Pharmacology

Subject :

Lec no : 10

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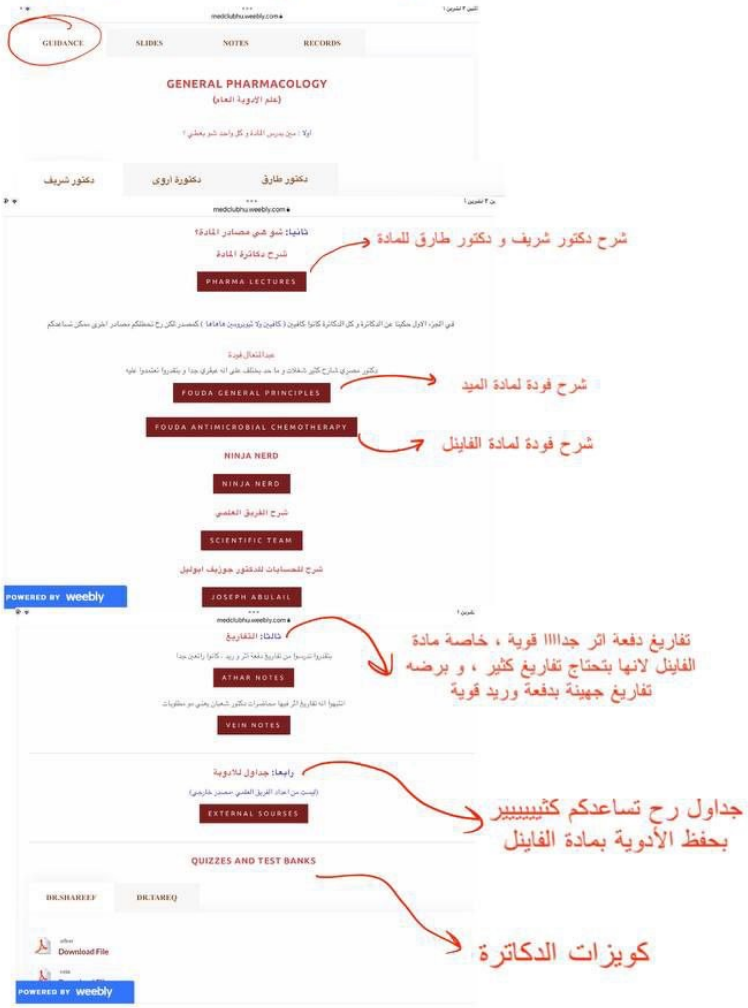
وَقُل رَّبِّ زِدْنِي عِلْمًا

للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

تجدون في guidance مادة الفارما على موقع النادي :



شرح دكتور شريف و دكتور طارق للمادة

شرح فودة لمادة الميد

شرح فودة لمادة الفاينل

تفاريغ دفعة اثر جداااا قوية ، خاصة مادة الفاينل لانها بتحتاج تفاريغ كثير ، و برضه تفاريغ جهينة بدفعة وريد قوية

جداول رح تساعدكم كثيييير بحفظ الأدوية بمادة الفاينل

كويزات الدكاترة

DOSE-RESPONSE RELATIONSHIP

Dose-response curves

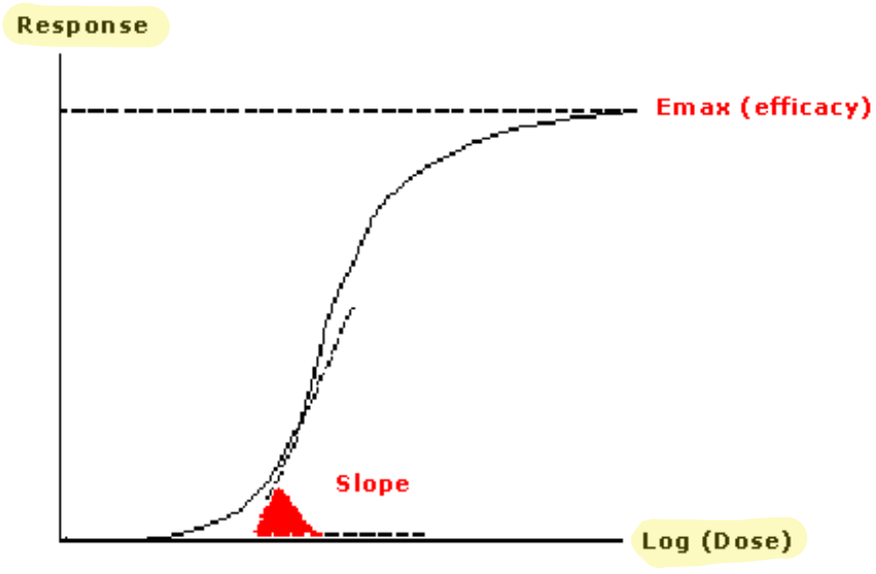
- The dose-response relationship can be represented graphically by 2 types of curves: the graded dose-response curve and the quantal (All/None) dose-response curve:

بسبب اختلاف الـ response

slide 32 Lec 8

I. Graded dose-response curve is obtained if the degree of response is depicted against log the dose e.g. increases of heart rate against the dose.

