WITH NOTES

GENERAL TOXICOLOGY

الدكتورة نبهت زمايلنا على الواتس ان "كل الأمثلة معانا" مع الأسف
احنا مطالبين بالهاند أوت بس
أي معلومات زيادة في الريكورد للتوضيح فقط ومش معانا

GENERAL TOXICOLOGY

Definitions:

Toxicology	▪ It is a **science dealing with** properties, actions, toxicity, fatal dose, detection, estimation, treatment & autopsy findings (in case of death, in relation to the poisonous substances).
Toxicant	▪ The specific chemical poisonous.
Toxic effects	▪ **Toxic effects are categorized according to the site of poison effect :** • **In some cases**, the effect may occur at only one site. - This site is referred to as the specific target organ. • **In other cases**, toxic effects may occur at multiple sites.

Types of systemic toxicity: (Depending on time)

Acute toxicity	• It occurs almost immediately (hours/days) after an exposure. • Acute exposure is usually: - A single dose or - A series of doses received within one day.
Subacute toxicity	• It results from repeated exposure for several weeks or months. • This is a common human exposure pattern for some **pharmaceuticals** and **environmental agents**
Chronic toxicity	• It represents **cumulative damage** to specific organ systems and takes many months or years to become a recognizable clinical disease. • Damage due to subclinical individual exposures may go unnoticed but with repeated subclinical exposures, cumulative damage slowly builds up until it exceeds the threshold for chronic toxicity.

Manner of poisoning:

Accidentally	▪ Most episodes of pediatric poisoning, dosage error or iatrogenic.
Suicidal (Deliberate)	▪ **Overdose** as self-harm.
Homicidal	--------

Classification of poisons:

I- According to their mode of action:

Poisons with local action	○ They act locally producing immediate destruction of the tissues with which they come in contact. ○ e.g., corrosives (except organic acids)
Poisons with remote action	○ They act only after absorption without any local effects ○ e.g., plant poisons which act mainly on CNS.
Poisons with both local & remote actions	○ As irritant metallic poisons which have a local irritant action on the tissues, they come in contact for some time and a remote action (on **parenchymatous organs**) after absorption.

II- According to the organs affected: (Target Organ Toxicity).

Neurotoxic	○ Alcohol and lead.
Hepatotoxic	○ Ethanol, Acetaminophen, Phosphorus & Carbon Tetrachloride. = Paracetamol
Nephrotoxic	○ Heavy metals e.g., mercury.
Cardiotoxic	○ Digitalis.
Immunotoxic	○ Isocyanates.
Respiratory System	○ Tobacco smoke, asbestos and ozone.
Reproductive System	○ Dibromochloropropane.

III- According to the chemical nature

Acids	○ As sulphuric, nitric and hydrochloric acid.
Alkalies	○ As caustic soda, caustic potash and ammonium hydroxide

Factors affecting the severity of toxicity:

I- Factors related to the person:

Age	▪ **Children and old people** are generally more susceptible to the toxic agents due to ↓↓ of detoxification power. ▪ However, children can tolerate the action of atropine, but NOT morphine.	
Genetic factors	▪ Persons suffering from g**lucose-6-phosphate dehydrogenase deficiency** are susceptible at therapeutic doses to hemolytic effect of some drugs like vitamin K & sulphonamides.	
Personal hypersensitivity	▪ Very small harmless doses can produce severe symptoms in sensitive patients e.g., therapeutic dose of penicillin or iodine may produce anaphylaxis in hypersensitive patients.	
Tolerance	▪ Repeated intake of substances of abuse leads to development of tolerance where addicts can stand big dose without ill-effect. So, they have to ↑↑ the dose to get the same effect.	
Idiosyncrasy	▪ **Abnormal response to some** drugs e.g., morphine may produce convulsions instead of depression of CNS.	
State of health	▪ Patients suffering from **liver or kidney diseases** may show signs of ↑↑ toxicity of the poisons.	
Condition of the stomach	**Type of food**	Fatty foods delay the absorption of arsenic while they ↑↑ the absorption of some poisons as DDT & phosphorus.
	Gastric secretion	Poisoning with potassium cyanide may not be fatal in case of achlorhydria as HCL in stomach is important to form the severely toxic hydrocyanic acid.

II- Factors related to the poison

State	▪ Poisons in gaseous form are more rapidly absorbed followed by liquid, fine powder, then big lumps.
Routes	▪ The quickest is inhalation followed by IV, IM then SC, oral, mucosal membranes, lastly cutaneous absorption which is minimal except in some poisons e.g., (organophosphates - phenol - tetraethyl lead)
Dose	▪ The bigger the dose, the more toxic effect "However, this is not a general rule as big doses of metallic poison may cause severe vomiting, so eliminate most of the poison"
Cumulation	▪ After repeated small doses of certain drugs which are **not readily metabolized**, the effect of a single large dose is reached leading to poisoning e.g., digitalis

Diagnosis of poisoning

I- History & Circumstantial evidence

- History of 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).
- History of intake a poison, financial problems, psychiatric troubles, previous attempts at suicide or threatening by somebody.
- History of presence of bottle of tablets or insecticide near the victim.
- History of patients rescued from fire (CO, cyanide).

☒ History should include:

Toxin information	○ Type of toxins (**What**) ○ Time of toxic exposure (acute versus chronic). (**When**) ○ Amount of toxin taken (**How much**) ○ Route of toxin administration (i.e. ingestion, intravenous, inhalation) (**How**) ○ Manner of the toxic ingestion or exposure. (**Why**)
Psychiatric Information	○ History of **psychiatric illness** or **previous suicide attempts**
Drug(s) Information	○ Information about all drugs taken, including prescription, over the counter (OTC) medications, vitamins, & herbal preparations.
Unavailable Information	○ If history is unavailable from the patient, information should be taken from family & friends. ○ Paramedics or emergency medical technicians are also good sources of information because they may be able to furnish details, such as the presence of empty pill bottles.

II- Clinical Examination: (General & Local)

Vital signs	○ Pulse, Blood Pressure, Respiratory Rate, Temperature & Pupils
Systems	○ Cardiovascular, Respiratory, Abdominal & Neurological Exam.
Mouth:	○ Perioral Acneiform Lesions, Dry Mouth, Hypersalivation & Breath Odor
Muscle condition	○ Muscle Rigidity or Muscle Fasciculation
Skin	○ Cyanosis, Blisters, Needle Tracks & Hot/Flushed

MCQ + Case

Toxidromes

مهم نعرف في الجدول دا الأعراض اللي بتظهر دي بتندرج تحت أي عيلة

- الجدول كله حفظ

	Examples	Vital signs	Pupils	Other findings
Sympatho-mimetic	**Cocaine.** Amphetamine. Pseudo-ephedrine.	Hyperthermia - Tachycardia. Hypertension - Tachypnea.	Mydriasis	Piloerection. Hyperreflexia. Diaphoresis - Tremors.
Anti-cholinergic	**Atropine.** Tricyclic-antidepressant. Antihistamine.	Hyperthermia - Tachycardia. Hypertension		Hot, dry, red. Blind - Seizures.
Hallucinogenic	**Δ 9-Tetra-Hydrocannabinol.** Phencyclidine. Lysergic acid diethylamide	Tachycardia - Hypertension. Tachypnea.	Mydriasis. Nystagmus	Hallucinations. Agitation. Disorientation
Opioid	Opiates - Heroin.	Hypothermia - Bradycardia. Hypotension - Hypopnea	Miosis	CNS depression. Coma.
Sedative-Hypnotic	**Benzodiazepines.** **Barbiturates.** Alcohol. Anticonvulsant.	Hypothermia. - Bradycardia Hypotension - Hypopnea		Hyporeflexia. Confusion. Stupor. Coma.
Cholinergic	**Organophosphates.** Carbamates. Mushrooms	Hypothermia - Bradycardia. Tachypnea		Lacrimation. Salivation. Incontinence. Bronchospasm. Seizures

Coma

مهمة جدا بتفاصيلها

☒ Causes:

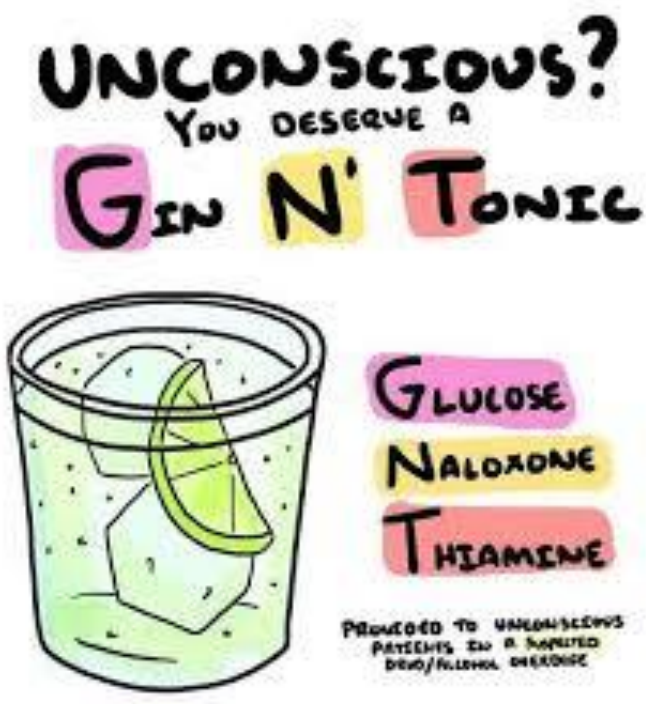
Toxic causes	▪ **Generalized CNS depression**: - e.g., ethanol, opiates, & sedative-hypnotics). ▪ **Post-ictal phenomenon** "after a drug-induced seizure" - e.g., anticholinergics. ▪ **Hypoglycemia**: (e.g., insulin, oral hypoglycemic drugs). ▪ **Cellular hypoxia**: (e.g., CO, cyanide).
Traumatic causes	▪ Head injuries.
Pathologic causes	▪ Liver and renal failure. ▪ Infections as encephalitis or meningitis.
Environmental causes	▪ Hypothermia or hyperthermia
Hysterical	▪ **NO** organic cause, normal vital signs, and negative investigations

☒ General lines of treatment of coma:

1) **Care of Airway & Breathing**: Maintain airway, administer supplemental O2 and assist ventilation if necessary.
2) **Coma cocktail**: (Dextrose, Naloxone & Thiamine) "NEXT PAGE "
3) **Control convulsions**: If they are present.
4) **Correct electrolyte, or acid-base disturbance.**
5) **CT scan**: If suspecting a brain lesion, perform a CT scan.

