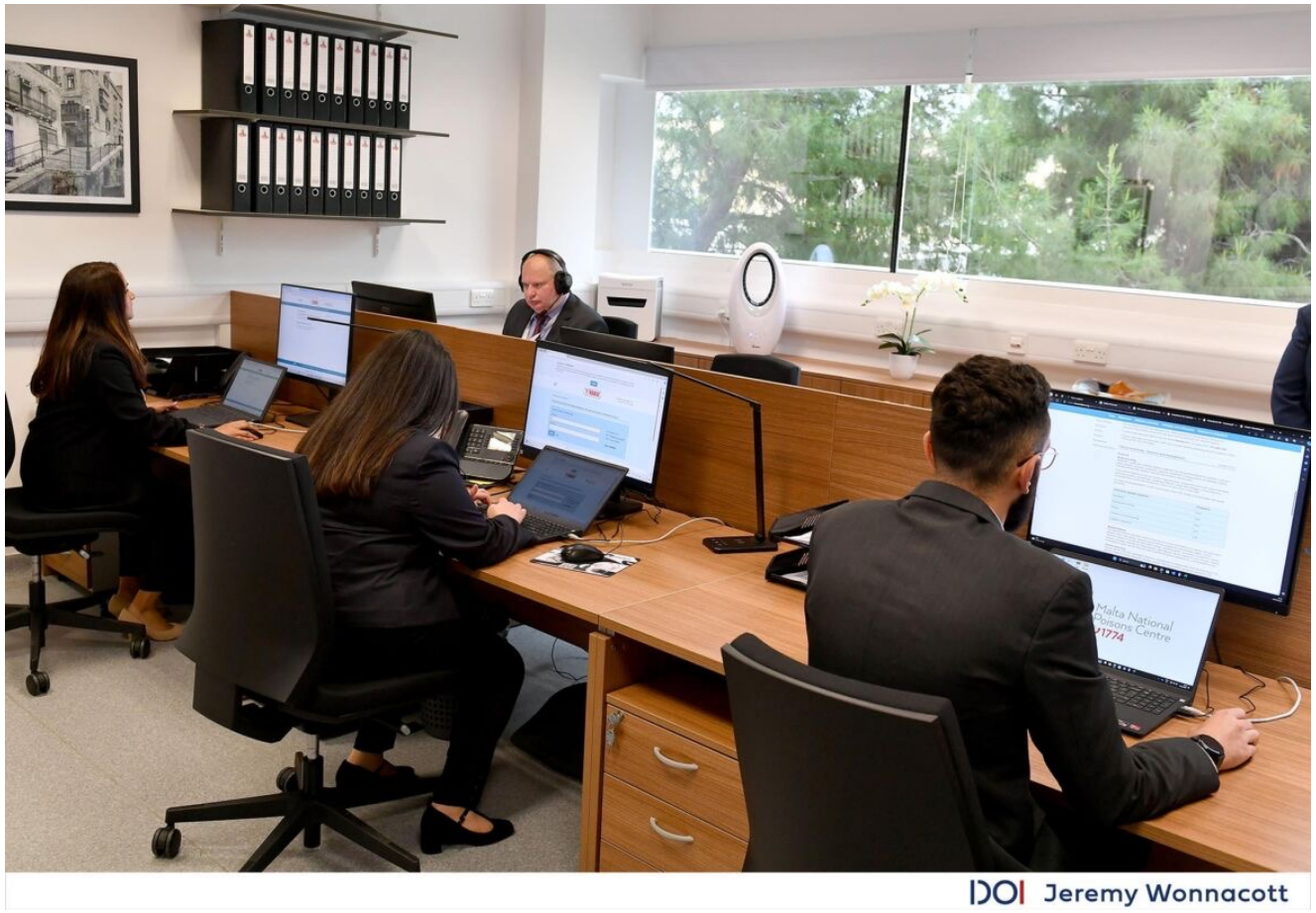
Let’s talk about Poisons

Dr Jeffrey Bonnici

Dr Robert Chircop

Mr Mark Zammit

The Malta National Poisons Centre



Life Science Park, Msida

Main objectives

- Understand how to approach a patient with an overdose in the Primary Care setting
- Conducting first assessment
- Identifying drug taken
  - History, Physical examination (vitals, toxidromes), Diagnostic tests
- Stabilisation
- Decontamination
- Prevention of drug absorption
- Enhancement of drug elimination
- Administration of antidote
- Specific cases

Determining Aquity

- **Critical –** Life-threatening illness or injury with a high probability of mortality if immediate intervention is not begun to prevent further airway, respiratory, hemodynamic, or neurologic instability.

