Clinical toxicology laboratory

5th. stage

By assistant lecturer

Dr. Nibrass Al Abdali

2023 - 2024

كلية الصيدلة
جامعة الفراهيدي
2012 - 1433
Al-Farahidi university

Lab. 1

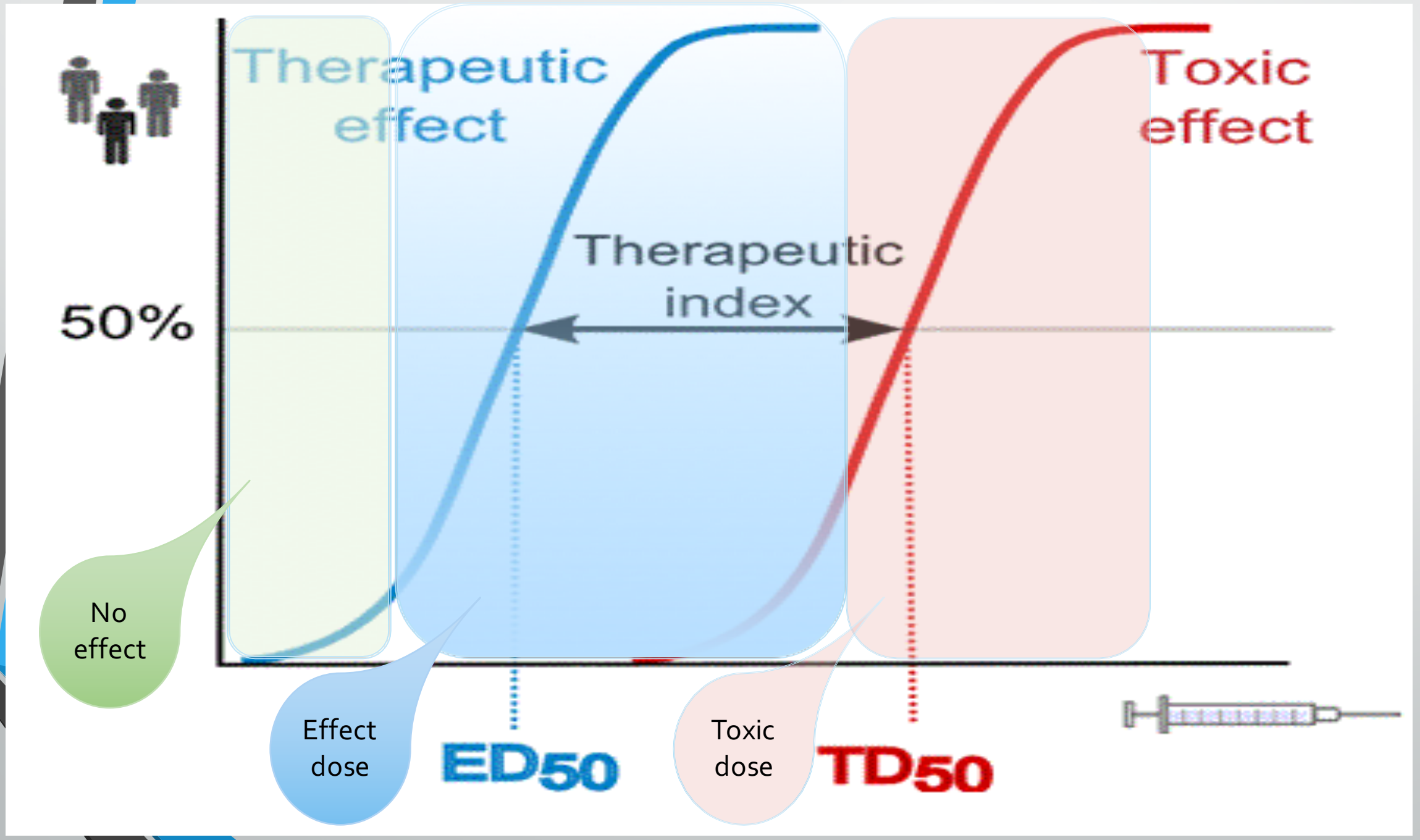
Clinical Toxicology

- Human toxicology deals with the general concern of exposure of humans to xenobiotics and toxic responses elicited.
- Clinical toxicology is a subspecialty of toxicology dealing with the bedside management of poisoned patients, including definitive toxicological diagnosis, assessment of immediate severity and , and selection of treatments including, antidotes.
- General considerations in management of the poisoned patient:

1. Patient: the first priority is the care of the patient.
2. Treatment of patient, no matter what the cause of their in toxicities.

❖ There are two main types of toxicity:

1. Acute toxicity occurs almost immediately (seconds/minutes/hours/days) after an exposure. Its usually occur via a single dose or a series of doses received within a 24-hour period. Death can be a major concern in cases of acute exposures.
2. Chronic toxicity represents cumulative damage to specific organ systems and takes many months or years to become a recognizable clinical disease.

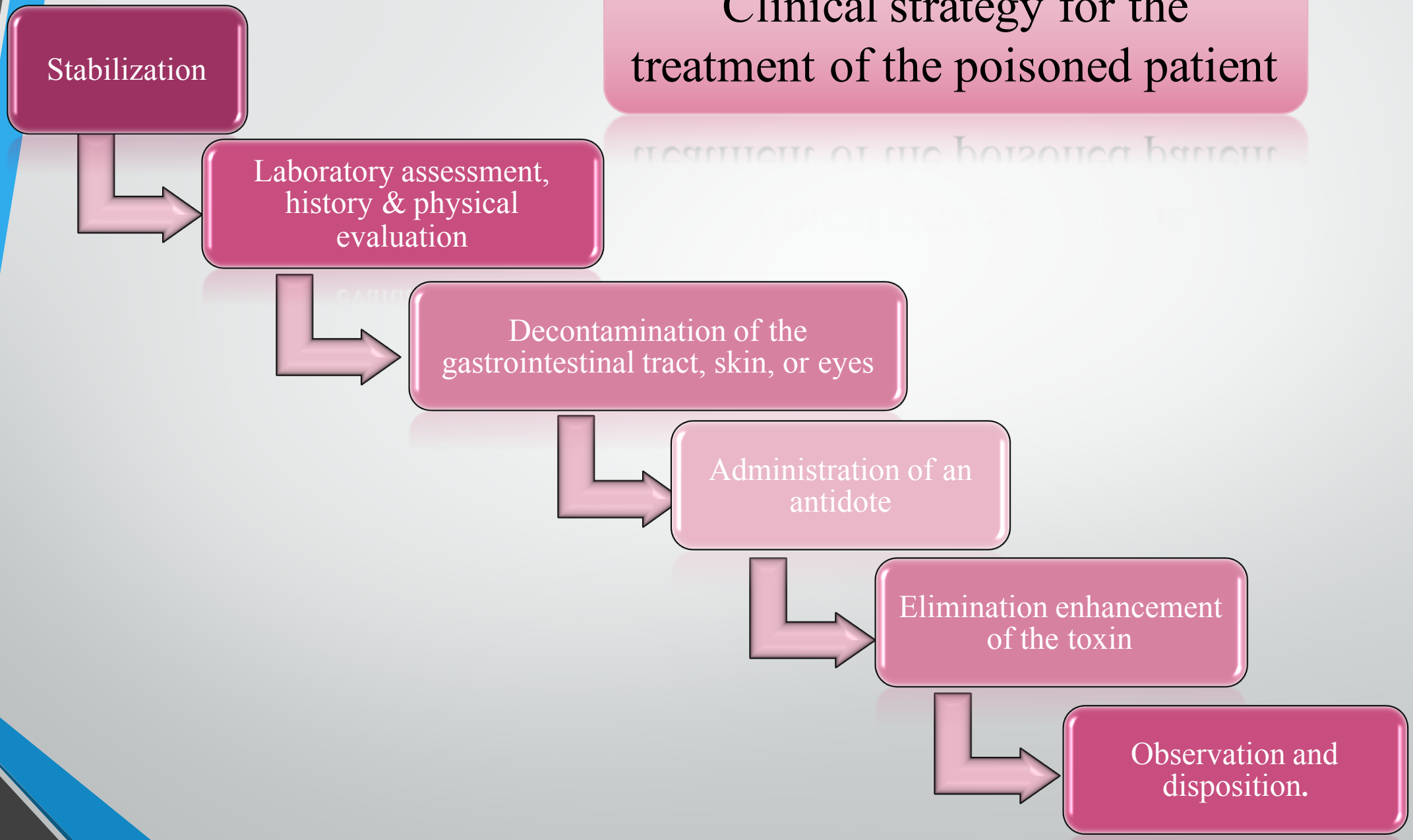

Therapeutic effect
Toxic effect
Therapeutic index
50%
No effect
Effect dose
ED50
Toxic dose
TD50

1- How do you remove the patient from the source of a toxicant and/or decontaminate

2- How do you treat the symptoms and signs of intoxication ranging from discomfort, organ distress, an organ failure

3- In selected poisonings how do you decide administration of antidotes

Clinical strategy for the treatment of the poisoned patient



Clinical strategy for the treatment of the poisoned patient:

1. Stabilization.

As with any unstable or critically ill patient, the resuscitation (Airway, Breathing, Circulation (ABC)) with basic life support takes priority.

