

Practical pharmacology

Part 1

21

pharma ology

It is science of the drugs

Drug

Science

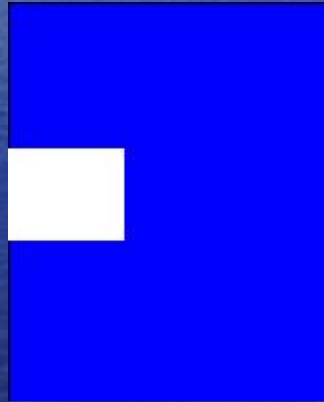
2 What is Drug

**It is the chemical that affect
physiological body function
through interaction with
receptors**

?What is Drug

**It is the chemical that affect
physiological body function
through interaction with
receptors**

A



Respon
se

Forces involved in D-R interaction

Covalent bonds

Ionic bonds

Hydrogen bonds

Vander waals bonds

Forces involved in D-R interaction

Covalent bonds

Ionic bonds

Hydrogen bonds

Vander waals bonds

Forces involved in D-R interaction

Covalent bonds

Strong

irreversible

Alkylating agents

Forces involved in D-R interaction

Covalent bonds

Ionic bonds

Hydrogen bonds

Vander waals bonds

Forces involved in D-R interaction

Ionic bonds

common

Affected by pH

Forces involved in D-R interaction

Covalent bonds

Ionic bonds

Hydrogen bonds

Vander waals bonds

Forces involved in D-R interaction

Hydrogen bonds

?

Forces involved in D-R interaction

Covalent bonds

Ionic bonds

Hydrogen bonds

Vander waals bonds

Forces involved in D-R interaction

Vander waals bonds

?

Receptors types

On cell membrane

Intracellular

GPCR

Receptor with intrinsic ion channel

Enzyme linked receptors

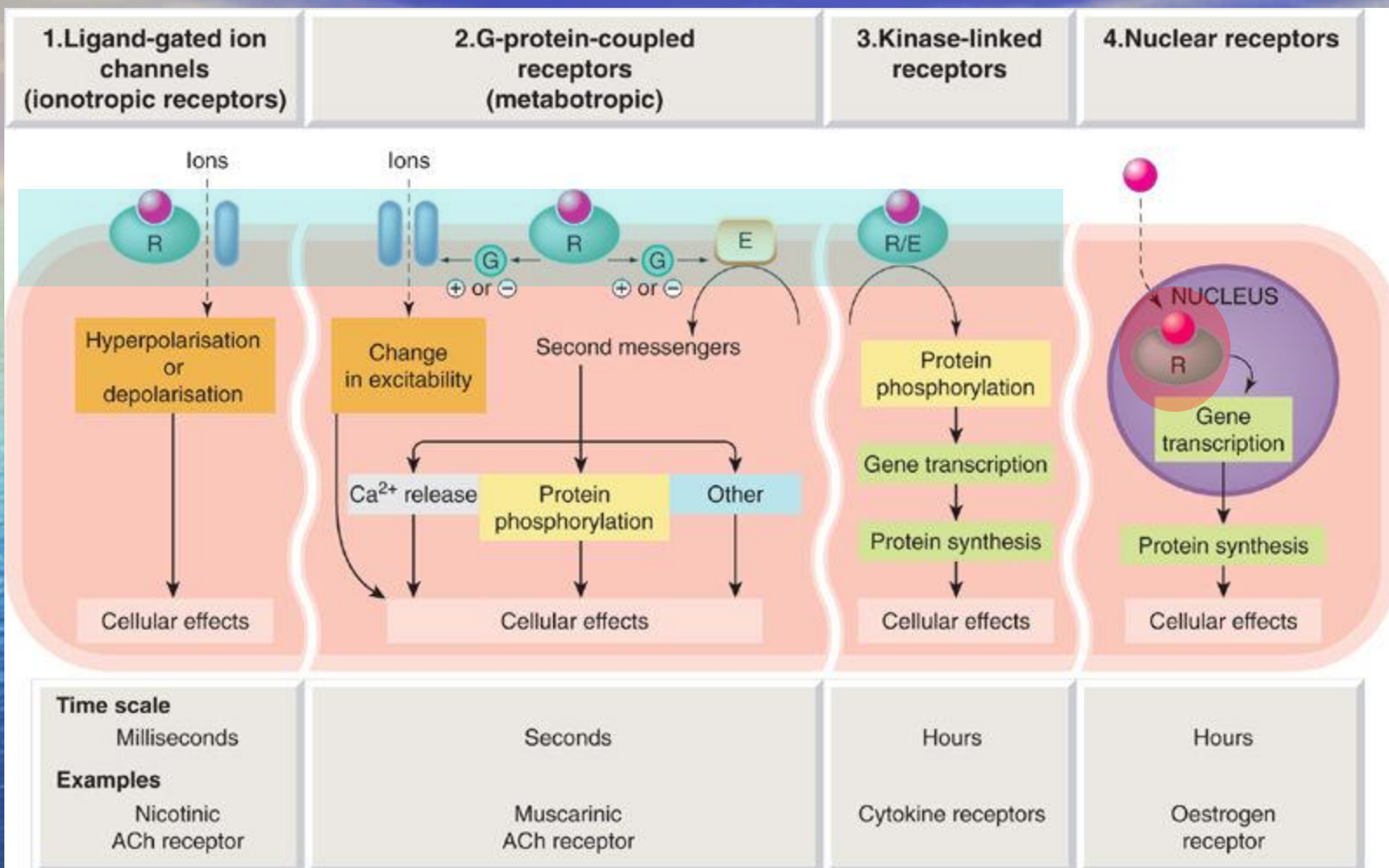
Receptors types

```
graph TD; A[Receptors types] --> B[On cell membrane]; A --> C[Intracellular]; C --> D[Transcription factors]
```

On cell membrane

Intracellular

Transcription factors



Rang et al: Rang & Dale's Pharmacology, 7e
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Drug-Receptor Interaction

