Adrenergic Drugs

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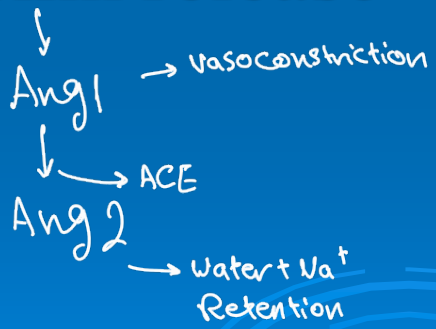
Beta-adrenoceptors (receptors)

Two subgroups β_1, β_2

β_1-adrenoceptors:

- **Heart** — Increase HR, contractility & conductivity ⇒ in cases of Heart failure
  - (main) — why? → more receptors in the heart than the kidney.
- **Kidneys** — Increase renin release
  - ↳ in cases of kidney dysfunction ⇒ we might use ACE inhibitors.



β_2-adrenoceptors

Bronchi	Bronchodilatation
Bladder wall	Relaxation
Skeletal M. arterioles	Vasodilatation
Glycogenolysis	Increase blood glucose
Gluconeogenesis	Increase blood glucose
Uterus	Relaxation
Enhances entry of K into cells	Hypokalemia

β-Stimulants

1. **Selective β_2 agonists:**

   Salbutamol (Albuterol) (Ventolin)

   USA

   tradename

- non-catecholamine
- can be given by **inhalation, orally** & **injection**
- **Short acting bronchodilator**
- Its t ½ is about **4 hours**

  short duration

- Has **a rapid onset of action (acute asthmatic attacks)**

  very effective why?

1. Selective β_2 agonists:

It is used in treatment of:

- **Acute bronchial asthma attacks**
- **Premature labour** or threatened abortion
- **Adverse effects:**

Tremor, tachycardia & hypokalemia, hyperglycemia

Because it causes relaxation of uterus

Salmeterol & Formoterol

- is a **long acting bronchodilator** similar to salbutamol with **longer t ½ (12 hr)**
- **Have a delay onset of action**
- It is useful in **prophylaxis of bronchial asthma**
  - Repeated attacks in a short specific time. ex→ cold weather in winter.
- **Not useful for acute attacks** ⇒ because of the delay onset
- Not recommended as **monotherapy** & highly efficacious **when combine with corticosteroid**
  - Anti-infection
  - Mucus + contraction of smooth M may cause an inflammation.

2. Selective β1-agonist

Dobutamine

- **Is a synthetic, direct acting catecholamine**
- **Inotropic sympathomimetic** ⇒ ↑↑ contractility.
- is used in **congestive heart failure (CHF)** to **increase cardiac output**
- **Inotropic support after cardiac surgery**
- **Septic and cardiogenic shock**

3. Non-selective β-stimulants:

Isoprenaline (Isoproterenol)

- **A synthetic, direct acting drug**
- It is a **catecholamine** with **non-selective β1 & β2** agonistic activities
- It increases **SBP & HR** (**β1** effect) & **decreases DBP** (**β2** effect)
- It is **rarely** used **to increase heart rate** in **heart block** & **to stimulate heart in cardiac arrest**

Mixed Alpha & Beta agonists

Adrenaline (Epinephrine)

- It is an **endogenous catecholamine synthesized** in **adrenal medulla** & **certain areas in brain**
- **Commonly used therapy (drug of choice in emergency situations)**

Why? Because of the Rapid onset.

Pharmacodynamic effects

- **On blood vessels:** → Vasoconstriction

Response differs according to site of vessels:

- **Skin, mucous membrane & viscera arterioles contain $\alpha 1$ receptors** & show **vasoconstriction**
- **Skeletal muscle vessels** contain mainly β_2-receptors that show **vasodilatation**

Remember :-
- α_1 ⇒ Smooth. M constriction ✓
- β_2 ⇒ Smooth. M + Skeletal. M arterioles dilatation ✓

Pharmacodynamic effects

- **Veins** contain $\alpha 1$ **vasoconstrictors**

- **Heart shows** β_1 **+ve inotropic** ⇒ Contractility

  +ve chronotropic effects ↘ HR

Effect on blood pressure:

- **Small doses** of adrenaline given by Sc or i.m will **increase SBP** (β_1 effect on heart) & **decrease DBP** (β_2 vasodilatation of skeletal BV) **(β effect predominate)**
- Giving adrenaline in **large doses** or **by IV administration** will **increase both SBP & DBP** (predominant **α1 effect**)

→ Radial Muscle

- **Iris (mydriasis), bronchi (bronchodilatation)**
- **Sphincters of gut & bladder show contraction**, while walls of gut & bladder show relaxation ⇒ Sympathetic effect ⇒ decrease GI motility.
- **Metabolic effects:** adrenaline **increases blood glucose** ⇝ β effect.

Adrenaline (Epinephrine)

Pharmacokinetics:

- Has rapid onset & brief duration of action
- **Is given Iv, Sc, by inhalation or topically to the eye**

for eye examination !