Coma Cocktail

Dextrose	○ It is given to all patients **with depressed consciousness & Hypoglycaemia.** • Child: 25 % (2 ml/kg) IV. • Adolescent/adult: 50 % (1 ml/kg) IV.
Naloxone Respiratory stimulus	○ It is given to all patients **with depressed respiration.** • Child: 0.1 mg/kg IV. • Adolescent/Adult: 0.4 mg IV & 0.1 mg IV "If suspected Opioid Abuse" • If no response give up to **2 mg IV.** • If no response, repeat the dose every 2 min. Till a total dose of 10 mg
Thiamine	○ It is given to **malnourished & chronic alcoholic patients.** ○ 100 mg IV or IM (It is not given routinely to children).



Convulsions

مهمة جدا بتفاصيلها

☒ Causes:

Toxic causes	Acting on the cerebrum	Causing muscular hyperactivity e.g., **amphetamine, cocaine, caffeine and atropine.**
	Acting on the brain stem	Causing clonic convulsions i.e., contraction & relaxation of the muscles e.g., **picrotoxin and lead.**
	Acting on the spinal cord	Causing tonic convulsions i.e. sustained hypertonia of the muscles e.g., **strychnine.**
	Cerebral anoxia	e.g., **cyanide.**
Metabolic causes		▪ Hypoglycemia, hyponatremia, hypocalcemia, or hypoxia
Traumatic causes		▪ Head trauma with intracranial injury. ▪ Idiopathic epilepsy. ▪ Exertional or environmental hyperthermia
Pathologic causes		▪ CNS infection (meningitis or encephalitis) ▪ Febrile seizures in children.

☒ General lines of treatment of coma:

1) **Maintain an open airway and assist ventilation.**
2) **Use one or more of the following anticonvulsants:**

Diazepam	**1st** Line of therapy
Phenobarbitone	2nd Line of therapy
Phenytoin	It is not indicated in the management of toxic seizures.

MCQ common

- MCQ (common) : Which of the following is not indicated to treat toxic seizures?
A) Phenytoin

3) **Specific measures** as:
   - Glucose for hypoglycemia.
   - Cool Immediately for hyperthermia.
   - Fluids for dehydration.
4) **Consider specific antidotes.**

Non-Toxic Ingestion

Def	▪ Nontoxic ingestion, is defined as producing little to no toxicity when ingested in small amounts. ▪ They are not true poisoning and can be managed by reassurance.

☒ Types:

• Antacids	• Shampoo	• Hand lotions	• Cigarette butts
• Fertilisers	• Bath oil	• Shoe polish	• Inks
• Paint	• Hair products	• Chalk	• Soap
• Antibiotics	• Shaving cream	• Incense	• Colognes & perfumes
• Glues	• Candles (wax)	• Silica	• Laxatives
• Corticosteroids	• Deodorants	• Cosmetics	• Matches (red phosphorus)
• Lipstick	• Vaseline (petroleum jelly)		• Newsprint
• Detergents (sips)	• Thermometer mercury		• Oral contraceptives

☒ Criteria: مهمة جدااا وموضع سؤال

- To diagnose a non-toxic exposure; ALL the Criteria should be Present: (6A)

1) **Absolute identification** of the product.
2) **Absolute assurance** that only 1 product was ingested.
3) **Absence** "NO" signal word (Danger, Poison, Warning, Caution) on the container
4) **A good approximation** of the amount ingested.
5) **Assurance** that the victim is free of symptoms.
6) **Ability** to call back at intervals to determine that no symptoms have developed.

Asymptomatic Patient

✖ The patient with exposure to toxin may remain asymptomatic due to:

1) Non-toxic substance: The substance may be nontoxic.
2) Insufficient amount: An insufficient amount has been ingested
3) Insufficient absorption: A sufficient amount has not been absorbed

III- Investigations

☒ **Value:** To assess base line of the patient and follow up target organs.

☒ **Include:**

1) General Investigation "**Routine Investigations**":
2) Specific Investigation "**Toxicological Investigations**" "Toxicology Screen"

➲ General Investigation "Routine Investigations":

1) ECG.

2) Laboratory:

- **Blood Glucose Level.**
- **Arterial blood gases:**

- High anion gap metabolic acidosis (**MUD PILES**):

Methanol	**P**ropylene glycol
Uremia	**I**ron
Diabetic ketoacidosis	**L**actic Acidosis
--	**E**thanol
--	**S**alicylates

- Liver function tests " clotting profile for paracetamol & anticoagulants toxicities"
- **Renal functions tests** "urine analysis for rhabdomyolysis"
- **Complete Blood Picture.**

3) Radiological:

<table>
<tr><td>Chest X ray</td><td>

If pulmonary edema/aspiration is suspected.
Drugs causing pneumonitis or pulmonary edema (MOPS)

<table>
<tr><td>Meprobamate & Methadone</td></tr>
<tr><td>Opioids</td></tr>
<tr><td>Phenobarbital, Propoxyphene, Paraquat & Phosgene</td></tr>
<tr><td>Salicylates</td></tr>
</table>
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<tr><td>Abdominal X ray</td><td>

Common radio-opaque medications by abdominal X ray (BETA CHIP)

<table>
<tr><td>Barium</td><td>Chloral hydrate, Cocaine & Calcium</td></tr>
<tr><td>Enteric coated tablets</td><td>Heavy metals</td></tr>
<tr><td>Tricyclic antidepressants</td><td>Iodides</td></tr>
<tr><td>Antihistamines</td><td>Phenothiazines, Potassium</td></tr>
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➲ Specific Investigation "Toxicology Screen"

Samples	▪ Blood & Urine "**Most Indicated**" ▪ Vomitus, Gastric Lavage & Stool "May Indicated"
Value	▪ The most important evidence of poisoning is by chemical analysis
Categories	1) Blood Levels : next page 2) Urine Screen: next page 3) Specific Test: Carboxyhemoglobin levels "if carbon monoxide poisoning is suspected"

1) Blood Levels: 3A & 3I

Alcohols "Ethanol & Methanol"	**I**notropic "Digoxin & Theophylline"
Analgesic "Paracetamol & Salicylates"	**I**ron
Anti-Epileptics "Carbamazepine, Phenobarbital"	**I**mmunosuppressant "Methotrexate"

2) Urine Screen: In cases of suspected substance of abuse: ABC+

Amphetamine
Benzodiazepines & **B**arbiturates
Cannabis & **C**ocaine
+ Opioids, Tramadol, Pregabalin, Synthetic Cannabinoids.

IV- Treatment

General lines of treatment of poisoned patient:

- **Good supportive care is the backbone of any successful therapy of poisoned patients.**

1) **Stop Exposure & Emergency Treatment**

   "Prevent further exposure to the poisons & Supportive measurement"

2) **Emergency and supportive measures** (ABCDE)

3) **Decontamination.**

4) **Enhancement of Elimination** "Enhancement of poison Excretion".

5) **Antidotes** "Administration of toxin-specific antidotes".

6) **Symptomatic Treatment.**

1) Stop Exposure & Emergency Treatment

☒ **Prevent Further Exposure to The Poison:**

- **In industrial or agricultural exposure**: Remove the patient from the polluted area.
- **In cases of toxic inhalants**: Transfer the patient to fresh air and giving oxygen.
- **In suspected suicidal cases**: The patient hospitalized & observed to prevent other trials.
- **During medical treatment**: If toxic manifestations appear, the drug should be stopped immediately.

2) Emergency and supportive measures (ABCDE)

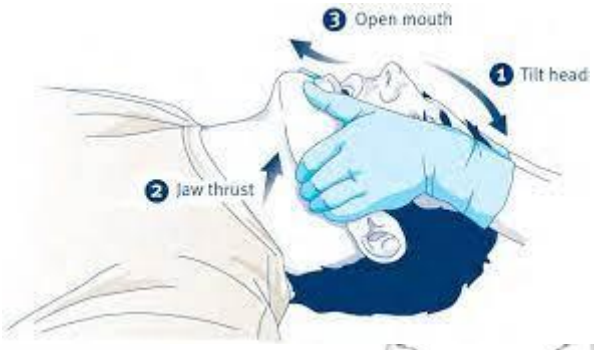
☒ **The first step is to recognize and treat life threatening conditions:**

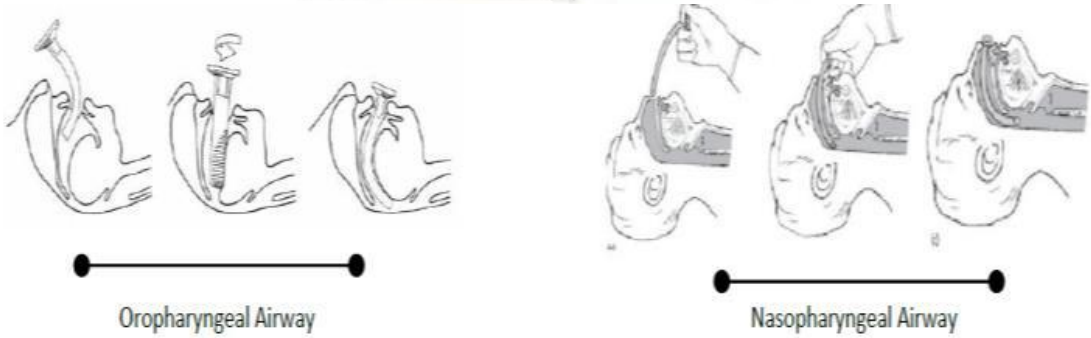
- A=Airway
- B=Breathing
- C=Circulation
- D=Disability
- E= Emergency Antidote

Airway opening & clearance.

N.B: The greatest contributor to death from drug overdose or poisoning is resp. failure.

