Introduction to Toxicology

Team Leaders

Khalid Aleedan & Aseel Badukhon

Done by

Shrooq Alsomali Allulu Alsulayhim

Nawaf Alkhudhayri Weam Babaier

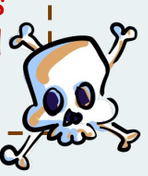
Mohammed Alyousef

Revised by: Yara & Basel

Objectives

1. Definition and Terminology
2. Classification of Toxic agents
3. Assessment [History, Examination, Investigation]
4. Management
5. Disposition
6. Poison center No.

This lecture is extremely important! It sums up all lectures of the course. It is essential to understand and study this lecture first!!



Introduction to toxicology

Definition of Toxicology:

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[1])

[1] common when doctors write the prescription by handwriting, so instead of writing 10 units they write 10 U and the U look like 0, so the nurse give 100 units

- Symptoms control (i.e. paracetamol for pain[2])

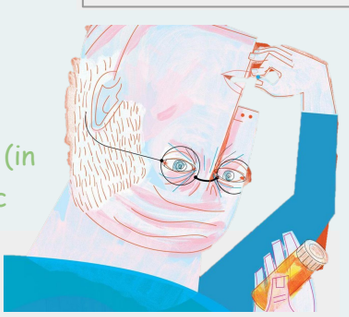
[2] common seen with toothache, the patient may take 10 tablets "depends on age; go back to APAP lecture" and come to ER with liver problems

- Exposure i.e. radiation, organophosphate[3]

[3] commonly used by farmers as pesticide or used to treat lice in young girls

- Bite i.e. snake bite

What are the routes of exposure?



- Inhalation (i.e. Nitrous oxide, CO) trick in the MCQs (in the question they always say: 3 people were in campus or picnic all of them have headache, nausea, irritability. What is your diagnosis? CO poison)
- Skin or eye absorption (i.e. organophosphate)
- Ingestion : major one (i.e. paracetamol….etc)
- Injection (i.e. Opioids, insulin)

CO commonly seen in fire or from vehicle exhaust. We commonly see it during summer bc of firewood. The problem of CO that it is odorless and painless, so people die without noticing or suffocation. CO can mimic stroke, how to differentiate? Once you give O_2 in CO poison they improve unlike stroke

Assessment

History:

- May be unclear Because if they are addicted or had used the drug for suicide . they won't tell you that. Also, they could be unconscious hence won't know what happened (Someone put something in their food or drink)
- Substance abuse!, if the patient was comatosed, we ask relatives or EMS if they saw any tablet or bottles or gases in the seen
- Dose (hard to estimate cuz they gonna tell you I took the whole bottle but they don't know how many pills was in the bottle)
- Route of exposure you know by seeing black discoloration of nose or injection marks
- Collateral Hx (i.e. family, friends, medical records)
- Prehospital medical staff (i..e empty containers)

- Other (i..e hobbies like farming which can hint towards a snake bite "organophosphate" or مخيمات which point towards CO poisoning , occupation, suicide note, change in behaviour recently which can point out to suicide)

Examination:

Organ system	Example of finding
General appearance	Malnourished (IV drug user, HIV infection) IV users: dehydrated, cachexic, poor hygiene, poor selfcare
CNS	Miosis* (So if you find in the question miosis this means Opioids or organophosphate poison) Nystagmus**/ataxia*** (ethanol) *the pupil in constricted (less than 3 mm) **rapid movement of the iris ***unsteady gait
CVS	Murmur (Endocarditis/IV drug user) letting bacteria in with injection. Usually the question is: fit and healthy patient develop new onset of murmur and you find fresh mark on the vein
Respiratory system	Bronchorrhea/crepitations/hypoxia (Organophosphate)
GIT	Oral cavity burns (corrosive ingestion**** , hyper salivation cholinergic toxidrome) ****مثل الكلوركس، لمن نحطه في كاس يكون لونه أصفر فالأطفال ينجذبون له ويشربونه
Urology	Urinary retention (anticholinergic toxicity)
Peripheral nerves	Tremor (Lithium, seen in bipolar patient) Lead pipe rigidity***** (NMS) clonus/hyperreflexia (serotonin toxicity) *****if you ask the patient to flex, they will resist resist then they will flex
Dermal	Bruising (anticoagulant) flush, dry skin(anticholinergic toxicity) warm, moist skin(sympathomimetic toxicity)

DON'T FORGET!

