PHARMACOLOGY
TEAM 439

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MED439
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Quantitative aspects of drugs

If you didn't understand any part from this lecture Click here!

- Important
- In male and female slides
- Only in male slides
- Only in female slides
- Extra information

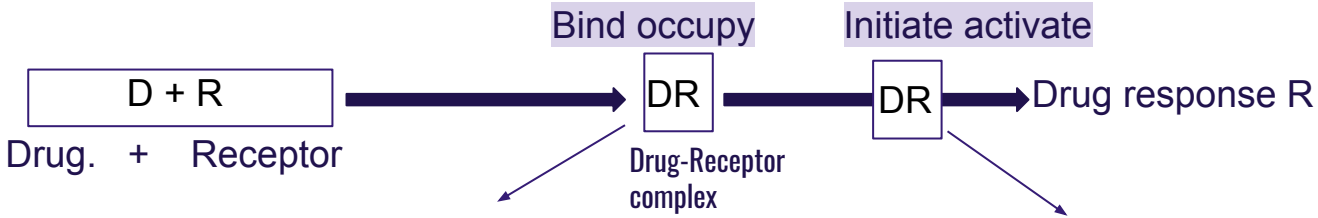
Objectives

- Determine quantitative aspects of drug receptor binding.
- Recognize concentration binding curves
- Identify dose response curves and the therapeutic utility of these curves.
- Classify different types of antagonism.

Any Future corrections will be posted on the editing file.
make sure to check it **frequently**

Click Here

Quantity aspects of drugs



Relate concentration [C] of D used (x- axis) the binding capacity at receptors (y-axis)

Concentration-Binding Curve
AFFINITY

The tendency of a drug to bind to the receptors is governed by its AFFINITY.

Potency

Relate concentration [C] of D used (x-axis) to response produced (y-axis)

Dose Response Curves
EFFICACY

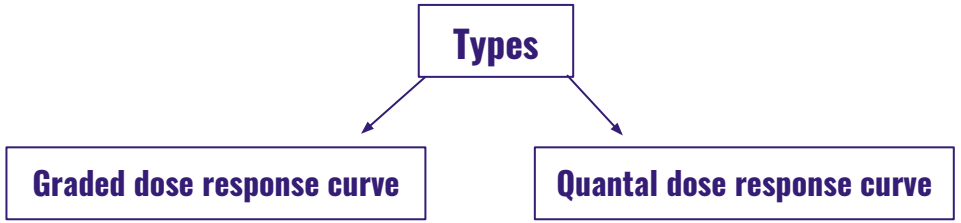
The ability for it, once bound, to activate the receptor is denoted by its EFFICACY.

Concentration binding curves:

- A correlation between **drug concentration [C]** used (x- axis) and drug binding capacity at receptors [B] (y-axis).
- Is a relation between **drug concentration** & drug binding
- i.e. Affinity

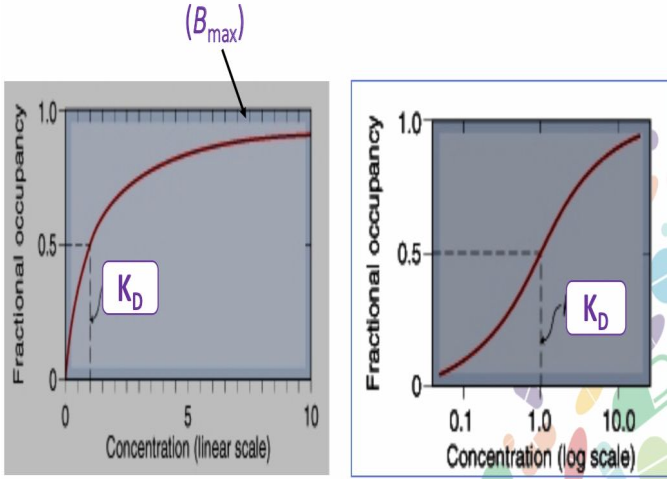
Dose- response curves:

- A correlation between **drug concentration** [D] used (x- axis) and drug response [R] (y-axis).
- Used to study how response varies with the concentration of the drug
- I.e. the relation between concentration and response



Concentration binding curves	• a correlation between **drug concentration [C]** used (x-axis) and **drug binding** capacity at receptors [B] (y-axis). i.e. Affinity	
Used to determine	(B_{Max})binding capacity	The total density of receptors in the tissue.
	K_{D50}	The concentration of drug required to occupy 50% of receptors at equilibrium.
	affinity of drug for receptor	The higher the affinity of drug for receptor = the lower is the K_{D50}. i.e. inverse relation (Binding potential = $Bmax/K_{D50}$).

Binding ability of drug with receptor (receptor complex)



Note: The higher the concentration, the higher the drug binding is going to be.(linear relationship)

Graded Dose-response Curve	• Relate drug concentration to response. • Response is gradual • Gradual increase in response by increasing the dose (continuous) • Curve is usual sigmoid in shape • Examples: low blood pressure, heart rate, blood glucose level cholesterol ..	
used to determine	(Emax) Maximum Efficacy	is the maximal biological response produced by a drug.
	(EC50) Median Effective concentration	is the concentration of the drug that produces a response equal to 50% of the maximal response (E_{max}).(concentration that effect 50% of (Emax))
	Potency	- The concentration of the drug required to produce a specified response (50% of the maximal response = EC_{50}) - Potency of drugs can be compared using EC_{50}, The smaller the EC_{50}, the higher the potent of drug. - It is inversely proportional to EC_{50}
	Efficacy	- The higher efficacy of drug at the Maximum Effect Potency higher at low Concentration of drug + we never look for efficacy or the Emax While the Efficacy we just look for the Emax

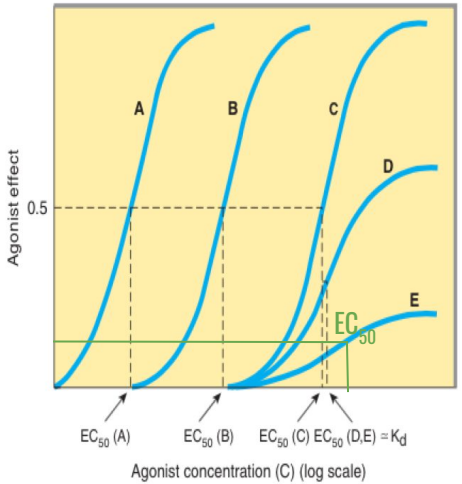
Graded dose - response curve

Which of the following curves represent the least potent drugs ? E

Potency = $\frac{1}{\text{Concentration}}$

Concentration يقل Potency كلما زاد

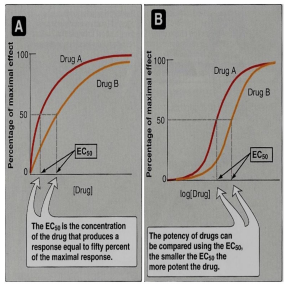
inversely proportional to each other

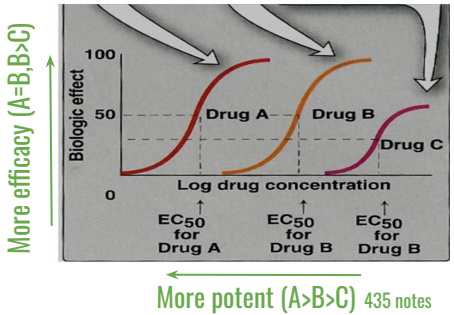


Which of the following drugs have the lowest efficacy ? E

It is better when the concentration is low
and the effect is high

Note: As "EC_{50}" increases, the response will also increase.



