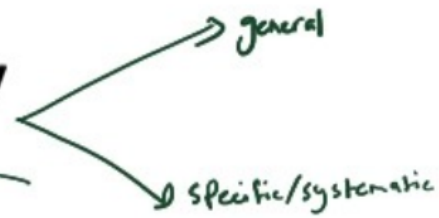
General Toxicology



Dr Melad Gad Paulis

- In case of suicide the harm is intentional so mostly the dose will be high.
- In case of accidental poisoning mostly it will be caused by a small dose.

} Not always true but mostly.

→ not all accidental poisoning is caused by a small dose, also not all suicidal or intentional should be caused by a small dose.

* rapid onset of action → cyanide
  delayed ... → Paracetamol, methanol
  ↳ signs and symptoms don't appear immediately, so the management and treatment will be more difficult.

{The dose makes the poison}

* supportive treatment is the main line of treatment.

- The more the dose the more & increased toxicity.
- Toxicity varies between variable substances, some need high doses to cause toxicity & some need high doses to be toxic.

⇒ Some drug may potentiate each other. (drugs (addiction)/snake venom)
⇒ mode of action (dermal, I.V., ...) / route of administration
↳ IV is the most dangerous because the bioavailability is 100%
⇒ Age, infants & children can be affected by doses less in amount than adult doses.
⇒ Presence of antidote (ترياق) for the poison can be a factor. (not all poisons have antidotes, and if someone had a delayed onset of action the effect of the antidote won't be high. Paracetamol's antidote has to be given after 8 hours.)
⇒ Mechanism of action affect management of case & not severity.
⇒ Problem in the organ responsible of excretion can affect & inhance toxicity.

غالبًا الأطفال ممكن يموتوا من لدغة العقرب وغيرها، الكبار شو السبب؟ (أهم سبب)
① size: the relation between the dose and body weight (distruption)
② faster absorption due to body circulation

* most common toxins in Jordan → Cleaning detergents, food poisioning, Snake and scorpion venom in Summer, Co poisioning in winter, chronic nicotine (Smoking)

Definitions:

Paracetamol

toxins → threpetic: HTN drugs, NSAIDs, paracetamol (toxic if reaches toxic doses)
toxins → non threpetic: cleaning detergents, organophosphates

→ The study of poison

❖ **Toxicology** is the word derived from the Latin word {Toxicum =poison. Logy=science} and it means the study the effects of poisonous substances on living organism.

→ A branch of medecine that deals with toxins.

❖ **Clinical toxicology** is the branch of medicine that deals with **forms and sources**, **mechanism(s) of toxicity**, **toxic dose**, **clinical picture**, **diagnosis** & **treatment** of poisoning.

❖ **A poison** is any substance that produces harm to the body.

* السموم ممكن نلاقيها بالبيت :- مواد كيميائية [كلور، gases, drugs (overdose), fertilizers, organophosphorus

Co, batteries, mercury, Snake scorpion venom, paint, food poisoning, mercury

* is there anything that isn't poisonous? No even water can be toxic, this depends on the dose

↳ if Someone took paracetamol in small doses it won't be toxic, if I drink a small amount of water .....

* واحد أخذ ٣ على Paracetamol (هو مرض أعلى) toxicity ال ← acute / chronic

Toxicity may be

sudden appearance of symptoms and signs طفل شرب علبة كلور

- Acute: exposure to a single large dose in short period of time.
- Chronic toxicity: exposure to repeated small toxic doses for large period led to gradual worsening as chronic lead, ethanol toxicity. [addiction]

> 6 months

- Subacute toxicity: shows the features of acute and chronic toxicity.

[or Sub chronic [both depend on the dose and duration]]

- Fulminant toxicity: ingestion of massive dose that produce multiple organ failure.

multiple organs

* lethal dose → highly toxic ← (low lethal dose) جرعة صغيرة بتموت بسرعة بتموت → cyanide
high lethal dose → methanol
بحتاج جرعة كبيرة حتى يموت

Classification of poisons:

1. Site of action:

Iron supplements have a mild toxic effect, affecting the liver mainly

a. Toxin has **local effect**: they act only in the site come in contact with.