Airway opening	○ Triple airway maneuver: (Head tilt, jaw thrust, mouth opening). ○ If there is any suspicion of neck injury: Place the patient in left lateral position with the head downwards which allows the tongue to fall forwards and vomitus or secretions to drain out of the mouth.
Airway clearance	○ Finger sweep technique to remove any F.B. or denture ○ Suctioning of the mouth and oropharynx to remove secretions.
Maintain airway opened	○ Either by oro or nasopharyngeal airway





Toxic causes of respiratory failure: (The commonest cause of death)

- **Central Causes:** As opiates, barbiturates, alcohols.
- **Peripheral Causes:**

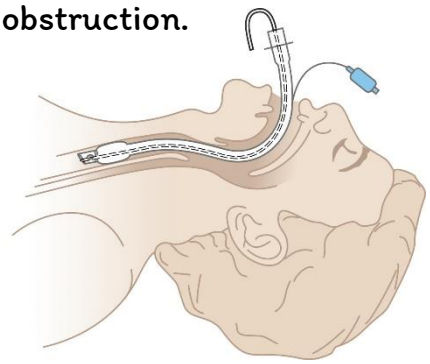
Airway obstruction	1. **Falling Back of The Tongue or Vomitus**: As in comatose patient. 2. **Laryngeal Spasm**: As in cyanide poisoning. 3. **Oedema of the airway**: As in irritant fumes or gas such as chlorine inhalation. 4. **Bronchospasm**: As in organophosphates compounds. 5. **Excessive Secretions**: As in organophosphate or carbamate toxicity. 6. **Pneumonia**: From aspiration of Gastric Contents, or hydrocarbons such as Kerosene. 7. **Pulmonary Oedema**: As in Organophosphates.
Neuro-muscular block	Neostigmine & physostigmine
Paralysis of respiratory muscles: **BOSP**	1. **B**otulinum toxins 2. **O**rganophosphates 3. **S**nake bites 4. **P**ost convulsive muscle exhaustion.

Breathing support

- O2 mask (Face mask) or bag valve mask (Ambu bag) or Endotracheal intubation (ETT)
- Pulse oximeter to assess O2 saturation

Advantages of ETT

1. It protects the airway and prevents aspiration & obstruction.
2. It allows for mechanically-assisted ventilation.
3. Some emergency drugs can be given through it
   e.g., naloxone, atropine & epinephrine



Circulatory support

(1) Check (3 Ps) Blood Pressure, Pulse rate and Perfusion (Capillary Refill Time; CRT):

- Perform cardiopulmonary resuscitation if there is no pulse.
- Treat shock and arrhythmia if present

(2) Begin Continuous ECG monitoring:

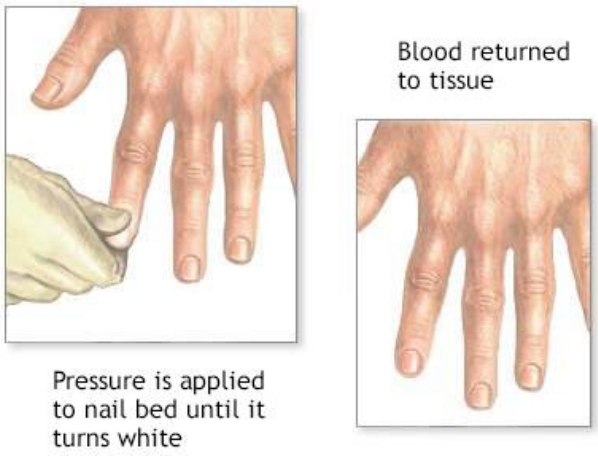
- This is essential for comatose patients and cardiotoxicity.

(3) Establish an intravenous line.

(4) Draw blood for routine studies.

(5) Foley's catheter:

- It is placed in the bladder if the patient is seriously ill :
  - (shocked, convulsing or comatose).
- Obtain urine for routine & toxicologic testing and measure hourly urine output.



Disability

1) Neurological Status:

- Once ABC is addressed, the neurological status should be assessed, mainly level of consciousness; pupils and random blood sugar (RBS).

2) Level of Consciousness:

Stupor	▪ It is a grade of unconsciousness in which the patient can be aroused (awakened) only by painful stimuli .
Coma	▪ It is a state of prolonged unconsciousness in which the patient cannot be aroused by painful stimuli.

3) AVPU Scale: evaluate Consciousness level

	A	Awake and Alert
	V	Respond to Verbal stimuli
Stupor →	P	Respond to Pain.
Coma →	U	Unresponsive

4) Reed's Classification:

Stage	Conscious level	Pain response	Reflexes	Respiration	Circulation
0	Asleep	Arousable	Intact	Normal	Normal
I	Comatose	Withdrawal	Intact	Normal	Normal
II	Comatose	None	Intact	Normal	Normal
III	Comatose	None	Absent	Normal	Normal
IV	Comatose	None	Absent	Cyanosed	Shock

3) Decontamination

1. Skin decontamination

☒ Indications:

Corrosives	To prevent skin injury
Toxins	▪ Which are readily absorbed through the skin As: - Organophosphates Insecticides, Paraquat, Phenol & Oxalic Acid. ▪ To prevent systemic absorption.

☒ Steps:

1st	Wear protective clothes and gloves
2nd	Remove the patient's contaminated clothing
3rd	➲ Flush exposed areas with copious quantities of tepid water or saline. ▪ For at least 30 minutes. ▪ Use soap for oily substances.

2. Eye decontamination

☒ Indications:

Corrosive & hydrocarbon	That can rapidly **damage the cornea**
Toxins	▪ That are readily skin absorption, can also be absorbed through the conjunctiva.

☒ Steps:

1st	Flush exposed eyes with copious quantities of tepid water or saline for up to 20 min.
2nd	Ophthalmologic consultation in patients with serious injury is required

3. Lungs decontamination

☒ Indications:

Irritating gases & fumes	As chlorine gas
Toxins	▪ That are absorbed through the respiratory tract (Inhalation) as: - CO , Cyanide & Hydrogen Sulphide - Organophosphates Insecticides

☒ Steps:

1st	Ensure adequate respiratory protection for yourself & Other care providers (wear protective mask).
2nd	Remove the victim from exposure to fresh air.
3rd	➲ Care of respiration is started after cleaning the mouth: ▪ Administer humidified O2 (if available) ▪ Assist ventilation (if necessary). ▪ Apply Tracheostomy or ETT (if indicated).

4. GIT Decontamination

(1) Emesis : It Is Currently Abandoned

(2) Cathartics.

(3) Gastric Lavage.

(4) Whole Bowel Irrigation.

(5) Activated Charcoal (Local Antidote).

Cathartics

Def	▪ Cathartics are **substances that enhance the passage of materials through the GIT** thus ↓↓ the time of contact between the poison & the absorptive surface of the stomach and intestine

☒ Types:

	Osmotic	Irritant
Examples	**Magnesium Sulfate & Sorbitol**	**Castor oil**
Mechanism	These are substances that ↑↑ the osmotic pressure in the intestinal lumen, thus causing fluid to be drawn into the lumen causing evacuation.	• They act by stimulation of motility • **Continuations**: in fat soluble toxic substances because they ↑↑ their absorption. As yellow phosphorus, CCl4 & chlorinated insecticides.
Dose	1-2 g/kg "Sorbitol"	60-100ml

☒ Contraindications:

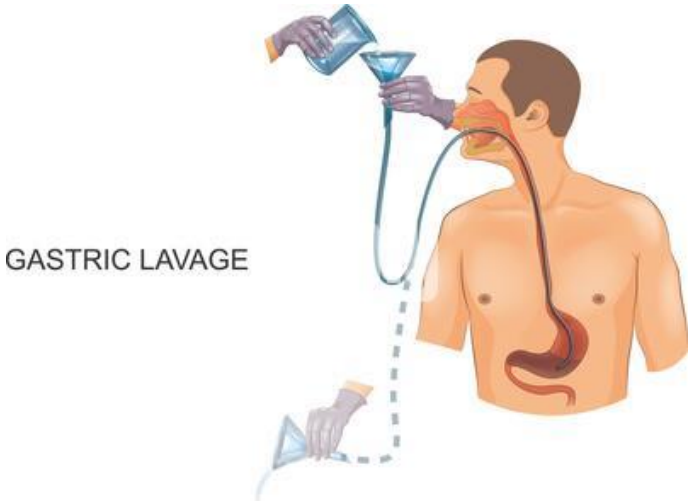
1. GIT hemorrhage.
2. Recent bowel surgery.
3. Intestinal obstruction and ileus.
4. Renal failure for risk of magnesium load.

☒ Complications:

1. Dehydration particularly in children & elderly.
2. Electrolyte imbalance.

Gastric lavage

Indications	▪ A significant amount of Ingested Toxic Substance Within 1 Hour ▪ It is usually used for extremely toxic substances. ▪ When patient is unable to protect their own airway, intubate before proceeding.
Procedure	▪ Place large bore orogastric or nasogastric tube. ▪ Confirm placement.
Contraindication	▪ In cases of CORROSIVES, sharp objects, large pills.



Whole bowel irrigation

Technique	▪ Using a gastric tube, give a surgical bowel-cleansing solution containing a non-absorbable polyethylene glycol until rectal effluent is clear.
Indications	▪ **Ingestion of large dose of iron or lithium** or "Other drugs poorly adsorbed to activated charcoal" ▪ **Ingestion of Large amount of sustained release** or **enteric coated tablets.** ▪ **Ingestion of foreign bodies** or drug filled packets or condoms..

Contra-indications	▪ Ileus or intestinal obstruction. ▪ Comatose or convulsing patient unless the airway is protected by endotracheal tube.
Side effects	Nausea - regurgitation - pulmonary aspiration

Activated charcoal (AC) مهم ويعتبر البطل

Mechanism	▪ Almost irreversibly adsorbs drugs & chemicals, preventing absorption
Indication	▪ Consider for all significant toxic ingestions; except poorly binds substances "**PGAIS**"
Dose	▪ Give **50 g (adults)** or **1 g/kg (children)** as a single oral dose placed in a cup for self-administration. ▪ Prepared with a ratio 1:4 charcoal to water →→ Goal is to have a charcoal to toxin ratio > 10:1 ▪ Mixing with ice cream improves palatability for children. ▪ In the intubated patient, AC may be given via **oro- or nasogastric tube**.

☒ **Contraindications:** Substances **NOT** adsorbable by activated charcoal (**PHAILS**)

P	**P**esticides - **P**otassium.
H	**H**ydrocarbons.
A	**A**cids - **A**lkali "Poor binding and makes endoscopy difficult" & **A**lcohols.
I	**I**ron & **I**nsecticides.
L	**L**ithium
S	**S**olvents

4) Enhanced Elimination

☒ Principles:

- It is used in drug intoxication when the renal route is a main route to its total clearance.
- Forced diuresis may ↑↑ glomerular filtration rate & ion trapping by urinary pH manipulation may enhance elimination of polar drugs.
- It is used in case of **healthy kidney**.