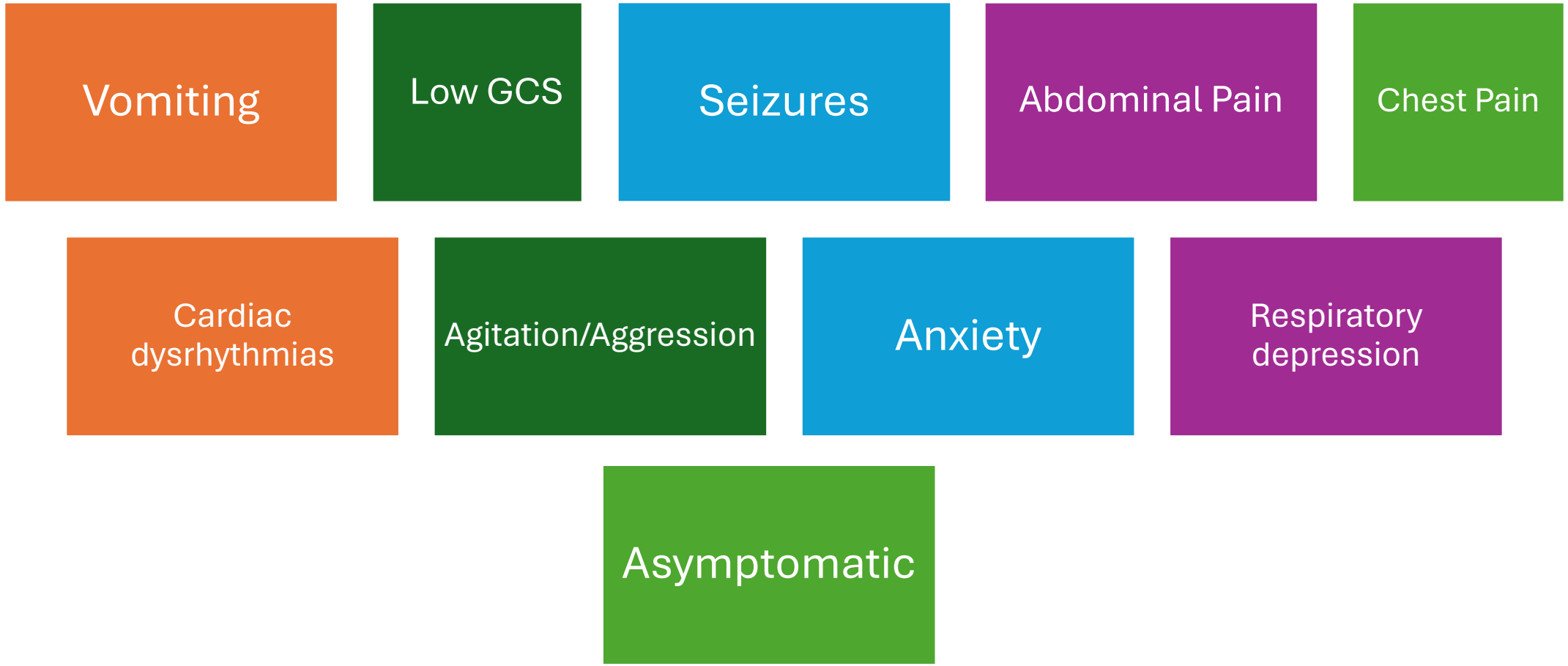
- **Emergent** - Patient presents with symptoms of an illness or injury that may progress in severity or result in complications with a high probability for morbidity if treatment is not begun quickly.

- **Low acuity** - Patient presents with symptoms of an illness or injury that have a low probability of progression to more serious disease or development of complications.

- Conduct primary assessment and take steps to stabilise patient accordingly

Counselman FL, Babu K, Edens MA, Gorgas DL, Hobgood C, Marco CA, Katz E, Rodgers K, Stallings LA, Wadman MC; 2016 EM Model Review Task Force, Beeson MS, Keehbauch JN; American Board of Emergency Medicine. The 2016 Model of the Clinical Practice of Emergency Medicine. J Emerg Med. 2017 Jun;52(6):846-849.

Acute overdose patient



- Taking a focused history
- Identify risk factors
- Identify the patient’s appearance, vital signs
- Recognise physical findings, toxidromes

- Associated factors – age, gender, ethnicity, communication barriers, socioeconomic factors, underlying disease

Approach to a patient with an acute overdose will depend on what drug/s have been taken, amount taken, route taken, time since ingestion, and the accompanying signs and symptoms

Knowledge of the drug/s taken

Patient history (including collateral)

Physical examination

Toxidrome recognition

Diagnostic tests

Patient history

- Diagnosis can’t be reached without information
- High index of suspicion
- Possible differential diagnosis
  - e.g. Coma – vascular event in brain, trauma, CNS infections, sepsis, metabolic abnormalities, toxins etc.
- Chance of polypharmacy +/- use of alcohol

Physical Examination

- Poisoning may affect one organ only or damage several simultaneously.
- Diagnosis of acute poisoning cannot be made on the basis of a single physical sign.
- Clusters of clinical features comprise syndromes that help establish a diagnosis.
- **Vitals signs** may give a clue of drug/s taken, if no history obtainable/unreliable

Physical examination findings: Vitals

Tachycardia (TACH)

