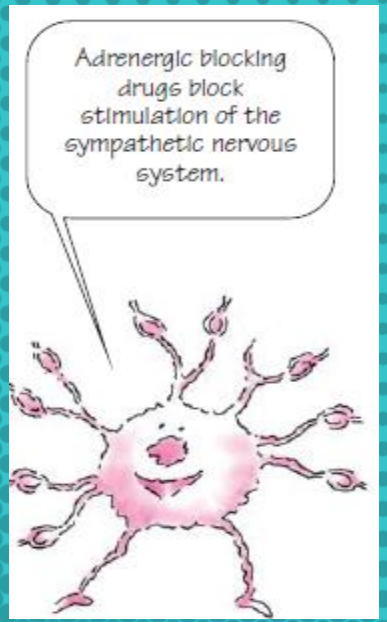
SYMPATHOLYTIC DRUGS

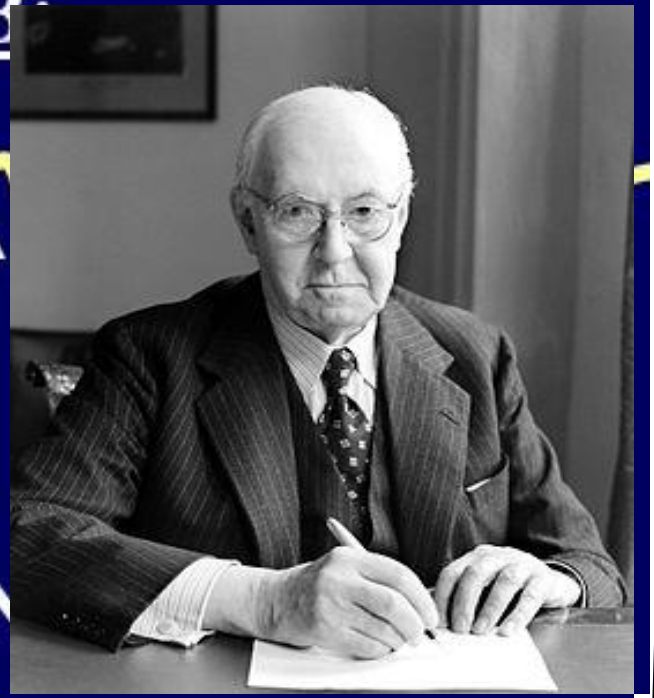


ADRENERGIC NEURON BLOCKERS

ADRENERGIC RECEPTOR BLOCKERS

ADRENALINE REVERSAL

Sir Henry Dale, awarded the Nobel prize in 1936



▪ILOS

Outline the mechanisms of action of adrenergic neuron blockers

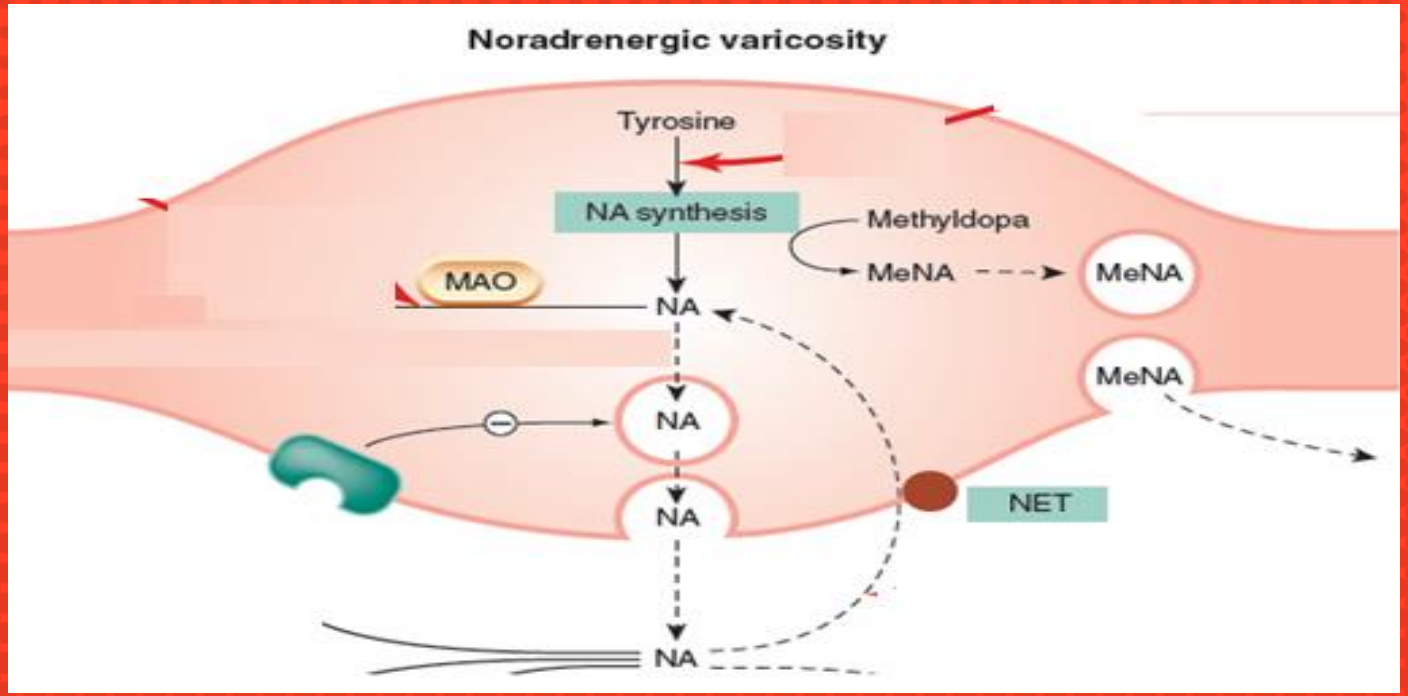
Classify α-receptor blockers into selective & non- selective

