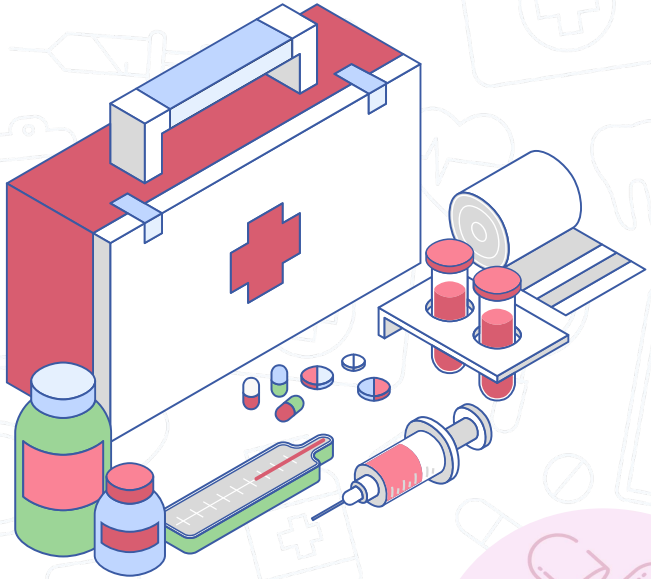
QUANTITATIVE ASPECTS OF DRUG ACTION 442



EDITING FILE

Pharmacology
Team 442

Important
Main text
Male slide
Female slide
Extra info
Doctor notes

Objectives:

1-Determine quantitative aspects of drugs receptor binding.

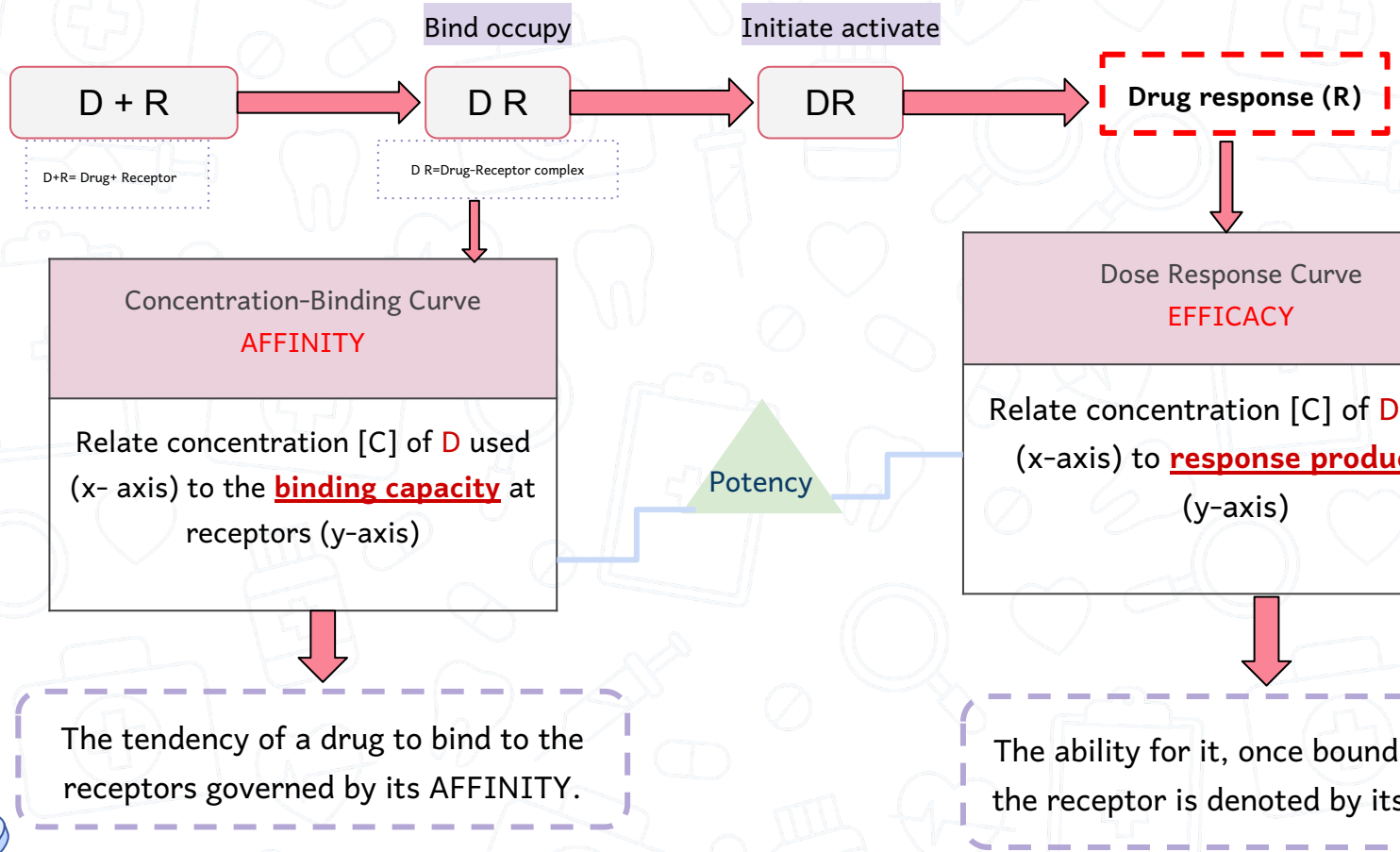
2-Recognize concentration binding curves.