Examine skin folds, clothes and bags for retained tablets or substances
usually drug users hide their drugs under their skin fold. Couples of days ago we found amphetamin hidden under the patient's scrotum :) so look carefully

Toxidrome

All toxidrome are important!

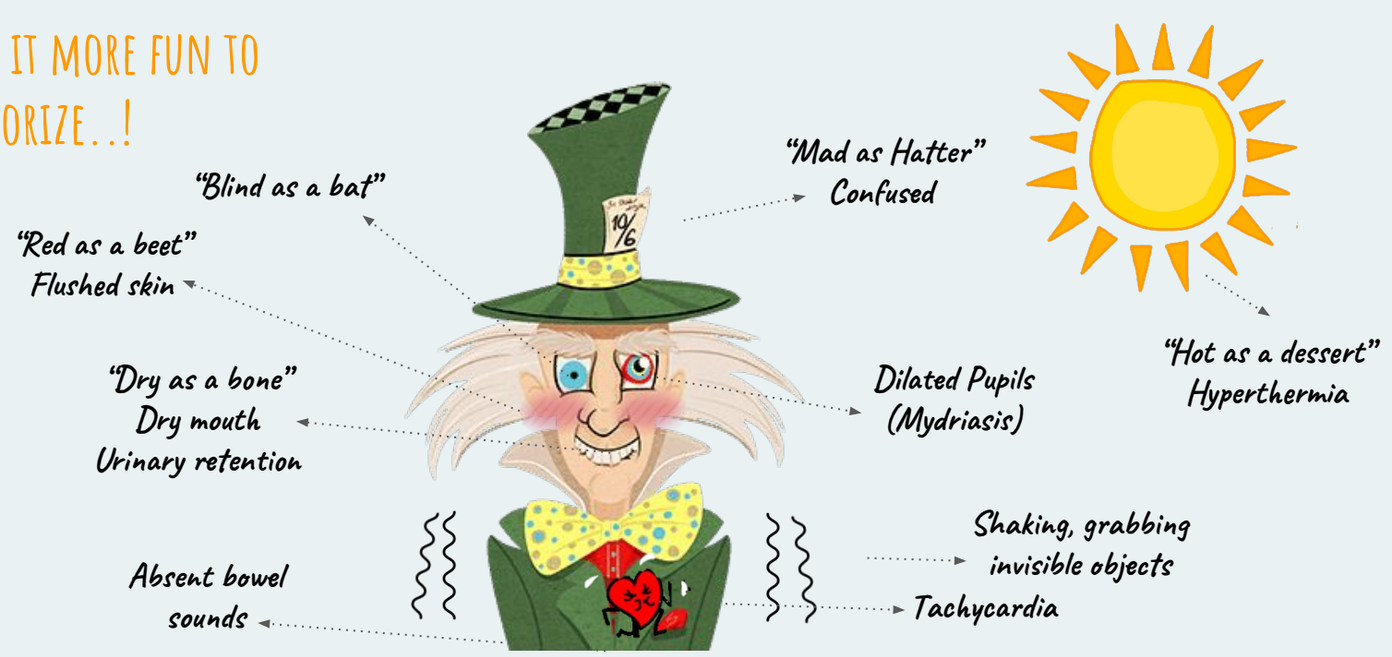
Definition of Toxidrome:

Cluster of symptoms and signs enabling the identification of potential toxins when a clear history is unavailable.
(gathering the symptoms and signs and getting an idea about what the patient used.)

Anticholinergic (Antimuscarinic) e.g. Atropine

Clinical features (NO WATER)	Agent	Potential interventions
- Altered mental status - Mydriasis - Dry flushed skin - Urinary retention - Decreased bowel sounds - Hyperthermia (cause of death) - Dry mucus membrane - Other: -Seizure -Rhabdomyolysis -Arrhythmia	- Scopolamine - TCA - Olanzapine - Antihistamine - Diphenhydramine	- Physostigmine - Benzodiazepine for sedation (MCQs) - Cooling - Supportive management like IV fluid

Make it more fun to memorize..!