- **T**CAS, Thyroid meds, Theophylline
- **A**nticholinergics, antihistamines, drug and alcohol withdrawal, antipyschotics
- **C**ocaine, caffeine, PCP, amphetamines
- **H**ydralazine

Bradycardia (BRAD_C)

- **B**eta-blockers, benzodiazepines
- **R**ivastigmine and other anticholinesterase drugs
- **A**nti-arrhythmics, Alcohols
- **D**igoxin, digitalis
- **C**alcium channel blockers, Clonidine

Hyperthermia (NASA)

- **N**euroleptic malignant syndrome
- **A**nticholinergics, **A**ntihistamines, antipsychotics, antidepressants
- **S**ympathomimetics, salicylates, serotonin syndrome
- **A**lcohol withdrawal

Physical examination findings: Vitals

Hypothermia (COOL_B)

- **C**arbon monoxide
- **O**ral-hypoglycaemiac agents, Insulin
- **O**pioids
- **L**iquer (alcohol)
- **B**eta-Blockers, benzodiazepines (sedatives)

Bradypnoea (LOGS)

- **L**iquer (alcohol)
- **O**pioids
- **G**HB and related compounds
- **S**edatives (Benzodiazepines, etc)

Physical examination findings: Vitals

Tachypnoea (TACH_PNOEA)

- **T**oxin-induced metabolic acidosis
- **A**spirin
- **C**yanide
- **H**ydrogen sulphide
- **P**araquat, Phosgene, PCP
- **N**erve agents
- **O**piate withdrawal
- **E**thanol Withdrawal
- **A**gitation/Anxiety inducing drugs

Hypotension (TABACCO)

- **T**CA
- **A**nti-arrhytmics
- **B**eta-blockers, benzodiazepines
- **A**nti-hypertensives, antihistamines
- **C**alcium channel blockers
- **C**lonidine
- **O**pioids

Hypertension (MATS)

- **M**onoamine oxidase inhibitors
- **A**nticholinergics
- **T**hyroid meds
- **S**ympathomimetics (Cocaine, caffeine, amphetamines)

Physical examination findings: Vitals

COMA (GCS≤8 or U on AVPU) – (LETHARGIC)

- **L**ead, lithium
- **E**thanol, ethylene glycol,
- **T**ricyclic antidepressants, thallium, toluene
- **H**eroin, hemlock, hepatic encephalopathy, heavy metals, hydrogen sulphide, hypoglycaemics
- **A**rsenic, antidepressants, anticonvulsants, antipsychotics, antihistamines
- **R**ohypnol (sedative hypnotics), risperidone
- **G**amma-hydroxybutyrate (GHB)
- **I**soniazid, insulin
- **C**arbon monoxide, cyanide, clonidine

Physical examination findings: Vitals

Seizures (OTIS CAMPBELL)

- **O**rganophosphates
- **T**ricyclic antidepressants
- **I**soniazid, **I**nsulin
- **S**ympathomimetics
- **C**amphor, **C**ocaine
- **A**mphetamines
- **M**ethylxanthines
- **PCP**, **P**ropoxyphene, **P**henol, **P**ropranolol
- **B**enzodiazepine withdrawal, **B**otanicals
- **E**thanol withdrawal
- **L**ithium, **L**idocaine
- **L**indane, **L**ead

Erickson TB, Thompson TM, Lu JJ. The approach to the patient with an unknown overdose. Emerg Med Clin North Am. 2007 May;25(2):249-81

Physical Examination findings: Neurology Exam

The GCS/AVPU are useful in head trauma and also in the assessment of the need for intubation, HOWEVER, have a limited role in predicting outcome in the poisoned patient.

Cardinal sign – symptoms only down one side of the body – not poisoning.

Classic pupillary findings:

- **Miosis** – Opioids, organophosphates, clonidine, carbamates
- **Mydriasis** – Sympathomimetics, withdrawals, anticholinergics
- **Nystagmus** – Phenytoin, PCP (Rotary), ethanol, carbamazepine, lithium, barbiturates, sedative hypnotics.
- **Vertical Nystagmus** – Brainstem bleed until proven otherwise
- **Optic neuritis/vision loss** – methanol (or MS)

Fasciculations – Organophosphate/Nicotine
Rigidity – Tetanus/Strychnine
Tremors – Methylxanthines, withdrawal, lithium
Dystonia – Neuroleptics

Toxidrome recognition

Anticholinergic (cyclic antidepressants, antihistamines, phenothiazines)

- Hyperthermia (hot as a hare)
- Dry skin (dry as a bone)
- Flushed (red as a beet)
- Mydriasis (blind as a bat)
- Delirium/hallucinations (mad as a hatter)
- Urinary retention (full as a flask)
- Tachycardia

Sympathomimetic (cocaine, amphetamines, pseudoephedrine)

- Tachycardia
- Mydriasis
- Agitation/Aggression
- Hypertension
- Hyperthermia
- Seizures

Erickson TB, Thompson TM, Lu JJ. The approach to the patient with an unknown overdose. Emerg Med Clin North Am. 2007 May;25(2):249-81

