



Adverse drug reactions

By

Dr. Lamiaa Mohammed Meghawery

Associate professor of pharmacology

Faculty of dentistry

Mutah university



Intended learning outcomes (ILOS):



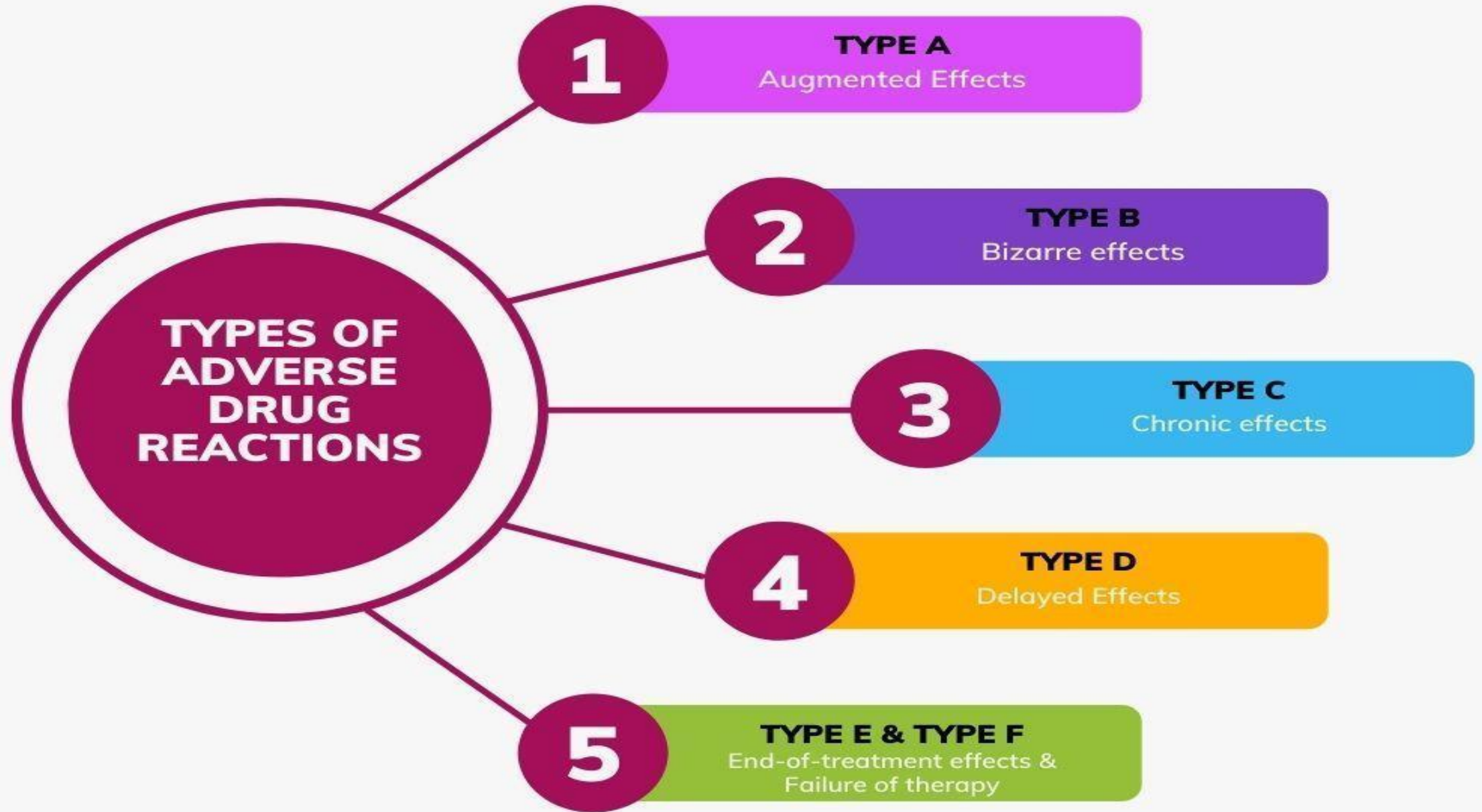
- **Identify types of adverse drug reactions**
- **Interpret difference between tolerance and intolerance .**
- **Discuss type D adverse drug reactions.**
- **Identify net results of chronic use of drugs.**

ADVERSE DRUG REACTION

*A noxious and unintended response to a medicine.
(European Medicines Agency definition)*

- Are harmful effects of a drug at doses used in therapy, which calls for

Decrease dosage, Stop drug & or immediate treatment



- Are harmful effects of a drug at doses used in therapy, which calls for

Decrease dosage, Stop drug & or immediate treatment

They are classified into:

- 1- **Type A** = **A**ugmented and Predictable = Related to the normal pharmacology of the drug.
- 2- **Type B** = **B**izarre and unpredictable = Not related to the normal pharmacology of the drug.
- 3- **Type C** = **C**hronic effects after long use of drugs.
- 4- **Type D** = **D**elayed effects of the drugs.
- 5- **Type E** = **E**nd of dose effects.
- 6- **Type F** = **F**ailure of therapy.