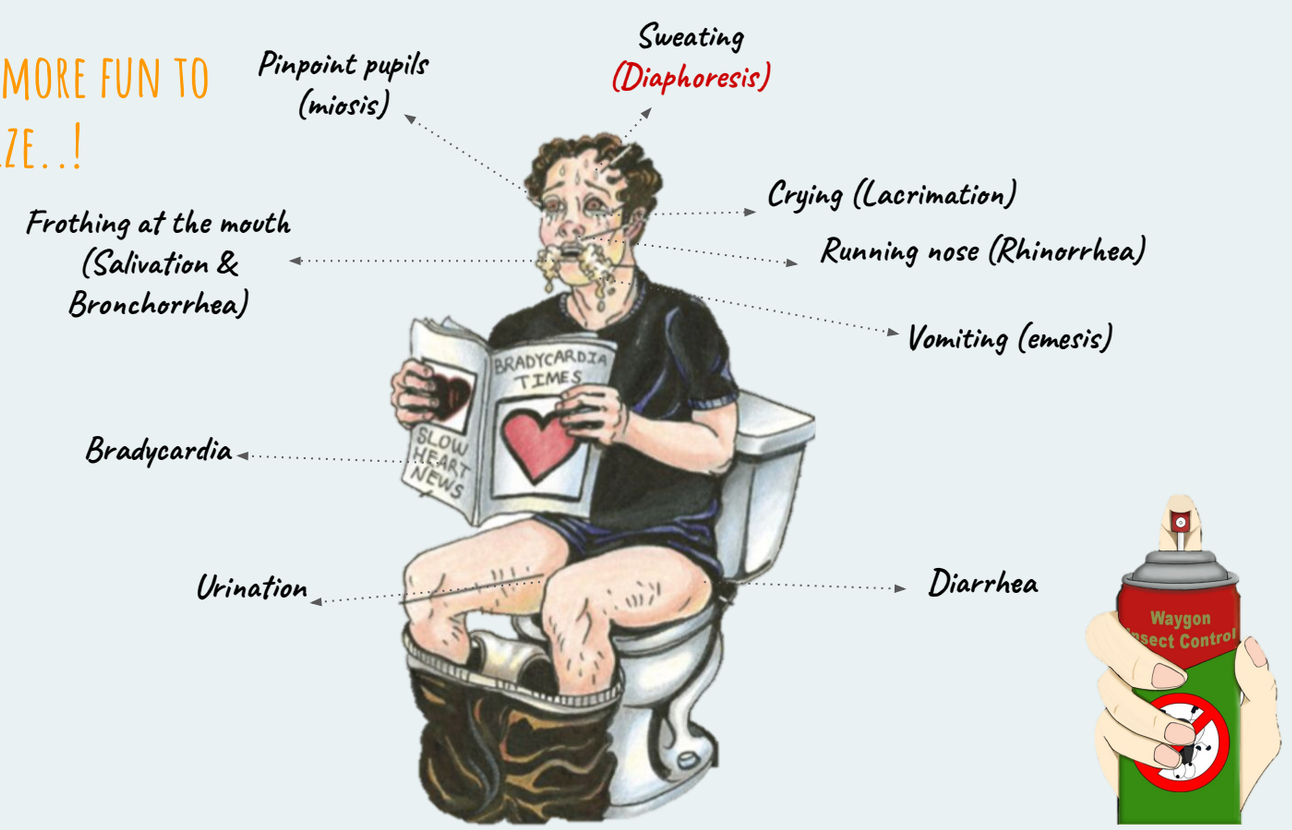


Toxidrome

Cholinergic (Muscarinic)

Clinical features (TOO MUCH WATER)	Agent	Potential interventions
-Muscarinic effect: -Salivation -Lacrimation -Diaphoresis -Nausea -Vomiting -Urination -Defecation -Bronchorrhea **- Nicotine effect** -Muscle fasciculations-Weakness **- Other** -Bradycardia -Miosis/Mydriasis - Cause of **Death** -> respiratory arrest from muscle paralysis	- Organophosphate insecticides - Carbamate insecticides	- Airway protection + ventilation - Atropine the antidote - Pralidoxime

MAKE IT MORE FUN TO MEMORIZE..!



