Sympatholytic & adrenergic blockers
α-receptor Antagonists

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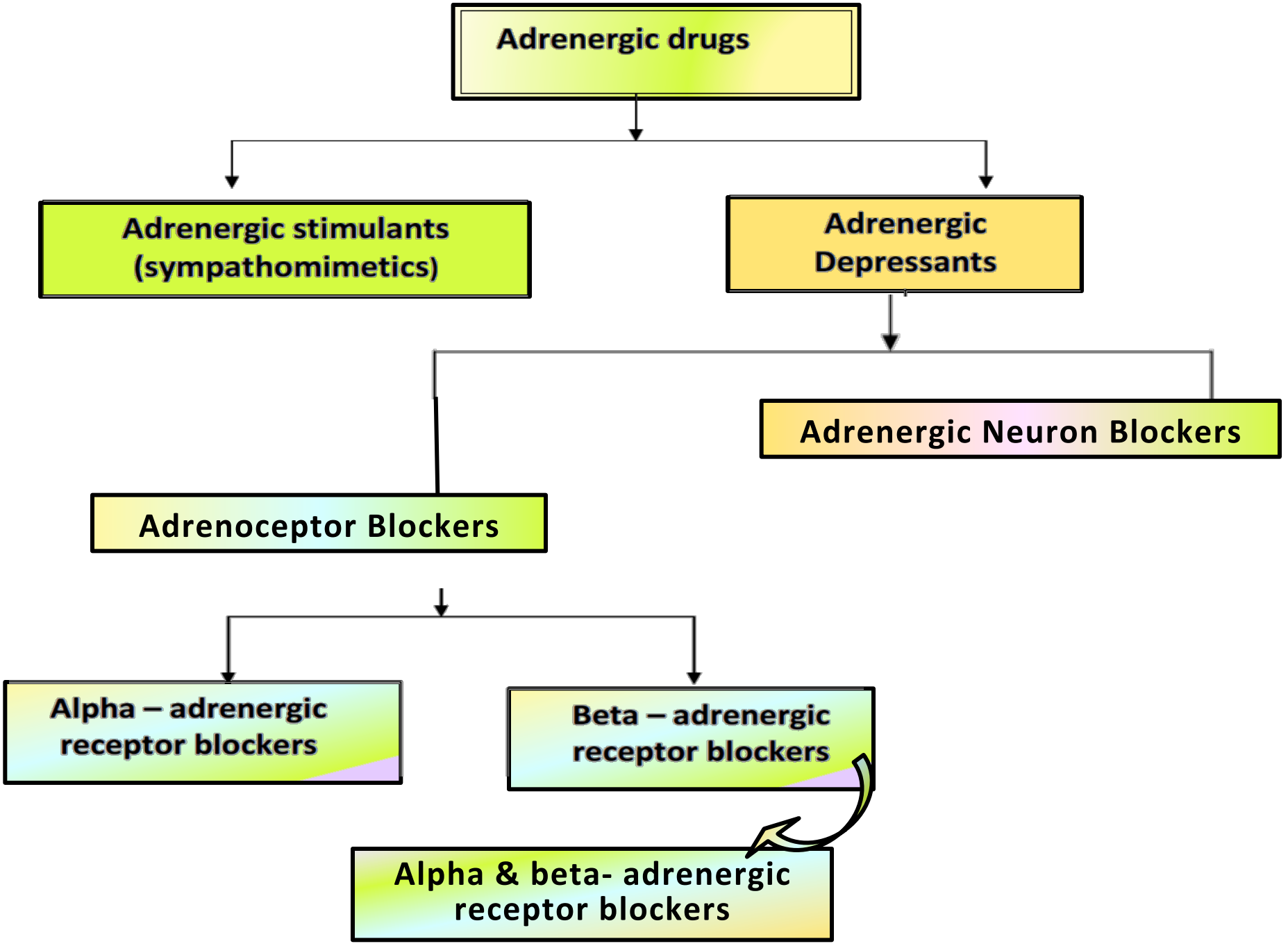

