



Introduction to Toxicology

➤ Objectives:

- definition,terminology.
- classification of toxic agents
- assessment (history,examination,investigation)
- management
- disposition
- poison center

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TOXICOLOGY

Definition and terminology

Don't memorise it just understand it i will not ask about it. most important is Systemic and Organ toxin

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.

It 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 e.g. **Cyanide**

Organ toxin: toxin that affects only **specific tissue or organs** i.e. **Lead, Paracetamol**

causes and routes to get toxic

Causes include	Routes include
Intentional: i.e. suicide.	Inhalation: i.e. Nitrous oxide, CO.
Wrong dose: i.e. Insulin.	Skin or eye absorption: i.e. organophosphate.
Symptoms control: i.e. paracetamol for pain.	Ingestion : major one: i.e. paracetamol....etc.
Exposure: i.e. radiation, organophosphate . عمال المزارع يستخدموه كمبيد	Injection: i.e. Opioids, insulin.
Bite: i.e. snake bite.	

Assessment

1-History:

it may be unclear **unconscious, child, doesn't know that he have had poisoned**.

you should ask about:

- substance?
- dose?
- route 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.

Toxidrome:

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

	Agents examples	Features	Potential interventions
Anticholinergic MOA: ANTAGONIZE the effects of endogenous Acetylcholine by blocking the receptors	-Atropine -Scopolamine -Amantadine -Tricyclic and tetracyclic antidepressants(TCA), -Olanzapine -Antihistamines	-Peripheral muscarinic blockade: Mydriasis, Anhidrosis, Tachycardia, Urinary retention and Ileus. -CNS muscarinic blockade: Confusion, Agitation, Hyperthermia can cause death , Myoclonus, Tremor, Abnormal speech, Hallucinations or Coma.	-Physostigmine - Benzodiazepines for sedation(MCQ) -cooling and Supportive care
Cholinergic MOA: Block acetylcholinesterase from working (prevent Ach degradation)	- Organophosphate and carbamate insecticides	-SLUDGE syndrome Salivation, Lacrimation, Urination, Diaphoresis, GI upset: Diarrhea, vomiting. Or Eye: Miosis. -Other: Bradycardia. Death due to respiratory arrest from muscle paralysis.	-Airway protection and ventilation - Atropine and Pralidoxime
Sympathomimetics Excessive sympathetic stimulation involving epinephrine, norepinephrine and dopamine	- Amphetamine - cocaine	-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	-Cooling -sedation with benzodiazepine -hydration.
Opioid	- Heroin - Morphine - Oxycodone	-CNS depression, Miosis (pinpoint pupil) - Respiratory depression : could cause death - hypothermia or bradycardia. pupil is constricted and RR 4 ?MCQ	-Naloxone: Competitive opioid antagonist - +/- airway support and ventilation
Sedative-hypnotic	- Benzodiazepines e.g.Diazepam - Barbiturate.	-Depressed level of consciousness , ataxia, slurred speech - respiratory depression -bradycardia or hypotension	Ventilatory support. dont choose flumazenil only in OR not for overdose out outside the hospital (MCQ)
Hallucinogenic	-Phenocyclidine - Lysergic acid diethyl amide (LSD) - psilocybin - mescaline	-Hallucination, dysphoria, anxiety -hyperthermia, mydriasis, nausea or +/--sympathomimetic.	Supportive

Other Toxidromes:

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

2-Examination:

Organ system	example of finding
General appearance	Malnourished: i.e. IV drug user , HIV infection.
CNS	Miosis*: i.e.Opioids, organophosphate. *constriction of pupil. Nystagmus*/ataxia: i.e. ethanol. *fast, uncontrollable movements of the eyes
Peripheral nerves	tremor: i.e. Lithium. Lead pipe rigidity: i.e NMS clonus/hyperreflexia: i.e. serotonin toxicity
Respiratory system	Bronchorrhea/crepitations/hypoxia: i.e. Organophosphate
CVS	Murmur: i.e. Endocarditis, IV drug user.
GIT	oral cavity burns: i.e. corrosive ingestion hyper salivation: i.e. cholinergic toxidrome
Urology	urinary retention: i.e. anticholinergic toxicity
Dermal	bruising:i.e. anticoagulant flush, dry skin: i.e. anticholinergic toxicity warm, moist skin: i.e. sympathomimetic toxicity

- Do not forget examine skin folds, clothes and bags for retained tablets or substances.