Toxidrome

Sympathomimetics

Clinical features	Agent	Potential interventions
- Psychomotor agitation -Mydriasis -Diaphoresis -Tachycardia -Hypertension -Hyperthermia -Others: -Seizure -Rhabdomyolysis -MI - Death -> seizure, cardiac arrest, hyperthermia *NB/ very close to anticholinergics but the difference in diaphoresis (sweating) important for MCQs	-Amphetamine (very common in our society) -Cocaine	-Cooling -Sedation with benzodiazepine -Hydration

Opioids

Clinical features	Agent	Potential interventions
- CNS depression - Respiratory depression - Miosis - Others: -Hypothermia -Bradycardia - Death from respiratory depression	- Heroin - Morphine - Oxycodone Needs observation	- Naloxone - +\- airway support and ventilation

Sedative-Hypnotic

Clinical features	Agent	Potential interventions
- Depressed LOC (Level Of Consciousness) - Ataxia - Slurred speech - Respiratory depression - Bradycardia *NB/ very close to opioids but the difference is NO Miosis يقولكم الدكتور هنا نلعب في الام سي كويز فركزوا الله يرضى عليكم :)	- Benzodiazepines along with sympathomimetics sometimes - Barbiturate	- Ventilatory support (give them O_2, if it didn't work intubate them)

Toxidrome

Hallucinogenic

Rape drugs

Clinical features	Agent	Potential interventions
- Hallucinations - Dysphoria - Anxiety - Hyperthermia - Mydriasis - Nausea - +\- sympathomimetics	- Phencyclidine - Lysergic acid diethylamide (party drugs) - Psilocybin - Mescaline	-Supportive

Other Toxidromes

(These are not typical toxins)

Toxidrome	Examination finding
Hypoglycemic (i.e.insulin)	altered mental status, diaphoresis, tachycardia, HT You should give them dextrose if you are in hospital or in ambulans. If you are at home give sugar or honey under the tongue or on the buccal region)
Serotonin (i.e. SSRIs)	altered mental status, hyperreflexia, hypertonia(LL>UL), clonus, tachycardia
Neuroleptic Malignant (i.e.antipsychotics)	severe muscle rigidity, hyperpyrexia (fever) , altered mental status (Serotonin and neuroleptic are similar but you can differentiate by fever which occurs in neuroleptic)
Extrapyramidal (i.e.haloperidol)	Dystonia, torticollis, muscle rigidity
Ethanol	CNS depression, ataxia, dysarthria, **smell of ethanol**
Salicylate (i.e. Aspirin) know the findings	AMS, Resp Alkalosis, Metabolic Acidosis, Tinnitus, Tachypnoea, Tachycardia, diaphoresis, nausea vomiting

Step 3 in assessing after history and examination

Diagnostic tests

These tests are:

Bedside:

- Blood Glucose level : hypoglycemia You should give them dextrose if you are in hospital or in ambulans. If you are at home give sugar or honey under the tongue or on the buccal region)
- ECG: Arrhythmias anticholinergic drugs can cause them
- VBG: i.e. metabolic acidosis —> paracetamol

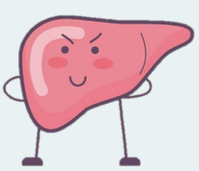
List of drug concentrations that may help in assessment!

Laboratory:

- Blood / urine drug level(actually it won't point out which exact drug the patient use, so it kind of pointless. except paracetamol but I should wait 4 hours from the ingestion time to see the result)

Electrolytes:

- K level :
  i.e. hyperkalemia in digoxin overdose



Liver Function Tests:

- Elevated liver enzymes in Paracetamol toxicity Ethanol and amphetamine level

Limitations of Drug screening assays:

1 Nonspecific

Most tests use enzyme-immunoassays that only detect typical drugs within class: opioids, amphetamines, benzodiazepines, cannabinoids, cocaine, barbiturates.
Amphetamine screens don't detect methylenedioxy-methamphetamine.
Opioid screens don't detect meperidine.
Benzodiazepines screens don't detect flunitrazepam.

2 Time Frame

Drugs may be detected days to weeks after exposure. A positive test may not account for current clinical findings

3 Noninclusive

A negative drug screen doesn't exclude a rare exposure.

4 Cross-reactivity

Carbamazepine, cyproheptadine and chlorpromazine test positive for tricyclic antidepressants.
Selegiline, methylphenidate and pseudoephedrine test positive for amphetamines.

5 Sampling error

Assay may be negative if dilute urine is tested.

