



PHARMACOLOGY

Team 434

Foundation Block

10-TOLERANCE AND ADR



Color Index

Red: Important Notes.

Orange: Further Explanation.

Purple: Additional Notes.

OBJECTIVES

- A- Distinguish difference between tolerance and desensitization (tachyphylaxis) and reasons for their development.
- B- Recognize patterns of **A**dverse **D**rug **R**eactions (ADR).

VARIATION IN DRUG RESONSIVNESS

- Decrease in drug effects or Development of side effects Between different individual or Within the same individual

TOLERANCE and DESENSITIZATION

- Phenomenon of variation in drug response, where by there is a gradual diminution of the response to the drug when given continuously or repeatedly

DIMINUTION OF A RESPONSE

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graph TD; A[DIMINUTION OF A RESPONSE] --> B[TACHYPHYLAXIS / DESENSITIZATION]; A --> C[TOLERANCE];
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TACHYPHYLAXIS / DESENSITIZATION

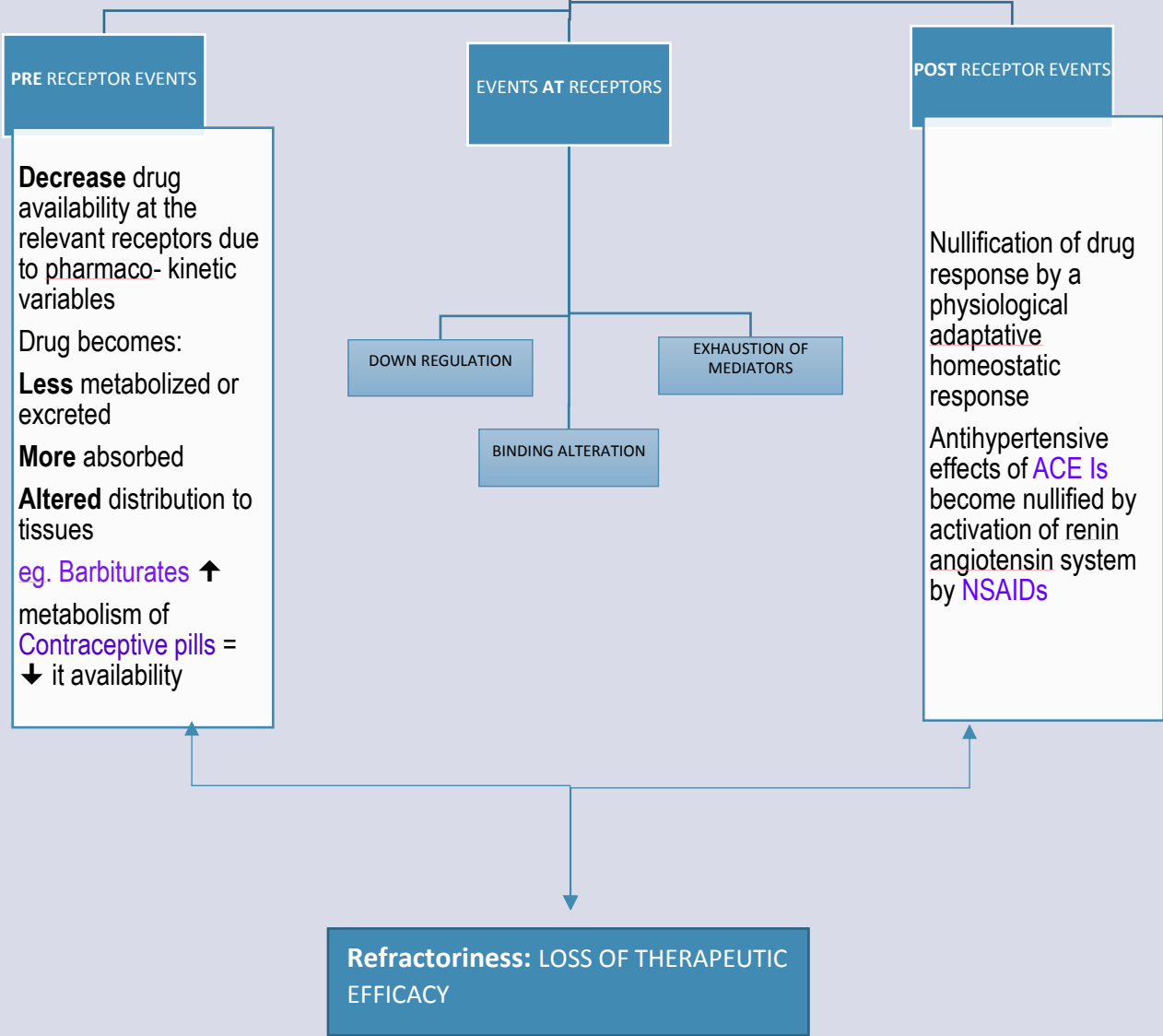
Rapid, in the course of few minutes.