It has no systemic toxicity. Example of these are corrosives (مواد حارقة). → local effect on lips, mouth esophagus, stomach.

b. Toxin has **systemic action**: they affect organs away from site of contact i.e., after absorption e.g., morphine, paracetamol…

c. Toxin has **dual action**: it has both local and systemic action. Example is heavy metals.

→ mercury

2. *Target organ classification*:

*CO affects the brain mainly, how? CO binds with hemoglobin and ↓ the affinity of O2. (after the brain the heart is affected ...)

This classification of poison according to the main organ affected by the poison:

I. **Hepatotoxic Agents:**

- The liver is a target organ for many chemicals and therapeutic drugs, e.g. paracetamol, iron, phosphorous.... ethanol

liver mainly then kidney

I. **Nephrotoxic agents**: such as aminoglycosides, NSAID, oxalic acid,

gentamycine

II. Agents affecting **nervous system**: as CNS depressants as morphine or stimulants as cocaine or affect neurotransmission as organophosphates.

III. **Cardiotoxic**: drugs as digitalis, aconite.

cause arrythmia

Aconitine intoxication by ingestion of aconitum roots can lead to ventricular tachycardia & cardiac arrest.

IV. **Pulmonary Toxic Agents**: as kerosene, chlorine gas.

V. **Gastrointestinal toxic agents**: as food poisoning, heavy metals...

opioids → constipation

VI. **Dermal**: as corrosives.

VII. **Ocular**: methanol.

*Plumbism → chronic lead toxicity, common poisoning in children (not rare)

chronicity

3- Origin and source of the poison:

a. Plant origin: as opium, digitalis, strychnine, and atropine. العشبي weed , marijuana, مخدرات

b. Animal origin: snake and scorpion venom.

c. Synthetic: as barbiturates, paracetamol.

4. Mode of toxicity:

Exposure to toxin may occur accidentally, homicidal or suicidal.

1. **Accidental Poisoning (nonintentional exposure):**

Most of the poisoning is accidental. In children most of the poisoning is accidental as they consume tablets or syrup in the household accidentally. Accidental poisoning can occur in agricultural workers when spraying insecticides. It can occur if a person drinks unsafe water contaminated with arsenic, etc.

2. **Suicidal Poisoning:** (intentional poisoning)

It usually occurs by available toxin the victim. Also, it is usually cheap and does not cause pain.

3. **Homicidal Poisoning:** intentional giving toxin to a person to induce harmful effect to him.

Toxin used usually has no smell or odour.

Factors which modify the actions of poisons:

1. ***Factors related to the toxin itself***: these factors are

I. **Dose:** as expected increase the dose increase the toxicity. As mentioned earlier poison is a matter of quantity.

II. **Form:** Poisons in gaseous form will act earlier than in other physical states. Poisons in solution act rapidly than the powdered form.

III. **Mode of administration:** Rapidity of action of a poison depends upon the mode of administration. The following are the routes in order of rapidity of onset of action of a poison

- IV injection: is the rapidest route "Then"
- Inhalation "Then"
- IM & SC injection "Then"
- Ingestion "Absorption from m.m. of vagina & rectum is more" "Then" intact skin absorption is the slowest route.

I. **Cumulative effect:** it occurs in toxin with repeated exposure to small doses not enough to cause acute toxicity. Also, drugs slowly excreted from the body as digoxin.

2- Factors related to the patient: it include the following

* Some toxins can be more effective on females like ethanol
* in a pregnant women, co poisioning will affect the baby more due to Hs f (fetal hemoglobin) which has high affinity for co. Pregnant women will be more effective than non-pregnant due to the high metabolic rate.