III - Type C (Chronic effects):

Effects of prolonged use of a drug:

III) Type C (Chronic effects after long use of drugs)

1- Tolerance:

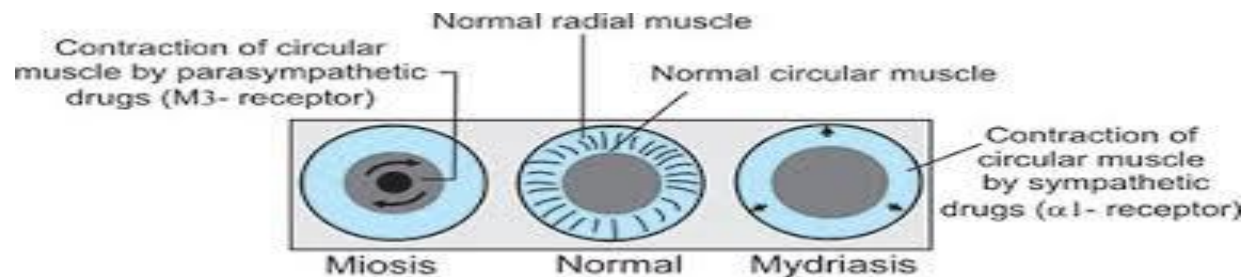
- Decreased or failed response to
drugs.
- Either ↑ dose of the drug or stop the
drug for some time.

* Types of Tolerance:

A) Congenital (Inborn) Tolerance:

1- Racial: Ephedrine does NOT produce mydriasis in **Negroes**.

2- Species: **Rabbits** tolerate Atropine. They have excess atropine-esterase enzyme.



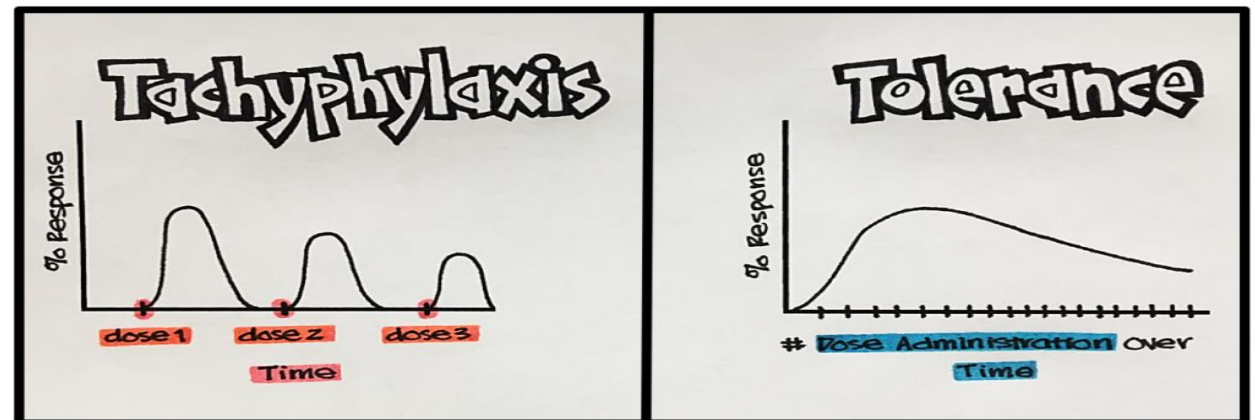
3- Individual (Biological) variations within any population.

