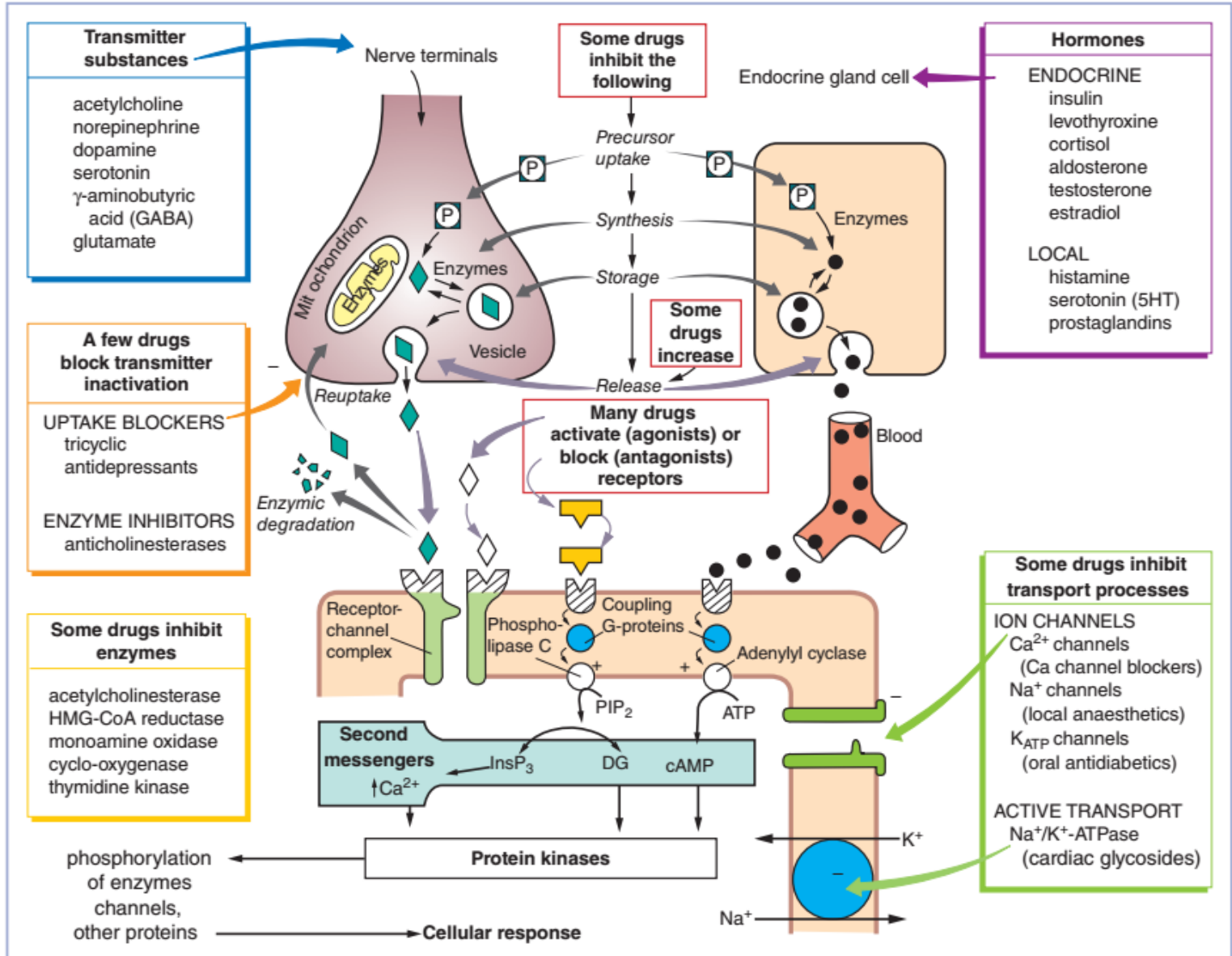


Pharmacodynamics

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Neurobiology

Principles of drug action



Principles of drug action

Drugs: natural, semisynthetic or synthetic small molecules, which interact with a specific component of the target organism.