TOLERANCE

Gradual, in the course of few days to weeks.

These should be distinguished from loss of effectiveness of antimicrobial agent (**Resistance**).

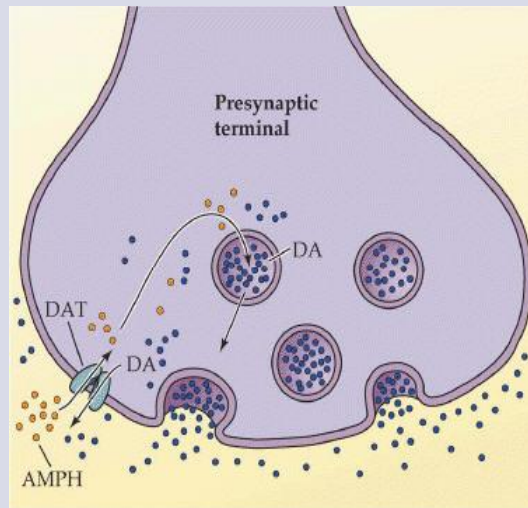
REASONS FOR DEVELOPMENT OF TOLERANCE



EVENTS AT RECEPTORS

1. EXHAUSTION OF MEDIATORS

Depletion of mediator stores By Amphetamine.



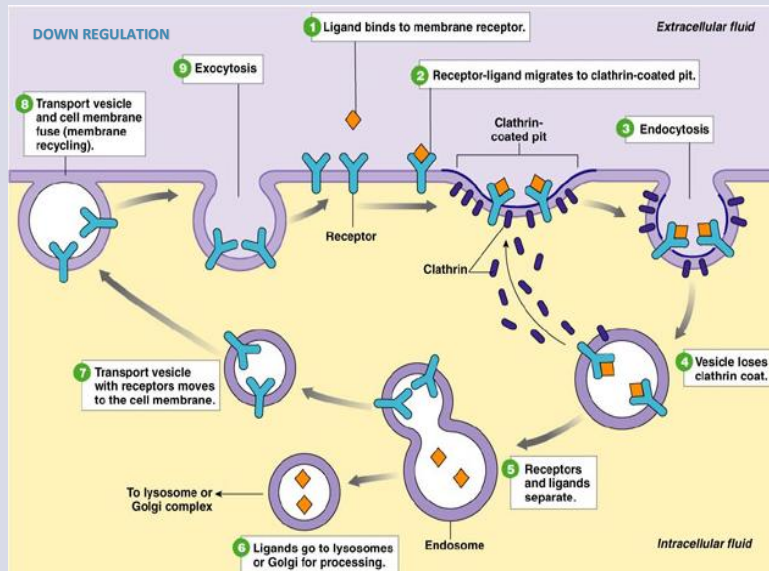
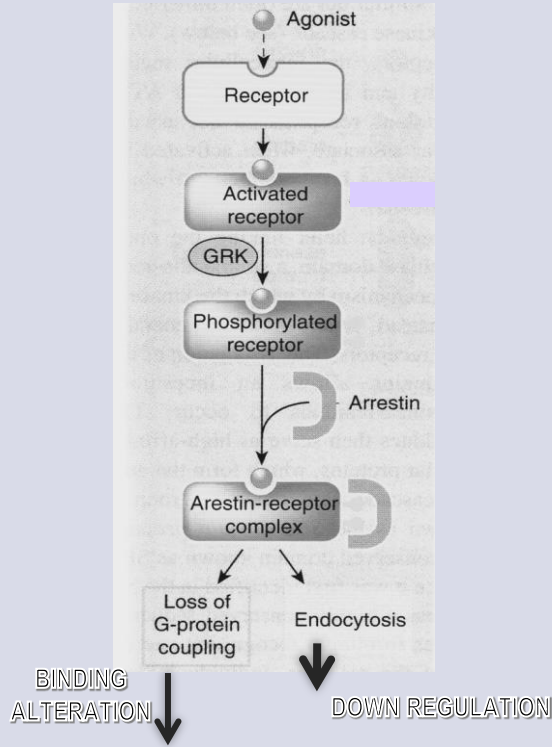
2. BINDING ALTERATION

Phosphorylation of receptor

I.e. β -adrenoceptors \rightarrow \downarrow Activation of **AC** to related ionic channel [functional defect].

