Sympatholytic & adrenergic blockers

α-receptor Antagonists

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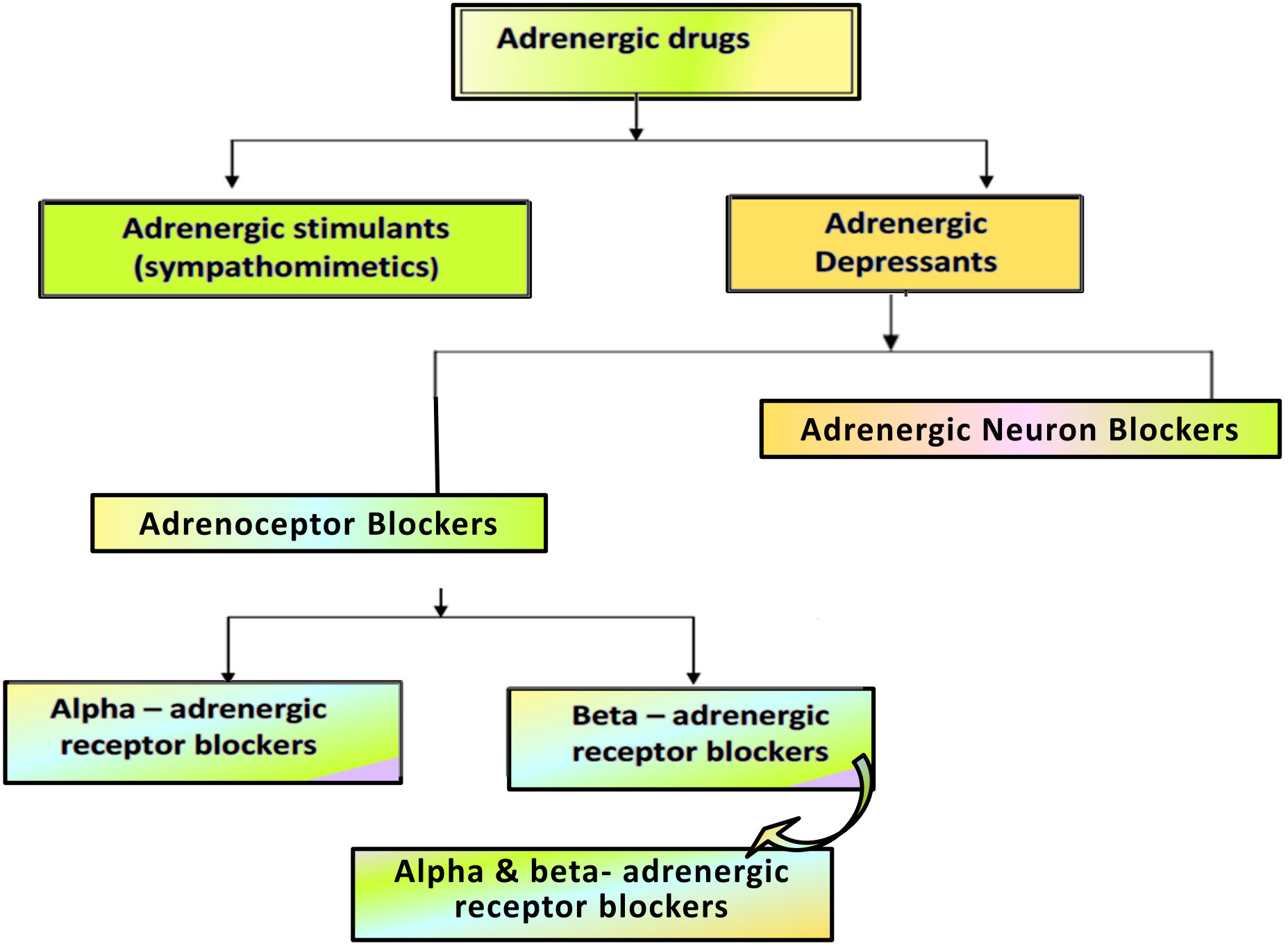
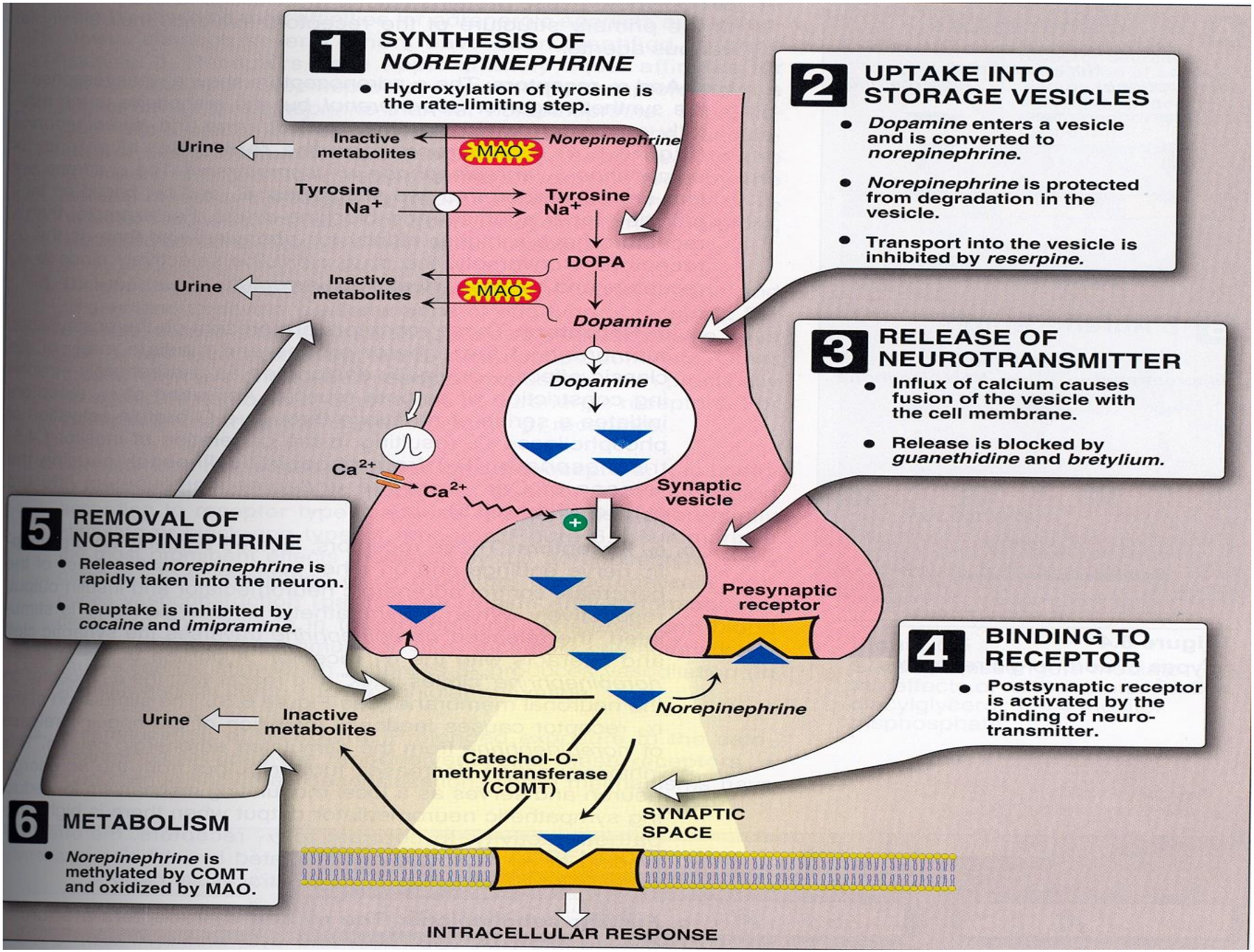

