Introduction to Toxicology

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Topics

- Definition
- Terminology
- Classification of Toxic agents
- assessment
  - history
  - Examination
  - investigation
- Management
- Disposition
- Poison center No.

Definition

a science that deals with the adverse effects of chemicals on living organisms and assesses the probability of their occurrence

Why people get toxic?

intentional i.e. suicide

wrong dose (i.e. Insulin)

symptoms control (i.e. paracetamol for pain)

exposure i.e. radiation, organophosphate

bite i.e. snake bite

what are the routes of exposure?

inhalation (i.e. Nitrous oxide, CO)

skin or eye absorption (i.e. organophosphate)

ingestion : major one (i.e. paracetamol….etc)

injection (i.e. Opioids, insulin)

Assessment

History

may be unclear

substance

dose

rout of exposure

collateral Hx (i.e. family, friends, medical records)

Prehospital medical staff (i..e empty containers)

other (i..e hobbies, occupation, suicide note, change in behaviour recently)

Examination

Organ system	example of finding
General appearance	Malnurished (IV drug user, HIV infection)
CNS	Miosis (Opioids, organophsophate) Nystagmus/ataxia (ethanol)
CVS	Murmur (Endocarditis/IV drug user)
Respiratory system	Bronchorrhea/crepitations/hypoxia (Organophosphate)

Examination

Organ system	Example of finding
GIT	oral cavity burns (corrosive ingestion hyper salivation (cholinergic toxidrome
Urology	urinary retention (anticholinergic toxicity)
Peripheral nerves	tremor (Lithium) Lead pipe rigidity (NMS) clonus/hyperreflexia (serotonin toxicity)
Dermal	bruising (anticoagulant) flush, dry skin(anticholinergic toxicity) warm, moist skin(sympathomimetic toxicity)

Do not forget . . . !

examine skin folds, clothes and bags for retained tablets or substances


KEEP
CALM
BY
FOCUSING ON
TOXICOLOGY

Toxidrome

Cluster of symptoms and signs

enabling the identification of potential toxins when a clear history is unavailable

Anticholinergic = Antimuscarinic

clinical features	agents	potential interventions
• altered mental status • mydriasis • dry flushed skin • **urinary retention** • decreased bowel sounds • **hyperthermia (cause of death)** • dry mucus membrane other • seizure • rhabdomyolysis • arryhythmia	• **Atropine** • scopolamine • TCA • Olanzepine • antihistamine • diphenhydramine	• physostigmine • **benzodiazepine for sedation (MCQs)** • cooling • supportive management