2. Laboratory assessment, history & physical evaluation

Physical examination of the patient is required to assess the patient's condition.

The substances belonging to a particular class of toxin produce characteristic combinations of symptoms and signs, which is called toxic syndrome (Toxidromes).

The toxidrome-oriented physical examination may provide valuable insight into the class of toxin involved.

3. . Decontamination of the gastrointestinal tract, skin, or eyes

In case of GI, in patients who present very early (less than an hour after their ingestion) or for those patients who have taken a very large or dangerous

- overdose. it should be done as early as possible in the emergency department GI decontamination is done by (dilution, emesis, lavage, adsorbents and cathartics).

A- Dilution: 1-2 cupful for child and 2-3 cupful for adult. Excessive liquid may distend the stomach wall causing premature evacuation of its content into duodenum & making it more difficult to remove the poison. Advantages of dilution are reducing gastric irritation & add bulk to the difficult to remove stomach that may be needed for emesis.

B- Emesis: should not attempt (hydrocarbon (e.g. gasoline), corrosive acid (HCl, H_2SO_4, H_2O_2) or alkali (NaOH, KOH) & if patient is unconscious.

- Ipecac syrup: expectorant syrup (when given in low dose) & as emetic syrup (when given in high dose). Early vomiting usually within 30 min. & second one occurs after 30 min.
- Dose of ipecac:

1. Adults and teenagers ----------15 to 30 mL + 240 mL water.
2. Children 1 to 12 years of age ---- 15 mL + 120-240 mL.
3. Children 6 months -1 year of age ---- 5–10mL+120-240 mL.

- **Symptoms** of overdose (ipecac toxicity) (may also occur if ipecac is taken regularly) Diarrhea, Fast or irregular heartbeat, Nausea or vomiting (continuing more than 30 minutes), Stomach cramps or pain, Troubled breathing, Unusual tiredness or weakness & Weakness, aching, and stiffness of muscles, especially those of the neck, arms, and leg

C- Lavage: or called (Gastric lavage) is an invasive procedure to decontaminate the stomach of patients. Indicated in treatment of Acute Lead Intoxication. Contraindicated in ingestion of a strong acid or alkali, ingestion of a hydrocarbon with a high aspiration potential.

D- Adsorbents: kaolin, pectin & activated charcoal, in which charcoal binds to diverse substances, rendering them less available for systemic absorption from the GIT.

- Single-Dose Activated Charcoal is administered as slurry, either in water or sorbitol, orally or via a nasogastric tube (0.5 to 1 g/kg in children or 25 to 100 g in adults).

E- Cathartics: one of the old ways for the purpose of eliminating toxicants from the GIT. The two most common categories of cathartics are the magnesium salts (e.g., magnesium citrate, magnesium sulfate) and non digestible carbohydrates (e.g., sorbitol)

4. Administration of an antidote

• Antidote is a substance that can prevent further poisoning from specific substances.

5. Elimination enhancement of the toxin.

- PH alteration & dialysis and Hemoperfusion: PH alteration: increased elimination of weak acid will occur when urinary pH is more alkaline, while enhanced elimination of weak base will occur when urinary pH is more acidic. Sodium bicarbonate.
- Dialysis and Hemoperfusion: Dialysis depends on the principle of diffusion from an area of high concentration to one of lower concentration• Dialysis and perfusion methods should never replace the use of more specific treatment or antidote.

6. Observation and disposition.

- If the patient has persistent and toxic effects, the patient will require prolonged care course. Admission is indicated for completing his treatment and observation; in the case of severe toxicity, the patient may need admission to intensive care unit.
- In the case of mild toxicity or asymptomatic patient, a 6-hour observation period is sufficient to exclude the development of serious toxicity.

THANK YOU

Clinical toxicology laboratory

5th. stage

By assistant lecturer

Dr. Nibrass Al Abdali

2023 - 2024

كلية الصيدلة
جامعة الفراهيدي
2012 - 1433
Al-Farahidi university

Lab.2

Poisoning with OTC

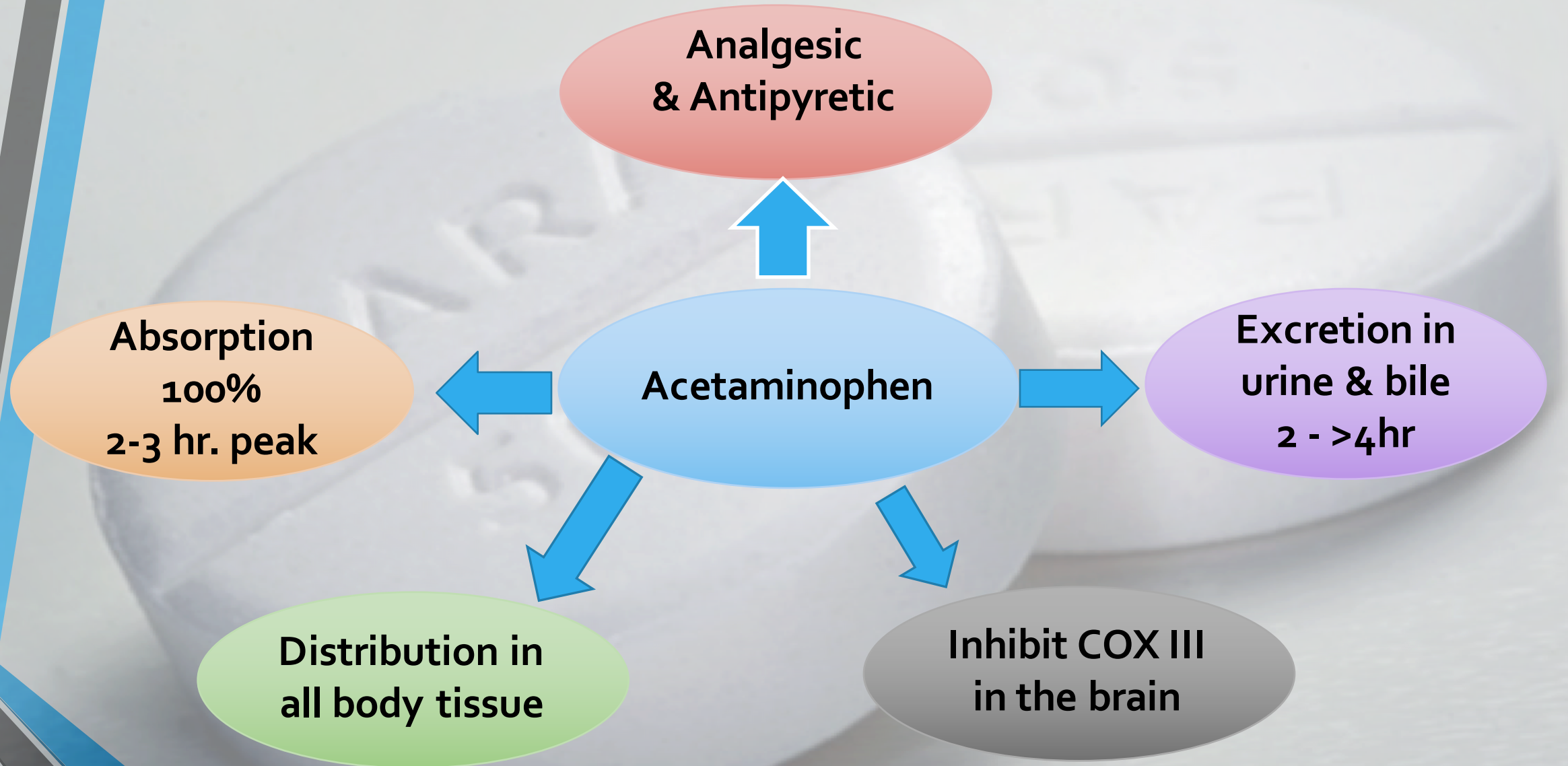
- Over the counter drugs (OTC) toxicity.
- The most important OTC with approximately daily using are [acetaminophen (Paracetamol) & acetyl salicylic acid (Aspirin)]
- The action of NSAIDs :