Step 4

Management

When a patient comes with a toxidrome, these steps must be followed accordingly:

1. Resuscitation
2. Decontamination
3. Disposition

(after assessment and running tests)

Resuscitation:

Airway (is the patient breath or not)

- Intubation: if compromised (the patient doesn't speak in normal way or the patient is choking)

Breathing (equal breath at two side)

- O_2 administration, if hypoxic (i.e. oxygen saturation <94%)
- Mechanical ventilation if intubated

Circulation (normal vital signs or not)

Hypotension:

- IV fluid like normal saline or blood (10-20ml /Kg) , avoid excess fluid administration
- specific antidote (Next slide to check that very good list of antidotes!)
- inotropic support 'vasopressin' (i.e.Adrenaline infusion)

Aim : systolic BP > 90mmHg or MAP (Mean Arterial Pressure) >65 mmHg

A B C

"Remember the ABC rule in resuscitation"

This table is very important through all toxicology lectures, memorize the drugs in your lectures!
At Least 3 will come in MCQs

Management

Poison	Antidote
Acetaminophen | Anticholinergic	N-acetylcysteine | Physostigmine
Anticoagulants	Vitamin K, FFP
Aspirin	Sodium Bicarbonate "NaHCO3"
Beta blockers	Glucagon, insulin
Benzodiazepines	Flumazenil
Ca channel blockers	Ca, glucagon, insulin
Carbon monoxide "CO"	Oxygen
Cholinergics	Atropine
Cyanide	Hydroxycobalamin,amyl nitrite, sodium thiosulfate
Digoxin | Heparin	Digoxin FAB | Protamine
Hydrofluoric acid	Calcium gluconate
Insulin | Iron	Glucose | Desferoxamine
Isoniazid | Methanol[4]	Pyridoxine | Ethanol[4]
Ethylene Glycol	Fomepizole, ethanol
Methemoglobin	Methylene blue
Opioids	Naloxone
Serotonin repute inhibitors	Cyproheptadine
Sulfonylurea	Octreotide, glucose
Tricyclic antidepressants	Sodium bicarbonate
Heavy metals: -Arsenic -Copper -Lead -Mercury	Dimercaprol EDTA Penicillamine Succimer (DMSA)

[4] Bc they believe ethanol is safe, but methanol, isobornyl alcohol, ethylene glycol are harmful

Management

Resuscitation:

Some specific presentations:

Hypoglycemia	- BGL (blood glucose level) : < 4 mmol - give IV dextrose (Glucose)
Cardiac Arrhythmias	- Antiarrhythmic drugs are not first line treatment in toxin induced arrhythmias - **Treatment:** - O_2 sat - antidote (i.e. digoxin Fab in digoxin overdose) NO Beta Blockers!
Seizure	- Treatment 1st : IV benzodiazepine (except in Isoniazid toxicity —> Pyridoxine) 2nd: Barbiturates - Treat hypoglycemia 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

Decontamination:

Here we either clean your gut (GIT decontamination) or your blood (enhanced elimination)!

1-GIT Decontamination:
-Activated Charcoal
-Whole Bowel irrigation prior to colonoscopy.
-Gastric lavage very bad
-Induced Emesis (Syrup or Ipecac) very bad

2-Enhanced Elimination:
-Multiple dose activated charcoal
-Urine alkalinisation
-Extracorporeal technique of elimination:(harm-dialysis and hemofiltration ,charcoal hemoperfusion)

{ Management }

GIT Decontamination:

تأكل المريض فحم :)

1-Activated charcoal (single dose)

Charcoal will bind to the drug and and excrete it outside the body

Indications	Contraindications	Complication	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-Dextropropoxyphene 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 and antidote -Risk assessment -> potential for seizure of decrease LOC -Decreased LOC, seizure (unless intubated) -Charcoal resistance agent (see below) -Corrosive ingestion ***Ileus is not a contraindication**	-Vomiting 30% -Messy -Aspiration -Direct administration into lung if NG tube placed in lung -Impaired absorption of subsequent oral antidote, therapeutic agent -Corneal abrasion -Staff distraction from resuscitation and supportive priorities	**-Dose:** -50 gm for adult -1 gm/kg for children -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 with other (sorbitol)**

Charcoal resistance substances:

(Doesn't bind to charcoal)