Toxidrome recognition

Opioid (Heroin, codeine, morphine, oxycodone)

- Miosis
- Bradypnoea
- Bradycardia
- Hypotension
- Coma

Cholinergic (SLUDGE) or (DUMBBELLS)

- **S**alivation
- **L**acrimation
- **U**rination
- **D**iarrhoea
- **G**astrointestinal distress fasciculations
- **E**mesis

Diarrhoea
Urination
Miosis
Bronchorrhoea
Body

Emesis
Lacrimation
Lethargy
Salivation

Toxidrome recognition

Nicotinic (nicotine, coniine (Conium maculatum)

- Miosis
- Tachycardia
- Weakness
- Tremors
- Fasciculations
- Seizures
- Somnolence

Withdrawal

- Diarrhoea
- Tachycardia
- Lacrimation
- Mydriasis
- Goose flesh
- Hypertension
- Yawning
- Cramps
- Hallucinations
- Seizures

Toxidrome recognition

Salicylism

- Nausea/vomiting
- Tinnitus/deafness
- Dizziness/lethargy
- Dehydration
- Restlessness
- Sweating
- Hyperventilation – Resp alkalosis
- Confusion/coma
- Metabolic + lactic acidosis
- Seizures
- Hyperthermia
- Cardiac dysrhythmias, NC-pulmonary oedema

Serotonin syndrome

- Triad of:
  - **CNS features** (agitation/coma) – 40% patients
  - **Autonomic instability** (e.g. hyperpyrexia) – 50%
  - **Neuromuscular excitability** (e.g. clonus, raised CK) – 50%
- May occur over a period of minutes to hours
- Death usually from hyperthermia - MOF

Diagnostic tests in identifying poisoned patient

- **ECG –** Tachycardia, bradycardia, QTC, QRS, SA and AV blocks, junctional rhythms, VT, AF, Premature ventricular contractions, non-paroxysmal atrial tachycardia with AV block.
- **High K^+**: K+ supplements, cardiac glycosides (digoxin), rhabdomyolysis, haemolysis, AKI
- **Low K^+:** theophylline, other sympathomimetic agents
- **Low HCO_3^-**:metabolic acidosis (usually from hypoxaemia, peripheral circ. failure), but also from **impaired cellular respiration** (salicylates, cyanide) or **toxins metabolised to acids** (methanol and ethylene glycol). Also **respiratory alkalosis** (salicylates/sympathomimetic agents)
- **Hypoglyacemia** – usually OHA, insulin but also ethanol (esp. in children) and in liver damage (e.g. paracetamol)
- **Anion & osmolal gaps** – should be requested in patients with suspected overdose in metabolic acidosis/if antifreeze or ethanol substitute suspected.

Diagnostic tests in identifying poisoned patient

- **Hyperglycaemia –** large no. of agents, partic. Sympathomimetic drugs (e.g. theophylline), calcium channel blockers.
- **Hypocalcaemia –** poisoning with flouride salts, hydroflouric acid burns and ethylene glycol ingest.
- **LFT's – Increased ALT –** espec. >1000units/litre – suspect paracetamol poisoning.
- **Screening for unknown and undisclosed toxins**
  - The only one toxin that should be routinely screened is **Paracetamol**
  - Should be taken in all deliberate OD's
  - All unconscious suspected OD's
  - Routine Salicylate levels are not justified. (Unlikely to cause coma, and highly improbable without signs of salicylism)*.

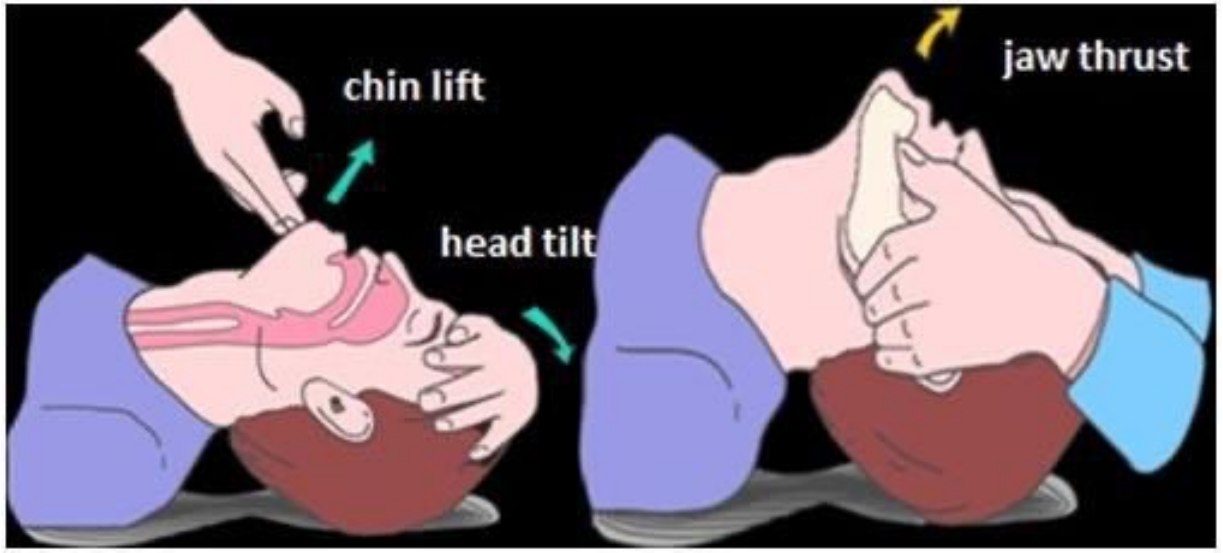
* Wood DM, Dargan PI, Jones AL. Measuring plasma salicylate concentrations in all patients with drug overdose or altered consciousness: is it necessary? Emerg Med J. 2005 Jun;22(6):401-3