3- Identify dose response curves and the therapeutic utility of these curves.

4- Classify different types of antagonism.

Click for Detailed explanation 1 Hour(:

Quantity aspects of drugs



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 or dose

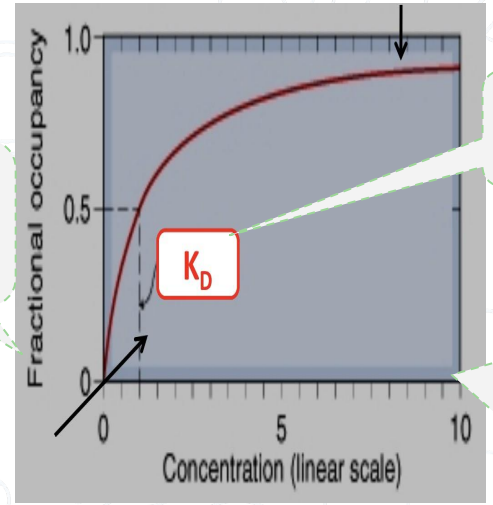
- I.e. the relation between concentration and response

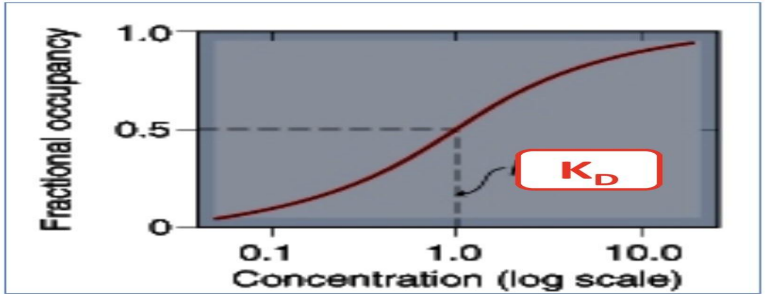
Concentration binding curves

must understand the terms may come SAQ

Used to determine

Bmax (binding capacity)	is the total density of **receptors** in the tissues.(100% bind)
KD50	is the **concentration**[C] of the drug required to occupy **50% of receptors** at equilibrium.
The affinity of drug for receptor	The **higher** the affinity of **D** for receptor, the **lower** affinity of is the **KD** i.e. inverse relation (Binding Potential = Bmax /KD)





Dose-Response curves

1-Graded Dose-Response Curve (تدريجي)

- Relate drug concentration (dose) to **response**.
- Response is gradual
- Continues response: increase in response by increasing the dose
- Curve is usual sigmoid in shape(s shape)
- Examples: low blood pressure, heart rate, blood glucose level cholesterol

Action
بيان مع كمية dose

Used to determine

(Emax) Maximum Efficacy

is the **maximal** biological response produced by a drug.

Efficacy

439: The higher efficiency of drugs at the Maximum Effect.