1. Reduce pain.
2. Decrease inflammation.
3. Prevent blood clot.
4. Decrease fever.

- The most common adverse effect (depend on specific drug) include:

1. Increase GI ulcers & bleeds
2. Heart attack
3. Kidney disease.

Acetaminophen (Paracetamol)


Analgesic
& Antipyretic
Absorption
100%
2-3 hr. peak
Acetaminophen
Excretion in
urine & bile
2 - >4hr
Distribution in
all body tissue
Inhibit COX III
in the brain

- Acetaminophen is the main analgesics and antipyretics treatment.
- Acetaminophen is not NSAID, most common over dose occur
- Acetaminophen metabolite in liver to NAPQI (N-acetyl-p-benzoquinone)
- NAPQI erase by GSH (Glutathione)
- NAPQI is toxic metabolite will lead to failure of ATP synthesis & release of sequestered Ca++
- Lethal dose 15-25 gm
- In adult: 15 gm will cause acute hepatic failure, in children 150 mg/kg

Stage I toxicity

Within 24 hr., no hepatic injury, asymptomatic, N/V, abdominal pain

Stage II toxicity

24 – 72 hr., right upper quadrant abdominal pain, anorexia, N/V, tachycardia& hypertension, rise liver function test

Stage III toxicity

72 – 96 hr., N\V, abdominal pain, maximal liver injury (jaundice, coagulopathy, hypoglycemia,& hepatic encephalopathy), acute renal failure, death from multi-organ failure

Stage IV toxicity

The recovery phase, patients who survive stage III

- Factors that may predispose patients to hepatotoxicity:

1. Increase frequency & duration of acetaminophen dosing.
2. Increase capacity for CYP2E1 activation to NAPQI
3. Decrease GSH availability.
4. Decrease capacity for glucuronidation & sulfation
5. Alcohol intake

Acetaminophen level	Result interpretation
10 – 20mcg/ml	**Therapeutic levels**
Less than 150 mcg/ml 4 hr. after ingestion	**Low risk of liver damage**
Greater than 200 mcg/ml 4 hr. after ingestion Or Greater than 50mcg/ml 12 hr. after ingestion	**Associated with toxicity & liver damage**

- **Laboratory tests:**

- **Liver function tests**:

1. Alanine aminotransferase (ALT) ⬆ ((4-36 U/L))
2. Aspartate aminotransferase (AST) ⬆ ((8-33 U/L))
3. Bilirubin (total & fractional) ⬆ ((0.1- 1.2 mg/L))
4. Alkaline phosphatase ⬆ ((44-147 IU/L))

- Prothrombin time (PT) with international normalized ratio INR) ⬆ ((11-13.5 sec.))
- Renal function (renal failure)

1. Electrolytes ⬇
2. BUN ⬆ ((6-24 mg/dL))
3. Creatinine ⬆ ((For men, 0.74 to 1.35 mg/dL & for women, 0.59 to 1.04 mg/dL))

- ECG
- Lipase & amylase (in patient with abdominal pain) (hyperamylasemia)
- Other tests:

1. Serum salicylate level (in unconscious or suspicion of co-ingestion of salicylates
2. Urine drug screen (in unconscious to determine if other substances have been taken) **nomogram**

Special clinical considerations

Glutathione deficiency

- Acute or chronic starvation
- Eating disorder (anorexia)
- chronic debilitating illness (ADIS, hepatitis C)

Prior medications

- Long-term with CYP 450 inducer (carbamazepine, rifampicin)
- Long standing alcohol

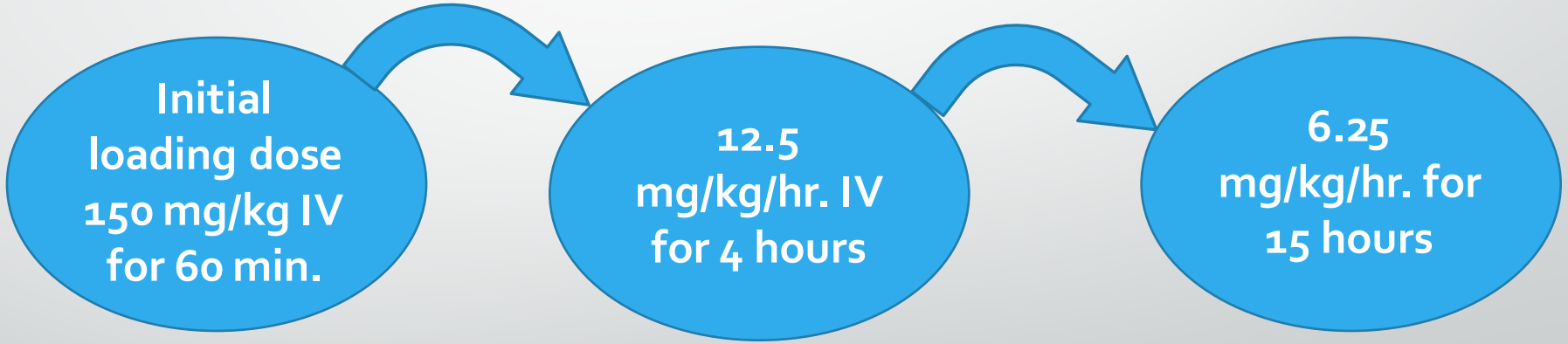
children

Treatment:

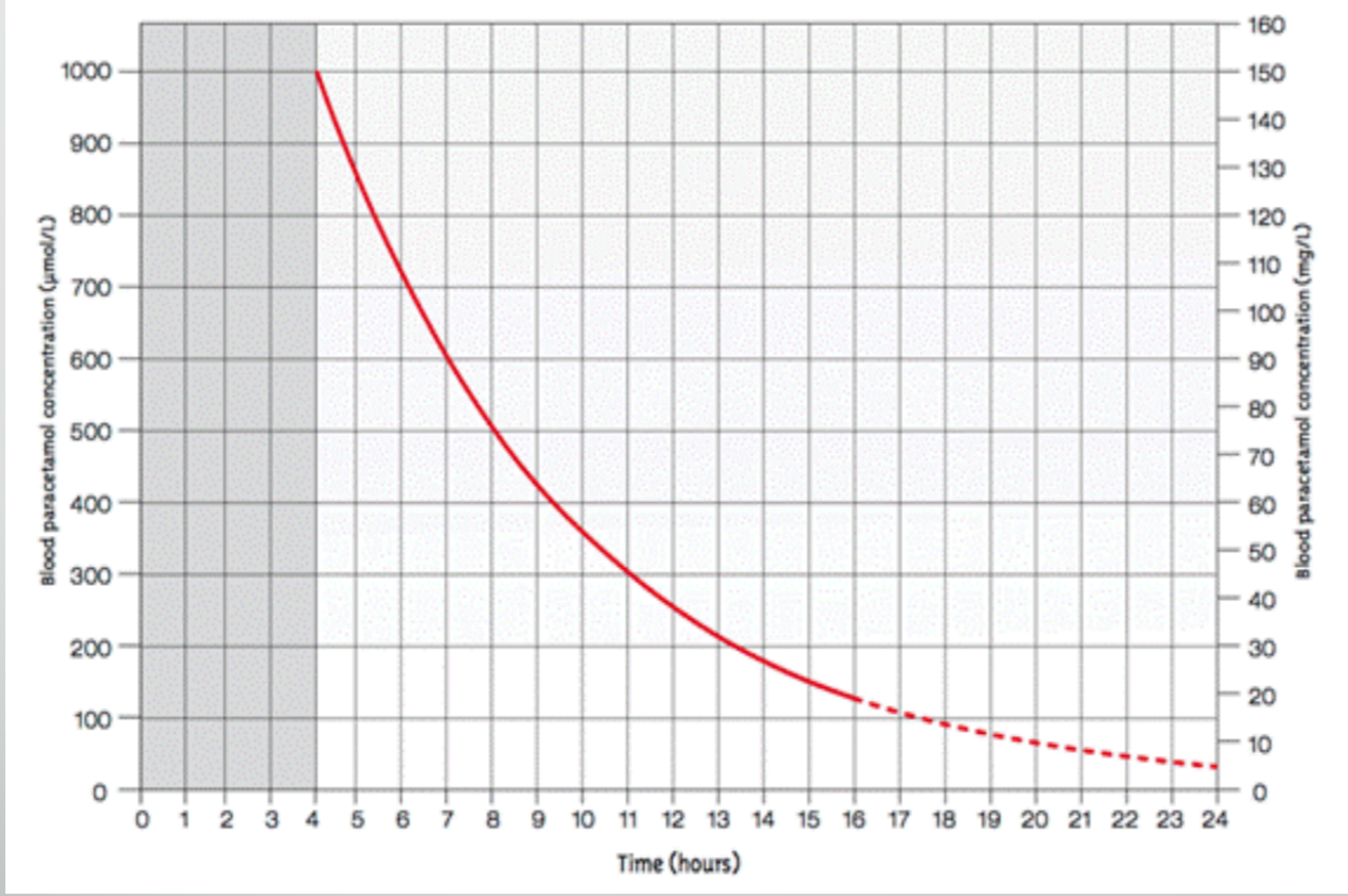
- **Gastric lavage:** as immediate as possible specially before 4 hr. even after that to eras any acetaminophen In stomach.
- **Antidote**: N-acetyl cysteine (NAC)
- **Hemodialysis**:
- **Liver transplantation:** in sever hepatotoxicity that will lead to hepatic failure.
- **Activated charcoal .**

