SYMPATHOLYTIC AGENTS USED IN HYPERTENSION

BY:

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SYMPATHOLYTICS :

- A **sympatholytic** (or **sympathoplegic**) drug is a medication which inhibits the postganglionic functioning of the sympathetic nervous system.

- **They can block at 3 different levels :**

✓ P**eripheral sympatholytic drugs** (α &β receptor antagonists) block the action of NA at the effector organ (heart or blood vessel).

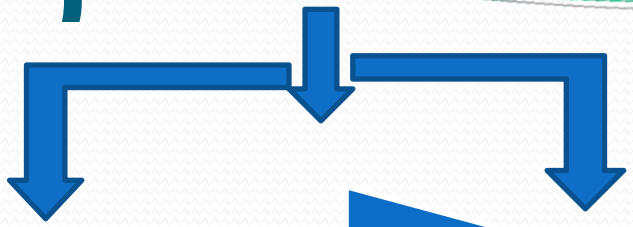
✓**Ganglionic blockers** that block impulse transmission at the sympathetic ganglia.

✓ Centrally acting sympatholytic drugs that block sympathetic activity within the brain.

CLASSIFICATION OF SYMPATHOLYTIC AGENTS

- ✓β -Blockers
- ✓α -Blockers
- ✓β+α -Blockers
- ✓Ganglion blockers
- ✓Neuronal blockers
- ✓Centrally acting sympatholytics

β-Blockers

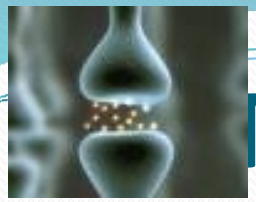


Non-selective (β1 + β2)

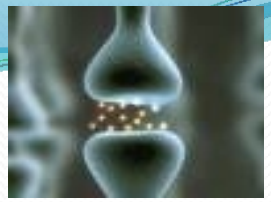
- Propanolol
- Pindolol
- Timolol
- sotalol

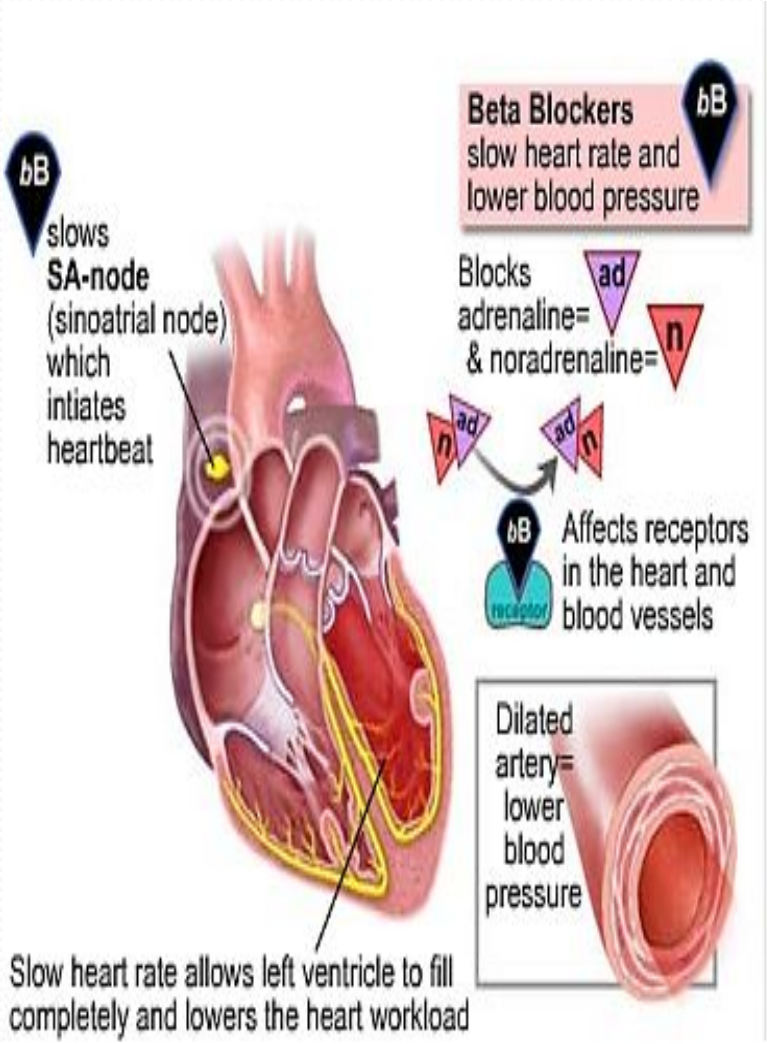
Cardioselective (β1)