(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))

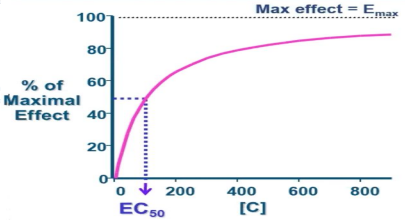
Potency

the concentration of the drug required to produce a specified response **(50% of the maximal response = EC50).**

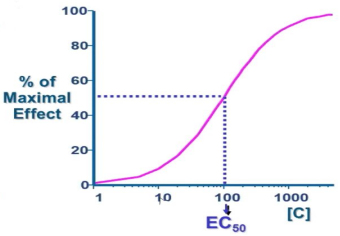
Potency of drugs can be **compared** using EC50, The smaller the EC50, the more potent the drug.(علاقة عكسية)

Potency is **inversely proportional** to EC50

Graded Dose-Response curves



As C ⬆ (Dose) Result In response ⬆

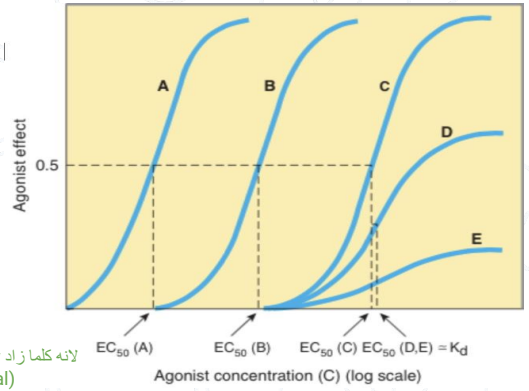


E_{max}:Effect when all the receptors are occupied by D

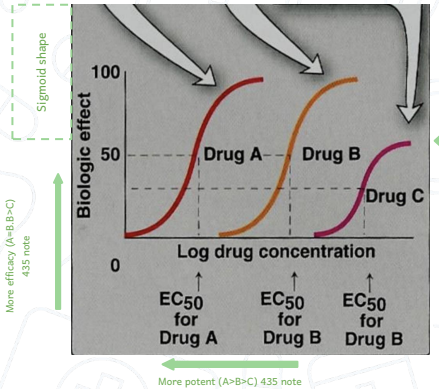
EC_{50}:that gives half the maximal effect

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

Which of the following drugs have the lowest efficacy ? E

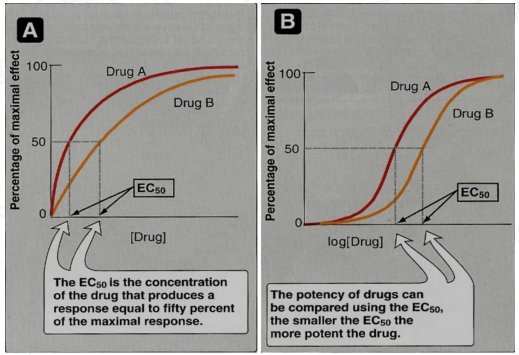


concentration يقل potency لانه كلما زاد
(Inversely proportional)

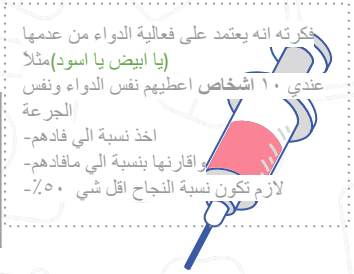


Drug A and B have the same **efficacy** but different **potency**, and they have **more** efficacy than drug c.
-Drug A is the most potent
-Drug C is the least potent

Only in girls slides



Dose-Response curves



2- Quantal Dose-response Curve

Relate drug concentration to % percentage of patients responding (all or none response).

- The response may be 1- therapeutic response 2-adverse effect 3- lethal effect
- Examples: prevention of convulsion(therapeutic) arrhythmias (adverse)or death(lethal)

Used to determine

(ED50)Median Effective Dose — is a dose of the drug required to produce a therapeutic effect in 50% of individuals

(LD50) Median Lethal Dose — Is the dose of a drug required to produce death (Lethal) in 50% of individuals.

(TD50) Median Toxic Dose — is the dose of a drug required to produce toxic effects in 50 % of individuals.