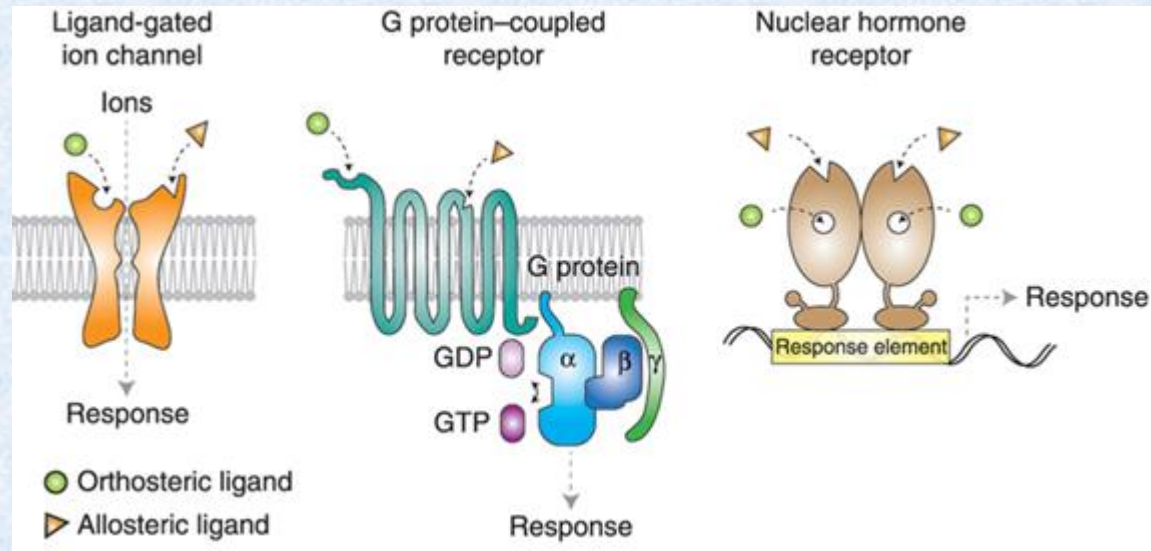
Most drugs act on macromolecules in the body:

- Enzymes
- Receptors
- Transporters
- Ion channels



signalization cascade,
change in cellular function

Main
receptor
types:

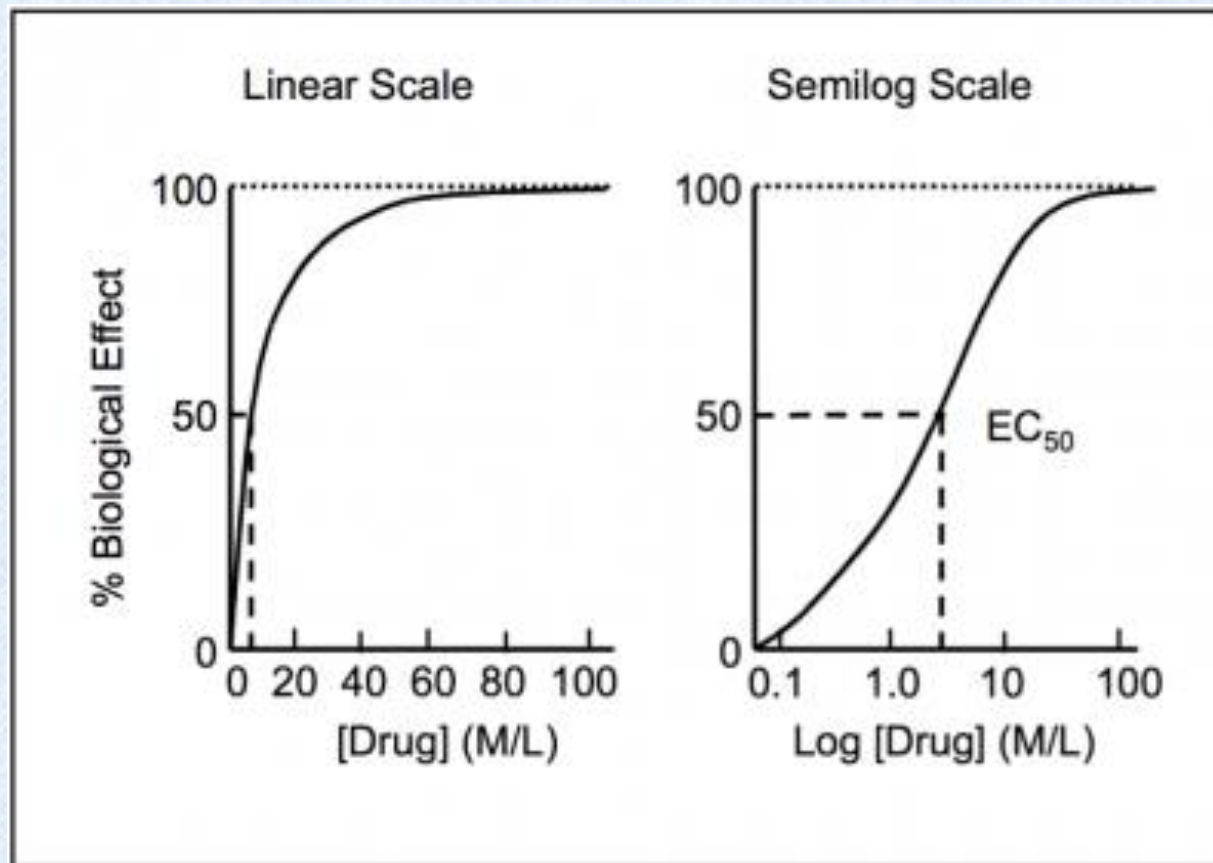


Dose-response relationship

$$[AR] = \frac{[R_0][A]}{K_D + [A]}$$

A: agonist, R: receptor,

K_D : equilibrium dissociation constant

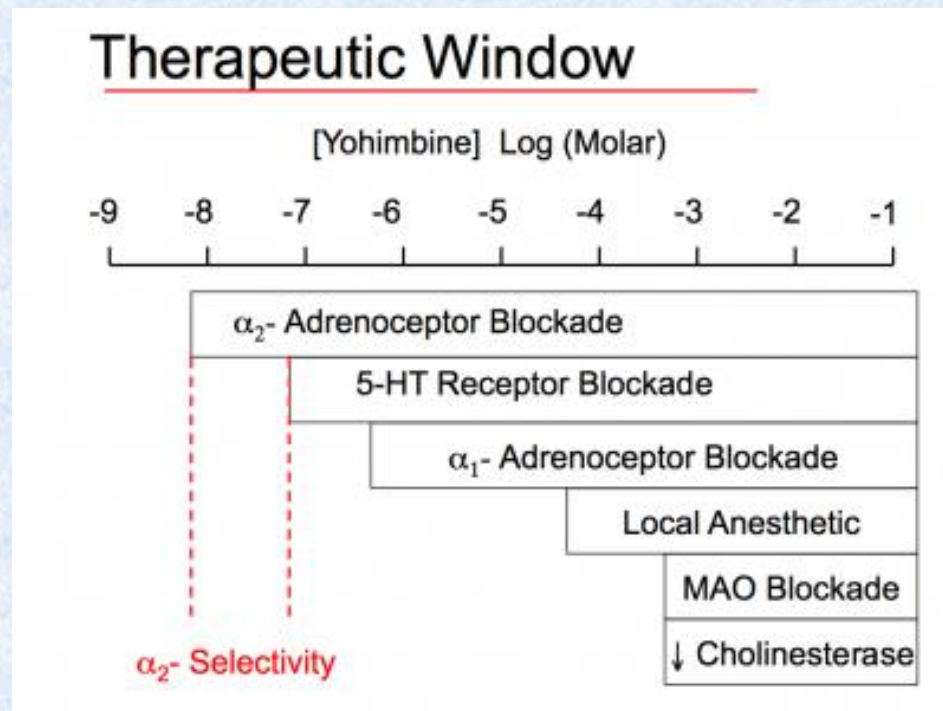


Principles of drug action

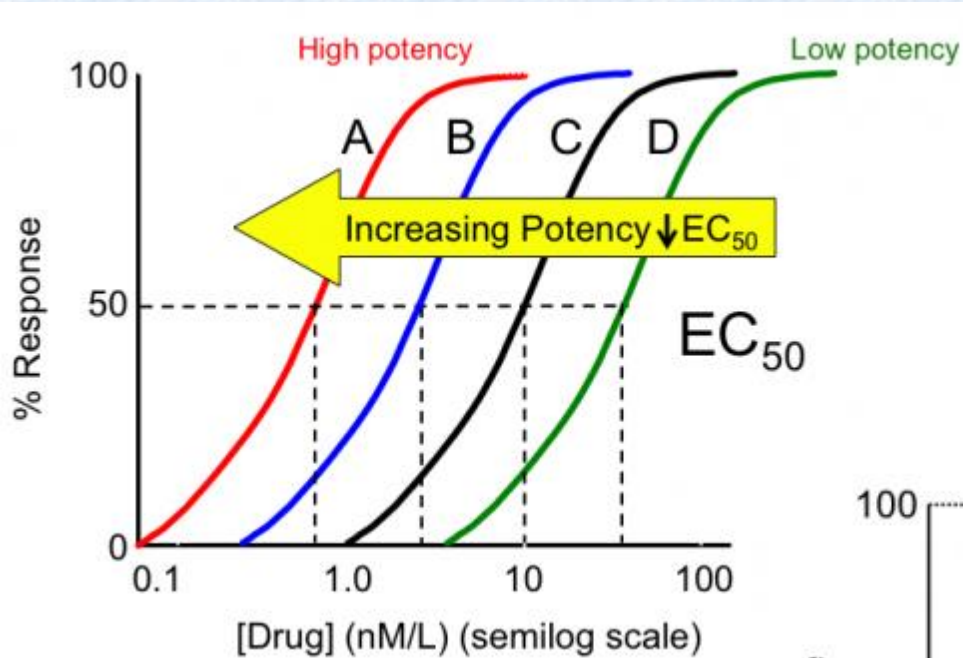
