* there is a lecture 7 which I did not include it in my summaries because it is full with understanding concept rather than memorizing information so it is important go and study it from the slides

Color ⇒ from my understanding (سمس)
Color ⇒ Extremly important

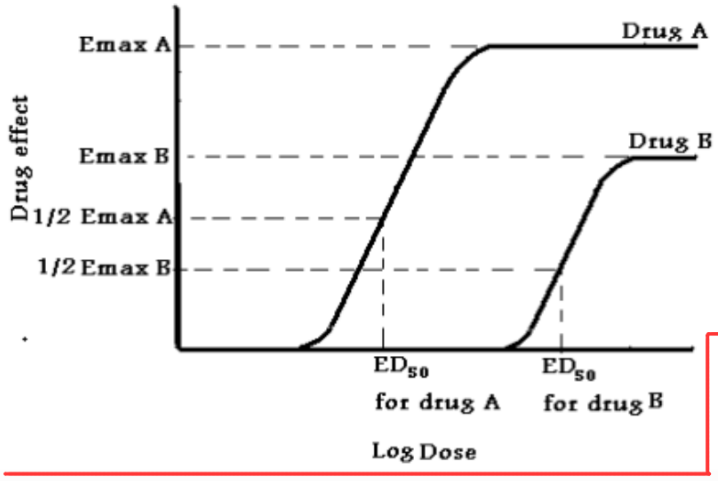
let's start Lecure number 8:

efficacy: is maximum effect of a drug (Emax) which depend on

- number of Drug-Receptor Complex (Receptor that got activated)
- efficiency of coupling receptor activation to Cellular response

example morphine and aspirine produce the same pharmacological effect But with different efficacy. (morphine is more powerful, it is from opioids)

* more efficacy = more production of biological response = more intrensic activity
* efficacy is not synonymous for intrestic activity but it has relation with it.
  ↳ refer to capacity of drug to produce an effect or overall magnitude of the maximum Response.
* Drug stimulate full response ⇒ full agonist ⇒ very efficacious.



in this picture Drug A has higher efficacy than Drug B because higer Emax the hight of the log

* smaller EC → greater potency

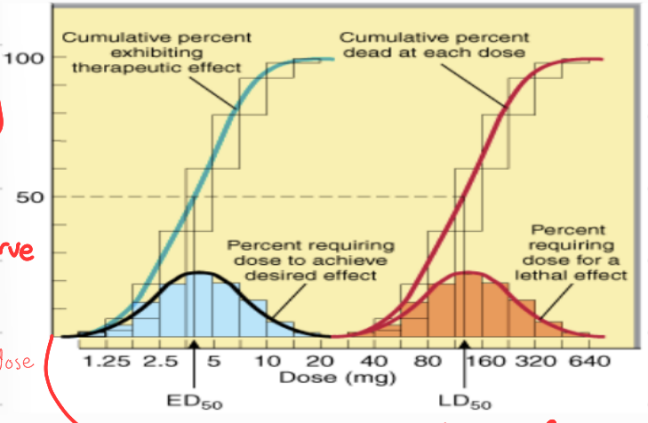
* Antagonism Between Drugs.

* pharmacological Antagonism: occure when an antogonist prevent Agonist from Binding the receptor and it might be competitive or non-competitive

competitive:
* in reversable fashion
* log dose-response curve shifted to the right
* higher concentration of Agnist is needed to acheive the response.

non-competitive:
* Bind irreversable to the receptor or allosterically (another side)
* independent on the concentration of Agonist
* log response Curve is non-parallel shift

* Quantal Dose-Response Curves.
  - involve all or non-Response (يعني يا طلب الدوا لا)
  - Obeys Normal frequency distribution
  - when transformed into cumulative will result into sigmoidal curve
  - Can calculate TI (therapeutic index) = LD50 / ED50



