

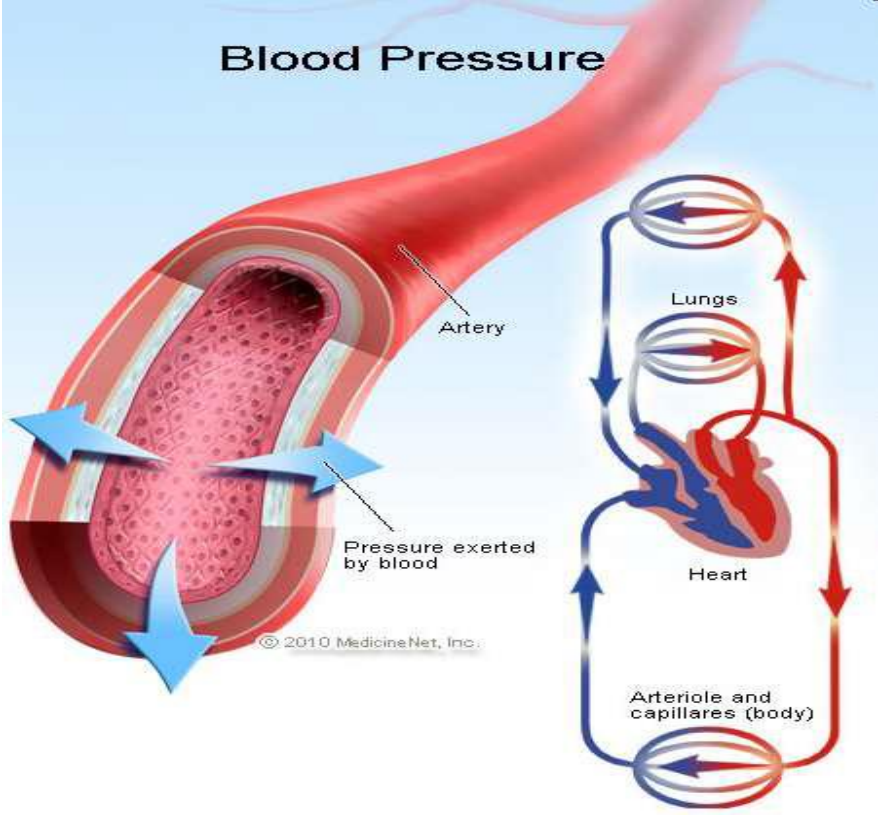


**CARDIOVASCULAR
DRUGS**

Antihypertensive drugs

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Blood Pressure.....



Normal Regulation of Blood Pressure

1.) Arterial blood pressure(BP) is directly proportionate to the product of the blood flow (cardiac output, CO) and the resistance to passage of blood through precapillary arterioles (peripheral vascular resistance, PVR)

- **$BP = CO \times PVR$**

Physiologically CO and PVR is maintained by **arterioles , postcapillary venules & Heart .**

2.) Local agents **like Nitric oxide**

3.) **Baroreflex**

4.) Renin-angiotensin- aldosterone system (RAAS)

HYPERTENSION

- Hypertension or High Blood Pressure is a chronic medical condition in which **blood pressure in the arteries is elevated.**
- Blood pressure is defined by two measurements, systolic and diastolic which depend on whether the heart muscle is contracting (systole) or relaxed between beats (diastole).
- Normal blood pressure at rest is within the range of 100–140 mmHg systolic and 60–90 mmHg diastolic.

Hypertension - **systolic BP more than 140mm Hg**

-diastolic BP more than 90mm Hg

Hypertension may be

- Primary hypertension/Essential hypertension
 - No specific cause
 - 95% cases

- Secondary hypertension
 - Due to specific disease or drug
 - 5% cases

Etiology

- ✓ **Age:** The risk of high blood pressure increases as age. Through early middle age, or about age 45, high blood pressure is more common in men. Women are more likely to develop high blood pressure after age 65.
- ✓ **Race.** High blood pressure is particularly common among blacks, often developing at an earlier age than it does in whites.
- ✓ **Family history**
- ✓ **Overweight or obese.**
- ✓ **Tobacco consumption**
- ✓ **Too much salt (sodium) in diet**
- ✓ **Too little potassium in diet.**
- ✓ **Too little vitamin D in diet**
- ✓ **Drinking too much alcohol**
- ✓ **Stress.**
- ✓ **Certain chronic conditions.** Certain chronic conditions also may increase risk of high blood pressure, such as kidney disease and sleep apnea.

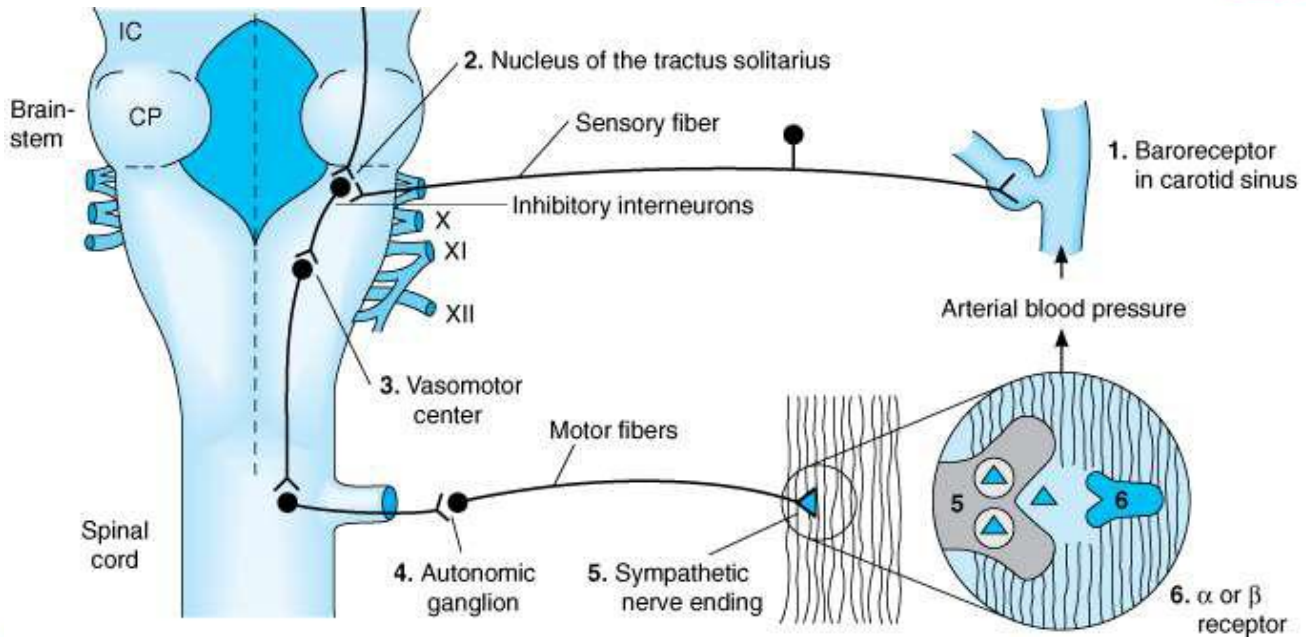
Pathophysiology

- Baroreflex
- Renin-angiotensin- aldosterone system (RAAS)