بقدر اعطي عن العرض بالرقم *



شو بستفيد من الـ curves؟

Parameters that can be obtained from the graded dose-response curve:

1. **Maximal Efficacy (E_{max})**: is the maximal **effect** produced by the drug *(= the maximum value of the dose-response curve)*

فايدتها

- Value of knowing the (E_{max}):
  - a) Knowing the maximal responding capacity of the organ
  - b) Differentiation between full agonist and partial agonist

power/force

2. **Potency** of the drug is assessed from 2 parameters:

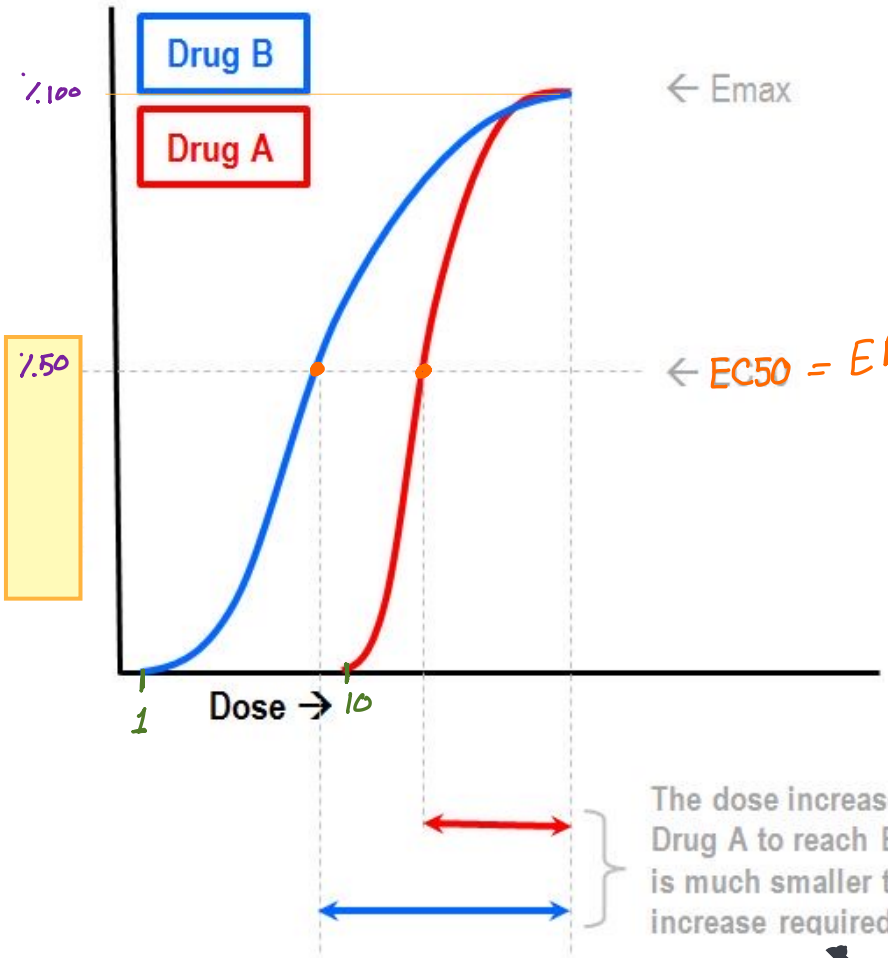
E: Effect / D: Doses

   a. **ED_{50}:** it is **dose** that produces 50% of the maximal response (E_{50}). The lower the ED_{50} the more potent the drug is.

فايدتها

- Value of knowing the (ED_{50}):
  - a) Calculation of drug potency
  - b) Comparing potencies of multiple drugs in one animal

Response



نفسها

* هيسا جهون انو drug إلو أعلى potency ؟

كلام الدكتور: دايمًا في الامتحان منغلط بنفس الغلط

← الـ drug (B) إلو أعلى potency

لانو احتاج لجرعة اقل حتى يعمل response ٪50 عكس (A) إلي احتاج جرعة أكبر حتى يعطي نفس response.

