Adrenergic Drugs

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Sympathomimetics (Adrenergic Agonists)

- Agents that **mimic actions of sympathetic system & stimulate adrenergic receptors (adrenoceptors)**
- Adrenergic neurons release norepinephrine as primary neurotransmitter

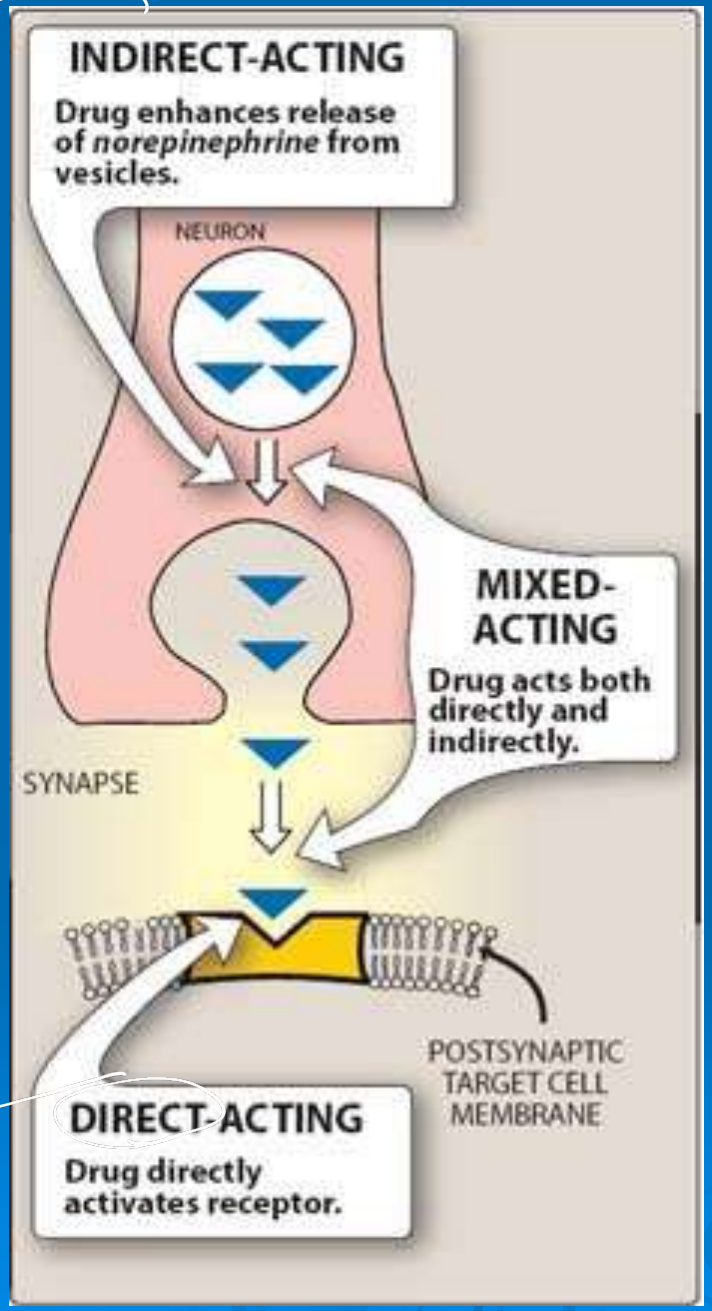
Nor- Adrenaline

Cholinergic ⇶ primary NT is Ach

Classification of Sympathomimetics

- **Direct-acting:** (Works on adrenergic Receptor directly)
  - **Selective:** salbutamol (B2), dobutamine (B1) (selective → Mainly in Bronchus; increase cardiac contractility ⇒ used in acute Heart Failure; → in Heart)
  - **Non-selective:** adrenaline, noradrenaline (B & alpha receptors) (Both β + α)
- **Indirect-acting** (Enhance the release of NE.)
  - **Releasing agents** (amphetamine)
  - **Uptake inhibitors** (cocaine, tricyclic antidepressants TCAs) (inhibit pre take from synaptic. Keep it in the System.)
  - **MAO Inhibitors** (Metabolism of NE and E. → so Inhibiton means No Metabolism and keep it in the System.)
- **Mixed-acting** (ephedrine, pseudoephedrine)

Pre synaptic



Post-synaptic

Actions of sympothomimetics

- These are mediated through stimulation of **alpha, beta & dopaminergic adrenoceptors**

Sympathomimetics

in emergency situations Adrenaline is amazing for shock.

They are also classified into:

- **Catecholamines:** (adrenaline, NA, dopamine, dobutamine, isoprenaline)
- **Non-catecholamines:** (synthetic alpha-agonists & beta-agonists, e.g. phenylephrine, ephedrine, amphetamine)

Not given during emergency!

