Selective β_1 agonists

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•***Dobutamine***

•Synthetic **catecholamine**

•It **increases cardiac output** with **little change in heart rate** (does not significantly elevate oxygen demands of the myocardium).

•It is used **i.v.**

•$t_{1/2}$ is about **2 minutes**.

•**Therapeutic uses:**

• In **cardiogenic shock with IHD** (if there is renal shutdown, dopamine is preferred)

•**Adverse effects:**

•**Arrhythmias** (↑ A-V conduction). Other adverse effects are less than adrenaline.

Selective β_2 agonists

Salbutamol (Albuterol in USA*), Terbutaline and Levosalbutamol* (new)

Short-acting β_2 agonists (SABA)

They are used primarily as **bronchodilators** and administered mainly by a **metered-dose inhaler**. **(MDI)**
Compared with the nonselective **β**-adrenergic agonists

these drugs produce equivalent bronchodilatation with **less cardiac stimulation**.

Salbutamol
(the **most widely used drug**) is **well absorbed** & mainly excreted **unchanged**, plasma **$t_{1/2}$ = 4 h**. It is most widely used for :

- Treatment of ***asthma***, given by nebulizers (in the treatment of acute attacks), metered-dose inhaler or orally.
- ***Premature labor*** (produce relaxation of uterine smooth muscles), given orally or parenterally.
- Treatment of ***hyperkalaemia*** (nebulizer)

Terbutaline use is similar to salbutamol but it is **poorly absorbed orally.**

- ***Unwanted effects :***
  - **Tachycardia**
  - **Dysrhythmias**
  - **Tremor**
  - **hypokalemia**
- **Levosalbutamol (levoalbuterol) produced less cardiac stimulation**

Salmeterol and Formoterol (Eformoterol)

Long-acting β_2 agonists (LABA)

Single dose by an inhaler, provides sustained bronchodilatation over **12 hours**, compared with less than **3 hours** for SABA.
Formoterol and **salmeterol** has **delayed onset** of action.

Both agents are **used** by inhalation (MDI) for controlling **asthma** symptoms (not used in acute attacks).
These agents are highly effective when combined with inhaled ***corticosteroids*** (ICS).

S.E. similar to those of SABA.

Other Selective β_2 agonists :

Ritodrine

Used mainly to **delay parturition (labour)**, poorly absorbed by mouth; given i.v. (rarely used)

Isoxsuprine is orally taken

Indirect Acting Adrenergic Agonists

•cause **NA release** from presynaptic terminals or **inhibit its uptake**.

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•***Amphetamine***

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•**CNS stimulant** drug of **high abuse** potential

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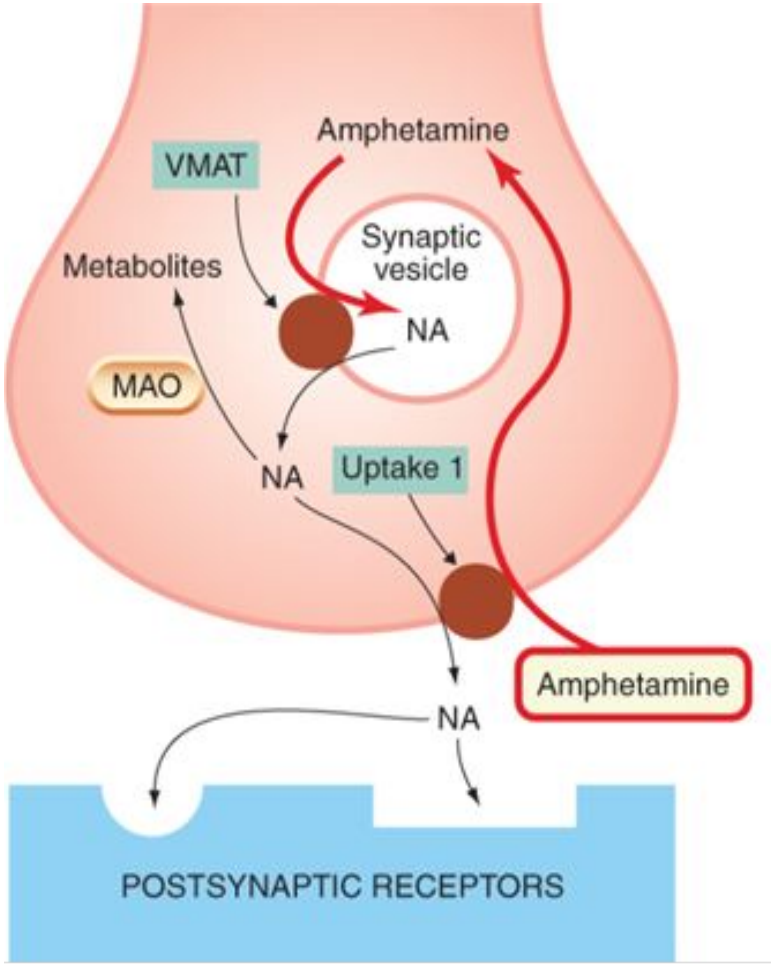
•**block NA uptake** and cause cellular **release of stored NA**.