▪Study in detail the pharmacokinetic aspects & pharmacodynamic effects of α adrenergic blockers

MECHANISMS OF ADRENERGIC BLOCKERS

- **1-Formation of False Transmitters**

α-Methyl dopa



MECHANISMS OF ADRENERGIC BLOCKERS

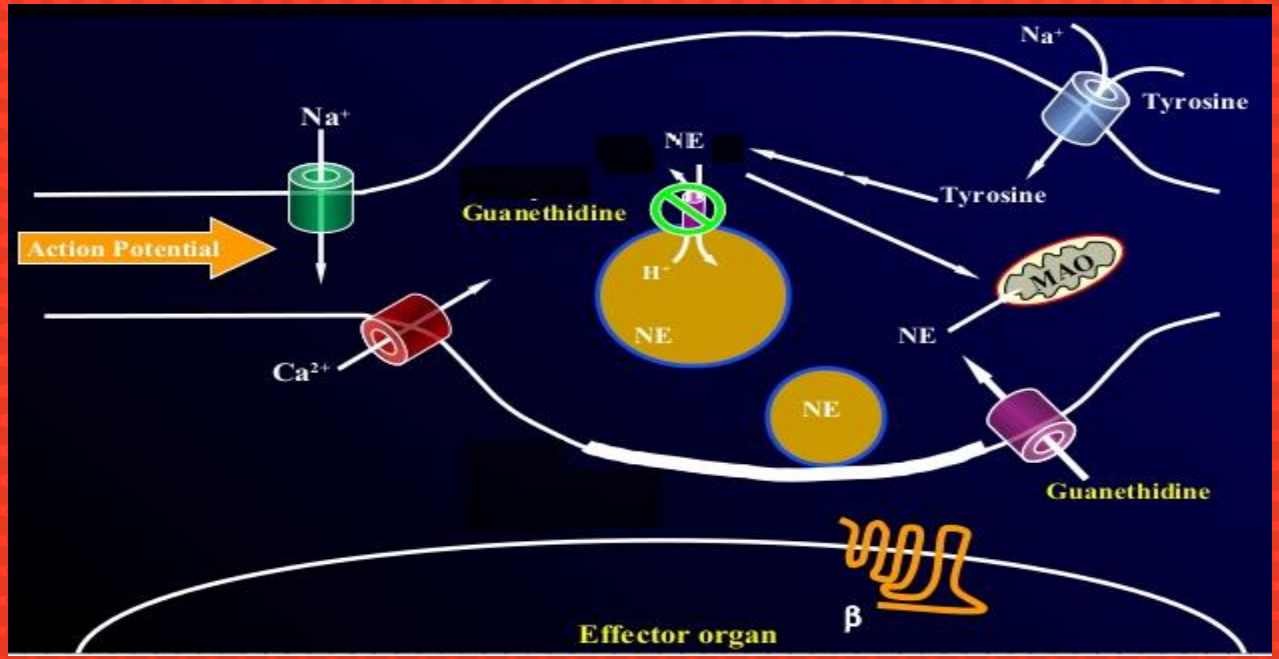
- 2-Depletion of Storage sites

Reserpine

MECHANISMS OF ADRENERGIC BLOCKERS

▪3-Inhibition of release

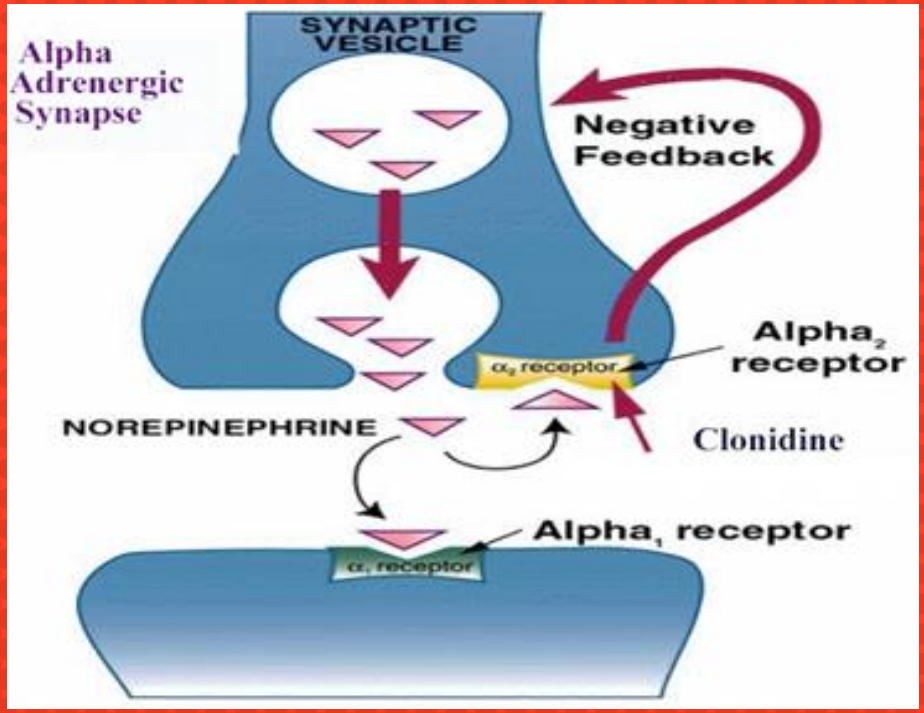
Guanethidine