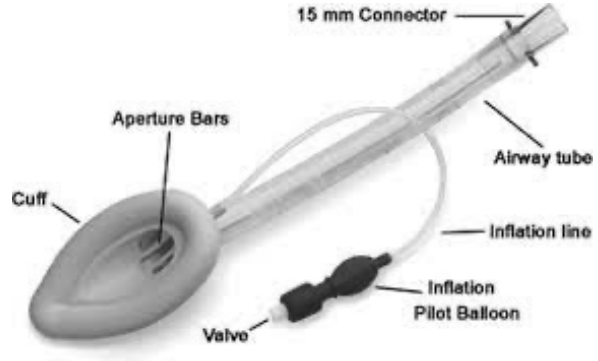
Further care:

- Patient stabilisation (ABC)
- Decontamination (GI)
- Prevention of drug absorption
- Enhancement of elimination
- Administration of antidote
- Observation/Disposition

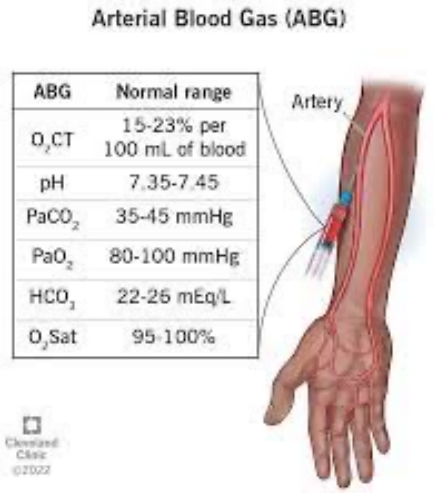
Patient Stabilisation – Airway, Breathing, Circulation

- Treatment includes
  - Assessment of the airway for obstruction, providing oxygen
  - Head tilt + chin lift **or Jaw thrust
  - Using airway adjuncts
  - Supraglottic devices – e.g. LMA
  - Intubation and ventilation





Patient Stabilisation - Breathing



- Toxins may interfere with ventilation due to central effects on the nervous system or local effects causing weakness of the chest musculature. If gastric contents or toxins have been inhaled gas exchange at the alveolar level may be impaired and the patient can become hypoxic even if ventilation is adequate.
- Clinically, a severely hypoxic may appear centrally cyanosed. **Arterial blood gases** are the best guide to the adequacy of **respiration**. They provide information about the effectiveness of ventilation, gas exchange and the metabolic state of the patient.
- **Pulse oximetry** is non-invasive, readily available and often used to provide information on the **oxygen saturation** of the blood. However, the result may be misleading
  - for example, in severe CO poisoning a patient may have severely impaired oxygen delivery but a normal oxygen saturation on the pulse oximeter.

Patient Stabilisation - Circulation

Hypotension is the commonest cardiovascular manifestation of poisoning

- May respond to elevation of legs.
- Crystalloids sometimes help
- Inotropes?

Hypertension

- **In many situations, may be best left untreated**
- In agitated patients may improved after benzo's
- IV GTN e.g. 1-2mg/hr up to 12mg/hr
- ?Calcium channel blocker/Labetalol/Phentolamine

Rhythm disturbances

- Usually settle with good oxygenation, norm. of electrolytes and acid base balance control.
- Prolonged QRS (e.g. TCA) – **Sodium Bicarbonate**
- Prolonged QTC – **Magnesium Sulphate**

GI decontamination, Prevention of absorption/enhanced elimination

- Gastric decontamination
  - Gastric lavage
  - Syrup of ipecac
- Activated charcoal
- Whole bowel irrigation
- Dialysis (haemodialysis/haemoperfusion)
- Urine alkalinization
- Lipid emulsion therapy
- V-A ECMO
- Antidotes

GI Decontamination

- Controversial topic in Toxicology.
- Limited number of studies demonstrating effect of GI decontamination to clinical meaningful endpoint, and ethical dilemmas in doing such studies.
- Clear limited value for the unknown drug at an unknown time. Most authors tend to agree that it should be done early (within 1 or 2 hours).
- Considerable decline in use of all methods of decontamination, possibly related to decline of more potent drugs like barbiturates and cyclic antidepressants (benzodiazepines and SSRI/SRNI).
- Gastric emptying is performed either through gastric lavage OR induction of emesis by syrup of ipecac.
- The use of syrup of ipecac declined significantly after joint position papers (AACT, EAPCCT) in 1997,2004 and 2013. Ipecac delays administration of activated charcoal and other oral treatment.
- The patient is usually on the steep portion of the dose-response curve.