3-Diagnostic tests:

3.1-Bedside:

- Blood Glucose level: example of findings is hypoglycemia.
- ECG: example of findings is Arrhythmias .
- venous blood gas: example of findings is metabolic acidosis due to paracetamol .
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3.2-Laboratory:

- blood / urine drug level [Dr said acetaminophen and salicylate is most frequent](#)

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 .

3.3-limitation of Drug screening assays

[we make the decision based on clinical judgment and these are the limitation:](#)

Nonspecific	Most tests use enzyme-immunoassays that only detect <i>typical</i> 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.

Management

Resuscitation:

- **Airway:** intubation: if compromised (mainly obstruction)
- **Breathing:** O₂ administration, if hypoxic i.e. O₂sat <94%, mechanical ventilation if intubated
- **Circulation:** if Patient is hypotensive :
 - IV fluid 10-20 ml /Kg.
 - Avoid excess fluid administration.
 - Specific antidote.
 - Inotropic support i.e. Adrenaline infusion.
 - **Aim** : systolic BP > 90 mmHg or mean arterial pressure (MAP) >65 mmHg

some specific presentations

Hypoglycemia: Blood Glucose Level < 4 mmol	give IV dextrose (Glucose)
Cardiac Arrhythmias	<input type="checkbox"/> O ₂ saturation <input type="checkbox"/> Antidote i.e. digoxin Fab in digoxin overdose <input type="checkbox"/> Anti-Arrhythmic drugs are not first line treatment in toxin induced arrhythmias.
Seizure Child presented with seizure his mother complaining of chest infection what is most likely drug? treatment?	<input type="checkbox"/> 1st : IV benzodiazepine except in Isoniazid toxicity we give Pyridoxine . MCQ <input type="checkbox"/> 2nd : Barbiturates treat hypoglycemia and hyponatremia. No rule for Phenytoin in toxin induced seizure
Agitation	<input type="checkbox"/> 1st line treatment : benzodiazepine <input type="checkbox"/> 2nd line treatment : antipsychotic agents
Hyperthermia	<input type="checkbox"/> core temperature* > 39° <input type="checkbox"/> aggressive cooling *Core temp can be obtained by Rectus, gastric tube or foley catheter
Hypothermia	<input type="checkbox"/> core temperature <32° <input type="checkbox"/> aggressive rewarming.

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 reupte inhibitors	Cyproheptadine
Sulfonylurea	Octreotide, glucose
Tricyclic antidepressant	Sodium bicarbonate

لازم تنحفظ من قلب لان يجي منها **اسئله كثيره** مو لازم تحفظوها من اول لكتشر لكن مهم تحفظوها Antidotes

Decontamination

Focus on what i had said and read the rest -contraindication is imp

1-GIT Decontamination: Removing an ingested toxin from the gastrointestinal (GI) tract in order to decrease its absorption.

- **Single dose Activated Charcoal:** dr focus on -time should be <1 hour -charcoal sensitive substances -ileus is not contraindication -decrease level of consciousness is most imp contraindication. (adsorption) *نستخدم الفحم في المواد التي يقدر الفحم بمتصفها*

indications	contraindications	complications	technique
<ul style="list-style-type: none"> • preferred method • < 1 hour from ingestion • charcoal sensitive substances: (MCQs) <ol style="list-style-type: none"> 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 	<ul style="list-style-type: none"> • 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 <p>ileus is not a contraindication</p>	<ul style="list-style-type: none"> • vomiting 30% • messy • aspiration • direct administration 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 	<ul style="list-style-type: none"> • dose <ul style="list-style-type: none"> - 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) <p>no difference between mixing AC with water or other (sorbitol)</p>