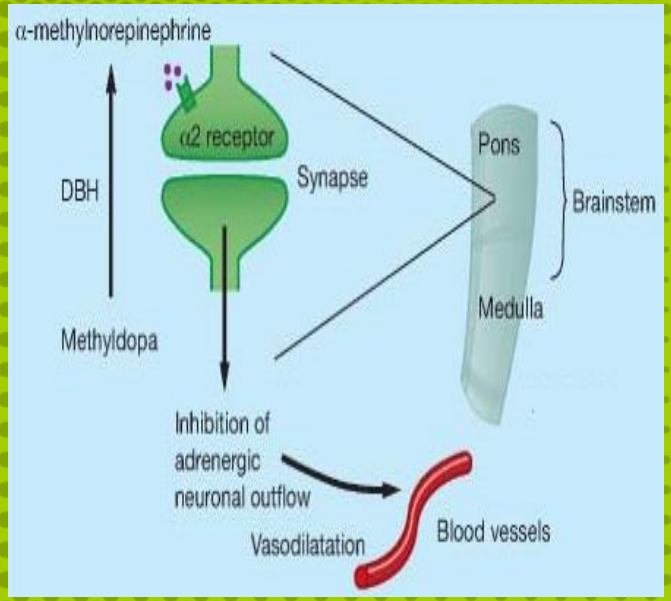
MECHANISMS OF ADRENERGIC BLOCKERS

- 4-Stimulation of presynaptic α_2 receptors

Clonidine and α-Methyldopa



α-Methyldopa



- Forms false transmitter that is released instead of NE
- Acts centrally as α_2 receptor agonist to inhibit NE release

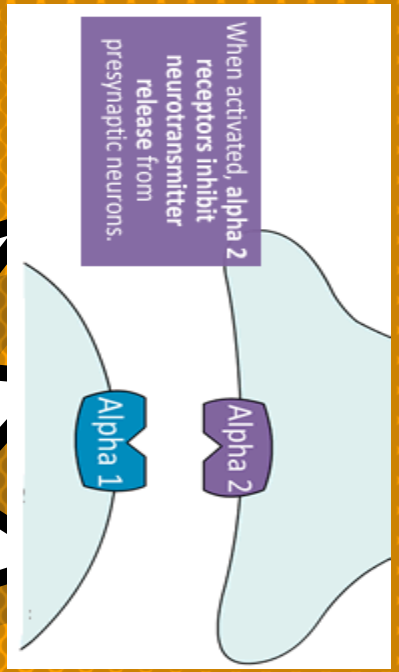
Drug of choice in the treatment of hypertension in pregnancy (pre-eclampsia - gestational hypertension)