Hydrocarbons and alcohol	Ethanol, Isopropyl alcohol	Ethylene glycol, Methanol
Metals	Lithium, Iron, K	Lead, Arsenic, Mercury
Corrosive	Acid	Alkalis

Management

2-Whole Bowel Irrigation (WBI)

Indications	Contraindications	Complication	Technique
-Iron overdose >60 mg/kg -Lead ingestion -Arsenic ingestion -Body packers (الناس اللي يهربون المخدرات ويخبونها في جسمهم) -Slow release preparation: 1-Lithium 2-Verapamil/diltiazem 3-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 - Ileus* - Intestinal obstruction -Intubated and ventilated patient (relative) *While in activated charcoal was NOT a contraindication	-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 No doses required	-Polyethylene glycol electrolytes solution (PEG-ELS) (Remember GNT block!) -Single nurse assigned -Enough supply of PEG-ELS -NG tube inserted and confirmed -**AC charcoal** -Administer PEG: 1-Adult 2L/hr 2-Child 25 ml/kg/hr -**Give metoclopramide** -> decrease vomiting and enhance motility -Explosive diarrhoea -Continue irrigation until it clear -**Stop** if abdominal distention or bowel sound lost

This method is not used anymore; not important, skip it (: Just know the name.

3-Gastric Lavage

Indications	Contraindications	Complication	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 -Decreased LOC -Risk assessment -> potential for decreased 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 (asprination and auscultation) -Administr 200 ml Aliquot of warm tab water or NS - Drain the fluid into dependent bucket -Repeat until it's clear -Give AC 50 G via the lavage tube once lavage is completed

{ Management }

This method is not used anymore; not important, skip it (: Just know the name

4-Induced Emesis (Syrup of Ipecac)

Indications	Contraindications	Complication	Technique
-Limited -Charcoal resistant poison -Serious risk of toxicities - < 1 hour after ingestion -Large fragments in stomach (**WBI is better**) -Fe (Iron) -Sustained release lithium -Enteric coated tab -Poisonous mushrooms	-Non toxic ingestions -Sub toxic doses -Seizures -Decreased LOC -Risk assessment >> Potential for seizure / Decreased 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	-Prolonged vomiting > 1 hour in 10%-20% -Diarrhea 20% -Lethargy 10% -Pulmonary aspiration if (Seizure / decreased 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

{ Management }

Enhanced Elimination:

"Be careful, we have single dose and multiple doses of AC!"

1-Multiple Doses of AC

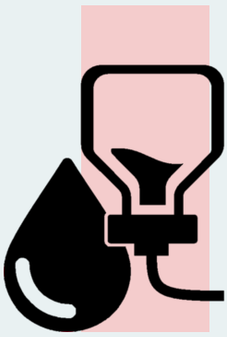
Indications	Contraindications	Complication	Technique
-Carbamazepine coma (most common indication) -Phenobarbital coma -Dapsone overdose -> methemoglobinemia -Quinine. Overdose -Theophylline overdose -Phenytoin	-Decreased LOC -Anticipate decrease of LOC -Bowel obstruction	-Vomiting 30% -Pulmonary aspiration -Constipation -Bowel obstruction -Bowel perforation -Corneal abrasion -Staff distraction from resuscitation and supportive care	-**Give the atoll dose:** -50 g for adult -1 gm/kg for children -**Repeat doses of:** -25 gm for adult - 0.5 g/kg for children -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

2-Urinary Alkalinisation

Indications	Contraindications	Complication	Technique
-Salicylate overdose -Phenobarbital coma (**not first line**) -Cyanide -Isoniazid -Toxic alcohol -Tricyclic antidepressants -Propranolol -Flecainide -Quinidine -Methotrexate	-Fluid overload **Mechanism** Make urine PH alkaline -> ionisation of highly acidic drug -> decrease renal absorption and increase renal excretion. Give them sodium bicarbonate to make them urinate	-Alkalemia -Hypokalaemia -Hypocalcaemia -Volume overload	-Sodium bicarbonate -1-2 mmol/kg IV bolus -Infusion @ 250 ml/hr - 100 mmol NaHCO3 in 1000 ml 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

Management

3-Extracorporeal Technique of elimination



Hemodialysis

Movement of solute down a concentration gradient across a semipermeable membrane
Contraindicated in hemodynamic instability, poor vascular access and significant coagulopathy