Gastric Lavage

- At present there is no evidence showing that gastric lavage should be used routinely in the management of poisonings.
- The evidence supporting gastric lavage as a beneficial treatment in special situations is weak, as is the evidence to exclude benefit in all cases.
- **Gastric lavage should not be performed routinely, if at all, for the treatment of poisoned patients*.**
- In the rare instances in which gastric lavage is indicated, it should only be performed by individuals with proper training and expertise.

*Position paper (2004) + update (2013) American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists.

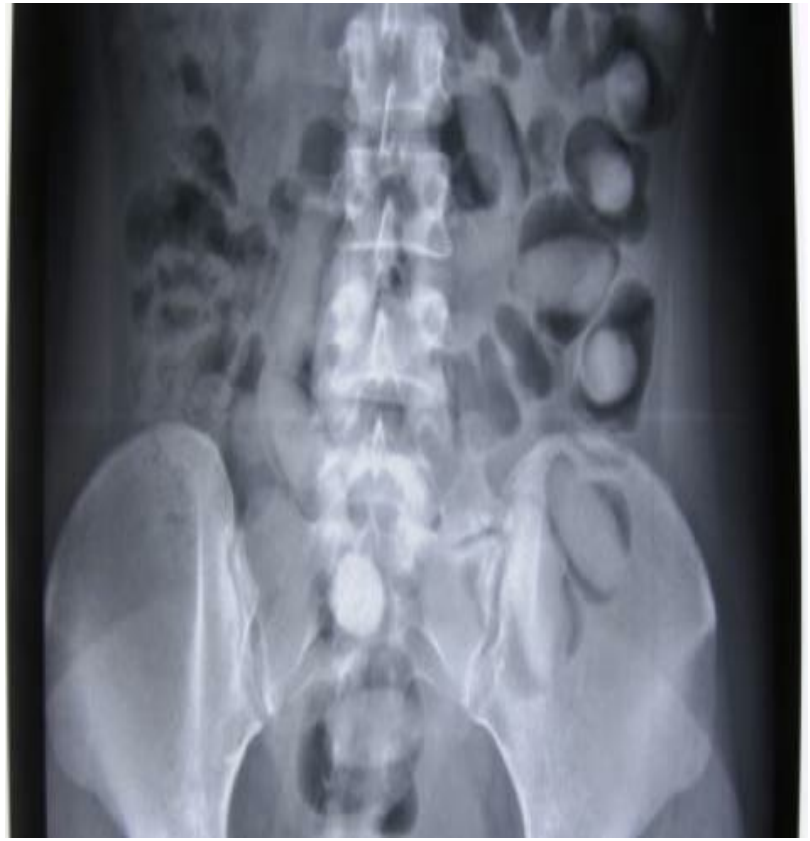
Prevention of absorption

Activated charcoal

- A single dose of charcoal (50g for adults and 1g per kg body weight for children)
- via mouth or NG tube up to 1 hour after ingestion of a potentially toxic amount of a well charcoal-adsorbed poison, (possibly beyond an hour in cases involving sustained or modified-release drug preparations).
- **C/I –** anatomical derangements of GI, unprotected airway, or when use may increase risk of aspiration esp. Hydrocarbons
- **Drugs poorly absorbed:** Cyanide, Lead, Alkali, D.D.T., Acids, Ethylene glycol, Methanol, Lithium, Organic solvents, Ethanol, Mercury, Ferrous salts,
- **Multiple dose activated charcoal – consider in** Phenobarbitone, Carbamazepine, Dapsone, Theophylline, Digoxin, Quinine
  - **50g followed by 12.5g hrly or 25g 2hrly in adults**
  - **1g/kg followed by 1g/kg/2hr in children**

Whole bowel irrigation

- Used for potentially dangerous ingestions of modif. Release/enteric coated drugs or if activ. Charcoal ineffective (iron, lithium, cocaine body packers) – 1.5-2litres/hr of PEG-ELS via NG tube (0.5L/hr in small children) for 4-6hours or until effluent is clear.
- Data from 10 **volunteer studies** using WBI for reducing absorption, showed three studies involving dosing with ampicillin, delayed-release aspirin, and sustained-release lithium with significant reduction in bioavailability of 67%, 73%, and 67%, respectively (all $p<0.05$).
- The concurrent administration of activated charcoal and WBI may actually decrease the effectiveness of the charcoal. The clinical relevance of this interaction is however uncertain.



