Pharmacology

Subject : PHARMACODYNAMICS

Lec no : 10

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وقل رب زدني علماً

تجدون في guidance مادة الفارما على موقع النادي :

للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

قبل ما نبلش المحاضرة... عشان أنا كتير منيحة الله يرضى عني😇😂
قررت أخليكم تكسبو أجر كبير بكل سهولة... شفتو محسني😌😂
طب شو هو الأجر وكيف يا لانا المتواضعة؟🤦🏻‍♀️😁
الأجر يا حلوين أنه تتبرعو برصيد الطباعة تبعكم اذا ما بتحتاجوه لطلاب بحاجته (قلتلكم اجر بسهولة)🤍💜
طيب شو لازم نعمل؟
أول شي لازم تفوتو ع بوابتكم ومن عند خدمات أخرى __ رصيد الطباعة
هلأ من هي الخطوة بس بدي تتأكدو انو رصيدكم موجود ولا خالص لو اعطاك (لا يوجد اي حركات طباعة حاليا) معناها الرصيد موجود وفيكم تتبرعو فيه
طيب تمام وكيف نتبرع؟
من بوبابتكم ومن عند خدمات أخرى __ الدخول لشبكة الانترنت (المختبرات واللاسلكية) بتاخدوا اسم المستخدم (والي هو رقمكم الجامعي) وبتنسخوا كلمة السر
واخر شي بتدخلو على QR code الي تحت👇 بتعبو فورم التبرع بالرصيد وبس.
سهلة القصة والله وفيها اجر كبير (اجر ع كل نقطة وحرف وكلمة انطبعت من رصيدك لشخص محتاج واجر بكل حرف اندرس من الورق الي انطبع برصيدك الي انت اصلا ما بتستخدمه).

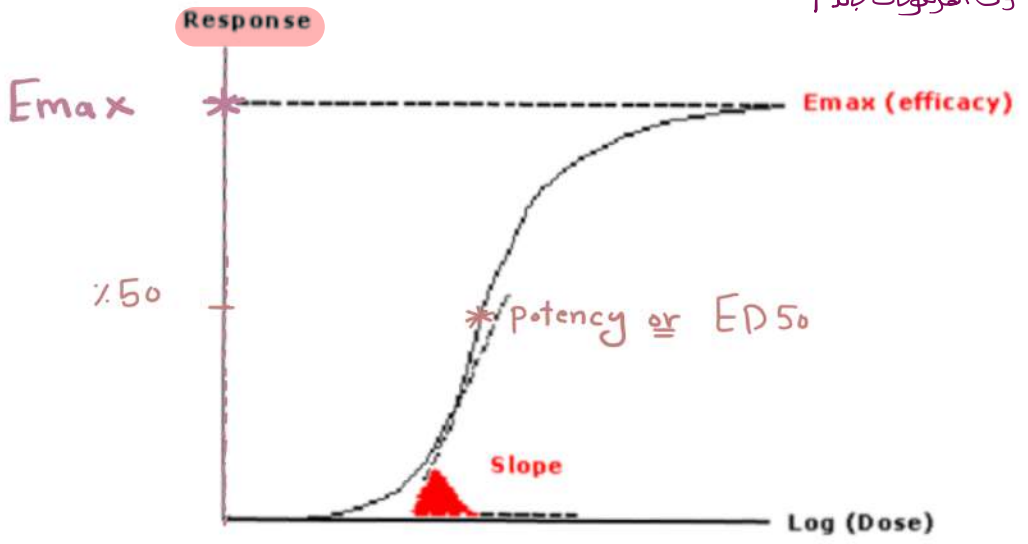
DOSE-RESPONSE RELATIONSHIP

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:

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.