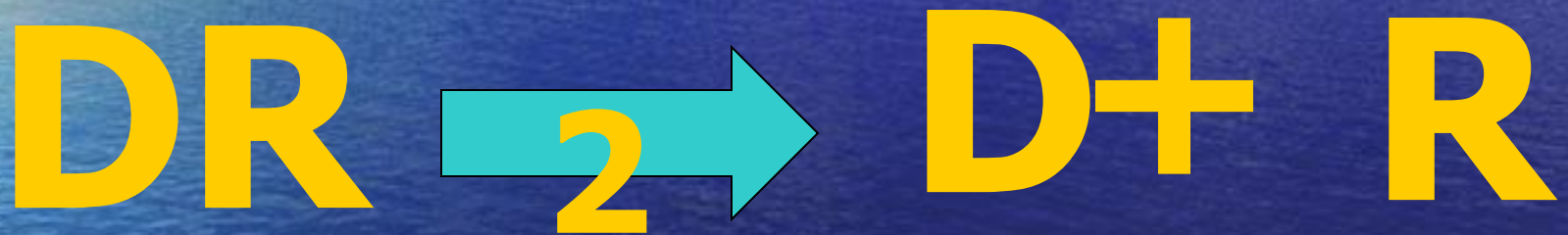
k



k_1 is association rate constant

Drug-Receptor Interaction

k



K_2 is dissociation rate constant

Drug-Receptor Interaction

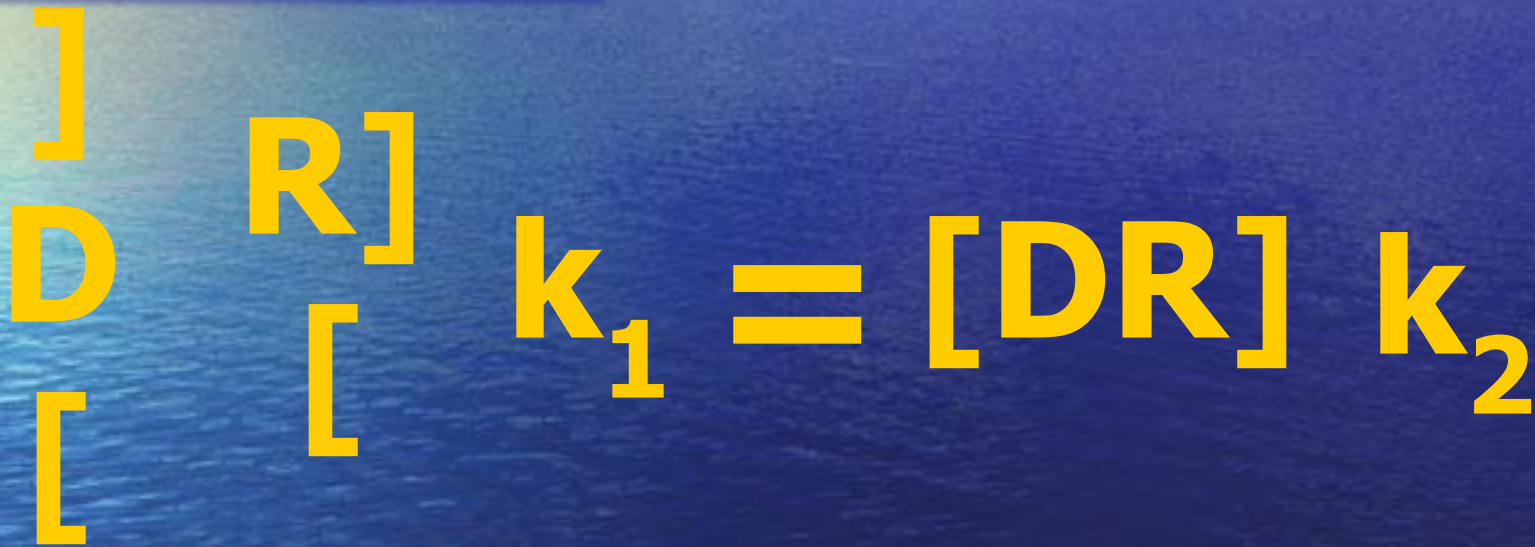
At equilibrium



2

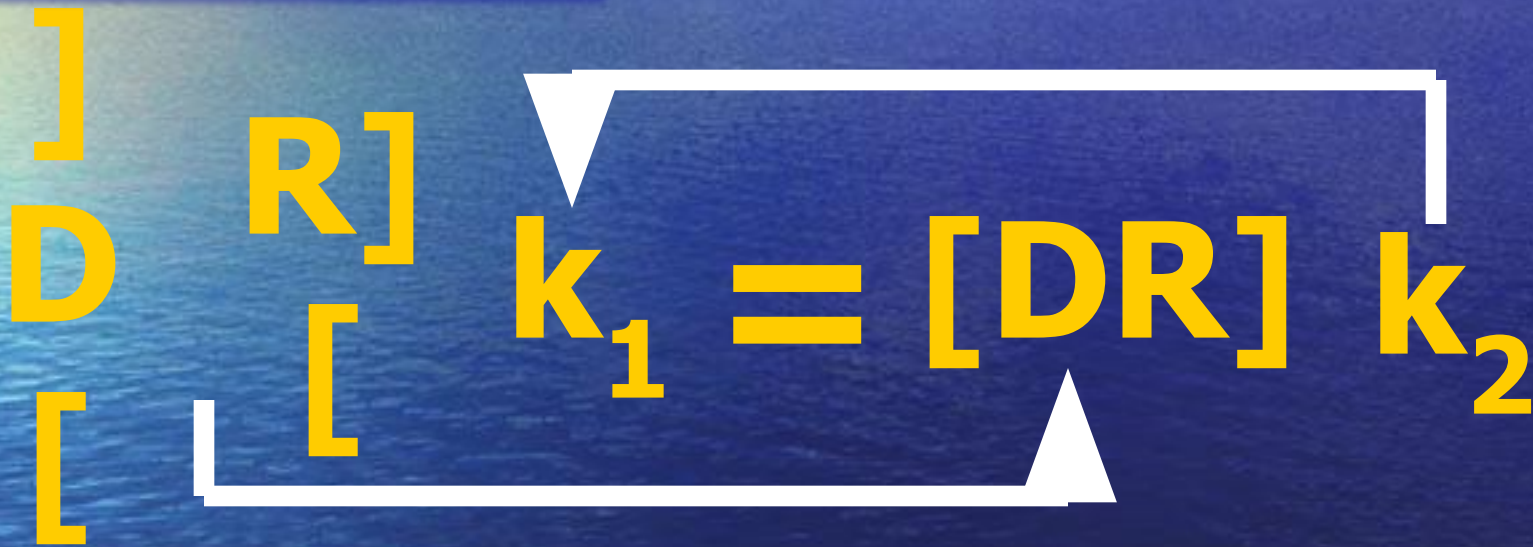
Drug-Receptor Interaction

At equilibrium



Drug-Receptor Interaction

At equilibrium



Drug-Receptor Interaction

$$K_d = \frac{[R][D]}{[DR]}$$

The equation shows the dissociation equilibrium constant K_d as the ratio of the concentration of free receptors $[R]$ and free drug $[D]$ to the concentration of the drug-receptor complex $[DR]$. The terms $[R]$, $[D]$, and $[DR]$ are crossed out with red diagonal lines in the original image.