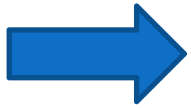
- Metoprolol
- Atenolol
- Acebutolol
- Esmolol

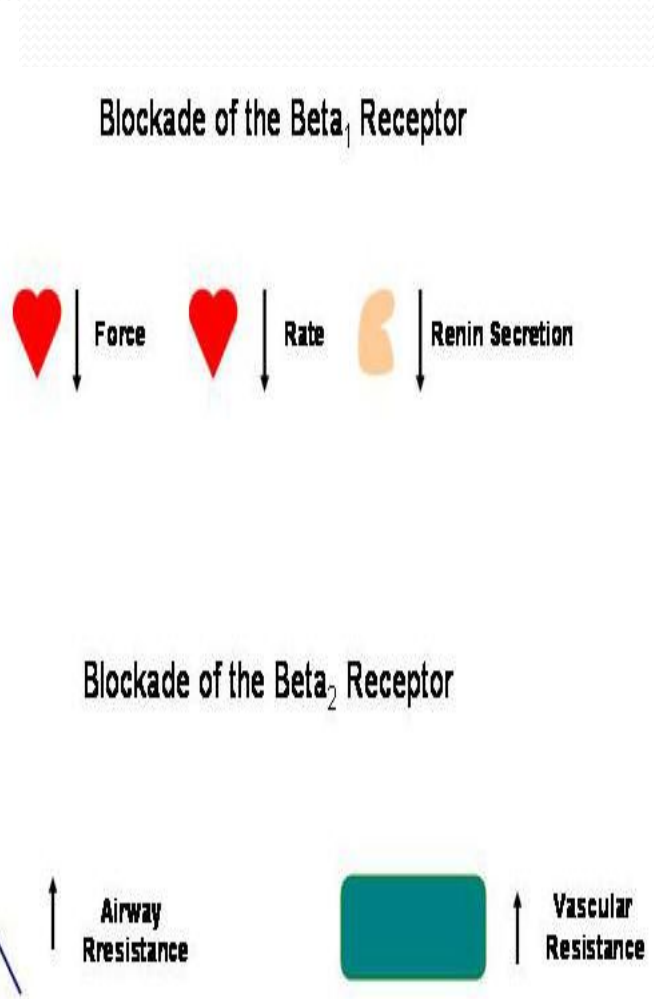


Mechanism of action









Uses :

- In mild hypertensive patients **(**stageI SBP-(140-159) & DBP-(90-99)**)**
- Hypotensive response develops over 1-3 weeks and is maintained over 24 hrs.

- **Other uses**:

✓ Angina.-decrease frequency of attack and Increase exercise tolerance

✓ Congestive heart failure.-antagonizes deletorios reflex of sympathetic system

✓ As a secondary prophylaxis in MI-By preventing reinfarction and ventricular fibrillation.

Ctd….

- ✓ Cardiac arrythmias-By suppressing extrasystoles & bradycardia.
- ✓ Supraventricular tachycardias are reduced due to prolonged systoles.(esmolol)

Adverse effects :

- ✓ Rebound hypertension on sudden withdrawl.
- ✓ Bradycardia in patients of sick sinus
- ✓ Bronchoconstriction
- ✓ GIT upset,
- ✓ Night mares, forgetfullness