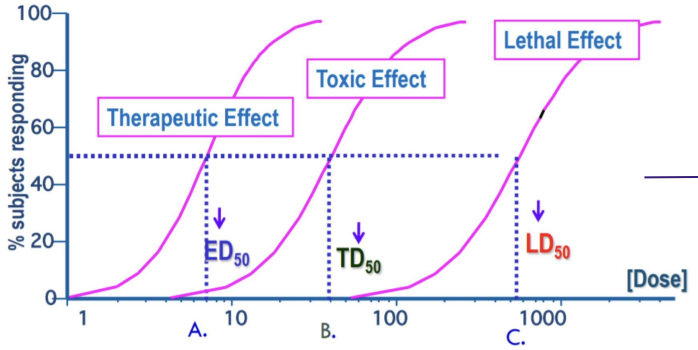


435 notes

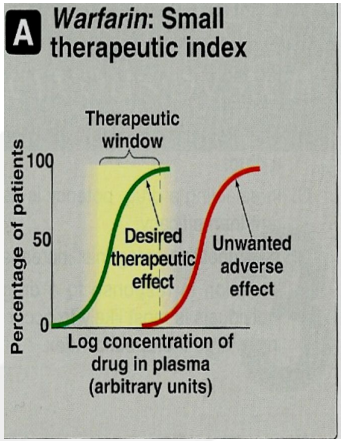
436 notes:
The potency of drug A is more than drug B&C.
The efficacy of drug A&B are the same and they are have more efficacy than drug c.

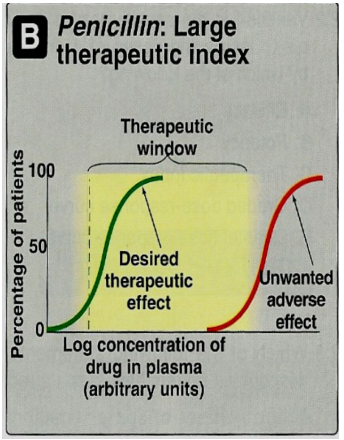
Quantal Dose-response Curve	• Relate drug concentration to % percentage of patients responding (all or none response). • The response may be therapeutic response, adverse effect or lethal effect • Examples: prevention of convulsion, arrhythmias or death.	
used to determine	(ED50) Median Effective Dose	is a dose of the drug required to produce a therapeutic effect in 50% of individuals (present of response of action in 50% of the patients)
	(TD50) Median Toxic Dose	is the dose of a drug required to produce toxic effects in 50 % of individuals.(Toxic effects=Side effects)
	(LD50) Median Lethal Dose	is the dose of a drug required to produce death in 50 % of individuals.
	Therapeutic index (TI)	• Therapeutic index = TD50/ED50 or LD50/ED50 • Is a measure of safety profile • High value =drug with wide margin of safety e.g diazepam, penicillin • Small value = a narrow margin of safety e.g. digoxin, warfarin The larger the therapeutic index the more safe the drug e.g: $\frac{100}{1}$ Is better than $\frac{4}{1}$

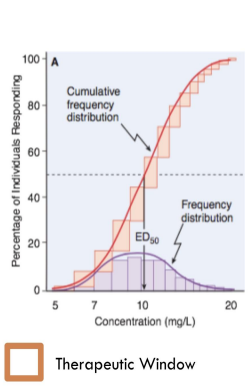
Quantal dose - response curve

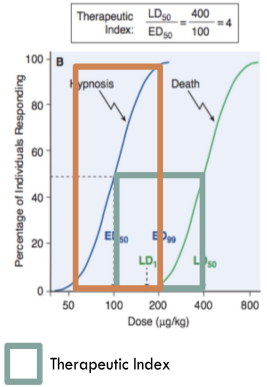


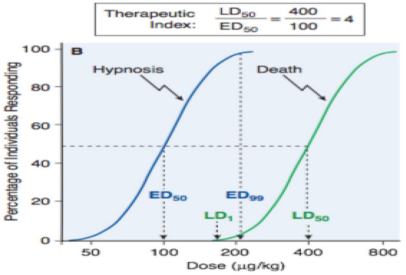
ED50= 50% of individuals exhibit the specified therapeutic response
TD50= 50% of individuals exhibit toxic effects
LD50= 50% of individuals exhibit death