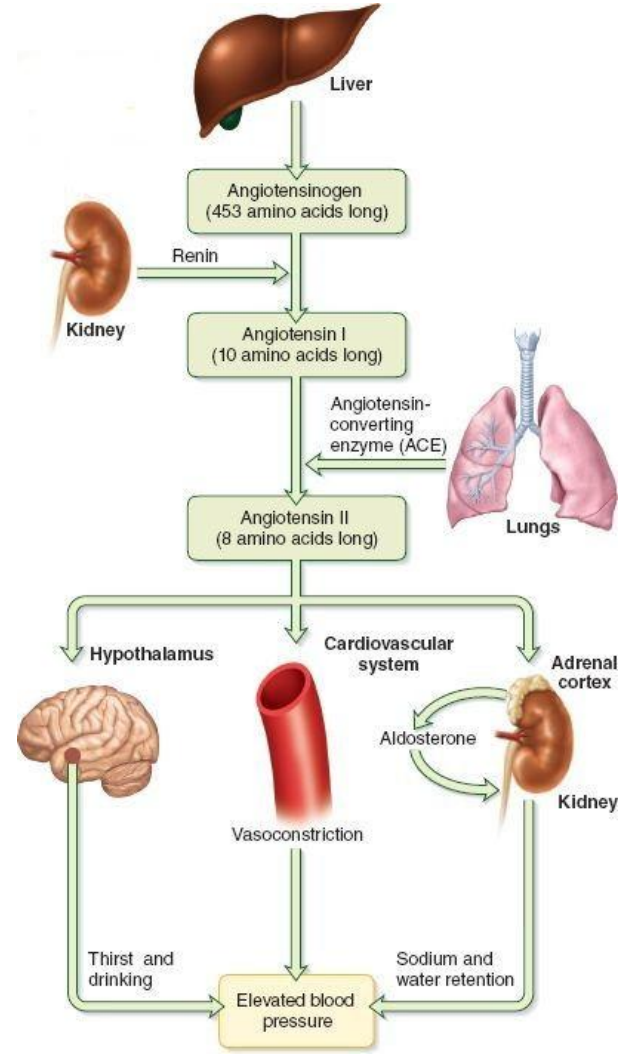
Baroreflex: Baroreceptor reflex arch

- Baroreflexes involving the sympathetic nervous system are responsible for the rapid, moment-to-moment regulation of blood pressure.
- A fall in blood pressure causes pressure-sensitive neurons (baroreceptors in the aortic arch and carotid sinuses) to send fewer impulses to cardiovascular centers in the spinal cord.
- This prompts a reflex response of increased sympathetic decreased parasympathetic output to the heart and vasculature, resulting in vasoconstriction and increased cardiac output.
- These changes result in a compensatory rise in blood pressure

Baroreflex.....



Renin-angiotensin- aldosterone system (RAAS)



Symptoms

- ❖ Severe headaches
- ❖ Fatigue or confusion
- ❖ Dizziness
- ❖ Nausea
- ❖ Problems with vision
- ❖ Chest pains
- ❖ Breathing problems
- ❖ Irregular heartbeat



Complications of Hypertension

Brain Stroke

Reduced blood supply to the brain can lead to rapid loss of brain function or stroke.

Vision Loss

Hypertensive Retinopathy
High blood pressure can damage blood vessels in the retina, resulting in loss of vision.

Blood Vessel Damage

Atherosclerosis

Hypertension is a leading cause of atherosclerosis, the artery-narrowing process that can result in heart attack and stroke.

Heart Attack

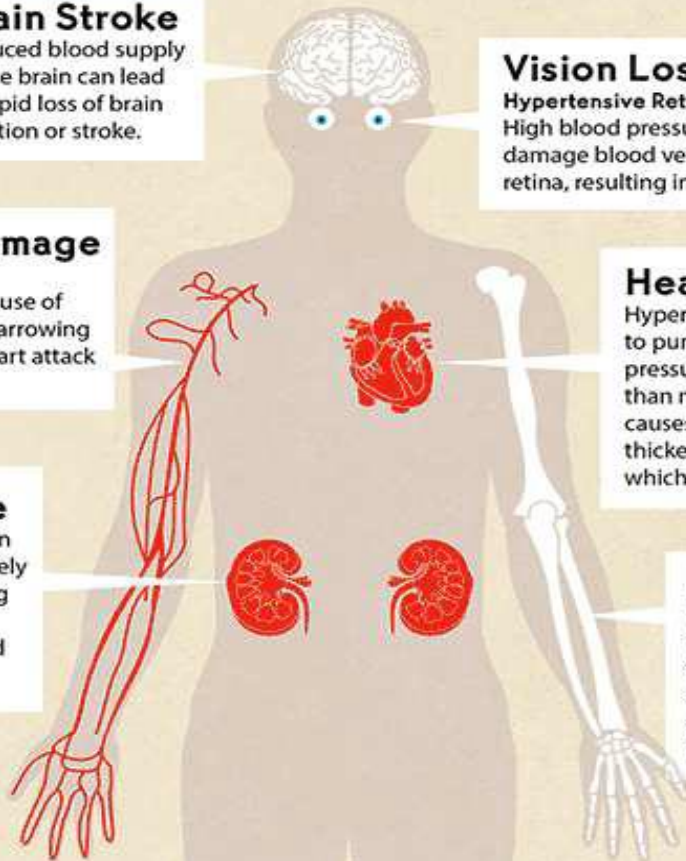
Hypertension causes the heart to pump against high blood pressure, making it work harder than necessary. Over time, this causes the heart muscle to thicken, restricting blood flow which can lead to heart failure.

Kidney Failure

Damaged blood vessels in the kidneys can't effectively filter your blood, resulting in a dangerous accumulation of fluid and waste.

Bone Loss

High blood pressure may increase the amount of calcium in your urine. That excessive elimination of calcium may lead to loss of bone density (osteoporosis).



Treatment

Non-Pharmacological Treatment:

- Quitting cigarette smoking,
- regular exercise,
- restricting dietary intake of: salt, saturated fats and calories

will improve peripheral circulation, prevent increases in blood volume, reduce plasma cholesterol levels and total body weight.

Pharmacological Treatment: AntiHypertensive drug

The image features decorative wavy lines in the corners. The top-right corner has a wave transitioning from purple to red to yellow. The bottom-left corner has a wave transitioning from yellow to red to purple.

ANTIHYPERTENSIVE DRUG

The image features decorative wavy lines in the corners. In the top right, there are overlapping, semi-transparent waves in shades of purple, red, and orange. In the bottom left, there are similar waves in shades of green, yellow, and red. The background is plain white.

*The substance which is used to reduce elevated blood pressure-
Antihypertensive drug*

CLASSIFICATION OF ANTIHYPERTENSIVE DRUGS

1. ACE inhibitors
2. Angiotensin receptor antagonist
3. Calcium channel blockers
4. Diuretics
5. β blockers
6. α blockers
7. $\alpha+\beta$ blockers
8. Central Sympatholytics
9. Vasodilators

