



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 super sensitivity and hypersensitivity.**
- **Discuss idiosyncrasy and side effects.**
- **Identify net results of secondary effects of drugs.**



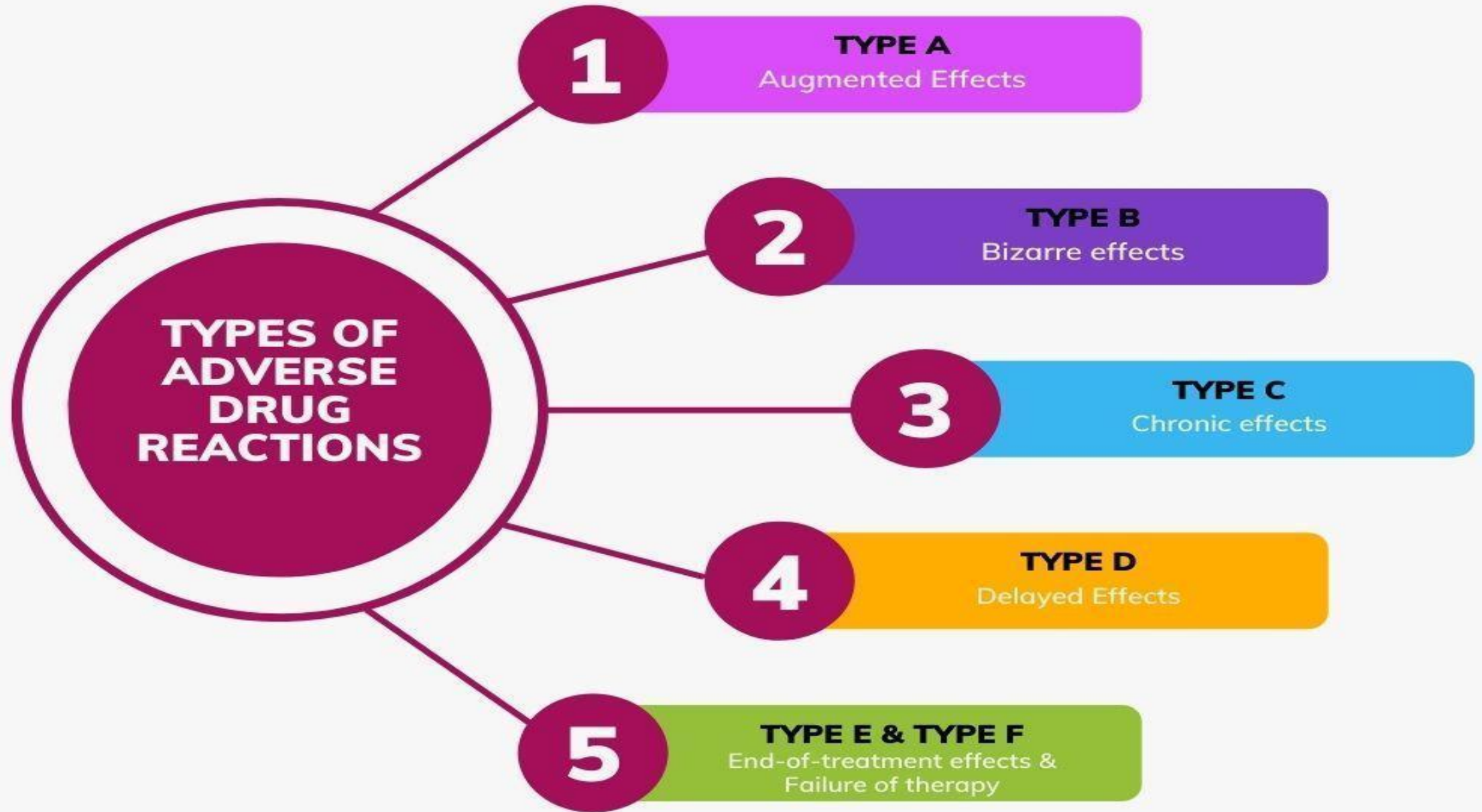
Adverse Drug Reactions

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



Types of adverse drug reactions

- 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.

