

pharmacology



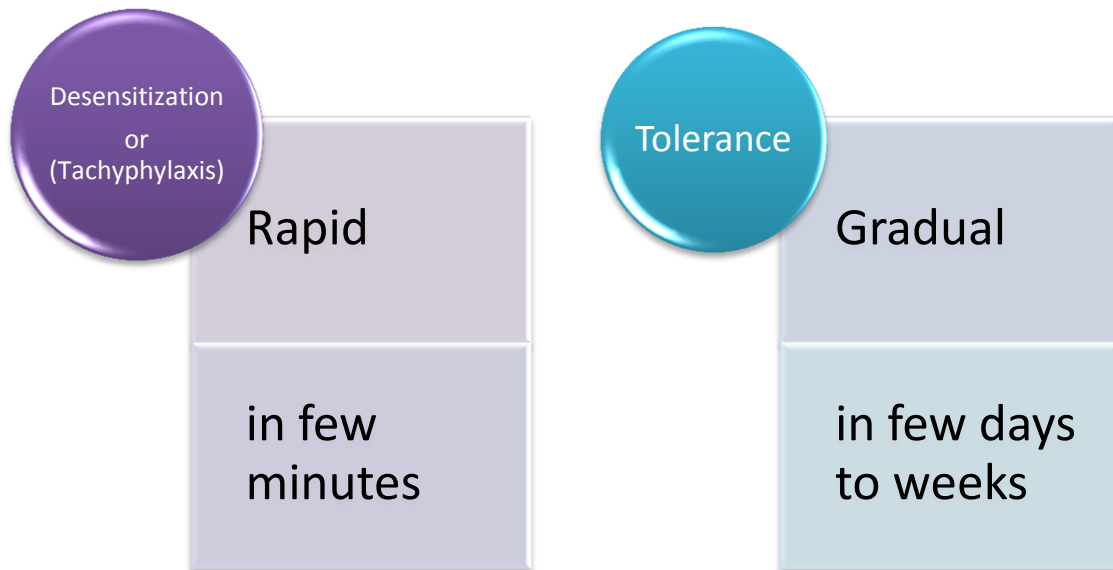
By:.

Team of pharmacology

Pharmacology 6th lecture (Tolerance dependence and concepts of ADR)

Lecture's objectives :

1. Know some pharmacological terminology
(Desensitization , Tachyphylaxis , Tolerance , Resistance , Refractoriness)
2. Reasons for development of tolerance (Pre-receptors events , Events at receptors , Post-receptors events)
3. The meaning of ADRs (**Adverse Drug Reactions**) and its types in addition to the comparison between types A & B
4. The meaning of Hypersensitization and its types.



Diminution of a response : between our body and the drug
Resistance: the loss of effectiveness of antimicrobial agent.
Refractoriness: the loss of therapeutic efficacy, pre & post receptor events lead to Refractoriness (unmanageable).

Tolerance:
Diminution of a response.

Reasons for development of tolerance:

Pre receptor events

Events at receptor

Post receptor events

↓ drug availability because of pharmacokinetic variation
So ↑ enzymes lead to ↑ metabolize = drug reduce concentration

-ex : barbiturates ↑ metabolize
Contraceptive pills so it becomes less availability.

-is the physiological adaption which leads to loss of response.