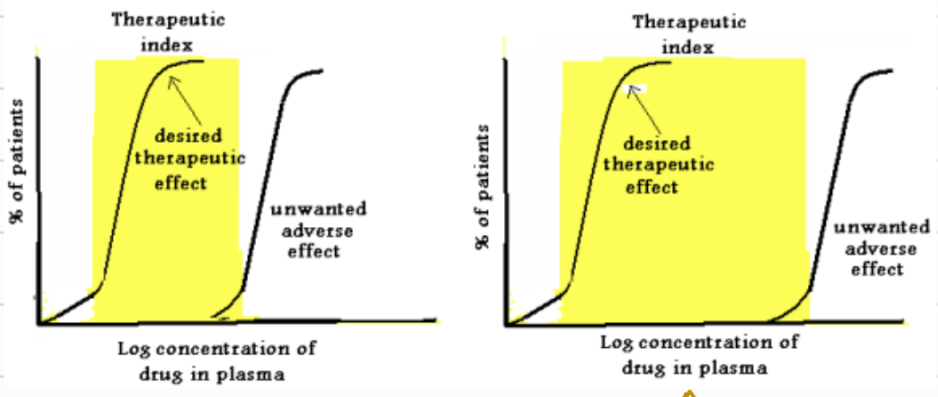
Lethal dose: dose required to produce death in 50% of animal

effective dose

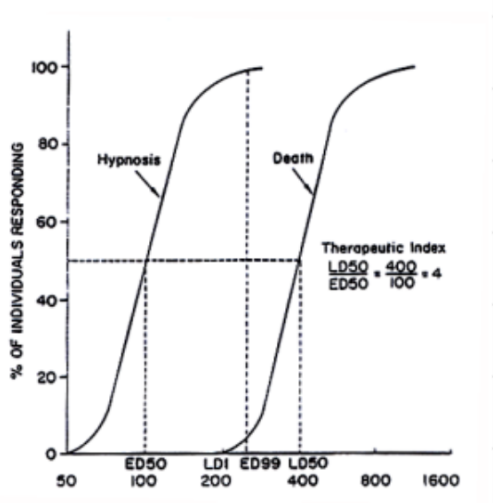
dose which 50% of individuals exibit the specific quantal effect

these are percentage of treated people.

* toxic Dose TD: dose required to produce particular toxic effect in 50% of animal.
* Therapeutic index of Drug is ratio of the dose that produce toxicity to the dose that produce effective response in a population individuals $TI = \frac{TD_{50}}{ED_{50}}$ or $\frac{ED_{50}}{TD_{50}}$



this is better



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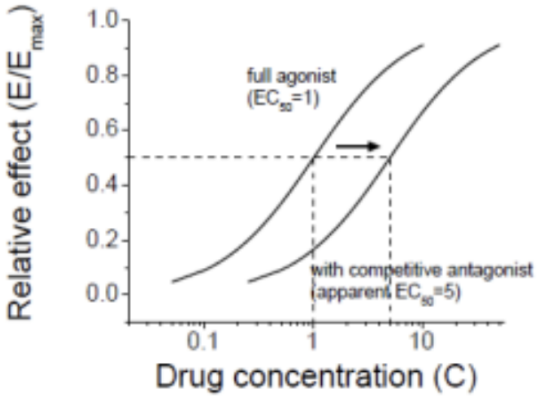
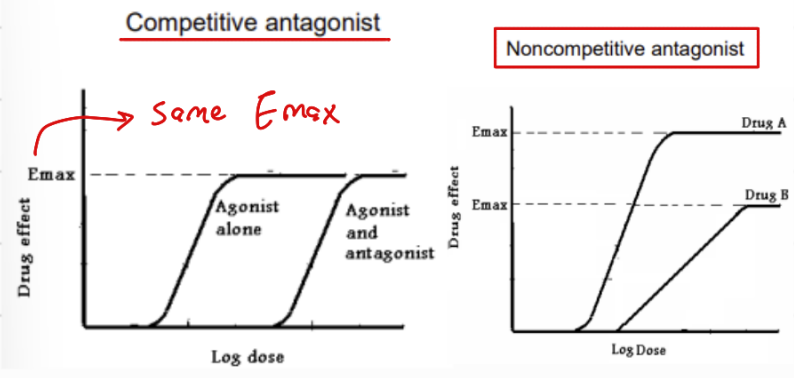
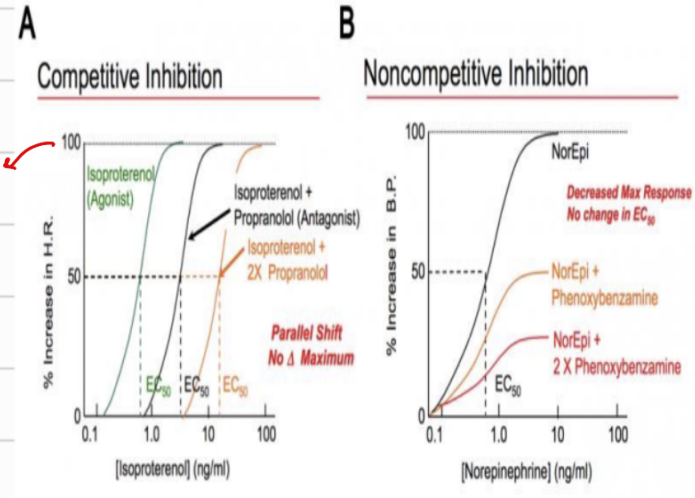
* Competitive Antagonists
  - Bind Agonist site
  - Do not shift equilibrium towards active or in active conformation
  - Neutral Antagonists