مستوى الجلوكوز أو مستوى الهرمونات بالدم



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

فعالية الدواء

1. **Maximal Efficacy (E_{max})**: is the maximal **effect** produced by the drug

(= the maximum value of the dose-response curve)

- Value of knowing the (E_{max}):

a) Knowing the maximal responding capacity of the organ

متل دواء اذا اشتغل على القلب بيعطيني استجابة 90% ولو اشتغل على عضو تاني بيعطيني استجابة 70%... انا هون بامكاني اعرف الاستحابة لل tissues وللدواء برضو

b) Differentiation between full agonist and partial agonist

■ Efficacy

- It is the ability of a drug to produce response (effect) after binding to the receptor.
- It is measured by the Emax (the maximal response that a drug can elicit at full concentration):

Full agonist is the drug that gives maximal response at full concentration (at full occupancy).

Partial agonist is that agonist gives submaximal response even at full concentration i.e.never gives Emax

ببلش اجرب لو مثلا على مريض عنده زيادة بال HR هلا بأول جرعة بعطيه 1mg وبنشوف ال HR قديش قل (نفرض كان HR عنده 100 وصار 90 يعني الاستجابة عندي 10%) هلأ انا بضل أزيد الجرعات لحد ما أول Emax يلي مهما زودت الجرعة بكون ال effect ثابت

قوة الدواء

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

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.

لاتنظر الى الرقم الكبير بالإمتحان

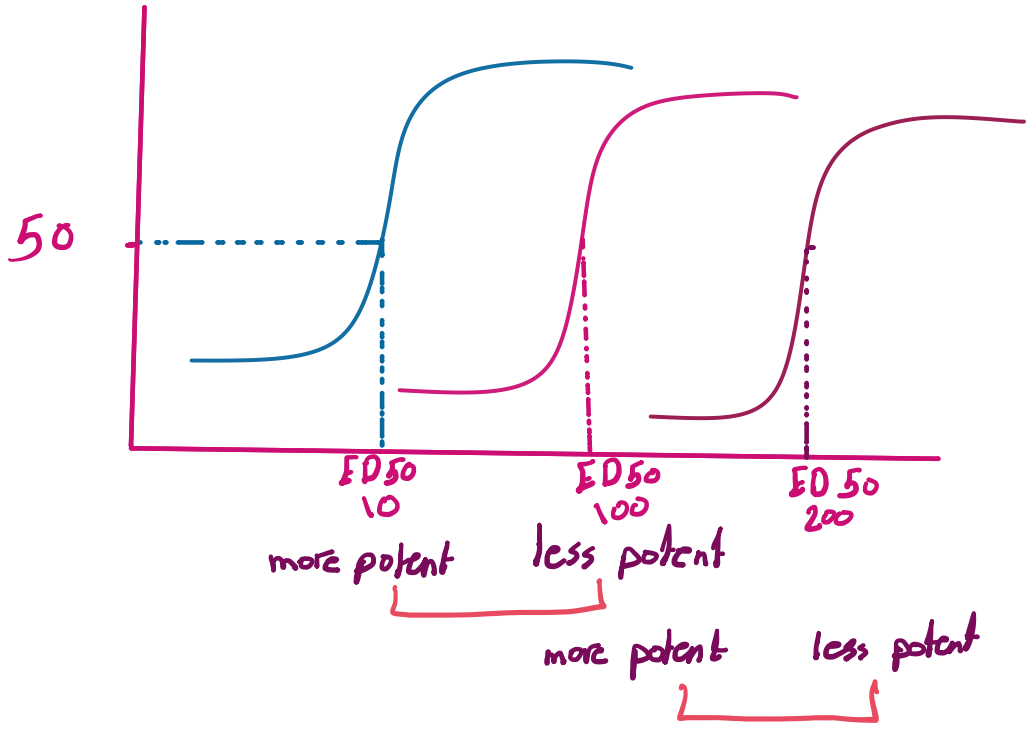
- Value of knowing the (ED_{50}):

a) Calculation of drug potency

b) Comparing potencies of multiple drugs in one animal

Potency

- ED50 (Effective Dose) is the dose of the drug that gives 50% of the Emax, or it is the dose that gives the desired effect in 50% of a test population of subjects.
- A drug that gives ED50 by smaller doses is described as "potent" drug.
- Potency of drugs is generally less clinically important than efficacy because you can increase the dose of a less potent drug to obtain the effect of a more potent one (provided that it is not toxic).