عشان توضح أكثر :- لوعندك  وجبنا (5) شباب حتى يشيلوها

نفس هاي الطاولة جبنا زلمة وشالها لحاله ، مين أقوى ؟

الزلمة أقوى (واحد بقوة 5) .

** الدوا كل ما زادت الجرعة بتروح ناحية اليمين أو الشمال ؟

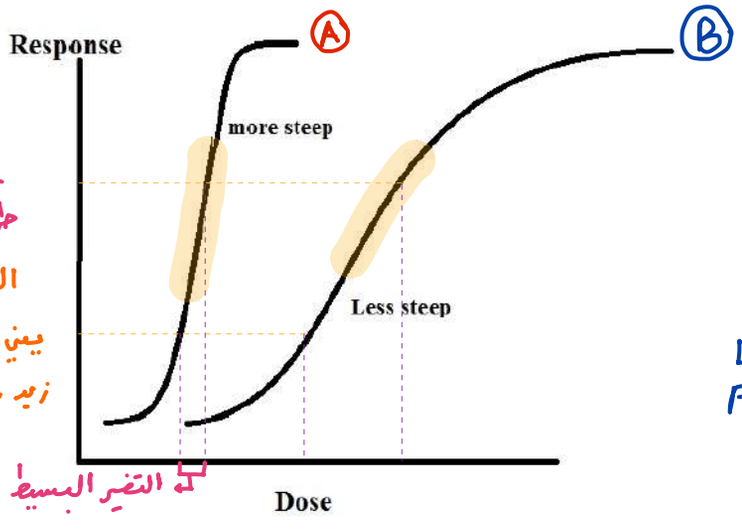
← اليمين ← كل ما راحت ناحية اليمين بتصير Less potency

وإلى ناحية الشمال high potency

b. Steepness (Slope) of the middle portion of the curve: meams sharpness of the response i.e. minimal change of the dose may lead to dramatic response

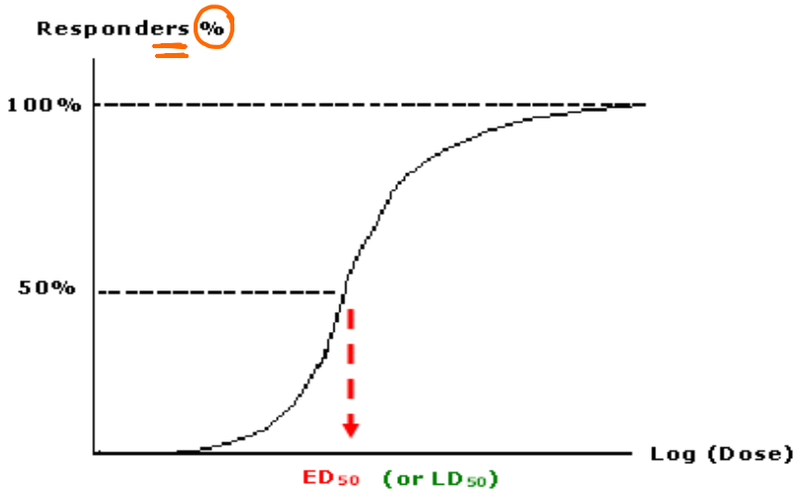
- Value of knowing the slope of the curve:

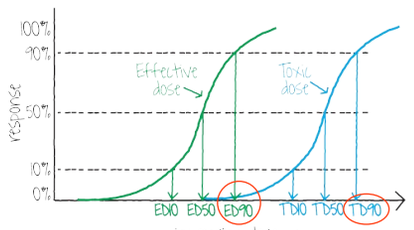
a) Comparing potencies of multiple drugs: the steeper the curve (the higher the slope) the more potent the drug is.



b) A drug having a steep curve may have multible actions e.g. effects on heart, brain, blood vessels; all decrease blood pressure

II. Quantal (All/None) dose-response curve: is obtained if the percentage of patients who respond to the drug is depicted against log the dose e.g. the % of epileptic patients who are treated by different doses of an antiepileptic drug





Parameters that can be obtained from the All/None curve:

1. **ED_{50}:** It is the **dose** that **cures 50%** of cases (E_{50}). It is used for comparison between drugs e.g. drug with a lower ED_{50} → more potent than that with a higher ED_{50}.

2. **LD_{50}:** The **dose** that **kills 50%** of animals. lower LD_{50} → more toxic. The dose used should not exceed 10% of the estimated LD_{50}.

3. **Therapeutic index (TI):**

   - It is the ratio between LD_{50} & ED_{50} → **$TI = LD_{50}/ED_{50}$**.
   - The **higher TI** ratio (i.e. the LD_{50} is much higher than the ED_{50}) → **the safer the drug**.