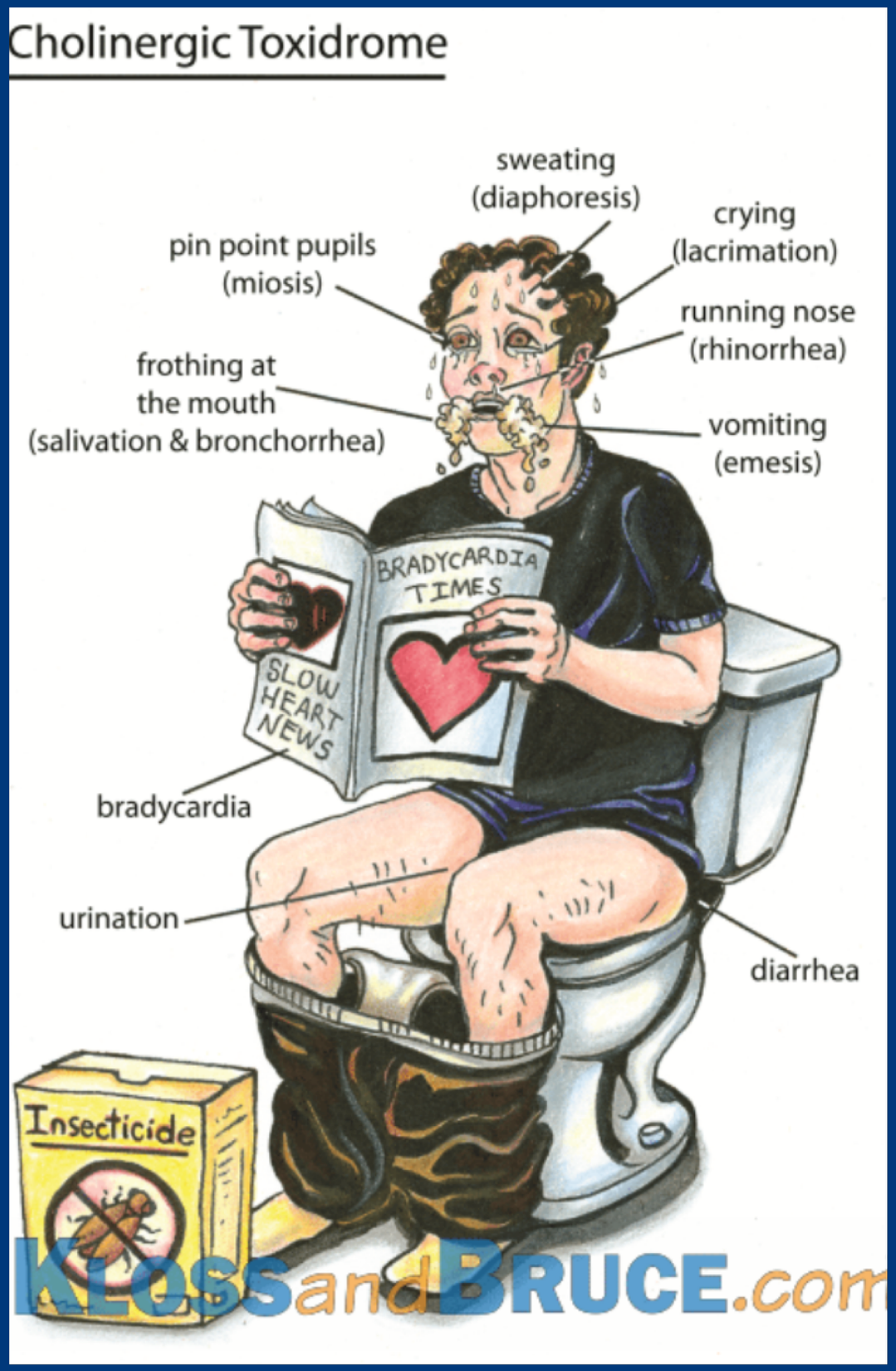
Anti-cholinergic

Cholinergic = Muscarinic

clinical features	agents	potential interventions

• **muscarinic effect**
  • salivation
  • lacrimation
  • diaphoresis
  • nausea
  • vomiting
  • urination
  • defecation
  • bronchorrhea
• **nicotinic effect**
  • muscle fasciculations
  • weakness
 	
other
• bradycardia
• miosis/mydraisis
 	
death—> respiratory arrest from muscle paralysis
	• organophosphate insecticides
	• carbamate insecticides
		• Airway protection + ventilation
		• **atropine**
		• **pralidoxime**

Cholinergic



Sympathomimetics

clinical features	agents	potential interventions
• psychomotor agitation • mydriasis • diaphoresis • tachycardia • hypertension • hyperthermia other • seizure • rehabdomyolysis • MI Death—> seizure, cardiac arrest, hyperthermia NB / very close to anticholinergics but the difference in **Diaphoresis**	• Amphetamine • cocaine	• cooling • sedation with benzodiazepine • hydration

Opioid

clinical features	agents	potential intervention
• CNS depression • respiratory depression • miosis others • hypothermia • bradycardia death from respiratory depression	• Heroin • morphine • oxycodone	• Naloxone • +/- airway support and ventilation

Sedative-hypnotic

clinical features	agents	potential interventions
• depressed LOC • ataxia • slurred speech • respiratory depression • bradycardia	• benzodiazepines • barbiturate	• ventilatory support

Hallucinogenic

clinical features	agents	potential intervention
• hallucinations • dysphoria • anxiety • hyperthermia • mydriasis • nausea • +/- sympathomimetics	• phenocyclidine • Lysergic acid diethyl amide • psilocybin • mescaline	• supportive

Other toxidromes

Toxidrome	Examination finding
Hypoglycemic(i.e.insulin)	altered mental status, diaphoresis, tachycardia, HT
Serotonin (i.e.SSRIs)	altered mental status, hyperreflexia, hypertonia(LL>UL), clonus, tachycardia
Neuromuscular Malignant(i.e.antipsychotics)	sever muscle rigidity, hyperpyrexia, altered mental status
Extrapyramidal (i.e.haloperidol)	Dystonia, torticollis, muscle rigidity
Ethanol	CNS depression, ataxia, dysartheria, smell of ethanol
Salicylate(i.e. Aspirin)	AMS, Resp Alkalosis, Metabolic Acidosis, Tinnitus, Tachypnoea, Tachycardia, diaphoresis, nausea vomiting