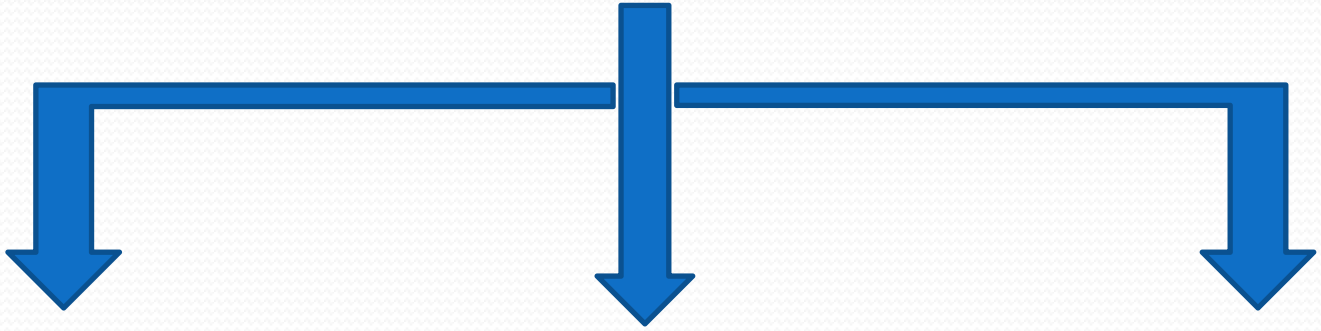
	Non-selective(β1+β 2)	Cardio selective (β1)
Pharmacological actions	• Decrease renal blood flow which ultimately decrease GFR. • Plasma LDL/HDL ratio is increased. • Most of them are lipid soluble. • Carbohydrate tolerance is impaired in prediabetis .(inhibits glycogenolysis due to	•Minimal effect on renal blood flow & GFR. •Little/no deletorious effect on blood lipids. •Most of them are lipid insoluble.

Ctd....

Adverse effects	**• Fatigue, unconciousness , subtle congnitive effects, loss of libido.** **•Cold hands and feet syndrome.** **•C/I in partial and complete heart block (propanalol)** **•Accenuates MI.**	- - -

Esmolol :Short lasting fall in B.P when given by i.v infusion(Rapid onset)