Same full effect

Enhancement of Drug effects:

Additive drug effect
* two drug with the same effect when given togather → produce effect equal to the sum of magnitude to the sum of the effects

$E_{AB} = E_A + E_B$

$2 = 1 + 1$

Synergic drug effect
* two drug with same effect when given togather → produce effect greater in magnitude than sum of the effects

$E_{AB} > E_A + E_B$

$2 < 1 + 1$

Potentiation drug effect
* Drug lacking an effect to it's own, increase the effect of a second active Drug

$E_{AB} > E_A + E_B$

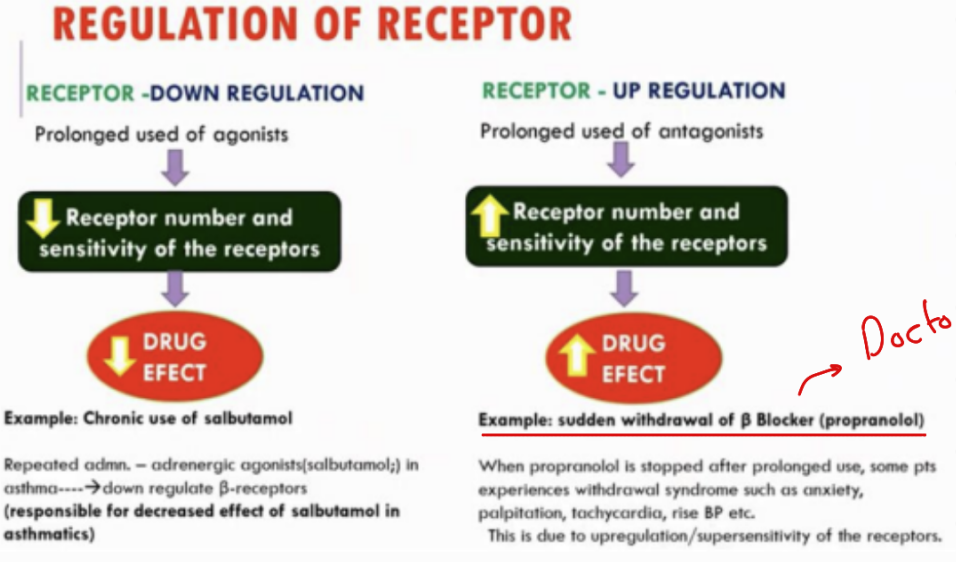
$1 < 1 + 0$

هكذا مكتوبة بالسلايدات
بس انا اعتقد انو خطأ و معكوسات

* Receptor Regulation:

Sensitization (up-regulation)
- Prolonged use of receptor blocker
- inhibition of synthesis or release Hormone or neurotransmitter - Denervation