1. **Age:** Poisons have greater effect on extremes of age.
2. **State of health:** Diseases of kidney and liver increase the effect of most of the poisons as they are the main sites of metabolism and excretion of toxin.
3. **Stomach state:**
   - Amount of food:
   - On empty stomach: poisons have faster action.
   - On full stomach: poisons have slower action.
4. **Genetic Condition:**

   Decrease glucose 6 phosphate dehydrogenase enzymes lead to haemolytic effect of some drug "Even in therapeutic doses" e.g. antimalarial, sulphonamides, vitamin K, naphthalene and benzene.

*drug toxicity either → taking 2 therapeutic drugs (drug interactions)
→ drug overdose

5. **Hypersensitivity**: In hypersensitive persons may produce severe symptoms even fatal anaphylaxis by therapeutic dose.

6. **Idiosyncrasy**: abnormal response to drug. Morphine In abnormal response may produce CNS excitation.

Common in addiction, Studies of tolerance were made on drugs not toxins.

7. **Tolerance**: it is decreasing the response to the drug in repetition of the dose or increase the dose gradually to obtain the same original response. So persons who tolerated, habituated or addicted to some drugs can stand big doses of these drugs without toxicity e.g. alcohol.

8. **Drug interaction**: in case of ingestion of more than one drug, they may interact to affect action of each other by one of the following:

    1. Synergism: effect of poison increase if combined with another; such as alcohol and barbiturate.
    2. Antagonism: effect of poison is counteracted by another such as ethanol and methanol.

*Coingestion → drug combination, example a person who is diabetic and has HTN, if the person takes ACE inhibitors with Ca^{+2} channel blockers

History → examination → investigations → treatment → general / specific / supportive management

General Diagnosis of Poisoning Cases

* Some Poision cases are really difficult to diagnose
* Some are simple to diagnose like co Poisioning in winter. Or scorpion/snake attack

- **Diagnosis of Poisoning:**

I. History and circumstantial evidences.

II. Clinical manifestations.

III. Investigations.

a toxic case?

- Some cases may come to emergency with recognized & well-identified cause of intoxication so this may make the process of treatment more easier.
- Some cases may present with unknown causes of intoxication or even we don't know if the patient is toxicated at all.
- Young age + coma + unknown cause ⟹ we should consider toxicity (suicide)
- Young age + arrythmia ⟹ one of d.dx is toxicology, because arrythmia is abnormal at that ages.

a- Sudden appearance of toxic manifestations in a healthy person or a group of persons after taking certain food or drink (as food poisoning. methanol and carbon monoxide toxicity),

b- History of intake a poison, financial problems, psychiatric troubles, previous attempts at suicide or threatening by somebody.

c- Presence of bottle of tablets or insecticide near the victim.

d- Patients rescued from fire (CO. cyanide),

e- Accidental intake of toxin.

GENERAL MANAGEMENT

You must suspect poisoning when the history is inclusive:

- **A comatose patient in whom the etiology is unknown.**
- **Arrhythmias of unknown etiology.**
- **Patients with metabolic acidosis of unknown etiology.**
- **A trauma victim especially if young.**
- **Bizarre symptoms.**
- **Psychiatric patient**

by methanol

especially in young age patients.

* make sure to diagnose the patient right, a patient who was Stinged by a scorpion might have tachycardia/bradycardia and parasympathetic over stimulation, so if given atropine (anticholinergic) this will make him worse.

asking for the substance will help us confirm if the patient is being honest or lying, Suicidal patients are called bad historians → example: the patient says the substance is paracetamol but his liver enzymes are normal, or in cases of methanol (the patient might be embarrassed to say that he was drinking)

• I. History: 'SATS"

methanol poisioning usually effects groups of people

- **S:** substance taken.
- **A:** amount ingested.
- **T:** time of ingestion.
- **S:** symptoms appeared.

It is very important to know the severity & how to deal with the admitted patient.