Adrenergic drugs
Adrenergic stimulants (sympathomimetics)
Adrenergic Depressants
Adrenergic Neuron Blockers
Adrenoceptor Blockers
Alpha – adrenergic receptor blockers
Beta – adrenergic receptor blockers
Alpha & beta- adrenergic receptor blockers

Classification of sympatholytics

- *Adrenergic neuron blockers*
- *Adrenergic receptor blockers*


1 SYNTHESIS OF NOREPINEPHRINE
Hydroxylation of tyrosine is the rate-limiting step.
2 UPTAKE INTO STORAGE VESICLES
Dopamine enters a vesicle and is converted to norepinephrine.
Norepinephrine is protected from degradation in the vesicle.
Transport into the vesicle is inhibited by reserpine.
3 RELEASE OF NEUROTRANSMITTER
Influx of calcium causes fusion of the vesicle with the cell membrane.
Release is blocked by guanethidine and bretylium.
4 BINDING TO RECEPTOR
Postsynaptic receptor is activated by the binding of neuro-transmitter.
5 REMOVAL OF NOREPINEPHRINE
Released norepinephrine is rapidly taken into the neuron.
Reuptake is inhibited by cocaine and imipramine.
6 METABOLISM
Norepinephrine is methylated by COMT and oxidized by MAO.
Urine
Inactive metabolites
MAO
Norepinephrine
Tyrosine
Na+
DOPA
Dopamine
Ca2+
Synaptic vesicle
Presynaptic receptor
Catechol-O-methyltransferase (COMT)
SYNAPTIC SPACE
INTRACELLULAR RESPONSE

Classification of sympatholytics

➢ *Adrenergic neuron blockers*

- **Formation of False Transmitters**

  e.g. α-Methyl dopa

- **Depletion of storage sites**

  e.g. reserpine

- **Inhibition of release & enhance uptake**

  e.g. guanethidine

- **Stimulation of presynaptic α_2 receptors**

  e.g. Clonidine and α-Methyl dopa

Classification of sympatholytics
Adrenergic neuron blockers

α-Methyl dopa

- Forms false transmitter that is released instead of NE
- Acts as central α_2 receptor agonist to inhibit NE release
- Drug of choice in
  - Treatment of hypertension in pregnancy (gestational hypertension- pre-eclampsia).

Classification of sympatholytics

Clonidine

- Acts as central α_2 receptor agonist to inhibit NE release
- suppresses sympathetic outflow activity from the brain.
- Little used as antihypertensive agent due to rebound hypertension upon abrupt withdrawal.

Apraclonidine

- is used in open angle glaucoma as eye drops.
- acts by decreasing aqueous humor formation.