Diagnostic tests

Bedside :

Blood Glucose level : hypoglycaemia

ECG: Arrhythmias

VBG: i.e. metabolic acidosis —> paracetamol

Diagnostic tests

Laboratory:

blood / urine drug level

TABLE 176-5 Drug Concentrations That May Assist Patient Assessment or Management

Acetaminophen	Methanol
Carbamazepine	Methotrexate
Carbon monoxide	Paraquat
Digoxin	Phenobarbital
Ethanol	Phenytoin
Ethylene glycol	Salicylate
Iron	Theophylline
Lithium	Valproic acid
Methemoglobin	

Diagnostic tests

what are the limitation of Drug screening assays?

TABLE 176-6 Limitations of Toxicologic Drug Screening Assays

Nonspecific	Most tests use enzyme-immunoassays that only detect *typical* drugs within a class: opioids, amphetamines, benzodiazepines, cannabinoids, cocaine, barbiturates. Amphetamine screens do not detect methylenedioxy-methamphetamine. Opioid screens do not detect meperidine. Benzodiazepine screens do not detect flunitrazepam.
Time frame	Drugs may be detected days to weeks after exposure. A positive test may not account for current clinical findings.
Cross-reactivity	Carbamazepine, cyproheptadine, and chlorpromazine test positive for tricyclic antidepressants. Selegiline, methylphenidate, and pseudoephedrine test positive for amphetamines.
Noninclusive	A negative drug screen does not exclude a rare exposure.
Sampling error	Assay may be negative if dilute urine is tested.

Diagnostic tests

Electrolytes:

K level : i.e. hyperkalemia in digoxin overdose

LFT:

elevated liver enzymes in Paracetamol toxicity

Management:

Resuscitation

Airway:

intubation: if compromised

Breathing:

O2 administration, if hypoxic (i.e. O2sat <94%)

mechanical ventilation if intubated

Circulation :

hypotension

IV fluid (10-20ml /Kg) , avoid excess fluid administration

specific antidote

inotropic support (i.e.Adrenaline infusion)

aim : systolic BP > 90mmHg *or* MAP >65 mmHg

Resuscitation

Antidotes list

Poison	Antidote
Acetaminophen	N-acetylcysteine
Anticholinergics	Physostigmine
Anticoagulants	Vitamin K, FFP
Aspirin	Sodium bicarbonate
Beta blockers	Glucagon, insulin
Benzodiazepines	Flumazenil
Calcium channel blockers	Calcium, glucagon, insulin
Carbon monoxide	Oxygen
Cholinergics	Atropine, pralidoxime (2-PAM)
Cyanide	Hydroxycobalamin, amyl nitrite, sodium thiosulfate
Digoxin	Digoxin FAB
Heparin	Protamine
Heavy metals • Arsenic • Copper • Lead • Mercury	Dimercaprol EDTA Penicillamine Succimer (DMSA)
Hydrofluoric acid	Calcium gluconate
Insulin	Glucose
Iron	Desferoxamine
Isoniazid	Pyridoxine
Methanol	Ethanol
Ethylene glycol	Fomepizole, ethanol
Methemoglobin	Methylene blue
Opioids	Naloxone
Serotonin repute inhibitors	Cyproheptadine
Sulfonylurea	Octreotide, glucose
Tricyclic antidepressant	Sodium bicarbonate

Resuscitation

some specific presentations

Hypoglycemia

- BGL : < 4mmol

- give IV dextrose (Glucose)

Cardiac Arrhythmias

Anti-arrythmic drugs are not first line treatment in toxin induced arrhythmias

treatment:

O2 sat

antidote (i.e. digoxin Fab in digoxin overdose)

Seizure

treatment

1st : IV benzodiazepine (except in Isoniazed toxicity —> Pyridoxine)