**K_d (dissociation equilibrium constant)
is conc. of the drug that
bind 50 % of the receptors**

k_d

- It is a measure of drug affinity

- Its units is conc. units

Drug A

Has higher K_d than

Drug B

? Which one has a higher affinity

Important concepts

- Affinity
- Efficacy
- potency

Affinity

- **The ability of the drug to bind to the receptor**
- **Measured by K_d**
- **Both agonist and antagonist have affinity to their receptors**

Efficacy

- It is the ability of the drugs to elicit pharmacological effect
- Measured by E_{\max}
- Agonist has efficacy and antagonist has no efficacy

potency

- The ability of the drug to produce response at lower conc.
- Measured by ED50

The drug may be

- Agonist
- Antagonist
- Partial agonist

Agonist

- Has affinity and efficacy
- $IA=1$

Antagonist

- Has affinity but no efficacy

- $IA=0$

Partial agonist

- Has affinity and efficacy
- $IA=0-1$

antagonism

- Physical
- Chemical
- Physiological
- Pharmacokinetic
- pharmacodynamic

Chemical antagonism

- One drug reacts chemically with an active drug to form an inactive compound,
- It involves precipitation, complexation, neutralization redox reaction.
- Intended □ treatment of heavy metal toxicity by complexation with chelators.
- Incidental □ complexation of tetracycline calcium in dairy products.

Physiological antagonism

- 2 drugs act on different sites in the same or different system.
- a- Intended Norepinephrine in case of anaphylaxis.
- b-Incidental patient taking barbiturates for anxiety, co-administration of anti-tussive (ephedrine).

Pharmacokinetic antagonism (ADME)

- a- Intended □ forced alkaline diuresis in management of barb Poisoning.
- b- Incidental □ Barb. + other drugs



Induction of the metabolism of concomitant drugs, their decrease plasma level.

Pharmacodynamic antagonist

Competitive

Non-competitive

Reversible

Surmountable antagonism

Ach. + atropine

Pharmacodynamic antagonist

Competitive

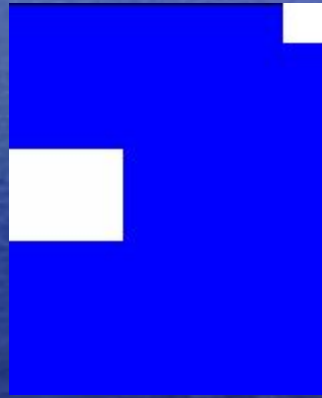
Non-competitive

Reversible

Irreversible

Non-surmountable antagonism

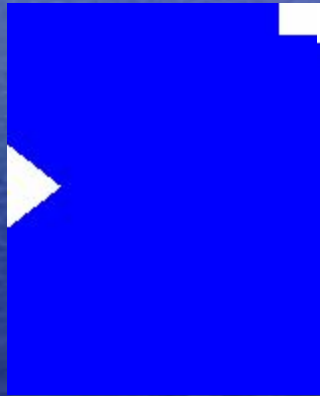
Ach. + succinylcholine



A

A

X



An

Dose-Response Curve

- What ?

- Types ?