Affinity: EC_{50} : drug concentration at which 50% of receptors are occupied

Selectivity: difference in affinity for similar targets
(100x-1000x means high selectivity)

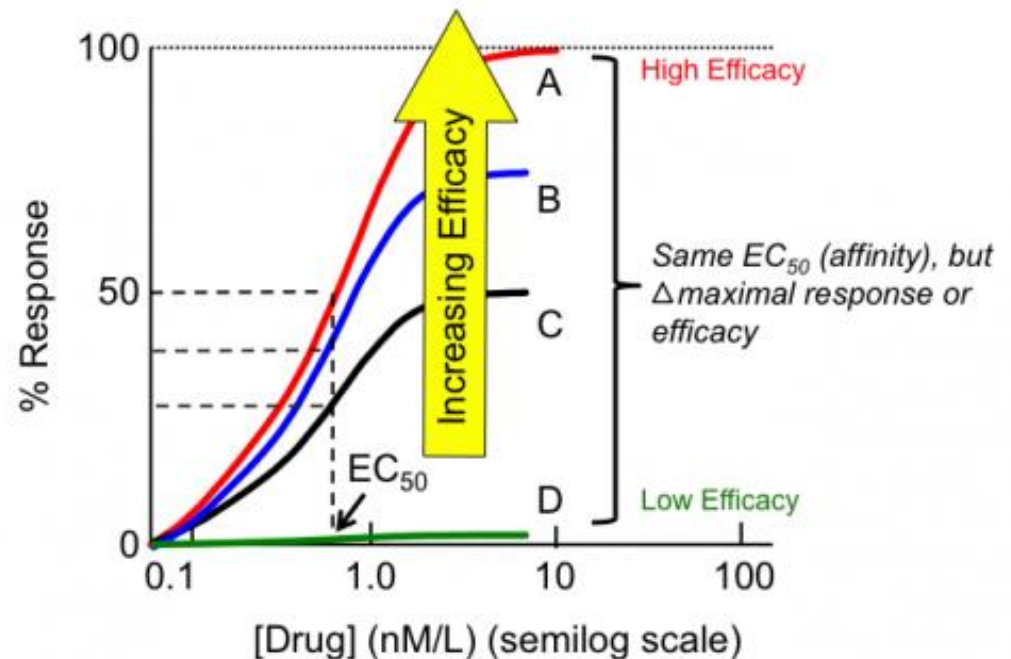
Most drugs don't have true specificity for one target.



