TOXOCOLOGY 434

Lecture 1

Introduction to Toxicology

Color Index : Important , doctor`s note

Editing File

Definitions

Toxicology	a science that deals with the adverse effects of chemicals on living organisms and assesses the probability of their occurrence
Toxicants	substance that produce adverse biological effects of any nature it may be *chemical or physical* effects may be *acute or chronic*
Toxins	specific portions produced by living organisms (i.e. mushroom toxin or tetanus toxin) most exhibit *immediate effects*
Poisons	Toxicants that cause *immediate death or illness* when experienced in very *small amounts*
Toxic Agents	anything that can produce an adverse biological effect *may be*: chemical (i.e. Cyanide) ,Physical (i.e. radiation),Biological (i.e. snake venom)
Toxic substance	a material which has toxic properties
Systemic Toxin	toxin that affects the entire body or many organs rather than a specific site for example: Cyanide
Organ toxin	toxin that affects only specific tissue or organs examples: Lead, Paracetamo

Doctor said this is just an introduction !

Why people get toxic?

1. intentional i.e. suicide
2. wrong dose (i.e. Insulin)
3. symptoms control (i.e. paracetamol for pain)
4. exposure i.e. radiation, organophosphate(الجره تستخدم كمبيد حشرات في المزارع)
5. bite i.e. snake bite

Routes of exposure:

1. inhalation (i.e. Nitrous oxide, CO)
2. skin or eye absorption (i.e. organophosphate)
3. ingestion : major one (i.e. paracetamol….etc.)
4. injection (i.e. Opioids, insulin)

Toxidrome:

Is a cluster of symptoms and signs enabling the identification of potential toxins when a clear history is unavailable.

Six basic toxidrome :

1. Anticholinergic
2. Cholinergic
3. Sympathomimetics
4. Opioid
5. Sedative-hypnotic
6. Hallucinogenic

Anticholinergic: MOA: ANTAGONIZE the effects of endogenous Acetylcholine by blocking the receptors	
Agents(examples)	Atropine, Scopolamine, Amantadine, Tricyclic and tetracyclic antidepressants(TCA), Olanzapine and Antihistamines .
Features	Peripheral muscarinic blockade: Mydriasis, Anhidrosis, Tachycardia, Urinary retention and Ileus. CNS muscarinic blockade: Confusion, Agitation, Hyperthermia (cause of death),Myoclonus, Tremor, Abnormal speech, Hallucinations or Coma.
Potential interventions	Physostigmine, Benzodiazepines for sedation (MCQs), cooling and Supportive care

Cholinergic : MOA: Block acetylcholinesterase from working (prevent Ach degradation)	
Agents	Organophosphate and carbamate insecticides.
Features	(SLUDGE syndrome) Salivation, Lacrimation, Urination, Diaphoresis, GI upset: Diarrhea, vomiting. Or Eye: Miosis. Other: Bradycardia. Death due to respiratory arrest from muscle paralysis.
Potential interventions	Airway protection+ ventilation, Atropine and Pralidoxime

Sympathomimetics: Excessive sympathetic stimulation involving epinephrine, norepinephrine and dopamine	
Agent	Amphetamine and cocaine
Features	Tachycardia +/- arrhythmias, Mydriasis, Diaphoresis , Hypertension +/- Intracerebral hemorrhage ,Confusion with agitation ,Seizures or Rhabdomyolysis (due to excess movement) Death can result due to Seizures, hyperthermia and cardiac arrest. NB/ very close to anticholinergic but the difference in Diaphoresis
Potential interventions	Cooling, sedation with benzodiazepine and hydration.

Opioid:	
Agent	Heroin, Morphine and Morphine.
Features	CNS depression, Miosis (pin point pupil), Respiratory depression (could cause death), hypothermia or bradycardia.
Potential interventions	Naloxone(Competitive opioid antagonist) and +/- airway support and ventilation

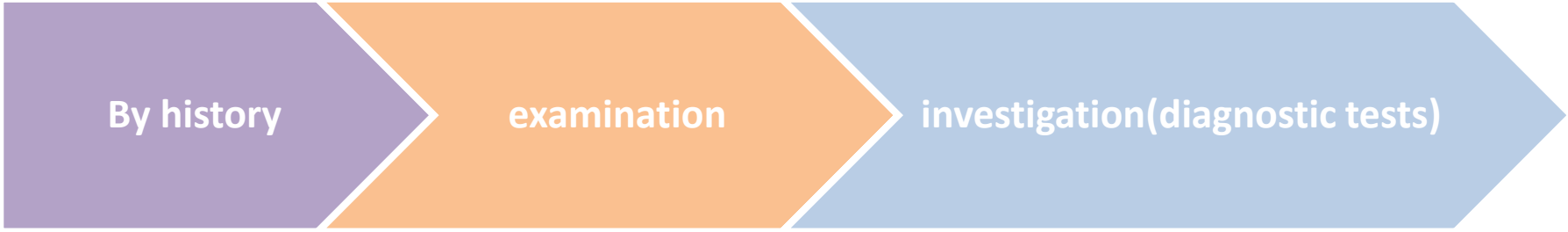
Sedative-hypnotic	
Agent	Benzodiazepines, Diazepam and Barbiturate.
Features	Depressed level of conciseness, ataxia, slurred speech, respiratory depression ,bradycardia or hypotension
Potential interventions	Ventilatory support.