•***Centrally*** it **increase alertness**, **decrease fatigue**

and **depress appetite**, also cause **insomnia** and produce **euphoria**.

•***Peripherally*** it **increase BP** significantly



•**Therapeutic uses:**

- Used as CNS stimulant in **narcolepsy**
- Also used in **attention deficit hyperactive children**
- **Appetite suppressant**

•**Well absorbed** orally, penetrates freely into **brain**, excreted **unchanged in urine**, plasma $t_{1/2}$ =12 hours , depending on **urine flow and pH** **(Acidification of urine significantly increases its elimination since it is weak base)**

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•**S.E. : Hypertension**, **tachycardia**, **insomnia**, **acute psychosis** with overdose, **dependence**, **teratogenic effects** .

•Mostly **abused** by : **athletes** , **drivers** (over night) and **medical students.**

•***Methylphenidate, methamphetamine and MDMA (methylenedeoxymethamphitamine) are similar agents.***

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•***Cocaine***

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•**CNS stimulant** drug (from **coca leaves**) of high **abuse** potential

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•block **NA uptake** in noradrenergic neurons.

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•Like amphetamines, it can **increase BP**

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•Rarely used **local anesthetic** and it is major drug of abuse, well absorbed orally or intranasally

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•**S.E. : Hypertension**, **excitement**, **convulsions** , **dependence**


LACK OF ATTENTION
ADHD
IMPULSIVE
HYPER-ACTIVITY
ADHD

•***Tyramine***

•Normal byproduct of **tyrosine** metabolism **not a clinically useful drug**

•important because it is found in **fermented foods**, such as **yoghurt**, **cheese** and **wine**.

•Tyramine can enter the nerve terminal and **displace stored NA**.

•Normally, tyramine is **oxidized by MAO in the GIT**, but if the patient is taking **MAO inhibitors**, it can precipitate serious vasopressor episodes (**hypertensive crisis**)

•**Tyramine rich foods** are **contraindicated** with **MAO inhibitors**.

•Mixed-Action Adrenergic Agonists

•induce the **release of NA** and **activate adrenergic receptors**

•*Ephedrine and Pseudoephedrine*

•**Release stored NA** from nerve endings and directly **stimulate both α and β receptors**. (non-selective) Thus, they produce a **wide variety of adrenergic actions**.

•Not metabolized by **COMT** and **MAO**; thus, these drugs have a **long duration of action**.

•They have **excellent absorption** orally and **penetrate into the CNS**; however, ***pseudoephedrine has fewer CNS effects***.

- **Therapeutic uses of *ephedrine*:**
  - **Chronic treatment asthma**
  - **Cold-preparations**
  - **Nasal decongestant (systemic use)**
  - **To raise blood pressure.**
- **S.E. : Hypertension, tachycardia, insomnia, dependence.**
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- **Pseudoephedrine** is primarily used to treat **nasal and sinus congestion or congestion of the eustachian tubes**. It is preferred than ephedrine because of less CNS effects.

ADRENERGIC ANTAGONISTS

(*Adrenergic blockers* or *sympatholytic* agents)

•α-Adrenergic Blocking Agents (α-blockers):

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•Drugs profoundly affect **BP**. **decrease peripheral vascular resistance**. This induces a **reflex tachycardia**.

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•Non-selective α-blockers:

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•Phenoxybenzamine

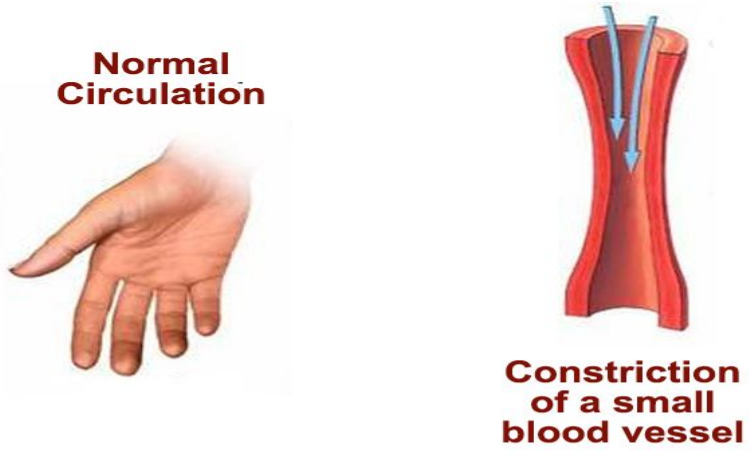
•nonselective, **bind covalently** to both **α_1** and **α_2** adrenoceptors. The block is **irreversible**. Therefore, the actions of phenoxybenzamine last about 24 hours after a single administration.