1.) ACE inhibitors

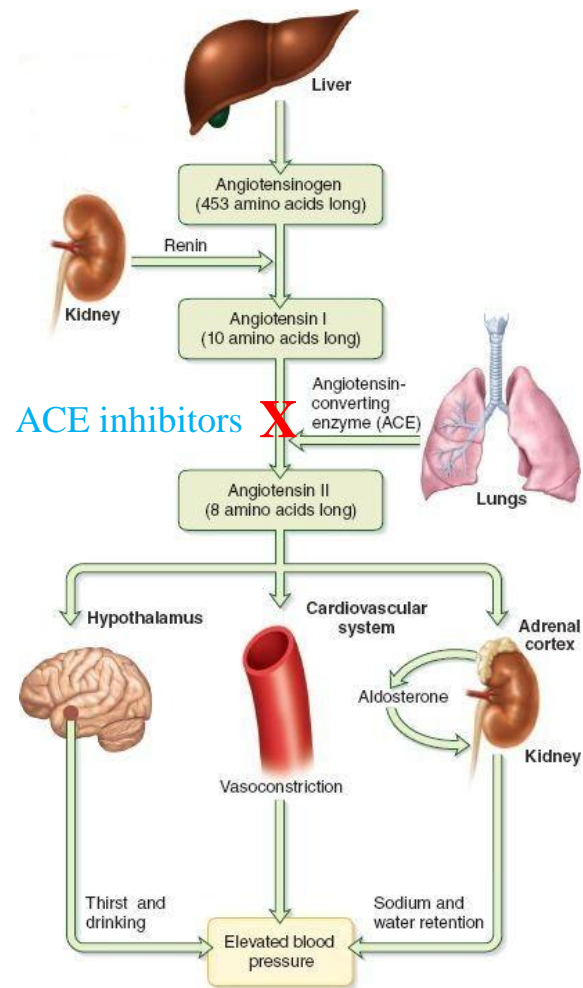
- ACE inhibitors-**Angiotensin Converting Enzyme inhibitors**
- The ACE inhibitors are one of the first choice drugs in all grades of essential as well as renovascular hypertension.

Eg:

- Captopril
- Enalapril
- Ramipril
- Lisinopril

ACE inhibitors.....

Mechanism of Action



ACE inhibitors.....

Adverse effects

- ✓ Cough(dry cough)
- ✓ Angioedema
- ✓ Proteinuria
- ✓ Teratogenic
- ✓ Severe hypOtension : first dose phenomenon
- ✓ Neutropenia
- ✓ Rashes
- ✓ Itching
- ✓ Loss of appetite, nausea, vomiting, diarrhoea

ACE inhibitors.....

Therapeutic uses

❖ Hypertension:

Use of ACE inhibitors reduces the incidence of complications in hypertensive patients. ACE inhibitors are useful in all grades of hypertension.

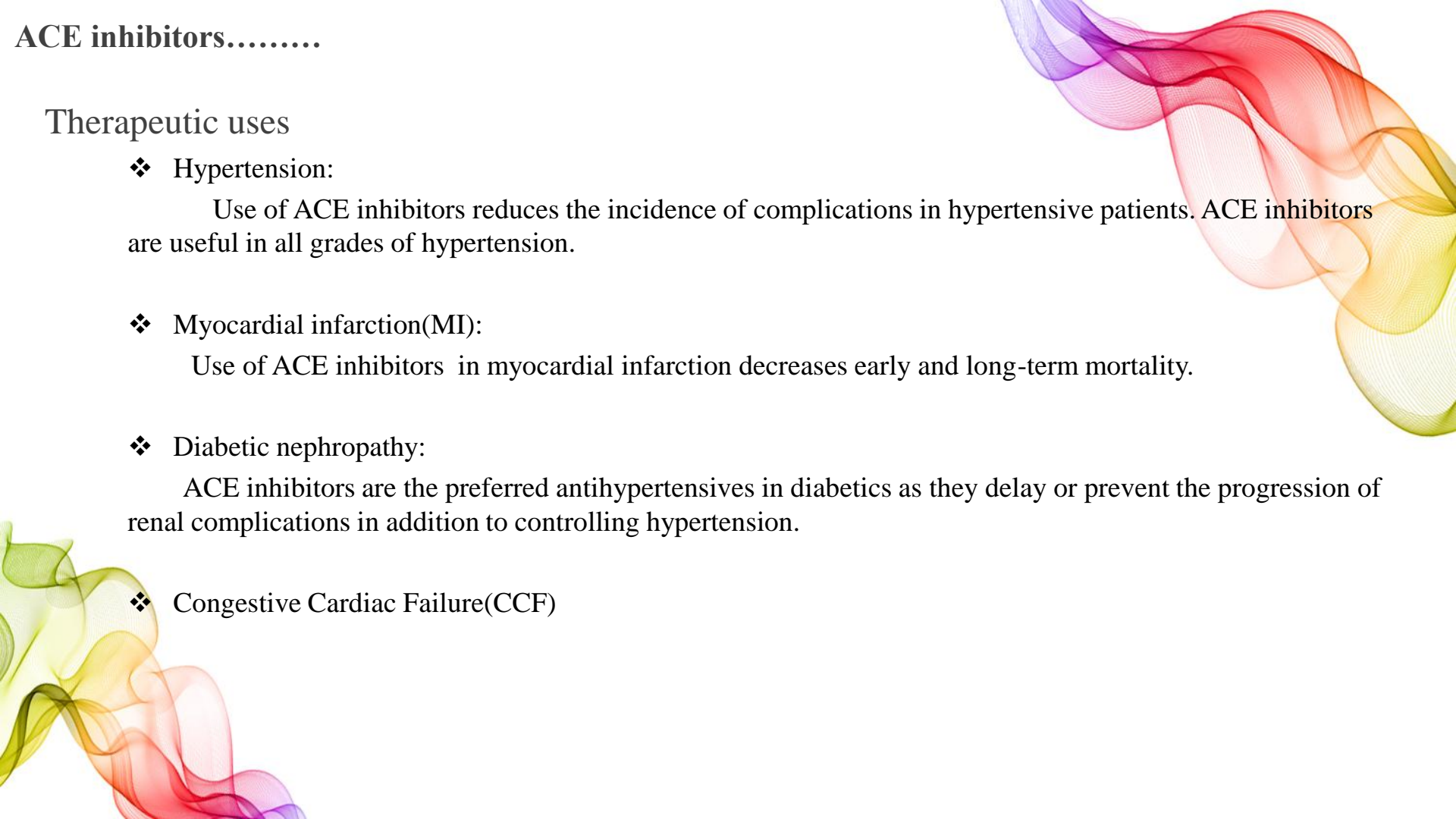
❖ Myocardial infarction(MI):

Use of ACE inhibitors in myocardial infarction decreases early and long-term mortality.

❖ Diabetic nephropathy:

ACE inhibitors are the preferred antihypertensives in diabetics as they delay or prevent the progression of renal complications in addition to controlling hypertension.

❖ Congestive Cardiac Failure(CCF)