Adrenergic drugs
Adrenergic stimulants (sympathomimetics)
Adrenergic Depressants
Adrenergic Neuron Blockers
Adrenoceptor Blockers
Alpha – adrenergic receptor blockers
Beta – adrenergic receptor blockers
Alpha & beta- adrenergic receptor blockers

Classification of sympatholytics

➢ *Adrenergic neuron blockers*

- **Formation of False Transmitters**

  e.g. α-Methyl dopa

- **Depletion of Storage sites**

  e.g. reserpine

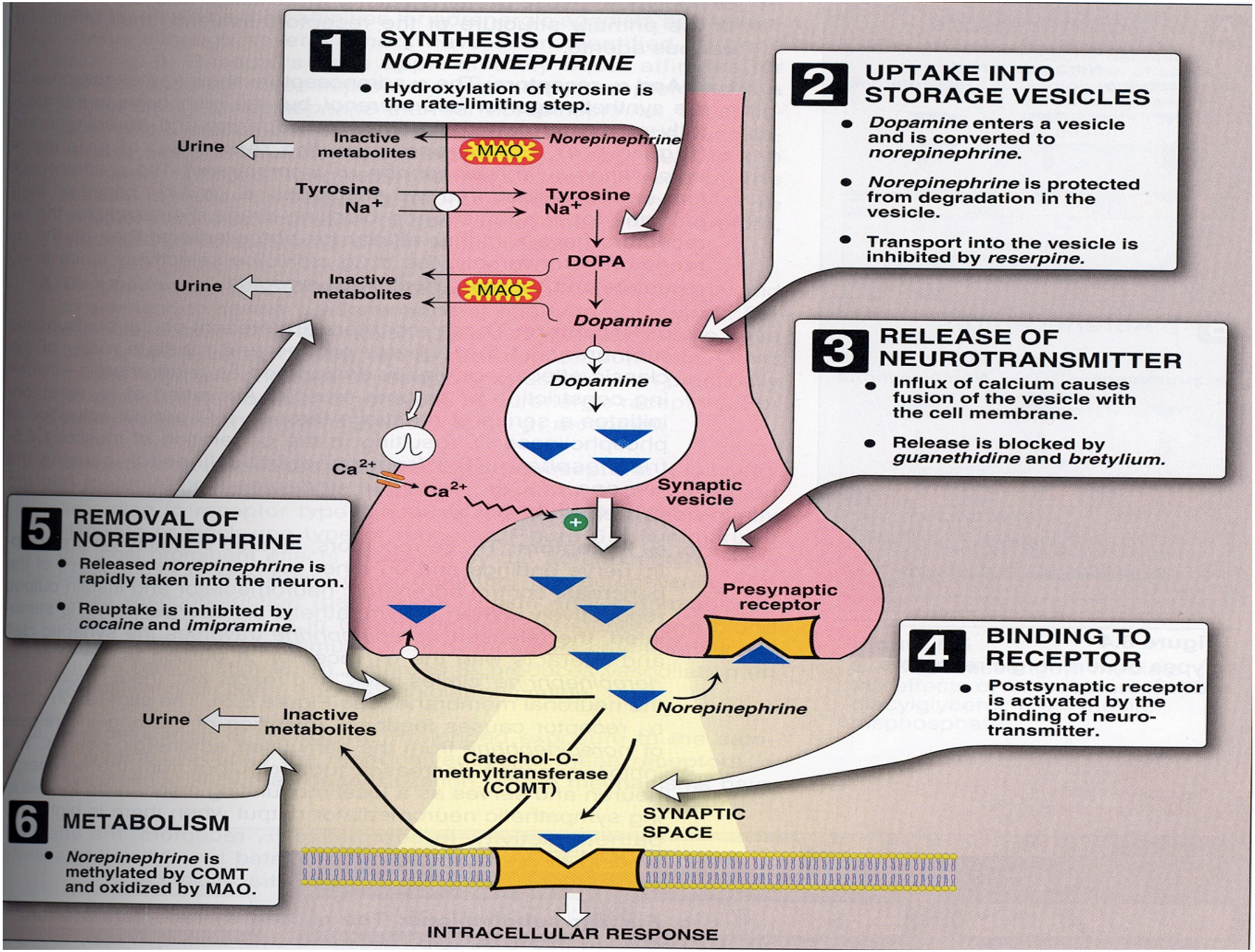
- **Inhibition of release & enhance uptake**