☒ Types:

1. Urinary Manipulation
2. Hemodialysis
3. Hemoperfusion
4. Hemofiltration
5. Peritoneal Dialysis
6. Repeated Dose Activated Charcoal (Gut Dialysis)

Urinary Manipulation

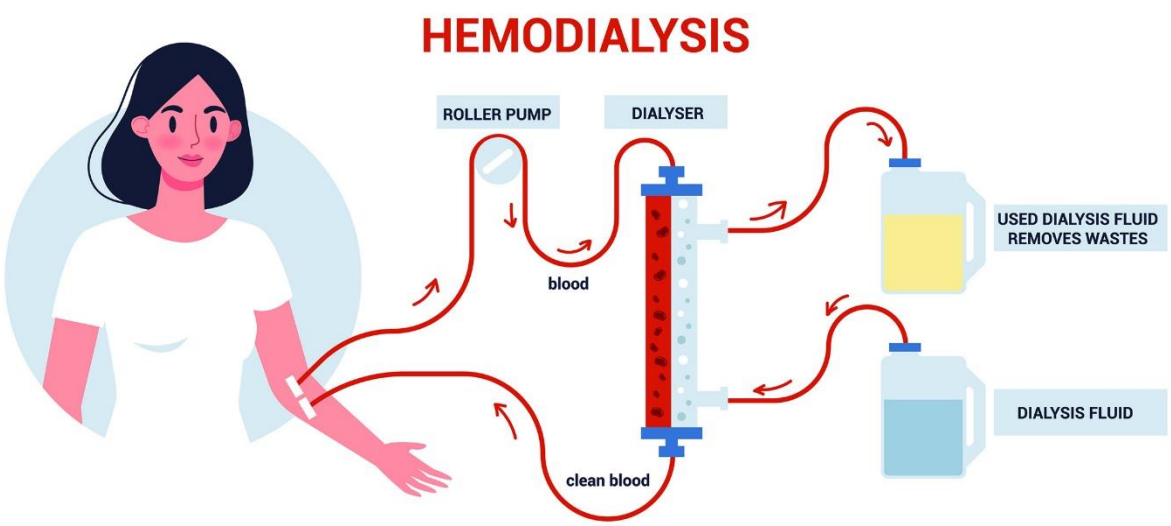
Urinary alkalization	○ It is commonly used for: - Salicylate overdose, - Isoniazid, - Phenobarbitone, - Methanol & methotrexate ○ But forced diuresis is generally not used because of the risk of fluid overload.
Urinary acidification	○ By using **ammonium chloride** has previously been used to enhance excretion of weakly alkaline drugs: - Amphetamine, - Strychnine, - Quinine - phencyclidine

Hemodialysis

Principle	▪ **For dialysis to be effective, toxin must be of:** 1. Small size (molecular weight < 500 Daltons) 2. Highly water soluble 3. Low protein binding 4. Small volume of distribution **(< 2 L/kg).** ▪ This occurs through **semi-permeable** membrane.

☒ Indications: (UNSTABLE)

U	**U**raemia.
N	**N**o response to conventional therapy.
S	**S**alicylates,
T	**T**heophylline
A	**A**lcohols (MethanoL & isopropanol)
B	**B**oric acid, **B**arbiturates,
L	**L**ithium
E	**E**thylene glycol



Hemoperfusion

Principle	○ Because the drug or toxin is in **direct contact** with the adsorbent material, drug size, water solubility and protein binding are not important limiting factors in cases of haemofilteration procedure
Indications:	○ **Substances have a great benefit for clearance by Haemoperfusion:** - Carbamazepine, Barbiturates & Theophylline.

Advantages	Disadvantages
For most drugs, hemoperfusion can achieve greater clearance rates than hemodialysis.	1. Systemic anticoagulation is required, often in higher doses than for hemodialysis. 2. **Thrombocytopenia** is a common complication.

Hemofiltration

Principle	It can remove compounds with **large molecular weight** through porous membrane.
Indications	It is used in aminoglycoside, theophylline, iron and lithium overdoses
N.B	Substances NOT amenable to significant extracorporeal removal include: 1. Benzodiazepines - Tricyclic Compounds - Phenothiazines, 2. Chlordiazepoxide - Dextropropoxyphene

Peritoneal Dialysis

Advantages	Disadvantages
○ It is easier to perform than hemodialysis or hemoperfusion ○ It does not require anticoagulant.	○ However, it can be performed continuously, 24 hours a day, 24-hour peritoneal dialysis with dialysate exchange every 1-2 hours is **approximately equal to four hours of haemodialysis.**

Repeated Dose Activated Charcoal (Gut Dialysis)

Indication	○ It will help **clear enterohepatic circulation of some drugs**: (Phenobarbital – Theophylline – Carbamazepine – Dapsone – Digitoxin – Phenytoin – Phenylbutazone – Salicylates - Quinine - Paraquat)
Dose	▪ Give 1 gm/Kg od AC as 1st dose & 0.5 gm/kg of AC /2 hours as repeated doses. ▪ Give cathartics as sorbitol with first dose of charcoal to prevent constipation, but cathartics should not be used repetitively "only single dose" as they will cause fluid and electrolytes disturbances. ▪ **Check**: bowel sound & nasogastric aspirate, before given each dose ▪ **Clinical reassessment** & taken end point decision for MDAC, every 6 hours
Route	It is given **orally or via gastric tube**.

5) Antidotes

☒ Types:

1) **Antagonist**
2) **Competitors**
3) **Chelators**
4) **Inactivators**

➲ Antagonist:

Principle	Substance which antagonizes the action of the poison
Examples	1. Atropine antagonizes the muscarinic action of the organophosphate 2. Pilocarpine antagonizes the peripheral action of atropine.

➲ Competitors:

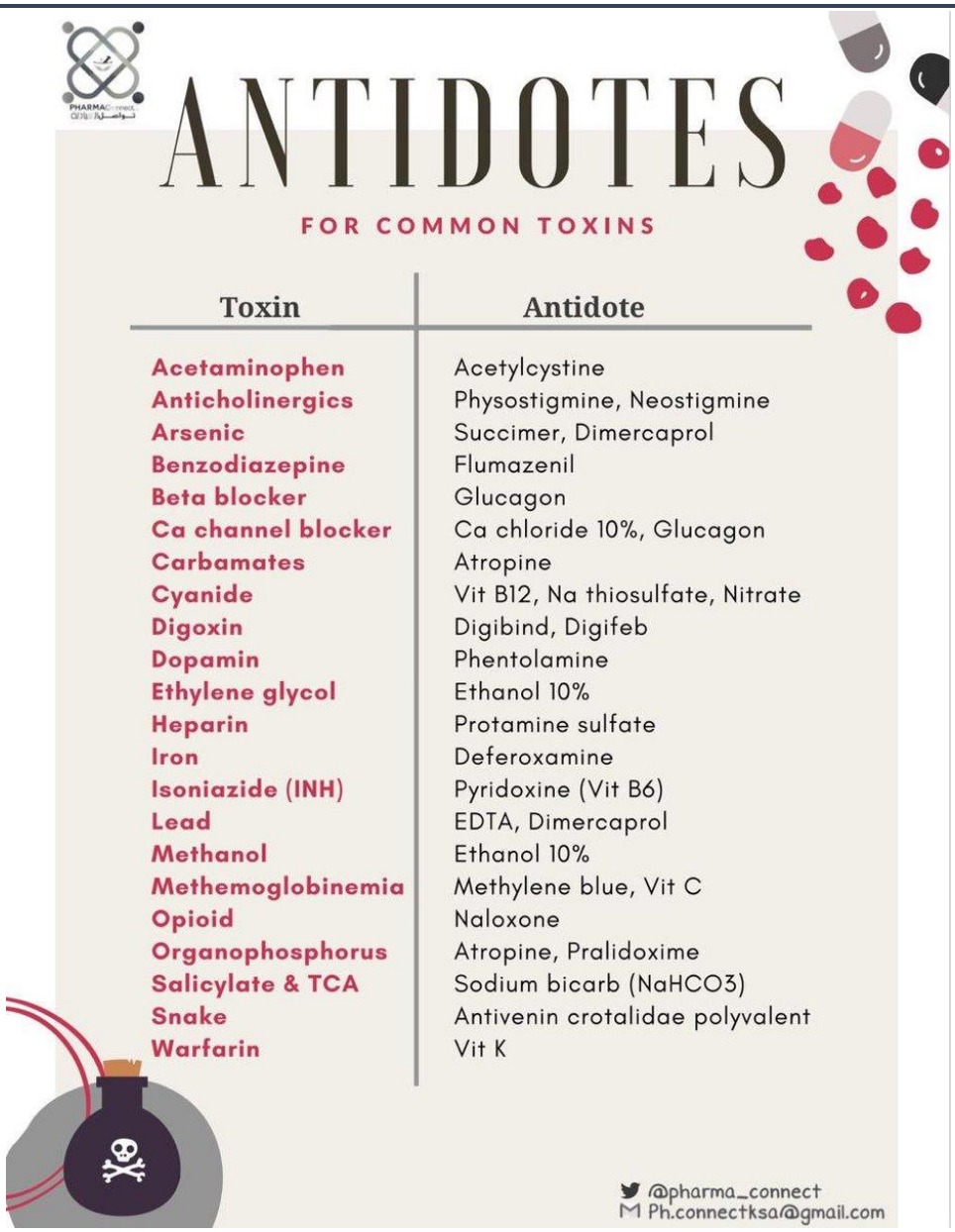
Principle	▪ A substance which competes with the poisons at the sites of their action preventing them from exerting their effects. ▪ They are characterized by having similar chemical formula to the poison.	
Examples	Narcotic antidotes	1. Naloxone (Narcan, N-allyl oxymorphine): • It acts as a pure antagonist. • It is potent with no depressant action on CNS. • It provides both a therapeutic & diagnostic modality for opioid poisonings. 2. Nalmefene (Revex): It acts as a pure antagonist. 3. Nallorphine (N-allyl morphine, lethidrone): . It acts as agonist-antagonist
	Ethyl alcohol	• It is the antidote for **methanol poisoning**. • It competes with the enzyme alcohol dehydrogenase, so methanol doses do not change into toxic formaldehyde & formic acid.

➲ Chelators:

Principle	A substance which unites with the absorbed poison forming soluble less toxic and easily excreted complex.
Examples	All antidotes of heavy metals are chelators

➲ Inactivators:

Principle	A substance which **unites with the poison to form non-toxic complex**
Examples	Hydroxocobalamin (Vit. B12a): • It unites with cyanide forming cyanocobalamin (Vit. B12).



Summary of Antidotes

MCQ + Case مهم وموضع

Poison	Antidote (S)
Acetaminophen	N-Acetylcysteine (Mucomyst).
Anticholinergics.	Physostigmine "Caution: may cause seizures, asystole, cholinergic crisis".
Organophosphates (Anticholinesterases)	Atropine - Pralidoxime
Carbamates (Anticholinesterases)	Atropine
Benzodiazepines.	Flumazenil
Beta- blockers.	Glucagon
Calcium channel blockers	Calcium chloride - Glucagon.
Carbon monoxide	Oxygen - Hyperbaric O2 in severe cases.
Digitalis.	Fab antibodies (Digi-bind).
Heavy metals	BAL (dimercaprol) – EDTA – Penicillamine – DMSA - Unithiol - DMPS
Iron	Deferoxamine.
Methanol & Ethylene glycol	Ethanol – Folate - Fomepizole.
Methemoglobinemia agents	Methylene blue
Opioids	Naloxone.
Warfarin & super warfarin	Vit. K.