**Respon
e**



Hyperbolic curve

Dose

**Respons
e**

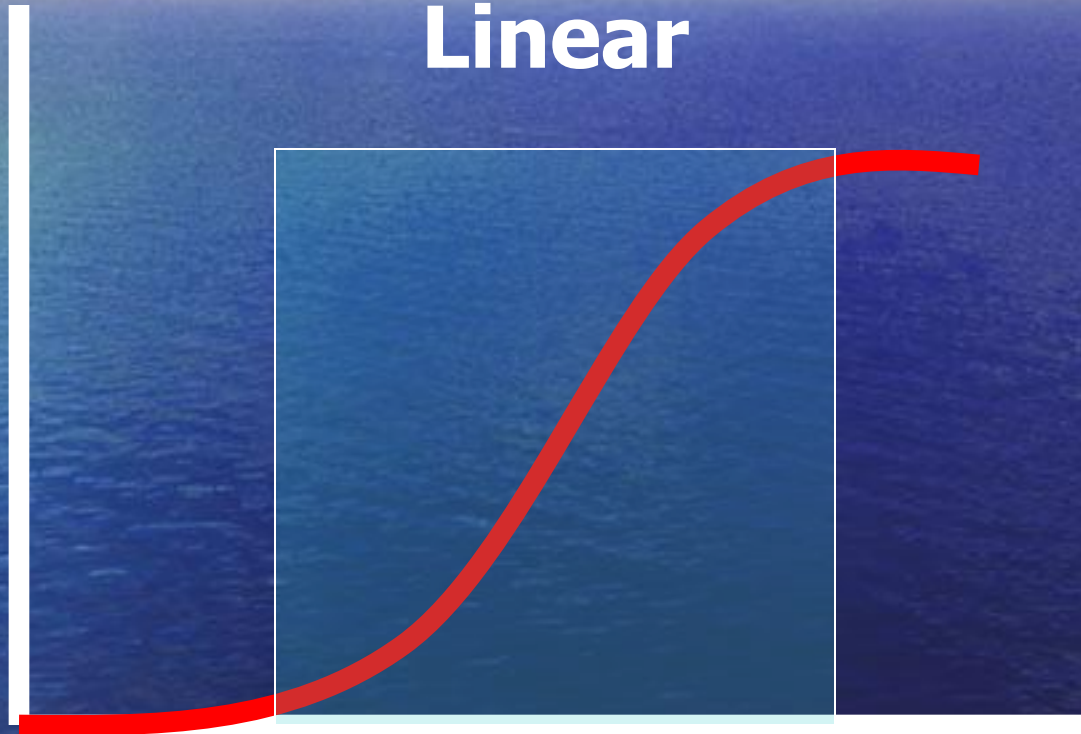


Sigmoidal shaped curve

Log dose

**Respons
e**

Linear

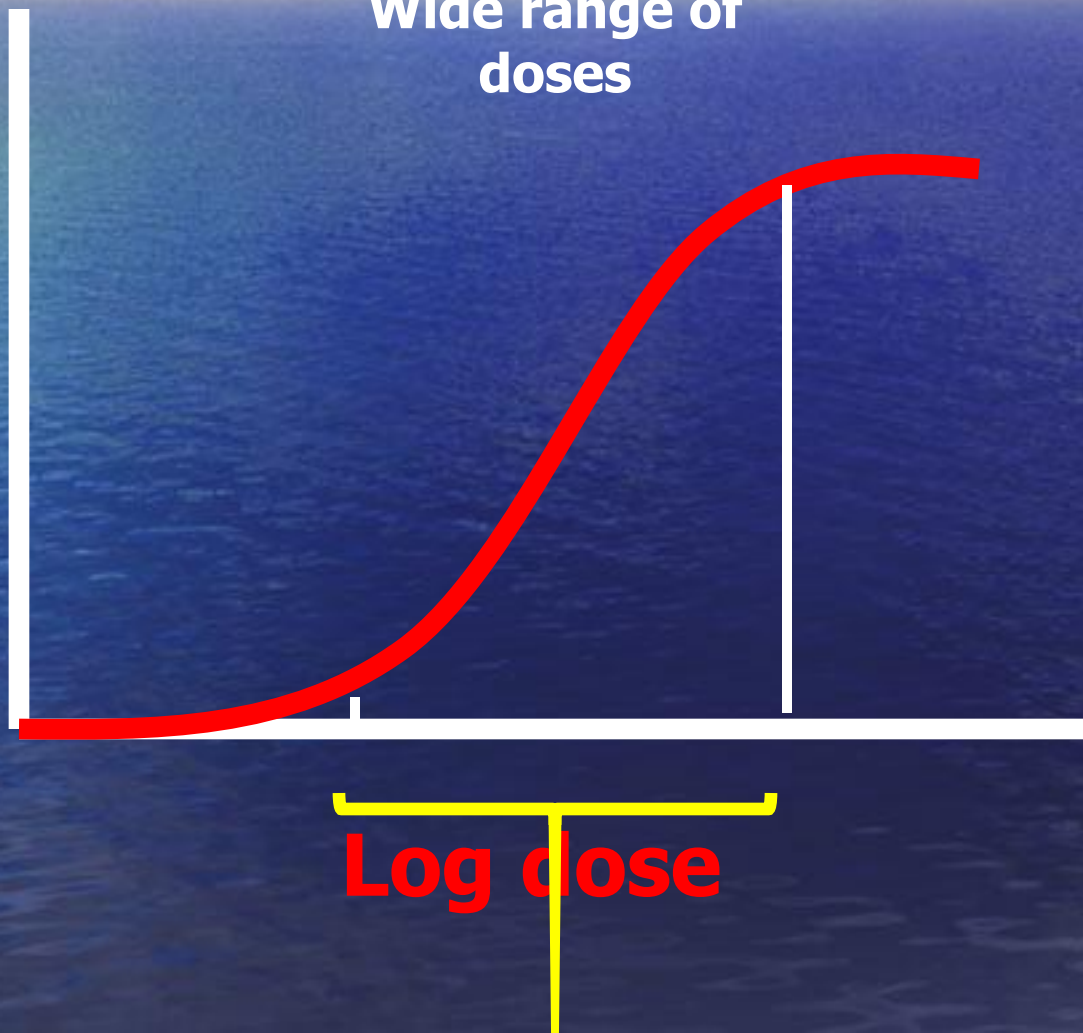


Log dose

**Respon
e**

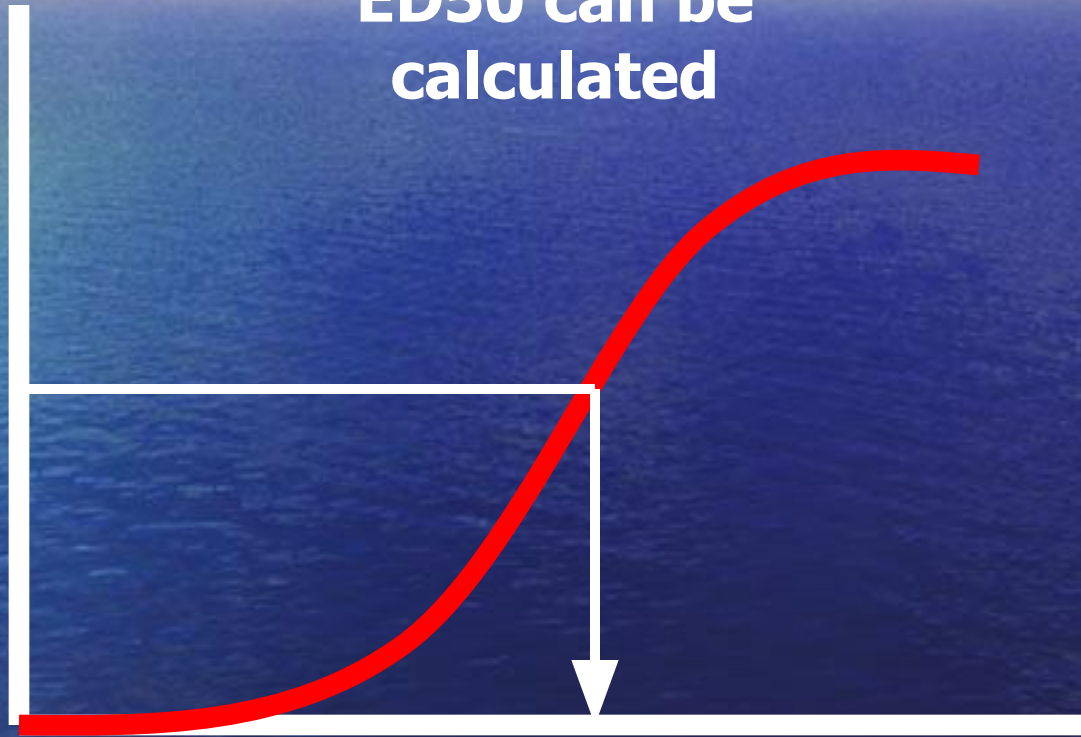
**Wide range of
doses**

Log dose



**Respons
e**