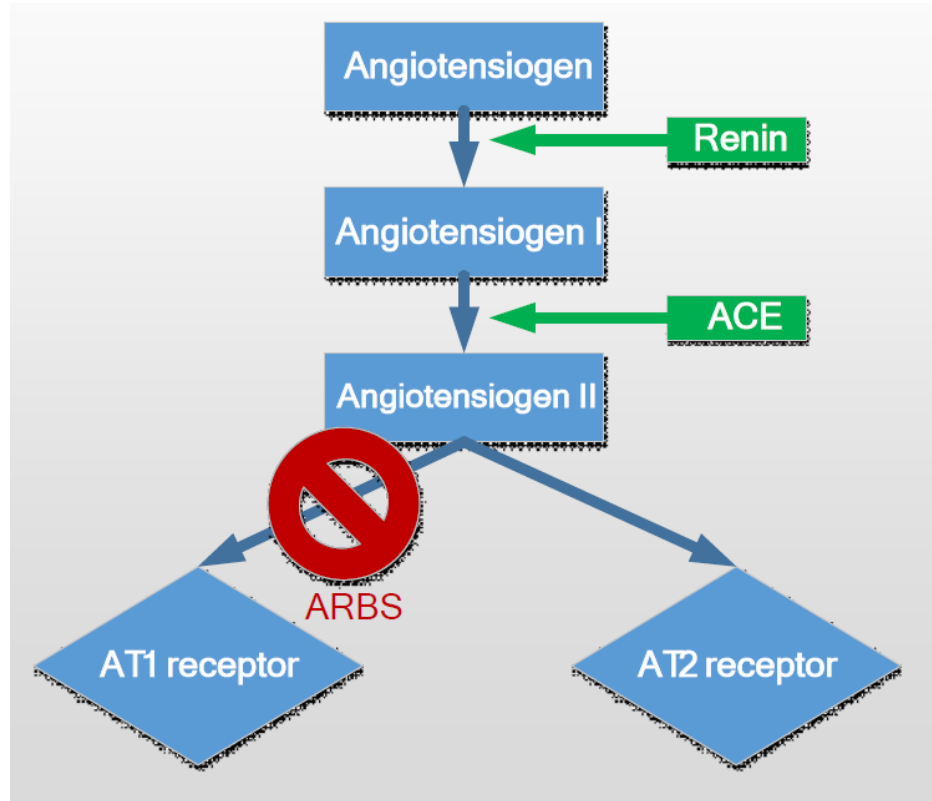
2.) Angiotensin receptor antagonist

- The Ang- II-receptor blockers (ARBs) are alternatives to the ACE inhibitors.
- Their pharmacologic effects are similar to those of ACE inhibitors in that they produce vasodilation and block aldosterone secretion, thus lowering blood pressure and decreasing salt and water retention.



ARBs.....

Mechanism of Action



ARBs.....

- ARBs decrease the nephrotoxicity of diabetes, making them an attractive therapy in hypertensive diabetics.
- Their adverse effects are similar to those of ACE inhibitors, although the risks of cough & angioedema are significantly decreased. They are fetotoxic.

Eg:

- Losartan
- Valsartan
- Irbesartan
- Candesartan
- Telmisartan

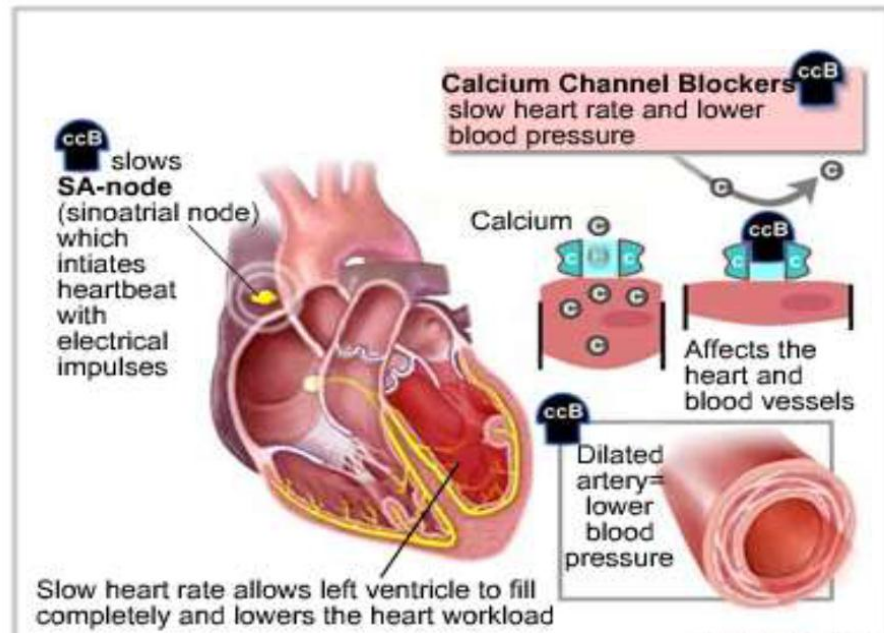
Angiotensin receptor blockers(ARBs) are used in the treatment of hypertension, CCF and diabetic nephropathy. They are mainly indicated in patients who develop cough with ACE inhibitors.

3.) Calcium channel blockers (CCBs)

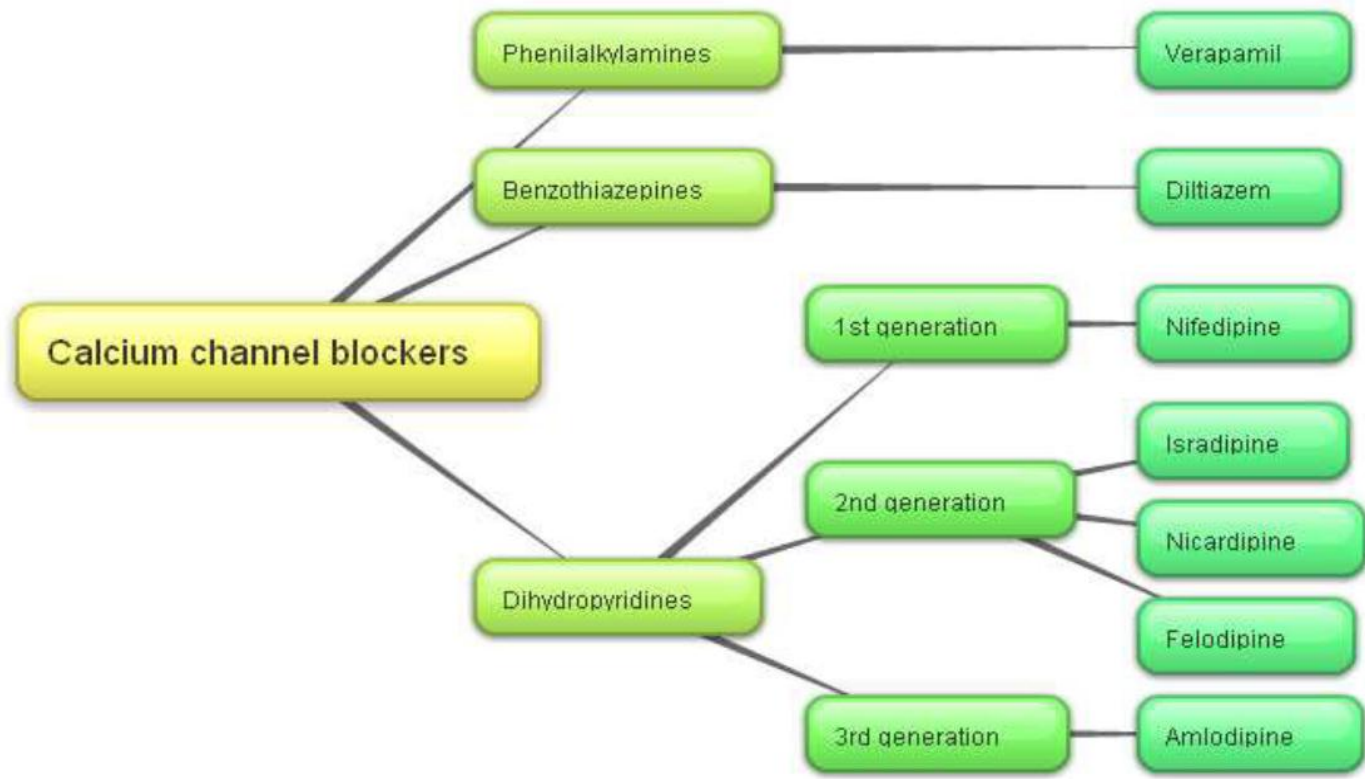
- CCB block the inward movement of calcium
----- by binding to L type calcium channels in the heart and
-----in smooth muscle of the coronary and peripheral vasculature.
- This causes vascular smooth muscle to relax, dilating mainly arterioles.