  e.g. guanethidine

- **Stimulation of presynaptic α_2 receptors**

  e.g. clonidine and α-methyl dopa

➢ *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

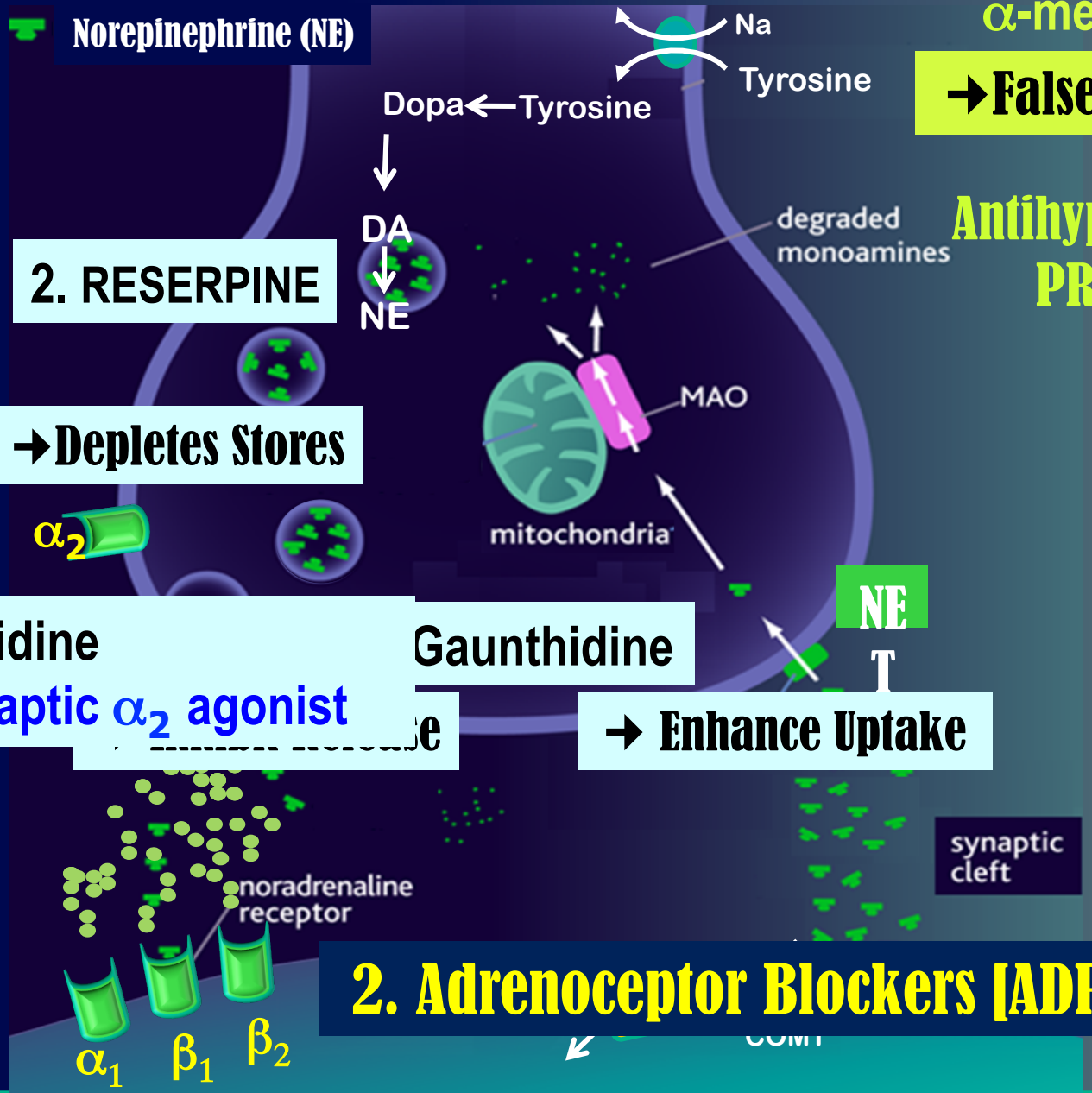
1. Adrenergic Neuron Blockers [SYMPATHOLYTICS]