**ED50 can be
calculated**



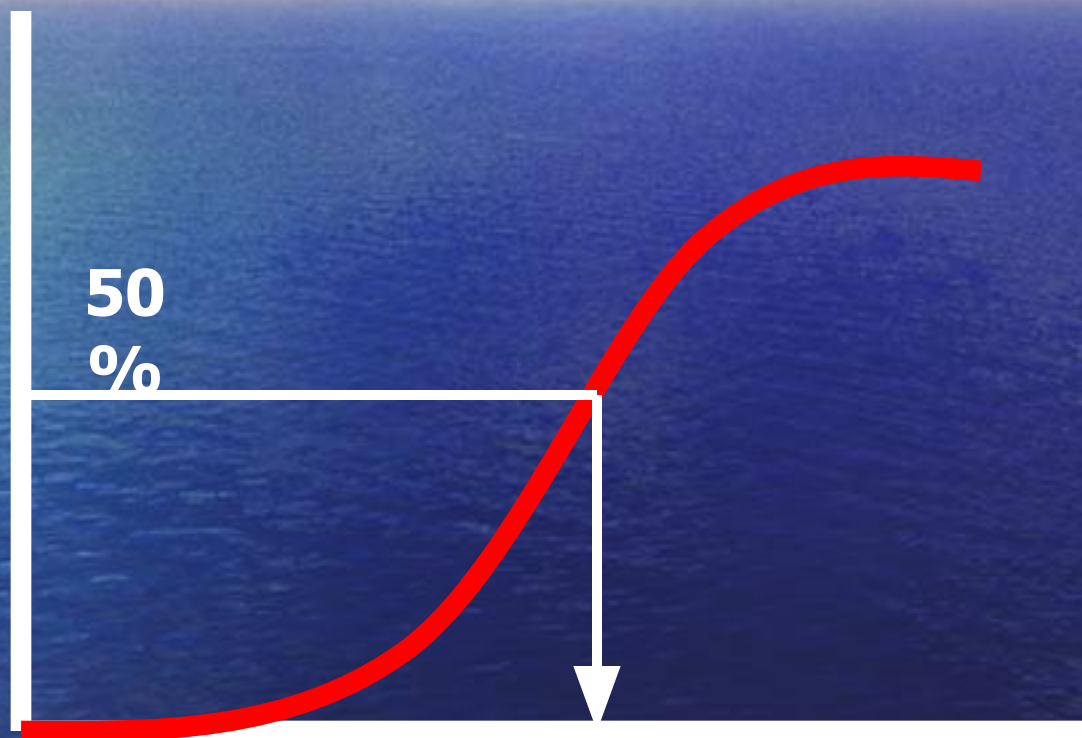
**ED50
Log dose**

Graded DRC

- Depends on graded response
- ED50 ?

The dose that give 50% of maximal response

Respons
e



50
%

ED50

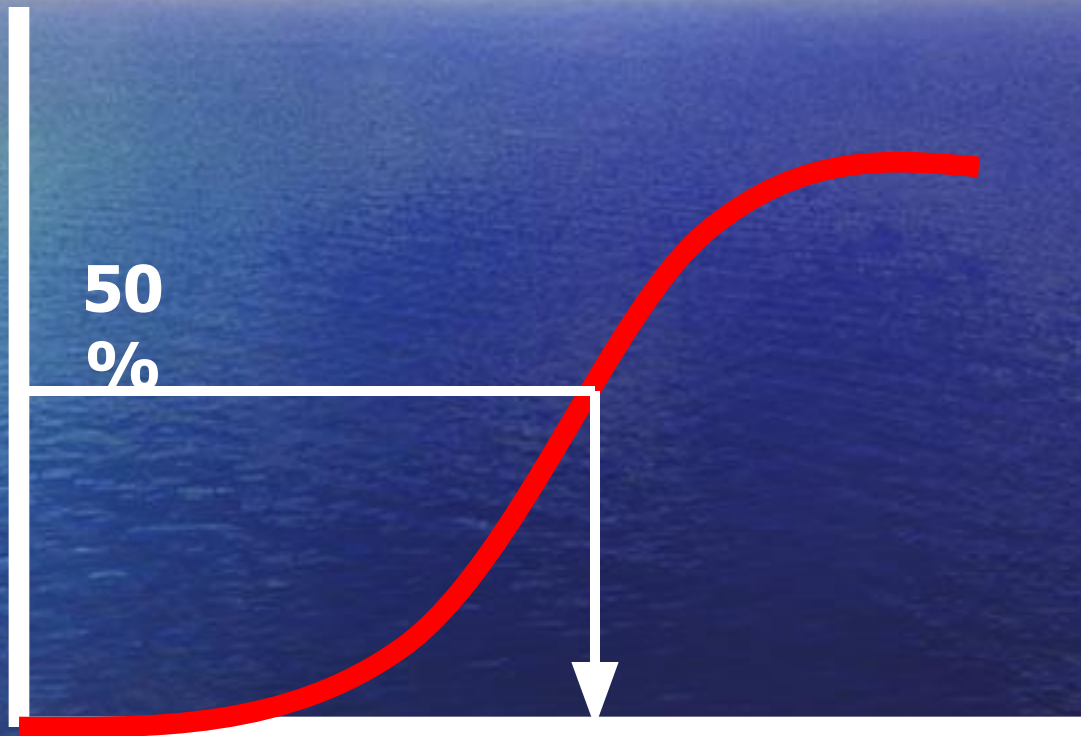
Log dose

Quantal DRC

- Depends on quantal response
- ED50 ?