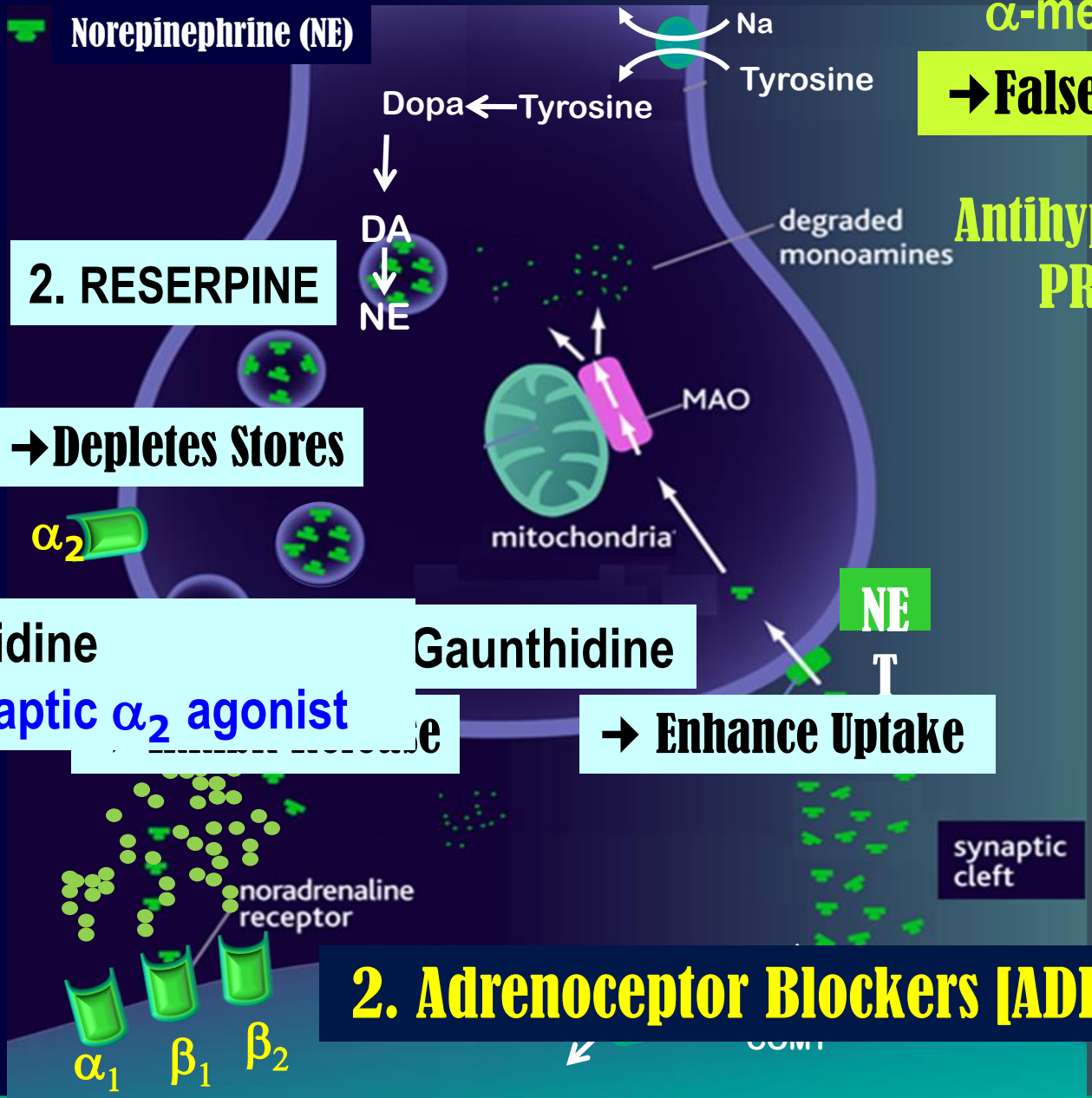
1. Adrenergic Neuron Blockers [SYMPATHOLYTICS]

1. METHYLDOPA

α-methyl tyrosine

→ False Transmitters

→ Antihypertensive in PREGNANCY



2. RESERPINE

→ Depletes Stores

4. Clonidine

Presynaptic α_2 agonist

Gaunthidine

→ Enhance Uptake

2. Adrenoceptor Blockers [ADRENOLYTICS]

Adrenergic receptor blockers

Include

- **α-receptor antagonists**
- **β-receptor antagonists**

Classification of α-receptor Antagonists

- **Non-selective antagonists e.g. phenoxybenzamine & phentolamine.**
- **α_1-selective antagonists e.g. prazosin, doxazosin.**
- **α_2-selective antagonists e.g. yohimbine**

Non-Selective α- Adrenoceptor Antagonists

Phenoxybenzamine:

Irreversible block of both α_1 and α_2 receptors

Long-acting (24 hrs)

Phentolamine:

reversible blocking of α_1 & α_2 receptors.

Short acting (4 hrs).