Xray of a bodypacker

Tenenbein et al, 1987, Kirshenbaum et al, 1989, Smith et al, 1991, Lapatto-Reiniluoto et al, 2001

Extracorporeal removal - **Dialysis**

- The construction of the first artificial kidney is attributed to Abel and colleagues in 1913.
- By the end of the 1950s, several poisons had been shown to be dialyzable, including barbiturates, salicylates, and hypnotics.
- Intermittent Hemodialysis remains a valuable therapeutic option for severe poisonings today. Haemodialysis has surpassed haemoperfusion as the modality of choice in poisoning because of improved clearance and better safety profile.
- Use of **high-flux** and high-efficiency dialysis membranes is now standard practice in dialysis centers. This is contributing to the possibility of dialysis being used for drugs that were considered not dialysazable before for instance, severe vancomycin overdose (1486 daltons).

Extracorporeal removal - **Dialysis**

- May be of some value in the treatment of ill patients with high plasma concentrations of salicylates, methanol, ethanol, ethylene glycol, lithium, phenobarbital, metformin, paracetamol, isopropanol and sodium chloride.
- Effectiveness of dialysis is limited by high levels of **protein binding** (e.g. warfarin), **high lipid solubility** and **high volumes of distribution** (amitriptyline) together with **high molecular weight** (heparin) and **poor diffusibility** across dialysis membranes.
- Contraindications to haemodialysis include haemodynamic instability and in particular hypovolaemic shock, and coagulation disorders. Severe respiratory disease and intra-abdominal sepsis are additional contraindications to peritoneal dialysis.

Intravenous lipid emulsion

- **Intravenous lipid emulsion** (ILE) is well known in the Emergency Department.
- The ’lipid sink’ is a term coined by Weinberg in 1998*, and postulates that the Lipid emulsion infusion creates an expanded lipid phase, and the resulting equilibrium drives toxic drug from tissue to the aqueous plasma phase then to the lipid phase.
- A treatment in life-threatening cardiotoxicity due to local anaesthetics.
- Based on this hypothesis, lipid emulsion has been considered a candidate for generic reversal of toxicity caused by overdose of **any lipophilic drug**

Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anesthesiology. 1998 Apr;88(4):1071-5.

Intravenous lipid emulsion

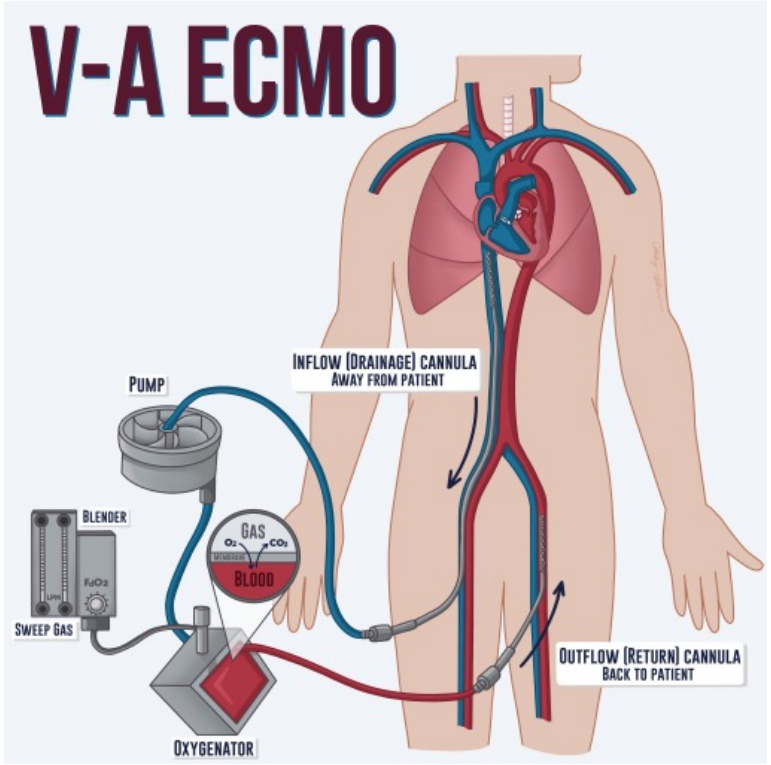
- There seems to be growing evidence of **inherent positive publication bias** in case reports and series.
- **Slowly but surely losing its importance in Toxicology.**
- Recommendation of ILE use in non-local anaesthetic drug poisoning remains controversial.[1]

In cardiac arrest or life-threatening cardiotoxicity secondary to poisoning where other therapies have been ineffective, consider the use of ILE, but evidence of benefit is weak.

1. Grant Cave and Martyn G Harvey. Should we consider the infusion of lipid emulsion in the resuscitation of poisoned patients? Crit Care. 2014; 18(5): 457.

Use of ECMO in Poisoned patients – ‘BRIDGE TO RECOVERY’

- Veno-venous (VV-ECMO) or veno-arterial (VA-ECMO) in poisoned patients?
- VA-ECMO!