Potency and efficacy

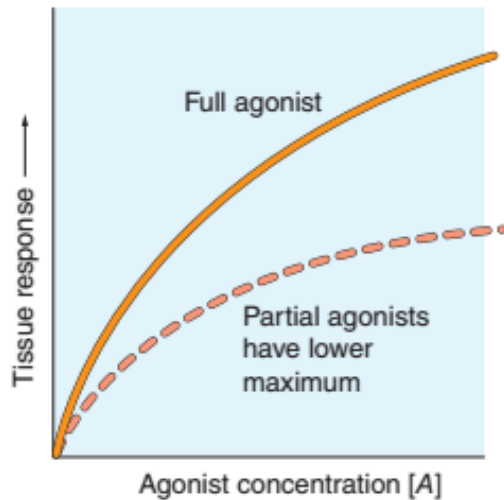


Characterization of agonists acting on the same target

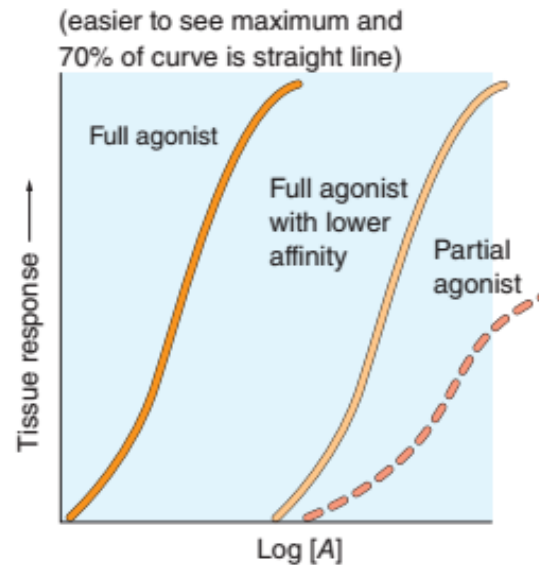


Drug-receptor interactions

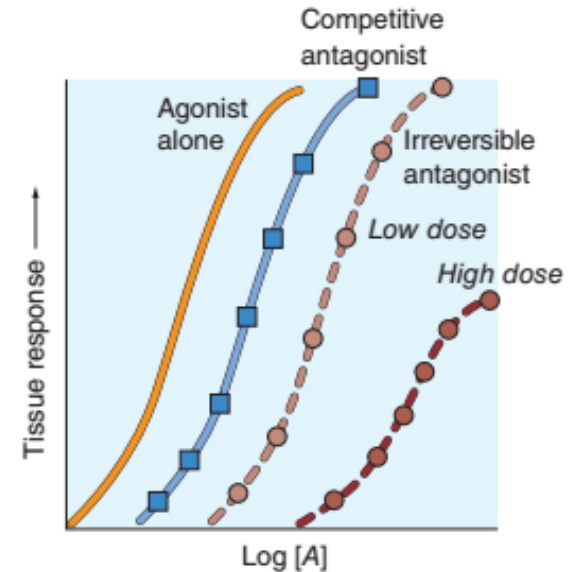
Concentration–response curve



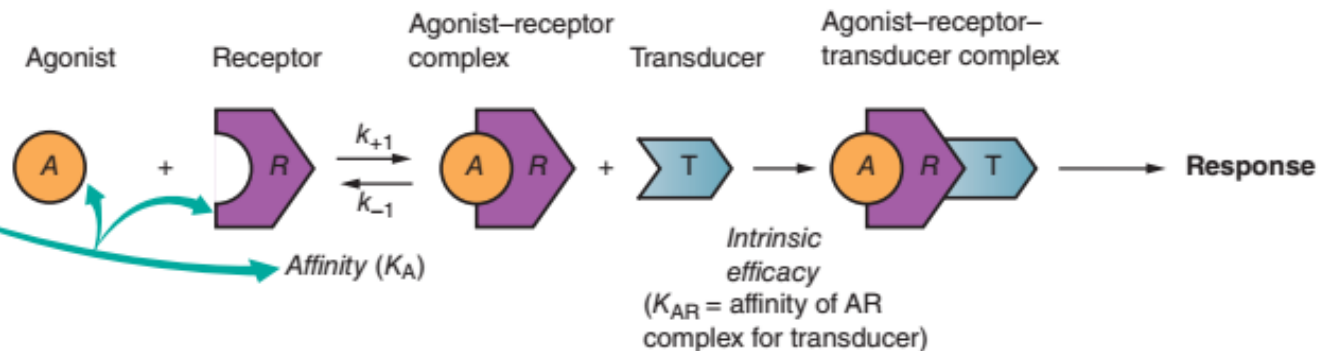
Log concentration–response curve



Effect of antagonists



Intermolecular forces
electrostatic H-bonding van der Waals hydrophobic

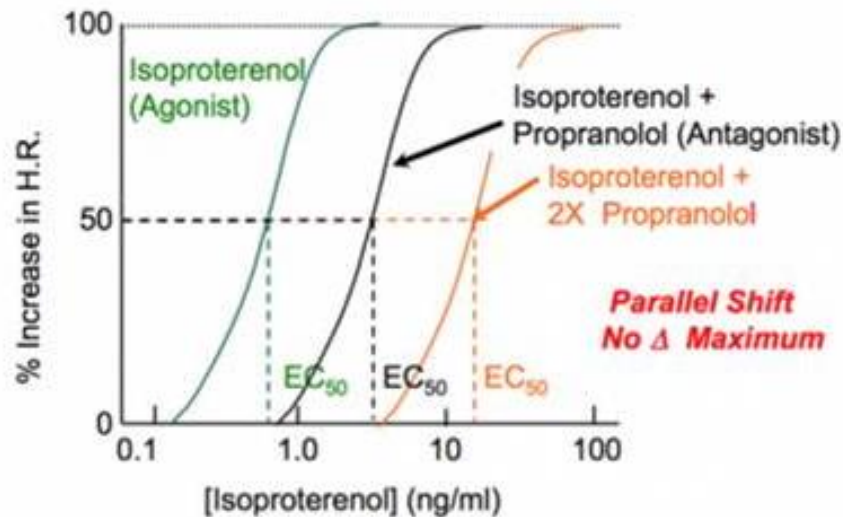


Types of antagonism

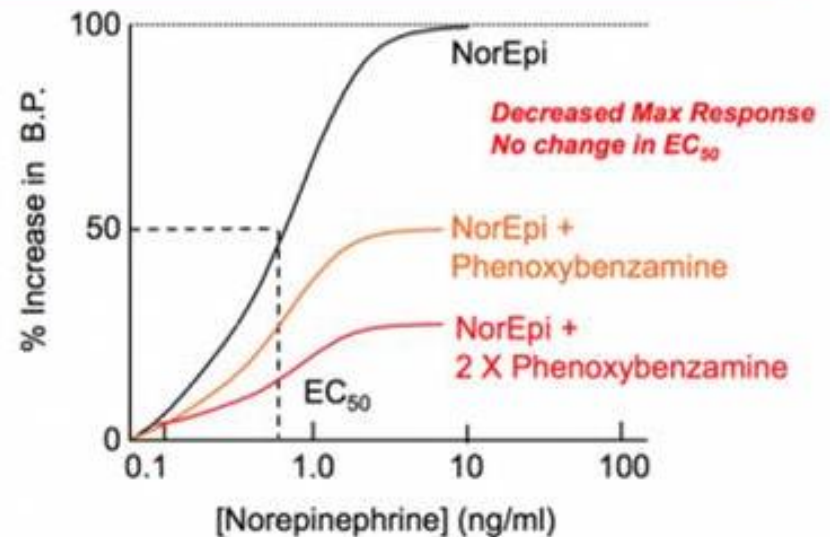
Competitive antagonist: binds to the receptor at the same location as agonist

Noncompetitive antagonist: allosteric

Competitive Inhibition



Noncompetitive Inhibition



Changes in sensitivity

Tolerance: effect of a certain drug decreases.

- Pharmacokinetic reasons e.g. metabolic enzyme induction
- Pharmacodynamic reasons e.g. decrease in receptor number, drug affinity, signalisation efficacy
- Sensitization occurs more rarely (antagonist \uparrow receptor number)
- Adaptive, homeostatic changes
- Tolerance may lead to **dependence!**

Antimicrobial drugs

Antibiotics: drugs killing/inhibiting the reproduction of bacteria.

Bacteriostatic vs. bactericide drugs

1929. Fleming – penicillin against *Staphylococcus*

Natural, then semisynthetic compounds (fermentation)

Targets:

- enzymes synthesizing bacterial cell wall (penicillin, vancomycin)
- enzymes responsible for DNA replication
- Ribosomes, protein synthesis (aminoglycosides, tetracyclin, erythromycin)

Efficacy against pathogen and sufficient cc. at infection site!