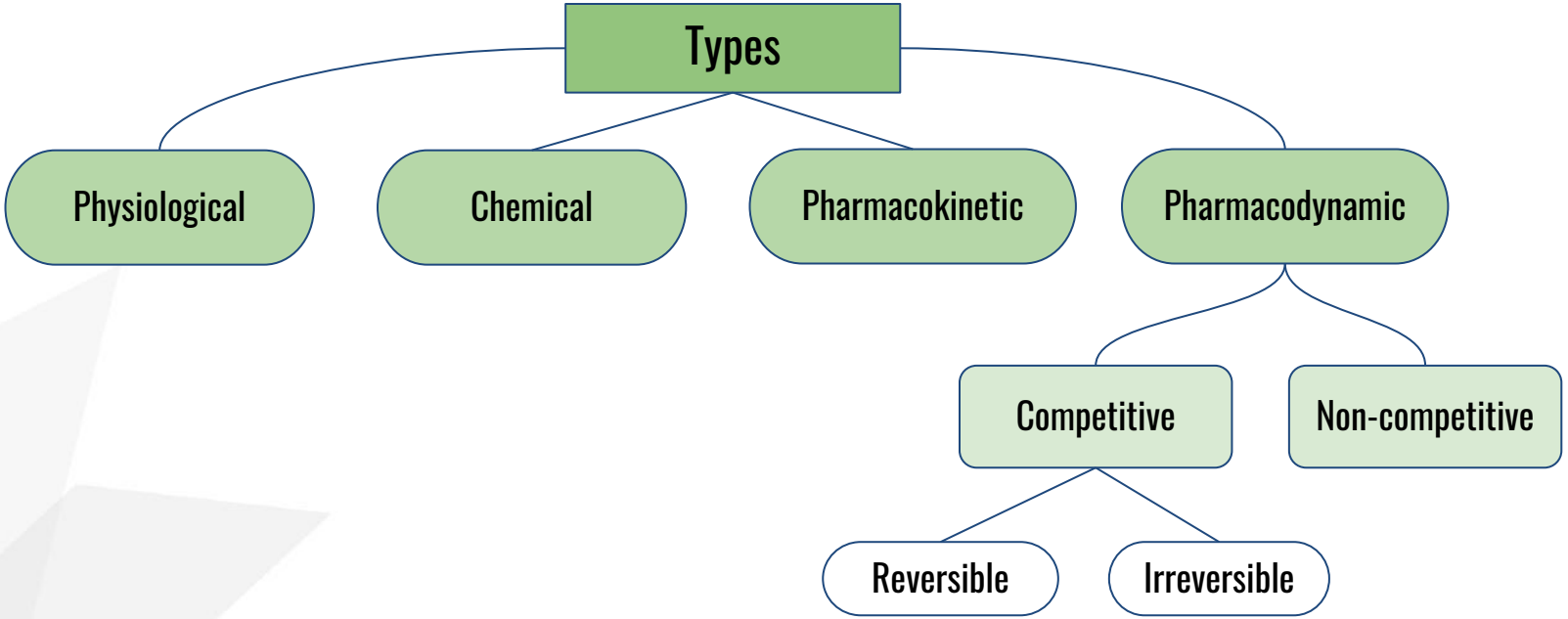
Therapeutic Window

Therapeutic Index

Note: Penicillin is safer than warfarin to take, due to having a larger therapeutic index.