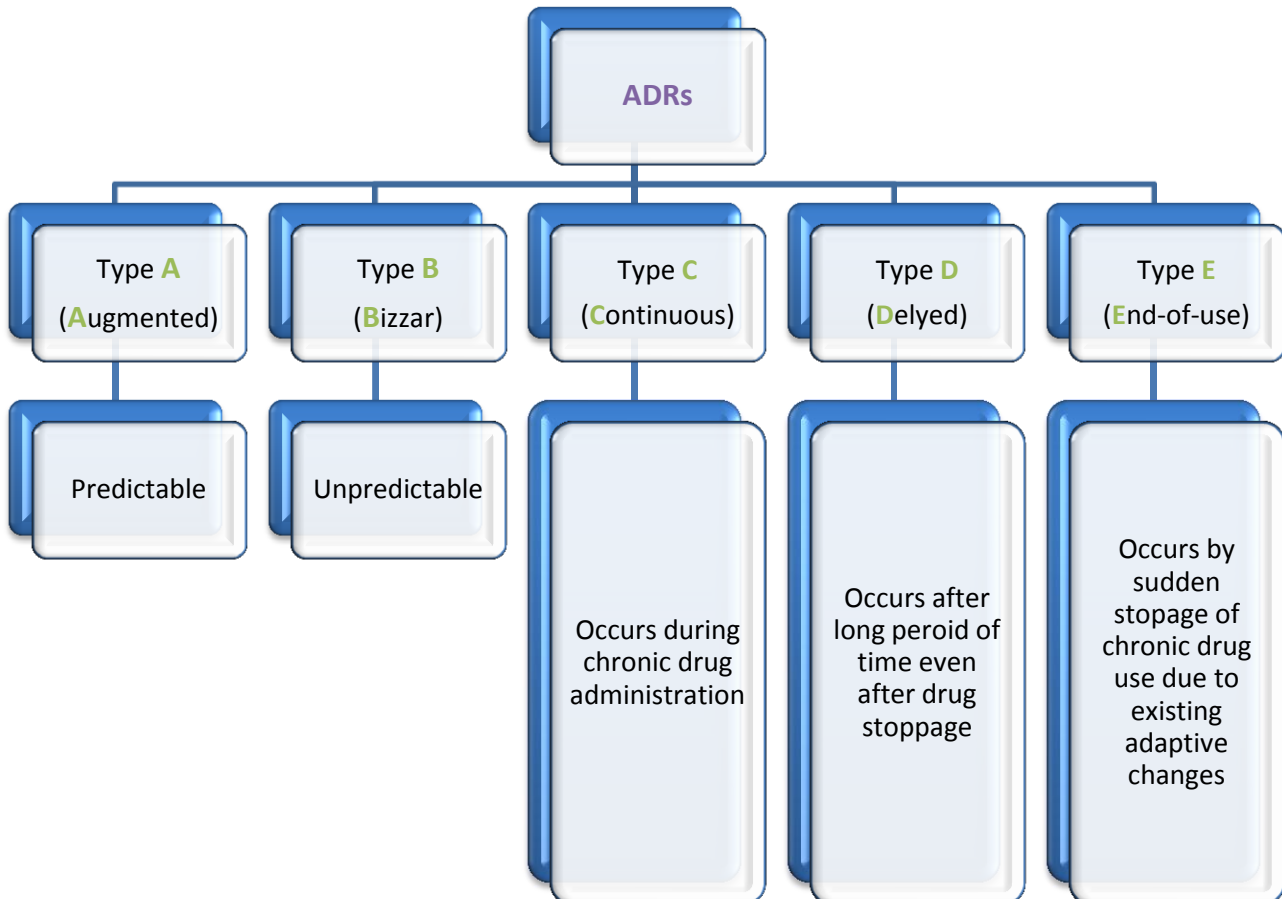
-Antihypertensive effects of **ACEIs** (angiotensin-converting-enzyme-inhibitors) become nullified by activation of renin angiotensin system by **NSAIDs** (non-steroid anti-inflammatory drugs).

EXHAUSTION OF MEDIATORS	BINDING ALTERATION	DOWN REGULATION
Depletion of mediator stores by Amphetamine it cause displacement of catecholamine from nerve until it depletion then response is decreased.	Phosphorylation of receptor when the drug bind to it, then it will be able to bind with (arrestin protein) β-adrenoceptors [functional defect]	Number of receptor is reduced after binding of (arrestin protein) Isoprenaline activation to β receptors [structural defect]

Barbiturate : دواء لمرضى الصرع يعمل على تكسير نفسه و تكسير الادويه الاخرى
Contraceptive pills : دواء منع الحمل
مريضة صرع تأخذ barbiturate و تأخذ contraceptive pills فيؤدي هذا الى الحمل

Adverse drug reaction (ADR): Development of side effects

Drug side effect classified alphabetically: A, B, C, D & E



	Type A Augmentation	Type B Idiosyncrotic
predictability	yes	No
Nature	Quantitative [extension of pharmacology effect]	Qualitative [immune or genetic base]
Does dependent	Yes (dose response relationship present)	No (dose response relationship absent)
Onset of symptoms	Usually Rapid	Usually delayed
Incidence & morbidity	High	Low
Mortality	Low	High
treatment	Dose adjustment or Substitute by > selective + Antagonize unwanted effect of 1 st drug	Stop drug + Symptomatic treatment
Example	Hemorrhage caused by <u>Warfarin</u>	Thrombocytopenia caused by <u>Quinine</u>

Drug	Type A	Type B
Chlorpromazine	Sedation	Cholestatic jaundice
Naproxen	GIT hemorrhage	Agranulocytosis
Phenytoin	Ataxia	Hepatitis, lymphadenopathy
Thiazides	Hypokalemia	Thrombocytopenia
Quinine	Tinnitus	Thrombocytopenia
Warfarin	Bleeding	Breast necrosis

Type	Explain	Example
C (Continuous)	Whose administer a chronic drug (for long time).	Osteoporosis is caused by <u>Corticosteroid</u>
D (Delayed)	Occurs after long time from administration a drug, even after stoppage	TERATOGENICITY caused by <u>Retinoids</u> & CARCINOGENICITY by <u>smoking</u>
E (End-of-use)	Occurs because of sudden stoppage of chronic drug.	Withdrawal syndrome caused by <u>Morphine</u>

Immunological Predisposition:

1st Exposure to drug will lead to **Sensitization**

2nd Exposure Lead to **Hypersensitivity**

Type B is due to immunological response (Hypersensitivity) classified to 4 Types:

TYPE I Anaphylaxis	TYPE II Cytotoxic	TYPE III Immune complex	TYPE IV Cell mediated
Urticaria rhinitis bronchial asthma by <u>Penicillin</u>	Haemolytic anaemia & thrombocytopenia by <u>Quinidine</u>	Serum sickness by <u>Sulphonamides</u>	Contact dermatitis by <u>local anaesthetics creams</u>