اليمين هو الأقل potent بتكون الجرعة أكبر

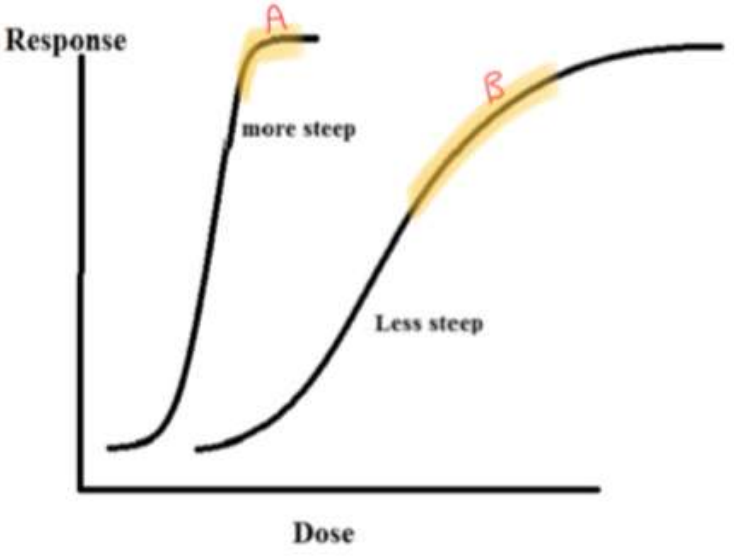
الشمال هو الأكثر potent بتكون أقل جرعة

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

more potent drug ← كلما زاد الميل

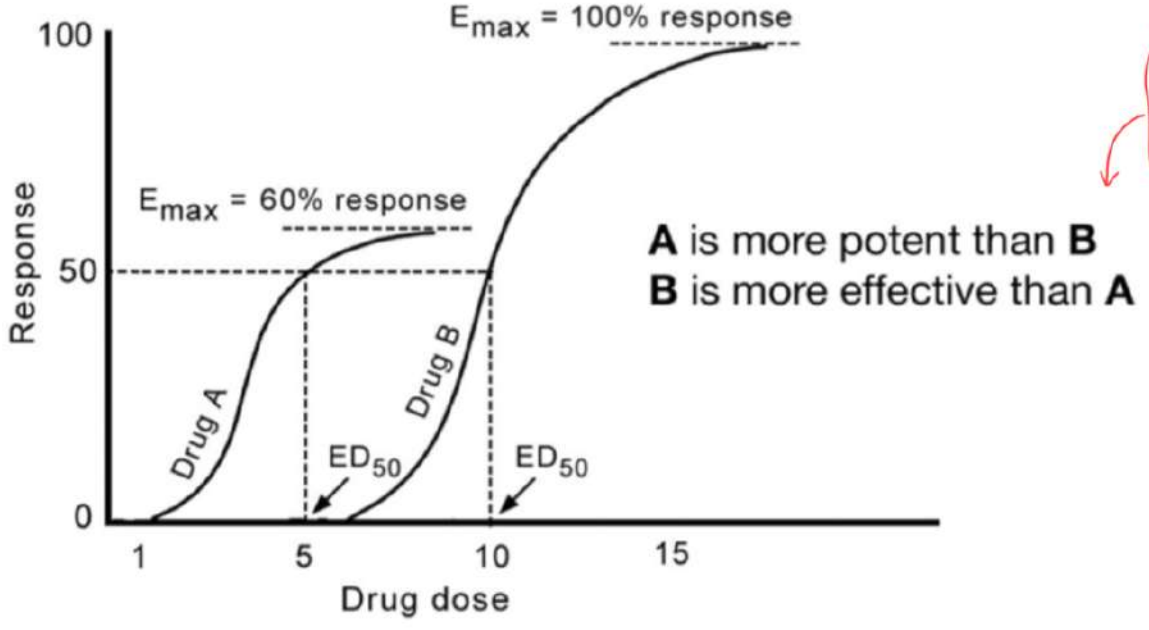
- Value of knowing the slope of the curve:

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



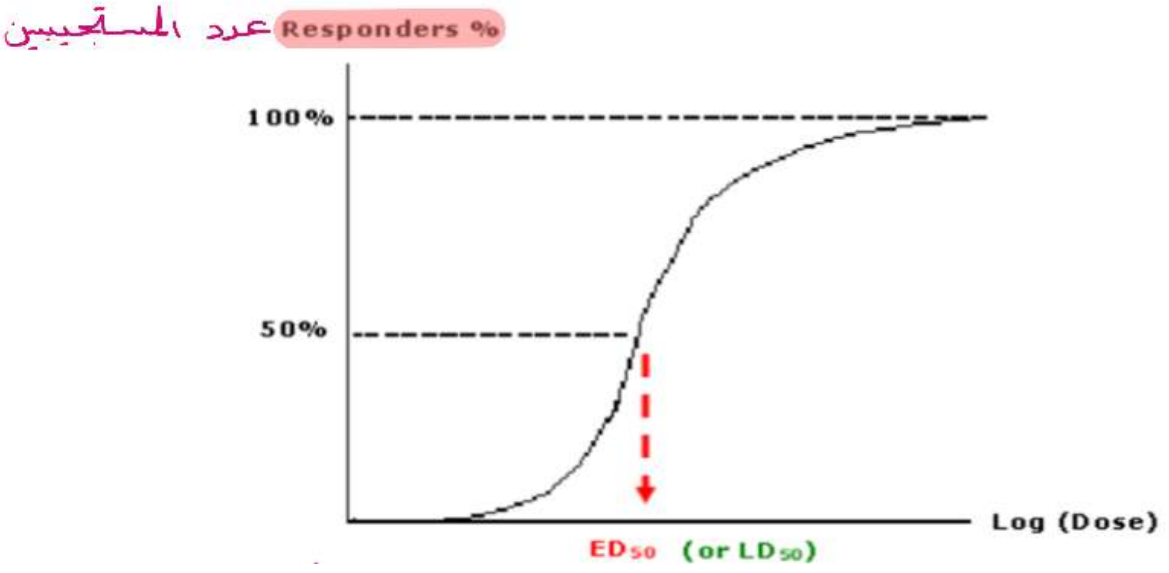
b) A drug having a steep curve may have multible actions e.g. effects on heart, brain, blood vessels; all decrease blood pressure

more than one mechanism



مثل هيك نمط الأسئلة

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



هون هو graded (أرقام) متل شخص عنده headache (صداع) وأنا أعطيته دواء هلأ الي رح يصير إما الصداع بيتحسن أو بزبل الصداع متل ماهو

ملاحظة
هذه التجارب تطبق على الحيوانات

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

1. **ED_{50}:** It is the **dose** that **cures 50%** of cases (individual) (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}.

هي الجرعة الي بتشفي نص المرض ED50

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):**

هي الجرعة الي بتسمم نص المرض [موت] LD50

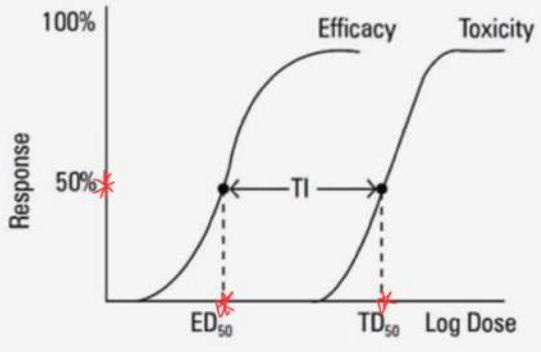
- It is the ratio between LD_{50} & ED_{50} → **$TI = LD_{50}/ED_{50}$**.
- The **higher TI** ratio (i.e. the LD_{50} is much higher than the ED_{50}) → **the safer the drug**.