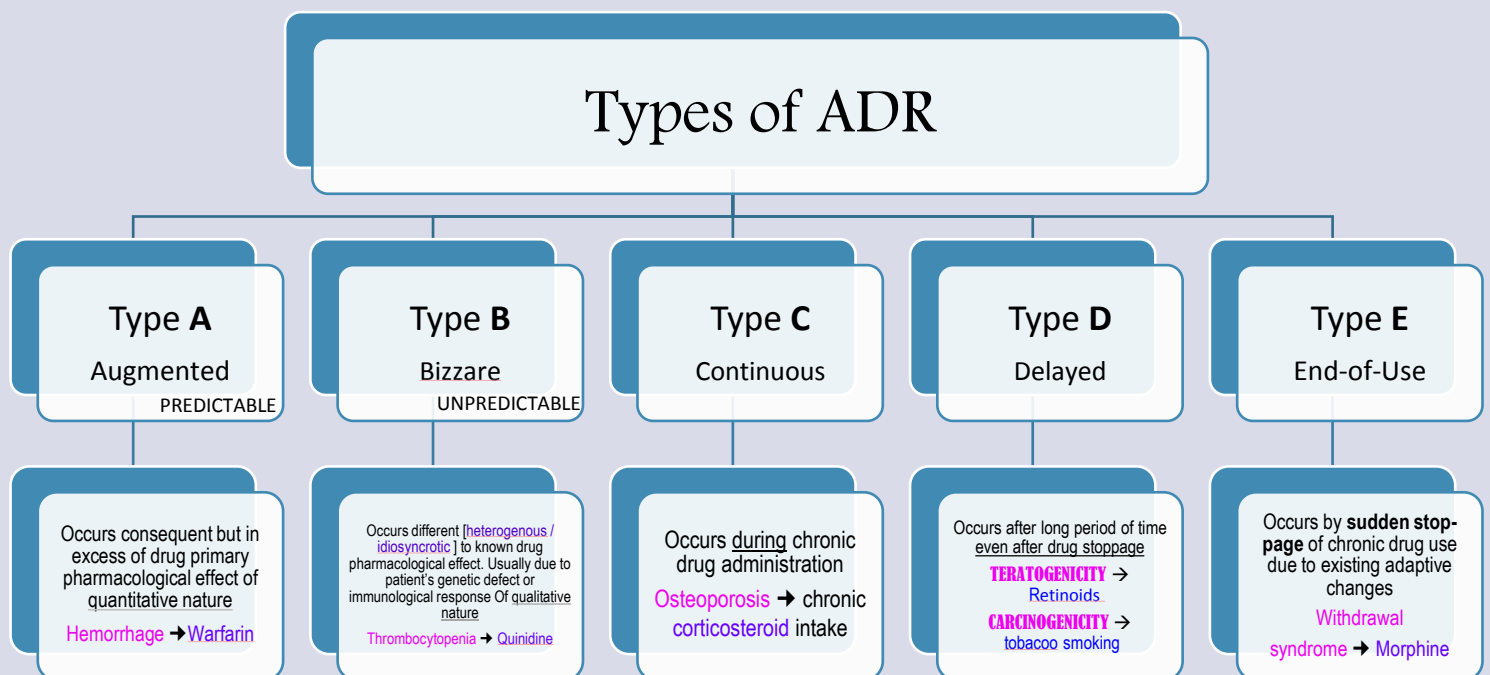
3. DOWN REGULATION

↓ Number of receptors. Isoprenaline activation to β receptors → ↑ R recycling by endocytosis [structural defect].