2nd: Barbiturates

treat hypoglycaemia and hyponatremia

No rule for Phenytoin in toxin induced seizure

Agitation

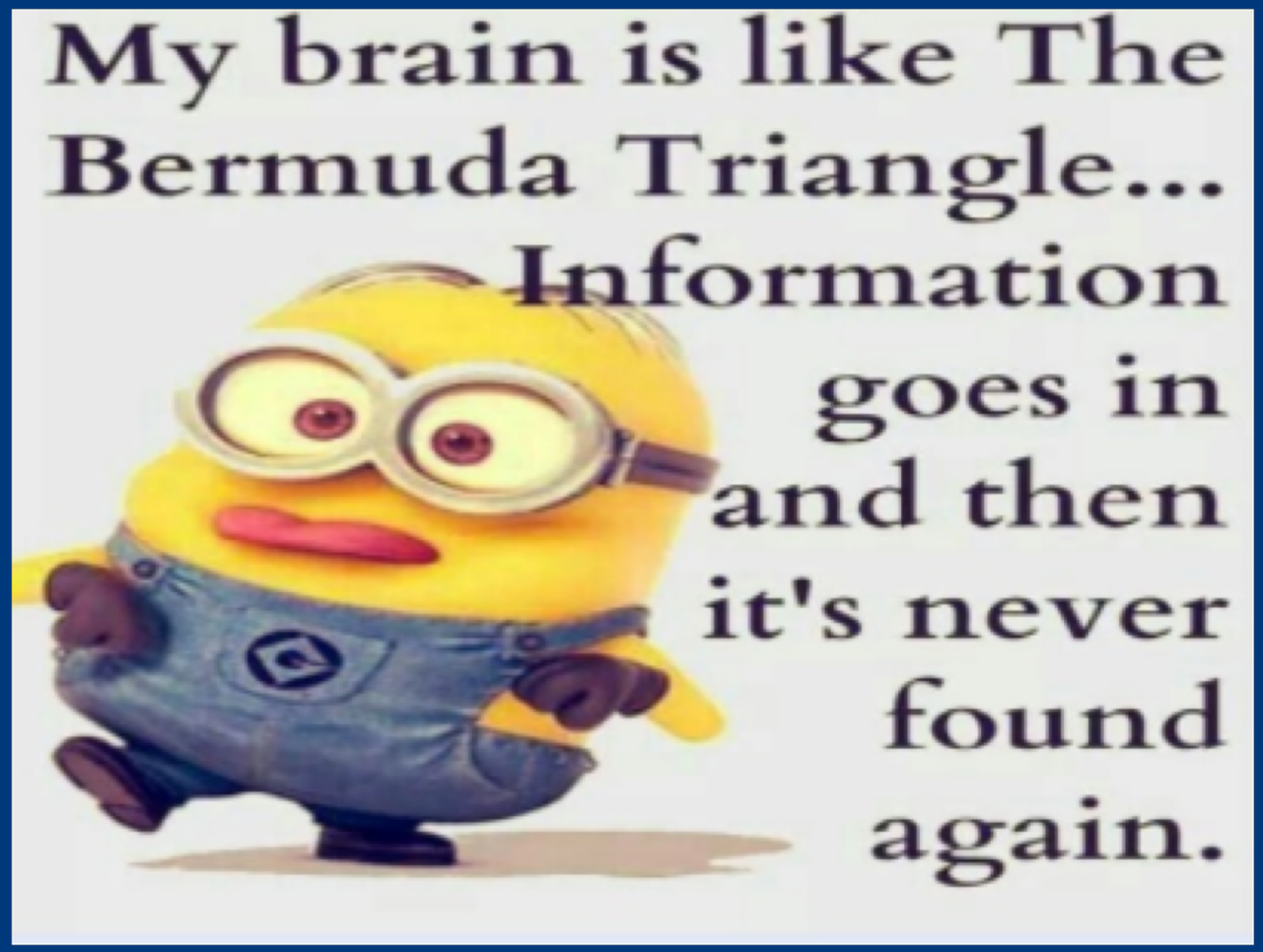
1st line treatment : benzodiazepine

2nd line treatment : antipsychotic agents

Hyperthermia and hypothermia

core temperature > 39* —> aggressive cooling

core temperature <32* —> aggressive rewarming


My brain is like The Bermuda Triangle...
Information goes in and then it's never found again.

Decontamination

two ways

GIT Decontamination

Enhanced Elimination

GIT decontamination

Activated Charcoal

whole bowel irrigation (WBI)

Gastric lavage

Induced emesis (Syrup or Ipecac)