The dose that give response in 50% of population

**Respo%
nse**



**50
%**

ED50

Log dose

ED50

- Compare between potencies of two drugs

Drug A

Has higher ED50
than

Drug B

? Which one is more potent

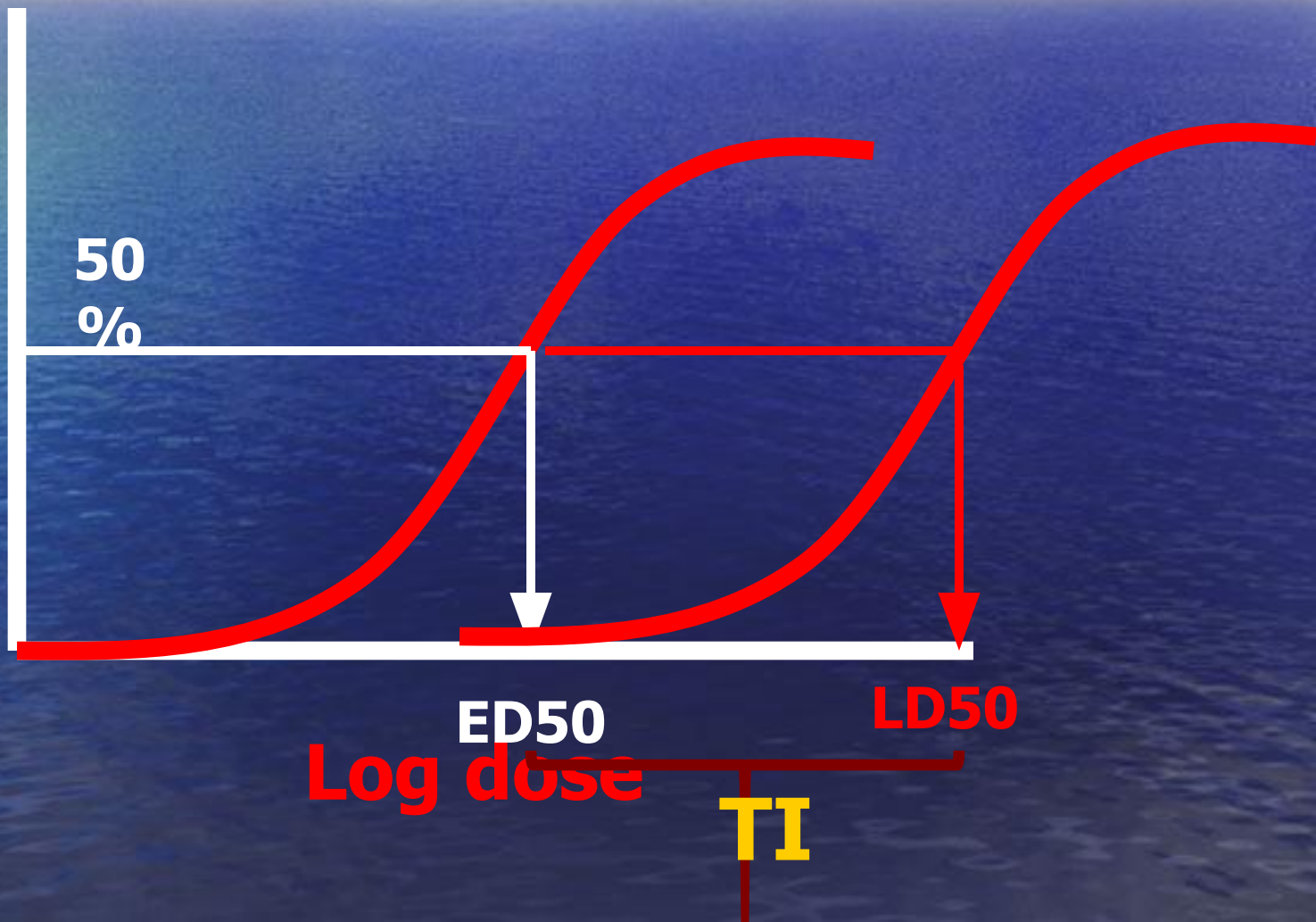
ED50

- Calculation of the therapeutic index

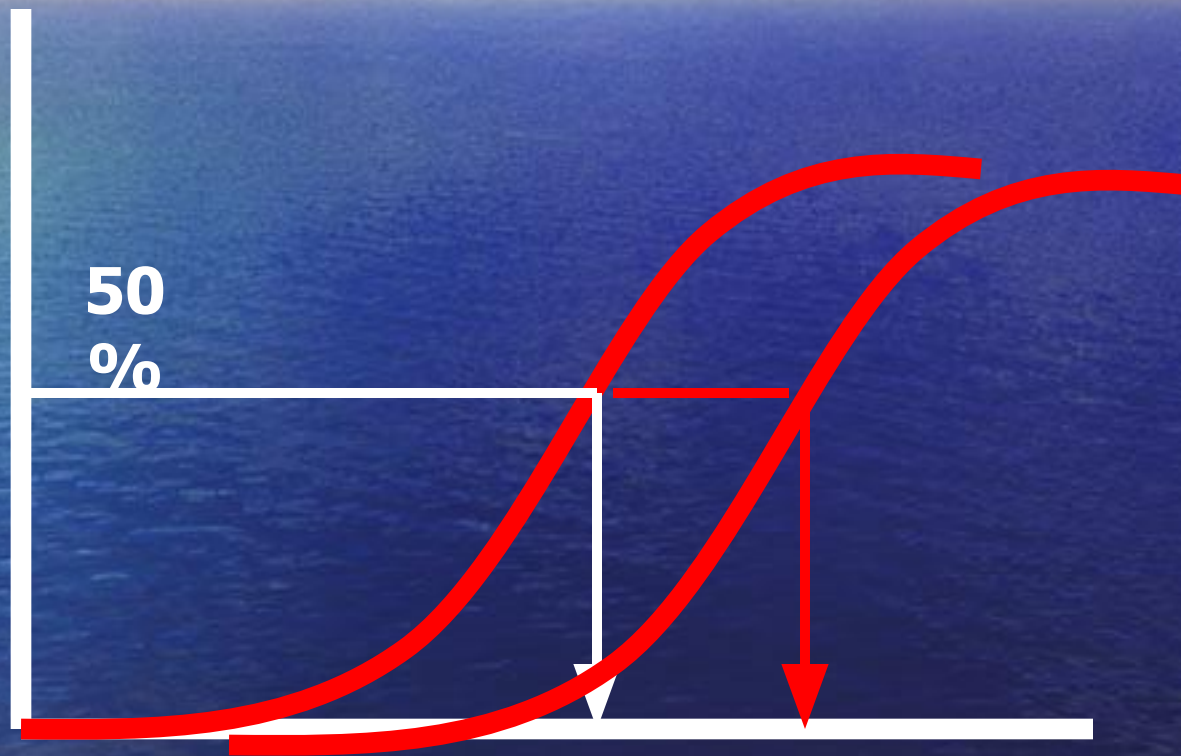
$$\text{TI} = \frac{\text{LD50}}{\text{ED50}}$$