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]

α-Methyl dopa

- **Forms false transmitter that is released instead of NE.**
- **Is a centrally acting α_2 adrenergic agonist that inhibits NE release.**

Drug of choice in:

Treatment of hypertension in pregnancy (pre-eclampsia - gestational hypertension).

Clonidine

- **Acts as 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.**

Uses: the management of withdrawal symptoms of opiate treatment, alcohol withdrawal, benzodiazepines and nicotine dependence.

Apraclonidine

is used in open angle glaucoma as eye drops.

acts by decreasing aqueous humor formation.

Adrenergic receptor blockers

Adrenergic receptor blockers or adrenolytics

They block sympathetic actions by antagonizing α or B-receptors.

Types

- **α-receptor antagonists**
- **B-receptor antagonists**

Classification of α-receptor Antagonists

Non-selective antagonists

e.g. phenoxybenzamine & phentolamine.

α_1-selective antagonists

e.g. prazosin, doxazosin, tamsulosin, terazosin.

Selective α_2- adrenoceptor antagonists

e.g. yohimbine

Non-Selective α - Adrenoceptor Antagonists

Phentolamine

Reversible blocking of α1 & α2 receptors.

Short acting (4 hrs).

Phenoxybenzamine

Irreversible block of both α_1 and α_2 receptors

Long-acting (24 hrs).

Both drugs cause:

1) Vasodilatation of blood vessels (α_1 block).
2) Decrease peripheral vascular resistance
3) Postural hypotension.
4) Increase cardiac output (α_2 block).
5) Reflex tachycardia.
6) Increase in GIT motility and secretions

Reflex tachycardia occurs by two mechanisms:

- **Stimulation of baroreceptor reflex that increase NE release.**
- **α2 blockade in heart that abolishes pre-synaptic negative feedback for NE release.**

Therapeutic Uses:

- **Pheochromocytoma: Before surgical removal to protect against hypertensive crisis.**

Adverse Effects of non-Selective α- Adrenoceptor Antagonists :

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

Non-Selective α- Adrenoceptor Antagonists

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

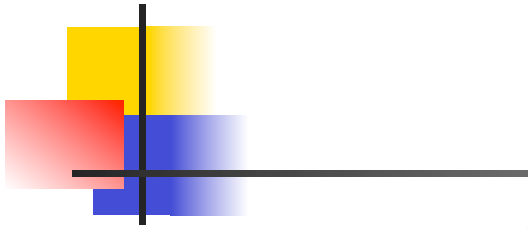
Selective α_1- adrenoceptor Antagonists

Drugs as

Prazosin, doxazosin, terazosin .