Clonidine

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

- Acts directly as α_2 receptor agonist to inhibit NE release

Suppresses sympathetic outflow activity from the brain

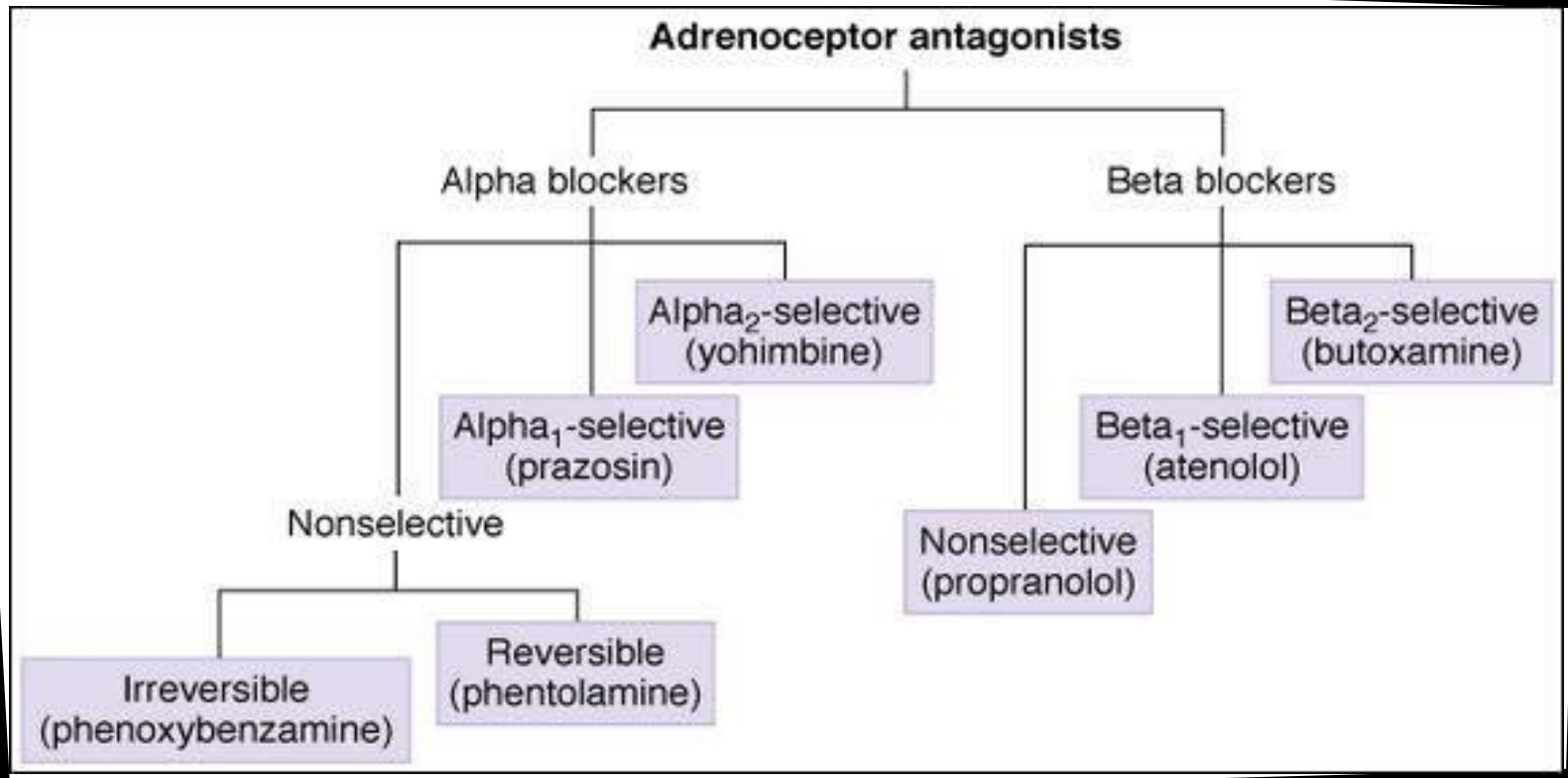


Little Used as Antihypertensive agent due to **rebound hypertension** upon abrupt withdrawal

SYNOPSIS

Adrenergic neuron blockers

- False neurotransmitter formation
  - α-Methyldopa
- Depletion of stores
  - Reserpine
- Inhibition of release
  - Guanethidine
- Stimulation of presynaptic α-receptors
  - Clonidine


Adrenoceptor antagonists
Alpha blockers
Beta blockers
Alpha2-selective (yohimbine)
Alpha1-selective (prazosin)
Nonselective
Irreversible (phenoxybenzamine)
Reversible (phentolamine)
Beta2-selective (butoxamine)
Beta1-selective (atenolol)
Nonselective (propranolol)