To know if the patient actually has taken a toxic dose of that drug or if he didn't reach it & won't be harmed so this may help us. ⇒ especially in patients who are lying. أو المرضى اللي بنداري

* Paracetemol toxicity dose is 12 pills letter than that won't cause toxicity.

also to know the severity the more the amount the more the severity.

- Help in diagnoses
- can help us to know the stage has been reached.
- can indicate severity

To know the stage of toxication that the patient reach.

- Some drugs causes late manifestations such as paracetamol & methanol.
- T know how to treat the drug & if a certain treament would be effective or not

* In some cases, the treatment is supportive and symptomatic (high fever → put the patient in an ice bath, Pain → give analgesic, hypoglycemia → give dextrose) Some times the patient has no symptoms example: if a patient was bitten by a snake but has no symptoms or investigations, the antidote is given for 8-12 hours.

* The toxins that have antidotes are 5% → 10% so antidotes aren't the main treatment for toxins.

* The main treatment for toxicity
  1) Decontamination (removal of cause)
  2) Treatment of symptoms & signs 3) Supportive treatment.

It should include:

- **Route of administration** (i.e., ingestion. intravenous. inhalation).
- **Reason for the ingestion** or exposure (accidental, suicidal, or homicidal.
- Presence of history of psychiatric illness or previous suicide attempts.
- Patient must be asked about **all drugs taken**; including: prescription, over-the-counter medications, vitamins, and herbal preparations.
- Patients may **incorrectly name the drugs** they have ingested; for example; they may refer to ibuprofen as acetaminophen or vice versa.
- Patients can be **unreliable historians**; particularly if suicidal, psychotic, presenting with altered mental status, or under the influence of recreational drugs. In this case information taken from family and friends may also prove helpful.

Examination

* toxicity of drugs isn't related to mechanism of action [NSaids are Pain analgesics but with toxicity there can be Pain] → paracetamol

Salicylate is anti-Pyertic with toxicity it's hyperthermic.

Physical Examination

Vital data:

1. **Temperature:** hyperthermia can occur in salicylate and anticholenrgic poisons, while hypothermia may occur in barbiturates, narcotics, sedative hypnotics and alcohol.

fever ← hyperthermia → Scorpion Poison, cocaine

Normally used to lower fever in cases of toxicity it causes ↑ fever. ← salicylate → aspirin (anti-pyretic)

2. **Pulse**: bradycardia is seen in opiate, digitalis, cholinergic, beta blockers, and calcium channel blockers, while tachycardia occurs in amphetamine, cocaine & anticholenrgic.

bradycardia → organophosphates.

tachycardia ← [CNS Stimulatants]

* opiods in normal doses have no effect on the heart rate, in high doses it depresses the vasomotor center and causes bradycardia

3. **Blood pressure:** hypertension in amphetamine and cocaine.

cocaine → Stimulantants

(mostly normal

C. Skin:

1. Flushing: in anticholinergic & alcohol. UD

2. Diaphoresis: in OPI, salicylate & cocaine.

3. Bullous lesion: in sedative hypnotics especially barbiturate & carbon monoxide poisoning.

D. Breath: it is important to smell the patient's breath. Alcohol, cyanide, phenol, organ phosphorous and H2S have characteristic odor.

E. Pupil:

size → constricted / normal / dilated
response → reactive / non-reactive
constricted
organophosphorus

* Quality of both pupils (both pupils effected or ipsilateral (1 side))?
if both are the same (size, response) → toxin (ethanol...) [general effect]
if ipsilateral → local problem in brain

1. **Pin-pointed:** with opiates, OPI, phenothiazines and pontine lesions.
2. **Reactive dilated:** with sympathomimetics (amphetamine, cocaine). → pubil constricted with light exposure. → stimulatory → sympathomimetic
3. **Non reactive dilated:** occurs with anticholinergics.
   - → No constriction by light exposure
   - → Atropine

F. Respiratory system:

1. **Tachypnea:** occur in aspiration pneumonia, toxic hypoxia & CNS stimulants (amphetamine, cocaine). → stimulatory
2. **Bradypnea:** occur in CNS depression as in ethanol and barbiturate. → inhibitory

3. Pulmonary edema: → right side heart failure (cardiogenic)

- Cardiac: in beta blockers and cyclic antidepressants (also digitalis)
- Non cardiac: in opiate, barbiturate, OPI & salicylate. (CO, barbiturates, gases)

(→ local effect on lung)

4. Wheezes: in organophosphorous, cholinergic medications and irritant gases.

G. Neurological: careful neurological examination should be done, grading of coma should be assessed in comatose patient.