مهم **

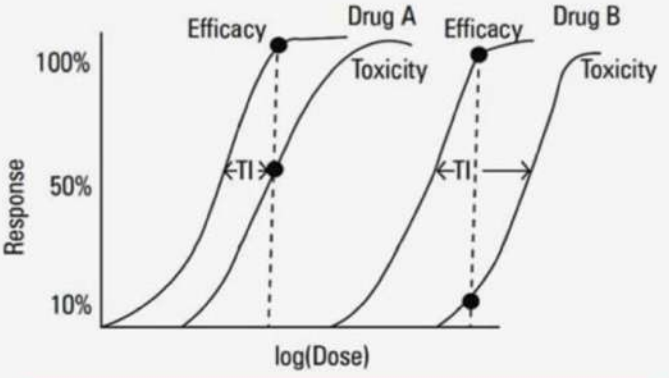
4. **Safety index (SI):** أكثر دقة

LD1 ← الجرعة الي قتلت 1٪ من الحيوانات (خطر)
ED99 ← الجرعة الي عملت response لـ 99٪ من الحيوانات

- 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**.



The therapeutic index (TD_{50}/ED_{50}) is a measure of the margin of safety of a given drug



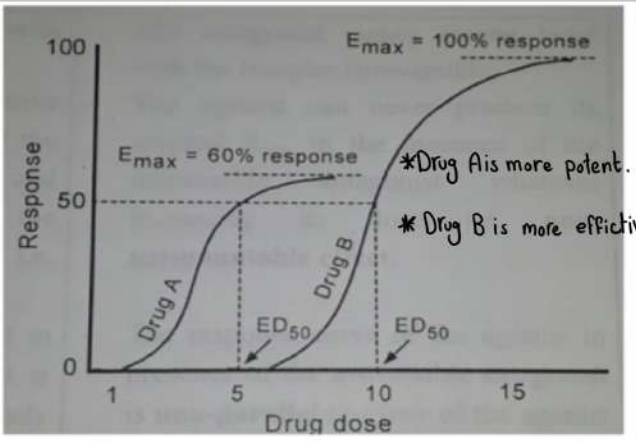
Drug A has a much narrower therapeutic index than Drug B. The dose of Drug A required to achieve a 100% therapeutic response will be toxic in 50% of patients. For Drug B, this is only 10%

Drugs with narrow (small) therapeutic index: أدوية خطيرة

Aminoglycosides (1), anticoagulants (2), antiepileptics (3), lithium (4), quinidine (5), theophylline (6).

+ digoxin

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??)

a drug with greater efficacy than greater potency is more therapeutically beneficial

• في حالة إستثنائية (Morphine) بهمنا فيهم Potency.

لقوا في هي المجموعة انه من ضمن ال action على CNS انها بتعملي depression ل respiratory center (بوقف النفس) وشافوا بالتجربة هاد depression انه dose dependent يعني كلما زادت الجرعة بزيد depression ل respiratory center وبالتالي الأدوية هي لما تجي تبدلها يفضل تستخدم more potent دواء مكانها عشان الجرعة الأصغر رح تخلي ال depression أقل.

موضوع المحاضرة عن العوامل الي بتخلي تأثير دواء معين يختلف من مريض لآخر

- مصادر قد تفيدكم لهاي المحاضرة :

Factors Modifying Dose-Response Relationship

A. Factors related to drug:

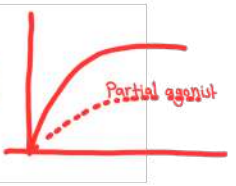
[1] Dose: is the main factor modifying drug action.