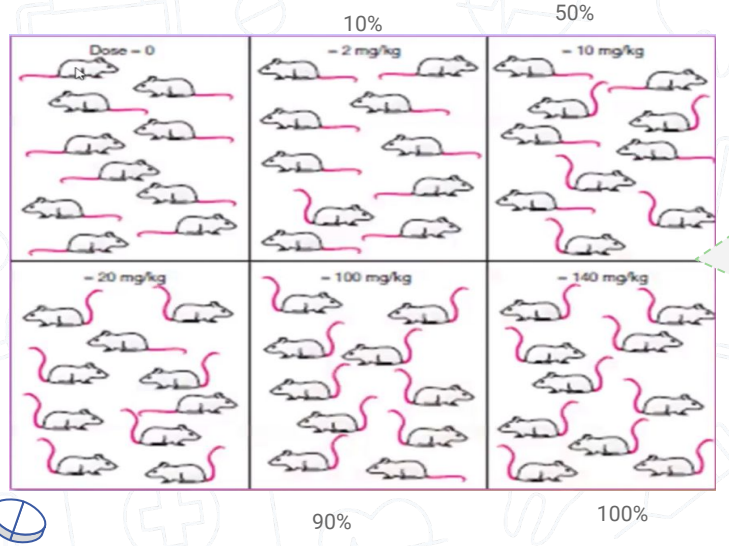
Therapeutic index (TI) — A measure of safety profile "The ratio of the dose that produces toxicity to the dose that produces a clinically desired or effective response in a population of individuals"

Therapeutic Index = TD50/ED50 or LD50/ED50.

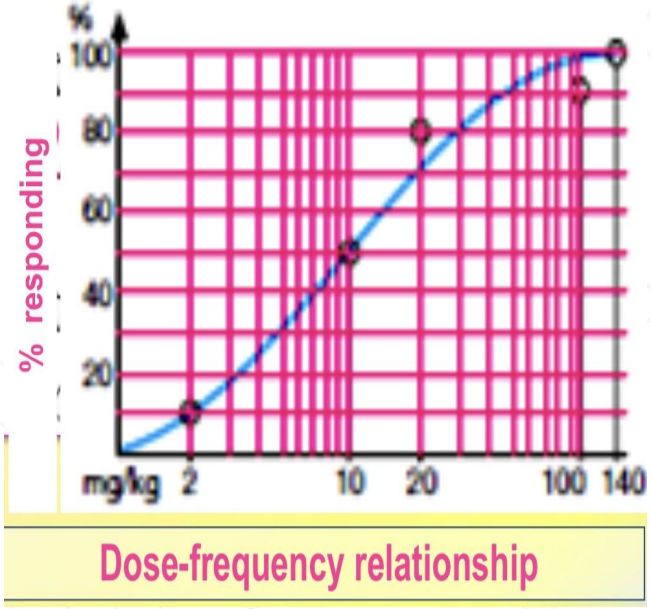
Large /high value = drug has **wide** margin of safety **e.g. diazepam, penicillin.**

Small value = a **narrow** margin of safety e.g. **digoxin, warfarin.**

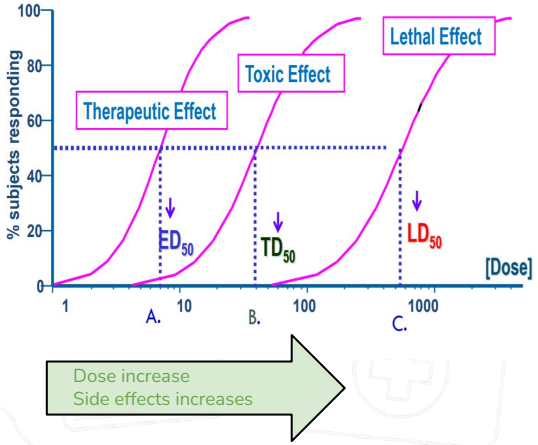
Quantal Dose-Response Curve (just to understand the concept)



10 فئران عطيناهم دواء
فنلاحظ المرة الأولى مع 2mg
فقط واحد اللي استجاب
واعطى response
والمرة الثانية زدنا الجرعة 10mg
فاستجاب نصفهم (50%)
فكل ما زدنا الجرعة بيزيد ال
response حتى نوصل 100%