PK of Sympathomimetics

- **Catecholamines**
  - Parenteral
  - Rapid onset of action, brief duration of action (have short t ½)
  - Enzymatic metabolism by (MAO & COMT)
  - Poor penetration into CNS

That's why it dosen't have long duration!

PK of Sympathomimetics

- **Non-catecholamines**
  - Oral & parenteral
  - Slower onset & longer duration of action
  - Less enzymatic degradation
  - More central effects (CNS effects)

Locations & Functions of adrenoceptors

- α-adrenoceptors: α1 & α2
- β-adrenoceptors: 2 subtypes of β-receptors
- Dopamine receptors: 4 subtypes

α1-Adrenoceptors

- Vascular smooth M ⇒ Vasoconstriction
- Radial M. of iris ⇒ Mydriasis
- Bladder sphincter ⇒ Contraction
- Intestine sphincter ⇒ Contraction
- Male sex organs ⇒ Ejaculation
- Inhibits entry of K into cells ⇒ Hyperkalemia
- **Increase peripheral vascular resistance (PVR)** ⇒ Pressure Agent ⇒ Hypertension

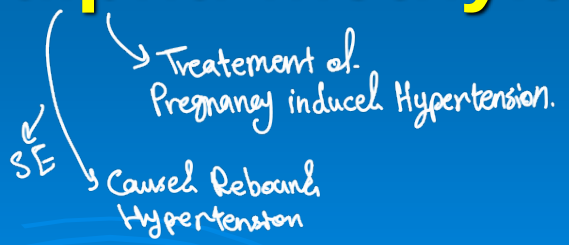
α2-adrenoceptors ⇒ Selective

Aldomit ⇒ centrally active → inhibit Release of NE or G
Hypertension drug.

- **Presynaptic** **Inhibits NA release**

Alpha-stimulants

- **Pressor agents:**
  - **Phenylephrine** ⇒ ↑ Tension, Vascular constriction.
- **Mucosal decongestants:**
  - **Pseudoephedrine, Oxymetazoline**
- **Alpha 2-agonists:**
  - **Clonidine** & **alpha-methyldopa**



Alpha-stimulants

1- Pressor agents

- These are **non-catecholamines** that **increase peripheral vascular resistance (PVR)** & **arterial blood pressure (both SBP & DBP)**
- They **reduce renal blood flow** (RBF) **& splanchnic blood flow** due to **α1-vasoconstriction**

Phenylephrine

- Is a **direct acting**, synthetic adrenergic drug
- It has predominantly direct **α1-agonist** effect, **a vasoconstrictor** & It is used as:
- **Pressor** agent (Pressure)
- **Nasal decongestant** agent (vasoconstriction)
- **Mydriatic** agent (ophthalmic solutions)
- **Vasoconstrictor** agent with local anesthetics (LA) (increase the duration)

2. Mucosal decongestants: Pseudoephedrine, Oxymetazoline

- Oxymetazoline **(Otrivin)**
- Useful in **allergic rhinitis, common cold & sinusitis**
- **Oxymetazoline is used in Ophthalmic drops** for relief of redness of eye associated with swimming, colds or contact lens

⇒ Vasoconstriction in Sinuses

- Relieve Sinus congestion and pressure ⇒ Reduce the pain.

2. Mucosal decongestants: Pseudoephedrine, Oxymetazoline

- **Avoid:**
  - **Prolonged use (rebound congestion)**
  - **In hypertensive patients**
  - **Children below 2 years of age**

Alpha 2-agonists (Clonidine & methyldopa)

- **Centrally acting antihypertensive drugs**: **clonidine** & **methyldopa** (Aldomet)
- These act centrally to produce inhibition of sympathetic vasomotor centers, decreasing sympathetic outflow to the periphery
- Methyldopa is used in hypertension during pregnancy
- They are **rarely used** because of risk of **rebound hypertension on withdrawal** of therapy

Beta-adrenoceptors (receptors)

Two subgroups β_1, β_2

β_1-adrenoceptors:

- **Heart** ⟹ Increase HR, contractility & conductivity
  - ⇒ chronotropic effect
  - ⇒ Inotropic
  - ⇒ chronotropic effect.
- **Kidneys** ⟹ Increase renin release
  - ⇓
  - Ang I → Vasoconstrictor
  - ⇓
  - Ang II → Sodium + Water Retention.

β_2-adrenoceptors

- Bronchi ⇒ Bronchodilatation
- Bladder wall ⇒ Relaxation
- Skeletal M. arterioles ⇒ Vasodilatation
- Glycogenolysis ⇒ Increase blood glucose
- Gluconeogenesis ⇒ Increase blood glucose
- Uterus ⇒ Relaxation → in cases of Abortion.
- Enhances entry of K into cells ⇒ Hypokalemia