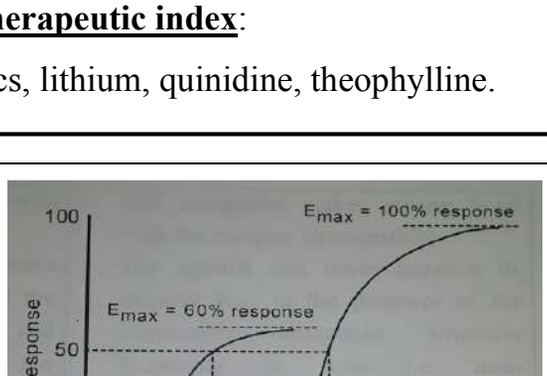
4. **Safety index (SI):**

   - It is the ratio between LD_1 & ED_{99} → **$SI = LD_1/ED_{99}$**.
   - LD_1: the lowest toxic dose – ED_{99}: the highest therapeutic dose
   - The **higher SI** ratio → **the safer the drug** .

Drugs with narrow therapeutic index:

Aminoglycosides, anticoagulants, antiepileptics, lithium, quinidine, theophylline.

Potency versus Efficacy



- **Potency**: it is the effect of drug in relation to dose.
  - Potent drug means that the drug can give certain E_{50} by a small dose, but this does not necessarily mean that it can give high E_{max} by increasing its dose.
- **Efficacy**: it is the ability of the drug to give certain E_{max}
  - Efficacious drug means that the drug can give high E_{max} by increasing its dose

Clinically: Efficacy is more important than potency (why??)

Why efficacy is clinically more important than potency?

Results: Potency is an expression of the activity of a drug in terms of the concentration or amount of the drug required to produce a defined effect, whereas clinical efficacy judges the therapeutic effectiveness of the drug in humans.

Factors Modifying Dose-Response Relationship

A. Factors related to drug:

[1] Dose: is the main factor modifying drug action.

[2] Drug shape:

- Most drugs have multible streoisomers e.g. D-glucose & L-glucose
- The receptor site is usually specific for one stereoisomer and not suitable for another like the hang and glove.
- Example: the S (+) isomer of methacholine is 250 times more potent than the R (-) isomer
- This phenomenon may explain how partial agonist is an agonist and antagonist in the same time because many drugs are used as "racemic mixtures" rather than pure isomers.

[3] Drug size:

- Most drugs have MW 100-1000 units.
- Drugs > MW 1000 cannot be absorbed or distributed.
- Drugs > MW 600 cannot cross placental barrier

[4] Time of administration (chronopharmacology):

- Many body functions (RBF, BP, HR….) have circadian rhythm and also many diseases (asthmatic attacks, anginal attacks…) are circadian phase dependent.
- ***Chronopharmacology:*** is the science dealing with tailoring drug medication according to the circadian rhythm of the body to get better response or to avoid possible adverse effects
- Examples:
  - Attacks of bronchial asthma are common at night (circadian variation of cortisol and inflammatory mediators) → better to give anti-asthmatic treatment in the evening

- Attacks of MI are common in early morning (circadian variation of sympathetic activity) → better to give anti-ischemic treatment before sleep.
- Irritant drugs should be given after meals to avoid gastric irritation e.g. iron
- C.N.S stimulant: should be given at day time.
- Drugs producing drowsiness as antihistamine drugs should be given at night

[5] Route of administration

- Magnesium sulfate: orally act as a purgative, while IV it cause depression to cardiac, skeletal, smooth muscles and C.N.S.
- Doses of drugs given by injection route are less than that by oral route and have rapid onset of action

[6] Drug combination (drug interaction):

- When two drugs are combined together, this may lead to:

1- Antagonism: one drug abolish the effect of the other (i.e. 1 + 1 = 0).

2- Addition or summation: the combined effects of two drugs are equal to the sum of their individual effects (i.e. 1 + 1 = 2) e.g. histamine and ACH on B.P.

3- Synergism: the combined effects of two drugs are greater than the sum of their individual effects (i.e. 1 + 1 = 3) e.g. sulphonamide and trimethoprim.

4- Potentiation: one drug lacks the specific effect but can potentiate the effect of another drug (i.e. 0 + 1 = 2) e.g. barbiturates has no analgesic effect but it can potentiate the analgesic effect of aspirin.

[7] Cumulation:

- This occurs when the rate of administration of the drug exceeds the rate of its metabolism or excretion which leads to drug accumulation in the body and toxic effect e.g. digitalis.