- If we know the the amount of tablets that taken by the patient >10 gm, it better to give the antidote **N-acetyl cysteine (NAC)** even before the acto. test concentration is appear .

The 20 hr. IV protocol of NAC



- If we don't know, It is safe to wait for the acetaminophen concentration to decide on the need for NAC in all cases that present within 8 hours of ingestion


Blood paracetamol concentration (μmol/L)
1000
900
800
700
600
500
400
300
200
100
0
Blood paracetamol concentration (mg/L)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)

nomogram

Single acute Acetaminophen ingestion

>200 mg/kg or unknown dose

<4 hr. post ingestion
Acet. Conc. At 4 hr. post ingestion
Plot on nomogram & treat if indicated

4-8 hr. post ingestion
Immediate Acet. Conc.
Plot on nomogram & treat if indicated

8 hr. post ingestion
Start NAC, immediate Acet. Conc. & ALT
Plot on nomogram & continue NAC or cease

Multiple supratherapeutic Acetaminophen

>200 mg/kg over 24 hr., or
>150 mg/kg/d over 48 hr., or
>100 mg/kg/d over 72 hr. or several days

→

Measure ALT & acetaminophen conc.
No risk if ALT normal & acet. Conc. <120 micromole/L
Start NAC

Acetyl Salicylic Acid ((Aspirin))

- Early symptoms and signs are **Nausea, vomiting, diaphoresis, and tinnitus, vertigo, hyperventilation, tachycardia, and hyperactivity**
- Salicylates are generally absorbed quickly through the GIT. The elimination half-life is generally **between 3 and 12 hours at therapeutic doses**, but this can increase unpredictably up to 30 hours in the setting of an overdose
- Generally, doses **less than 300 mg/kg** result in mild toxicity, **300-500 mg/kg** causes moderate toxicity, and **greater than 500mg/kg** will result in death
- Aspirin is a type of nonsteroidal anti-inflammatory drug (NSAID) which also has ***anti-platelet*** effects
- its mechanism of action is to **irreversibly** inactivate the cyclooxygenases enzyme through acetylation, thereby suppressing prostaglandin and thromboxane synthesis.

- Aspirin → (Hydrolyzed) salicylate (GIT & serum), $t_{1/2}$ 15 min.
- **Aspirin** toxicity ***initially*** causes a **respiratory alkalosis** because of its direct stimulatory effects on respiratory centers in the medulla.
- The ***second phase*** of aspirin toxicity results in an **anion gap metabolic acidosis**.

Clinical Features:

- **Vital signs**: tachypnea, hyperthermia, tachycardia, hypotension
- **Nausea and vomiting**: GI irritation or stimulation of chemoreceptor trigger zone in medulla
- **Ototoxicity**: tinnitus or deafness
- **Hypoglycemia**, **Hypokalemia**
- **Bruising**
- **Anion gap metabolic acidosis**: although a mixed respiratory alkalosis-metabolic acidosis is seen in adults, children frequently present with pure metabolic acidosis
- **CNS toxicity**: confusion, dizziness, seizures are more common in children than adults
- **Pulmonary or cerebral edema:** result of severe acidosis, more common in adults but can occur in children

Laboratory evaluation:

- Plasma salicylate levels should be checked **4 hours** after ingestion and then **every 3 hours** until levels start to decline.
- **Mild symptoms** 30-50 mg/dL
- **Moderate toxicity** 50-100 mg/dL
- **Severe toxicity** >100mg/dL is
- **Additional labs:** blood gases, BMP [glucose, Ca,(Na, K, CO_2 & Cl), & BUN], urinalysis
- **Aspirin nomogram**, also known as Done nomogram, is no longer considered to be predictive of toxicity and **should not be used**. Instead plasma concentration as well as clinical judgment should be used to make decisions.

THANK YOU

Clinical toxicology laboratory

5th. stage

By assistant lecturer

Dr. Nibrass Al Abdali

2023 - 2024

Lab. 3

Toxicity of Digitalis Glycosides

- **Digitalis** glycosides are life-saving drugs when used in therapeutic doses in the treatment of congestive heart failure (CHF), & for management of certain supraventricular arrhythmia, It protects ventricles during certain atrial arrhythmias
- It has wide-ranging beneficial effects and continues to play an important role in the modern management of appropriately selected patients with heart failure and atrial fibrillation. Digitalis has two-medicine form (digoxin & digitoxin)
- It consider safe, digoxin has a **narrow therapeutic window**, and it's proper dosing requires by doctors to be careful of various patient characteristics including age, gender, kidney function and accompanying use of other drugs to avoid potentially life-threatening toxicity

- A lower tolerance to the drug can also cause digitalis toxicity.
- It is estimated that 20-30% of patients taking a digitalis preparation will **experience** toxicity because the drugs have an extremely narrow therapeutic index.
- Digitalis was derived from **foxglove plant (Digitalis purpurea).**

Poisoning with digitalis

acute over-ingestion of medication

chronic toxicity (old patients) most commonly due to decreased renal clearance

Factors that increase the risk of digoxin toxicity include:

- Hypothyroidism/hyperthyroidism
- Advanced age
- Myocardial Infarction (MI)
- Renal insufficiency
- Hypercalcemia
- Alkalosis & Acidosis
- Hypoxemia

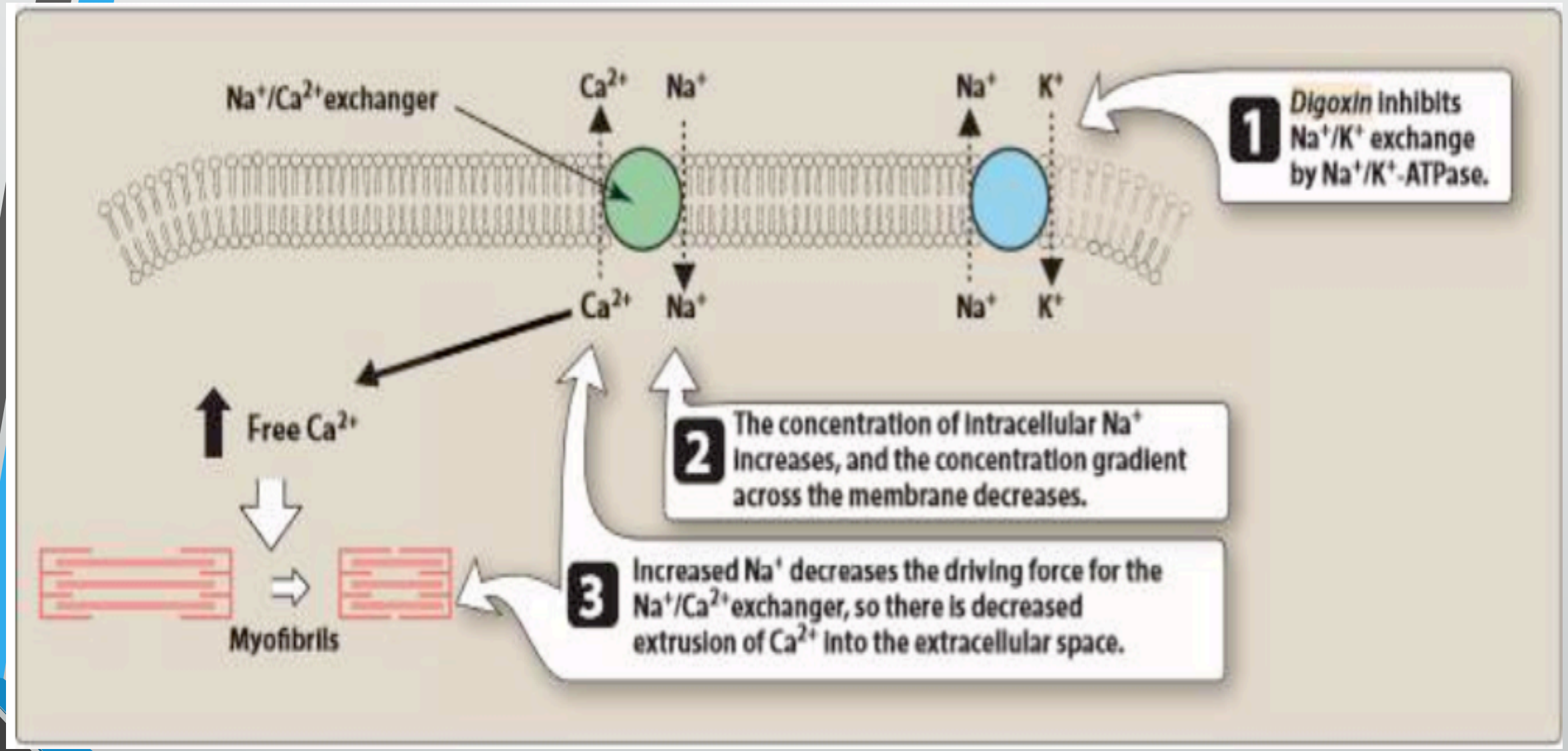
Medications that are associated with digoxin toxicity include:

- Diuretics
- Amiodarone
- Beta-blockers
- Benzodiazepines
- Calcium channel blockers
- Macrolide antibiotics
- Propylthiouracil
- Amphotericin

Pathophysiology:

1. The main mechanism of action of digitalis is inhibiting **Na+/K+ ATPase of the myocyte** (reversibly) resulting in increased intracellular Na+ levels. The accumulation of intracellular Na+ leads to a shift of Na+ extracellularly through another channel in exchange for Ca2+. This influx of intracellular Ca2+ assists with myocyte contractility.

2. Digoxin also has direct effects on conduction through increased vagal tone. Digoxin stimulates the vagus nerve leading to prolonged conduction through the sinuatrial (SA) and atrioventricular (AV) nodes.


Na+/Ca2+ exchanger
Ca2+
Na+
Na+
K+
1 Digoxin inhibits Na+/K+ exchange by Na+/K+-ATPase.
Ca2+
Na+
Na+
K+
Free Ca2+
2 The concentration of intracellular Na+ increases, and the concentration gradient across the membrane decreases.
3 Increased Na+ decreases the driving force for the Na+/Ca2+ exchanger, so there is decreased extrusion of Ca2+ into the extracellular space.
Myofibrils

Toxicity

- Therapeutic levels of digoxin typically range from 0.5 to 2.0 ng/mL. toxic concentration 3-4 times.

❖ The most accurate measurement of digoxin levels should measured 6 hr. after last ingestion **due to** Distribution of digoxin to various tissues normally takes several hours.

❖ Digoxin will lead to:

1. **Increased** intracellular Ca2+ that lead to premature contractions of the myocytes.
2. **Decreased** refractory period leading to increased automaticity and makes the myocytes more prone to the induction of arrhythmias.

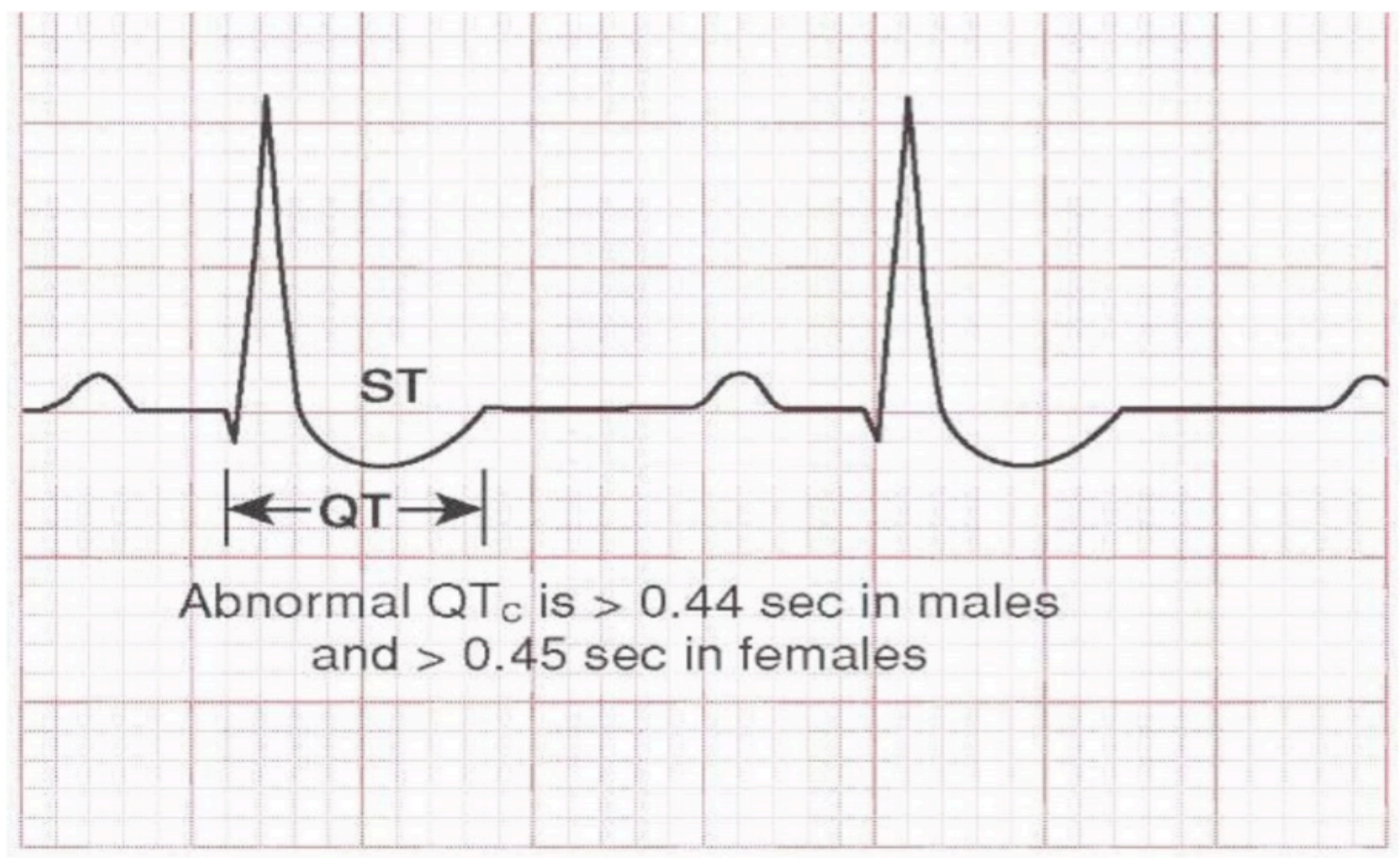
❖ In chronic toxicity with digoxin the excretion occur by kidney, usually seen in those with renal impairment. Clearance of digoxin decrease

with another treatment **verapamil, macrolides, and antifungals**.

- Individuals with Eubacterium lentum in their colon may require **larger** doses of digitalis to achieve the desired therapeutic serum concentrations. This microorganism reduces the lactone ring of digitalis. Digitalis blood concentrations may become toxic when these patients receive antibiotics, such as tetracycline or erythromycin, which eradicate the organism.
- There have been documented cases of clinical toxicity with digoxin levels in the therapeutic range.
- Electrolyte disturbances such as hypomagnesemia, hypercalcemia, and hypokalemia lead to **increased** sensitivity to digoxin making toxicity more likely even with a lower concentration of serum digoxin.
- Hypokalemia is the most common trigger of digoxin toxicity, which may also
  - occur as a result of diuretic therapy.