VS

Hemoperfusion

Movement of toxin from blood, plasma or plasma protein into a bed of activated charcoal (or other adsorbent) (It uses dialysis but the filter is different here)
(Blood is taken from a vein or artery then returned via VEIN)

Indications

-Severe life threatening
-Deterioration despite full supportive care
-Carbamazepine
-K overdose
-Sodium Valproate
-Metformin
-Phenobarbitone
-Chronic lithium
-Salicylate
-Toxic alcohol
-Methanol, Ethylene Glycol
-Theophylline

Contraindications

-Hemodynamic instability
-Poor vascular access
-Significant coagulopathy

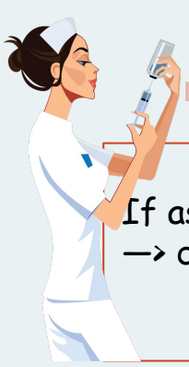
Complications

-Hypotension (most common)
-Bleeding from vascular access
-Air emboli
-Blood loss
-Systemic heparinisation
-Thrombocytopenia
-Neutropenia

Technique

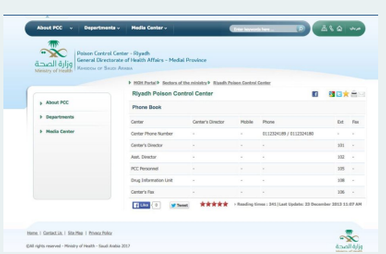
-Invasive
-Special; staff
-Special equipment
-Monitoring

Disposition:



If asymptomatic for 6 hours in ED —> discharge, otherwise admission to hospital is required

Poison Center number: 0112324189/0112324180
Be safe (:



How toxic your knowledge is!

1-Which of the following toxin-antidote combination is the most appropriate?

A) Iron - Insulin
B) TCA - Sodium bicarbonate
C) Aspirin - Glucagon
D) Lead - H2O2

2-Ethanol resists which of the following?

A) Charcoal
B) Lead
C) PEG
D) Methanol

3-In hemoperfusion, blood is returned after filtering to patient via artery.

A) True
B) False

4-When should you stop the administration of multiple doses of AC?

A) When you are able to hear 3 bowel sounds per minute
B) When you hear none
C) When you hear 2 bowel sounds per minute
D) You should never consider this until patient improves

5-Anticholinergic and stimulants are similar but

A) Anticholinergic causes sweating while stimulant doesn't
B) Anticholinergic causes miosis while stimulant causes mydriasis
C) Anticholinergic doesn't cause diaphoresis while stimulant causes it
D) None of the above

1-B
2-A
3-B
4-B
5-C

Summary

Introduction

Definition of Toxicology	Why people get toxic?	What are the routes of exposure?
A science that deals with the adverse effects of chemicals on living organisms and assesses the probability of their occurrence.	• Intentional • Wrong dose • Symptoms control • Exposure • Bite	• Inhalation • Skin or eye absorption • Ingestion • Injection

Toxidrome

- Anticholinergic (antimuscarinic)
- Cholinergic (muscarinic)
- Sympathomimetics
- Opioids
- Sedative-hypnotic
- Hallucinogenic

Important!

How to differentiate ?!

Anticholinergics and sympathomimetics have same clinical features But anticholinergics don't cause diaphoresis (sweating), while sympathomimetics cause diaphoresis.

The difference between **Opioid and Sedative-hypnotic** is that the opioid affects the pupil, while the Sedative-hypnotic doesn't affect the pupil.

When we have a toxidrome, we need an antidote! Remember to memorize them all!

Diagnostic tests

These tests are:	Limitations of drug screening assays
• Bedside • Laboratory • Electrolytes • Liver Function Tests	• Nonspecific • Time frame • Non inclusive • Cross-reactivity • Sampling error

Management

If asymptomatic for 6 hours in ED —> discharge, otherwise admission to hospital is required

Resuscitation	GIT decontamination	Enhanced elimination
• Airway • Breathing • Circulation	• Activated Charcoal (single dose) • whole bowel irrigation • Gastric Lavage	• Multiple doses of AC: • Urinary alkalinisation • Extracorporeal technique of elimination

Thank you and good luck!

Very Toxic but you are gonna do it!

A+ is yours (:

- Email us at:

436toxicology@gmail.com

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