[2] Drug shape:= Chemical shape = Drug isomerism

- 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

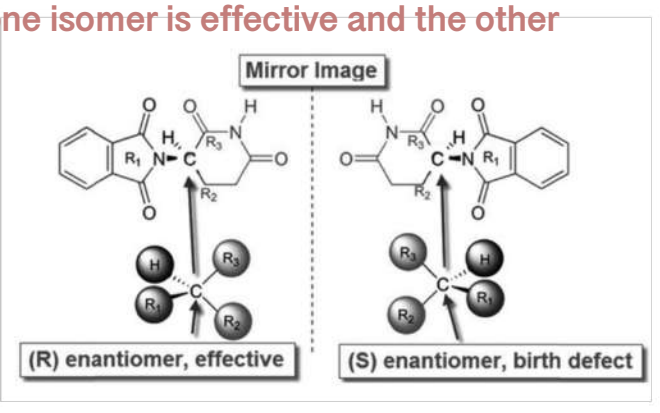
Methacholine is a non-selective muscarinic receptor agonist that acts directly on airway smooth muscle receptors to induce bronchoconstriction. (بضيق الشعب الهوائية)

- 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.



لـ مثال : 50٪ منها بكون D ، و 50٪ منها L
الدواء بكون خليط بين isomer ممكن يجيب نتيجة و isomer يعتبر toxic و بعمل مشاكل

This means that one isomer may be hundred times more potent than the other.
In other instances one isomer is beneficial while the other is toxic.
This phenomenon may explain how a single drug could act as agonist and antagonist (i.e. partial agonist) because many drugs are present in “racemic mixtures” rather than as pure isomers; or how one isomer is effective and the other isomer is toxic.



الأرقام مش للحفظ... الحمدلله

[3] Drug size: = molecular weight

- Most drugs have MW 100-1000 units.
- Drugs > MW 1000 cannot be absorbed or distributed. They should be given parenterally by IV
- Drugs > MW 600 cannot cross placental barrier (مشيمية)

بتغيبنا هاي الأدوية حالة أنا ما بدي الدواء يوصل للـ fetus.

[4] Time of administration (chronopharmacology): (زمن)

- Many body functions (RBF, BP, HR….) have circadian rhythm (توضيحها تحت) and also many diseases (asthmatic attacks, anginal attacks…) are circadian phase dependent.
- ***Chronopharmacology:*** is the science dealing with tailoring (تفصيل) drug medication according to the circadian rhythm of the body to get better response or to avoid possible adverse effects

مُعظم الـ functions بأجسامنا بتختلف بين الليل والنهار، مثل: Heart Rate, Blood pressure

وهاد بنسميه Circadian rhythm.

بدكم تكونوا كأطباء عارفين انه كل مرض الله وقت معين بتزداد الـ Severity تبعته وزاد العلم بنسميه Chrono biology.

انك تعرف الوقت المناسب لإعطاء دواء مُعين للمريض هاد العلم بنسميه Chronopharmacology.

- 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 → Drugs that can cause inflammation, pain or irritation at the extravasation (أي مُمكن يفضل يوخذ بعد الأكل)
  - C.N.S stimulant: should be given at day time.
  - Drugs producing drowsiness (خمول) as antihistamine drugs should be given at night

[5] Route of administration

GIT ملين عال

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

لما نعطي ال MgSO4 عبر IV حيأثر على ال electricity تبعت ال Cell membrane ال Muscles

حيزيد ال (+) داخل الخلايا ، بالتالي يمنع ال depolarization و بيعمل inhibition و بيقلل من Contraction.

الأسئلة ممكن تكون لمحاضرات سابقة

Quiz Time ⏰👏

1) In the presence of picrotoxin, diazepam is less efficacious at causing sedation, regardless of the dose. Picrotoxin has no sedative effect, even at the highest dose. Which of the following is correct regarding these agents?

A. Picrotoxin is a competitive antagonist.

B. Picrotoxin is a noncompetitive antagonist.

C. Diazepam is less efficacious than is picrotoxin.

D. Diazepam is less potent than is picrotoxin.

2) If 1 mg of lorazepam produces the same anxiolytic response as 10 mg of diazepam, which is correct?