- From the history of exposure to digoxin we can classify the poisoning is acute or chronic.
- Clinical **signs** of toxicity include (gastrointestinal, neurological and the most concerning cardiac). Most **symptoms** are non-specific findings and include (headache, malaise, insomnia, altered mental status, abdominal pain, nausea, and vomiting).
- Also, **visual changes** especially changes involving colors such as seeing a yellow hue are better known and specifically seen in digitalis toxicity (early-appearing symptoms), Blurred vision & loss of visual acuity.
- Cardiac manifestations include arrhythmias and rhythm disturbances.
- The mortality rate with toxic dose is reported to be as great as 25%.

- ECG changes include **shortening QT interval**, **scooping ST depression & flat, inverted or biphasic T waves** as shown below.



- Endogenous digoxin like immunoreactive proteins can result in a **false- positive result.**
- This is more likely to occur in patients with (Liver or renal disease, Chronic heart failure, Subarachnoid hemorrhage, Acromegaly, Diabetes, Pregnancy)

Treatment:

1. Early recognition and the administration of antidote **(immune Fab),** the trade name **Digibind**, depend on the digoxin concentration. It is first-line therapy for dysrhythmias including AV block and ventricular tachycardia caused by suspected digoxin toxicity. Digoxin with form complexes and are secreted via the urine. 10 vial for adults & 5 for children. The uses of antidote will lead to hypokalemia so, serum potassium should monitor.
2. Activated charcoal could use in **acute** ingestion within two hours.

3. Hydration, oxygenation, and close monitoring are necessary
4. Keep ECG monitored for dysrhythmias.
5. All electrolyte disturbances need to be corrected.
6. Short-acting beta-blockers to managed Supraventricular.
7. Phenytoin as been shown to suppress digoxin induced tachyarrhythmia
8. Lidocaine for managing ventricular arrhythmias.
9. Atropine may be used to manage bradycardia.

THANK YOU

Clinical toxicology laboratory

5th. stage

By assistant lecturer

Dr. Nibrass Al Abdali

2023 - 2024

Lab. 4

color, clarity, odor, and specific gravity

Urine analysis of toxins and c[illegible]is

- **Urinalysis** is of medical tests that includes (a) physical macroscopic examination of the urine, (b) chemical evaluation using urine test strips examination & (c) microscopic examination

cells, urinary casts, crystals, and organisms

The tests done on urine

- Red blood cell urine test
- Glucose urine test
- Protein urine test
- Urine pH level test

- Chemical examination of urine includes **the identification of protein, blood cells, glucose, pH, bilirubin, urobilinogen, ketone bodies, nitrites, and leukocyte esterase**.
- The commons chemical urine tests are:

1. Examining chemical aspects of a urine,
2. Healthcare providers or lab technicians

- They often use special test strips called **dipsticks** to test for certain chemical substances in the urine sample. The strips have pads of chemicals that change color when they come in contact with specific substances

- Normal urine color ranges from pale to deep amber & this depending on how much water person drink
- the result of a pigment called **urochrome**
- **Bloody urine** (UTI & kidney stones) and usually cause pain. Painless bleeding might signal a more-serious problem (cancer).
- Urinary blood (**hematuria**)
- **Dark or orange urine** if also have pale stools & yellow skin and eyes (liver malfunctioning)
- **Hematuria** (UTI, enlarged prostate, cancerous or noncancerous tumors, kidney cysts, long distance running & kidney or bladder stones)
- Foods (beets, blackberries & rhubarb) can turn urine red to pink.
- **Medications** Rifampin (Rifadin, Rimactane) TB ((reddish orange urine)), Phenazopyridine (Pyridium) numbs urinary tract discomfort, & laxative containing Senna

- Leukocytes
- Nitrite
- Urobilinogen
- Protein
- Ketone
- Specific gravity
- Hemoglobin
- PH
- Bilirubin
- Glucose

- Urine is mostly water, and contains mineral salts, and **about 2% urea**, which is produced in the liver to remove ammonia, which is a very toxic substance. Urea has a very low toxicity, although a continuous high level of urea in the blood called (**hyperuremia**) can cause disease, (due to increase in ammonia level which represent the most poisonous excretory substance)
- Abnormal constituents of urine are **sugar, proteins, blood, bile salts, bile pigments and ketone bodies**

THANK YOU

Clinical toxicology laboratory

5th. stage

By assistant lecturer

Dr. Nibrass Al Abdali

2023 - 2024

Lab. 5

Arsenic poisoning :

- Arsenic poisoning, or arsenicosis, occurs after the ingestion or inhalation of high levels of arsenic. Arsenic is a type of carcinogen that's gray, silver, or white in color.
- It is extremely poisonous to humans
- arsenic especially dangerous because it is test less & odorless that could be exposed to it without knowing it.
- Arsenic found in two formula:

a) Organic (natural) found in deep water (groundwater) and in seafood

b) Inorganic (manufactured) used in agriculture, mining, and manufacturing (lead arsenate pesticide)

Mechanism of action

Arsenite will:

- ↓ the formation of acetyl-CoA
- ↓ the enzyme succinic dehydrogenase
- ↓ the energy system of the cell & lead to ↑ cellular apoptosis
- prevents use of thiamine
- ↑ lactic acidosis
- ↑ production of hydrogen peroxide (H_2O_2)

Two types of toxicity with arsenic :

1. **Acute**: The immediate symptoms of acute arsenic poisoning include vomiting, abdominal pain and diarrhea. These are followed by numbness and tingling of the extremities, muscle cramping and death, in extreme cases.
2. **Chronic**: usually observed in the skin, and include pigmentation changes, skin lesions and hard patches on the palms and soles of the feet (hyperkeratosis). These occur after a minimum exposure of approximately five years and maybe a precursor to skin cancer, also cause cancers of the bladder and lungs.

- Arsenic is also associated with another adverse effect:

A. adverse pregnancy outcomes and infant mortality, with impacts on child health, and
B. exposure in utero and in early childhood has been linked to increases in mortality in young adults due to multiple cancers, lung disease, heart attacks, and kidney failure.

Symptoms of arsenic poisoning:

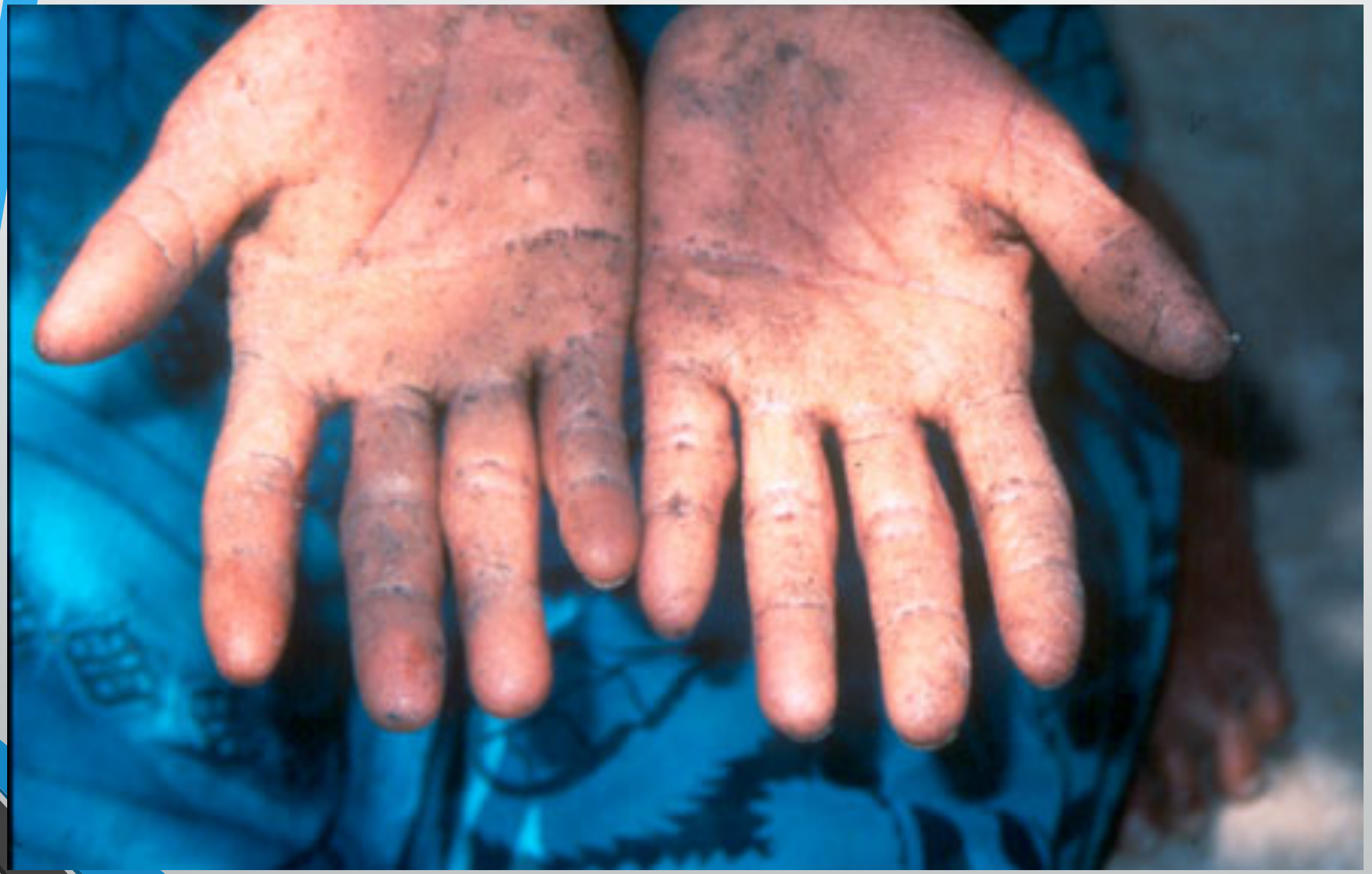
1. red or swollen skin
2. skin changes, such as new warts or lesions
3. abdominal pain
4. nausea and vomiting
5. diarrhea
6. abnormal heart rhythm
7. muscle cramps
8. tingling of fingers and toes