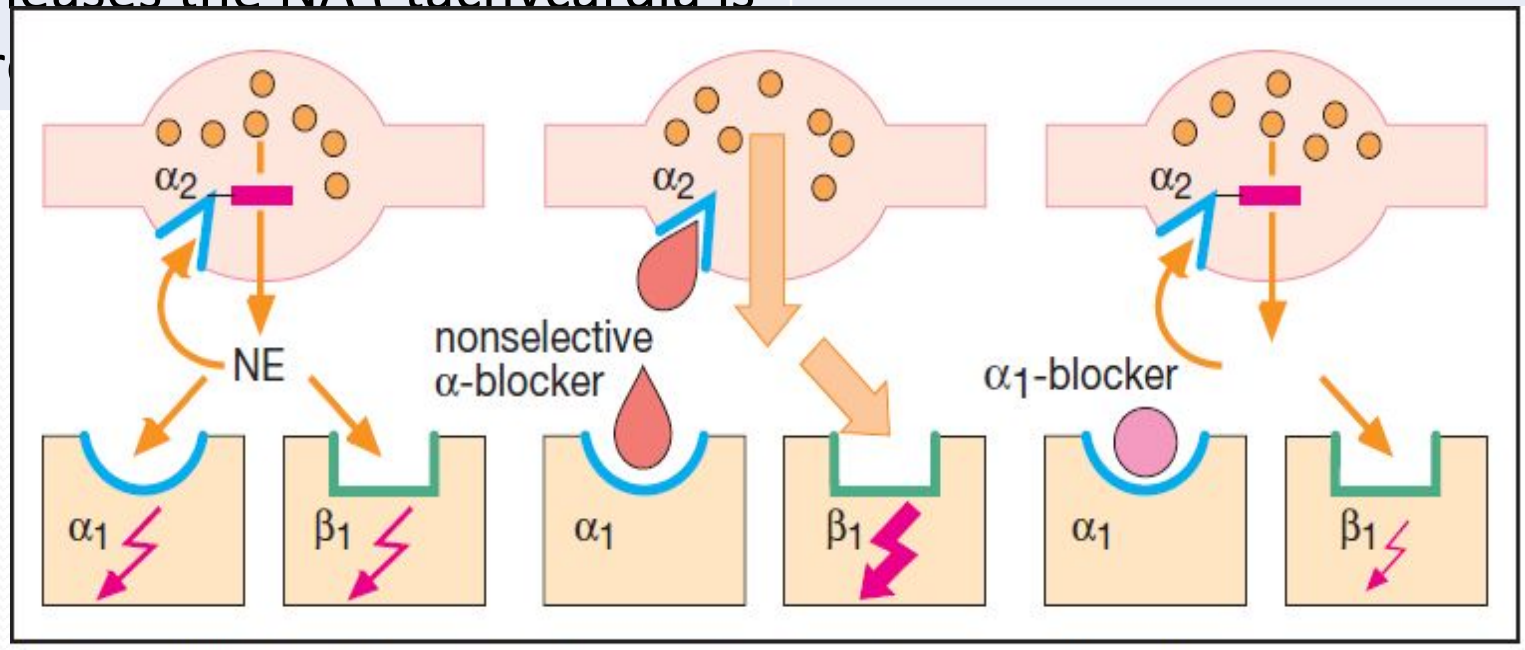
α -Blockers



Non selective	α 1 Selective	α 2 selective
• Phentolamine • Chlorpromazine • Phenoxybenzamine	• Prazosin • Terazosin • Doxazosin	• Yohimbine