Wide vs. narrow spectrum antibiotics

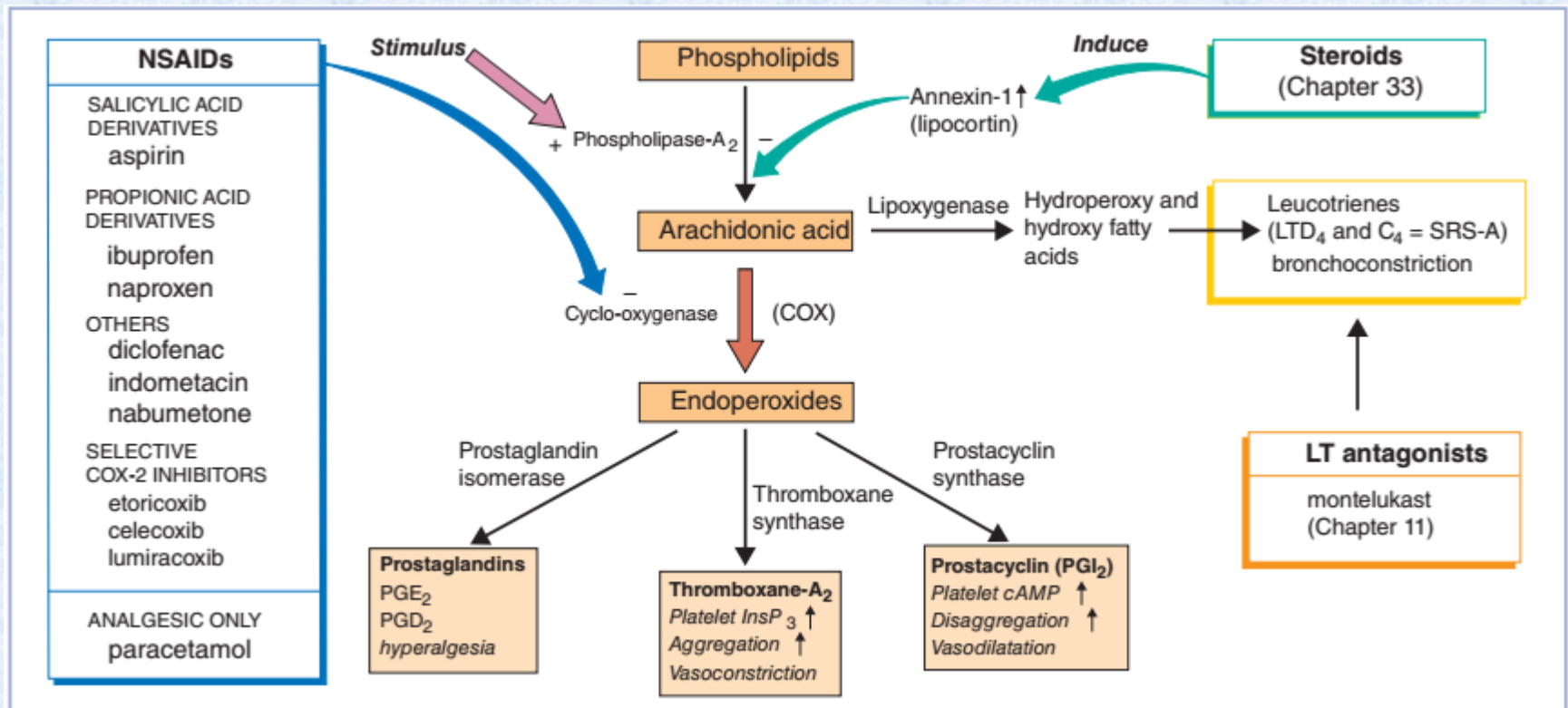
Effect on gut microflora, environmental microbes!

Antibiotic resistance

Pain killers, anti-inflammatory drugs

Inflammation: activation of mast cells, release of histamine,
 arachidonic acid → COX → prostaglandins

Inflammation inhibited by corticosteroids + NSAIDs



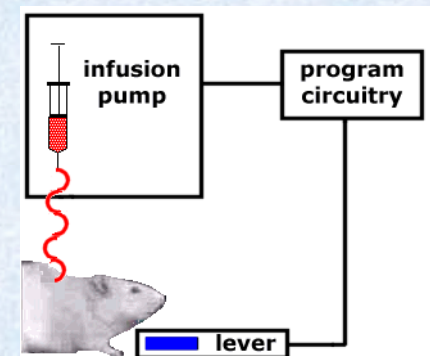
Pain killers, anti-inflammatory drugs

NSAIDs: non-steroid anti-inflammatory drugs

- Analgesic, antipyretic, anti-inflammatory
- Prescribed, sold over the counter (OTC)
- Aspirin, ibuprofen, paracetamol, diclofenac...
- Risk of gastric mucosa irritation (lack of PGs)

Opioids: agonists of opioid receptors, potentiate the endogenous analgesic pathways in the brain

- Morphine, codeine, fentanyl...
- Severe visceral pain
- Risk of overdose – respiratory arrest
- Risk of dependence



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