Desensitization (Down-Regulation)
- Prolonged use of Agonists
- inhibition of Degredation or uptake of Agonist



Doctor talked about this

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* Two state model of Drug-receptor interaction

* full Agonist shift equilibruim fully to the active conformation
* partial Agonist shift equilibruim partially to the active conformation
* Sub-maximal effect with receptors completly occupied → بصراحة مش عارف شو معناها بس اتوقع انه (على الجهتين راح يكون في تأثير)

The Receptor postulated to exist in two forms

R_i (inactive form) non-functinal form ⟷ R_a (active form) functional form

* even in absence of Agonist, some of the receptor pool is existing in Ra state and produce the same physiological effect as if Agoinst induced.

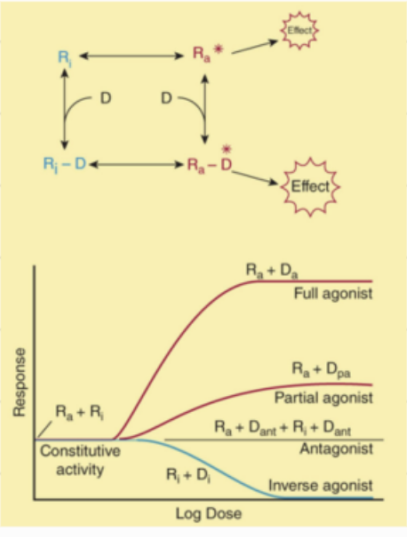
So what happen if Agonist is exist → it stabilize the receptor to stay in Ra form Because it (Agonist) has much higher affinity to Ra form so the larg % of Receptor pool will be in Ra-D fraction and large effect will be produced.

* The Effect of Receptor without Agonist is called Constitutive activity

* The recognition of constitutive activity depend on

- The receptor density
- Concentration of coupling molecules (if it was a coupled system)
- number of effector in the system

* So Antagonist has inhibitory function while Agonist is exist, But what the effect of Antagonism in absence of Agonist? some of them will act as inverse agonist so they reduce receptor activity under the basel level observed.



* Competitive & irreversable Antagoinst.

Receptor Antagonist

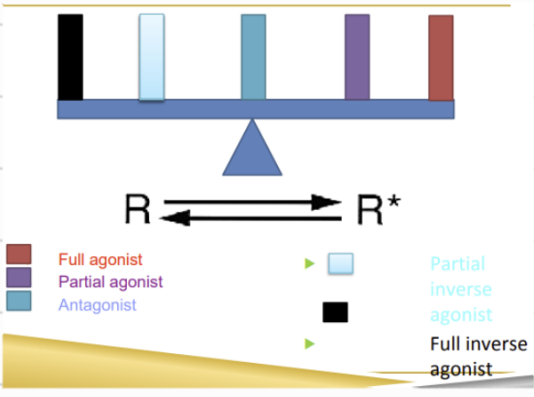
↓

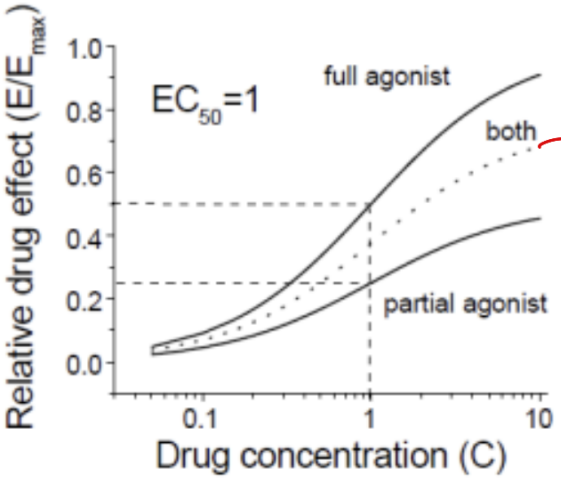
Bind to the receptor but it will not activate it, it will prevent Agonist from binding to the receptor

inverse Agonist

→ will shift equilibrium toward inactive form

* effect obvious if much constitutive activity





→ they will compete each other on the receptor.