One pill can kill in children

Def	Drugs with potential for severe toxicity if one or two tablets ingested by a 10-kg toddler

☒ **Types:**

1. **Beta blockers** e.g.: Propranolol
2. **Tricyclic antidepressants.**
3. **Diphenoxylate/Atropine.**
4. **Calcium channel blockers** e.g.: verapamil, diltiazem
5. **Theophylline SR.**
6. **Sulfonylureas.**
7. **Recreational sympathomimetic drugs** e.g.: amphetamines and ecstasy
8. **Opiates** e.g.: Methadone, Morphine & Oxycodone

Indications for ICU Admission

➲ For All Patients Who **Present with Poisoning** or **Potential Exposure to A Toxic Substance**

Neurological	▪ Toxin-induced seizures ▪ Unresponsiveness to verbal stimuli or Glasgow coma scale score <12.
Cardiac	▪ Cardiac arrhythmias. ▪ **Second- or third**-degree atrioventricular block. ▪ QRS duration > 0.12 s. ▪ Systolic BP <80 mm Hg. ▪ Anticholinergic cardiac toxicity.
Respiratory	▪ PaCO2 > 45 mm Hg. ▪ Need for endotracheal intubation
Metabolic & electrolytes	▪ Progressive metabolic acidosis. ▪ Electrolytes imbalance, especially severe hyperkalemia. ▪ **Management lines:** 1. Need for emergency dialysis or hemoperfusion. 2. Wide alterations in body temperature. 3. Antidotal therapy as naloxone, antivenin & antibotulinum abs


DEATH

DEATH

Def	The irreversible cessation of life and it is a process not an event.

☒ Phases of death:

1. 1st Phase: Somatic Death (Clinical Death)
2. 2nd Phase: Molecular Death (Cellular Death)

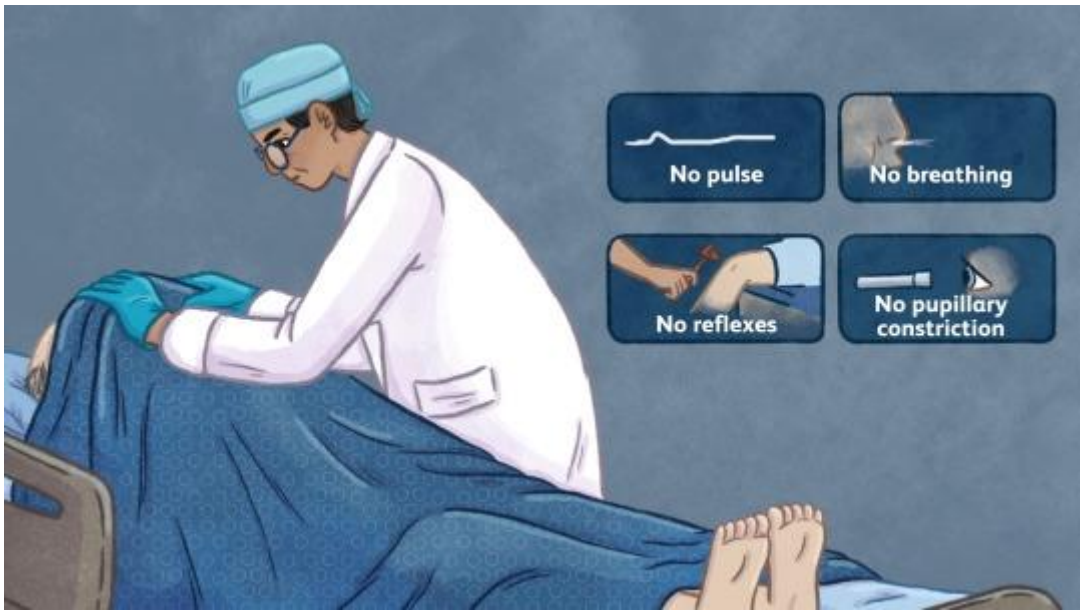
مهم نعرف الفرق بين somatic death وال cellular death وال

1st Phase: Somatic Death (Clinical Death)

Def	Complete & irreversible cessation of the vital functions of the brain, heart and lungs (**the tripod of life**)	
Characters	○ Tissues & cells continue to survive for variable periods of time, depending **upon their oxygen requirements.** ○ **After somatic death,** - The tissues and cells can respond to chemical & electrical stimuli, - The pupils also dilate and constrict. - Organs can be removed during this "**physiological gap**" from the cadavers for the transplantation.	
Diagnosis "3 facts"	**Cessation of heart beating:**	Absent heart sounds for a continuous period of 5- 10 minutes as well as flat ECG for a same period is accepted as evidence of death.
	Cessation of breathing:	Absent breath sounds
	Cessation of brain activity:	× Dilated fixed pupils and absence of pupillary and × corneal reflexes. × A flat Electroencephalogram (EEG) would confirm it.
Simulating Conditions مهم	1) Apparent death/suspended animation. 2) Coma following excess dose of sedatives or hypnotics. 3) Hypothermia in old age.	

2nd Phase: Molecular Death (Cellular Death)

Def	It is the **ultimate death** of all cellular elements
Characters	○ After somatic death, various tissues survive as long as oxygen supply to them is adequate. When the oxygen gets depleted, cellular death sets in. ○ Generally, it is completed within **2 to 4 hours of somatic death** and can be confirmed by absence of any response to an electrical, thermal or chemical stimulus in the tissues. ○ It is reported that **nervous tissue** dies rapidly (i.e. the vital centers of brain die in **about 5 minutes**), while the muscle tissue lives up to 3 to 4 hours after cessation of circulation.



☒ Medicolegal Importance (M.L.I.) of Distinction () Somatic& Molecular Death:

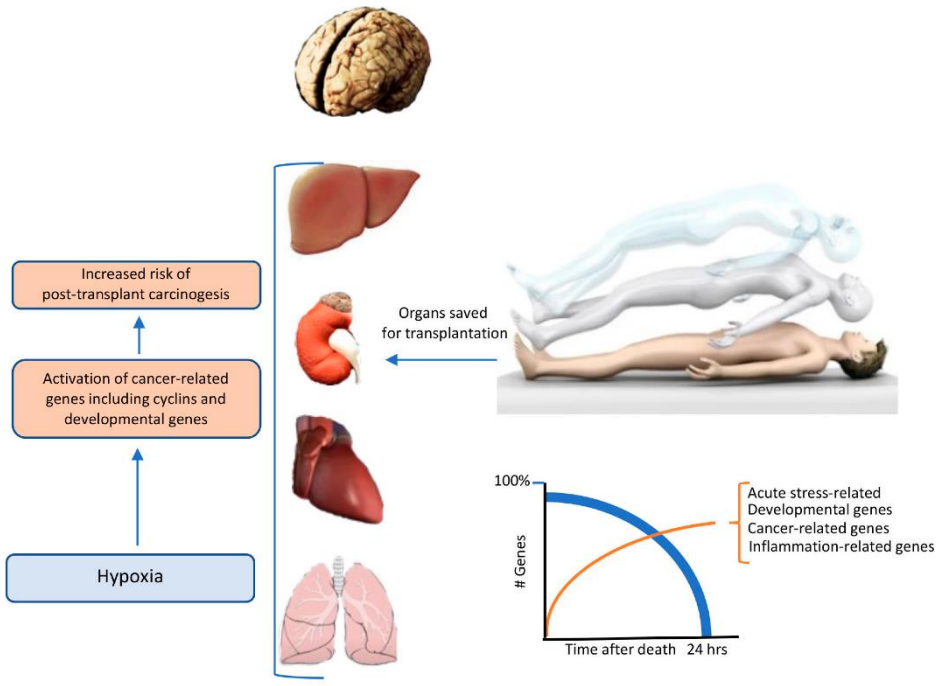
Premature Burial	○ **Prevent premature burial in cases of apparent death:** - Dead body is not transferred to the postmortem room unless **4 hours** have passed since somatic death. - Also, burial is not allowed before **8- 10 hours**.
Organ Transplantation	○ **The viability of the transplantable organs falls sharply after somatic death.:** • The liver within **15 minutes**, • The kidney within **45 minutes** • The heart within **one hour**.
Some cases of inheritance	○ When a family or more than one member of the family **dies in the same accident,** - The question is **who died first**? to know who will inherit the other.

☒ Signs of Death:

Immediate Changes (**Somatic Death**)	Early Changes (**Molecular Death**)
1) Insensibility & Loss of Voluntary Power. 2) Irreversible Cessation of Circulation & Respiration. 3) Brain/Brainstem Death 4) Cerebral/Cortical Death	1) Changes in the skin & facial pallor 2) Primary flaccidity 3) Contact flattening. 4) Ocular signs

Cerebral/Cortical Death

Characters	**In cortical death**,: ○ Brainstem is intact, ○ With continuous heart sounds and respiration ○ No muscular movement with **generalized flaccidity**. **Severe brain damage:** ○ Which does not involve the brainstem, may result in: A **persistent vegetative state** "Living Cadaver", **These patients:** 1. Breathe spontaneously, 2. Open and close their eyes, 3. Swallow, 4. Make facial grimaces 5. Have a preserved sleep-wake cycle. 6. However, they show no behavioral evidence of awareness (the patient does not speak or obey commands). **Flat EEG** alone should never be taken as conclusive evidence of death.
Diagnosis	The three cardinal findings in brain death are coma, absence of brainstem reflexes and apnea.