H. Abdomen:

***1.* Vomiting** with Digoxin, Theophylline, OPI. → one of the early manifestation of digitalis toxicity is vomiting.

***2.* Diarrhea** with OPI, iron, arsenic. → severe vomiting

***3.* Constipation:** with plumbism. → lead toxicity

Toxidromes (Fingerprints) in toxicology)

toxic syndromes

" A pattern of signs or symptoms that suggests a specific class of poisoning "

I. Anticholinergic toxidrome ⟹ Dilated nonreactive pubil

Characterictics

∴ toxidromes بال بعضونا أكثر شغلتين
① vital signs ② conscious levels

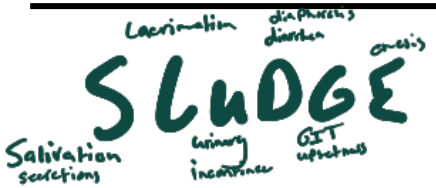
-altered mental status (hallucinations, agitation, coma) → initially CNS stimulation but then inhibition.
-large pupils Dilated non-reactive Pupil. (non responsable to light)
atropine is given in bradycardia
- tachycardia, high temperature
--dry flushed skin . flushed skin can be seen with ethanol.
-decreased bowel sounds. anticholinergic are given intestinal cholic to ↓ Spasms.
-urinary retention

كيف نفرق شو سبب الـ flushing ؟
-ethanol with chronic toxicity → hypothermia
-atropine with " " → hyperthermia

Common Causes

-Anticholinergic plants (e.g., Atropa beladona)-
-Atropine → Sedative ∴ has anti-cholinergic effect.
-Antihistamines (Benadryl- Diphenhydramine, Gravol - Dimenhydrinate) → non-Sedative
not an an anticholinergic drug but has it effect
-cyclic Antidepressants
-Antiparkinsonian agents
-Antiemetics
-Antispasmodics

III.Cholinergic toxidrome



Characterictics

-lacrimation, salivation

-bradycardia

-respiratory secretions

-hypoxia

-diaphoresis

-increased bowel sounds

-vomiting

-diarrhea and urinary incontinence

-fasciculations may occur and muscle weakness can result in respiratory failure

↑ secretions

↑ bowel activity

↓ bradycardia → hypoxia

↓ weakness & fasiculation in muscles → respiratory failure

Common Causes

organophosphate and carbamate insecticides

opiate / digitalis / B-blockers

→ CNS stimulation + vital signs

IV. Sympathomimetic toxidrome

Characterictics * excessive stimulation leads to depression and coma.
↳ hypoxia, hallucinations.

-agitated delirium is common

-large pupils ⇒ Dilated reactive pubil

-elevated vital signs

- -tachycardia
- -hypertension
- -hyperthermia
- -diaphoresis (unless severely dehydrated)

This can be used as a method to differentiate between symp. & anti-cholinergics.

while anti-cholinergic (parasympathetic) act on cholinergic receptors present in bowel so inhibit bowel sound

-bowel sounds present → Sympathomimetics doesn't act on bowel so doesn't affect bowel sound.

*Note: This toxidrome is usually differentiated from the anticholinergic toxidrome by the presence of marked diaphoresis (instead of dry skin). Also bowel sounds are not decreased + pallor.

Common Causes

-overdose of cocaine or amphetamine

-alcohol or sedative hypnotic withdrawal results in similar findings.