B) Acquired Tolerance:

_Decreased response to drugs after their repeated (long) use e.g. Morphine

*Types of Acquired Tolerance:

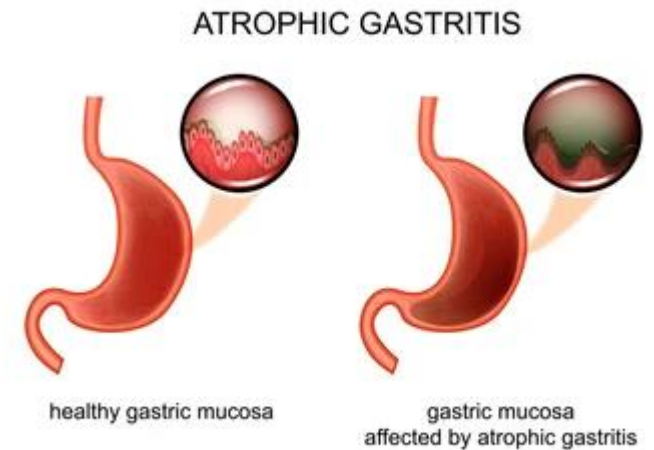
- a- **Cross Tolerance** between similar drugs in structure
- b- **Tachyphylaxis** (Acute acquired tolerance) e.g. Ephedrine on blood pressure.
- c- **Bacterial resistance** to antimicrobials



*Mechanism of Acquired Tolerance:

Change in Kinetics or Dynamics

- 1- **↓ Absorption:** Long use of Ethanol → Atrophic gastritis
- 2- **↑ Metabolism:** Phenobarbital (HME inducer → ↑ its own metabolism (Autoinduction).
- 3- **Down-regulation of receptors**
- 4- **↓ Endogenous substances:** Morphine → ↑ Endogenous Endorphins & Enkephalin.
- 5- **Antibody formation** e.g. Insulin.



shutterstock.com · 650112400

★ Characteristics of Acquired Tolerance:

1- Reversal, stop of the drug for sometime → Regain normal sensitivity.

2- Varies from one drug to another:

- **Rapid** with **ephedrine** & **very slow** with **adrenaline**

3- Does not affect all actions to the same extent :Long use of **morphine**

→ **Rapid tolerance to analgesia & ↓ of R.C. BUT NO tolerance to miosis or constipation**

4- Drug dependence (Habituation & Addiction) may follow tolerance.

III) Type C (Chronic effects after long use of drugs)

2-Drug Dependence:

a- Habituation:

- Psychic dependence.

- Sudden stop of the drug → **Psychic craving for the drug.**

- **Example:** Xanthine beverages (Coffee & tea).



b- Addiction:

- Psychic and Physical dependence.

- Sudden stop of the drug → **Withdrawal (Abstinence) syndrome .**

Usually the reverse of what the addicting agent does.

- **Example:** Amphetamine, Morphine, Ethanol, etc,



III) Type C (Chronic effects after long use of drugs)

3- Iatrogenic disease:

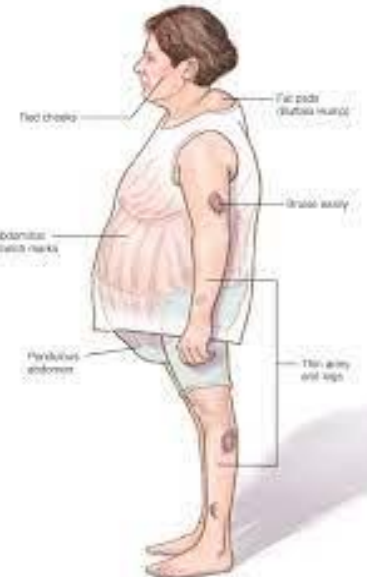
1- Drug-induced disease.

2- Examples:

Large dose of Reserpine → Iatrogenic Parkinsonism.

Large dose of Cortisol → Iatrogenic Cushing's disease.

Parkinsonism



IV- Type D (Delayed effects):

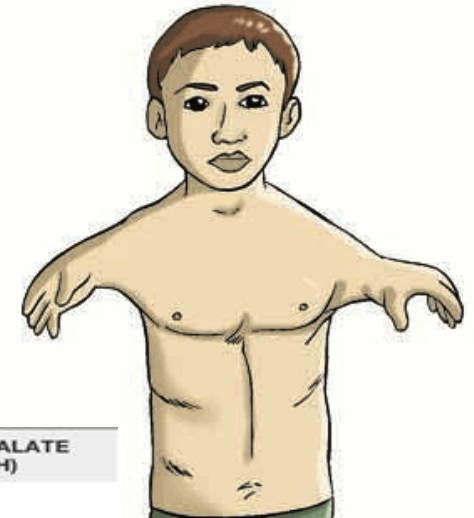
Delayed effects appearing after long use of the drug:

IV- Type D (Delayed effects):

1- Teratogenicity (Dysmorphogenesis):

- **Drug-induced fetal malformations.**

Especially when drugs are taken during the first trimester (First 3 months of pregnancy).



Examples:

a- **Thalidomide → Phocomelia (Absent long bones).**

b- **Phenytoin → Hare lip and cleft palate.**



c- **Tetracyclines → Teeth & Bone abnormalities.**



2- Mutagenicity & Carcinogenicity:

- Tobacco smoking → Bronchogenic carcinoma.