Brain Stem Death

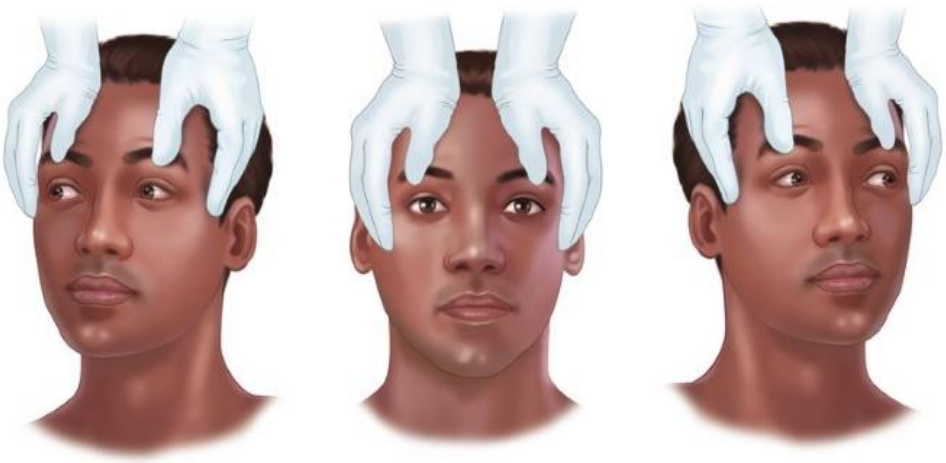
Characters	○ **Brain death is now accepted as brainstem death**. " The respiratory center and the reticular formation lie within the brainstem" ○ If these areas are dead→ the person is unable to breathe spontaneously or regain consciousness.

Diagnosis:

- **Brainstem reflexes test the function of the cranial nerves** which pass through the brain stem.
- If there is no response to these tests, the brain stem is considered to be irreversibly dead.

Examples of absence of brainstem reflexes:

1. Loss of pupillary reflex	No response of pupils to bright light
2. Loss oculocephalic reflex:	No ocular movement with head movement (**Doll's eye phenomenon**).
3. Loss of corneal reflex:	No blinking eye with corneal touch by a cotton swap "**No Facial sensation**"
4. Loss gag reflex:	No response after stimulation of posterior pharynx with tongue blade "**Pharyngeal reflexes absent**"



Exclusion Criteria:

- Certain prerequisites to be fulfilled before certifying brain stem death
- **Exclusion of the following reversible conditions is mandatory**:

1) Hypothermia.
2) Severe electrolyte, acid-base or endocrine abnormalities.
3) Drug intoxication: sedation, neuromuscular blockade or CNS depressant drugs.
4) Hypoxia, hypotension and shock.
5) Other conditions:

   Brainstem encephalitis - encephalopathies associated with hepatic failure, uremia and hyperosmolar coma of diabetes mellitus.

Whole Brain Death

- It is a combination of both cortical and brain stem death.
- This has allowed **the feasibility of removal of vital organs** such as the heart, kidney, liver, etc. from a donor body for the purpose of organ transplantation successfully **without any ethical or legal complications**.

Time of Death

- **Def**: the time at which brainstem death is established.
- This **does not coincide** with time when ventilator is switched off or heart stops.
- A physician should emphasize this fact to the relatives.
- He should clearly tell that ventilator is **not** withdrawn to let the patient die as the patient is already dead.
- So, **the modern concept of moment of death is brain death**

Organ Transplantation

- It's now - after established brain stem death- possible to harvest from a cadaver the eyes, kidneys, liver, pancreas, small intestine, lungs and heart.
- **The cornea of the eye** may still be suitable for transplant **up to 24 hours after death**.

Early Changes (Molecular Death)

Changes in the skin & facial pallor

Skin becomes pale	Due to stoppage of circulation & drainage of blood from the capillaries and the small vessels
The skin loses its elasticity & the face looks younger	Due to loss of creases
The lips appear brownish, dry and hard	Due to drying

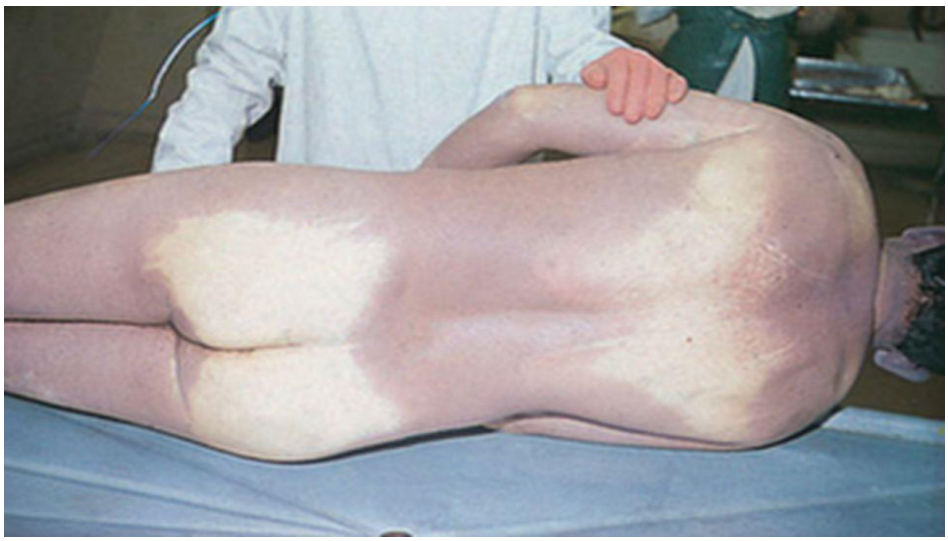
Primary flaccidity

Duration	It occurs immediately after death and ends after 2 hours in winter
Cause	• All muscles of the body lose their tonicity & become flaccid (complete relaxation) as the control from higher brain centers is lost. • Though, muscles are physically capable of responding to electrical & mechanical stimuli.
Changes	During this phase: - Jaw drops, - Pupils dilate, - limbs fall flat, - Thorax collapses, - Sphincters relax & there may be involuntary passage of urine & faeces.

Contact flattening

➲ **Def**: The areas which remain in contact with the ground **become flat & the blood from vessels of these areas is pressed out**, this continues even after the formation of postmortem staining over the surrounding areas.

➲ **For example**: flattening of the convex parts of the body (e.g., buttocks, calves, etc.) when the cadaver lies on its back.



Ocular signs

Loss of corneal reflex	It may be seen in all cases of deep coma & is **not a reliable sign**.	
Pupils	First	The pupils are **dilated**, due to the relaxation of muscles of the iris.
	later	Pupils are **constricted** with the onset of rigor mortis of the constrictor muscles. (In narcotic poisoning, pupils remain constricted).
Loss of intraocular tension	1. Intraocular tension falls rapidly after death. 2. It becomes **zero** in 4-8 h (10-22 mm Hg during life). 3. The eyeballs look sunken in the orbit.	

Suspended Animation (Apparent Death)

Def	○ It is a **death like state** in which vital signs of life (heart beat & respiration) are not detected by routine clinical methods as the functions are reduced to a minimum compatible with life.
Duration	It lasts for seconds to hours.
MLI	1) The patient can be resuscitated by cardiac massage or electric stimulator and artificial respiration. 2) The death certificate should not be issued without an ECG or EEG record.

➲ Types:

1) **Voluntary**: Seen in **practitioners of yoga**
2) **Involuntary**: Seen in:

- Freezing of body,
- Newborns,
- Electrocution,
- Heatstroke,
- Shock
- Poisoning with barbiturates or opiates,
- Drowning,
- Epilepsy,
- Post anesthesia,
- Cerebral concussion

Euthanasia

Eu = good , Thanatos = death.

It means "good death" or to "die well", with the basic theme of 'mercy killing".

Def	○ The **intentional killing** by act or omission of a dependent human being for his or her alleged benefit. ○ **In Egypt**, there is no legislation permitting euthanasia.

➲ Types:

Euthanasia by Action (active)	Euthanasia by Omission (passive)
• It is intentionally causing death by performing an action such as by **giving a lethal injection.**	• It is intentionally causing death by **not providing necessary and ordinary care** or food and water

➲ Indications of Euthanasia:

1) Unbearable pain (Euthanasia relieves suffering).
2) The patients' condition is terminal with no hope of recovery

Sudden Natural Death

Def	o It is unexpected death of an **apparently healthy person.** o WHO defines it as: "sudden death that occurs **within 24 h** from onset of symptoms".
Causes	The most common causes are **cardiovascular as coronary artery disease**

➲ M.L.I.:

1) The medicolegal expert should perform a thorough postmortem examination to exclude violence & poisons & to prove that death is due to natural causes (diseases).
2) An autopsy is necessary

POSTMORTEM CHANGES

POSTMORTEM CHANGES

☒ Postmortem Changes include:

1. **Cooling of the body**
2. **Postmortem Hypostasis (Lividity or Livor-Mortis)**
3. **Postmortem Rigidity or Rigor Mortis (Stiffness of Death)**
4. **Putrefaction or Decomposition**

1) Cooling of the body ≠ hypothermia

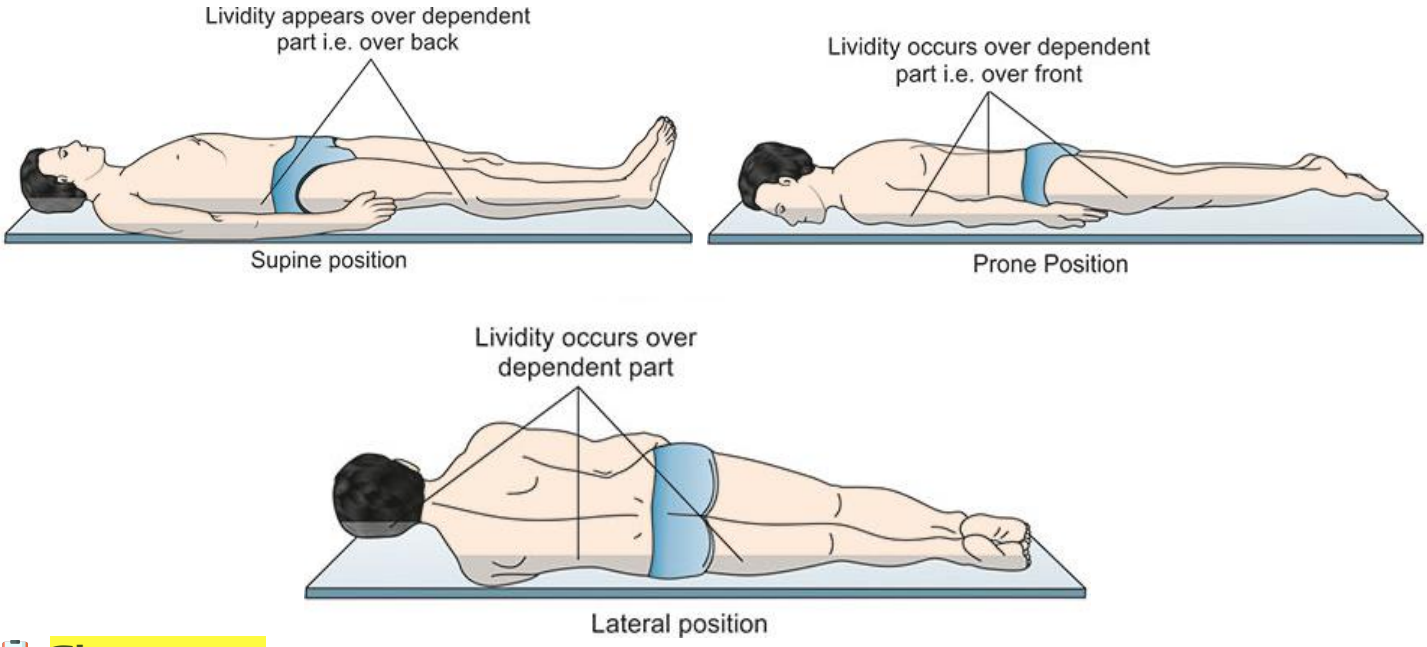
Def	Gradual cooling of the dead body until it comes in **equilibrium** with surrounding temperature.	
Mechanism	○ **During life**, there is balance between heat production & heat loss. ○ **After death**, heat production **stops** & the body loses heat.	
Rate	○ The average rate of heat loss is about **1-1.5^0 C/h** & the rate of cooling is not uniform. ○ Dead body attains environmental temperature "external surface cooling" in about **16-20hs** from death.	
Factors modifying rate of cooling	Environmental temperature (Major factor)	• The dead body cools rapidly when the difference between the environmental temperature and that of the corpses is **great as in the winter**.
	Media of disposal	• In case of **drowning in running** water, the rate of heat loss is double that in the air (**2-3^0 C /h**).
	Mode & cause of death:	• Slow cooling occurs in deaths due to infectious diseases or heat stroke (fever). • Rapid cooling occurs in deaths due to long wasting illness as T.B or shock.
M.L.:	1. It is a sign of death. 2. It helps in rough estimation of the time of death.	