CCBs are recommended when the preferred first line agents are contraindicated or ineffective.

Calcium Channel Blockers



CCBs.....



CCBs.....

Non-Dihydropyridines CCB

- Verapamil is the least selective of any CCB, and has significant effects on both cardiac and vascular smooth muscle cells. It is used to treat angina, supraventricular tachyarrhythmias, and migraine headache.
- Like verapamil, diltiazem affects both cardiac and vascular smooth muscle cells.

CCBs.....

Dihydropyridines CCB

- Dihydropyridines include nifedipine, amlodipine, felodipine, isradipine, nicardipine, and nisoldipine.
- These new-generation calcium channel blockers differ in pharmacokinetics, approved uses, and drug interactions.
- All dihydropyridines have a much greater affinity for vascular calcium channels than for calcium channels in the heart. They are therefore particularly attractive in treating hypertension.
- Newer agents, such as amlodipine and nicardipine, have the advantage that they show little interaction with other cardiovascular drugs, such as digoxin or warfarin, which are often used concomitantly with calcium channel blockers.

CCBs.....

Adverse effects

Dihydropyridines:

- ✓ Dizziness, headache, and a feeling of fatigue caused by a decrease in blood pressure.
- ✓ Peripheral edema is another commonly reported side effect of this class.
- ✓ Nifedipine and other dihydropyridines may cause gingival hyperplasia.

Verapamil and diltiazem

Constipation and AV block, should be avoided in patients with heart failure or with AV block.

CCBs.....

Therapeutic uses

- ❖ Calcium channel blockers have an intrinsic natriuretic effect & therefore, do not usually require the addition of a diuretic.
- ❖ These agents are useful in the treatment of hypertensive patients who also have asthma, diabetes, angina, and/or peripheral vascular disease.
- ❖ Most of these agents have short half-lives (3-8 hours). Treatment is required three times a day to maintain good control of hypertension.

4.) Diuretics

Thiazide diuretics

- Bendroflumethiazide
- Hydrochlorothiazides
- Chlorthalidone

Loop diuretics

- Furosemide

Potassium sparing diuretics

- Amiloride
- Triamterene
- Spironolactone

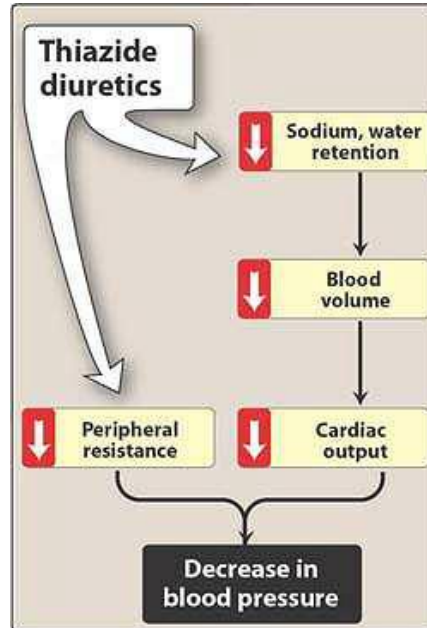


Diuretics.....

Thiazide diuretics

Thiazide diuretics lower BP initially by increasing sodium and water excretion.

This causes a decrease in extracellular volume, resulting in a decrease in cardiac output .



Diuretics.....

Thiazide diuretics

Therapeutic uses

- Thiazides are useful in combination therapy with β - blockers and ACE inhibitors.
- Spironolactone, a potassium sparing diuretic, is used with thiazides. Spironolactone has the additional benefit of diminishing the cardiac remodeling that occurs in heart failure.

Disadvantages of Thiazide Diuretics

They are not effective in patients with inadequate kidney function.

Loop diuretics may be required in these patients.

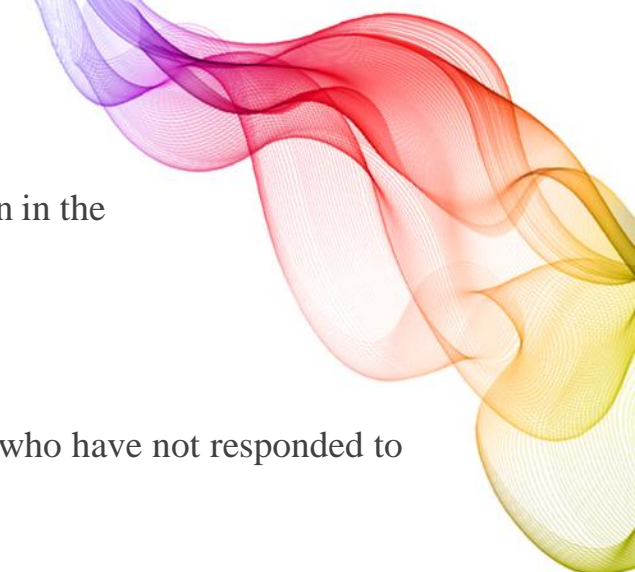
Diuretics.....

Loop diuretics

The loop diuretics act promptly by blocking sodium and chloride reabsorption in the kidneys.

It cause decreased renal vascular resistance and increased renal blood flow.

The loop diuretics act promptly, even in patients with poor renal function or who have not responded to thiazides or other diuretics.



Diuretics.....

Potassium sparing diuretics

- Amiloride and triamterene (inhibitors of epithelial sodium transport at the late distal and collecting ducts)
- spironolactone (aldosterone receptor antagonists) reduce potassium loss in the urine.
- Aldosterone antagonists have the additional benefit of diminishing the cardiac remodeling that occurs in heart failure.
- Potassium-sparing diuretics are sometimes used in combination with loop diuretics and thiazides to reduce the amount of potassium loss induced by these diuretics.

Diuretics.....

Adverse effects

- ❑ **Thiazide diuretics**-Hypokalemia, Hyperuricemia
- ❑ **Loop diuretics**-Ototoxicity
- ❑ **Potassium sparing diuretics**-Gastric upsets, Gynaecomastia in males, Menstrual irregularities in females

5.) β blockers

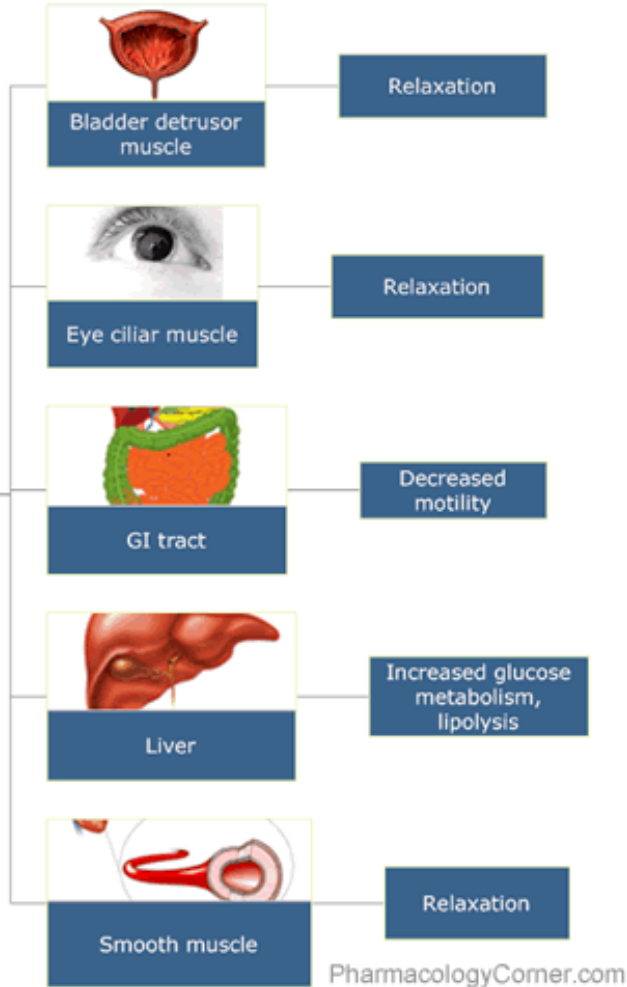
- ❖ β blockers are also referred as **β -adrenergic antagonist**.
- ❖ They block the β -receptors (β_1 , β_2 , and β_3) mediated effects of sympathetic stimulation and adrenergic agonists.