Antagonism

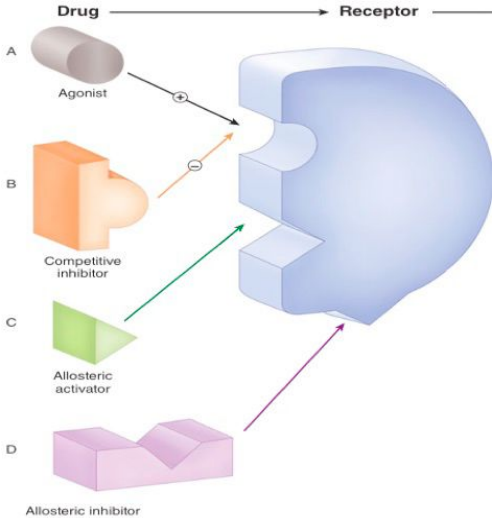
It is the decrease or the complete abolishment of the effect of one drug by the co-administration or combination with another drug.

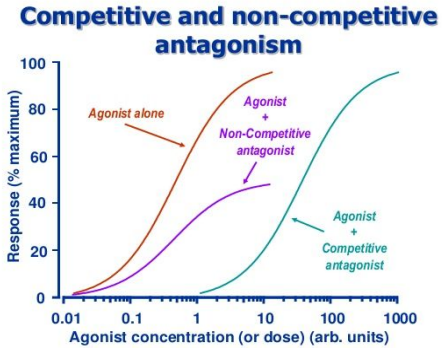


1- PHYSIOLOGICAL ANTAGONISM	2- CHEMICAL ANTAGONISM	3- PHARMACOKINETIC
• Two drugs act on different receptors to produce opposite physiological effects.	• Simple chemical reaction between 2 drugs resulting into loss of activity • No receptor	• The antagonist effectively reduces the concentration of the active drug at the site of action.
E.g. (Histamine) & (Adrenaline) •**Adrenaline** -> vasoconstriction and bronchodilatation -> increase blood pressure . -Adrenaline is used in anaphylactic shock. • **Histamine** -> vasodilatation and bronchoconstriction -> decrease blood pressure	E.g. Dimercaprol (which reduces heavy metal toxicity E.g. Lead)	E.g. Phenobarbitone (which accelerates hepatic metabolism of warfarin)

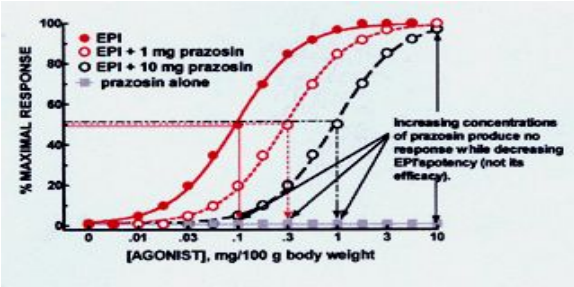
4- PHARMACODYNAMIC ANTAGONISM

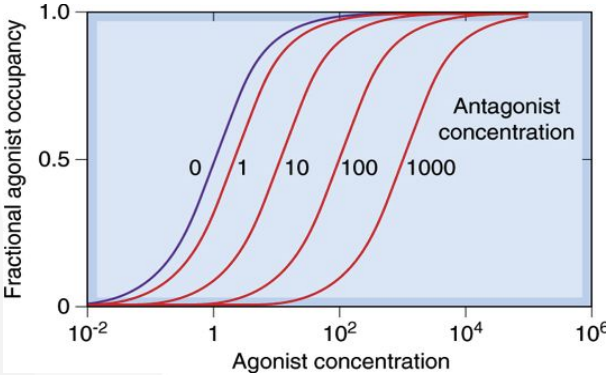
Competitive		Non-Competitive
reversible	irreversible	• Antagonist block at some point the chain of events that stimulate the response of agonist. • Agonist and Antagonist can be bound simultaneously (at the same time) • Antagonism cannot be overcome by increasing concentration of agonist.
• Two drugs compete for the same receptor (only one is bound). • The antagonist partially or completely prevents the pharmacological effect of agonist. • Antagonist dissociate rapidly from receptor. • Antagonism can be overcome by increasing the concentration of the agonist. • Parallel shift of the D-R curve to the right, without any change in slope or maximum.	• Two drugs compete for the same receptor • Antagonist forms stable,permanent chemical bond with receptor. • The original response can not be overcome even by increasing the dose of the agonist. • No parallel shift • A decrease in slope and a reduced maximum are obtained.	
e.g. acetylcholine and atropine	e.g. phenoxybenzamine and noradrenaline.	e.g. verapamil and noradrenaline.