Quantal Dose-Response Curve



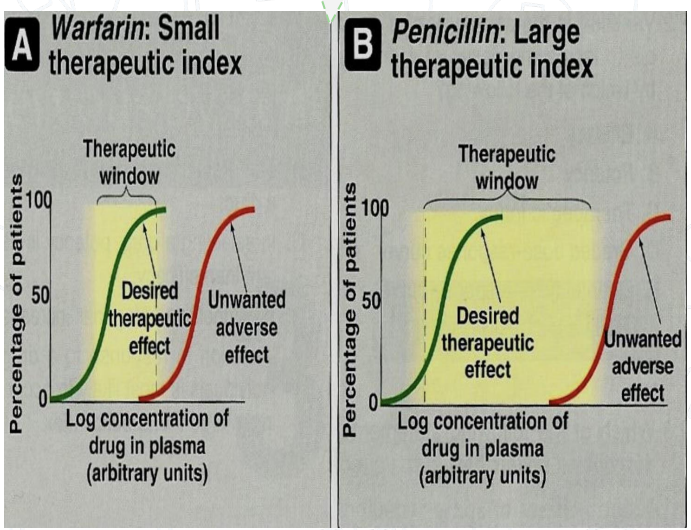
Dose increase
Side effects increases

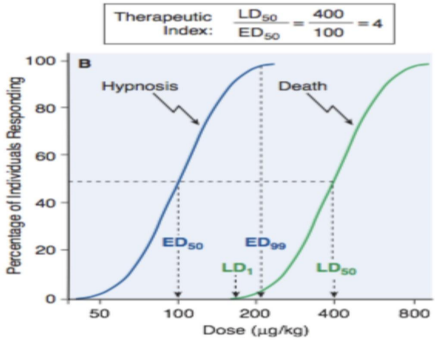
TD50= 50% of individuals exhibit toxic effects

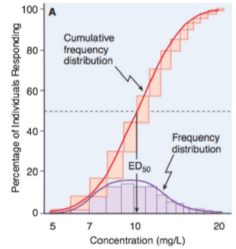
LD50= 50% of individuals exhibit death

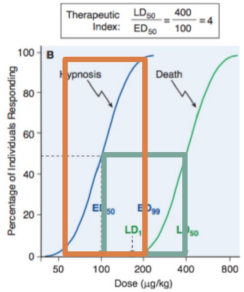
ED50= 50% of individuals exhibit the specified therapeutic response

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









Therapeutic Window

Therapeutic Index

Antagonism

(تضاد such as drug-drug interaction)

Definition:it is the decrease or the complete abolishment(remove) of the effect of one drug in the presence of another

Another definition:it is the decrease or the complete abolishment of the effect of one drugby the co-administration(مع بعض) (concurrent administration) or combination with another drug)

Click for Detailed explanation 30 min (:

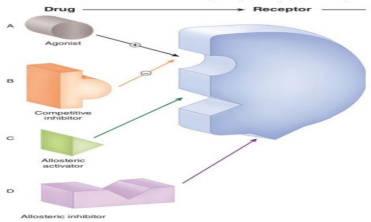
Types

- Physiological
- Chemical
- Pharmacokinetic
  ADME
- Pharmacodynamic
  (Receptor-blockade antagonism)
  Anything related to the receptor
  - Competitive
    - Reversible
    - Irreversible
  - Non-Competitive