Distribution & function of β -receptors

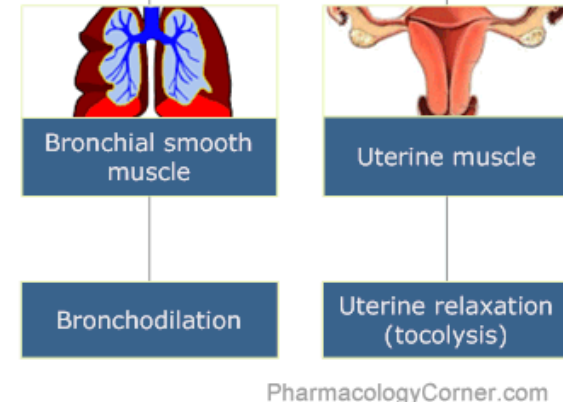
- ✓ **β_3 -receptor** is located in Adipose tissue-Lipolysis

β blockers.....

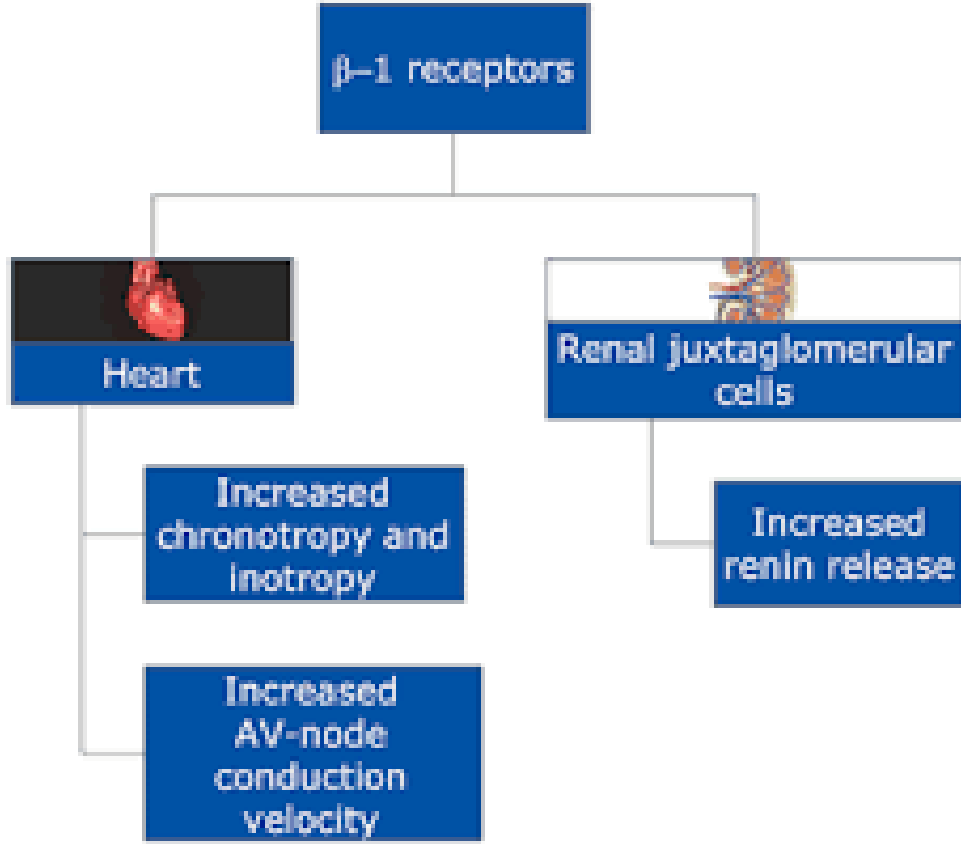
β -2 receptors



β -2 receptors



β blockers.....



β blockers.....

Classification of β blockers

- ✓ **Non-Selective β blockers** (block both β1 and β2 receptors)

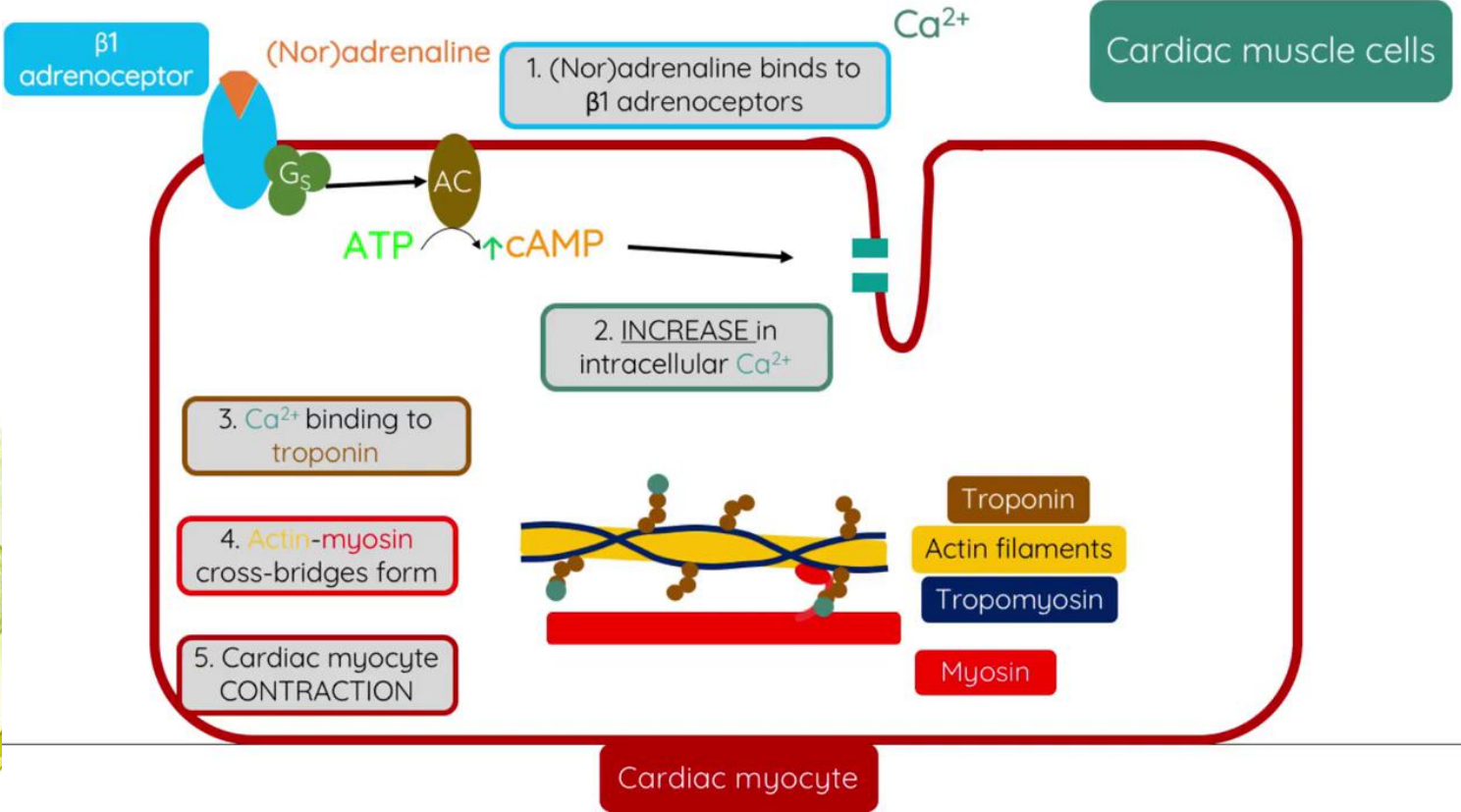
Propranolol, Sotalol, Timolol, Pindolol, Labetalol, Carvedilol