ADRENERGIC RECEPTOR BLOCKERS

They block sympathetic actions by antagonizing:-

- α-receptor
- β-receptor

CLASSIFICATION

α-Adrenoceptor Antagonists

Non-selective
block α_1 & α_2

Reversible
- Phentolamine

Irreversible
- Phenoxybenzamine

Selective

α_1-blockers
- Prazosin
- Terazosin
- Doxazosin

α_2-blockers
- Yohimbine

Selective α_{1A}

Tamsulosin

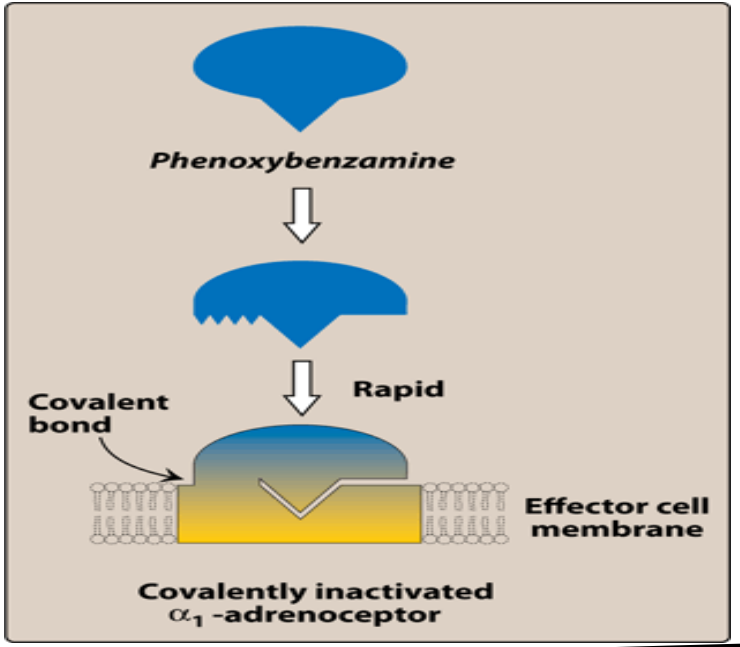
BPH

▪ *Non-Selective α- Adrenoceptor Antagonists*

Phenoxybenzamine:

Irreversible blocks both α_1 and α_2 receptors

Long-acting (24 hrs).