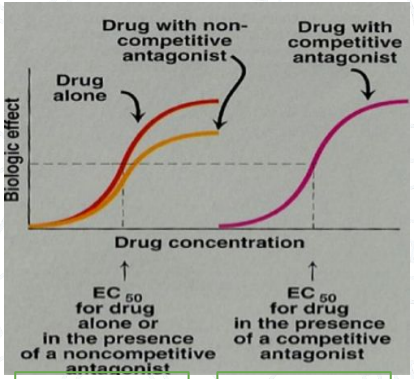
Types	Definition	Example حفظ
Physiological antagonism	-Two drugs act on **different receptors** to produce opposite physiological effect	Histamine & Adrinanile **Histamine** ⟶ vasodilation ⟶ (↓ blood pressure "hypotension") and bronchoconstriction الهيستامين يعطي شعور الاختناق وعدم القدرة على التنفس ف الادرينالين يعطي عكس المفعول **Adrenaline** ⟶ Vasoconstriction ⟶ (↑ blood pressure "hypertension") and bronchodilation -Adrenaline is used in anaphylactic shock.
Chemical antagonism Extra.:(Tetracycline can't take it with iron or calcium drugs)	-Simple chemical reaction between two drugs resulting into loss of activity - No receptor (both of the drugs won't work)	(**Dimercaprol**) used as antidote reduces heavy metal toxicity (as in **lead toxicity**). العمال اللي يشتغلون بمصانع الرصاص، الدواء راح يمسك ال lead toxicity وما يمتصه الجسم وبيطلع منه بدون اضرار، مثل: antacid Lead= رصاص
Pharmacokinetic	The antagonist effectively reduces the concentration of the active drug at the site of action.	e.g. (**Phenobarbitone -inducer-**) accelerates hepatic metabolism of warfarin. " Warfarin is anticoagulant " L3 enzyme induction

Pharmacodynamics (receptor-blocked antagonism)

Types	Competitive		Non-competitive
	Same receptor The strongest or with higher concentration will bind		
	Irreversible	Reversible (short duration)	
Definition	-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 of D-R curve -A decrease in slope and a reduced maximum are obtained. (treatment is hard) (the drug form a covalent bond with the receptor it can't be removed from its place) يعني بتكون الرابطة بينهم قوية ومهما زدنا من الجرعة ماراح تتأثر	-Two drugs compete for the same receptor**(only one 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 (treatment is easy) هذا النوع البقاء بيكون للدواء الاعلى تركيز	-Antagonist block at some point the chain of events that stimulate the response of agonist. يعني التغييرات اللي المفروض تحصل داخل الخلية راح تتوقف. -Agonist and Antagonist can be bound **simultaneously**. (at the same time but in different sites) - Antagonism cannot be overcome by increasing concentration of agonist. (the antagonist will enter in the signal transition pathway not in the receptor). في البداية على Surface -receptor and agonist سليمين ويشتغلون طبيعي في النهاية داخل الخلية Antagonist يوقف العملية
Example حفظ	-phenoxybenzamine (the antagonist) -noradrenaline (neurotransmitter in the parasympathetic, also have alpha and beta receptor)	-Acetylcholine (The agonist, also it's a neurotransmitter with Nicotinic/Muscarinic receptor in the sympathetic system) -atropine (the antagonist)	-verapamil (the antagonist) - noradrenaline (the agonist, with alpha and beta receptor)