- We should seek emergency help if:

1. darkening skin
2. constant sore throat
3. persistent digestive issues

possible causes of arsenic poisoning can include:

1. breathing air that contains arsenic
2. smoking tobacco products
3. breathing contaminated air from plants or mines that use arsenic
4. living near industrialized areas
5. being exposed to landfill or waste sites
6. breathing in smoke or dust from wood or waste that was previously treated with arsenic
7. eating arsenic-contaminated food , but some seafood and animal products may contain small levels of arsenic



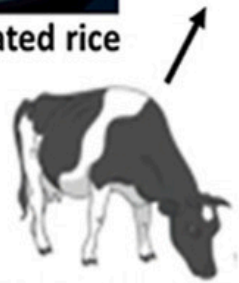
- Long-term exposure to arsenic can cause cancer. The most common types of arsenic-related cancers are associated with the:

1. bladder
2. blood
3. digestive system
4. liver
5. lungs
6. lymphatic system
7. kidneys
8. prostate
9. skin

Sources of arsenic exposure

Arsenic contaminated tube-wells

Arsenic contaminated rice

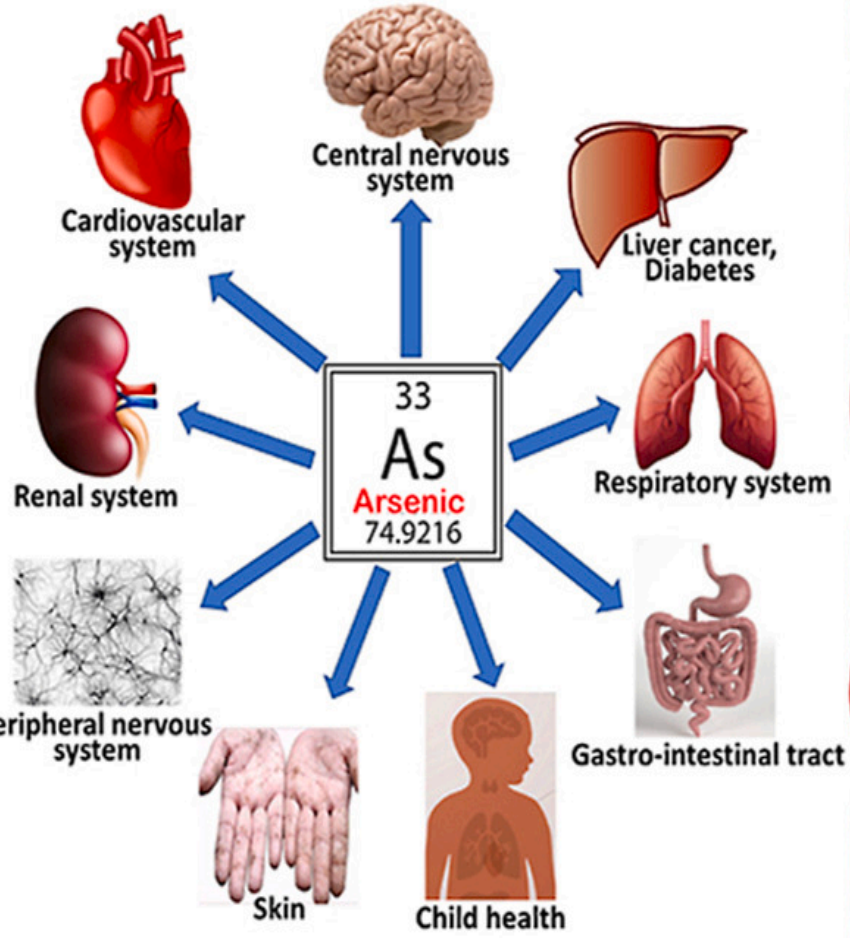


Arsenic-contaminated milk and meat

Irrigation with arsenic-contaminated water

Health consequences

- Arsenicosis
- Various cancers
- Child mortality
- Neurotoxicity



- Lifestyle-related diseases (Diabetes, hypertension)

Arsenic toxicity management

❑ Prevention

- ✓ Arsenic-free drinking water
- ✓ Arsenic-free food
- ✓ Completely avoiding arsenic exposure

❑ Mitigation

- ✓ Long-term sustainable arsenic remediation policies
- ✓ Arsenic separation from contaminated sources
- ✓ Alternative sources of water

❑ Treatment/amelioration

- ✓ Proper nutrition
- ✓ Antioxidant enriched food, vitamins, proteins, micronutrients
- ✓ Nano-drug delivery, combining both antioxidant and chelation therapy

There are tests to measure high levels of arsenic in the body via the:

- **blood**
- **Fingernails**
- **hair**
- **Urine** (**Acute exposure**)

long-term exposure of at least six months

Prevention and control

1. prevention of further exposure to arsenic by the provision of a safe water supply for drinking, food preparation and irrigation of food crops.
2. Education and community engagement
3. Should need to understand the risks of high arsenic exposure and the sources of arsenic exposure

Treatment

1. rapid stabilization with fluid and electrolyte replacement in an intensive care setting
2. Aggressive intravenous fluid replacement therapy may be life–saving in severe poisoning.
3. Gastric lavage may be useful soon after an acute ingestion to prevent further absorption.
4. Gastric lavage may be useful soon after an acute ingestion to prevent further absorption.
5. activated charcoal together with a cathartic is frequently recommended.
6. If profuse diarrhea is present, cathartics should be withheld.
7. Hemodialysis in a patient with concomitant renal failure.
8. Dimercaprol (2, 3 dimercaptopropanol, also known as British anti Lewisite or BAL) , was previously the most frequently recommended chelating agent for arsenic. **(DMPS) & (DMSA)** <u>These are more water soluble than BAL</u>

THANK YOU

Clinical toxicology laboratory

5th. stage

By assistant lecturer

Nibrass Al Abdali

2022 - 2023

Lab. 6

Parkinson's Disease

- **Parkinson's** disease is a brain disorder that causes *unintended* or *uncontrollable movements*, such as shaking, stiffness, and difficulty with balance and coordination
- Symptoms usually begin gradually and worsen over time. As the disease progresses, people may have difficulty walking and talking.
- They may also have mental and behavioral changes, sleep problems, depression, memory difficulties, and fatigue.
- The disease develop after age 60.
- **Symptoms:**

➢ **Bradykinesia -** slowness of movement, impaired dexterity, decreased blinking, drooling, expressionless face**.**

➢ **Tremor at rest** - involuntary shaking that decreases with purposeful movement. Typically starts on one side of the body, usually the hand.