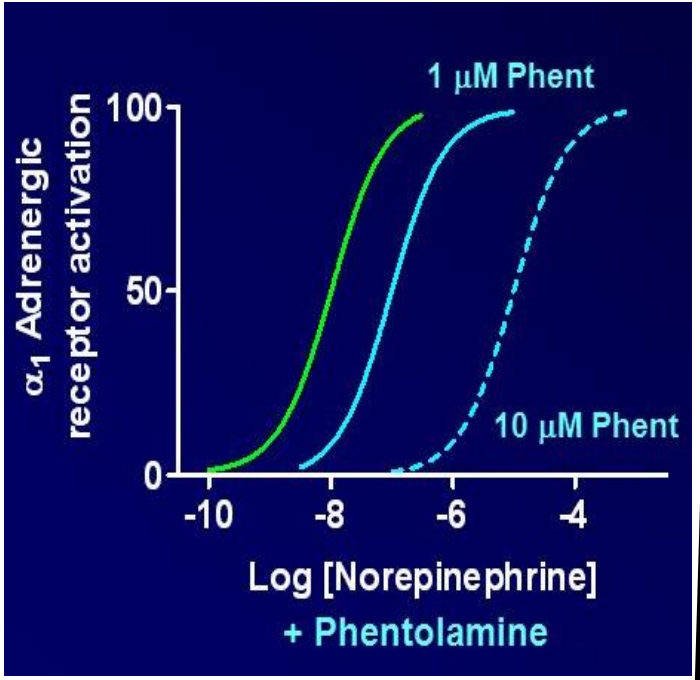


▪ *Non-Selective α- Adrenoceptor Antagonists*

Phentolamine

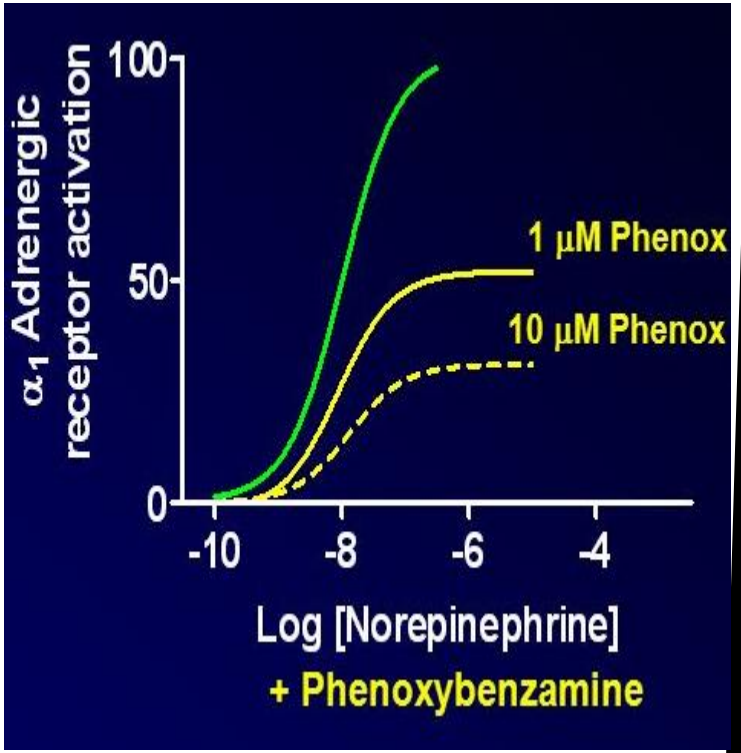
Reversible blocking of α_1 & α_2 receptors

▪ Short acting (4 hrs)

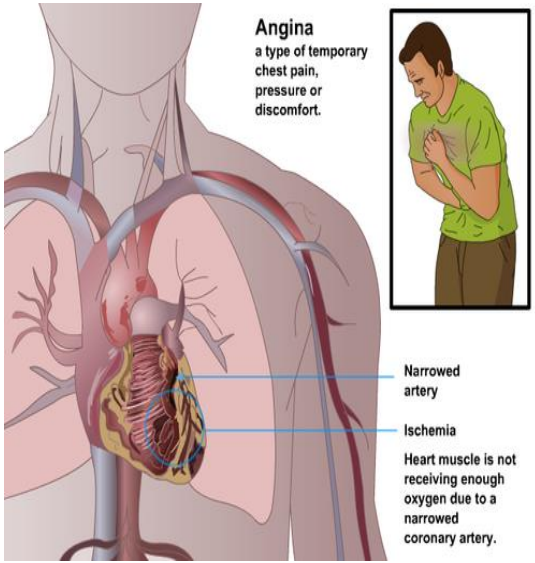


Both drugs cause:

- Postural hypotension
- Decrease peripheral vascular resistance
- Increase cardiac output (α_2 block)



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



- Reflex tachycardia

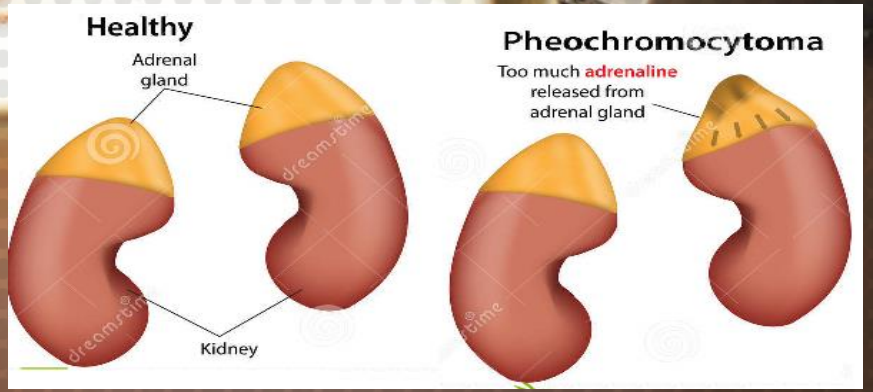
THERAPEUTIC USES:

- Pheochromocytoma:

Before surgical removal to protect against hypertensive crisis

"PHEochromocytoma"

- Palpitations
- Headache
- Episodic sweating (diaphoresis)



ADRS

Postural hypotension

Nasal stuffiness or congestion

Vertigo & drowsiness

ADRS

Tachycardia

Headache

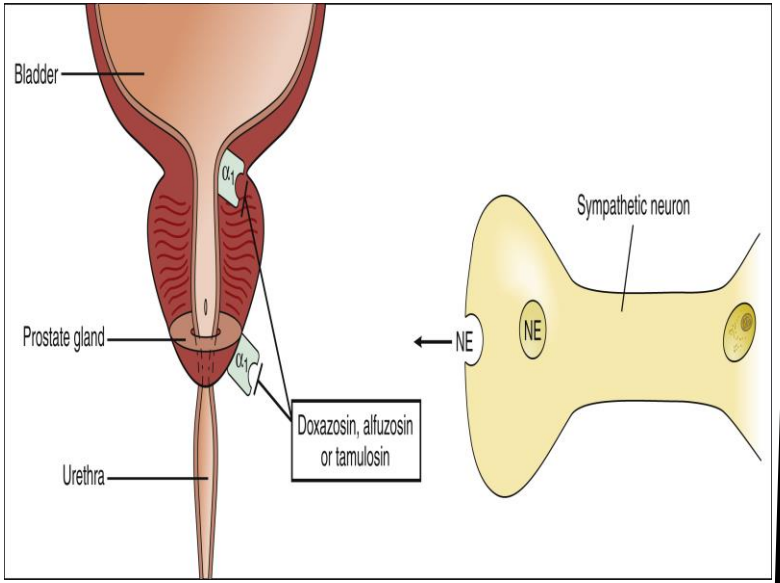
Male sexual dysfunction (inhibits ejaculation)