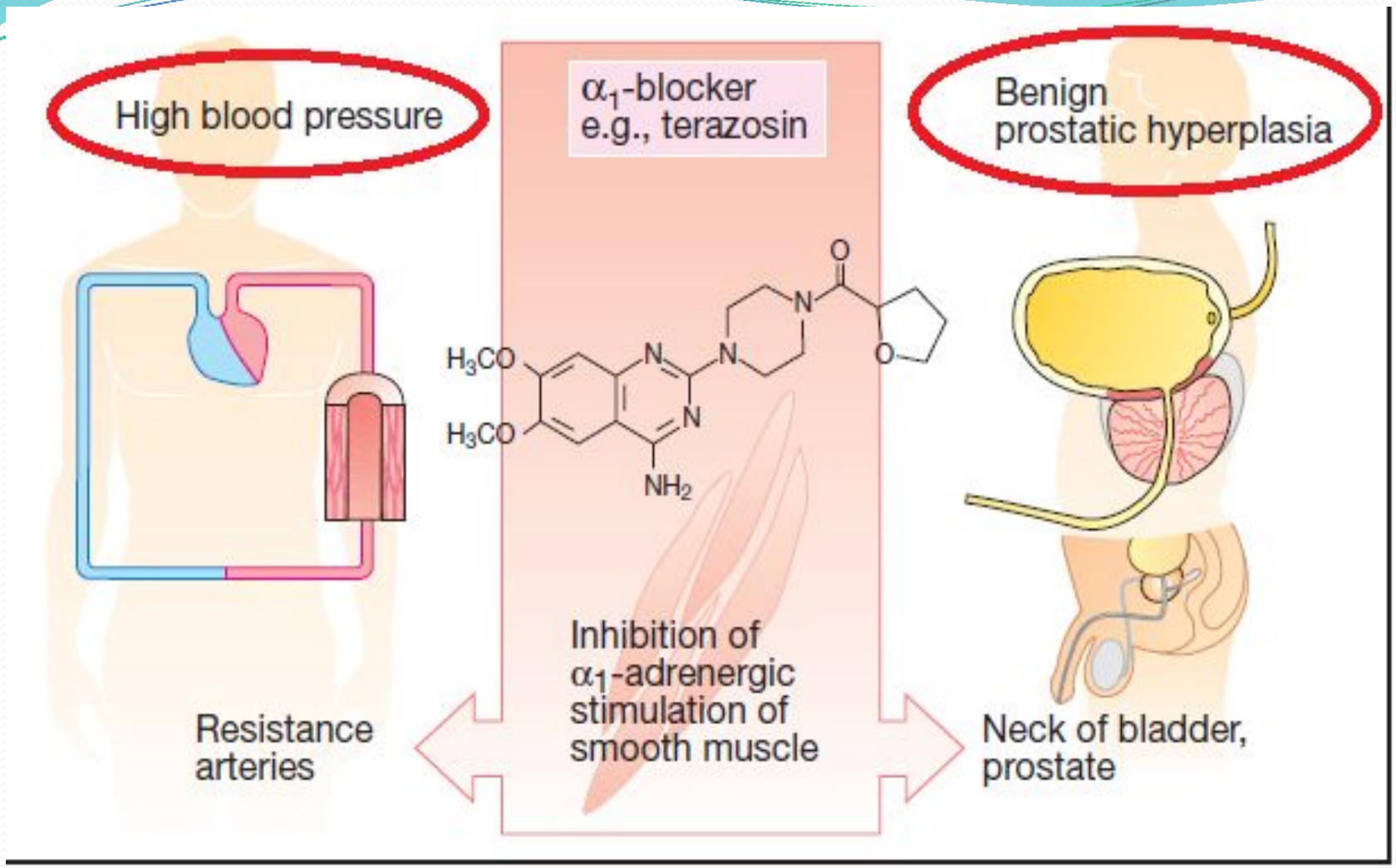
Mechanism of action

Non selective	Selective
Block both α1 and α 2 receptors	Block selectively α1 receptors.
Vasodilatation and fall in BP (α 1 blockade) - Presynaptic α2 blockade releases the NA (tachycardia is pr	Vasodilation and fall in BP (α1 blockade) - Tachycardia is minimal.



Uses :

- In mild to moderate hypertensive patients(prazosin)
- Clonidine withdrawl.
- Pheochromocytoma pts : Release of CA during surgery.
- Benign hypertrophy of prostate :By decreasing the tone of prostate /bladder neck muscles and by retarding progression.
- Raynauds disease .
- Used in diabetes patients.
- Increases the HDL and lowers the LDL & TGS



C. Indications for α_1-sympatholytics

Adverse effects:

- Postural hypotension.(Prazosin: first dose effect)
- Fluid retention and tolerance with monotherpy
- Head ache, drowsiness, dry mouth
- Miosis (α1 blockage)-blurred vision
- Nasal stuffiness
- Impotence(inhibits ejaculation)

α +β BLOCKERS

LABETELOL (β1 + β2 + α1)	CARVEDILOL (β1 + β2 + weak α1)
Fall in BP (Decrease in peripheral resistance)	Fall in BP (Vasodilation)
Uses: -Essential hypertension (absence of β blocker action) -Pheochromocytoma -Clonidine withdrawl.	**Uses:** -Anti- oxidation property -Hypertension. -Cardioprotective in CHF
ADR: -Postural hypertension -Failure of ejaculation. -Rashes -Liver damage	

GANGLION BLOCKERS

- **Quaternary ammonium compounds :** Hexamethonium , Pentolinium.
- **Monosulfonium compouds :** Trimethaphan, Camforsulfonate

ACTION:

- ✓ Ganglionic blockers inhibit autonomic activity by interfering with neurotransmission within autonomic ganglia.
- ✓ This reduces sympathetic outflow to the heart thereby decreasing CO by decreasing HR and contractility.
- ✓ Reduced sympathetic output to the vasculature decreases sympathetic vascular tone, which causes vasodilation & fall in B.P

Uses:

Trimethaphan- Used in hypertensive emergencies (aortic surgeries).

Adverse effects:

- ✓ excessive hypotension and impotence due to its sympatholytic effect.
- ✓ constipation, urinary retention, dry mouth due to it parasympatholytic effect
- ✓ Cannot be used in chronic HTN.