- ✓ **Selective β blockers** (block only β1 receptor)

Metoprolol, Atenolol, Acebutolol, Esmolol, Bisoprolol, Betaxolol, Celiprolol, Nebivolol

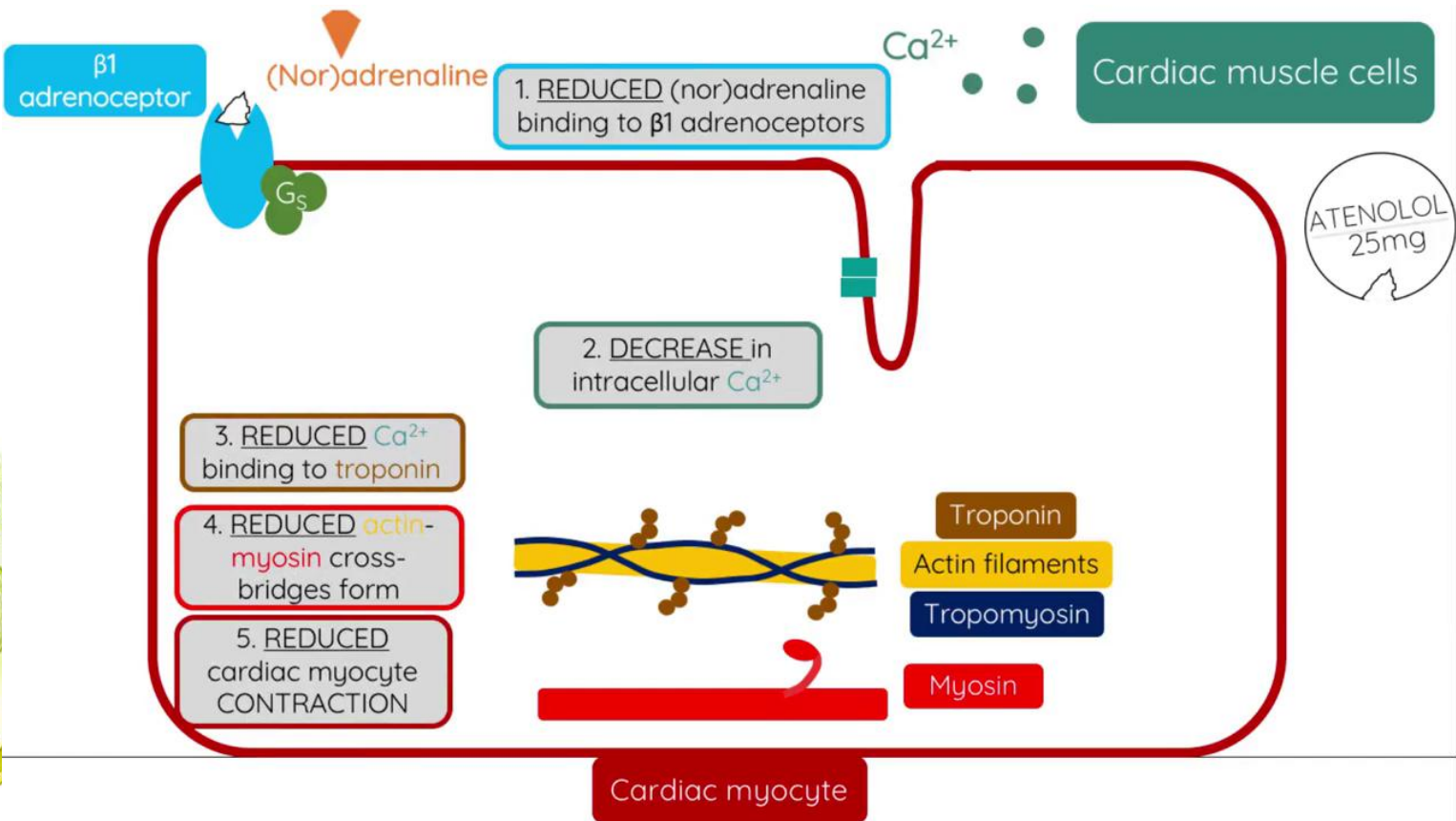
β blockers.....

Mechanism of action



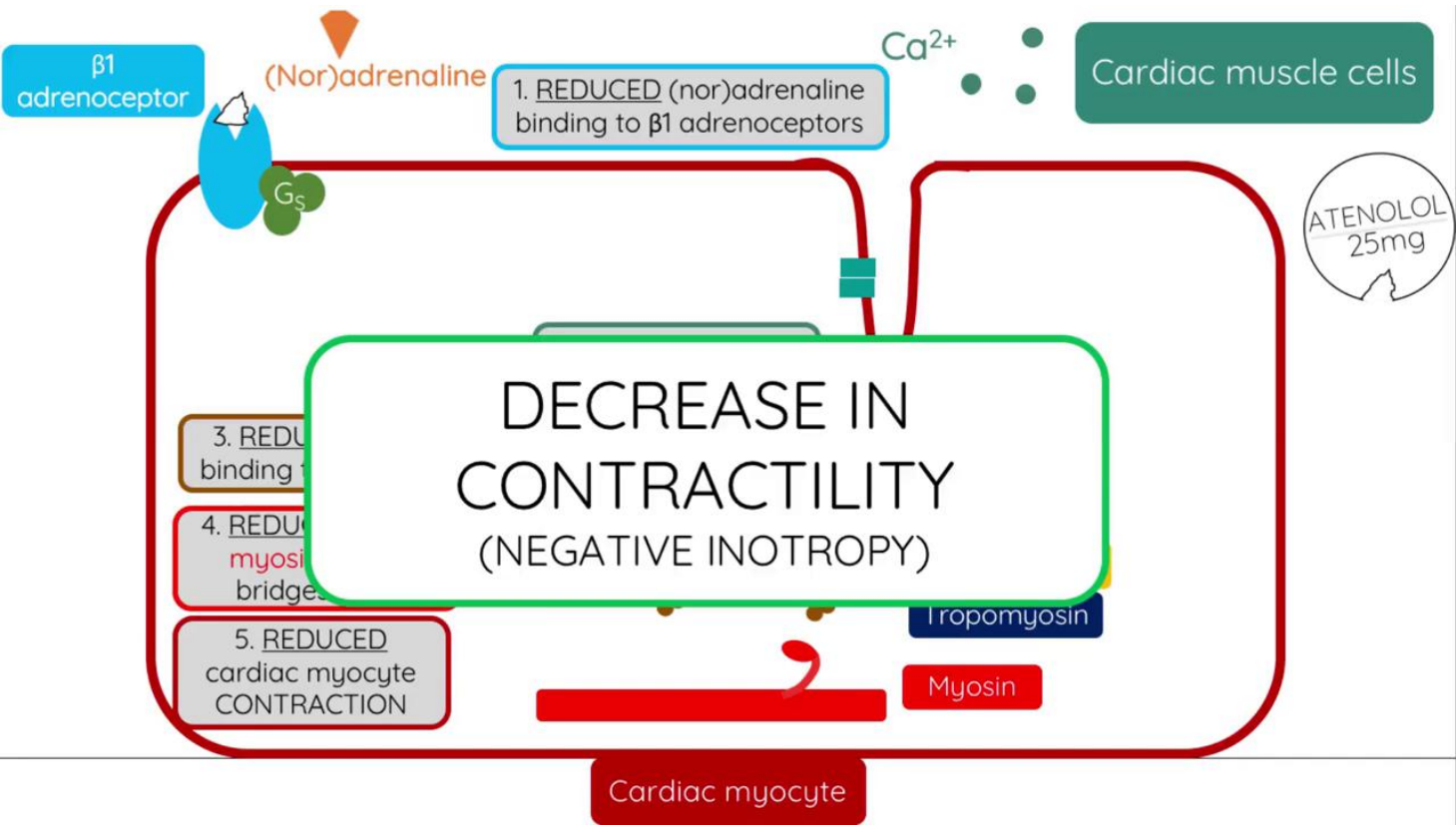
β blockers.....