•Effects :

- **α_1 block** will **decrease peripheral resistance** and provokes a **reflex tachycardia**.
- **α_2 block** will result in **more NA release**, which stimulates **β-receptors** on the heart to **increase HR & COP** (**α**-receptors are blocked).

•Therapeutic uses:

- in the treatment of ***pheochromocytoma***.
- **Raynaud's disease**.



•**Adverse effects:**

- **postural hypotension**
- **nasal congestion.**
- **inhibition of ejaculation (impotence).**
- **flushing**
- **reflex tachycardia (mediated by the baroreceptor reflex)**
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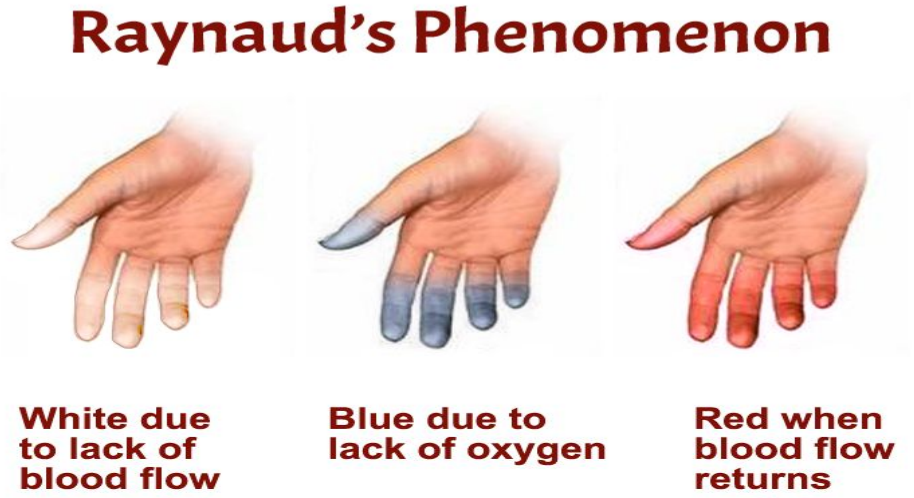

•***Phentolamine***

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•**reversible** competitive block of α_1 and α_2 adrenoceptors. Duration of action lasts for approximately **4 hours**.

•It used for the **short-term management of pheochromocytoma**. (it is rarely used now)

•Selective α_1- blockers :

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•Prazosin, Terazosin, Doxazosin, Alfuzosin, and Tamsulosin

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•selective competitive blockers of the **α_1** receptors.

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•They **decrease peripheral vascular resistance** and **lower arterial BP** (**Tamsulosin** has the **least effect on BP**).

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• **Doxazosin** is the **longest acting** of these drugs.

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•Therapeutic uses:

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- ***hypertension*** (mostly : **Prazosin**, **Terazosin**, **Doxazosin**)

•The **first dose** produces an **exaggerated orthostatic hypotensive** response that can result in syncope (***first-dose effect***) minimized by adjusting the **first dose** to **one-third or one-fourth** of the normal dose and by giving the drug at **bedtime**.

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- ***benign prostatic hypertrophy*** (also known as benign prostatic hyperplasia or **BPH**). (mostly : **Tamsulosin** and **Alfuzosin**)

•They are used alternative to surgery in patients with symptomatic BPH.

•**Tamsulosin** is a more potent inhibitor of the **α_{1A}-receptors** found on the **smooth muscle of the prostate.** This selectivity accounts for tamsulosin's minimal effect on blood pressure.

•**Adverse effects:**

- **dizziness, headache, drowsiness**
- **nasal congestion**
- **orthostatic hypotension**
- **male sexual function is not severely affected**

•**Selective α_2- blockers :**

•***Yohimbine***

•It is found as a component of the **yohimbe tree** and is sometimes used as a sexual stimulant (**aphrodisiac**).

•Yohimbine works at the level of the CNS to **increase sympathetic outflow to the periphery.**

•**Adverse effects:**

- Excitement
- Hypertension


'ANK YOU!