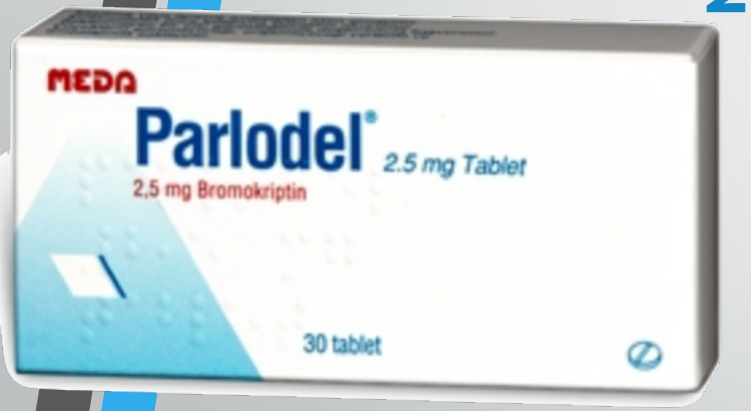
➢ **Rigidity -** stiffness caused by involuntary increase in muscle tone**.**

➢ **Postural instability -** sense of imbalance**.**

Causes:

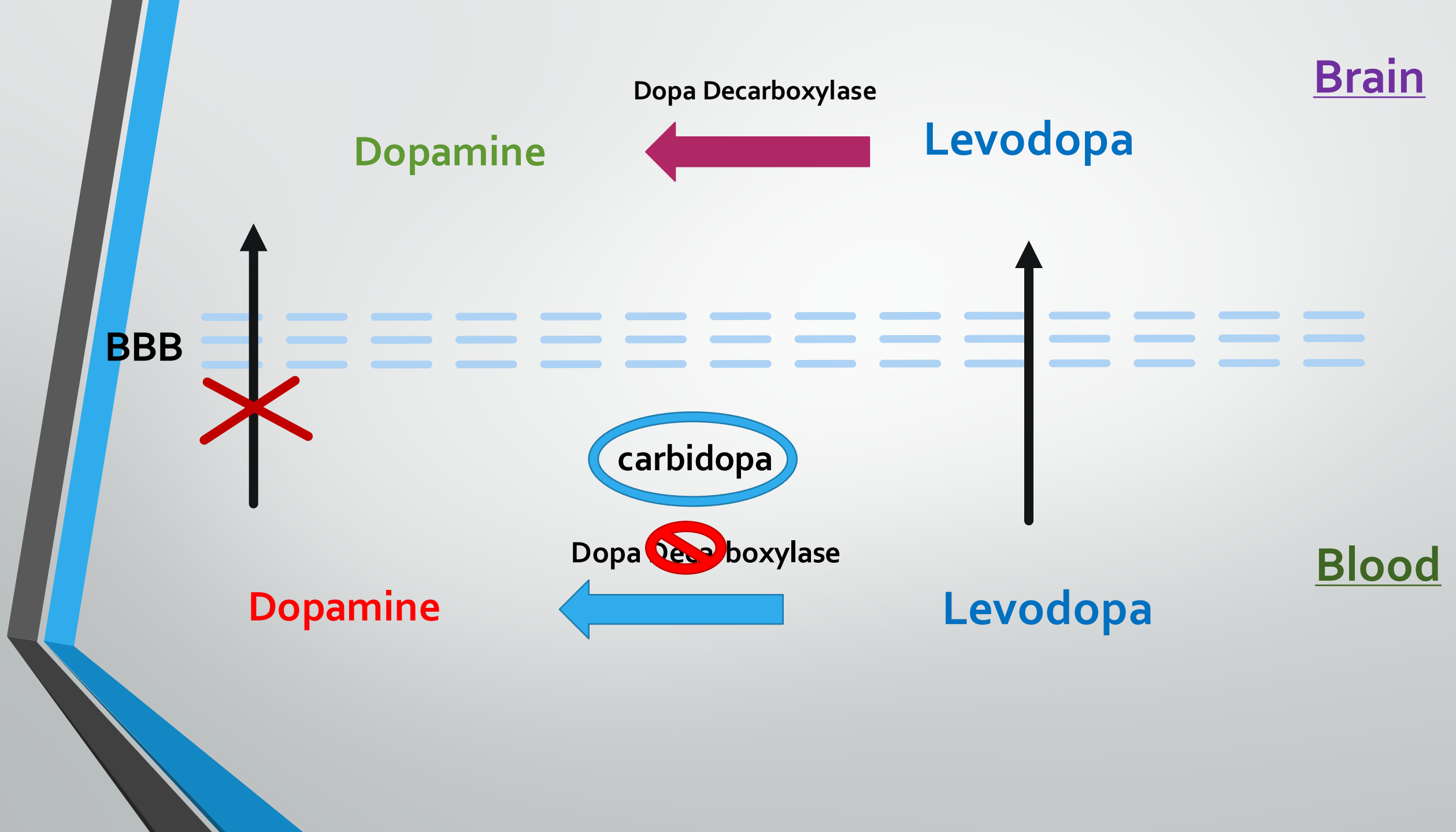
- ❑ There are no main cause for P.D. (genetics, environmental factors, and the natural process of aging have on cell death)
- ❑ There are also secondary forms of P.D. that are caused by medications such as **haloperidol** (a drug used to treat confusion and hallucinations), **reserpine** (an ingredient in some anti-hypertension drugs), and **metoclopramide** (an anti-nausea drug).
- nerve cells in the basal ganglia, an area of the brain that controls movement, become impaired and/or die.
- And this will lead to produce less dopamine, which causes the movement problems associated with the disease

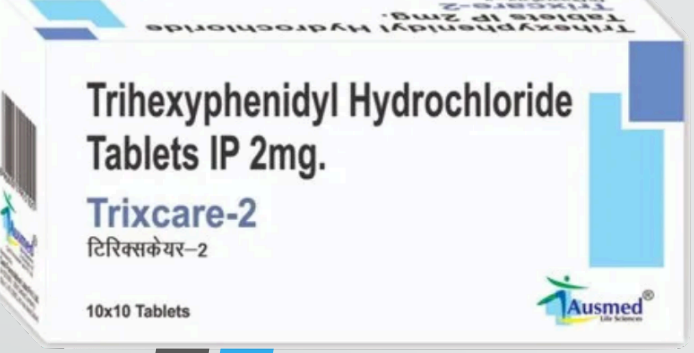
Anti- Parkinson toxicity:



- There are **5** main types of medications available to treat symptoms of Parkinson disease:

1. **Levodopa** (precursor of dopamine) which is the ***primary neuropathological*** feature of parkinsonism. (modifies the symptom of the disease). Extended-release (4-6) hr.
2. **MAO B** (monoamine oxidase type B) **inhibitors** and COMT (catechol-O-methyl transferase) **inhibitors**, they inhibit COMT degradation of levodopa in peripheral tissues, thereby increasing levodopa's half-life in the blood and enabling greater amounts of the drug to cross the blood-brain barrier. Ex. (levodopa/carbidopa **sinemet®**
3. **Dopamine** agonists, Stimulation of the receptors increases dopaminergic activity in the brain (bromocriptine **parlodel®**)


Brain
Dopa Decarboxylase
Dopamine
Levodopa
BBB
carbidopa
Dopa Decarboxylase
Blood
Dopamine
Levodopa



4. **Anticholinergic drugs**, agents that block the muscarinic receptors, such as trihexyphenidyl, are administered to reduce symptoms. *Trihexyphenidyl increased striatal dopamine release and efflux*

5. **Amantadine,** antiviral drug used for treatment of influenza A infection, also has ability to reduce symptoms of Parkinson disease (tremor & bradykinesia).

- Its mechanism of action is trigger the release of dopamine from neurons in brain. It also blocks excitatory signaling & neuronal overactivity associated with movement.

- ✓ Levodopa poisoning is very rare& induces neurological symptoms (**movement & heamodynamic disorders)The** primary side effect associated with large doses of **levodopa** is an increased risk for schizophrenia-like episodes and also nausea, sleepiness, dizziness & headache, presumably because of excess formation of dopamine.
- ✓ Symptoms are (**sever dizziness, irregular heartbeat, mental/mood changes** (schizophrenia-like episodes, agitation)**, nausea & vomiting**)
- ✓ **Phentolamine** is antidote
- ➢ Side effects of **dopamine-receptor agonists** include hallucination and mental confusion.
- ➢ Side effects of **anticholinergic treatment** , The onset of symptoms is rapid (30 min to 2 hr. after consumption) diaphoresis, excessive lacrimation, salivation, miosis, bradycardia, hypotension, urinary and fecal incontinence, and vomiting. Most is excreted in the urine within the first **12 h**
- ➢ The antidote is **physostigmine salicylate**

- **Amantadine** overdose can be fatal, the symptoms are confusion, agitation, behavior changes, hallucinations, sever headache or pounding in ears, muscle stiffness, problem with balance or walking, trouble breathing, fast heart beats, or seizure, dizziness, nausea, & vomiting.
- Clearance by kidney.
- **No** antidote for amantadine

THANK YOU