I) TYPE A (Augmented or predictable undesirable adverse effects):

Predictable undesirable effects related to the normal pharmacological actions of the drug:

1- Side Effect

2- Secondary Effect

3- Over-dose

4- Super-sensitivity

5- Drug Intolerance

6- Direct Cytotoxic Effects

7- Drug Interactions

I) TYPE A (Augmented or predictable undesirable adverse effects):

1- Side Effect:



1- An unintended (undesirable), inevitable (unavoidable), expected effect of a drug related to its pharmacological properties & produced by the therapeutic dose of the drug.

2- Usually unpleasant



Examples:

1- Dry mouth induced by atropine when used as antispasmodic

2- Gastritis induced by NSAIDs (as Aspirin) when used as antipyretic



I) TYPE A (Augmented or predictable undesirable adverse effects):

2- Secondary Effect:



An **indirect** consequence of a drug **related to its pharmacological properties** (pharmacodynamics) and produced by **the therapeutic dose of the drug**.

Drug	Primary Effect	Secondary Effect
Oral Broad spectrum antibiotics used to treat respiratory tract infection	Killing pathogenic bacteria in the respiratory tract	Killing intestinal flora → 1- <u>↓↓ synthesis of vitamin B & k</u> 2- overgrowth of resistant intestinal commensal bacteria → <u>super-infection</u>
Inhaled corticosteroid used to treat bronchial asthma	anti-inflammatory anti-allergic effect on the bronchi	suppress cell mediated immunity → overgrowth of oral commensal fungi → <u>oral candidiasis</u>

I) TYPE A (Augmented or predictable undesirable adverse effects):

3- Over-dose



- An exaggerated pharmacological action of the drug (side effect or direct cytotoxicity) occurs when the drug attains high toxic plasma levels.

- Causes:

1- Very large dose of a drug or sometimes just a larger than the therapeutic dose for drugs with narrow safety margin

2- Drug accumulation: on repeated drug administration with impaired drug elimination (liver or kidney failure).

- Examples:

1- Single large dose: Insulin L.D. → Hypoglycemia

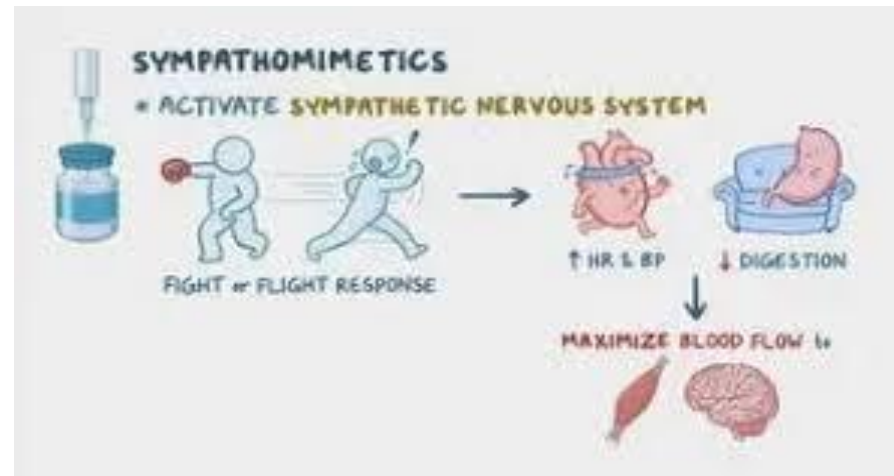
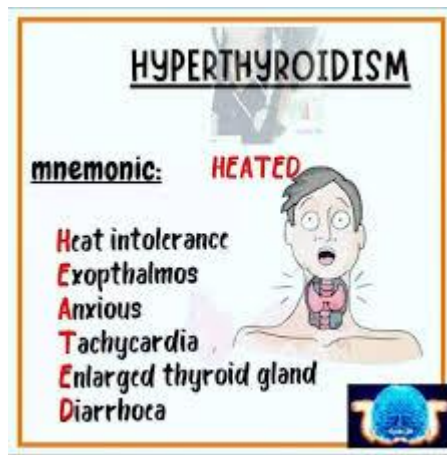
2- Accumulation of repeated doses: Digitalis (Long $t_{1/2}$)