2) Postmortem Hypostasis "Lividity" or "Livor-Mortis "

Def	➲ It is bluish or purplish discoloration or staining of **the most dependent parts of the body** skin and internal organs after death. ➲ It is called "**Postmortem staining**" or "**Darkening of death**".

Mechanism:

- It is due to **loss of the pumping action of the heart and cessation of circulation**, causing gravitational settling of blood in the toneless capillaries & venules of the dependent parts of the dead body
- Causing capillaro-venous distension and staining the dependent parts of the dead body with the **same color of the blood**

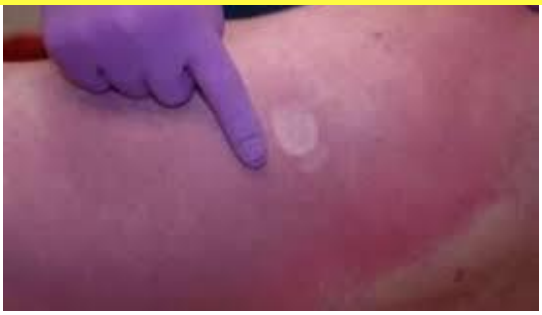


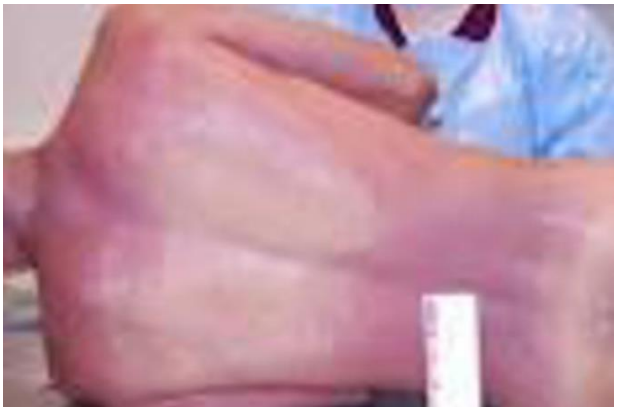
Characters:

Onset	Usually begins **immediately** after death
Shape	✖ It begins as small, mottled patches on the dependent parts of the body within 1-3 hs. → Mottled patches coalesce with each other to form uniformly stained large areas
Color	Has the **same color as blood** that can **be mistaken for bruises**

Blanching	× When lividity is still developing, pressing finger against the skin for a few seconds will cause blanching of lividity. × When the pressure is released, lividity will reappear. × If the body changes its position at this stage, all or some hypostasis may slip down to the most dependent areas making dual distribution of hypostasis (**change with position**)
Fixation	× PM staining becomes completely formed and fixed in 8-12 hs and persists until putrefaction sets in. × At this stage, lividity does not disappear if finger is firmly pressed against the skin. × If the position of the body is altered after fixation, the staining will not be changed.(**doesn't change with position**)
Absence	× Hypostasis **does not develop over areas of contact flattening**; - this phenomenon is known as **contact pallor** as vessels in these areas remain pressurized and the blood is compressed out.

MCQ مهم : Which of the following cases is characterized by absence of hypostasis?
A) Drowning in running water





M.L.I.:

1) **Sign of death**:

- A sure sign of death " **it is one of the best proofs for somatic death** "

2) **Time passed since death**:

- It helps to estimate the time passed since death from the formation, extension and fixation of the postmortem staining.
- There is **early onset** hypostasis in case of a person who died after prolonged recumbent position

3) Cause of death:

From its position	**In hanging**	- hypostasis is observed over the dependent lower limbs, the external genitalia & the distal parts of the forearms & hands.
	In drowning	- Hypostasis is observed on the face and the upper part of the chest, hands and lower arms as they are the dependent parts. - If the body is constantly changing its position as in case of drowning in moving water, **lividity may not develop.**
From its color	Bluish purple	In **natural death**.
	Very faint	In deaths from **haemorrhage** or severe **anemia**.
	Deep blue	In **asphyxia**.
	Red	In cases of **CO poisoning**

Differential Diagnosis:

- In certain cases, isolated patches of lividity remain separate from the large areas of lividity and may resemble **antemortem bruises**.

	Postmortem Lividity	Antemortem Bruises
Site	On the dependent parts.	Anywhere at the site of trauma.
Color	**Uniform** colour "according to cause of death".	**Different** colours
Margin	Merges with the surrounding area	**Clear & define**
Swelling	**No** swelling	Swelling of the affected area
Abrasions	**No** abrasions.	May be present

3) Postmortem Rigidity or "Rigor Mortis " "Stiffness of Death "

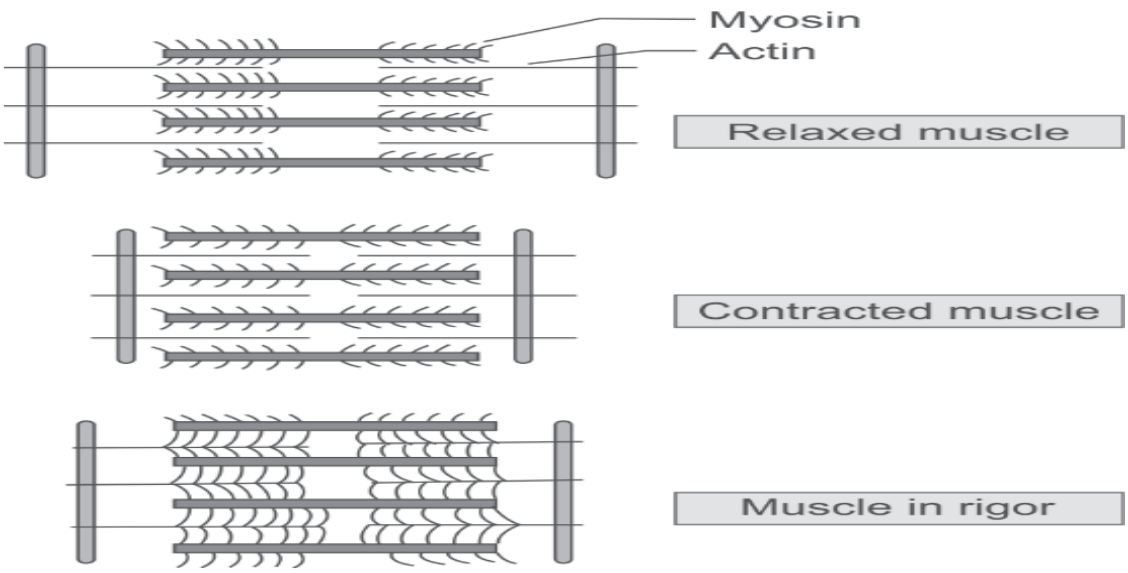
Rigor Mortis ≠ contraction

Def	➲ It is a condition of progressive stiffening and rigidity of **both voluntary & involuntary muscles**, ➲ **Preceded by** period of primary flaccidity. ➲ **Followed by** secondary flaccidity. **Primary flaccidity → Rigor Mortis → secondary flaccidity**

Mechanism:

- It is due to chemical changes involving proteins of the muscle fibers (Actin & Myosin)
- After death, ATP which is the principal factor concerned in the process of contraction & relaxation of the muscles is re **synthesized for a short time, depending on the glycogen stores.**
- **But after this glycogen is depleted,** ATP "required for active muscular relaxation" cannot be resynthesized
- It persists till autolysis of actin & myosin filaments occurs during the stage of **secondary flaccidity due to putrefaction**.

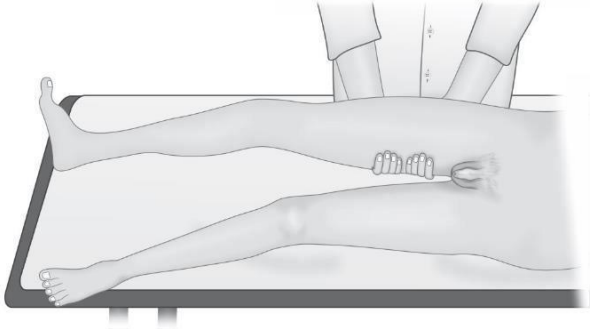
MCQ : A body is found with the upper half flaccid and the lower half stiff. This condition indicates which stage of postmortem muscle change?
A) Late stage of rigor mortis



Characters: "according to time "

2 h after death	○ Starts to appear in **the small muscles then spreads from above downwards.** ○ **Muscles affected:** • Firstly, the muscles of the eye lids, then jaw, • Muscles of the face, neck and trunk, • Followed by muscles of the upper limbs & then lower limbs.
12 h after death	○ Completed all over the body "**Fixed body**".
48 h after death	○ **Disappears completely** in about 36-48 hours after death. ○ The rigid muscles start to soften gradually in the same order of their occurrence (from above downwards)

How to test Rigor Mortis ???



× **It is tested by:**

- lifting the eyelids,
- Depressing the jaw,
- Gently bending the neck & joints of all four limbs.