Hallucinogenic	
Agent	Phenocyclidine, Lysergic acid diethyl amide, psilocybin and mescaline
Features	Hallucination, dysphoria, anxiety, hyperthermia, mydriasis, nausea or +/-sympathomimetic.
Potential interventions	Supportive

Other Toxidromes

Toxidrome	Examination finding
Hypoglycemic(i.e.insulin, sulfonylurea)	altered mental status(AMS), diaphoresis, tachycardia, hypertension.
Serotonin (i.e.SSRIs)	altered mental status, hyperreflexia, hypertonia(lower limb>upper limb), 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

How to assess the patients?



1) History:

- The history may be unclear
- Ask about the substance that was taken by patient and the dose
- Ask about the rout of exposure
- Take a collateral Hx (i.e. family, friends, medical records)
- Ask the prehospital medical staff (Emergency Medical Technician)about empty containers
- other (i..e hobbies, occupation, suicide note, change in behavior recently)

2) Examination:

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

3)Diagnostic tests:

Bedside :

- Blood Glucose level: example of findings is hypoglycaemia
- ECG: example of findings is Arrhythmias
- venous blood gas: example of findings is metabolic acidosis due to paracetamol

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	

Electrolytes: K level: example of findings is hyperkalemia in digoxin overdose

LFT :example of findings is elevated liver enzymes in Paracetamol toxicity

what are the limitations 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.

Doctor said the limitations without any examples!

Management

Resuscitation:

- Airway:

intubation: if compromised(mainly obstruction)

- Breathing:

O2 administration, if the patient is hypoxic (i.e. O2 saturation <94%)
mechanical ventilation if intubated

- Circulation :

  - For hypotensive patient gives IV fluid(usually normal saline 10-20ml /Kg) , avoid excess fluid administration.
  - specific antidote.
  - inotropic support (support the heart and vessels to increase the pressure, ex: Adrenaline infusion)

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

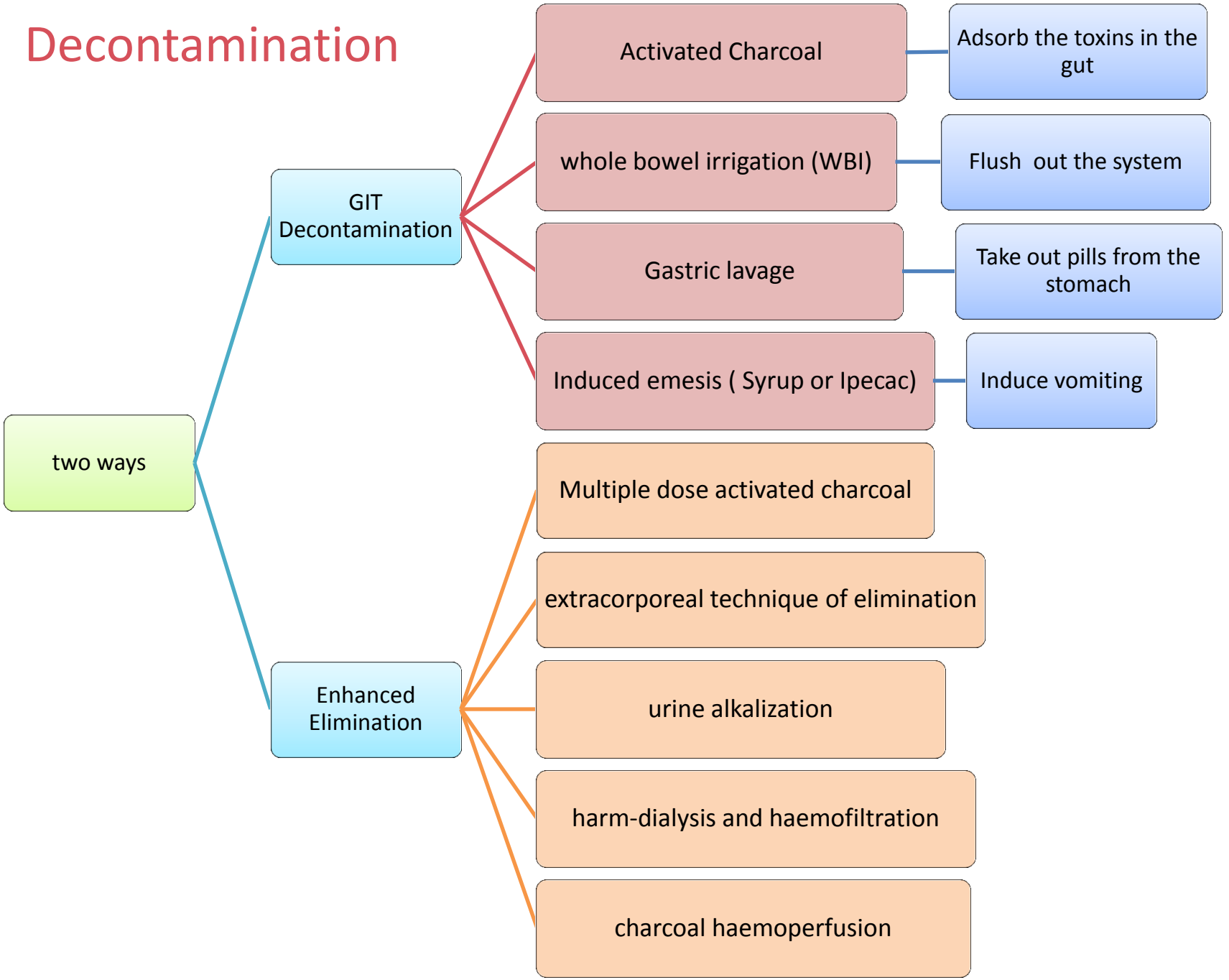
Doctor said we'll study them throughout the course ☺