Is a measure of drug safety

Respons
e



Respons
e



50
%

ED50

LD50

Log dose

TI

Drug A

Has higher TI than

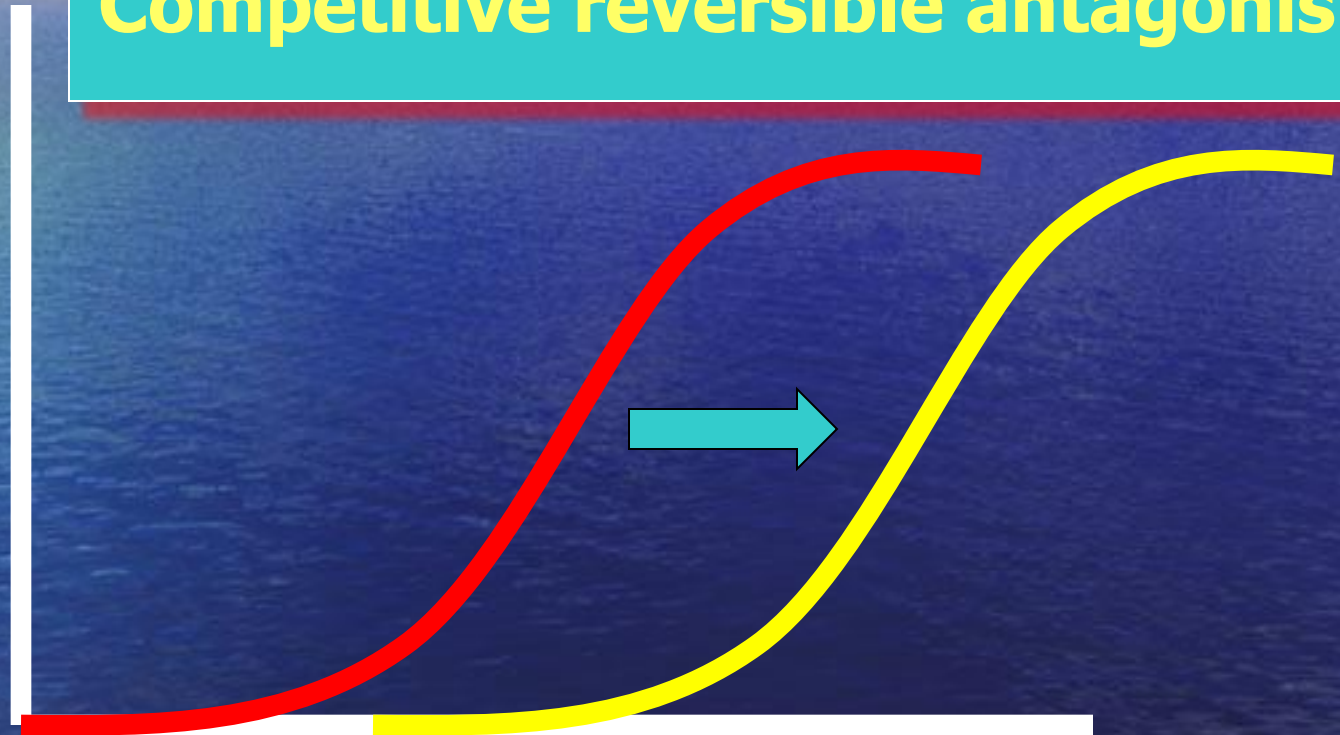
Drug B

? Which one is more safer

DRC & antagonists

Competitive reversible antagonist

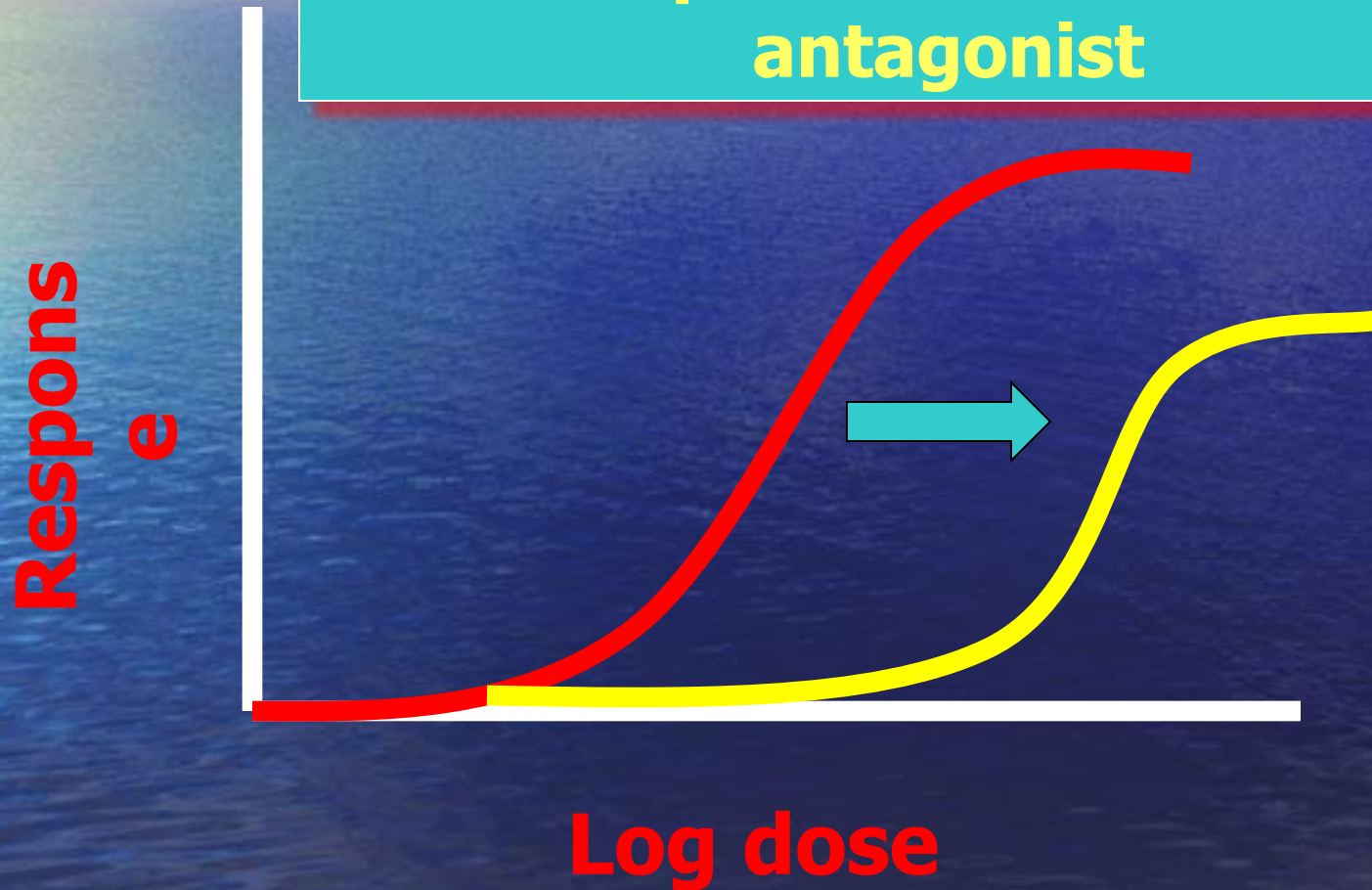