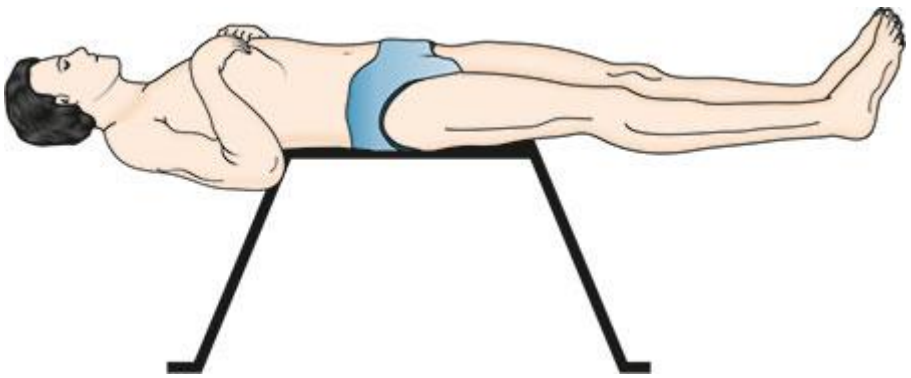
× Feeling of lower or higher **degree of resistance** is usually interpreted as rigor mortis.

Factors Affecting: depends upon rate of ATP depletion:

Temperature	In cold weather, its **onset is slow** with prolonged duration	
Age & condition of the body	**Infants & old people with weak musculature**	**Athletes with strong musculature**
	Rapid onset with short duration	**Slow onset** with long duration
Muscular activity before death	**Very rapid onset** in deaths from convulsions or after severe muscular exertion.	

M.L.I.:

1) Helps to estimate the time passed since death by **marching of rigor**.
2) Can give information about the **position** of the body at the time of death.



Cadaveric Spasm

Def	It is stiffening of **specific group of the voluntary muscles**, immediately after death, without being preceded by the stage of primary flaccidity.
Site	It is usually limited to a **single group** of voluntary muscles & frequently involves the hands

Examples:

➲ This condition occurs in cases of **extreme nervous tension** such as:

Suicidal cases	Accidental cases	Homicidal cases
The weapon used in suicide may be found firmly grasped by the cadaveric spasm of the hand muscles.	As in drowning, where **aquatic weeds, mud or sand** may be found firmly grasped in the victim's hand.	During struggle, the hand of the victim **may grasp hair, button, & piece of clothes** belonging to the assailant.

Differential Diagnosis:

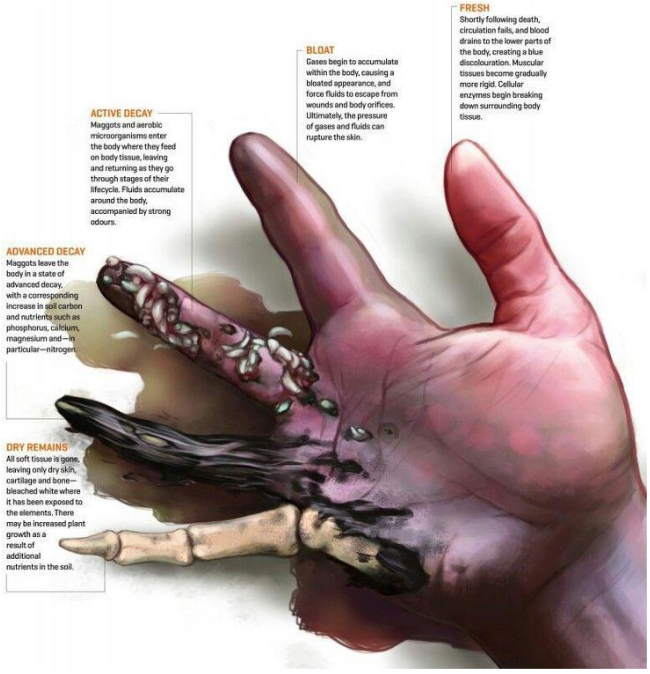
	Rigor mortis	Cadaveric Spasm
Occurrence	In all deaths	In some cases, & certain conditions.
Primary flaccidity	It is preceded by primary flaccidity	**Absent**
Onset	**2 hours** after death	**At the moment** of death
Muscles	Both voluntary & involuntary	Certain group of voluntary muscles
Cause	Due to chemical changes in the protein of the muscles.	The exact mechanism is not yet known but need certain conditions.

4) Putrefaction or Decomposition

Def	It is a **biological process** caused by growth of bacteria on the organic matter of the dead body transforming it into inorganic state.

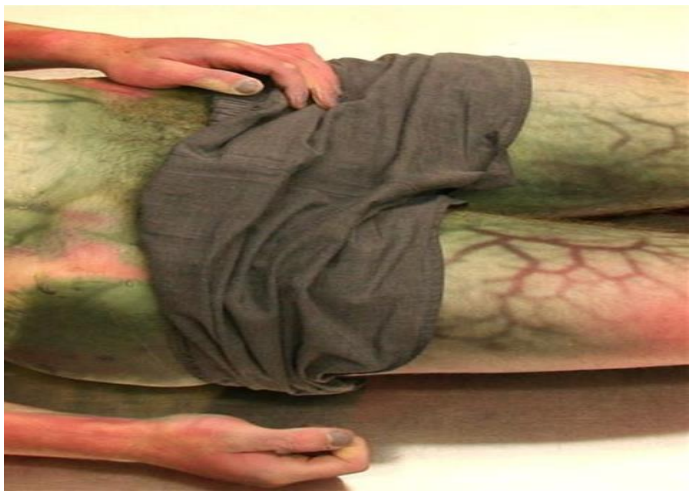
Mechanism: Putrefaction is caused by two processes:

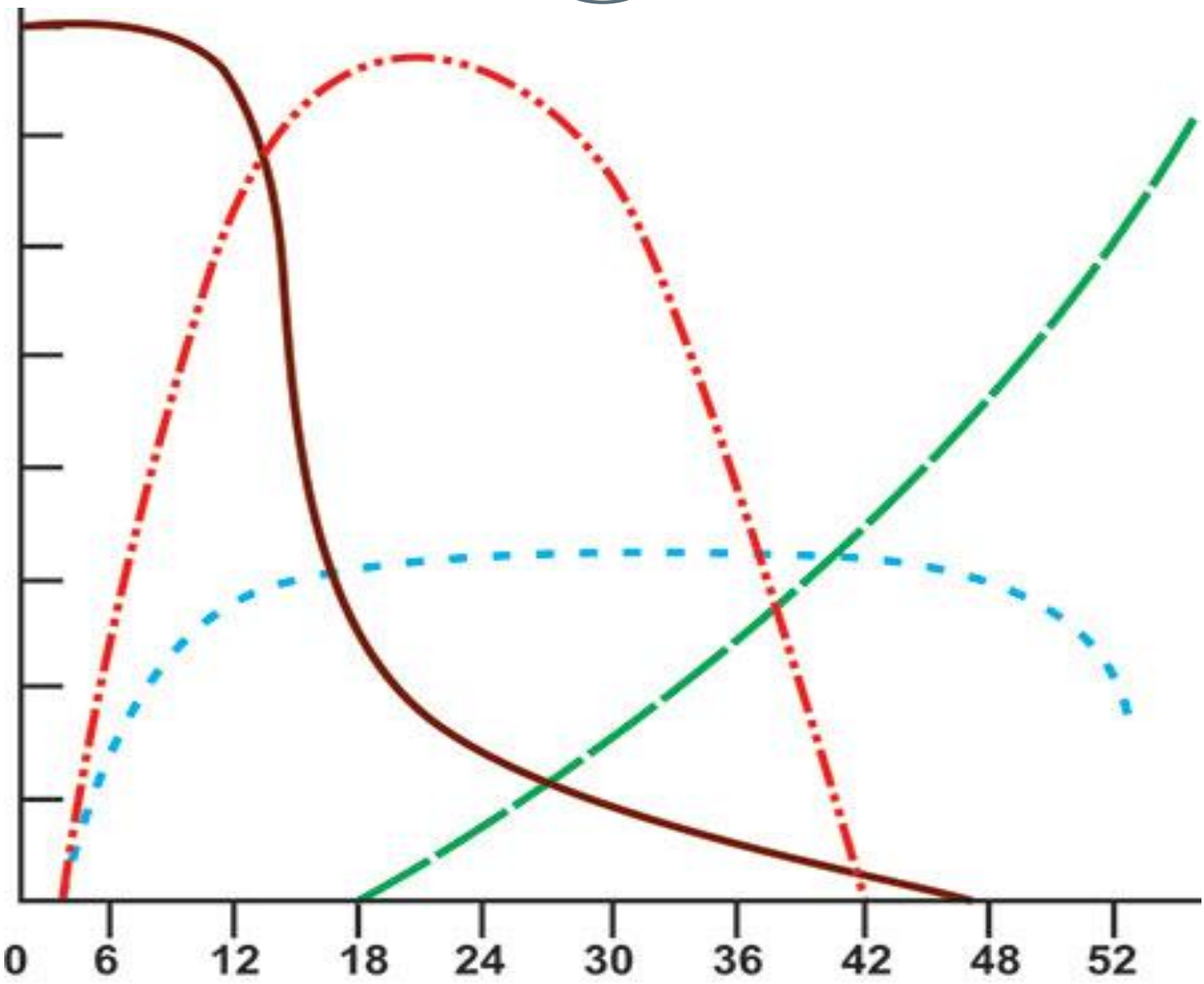
Autolysis effect:	○ Immediately after death, cell **membranes become permeable** and breakdown, releasing cytoplasm containing enzymes causing auto-digestion.
Bacterial effect:	○ The anaerobic gas-forming organisms mostly Clostridium Welchii present in large intestine, aided by aerobic bacteria, invade the tissues & blood ↓ 1. Softening & liquefaction of the tissues, 2. Hemolysis of blood 3. Gas formation.



Characters:

Onset	After 24 h after death in summer and 48hs in winter	
External Signs (3 D')	Discoloration	• The first external sign of decomposition is usually a greenish discoloration "Marpling" over the right iliac fossa over the region of the caecum which lies superficially. • The H2S gas combines with the hemoglobin released from hemolyzed RBCs & forms green sulphmethemoglobin which discolors the surrounding tissue.
	Distension	• **Various gases** produced during decomposition permeate into skin, soft tissue and organs which manifests as **crepitus and distension**.
	Dissolution:	• Progressive decomposition leads to **liquefaction and disappearance** of tissues and organs and eventual skeletonization




0
6
12
18
24
30
36
42
48
52
Postmortem cooling
Postmortem lividity
Putrefaction
Riogor mortis