I) TYPE A (Augmented or predictable undesirable adverse effects):

4- Super sensitivity

- An exaggerated pharmacological action of the drug in response to small therapeutic dose of the drug in some individuals due to tissue hyper-responsiveness (sensitivity).
- Management → decrease the dose
- Example: Hyperthyroidism → Super-sensitivity to sympathomimetics.



I) TYPE A (Augmented or predictable undesirable adverse effects):

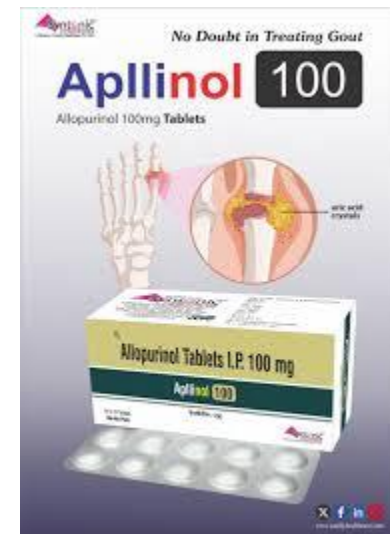
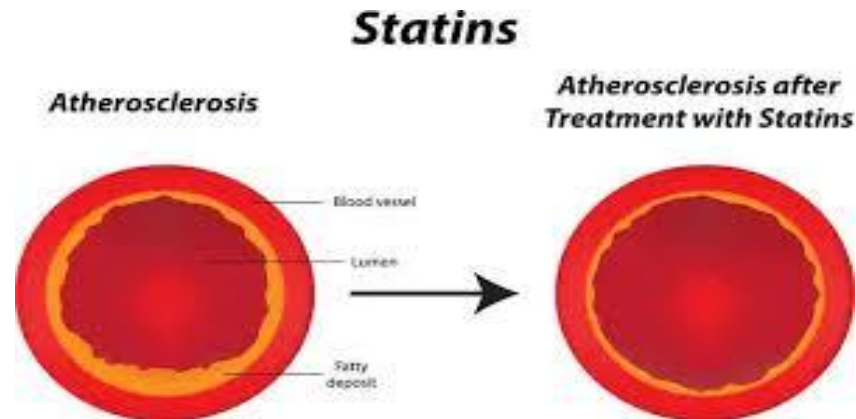
5- Drug Intolerance

- **A severe toxic effect** of the drug in response to the **usual therapeutic dose of the drug.**

- Examples:

1- Allopurinol intolerance: severe nausea, diarrhea, elevated liver enzymes.

2- Statin intolerance: severe liver & muscle injury.