Selective α_1- Antagonists

Prazosin & doxazosin

Prazosin (short half-life)

Doxazosin, terazosin (long half life)



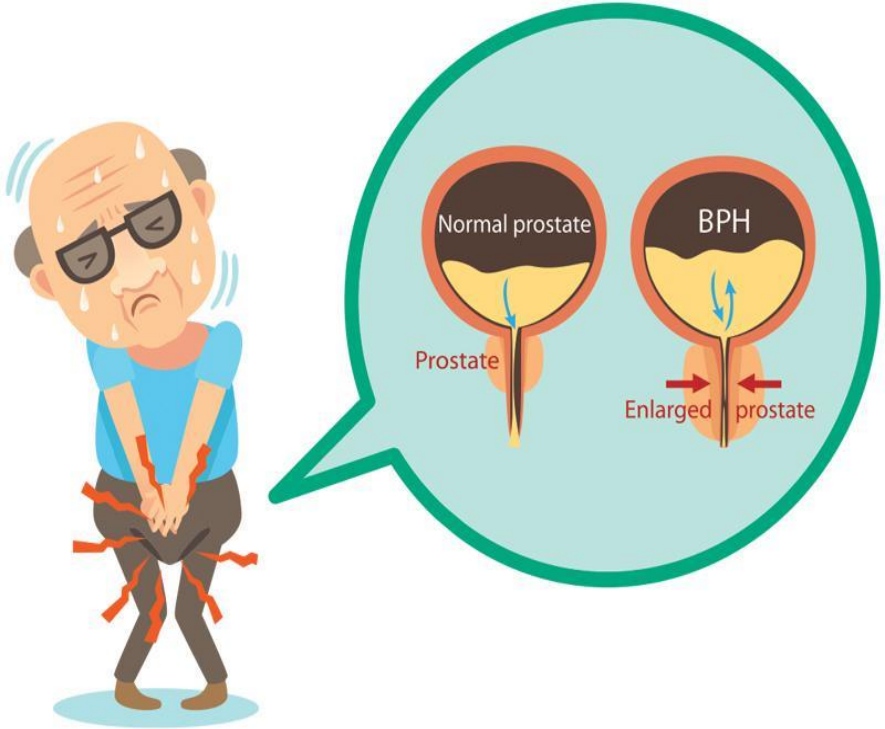
Selective α_1- Antagonists

- 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

First dose of α_1 receptor blocker may produce an orthostatic hypotensive response that can result in syncope (fainting).

Therapeutic Uses:

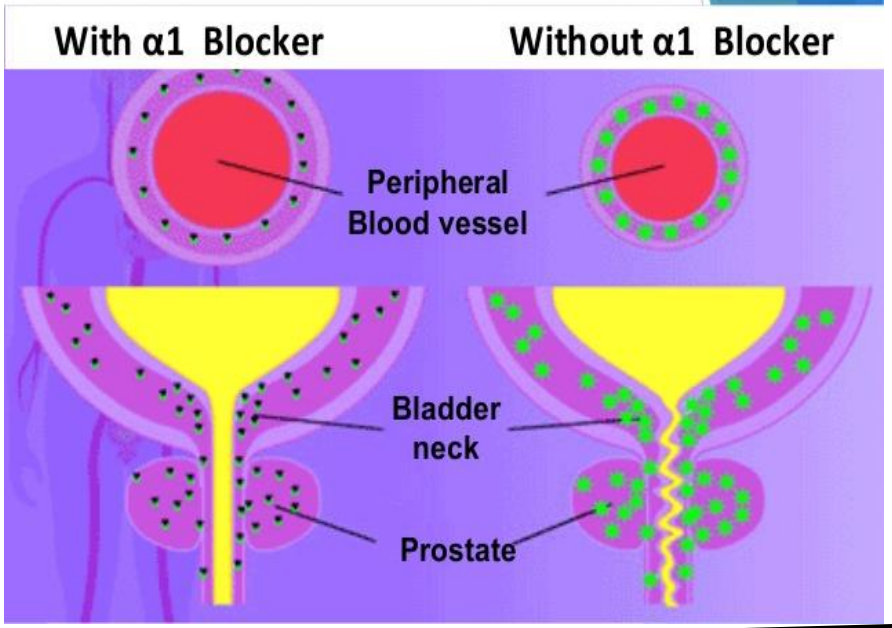
Benign Prostatic hyperplasia



Therapeutic Uses:

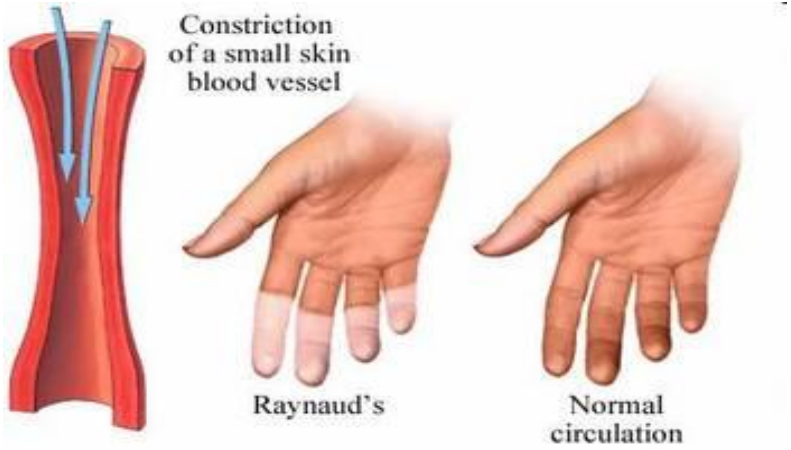
Treatment of hypertension with prostate enlargement

PRAZOSIN



Therapeutic Uses:

Reynaud's disease (vasospasm)



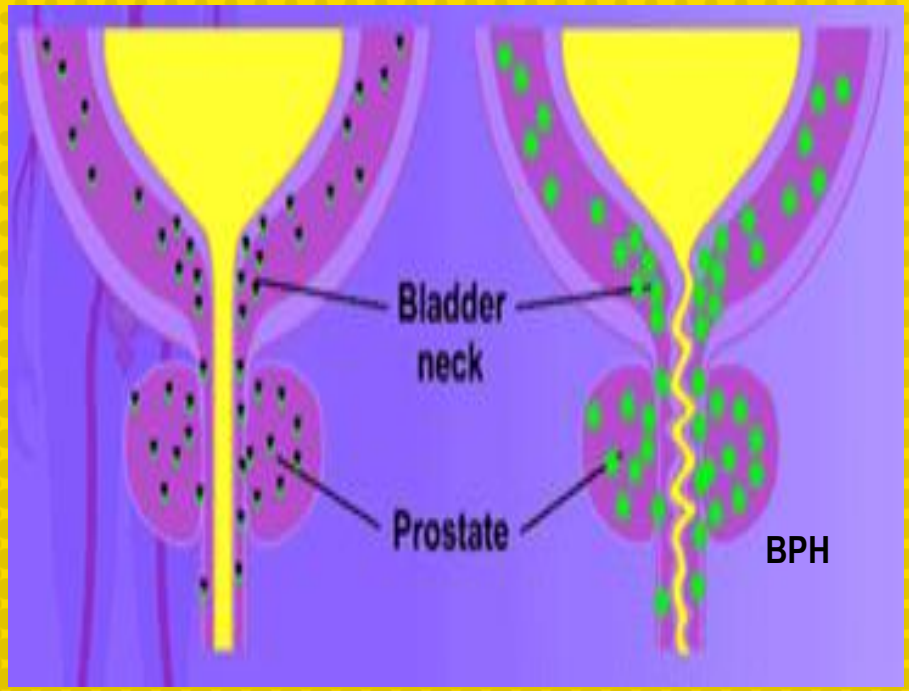
(**Reynaud's disease** causes some areas of the body such as fingers and toes to feel numb and cold in response to cold temperatures or stress)

Selective α1A–antagonist

Tamsulosin (Uroselective)

❖α1A receptors present in prostate

❖Tamsulosin is used in treatment of benign prostatic hypertrophy (BPH)



Selective α1A–antagonist

Tamsulosin (Uroselective)

Tamsulosin produces: relaxation of smooth muscles of bladder neck & prostate →improves urine flow

Has minimal effect on blood pressure

α_2-SELECTIVE ANTAGONISTS

Yohimbine

Used as aphrodisiac in the treatment of erectile dysfunction

Increase nitric oxide release in the corpus cavernosum thus producing vasodilator action and contributing to the erectile process