Sympathomimetic	anti-cholenergic
-Dilated reactive	-Dilated non-reactive
- present bowel sound	-Absent bowel sound
- Diaphoresis	-Dry skin.

II. Sedative hypnotic toxidrome → CNS Mainly in depressant effect.

(Vital signs affected in cases of severe toxicity)
↳ depressed effect.

depending on the degree of toxicity
Starting from slight drowsiness till deep coma

Characterictics

-depressed mental status

-relatively small pupils

-vital signs usually normal (unless severe dose) in mild / moderate toxicity.

- -significant respiratory depression is rare with pure benzodiazepine overdose
- -hypotension in large ingestions

* characters of addiction:
1- chronic intake → tolerance
2- Overpowering (craving) i.e. إذا ما أخذ جرعته اكتئاب ممكن يلجأ للقتل.
3- Bad facial expression and general appearance.
4- withdrawal manifestations: لما بقلل إدمان وقل الـ toxin في الدم بصير عنده أعراض الانسحاب

* أعراض انسحاب الـ depression بكون Stimulant
* ، الـ Stimulant بكون inhibitory (Sympathomimetic)

مثال: لو حاطه مدمن على الـ cocaine وما قدر يوخذ جرعة بتظهر عليه أعراض الـ depression of CNS

Common Causes

-overdose of benzodiazepines

-some sedative hypnotics

— withdrawal of stimulants

Toxidrome	Vital Signs	Signs
Anticholinergic	HR ↑	Bowel sounds ↓ Delirium[a] Dry mouth Mydriasis or normal Skin - dry, flushed
Sympathomimetic	HR ↑ BP ↑	Agitated Delirium[a] Mydriasis Skin—diaphoretic
Opioid	RR ↓ and/or shallow	Bowel sounds ↓ Mental status ↓ Miosis
Sedative-hypnotic	RR normal or ↓[b]	Mental status ↓
Cholinergic	HR ↓	Bronchoconstriction Bronchorrhea Diaphoresis Lacrimation Miosis Salivation Urination

[a]If severe
[b]If combined with other sedatives
BP, blood pressure; *HR*, heart rate; *RR*, respiratory rate; ↑, increased; ↓, decreased.

III. Investigations.

general (routine investigations)
specific

a- **Routine investigations**:

- blood glucose level
- **ECG**
- **LFT & Clotting (Paracetamol, anticoagulants).**
- **Arterial Blood Gases.**
- **Urinalysis**
- **Kidney function.**
- **Imaging: x-ray, CT, MRI.**

important for necrosis brain like in cases of CO poisoning

depending on the toxin
Can be specific for some types of information as in liver function test in case of paracetamol toxicity.

* كيف ممكن الـ x-ray يفيدنا بحالة الـ corrosive؟ حاد حارقة
Perforations ممكن يعبر عن stomach و esophagus ١- بتحرق
٢- ممكن تعمل مشاكل بالـ lung خصوصًا بحالة الـ inhalation [mine site of action in corrosive is upper GIT]

determines if +ve or -ve, after taking a sample of blood or urine then use the Kits that contains AB agonists (Paracetamol, tramadol, organ Phosphurus...) Screening test for multiple toxins at once.

- Elisa & specific Abs & kit for certain types of toxicity caused by certain drugs.

*if +ve quantative test are done to determine it's amount [not by elisa] use HPLC device / gas chromatography high Performance liquid chromatography.

- Chromatographic electrophoresis.

b- Chemical detection: (Analytical toxicology)

- The most important evidence of poisoning is by chemical analysis.
- Samples are taken from vomitus, gastric lavage, blood, urine and stool.
- Toxicological laboratory screen is important in (Come, Convulsion, Acute Delirium, Metabolic Acidosis & Hypoxia)
- Toxicological Laboratory serum level is important in:- (Alcohol - Aspirin - Paracetamol - Digoxin - Iron - Theophyline - salicylates)
- Carboxyhaemoglobin levels if carbon monoxide poisoning is suspected.