Q : what are the charcoal resistance substances ?

hydrocarbons and alcohol	metals	corrosive
<ul style="list-style-type: none"> • ethanol • isopropyl alcohol • ethylene glycol • methanol 	<ul style="list-style-type: none"> • lithium • iron • K • lead • arsenic • mercury 	<ul style="list-style-type: none"> • acids • alkalis

Charcoal resistance: *المواد التي ما يمتصها الفحم وماستخدمه معها كلها مهمة ولازم تحفظ*

- **Whole bowel irrigation (WBI):** indicated in body packers(drug smugglers)-non anion gap metabolic acidosis -(peg-sle) technique.

indications	contraindications	complications	technique
<ul style="list-style-type: none"> • iron overdose >60mg/kg • lead ingestion • arsenic ingestion • body packers • slow release preparations : <ul style="list-style-type: none"> • lithium • verapamil / diltiazem • potassium formulations 	<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • nausea /vomiting • abdominal bloating • <i>non anion gap metabolic acidosis</i> • pulmonary aspiration • staff distraction from resuscitation and supportive care priorities • delayed retrial to a hospital offering definitive care 	<ul style="list-style-type: none"> • Polyethylene glycol electrolytes solution (PEG-ELS) • single nurse assigned • enough supply of PEG-ELS • NG tube inserted and confirmed • AC charcoal • administer PEG <ul style="list-style-type: none"> • adult 2L/hr • child 25ml/kg/hr • give metoclopramide → decrease vomiting and enhance motility • explosive diarrhoea • continue irrigation until it clear • stop if abdominal distension or bowel sound lost

- Gastric lavage: we don't use it any more Dr did not read it

Gastric LAVAGE

indications	contraindications	complications	technique
<ul style="list-style-type: none"> • rare in ED • serious poisonings <1hr • other methods are unavailable • mercury ingestion • arsenic ingestion 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • pulmonary aspiration • hypoxia • laryngospasm • mechanical injury to GIT • water intoxication (children) • hypothermia • staff distraction form resuscitation and supportive priorities 	<ul style="list-style-type: none"> • 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):Not used any more Dr did not read it-may cause rupture and peritonitis"

indications	contraindications	complications	technique
<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • prolong vomiting > 1 hr in 10-20% • diarrhoea 20% • lethargy 10% • pulmonary aspiration if (seizure / Decrease LOC) • mallory weiss tear • pneumomediastinum • gastric perforation 	<ul style="list-style-type: none"> • 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

2-Enhanced Elimination:increase the rate of removal of an agent from the body.

- Multiple dose activated charcoal: most common indication carbamazepine did not said anything else

indications	contraindication	complication	technique
<ul style="list-style-type: none"> • carbamazepine coma (most common indication) • phenobarbitone coma • dapsone overdose —> methaemoglobinaemia • Quinine overdose • Theophylline overdose • phenytoin 	<ul style="list-style-type: none"> • Decrease LOC • anticipate decrease of LOC • bowel obstruction 	<ul style="list-style-type: none"> • vomiting 30% • pulmonary aspiration • constipation • bowel obstruction • bowel perforation • corneal abrasion • staff distraction from resuscitation and supportive care 	<ul style="list-style-type: none"> • give the atoll dose <ul style="list-style-type: none"> • adult 50 g • kids 1gm/kg • repeat doses of <ul style="list-style-type: none"> • adult 25gm • kids 0.5g/kg • every 2 hours • route <ul style="list-style-type: none"> • 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

- **Urine alkalisation:** Most imp indication salicylate did not say anything else.