V-Type E= End of dose effects.

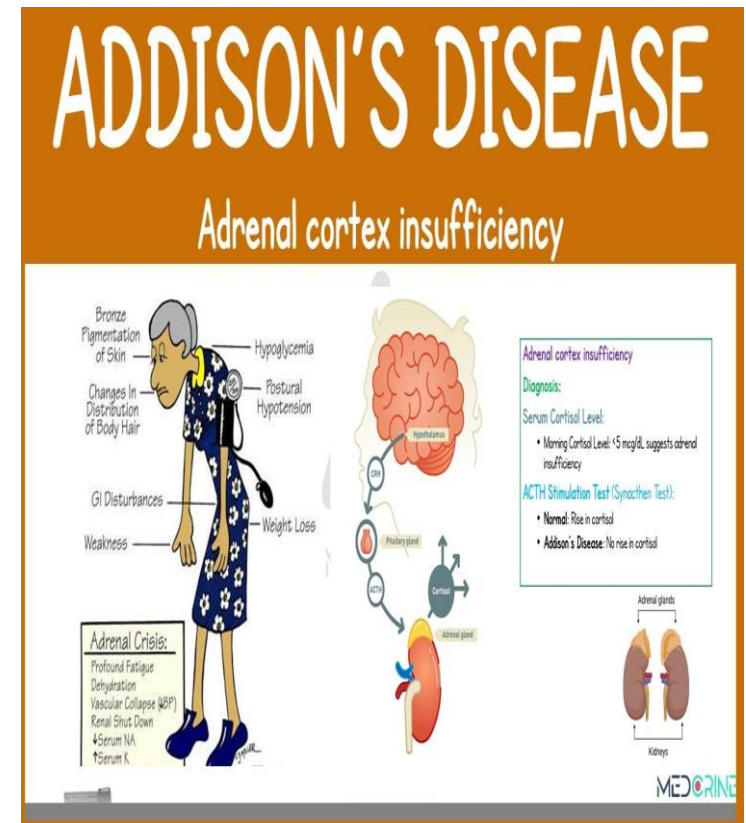
These are effects of sudden stopping of drug use (Drug Withdrawal), include:

1- Abstinence syndromes of **addicting drugs** as morphine.

2- Acute Addisonian crisis of **chronic steroid therapy**.

3- Worsening of existing disease.

• **Sudden Stopping β -blockers** → Myocardial infarction



VI- Type F (Failure of Therapy):

VI- Type F (Failure of Therapy):

1- Primary Failure:

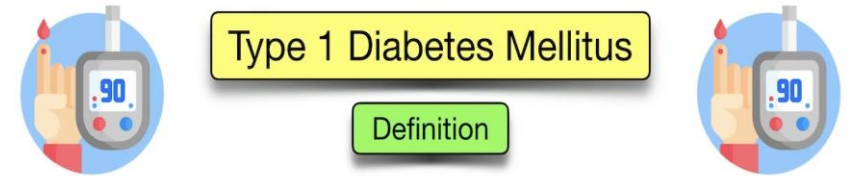
a- Genetic causes = Idiosyncratic reaction due to abnormal kinetics or dynamics

b- Patho-physiological causes: Failure of **insulin secretagogues** in treatment of **Type I diabetes** mellitus due to absolute deficiency of endogenous insulin.

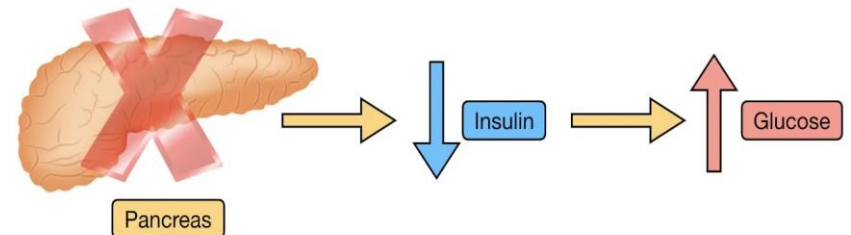
2- Secondary Failure:

a- Occurrence of tolerance.

b- Drug interactions.



Type 1 Diabetes - An autoimmune disease in which the insulin-producing cells of the pancreas are destroyed, leading to high blood glucose levels





Questions



1-Explain:

Steroids shouldn't be stopped suddenly .

2.Define teratogenicity with giving examples .

Put true or false:

iatrogenic cushing's disease is an example for drug tolerance.





Thank You