Therapeutic uses

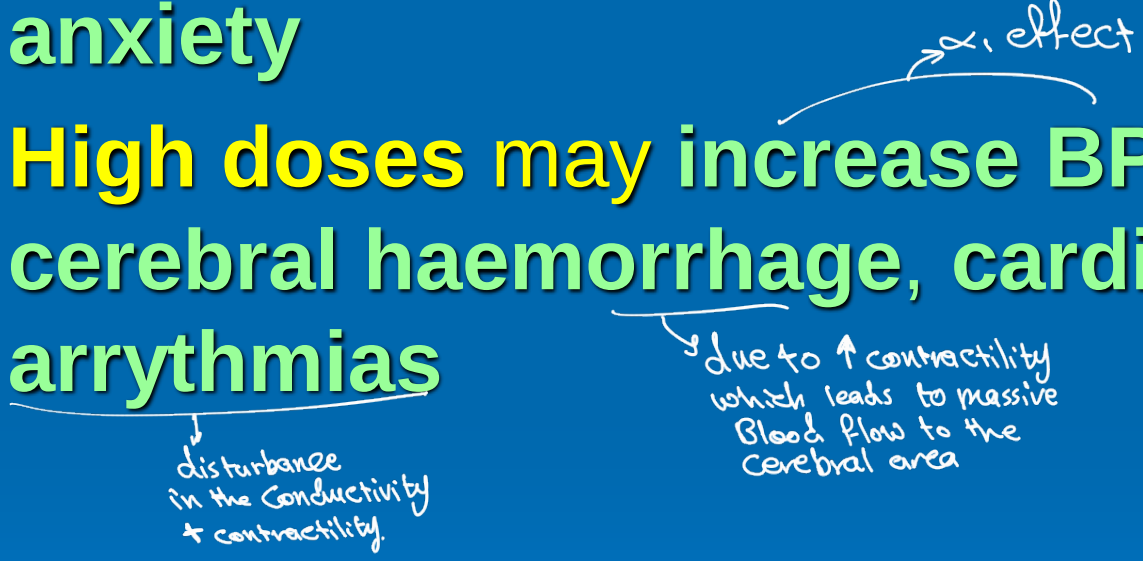
1 shot of Adrenaline is give directly in the chest toward the Heart.

- **Cardiac arrest (cardiopulmonary resuscitation-CPR)**
- **Severe allergic reactions (anaphylactic shock & angioedema):** Severe shortness of Breath due to Accumulation of Mucus in the Airway.
  - Physiological antagonist to histamine & stabilizer of mast cells
- **Vasoconstrictor with LA** Blurish in the eye due to ↑IOP
- **Chronic open angle glaucoma (topically):** vasoconstriction; reduces aqueous humor production & IOP

Relieve the pressure of the Abnormal Aquas humor amount in the eye with leads to IOP↓

Adverse effects

- **CNS disturbances:** Headache, tremor, anxiety
- **High doses** may **increase BP**, **precipitate cerebral haemorrhage**, **cardiac arrythmias**



Noradrenaline (Norepinephrine)

- It has **alpha agonist, β_1-agonist** & **weak β_2** agonist effects
- It **increases** both **SBP & DBP (potent α1 effect)**
- It is **mainly used to treat shock** as a **vasoconstrictor**

Dopamine

- It is an **alpha, beta & dopaminergic** agonist
- **Increases renal blood flow** due to **D1 vasodilatory** effect on **renal circulation**
- **At low dose, activates B1 receptors on heart, increases cardiac output, heart rate & BP**
- **At very high doses, activates alpha receptors, causes vasoconstriction**
- Is the drug of choice for **shock (cardiogenic & septic)** and is given by **continuous infusion to improve renal blood flow**

Indirect-acting sympathomimetics

Amphetamines

- Are important because can be **misused** as a **central psychostimulants** that **improve mood & alertness** منشطات
- **Acts by** Enhance **releasing endogenous NA** from adrenergic neurons after being taken up into neurons

Amphetamines

- Its effects include increase **alertness** & improved mood & **decreased fatigability** التعب
- It has also **central anorectic effects (depress appetite)** **due to its action in hypothalamic feeding center**

Amphetamines

- **Paradoxically,** it produces **sedation in children** Used in treatement of Hyperkinesia cases in children.
- **Peripheral** effects include **increase** in **BP** & **arrhythmias**
- It produces **emotional dependence**

Extra (حشى معلومات) ع
- state of Mind where a person is incapable of taking full responsibilty for thier own feelings.
⊕ معنى مشاعر بس ما بحشى فيها.

Therapeutic uses of amphetamines

- **Narcolepsy** (excessive abnormal sleep in adults- daytime)
- **Attention deficit hyperkinetic disorder (ADHD)** in **children** (abnormal pathological hyperactivity): **amphetamines improve attention, reduce hyperkinesia)**

Adverse effects

- **CNS: insomnia, irritability, dizziness, tremor**
- **CVS:** Palpitations, cardiac arrhythmias, HTN, angina pain
- **Emotional dependence**
- **Psychosis** (**Schizophrenia**-like with hallucinations & delusions)
- **Anorexia**

Direct & indirect sympathomimetics

Ephedrine

- **Mixed-action drugs** induce **release of NA from pre-synaptic terminals** and **they activate adrenergic receptor on postsynaptic membrane**
- **Non-catecholamine**

Ephedrine

- It is **non-selective agonist**, **stimulate both alpha & beta receptors** & its effects are **similar to that of adrenaline**
- **Ephedrine raises systolic & diastolic blood pressure** by **vasoconstriction & cardiac stimulation**
- **It causes bronchodilation**
- **Is give orally**

Therapeutic uses

- **Bronchial asthma** But NOT the Primary Choice!
- **Mydriatic agent** & **nasal mucosal decongestant**
- **Pressor agent** **in chronic orthostatic hypotension**
- **Heart block** **to increase heart rate**