Competitive reversible antagonist

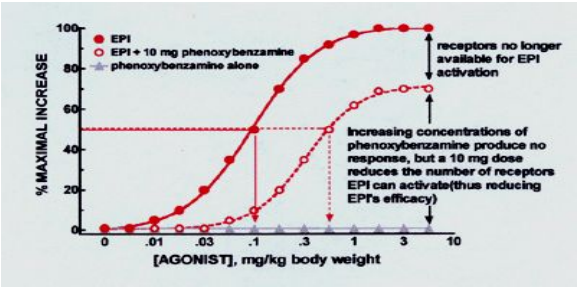


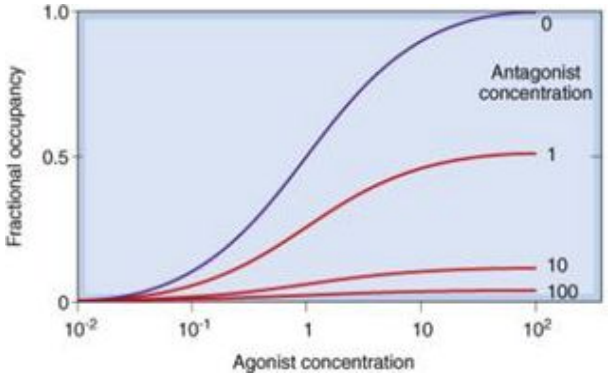


- Parallel shift to the right.
- No change in slope or maximum.
- Agonist is able to reverse the antagonist.

Vs

Competitive irreversible antagonist





- No parallel shift.
- Decrease in slope and a reduced maximum.
- Agonist has no effect on the antagonist

Only in male slides

EC100

- When a drug binds to a receptor the fraction occupancy equals D/(D+K).
- It is impossible for a drug concentration to reach EC100 and EC0.
- Even if you increase D to a million there will always be a K in the denominator and as such will never truly reach EC100.

D= concentration of drug

K= equilibrium binding dissociation constant

MCQ

Check out the questions made by MQ Team439 about this lecture here!!

1)	**The tendency of a drug to bind to the receptors is called?**			
A)	Affinity	B) Efficacy	C) Potency	D) EC50
2) Relate drug concentration to % percentage of patients responding is referred to?				
A)	Graded Dose-Response curve	B) Quantal dose-response curve	C) Concentration-Binding curves	D) -
3) Which type of Antagonism has No receptor involved?				
	A)Pharmacodynamic antagonism	B) Physiological antagonism	C) Chemical antagonism	D) Competitive (irreversible)
4) Two drugs compete for the same receptor and decrease in maximum effect are referred to?				
A)	Competitive (irreversible)	B) Competitive (reversible)	C) Non Competitive	D) Physiological

ANSWERS

1	A
2	B
3	C
4	A

SAQ

Check out the questions made by MQ Team439 about this lecture here!!

1) What's the main difference between reversible and irreversible Antagonism?

2) What is the total density of receptors in the tissues ?

3) Give an example of a drug that has a narrow margin of safety?

4)What is the relationship between KD50and affinity ?

ANSWERS

A1) In reversible antagonism the agonist is able to reverse the antagonist, while in the irreversible antagonism the agonist can't change the antagonist.

A2) The (BMax)binding capacity.

A3) Digoxin

A4) As the affinity gets higher, "(KD50)" decreases.(inversely proportional)

GOOD LUCK!

this lecture was done by :

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اسيل الشهري
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شادن العبيد
سديم آل زايد
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