Mechanism

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

indications	contraindication	complications	technique
<ul style="list-style-type: none"> • Salicylate overdose • phenobarbitone coma (not first line) • cyanide • isoniazid • toxic alcohol • TCA • propranolol • felcainide • quinidine • methotrexate 	<ul style="list-style-type: none"> • fluid overload 	<ul style="list-style-type: none"> • alkalemia • hypokalaemia • hypocalcaemia • volume overload 	<ul style="list-style-type: none"> • Sodium bicarbonate • 1-2 mmol/kg IV bolus • infusion @ 250ml /hr <ul style="list-style-type: none"> • 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:** Dr only said its invasive

Indications	Contraindications	Complications	Technique
<ul style="list-style-type: none"> • sever life threating • deterioration despite full supportive care <ul style="list-style-type: none"> • Carbamazepine • Potassium overdose • Sodium valproate • metformin • Phenobarbitone • chronic lithium • salicylate • toxic alcohol <ul style="list-style-type: none"> • methanol • ethylen glycol • theophylline 		<ul style="list-style-type: none"> • Hypotension (most common) • bleeding from vasclar access • air emboli • blood loss • systemic heparinisation • thromobcytopenia • neutropenia 	<ul style="list-style-type: none"> • invasive • special staff • special equipment • monitoring

- **Harm-dialysis and hemofiltration:** may cause severe hypotension
- **Charcoal hemoperfusion.**

Disposition:

- **If asymptomatic for 6 hours in ED → discharge.**
- **Otherwise admission to hospital is required.**

MCQs:

Q1) activated charcoal is used frequently for gastrointestinal decontamination in toxic ingestion . However It does not has a role in management of which of the following toxic ingestion ?

- A. Acetaminophen
- B. Ferrous sulphate
- C. Tricyclic antidepressant
- D. Beta Blockers

Q2) Which of the following agents and antidotes are correctly paired?

- A. Anticholinergic overdose –Flumazenil
- B. Aspirin overdose –N-acetyl cysteine (NAC)
- C. Iron overdose –Deferoxamine
- D. Paracetamol overdose –Physostigmine

Q3) an intravenous heroin user rushed to the ER after he found unresponsive with shallow breathing and weak pulses , which one of the following is the first in the management ?

- A. give him an IV bolus of normal saline .
- B. start a cardiac massage .
- C. control his airways and breathing .
- D. administer activated charcoal .

Q4) which on of the examples is a stimulant drug ?

- A. Barbiturate .
- B. Marijuana
- C. Morphine ,
- D. cocaine .

Q5) 20 year old patient present to you with sweating , agitation , tachycardia and mydriasis . This presentation can be caused by which of the following ?

- A. Depressant drugs .
- B. opioid .
- C. cannabis.
- D. Amphetamine

Q6) Which of the following drugs can be used as an antidote for cyanide?

- A. Hydroxocobalamin
- B. Sodium bicarbonate
- C. Atropine
- D. Naloxone

Q7) A young man was brought to the emergency by an ambulance, he has decreased level of consciousness, slow respiration and pinpoint pupils. Which of the following should be given to him?

- A. Atropine**
- B. Naloxone**
- C. Flumazenil**
- D. Fimopizole**

Q8) A 38-year-old man brought to the emergency department by Red Crescent after being found wandering in the street mumbling. His blood pressure is 148/80, heart rate is 112 b/m, temperature is 38.3°C, respiratory rate is 18 breath/minute, and oxygen saturation is 100% on room air. On examination, the patient is confused, his pupils are dilated and his face is flushed. His mucous membranes and skin are dry. Which of the following toxic syndromes is this patient exhibiting?

- A. Cholinergic syndrome**
- B. Sympathomimetic syndrome**
- C. Anticholinergic syndrome**
- D. Opioid syndrome**

Q9) Which one of the following is the antidote for organophosphorus poisoning?

- A- Atropine**
- B-Calcium gluconate**
- C-Potassium chloride**
- D-Hyoscine**

Q10) A 29-year-old male is brought to the emergency department after using amphetamine in a party. Which of the following complications may occur in this patient?

- a. Convulsions**
- b. Hypothermia**
- c. Hypotension**
- d. Bradycardia**

Answers: 1- B 2- C 3- C 4- D 5- D 6- A 7- B 8- C 9- A 10- A