Neuronal blockers

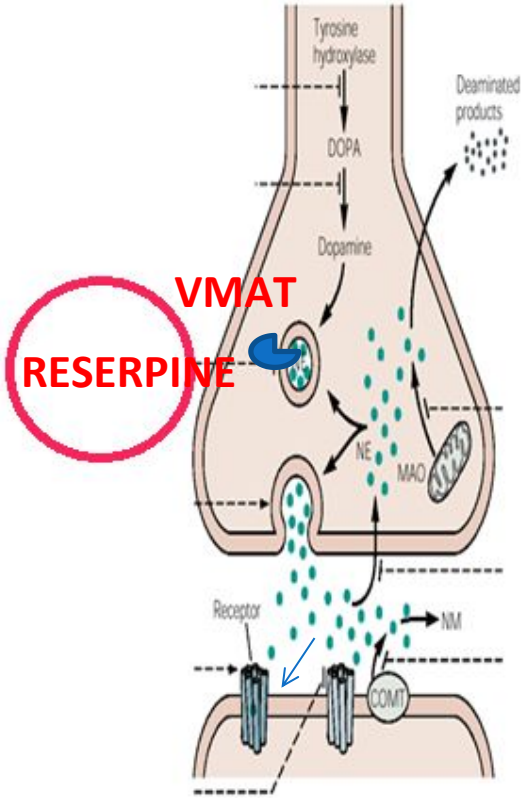
- ✓ **Reserpine :** Popular antihypertensive in 1950
- It inhibits the VMAT 2 (stores monoamines) at the neurons of intraneuronal vesicles

Monoamines get degraded by MAO.

- Effects are long lasting as the CA stores are restored gradually

Adverse effects:

At higher doses cause sedation, mental depression(deplete CA in brain)

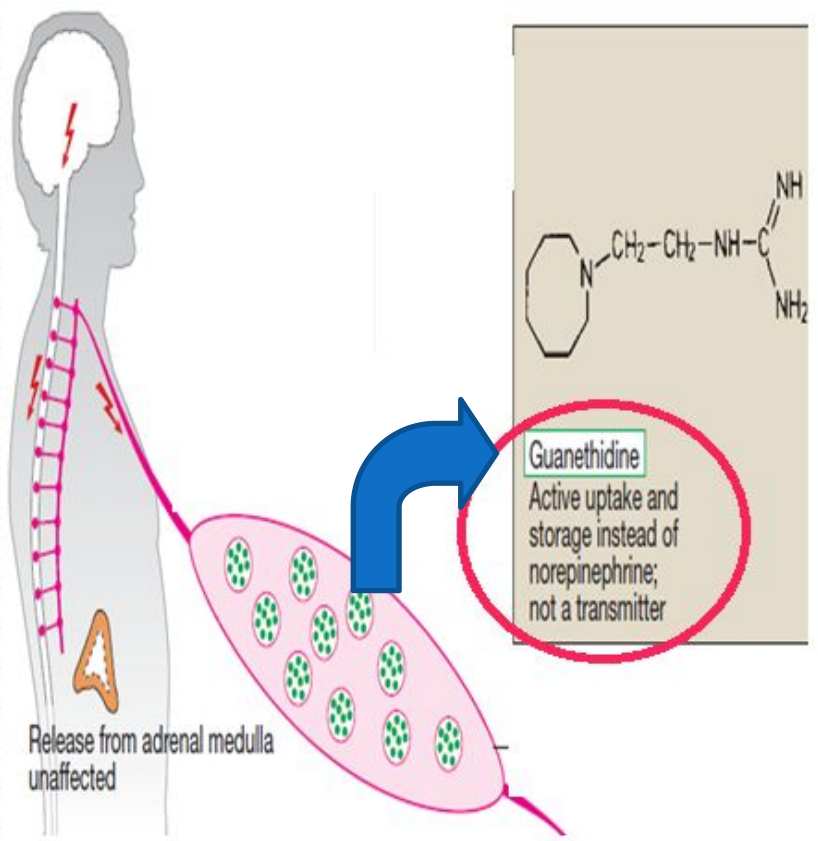


Guanithidine

- Polar guanidine compound
- Taken into adrenergic nerve endings by **active amine transporter.**

Actions:

- ✓ Engages & blocks NA uptake mechanism.
- ✓ Displaces NA in vesicles.
- ✓ Inhibits nerve impulse.
- ➢ Not used now because of side effects.



THANK YOU