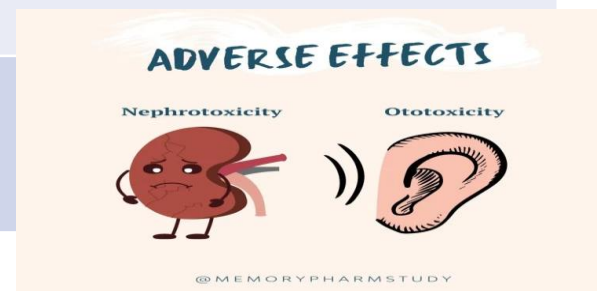
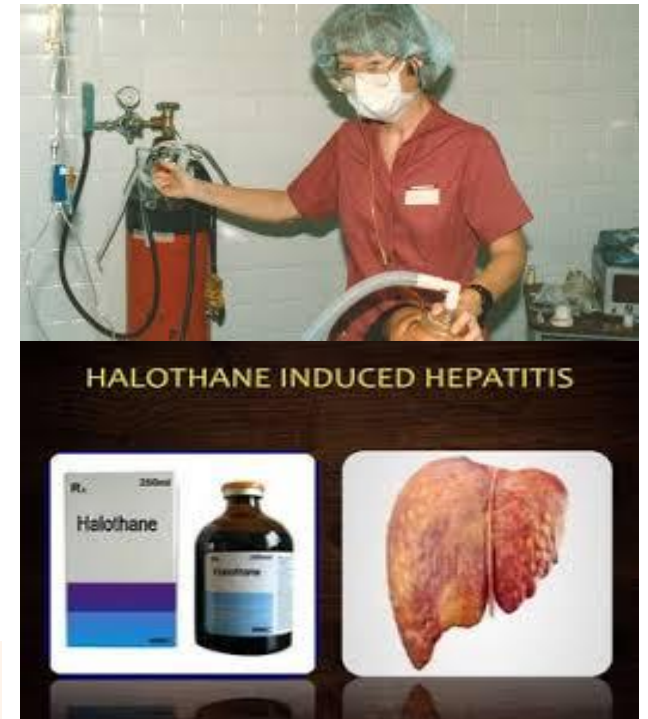


I) TYPE A (Augmented or predictable undesirable adverse effects):

6- Direct Cytotoxic Effects:

- The drug or its metabolites reacts with body tissues directly damaging cells.

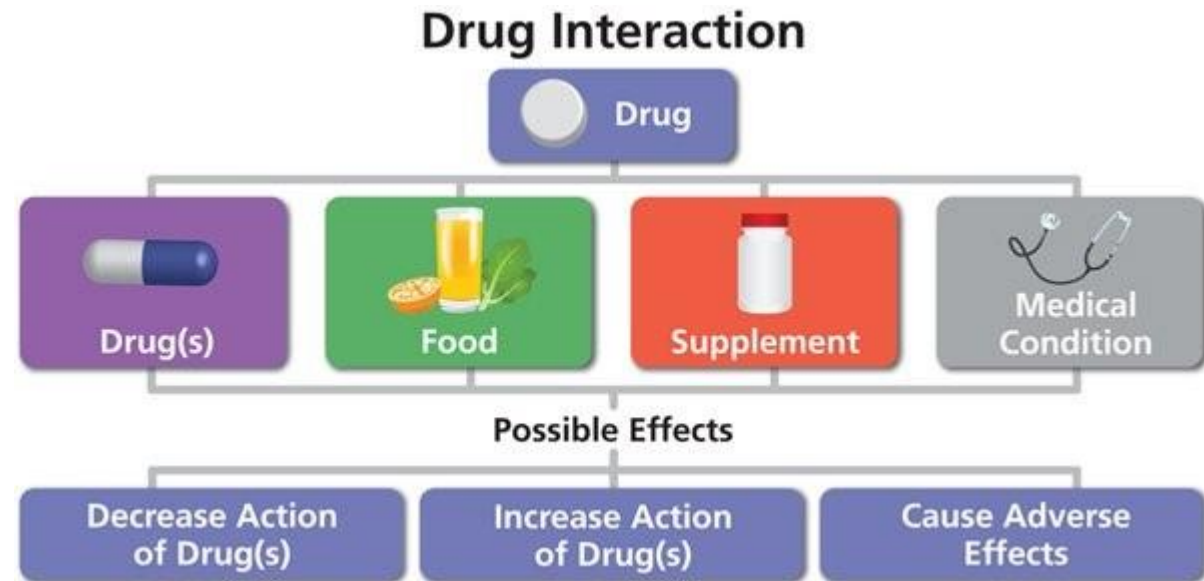
Cytotoxicity	Drug
1- Cardiotoxicity	Halothane
2- Hepatotoxicity	Halothane
3- Nephrotoxicity	Aminoglycosides
4- Neurotoxicity	Aminoglycosides → 8 th cranial nerve damage
5- Bone marrow inhibition	Chloramphenicol



I) TYPE A (Augmented or predictable undesirable adverse effects):

7- Drug Interactions

- Will be discussed later on.