Response



Log dose

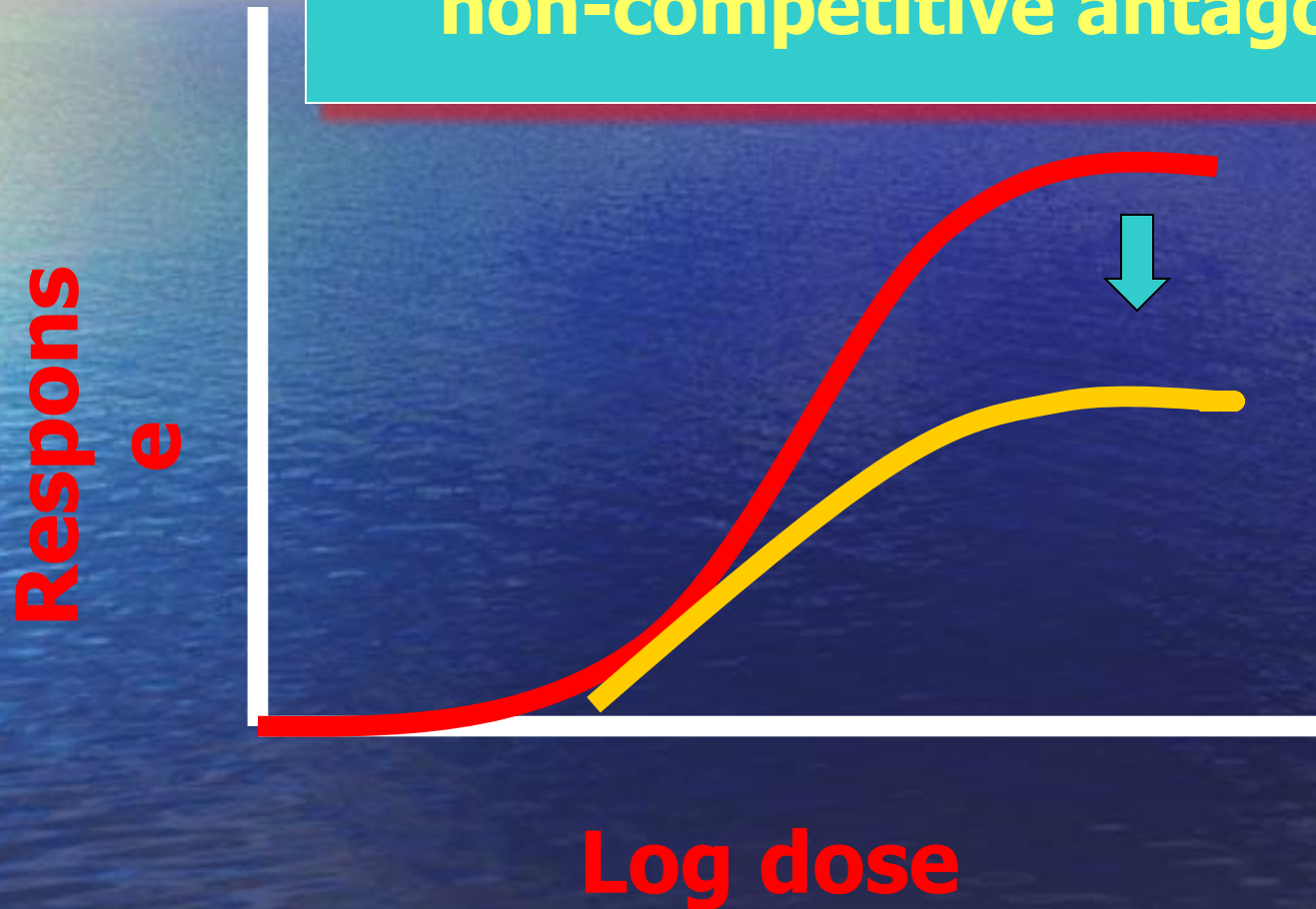
DRC & antagonists

Competitive irreversible antagonist



DRC & antagonists

non-competitive antagonist



Important notes

Parrallism

Indicate competition

Important notes

E_{max}

Indicate reversibility



Thank you