Activated Charcoal (single dose)

indications	contraindications	complications	technique
• preferred method • < 1 hour from ingestion • charcoal sensitive substances: (MCQs) 1. paracetamol 2. benzodiazepines 3. barbiturates 4. TCA 5. phenothiazines 6. most anticonvulsants 7. aspirin 8. theophylline 9. digoxin 10. dextropropoxyphen 11. amphetamines 12. quinine 13. morphine 14. ciclosporin 15. most NSAIDs 16. beta blockers	• incomplete initial resuscitation • non toxic ingestion • subtonic dose • risk assessment —> good outcome with supportive care & antidote • risk assessment —> potential for seizure of decrease LOC • decrease LOC , seizure (unless Intubated) • charcoal resistance agents (see below) • corrosive ingestion ***ileus is not a contraindication***	• vomiting 30% • messy • aspiration • direct admisntration into lung if NG tube placed in lung • impaired absorption of subsequent oral antidote, therapeutic agents • corneal abrasion • staff distraction from resuscitation and supportive priorities	• dose • adult 50 gm • children 1gm/Kg • mix with water • self administration if GCS 15 • via OG / Ng tube if intubated (first confirm tube position with chest X-ray) ***no difference between mixing AC with water or other (sorbitol)***

Activated Charcoal (single dose)

Q : what are the charcoal resistance substances ?

hydrocarbons and alcohol	metals	corrosive
• ethanol • isopropyl alcohol • ethylene glycol • methanol	• lithium • iron • K • lead • arsenic • mercury	• acids • alkalis

whole bowel irrigation

indications	contraindications	complications	technique

• iron overdose >60mg/kg
• lead ingestion
• arsenic ingestion
• body packers
• slow release preparations :
  • lithium
  • verapamil / diltiazem
  • potassium formulations
	• risk assessment —> good outcome with supportive care and antidote
	• risk assessment —> potential for seizure or decrease LOC
	• uncooperative patient
	• inability to place NG tube
	• uncontrolled vomiting
	• ielus
	• intestinal obstruction
	• intubated and ventilated patient (relative)
		• nausea /vomiting
		• abdominal bloating
		• *non anion gap metabolic acidosis*
		• pulmonary aspiration
		• staff distraction from resuscitation and supportive care priorities
		• delayed retrial to a hospital offering definitive care
			• Polyethylene glycol electrolytes solution (PEG-ELS)
			• single nurse assigned
			• enough supply of PEG-ELS
			• NG tube inserted and confirmed
			• AC charcoal
			• administer PEG
			  • adult 2L/hr
			  • child 25ml/kg/hr
			• give metoclopromide —> decrease vomiting and enhance motility
			• explosive diarrhoea
			• continue irrigation until it clear
			• stop if abdominal distension or bowel sound lost

Gastric Lavage

indications	contraindications	complications	technique
• rare in ED • serious poisonings <1hr • other methods are unavailable • mercury ingestion • arsenic ingestion	• incomplete initial resuscitation • risk assessment —> good outcome with supportive care and antidote • decrease LOC • risk assessment —> potential for Decrease LOC during the procedure • small children • corrosive ingestion • hydrocarbon ingestions	• pulmonary aspiration • hypoxia • laryngospasm • mechanical injury to GIT • water intoxication (children) • hypothermia • staff distraction form resuscitation and supportive priorities	• resuscitation area • GCS 15 / intubated Pt • left decubitus position, head down 20" • pass gastric lavage tube (36-40 G) (OG route) • confirm tube position (aspiration and auscultation) • administer 200 ml aliquot of warm tab water or NS • drain the fluid into dependent bucket • repeat until its clear • give AC 50 G via the lavage tube once lavage is completed

Induced emesis (Syrup or Ipecac)

indications	contraindications	complications	technique
• limited • charcoal resistant poison • serious risk of toxicities • < 1 hour after ingestion • large fragments in stomach (WBI is better) • Fe • sustained release lithium • enteric coated tab • poisonous mushrooms	• non toxic ingestions • sub toxic doses • seizures • Decrease LOC • risk assessment —> potential for seizure / decrease LOC within the next few hours • activated charcoal available within 1 hour and know to bind to the substance • infant < 12 months • corrosive ingestion • hydrocarbon ingestion	• prolong vomiting > 1 hr in 10-20% • diarrhoea 20% • lethargy 10% • pulmonary aspiration if (seizure / Decrease LOC) • mallory weiss tear • pneumomediastinum • gastric perforation	• children —> 15 ml • Adult —> 15-30 ml • with glass of water • usually vomit after 18 min • repeat the dose if no vomit after 30 min