- **Prazosin has short half-life.**
- **Doxazosin, terazosin have long half lives.**

Selective α_1- adrenoceptor Antagonists

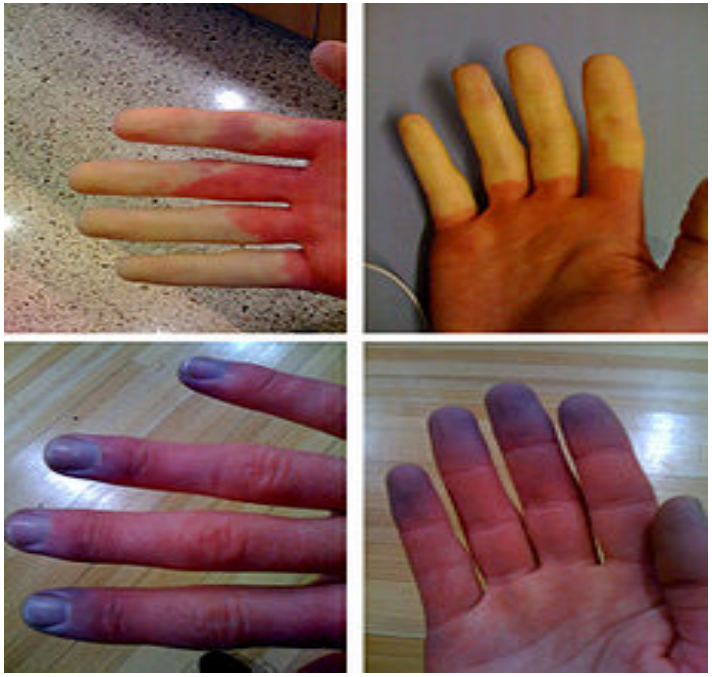


α_1–antagonists cause:

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

Therapeutic Uses:

- **Treatment of hypertension**
- **Urinary retention associated with benign prostatic hyperplasia.**
- **Reynaud's disease.**
- **Reynaud's disease** causes some areas of your body such as your fingers and toes to feel numb and cold in response to cold temperatures or stress).



Selective α_{1A}–antagonist
Tamsulosin

- a selective α_{1A}–antagonist.
- α_{1A} receptors present in prostate and bladder neck.
- Tamsulosin produce: relaxation of smooth muscles of bladder neck & prostate →improve urine flow.
- Has minimal effect on blood pressure.

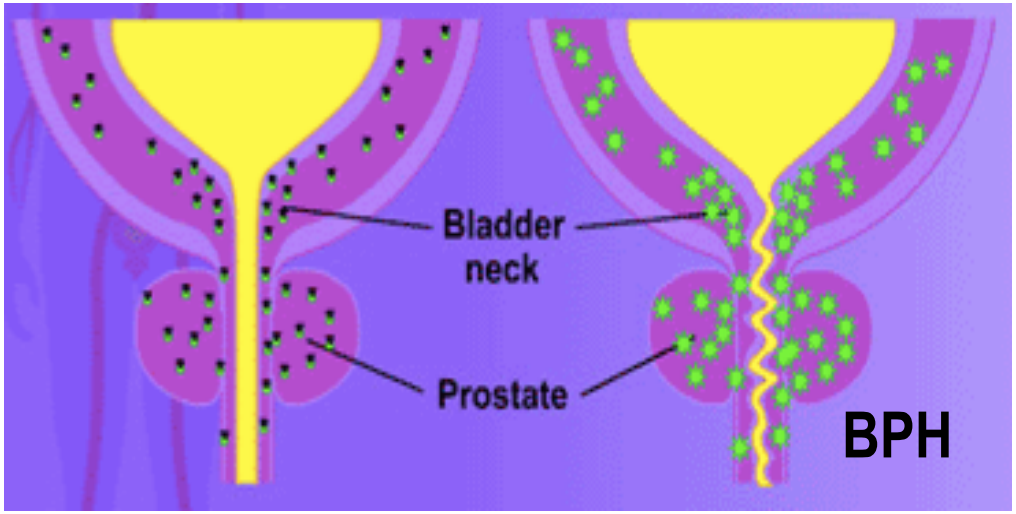
USES:

- Treatment of benign prostatic hypertrophy (BPH).
- Help with the passage of kidney stones.

Selective α1A–antagonist
Tamsulosin

Tamsulosin

Relaxation of bladder neck and prostate can improve urine flow



Adverse effects of α1- 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.**