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

some specific presentations	
Hypoglycemia	If the Blood Glucose Level : < 4mmol, give IV dextrose (Glucose)
Cardiac Arrhythmias	Anti-arrhythmic drugs are not first line treatment in toxin induced arrhythmias. treatment: O2 saturation antidote (i.e. digoxin Fab in digoxin overdose)
Seizure	Treatment 1st : IV benzodiazepine (except in Isoniazed toxicity we give Pyridoxine) 2nd: Barbiturates treat hypoglycemia and hyponatrmia *No rule for Phenytoin in toxin induced seizure, so phenytoin cannot treat seizure that caused by toxin.*
Agitation	1st line treatment : benzodiazepine 2nd line treatment : antipsychotic agents
Hyperthermia	core temperature* > 39° —> aggressive cooling
Hypothermia	core temperature* <32° —> aggressive rewarming

*Core temp can be obtained by Rectus, gastric tube or folly catheter

Decontamination



1)Activated Charcoal (single dose):

Indications: should be administered less than one hour from toxin ingestion
Charcoal sensitive substances: Paracetamol, benzodiazepines, barbiturates, TCA, phenothiazines, aspirin, digoxin, morphine, most NSAIDs and beta blockers.
Contraindications: incomplete initial resuscitation.
Complications: vomiting, messy, aspiration and aspiration pneumonia
What are the charcoal resistance substances?

- Hydrocarbons and alcohol (ethanol, isopropyl, ethylene glycol and methanol)
- Metals(lithium, iron, K, arsenic and mercury)
- Corrosive(acids and alkalis)

2)whole bowel irrigation:

Indications: many but it is usually used for **body packers**
Contraindication: decreased level of conciseness and dehydrated
Complications: non anion gap metabolic acidosis.
Technique: Polyethylene glycol electrolytes solution (PEG-ELS)

3)Gastric Lavage:

It is a nasty procedure. No more used.

4) Induced emesis (Syrup or Ipecac):

No more used.

I've put here only that points which mentioned by doctor

Enhanced Elimination:

1)Multiple dose activated charcoal :

Indications: Carbamazepine coma.

Contraindications: decreased level of conciseness. Complications: vomiting, messy, aspiration and aspiration pneumonia

Technique: give a dose of 50g then repeated doses of 25g every 2 h.

2)urine alkalization:

Mechanism: make urine PH alkaline by ionizing the highly acidic drug which leads to decrease renal absorption and increase renal excretion.

Indication: Salicylate (Aspirin) overdose

Contraindication: fluid overload

Technique: sadium bicarbonate 1-2 mmol/kg IV bolus.

3)extracorporeal technique of elimination:

It is invasive and the most common complication is Hypotension

4)harm-dialysis and haemofiltration

5)charcoal haemoperfusion

I've put here only that points which mentioned by doctor

Disposition(discharge):

if the patient is asymptomatic for 6 hours in ED —> discharge
otherwise admission to hospital is required.

GOOD LUCK ☺