agonistمن برا يسوي شغله
->receptor->(antagonist)تأثيره
داخل الخلية

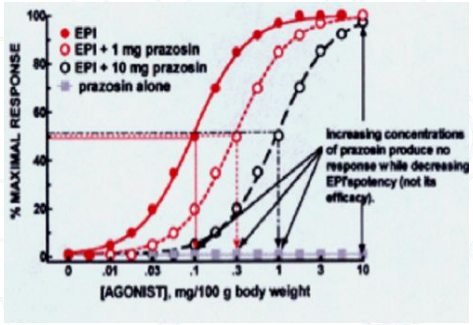


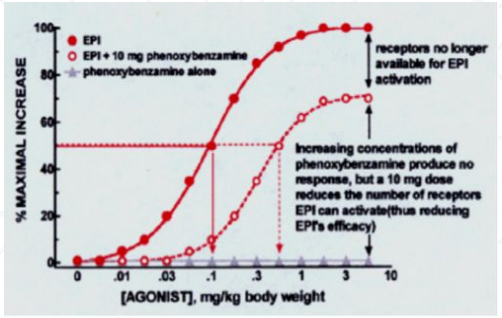
Ec is low because the drug is alone

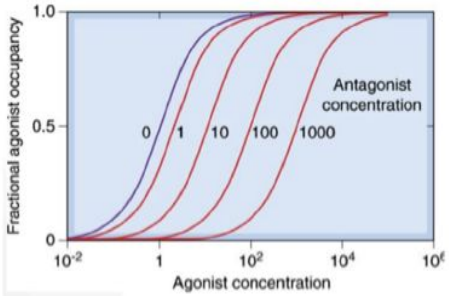
Ec is high because we have two drugs

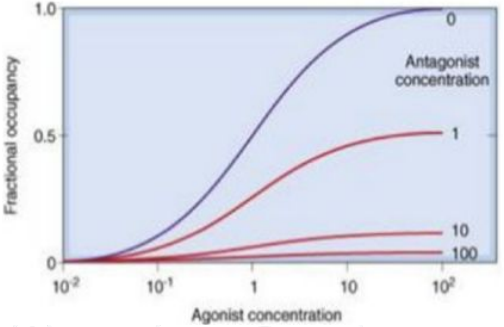
Important to know when it will be increased and when it will be decreased

Competitive reversible antagonist Vs Competitive irreversible antagonist









-Parallel shift to the right.
- No change in slope or maximum. -Agonist is able to reverse the antagonist.+ parallel يعني كلهم متوازيين

Thanks to 439

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

girls slides:

Antagonism can be overcome by increasing concentration of agonist = SURMOUNTABLE

Antagonism cannot be overcome by increasing concentration of agonist = NON-SURMOUNTABLE