Pharmacological actions

Both drugs cause:

1) **Decrease peripheral vascular resistance**
2) **Postural hypotension.**
3) **Reflex tachycardia.**
4) **Reflex tachycardia due to the fall in B.P, mediated by baroreceptor reflex and due to block α_2 in heart.**

Therapeutic Uses:

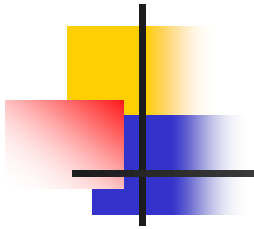
- **Pheochromocytoma:** Should be given before surgical removal to protect against hypertensive crisis.

Both drugs can precipitate arrhythmias and angina and are **contra-indicated in** patients with decreased coronary perfusion.

Adverse Effects of non-Selective α- Adrenoceptor Antagonists :

- **Postural hypotension**
- **Tachycardia**
- **Headache**
- **Nasal stuffiness or congestion**
- **Vertigo & drowsiness**
- **Male sexual dysfunction (inhibits ejaculation).**

Selective α1- Antagonists



Prazosin, doxazosin, terazosin .

Prazosin (short half-life)

Doxazosin, terazosin (long half life)

Selective α1- Antagonists

Pharmacological effects of α_1–antagonists:

- **Vasodilatation due to relaxation of arterial and venous smooth muscles**
- **Fall in arterial pressure**
- **less reflex tachycardia than with non-selective α blockers**

Therapeutic Uses:

- **Treatment of essential hypertension**
- **Urinary obstruction of benign prostatic hypertrophy (BPH).**
- **Raynaud's disease.**

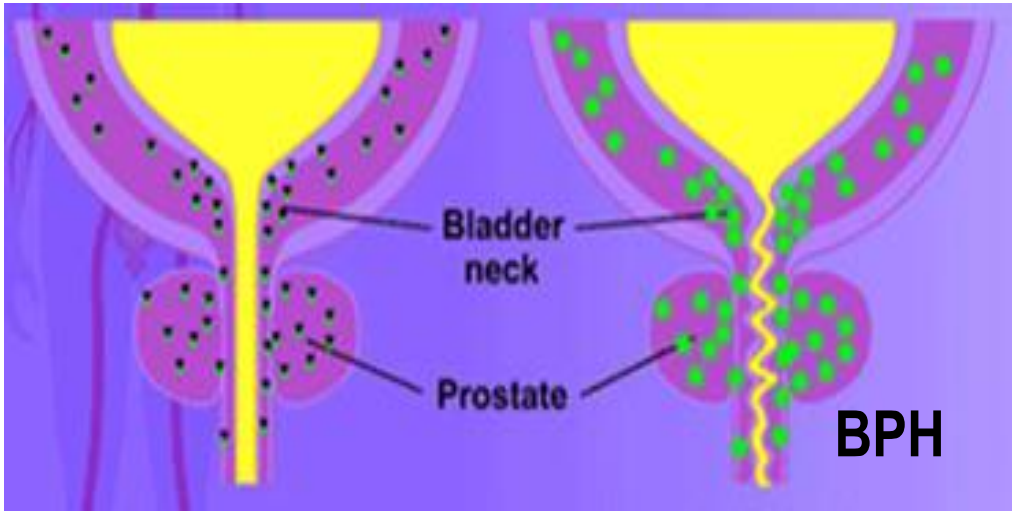
Selective α_{1A}–antagonists
Tamsulosin

- **Is a selective α_{1A} antagonist.**
- **Tamsulosin produce: relaxation of smooth muscles of bladder neck & prostate →improve urine flow.**
- **Has minimal effect on blood pressure.**
- **Tamsulosin is used in the treatment of benign prostatic hypertrophy (BPH).**

Selective α_{1A} antagonist Tamsulosin

Tamsulosin

Relaxation of bladder neck can improve urine flow



Adverse effects of α1A- Antagonists

as before with non selective but to a lesser degree

α_2-selective antagonists

- **e.g. yohimbine**
- **Used as aphrodisiac in the treatment of erectile dysfunction.**
- **Increase nitric oxide released in the corpus cavernosum thus producing vasodilator action and contributing to the erectile process.**