II) Type B (Bizarre or unpredictable adverse effects)

1- Allergy (Hypersensitivity)

2- Idiosyncrasy (Pharmacogenetics)

II) Type B (Bizarre or unpredictable adverse effects)

1- Allergy (Hypersensitivity):

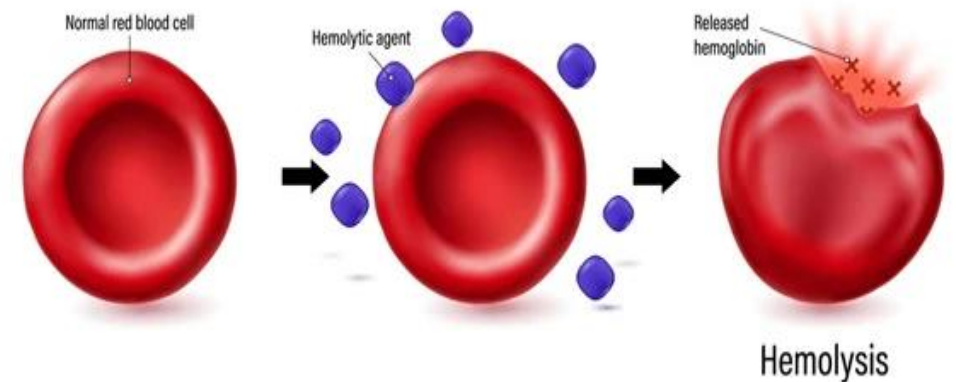
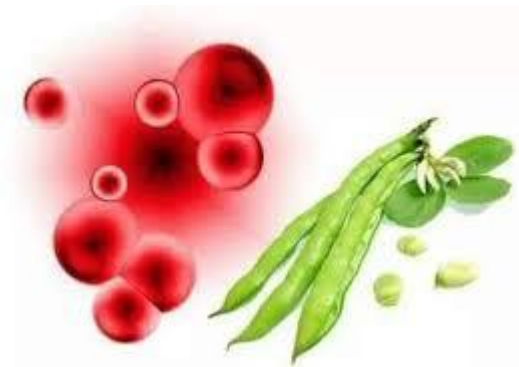
- Unpredictable abnormal response to drugs due to immune reaction.
 - The drug or its metabolites may act as an antigen or a hapten.
- Cross allergy can happen between chemically related drugs e.g. penicillins & cephalosporins
- Sometimes the excipient is the cause of allergy.
- Does not happen upon the first exposure to the drug. (IgE mediated only)
- Any drug may induce hypersensitivity reactions
- IgG mediated reactions may lead to drug resistance.
- Management: don't reuse the same or related drugs again.



II) Type B (Bizarre or unpredictable adverse effects)

2- Idiosyncrasy (Pharmacogenetics)

- Unpredictable abnormal response due to genetic abnormality.
- Occurs on first exposure.
- **Examples:**
 - a- **Hemolytic anemia** in patients with **Favism** (Glucose-6-Phosphate-Dehydrogenase enzyme deficiency) induced by: **Primaquine, aspirin & sulfonamides.**
 - b- **Succinylcholine apnea** in patients with abnormal Pseudo-Ch.E. activity.





Questions



Explain:

- 1. Aspirin can cause hemolytic anemia in favism.***
- 2. Succinylcholine apnea is considered as an idiosyncrasy reaction.***

Put true or false:

Allergic reactions with drugs is type A adverse drug reactions.





Thank You