Antidotes: Top 7

- **NAC -** Paracetamol
- **Naloxone -** Opioids
- **Atropine -** Organophosphates
- **Desferrioxamine -** Iron
- **Antivenims**
- **Flumazenil -** benzodiazepines
- **Ethanol** / Fomepizole - Toxic alcohols – Ethylene glycol + Methanol

References

- Counselman FL, Babu K, Edens MA, Gorgas DL, Hobgood C, Marco CA, Katz E, Rodgers K, Stallings LA, Wadman MC; 2016 EM Model Review Task Force, Beeson MS, Keehbauch JN; American Board of Emergency Medicine. The 2016 Model of the Clinical Practice of Emergency Medicine. J Emerg Med. 2017 Jun;52(6):846-849.
- Erickson TB, Thompson TM, Lu JJ. The approach to the patient with an unknown overdose. Emerg Med Clin North Am. 2007 May;25(2):249-81
- Wood DM, Dargan PI, Jones AL. Measuring plasma salicylate concentrations in all patients with drug overdose or altered consciousness: is it necessary? Emerg Med J. 2005 Jun;22(6):401-3
- Position paper (2004) + update (2013) American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists.
- Tenenbein M. Whole-bowel irrigation in iron poisoning. *J Pediatr.* 1987;111:142-145.
- Kirshenbaum LA, Mathews SC, Sitar DS, Tenenbein M. Whole-bowel irrigation versus activated charcoal in sorbitol for the ingestion of modified-release pharmaceuticals. Clin Pharmacol Ther. 1989 Sep;46(3):264-71.
- Lapatto-Reiniluoto, O., Kivistö, K.T. and Neuvonen, P.J. (2001), Activated charcoal alone and followed by whole-bowel irrigation in preventing the absorption of sustained-release drugs. Clinical Pharmacology & Therapeutics, 70: 255-260.
- Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anesthesiology. 1998 Apr;88(4):1071-5.
- Grant Cave and Martyn G Harvey. Should we consider the infusion of lipid emulsion in the resuscitation of poisoned patients? Crit Care. 2014; 18(5): 457.
- Duburcq T, Goutay J, Preau S et al., Venoarterial Extracorporeal Membrane Oxygenation in Severe Drug Intoxication: A Retrospective Comparison of Survivors and Nonsurvivors. ASAIO J. 2022 Jul 1;68(7):907-913
- Masson R, Colas V, Parienti JJ, Lehoux P, Massetti M, Charbonneau P, Saulnier F, Daubin C. A comparison of survival with and without extracorporeal life support treatment for severe poisoning due to drug intoxication. Resuscitation. 2012 Nov;83(11):1413-7. doi: 10.1016/j.resuscitation.2012.03.028. Epub 2012 Mar 31. PMID: 22469751.

Specific cases - 1

Private GP call:

A 3yr old boy *uncertain weight, but looks average*, is given Calpol suspension by his grandmother 10mls 4 times/24hrs for sore throat and now notices that it might be too much. Last given a few minutes ago

- The calpol package is purple and the bottle has a child on it and says sugar free, pain and fever relief for babies and infants.
- NO PMH, Child otherwise well.

120mg/5mls

2-6 months – 2.5mls every 4-6hrs (not more than 4 doses in 24hrs)
6-24 months – 5mls
2-4 years – 7.5mls
4-6 years – 10mls

Workings -1

- 3 years (age + 4 x 2) = 14kg.
- 10mls x 4 over 24hrs = 120x2x4 = 960mg over 24hrs

- 960/14 = **68.57mg/kg**

- Serious toxicity may occur if more than 150mg/kg but rarely toxicity ingestions 75-150mg/kg over 24hrs.

- Refer if symptomatic, more than 75mg/kg over 24hrs, or more than licenced dose but less than 75mg/kg/24hrs on each day of the last 72hrs.

Specific cases - 2

- Telemedicine call:
- A 45yr old male has been busy working on his pool pump room, from where he is calling and is now dizzy and short of breath and he thinks it might be the chlorine tablets. What would you tell this patient?

Specific cases - 3

Private GP call:

1) A grandmother is calling that her 2yr old grandson (?weight but probably around 2 stones) has just ingested some of her tabs (ferrous gluconate) – she thinks he took around 5 iron tablets and is wondering if this is worrying.
   - Child is asymptomatic

Workings - 3

- Ferrous gluconate 300mg (elemental iron 35mg). child = 12kg
- 35mg x 5 = 175mg/12kg = **14.58mg/kg**

- Children/adults who have accidentally ingested less than 20mg/kg of elemental iron and who have developed no new symptoms do not need referral for medical assessment.

Specific cases - 4

- A 80yr old gentleman attends the PHC claiming that he has taken 5 Xyzal tablets and is now worried. (on further enquiry, it transpires that he took them because his relatives want to put him in an elderly home…he also took them with half a bottle of jack daniels).

Specific cases - 5

- Telemedicine call:

- A 20yr old gentleman, has been to Golden bay for his first swim of the year and he was stung by a jellyfish over the back – he thinks it’s the common one.

Pelagia noctiluca

Thank You!

jeffreybonnici@gmail.com