A. Lorazepam is more potent than is diazepam.

B. Lorazepam is more efficacious than is diazepam.

C. Lorazepam is a full agonist, and diazepam is a partial agonist.

D. Lorazepam is a better drug to take for anxiety than is diazepam.

3) If 10 mg of oxycodone produces a greater analgesic response than does aspirin at any dose, which is correct?

A. Oxycodone is more efficacious than is aspirin.

B. Oxycodone is less potent than is aspirin.

C. Aspirin is a full agonist, and oxycodone is a partial agonist.

D. Oxycodone and aspirin act on the same drug target.

4) In the presence of propranolol, a higher concentration of epinephrine is required to elicit full antiasthmatic activity. Propranolol has no effect on asthma symptoms. Which is correct regarding these medications?

A. Epinephrine is less efficacious than is propranolol.

B. Epinephrine is a full agonist, and propranolol is a partial agonist.

C. Epinephrine is an agonist, and propranolol is a competitive antagonist.

D. Epinephrine is an agonist, and propranolol is a non-competitive antagonist.

5) The data presented in the figure below show that:

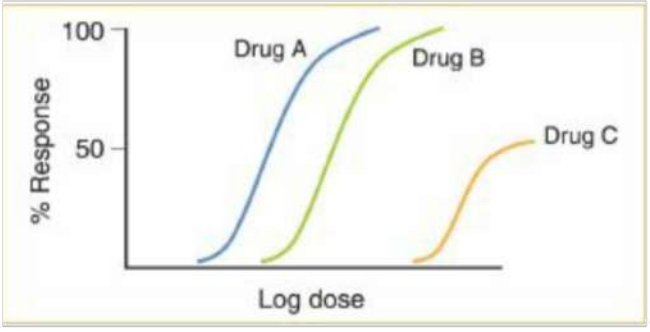
A. Drugs A and B have equal efficacy

B. Drug B and C have equal efficacy

C. Drug B is a partial agonist

D. Drugs A and C have the same affinity and efficacy

E. Drugs A and B have equal potency.



6) Which of the following best describes the effect of a competitive antagonist on the dose-response curve? (From USMLE🥺)

A. Non-parallel left shift

B. Non-parallel right shift

C. Parallel left shift

D. Parallel right shift

7. Identify the pharmacodynamic curve depicted in the picture:

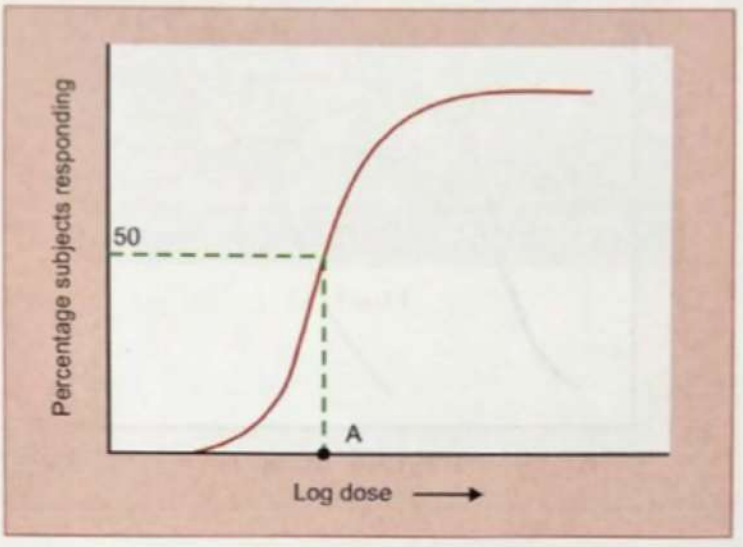


Fig. I 1

(a) Graded dose response curve
(b) Log dose response curve
(c) Quantal dose response curve
(d) Percentage dose response curve

8. Point A in the Fig. I 1 corresponds to:
(a) Potency
(b) Efficacy
(c) ED50
(d) LD50

ليس الطريق لمن سَبق ، إنَّما الطريق لمن صَدَق . 🧡

بالتوفيق 🔥