ADVERSE DRUG REACTIONS [ADR]

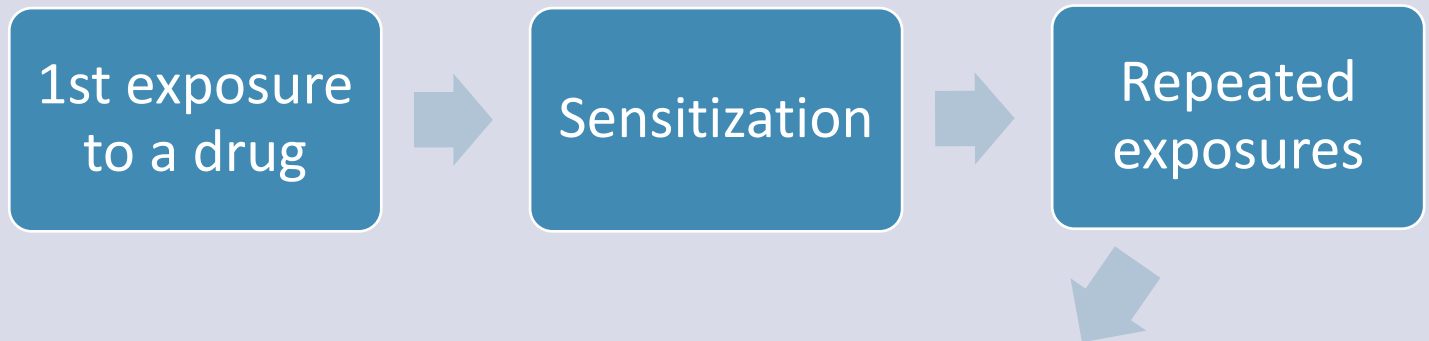
Harmful or seriously unpleasant effects occurring at doses intended for therapeutic effects.



Comparison between type A & B ADRs

	Type A Augmentation	Type B Idiosyncrotic
Pharmacological predictability	Yes	No
Nature	Quantitative [extension of pharmacology effect]	Qualitative [immune or genetic base]
Dose dependent	Yes (dose response relationship present)	No (dose response relationship absent)
Onset of symptoms	Usually Rapid	Usually delayed
Incidence	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 → Warfarin	Thrombocytopenia → Quinidine

Type B If due to immunological response



HYPERSENSITIVITY REACTION

- **TYPE I Anaphylaxis:** Urticaria, rhinitis, bronchial asthma by *Penicillin*.
- **TYPE II Cytotoxic:** Haemolytic anaemia, thrombocytopenia by *Quinidine*.
- **TYPE III Immune complex:** Serum sickness (fever arthritis enlarged lymph nodes, urticaria) by *Sulphonamides*.
- **TYPE IV Cell mediated:** Contact dermatitis by *Local anaesthetics creams*.

1) One of the reasons for the development of tolerance in pre receptor event is the :

- A. Decrease drug availability at the relevant receptors due to pharmacokinetic.
- B. Nullification of drug response by a physiological adaptive homeostatic response.
- C. Sudden stop- page of chronic drug use.
- D. Depletion of mediator stores.

2) Phosphorylation of a receptor by β -adrenoceptors causes.

- A. Decreases of adenylyl cyclase activation.
- B. Increase in receptor recycling.
- C. Increase metabolism of Contraceptive pills.
- D. Affect renin angiotensin system.

3) The other name for Bizzar (type B of ADR) :

- A. PREDICTABLE
- B. Heterogeneous
- C. End-of-Use
- D. Augmented

4) Sudden stoppage of chronic drug like Morphine can cause :

- A. Thrombocytopenia
- B. Osteoporosis
- C. Hemorrhage
- D. Withdrawal syndrome

5) A drug that causes Osteoporosis during chronic drug administration is :

- A. Warfarin
- B. Morphine
- C. Corticosteroid
- D. Quinidine

6) Hemorrhage is a predictable response for:

- A. Quinidine
- B. Warfarin
- C. Morphine
- D. Corticosteroid

7) Tobacco smoking could lead to _____ that could happen after a long period of time after stopping.

- A. Carcinogenicity
- B. Teratogenicity
- C. Osteoporosis
- D. Hemorrhage

8) The Incidence and morbidity of Type A (Augmentation) of ADR is :

- A. High
- B. Low
- C. Normal
- D. Unknown

9) The nature of Type B (Idiosyncratic) is:

- A. Quantitative
- B. Qualitative
- C. Usually Rapid
- D. Unknown

10) Penicillin could lead to Anaphylaxis reaction like :

- A. Bronchial asthma
- B. Haemolytic
- C. Anemia
- D. Thrombocytopenia

Answers: 1-A | 2-A | 3-B | 4-D | 5-C | 6-B | 7-A | 8-A | 9-B | 10-A

Done by Pharmacology Team

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Thanks to 433 team for making
this work possible <3