Enhanced Elimination

Multiple dose activated charcoal

urine alkalisation

extracorporeal technique of elimination

harm-dialysis and haemofiltration

charcoal haemoperfusion

Multiple doses of AC

indications	contraindication	complication	technique

• **carbamazepine** coma (most common indication)
• phenobarbitone coma
• dapsone overdose —> methaemoglobinaemia
• Quinine overdose
• Theophylline overdose
• phenytoin
	• Decrease LOC
	• anticipate decrease of LOC
	• bowel obstruction
		• vomiting 30%
		• pulmonary aspiration
		• constipation
		• bowel obstruction
		• bowel perforation
		• corneal abrasion
		• staff distraction from resuscitation and supportive care
			• give the atoll dose
			  • adult 50 g
			  • kids 1gm/kg
			• repeat doses of
			  • adult 25gm
			  • kids 0.5g/kg
			  • every 2 hours
			• route
			  • oral if GCS 15
			  • NG/OG tube after position confirmed by chest X-ray
			• check bowel sound before each dose ..
			• if no bowel sound stop doses
			• reconsider indication and endpoints every 6 hours
			• very rare therapy continue > 6 hours

Urinary Alkalinisation

Mechanism

- make urine PH alkaline —> ionisation of highly acidic drug —> decrease renal absorption & increase renal excretion

indications	contraindication	complications	technique
• Salicylate overdose • phenobarbitone coma (not first line) • cyanide • isoniazid • toxic alcohol • TCA • propranolol • felcainide • quinidine • methotrexate	• fluid overload	• alkalemia • hypokalaemia • hypocalcaemia • volume overload	• Sodium bicarbonate • 1-2 mmol/kg IV bolus • infusion @ 250ml /hr • 100 mmol NaHCO3 in 1000ml 5% dextrose • add 20 mol of KCL to the infusion to maintain the normokalaemia • follow serum HCO3 and K every 4 hr • aim urine PH >7.5 • continue till the lab and clinical evidence of toxicity is resolved.

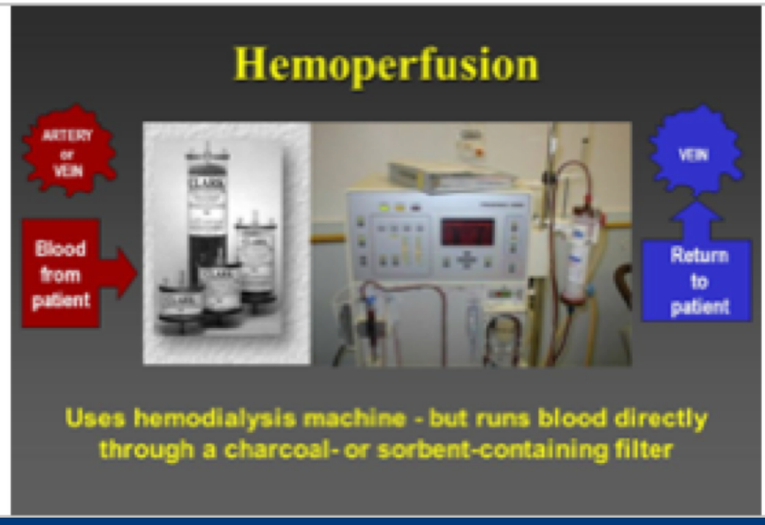
Extracorporeal technique of elimination

Hemodialysis

Movement of solute down a concentration gradient across a semipermeable membrane

Hemoperfusion

Movement of toxin from blood, plasma or plasma proteins onto a bed of activated charcoal (or other adsorbent)



Indications

- sever life threatning
- deteriration despite full supportive care
  - Carbamazepine
  - Potassium overdose
  - Sodium valproate
  - metformin
  - Phenobarbitone chronic lithium
  - salycilate
  - toxic alcohol
    - methanol
    - ethylen glycol
  - theophylline

Contraindications

- Hemodynamic instability
- Poor vascular access
- Significant coagulopathy

Complications

- Hypotension (most common)
- bleeding from vascclar access
- air emboli
- blood loss
- systemic heparinisation
- thromobcytopenia
- neutropenia

Technique

- invasive
- special staff
- special equipment
- monitoring

Disposition

if asymptomatic for 6 hours in ED —> discharge

otherwise admission to hospital is required

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Ministry of Health

Poison Control Center - Riyadh
General Directorate of Health Affairs - Medial Province
Kingdom of Saudi Arabia

- About PCC
- Departments
- Media Center

Riyadh Poison Control Center

Phone Book

Center	Center's Director	Mobile	Phone	Ext	Fax
Center Phone Number	-	-	0112324189 / 0112324180	-	-
Center's Director	-	-	-	101	-
Asst. Director	-	-	-	102	-
PCC Personnel	-	-	-	105	-
Drug Information Unit	-	-	-	108	-
Center's Fax	-	-	-	106	-

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Thank You

All the best !