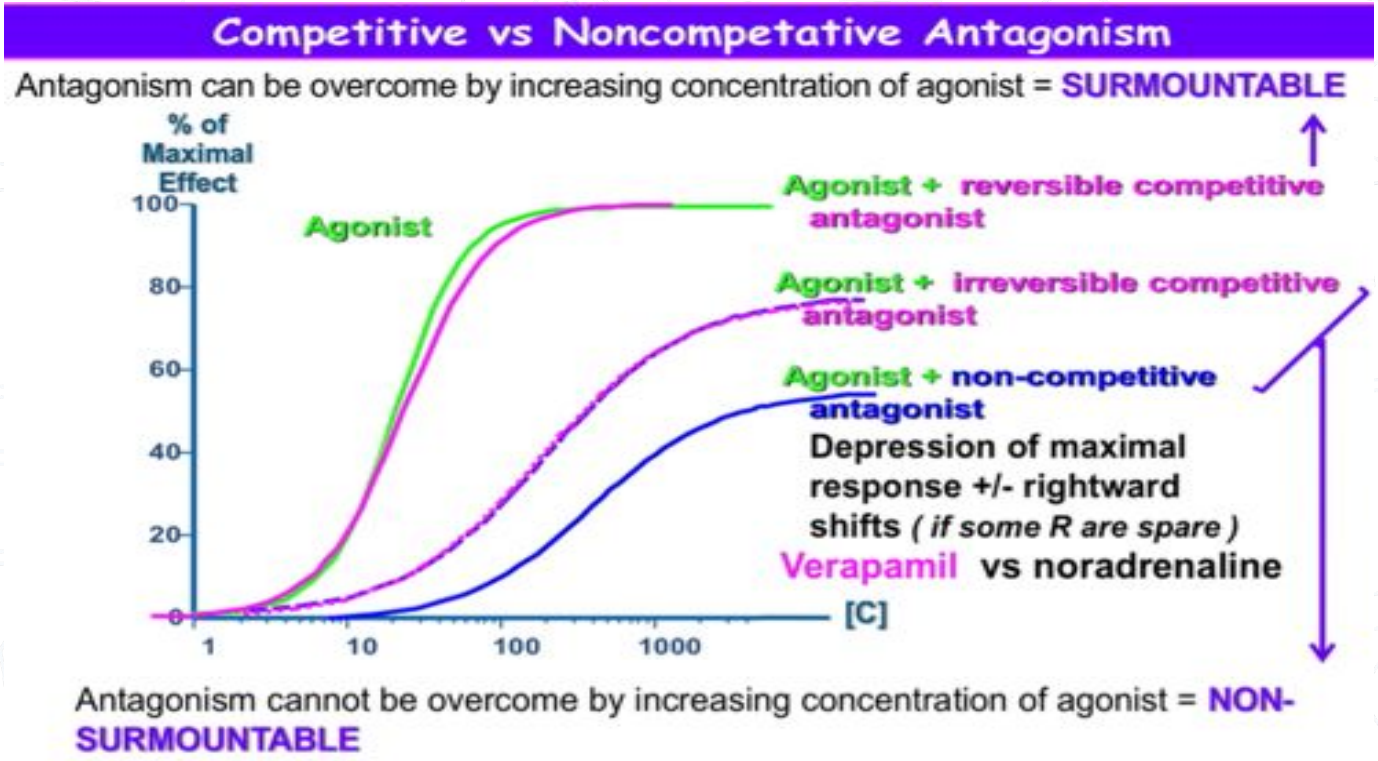
BOYS SLIDES

WHAT ABOUT EC100?

As the concentration (X) goes up, the dose-response equation computes the response (Y) as getting closer and closer to the Top plateau. But it never reaches it. When a drug binds to a receptor with mass action rules, the fraction occupancy equals D/(D+K), where D is the concentration of drug (that you vary) and K is the equilibrium binding dissociation constant, which is a fixed property of the drug and receptor. As D gets higher and higher, the fractional occupancy gets closer and closer to 1.0, but never reaches it. Therefore, there can be no EC100. And no EC0.

Summary:

Click for Useful **video**!!



MCQ

Q-1 When giving an example of a Agonist-Antagonist mechanism, which of the following is best mentioned?

A-Effect of Adrenaline & Penicillin **B**-Effect of Adrenaline & Histamine **C**-Effect of Penicillin & Histamine **D**-Effect of Aspirin & Adrenaline

Q-2 is the concentration of the drug that produces a response equal to 50% of the maximal response (Emax)?

A-EC50. **B-Emax.** **C-Potency.** **D- KD**

Q-3 The total density of receptors in the tissue?

A-Bmax. B-Emax. C-Kd50. D-Ed50

Q-4 Relate drug concentration to % percentage of patients responding (all or none response).?

A-Graded dose-response. **B-Dose-Response.** **C-Concentration-Binding.** **D-Quantal dose-response**

Q-5 Antagonist forms stable, permanent chemical bond with receptor is what kind of Antagonism?

A-Chemical. **B-Non competitive.** **C-Irreversible.** **D-Reversible**

1-B
2-A
3-A
4-D
5-C

SAQ

Q-1 What is the total density of receptors in the tissues ? med39

Q-2 Give an example of a drug that has a narrow margin of safety? med39

Answers

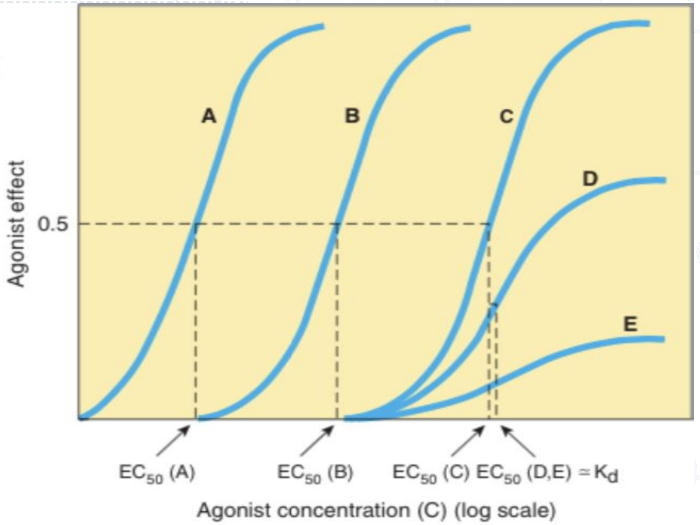
1- The (BMax)binding capacity.

2- Digoxin

SAQ

Q-3 define Bmax and KD50? from the DR

Q-4 which of the following have same efficacy ? From the DR



Answers

1- slide 5

2- A B C

SAQ

Q-5 supposed we have two medications one of them has therapeutic index with 4 and the other with 2000 what is better? From the DR

Answers

1- The second one with 2000 (the more therapeutic index the more drug safety)

DONE BY THE AMAZING TEAM

You GOT THIS!

Shahed Bukhari
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Hend Almogary
Razan Almohanna
razan almanjomi
Noura bin hammad
Lina alyahya
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