Mechanism of action



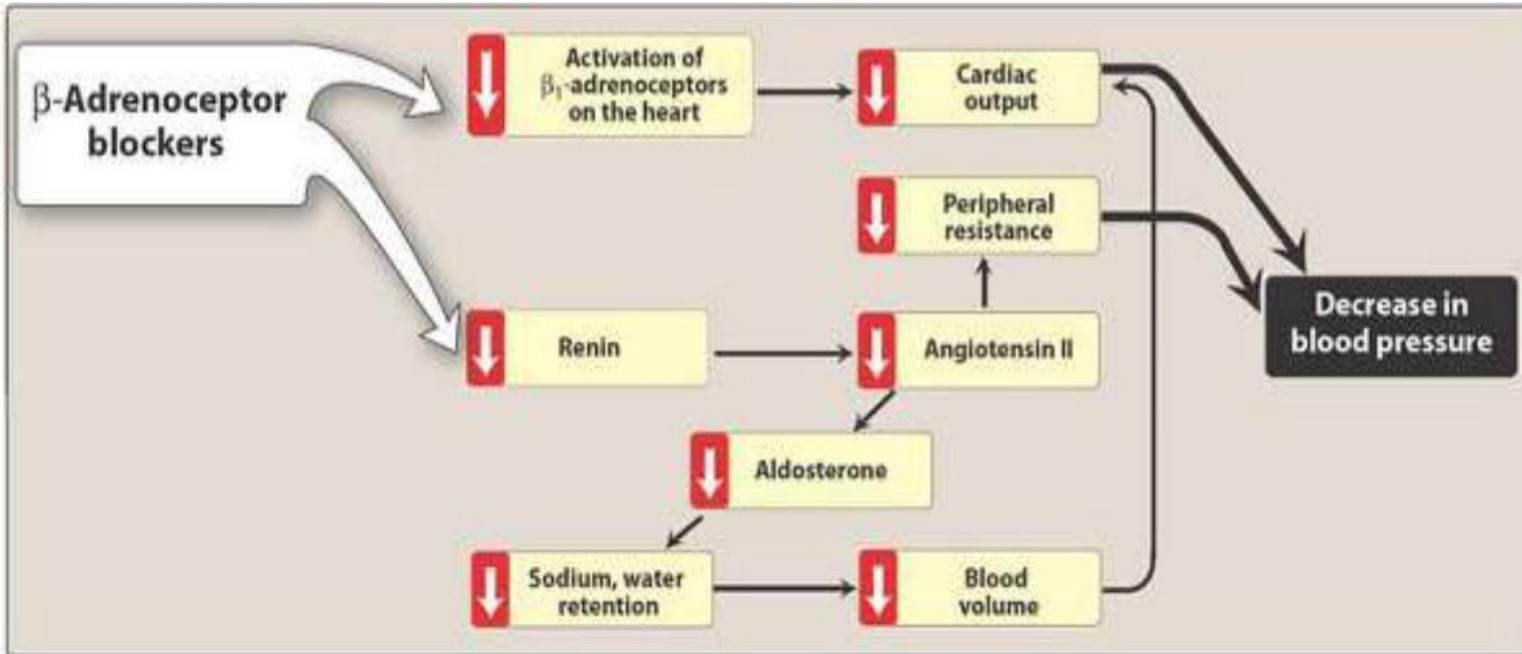
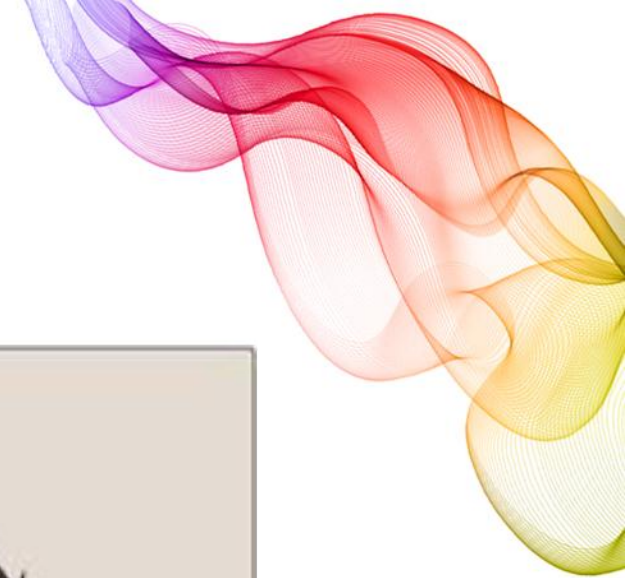
β blockers.....

Mechanism of action



β blockers.....

Mechanism of action



β blockers.....

Drawbacks of non-selective beta blockers:

- Fatigue, lethargy
- Bradycardia
- Loss of libido-impotence
- Cognitive defects-forgetfulness
- Bronchoconstriction-Asthma
- Hyperglycemia
- Sudden withdrawal-chance of rebound hypertension, precipitation of MI or angina

Advantages of cardio selective beta blockers over non-selective blockers

- ✓ Safer in asthmatics
- ✓ Safer in Diabetes mellitus

6.) α -blockers

Classification of α -blockers

Selective α -blockers

- ✓ Prazosin
- ✓ Terazosin
- ✓ Doxazosin

Non-Selective α -blockers

- ✓ Phentolamine
- ✓ Phenoxybenzamine

α blockers.....

Mechanism of action

It blocks post synaptic α -adrenoreceptors of veins and arterioles causing

- Vasodilatation (relaxation of both arterial and venous smooth muscle)
- Decrease the PVR
- Reduction in blood pressure.

α blockers.....

Adverse effects

- Postural hypotension
- Nasal stuffiness
- Dry mouth
- Miosis
- Syncope



α blockers.....

Therapeutic uses

- It is used as combination therapy along with diuretics/ β blockers for the treatment of hypertension.
- They are useful in diagnosis and treatment of Pheochromocytoma (Tumour of Adrenal gland).

7.) $\alpha+\beta$ blockers

Acting on Alpha as well as on beta receptors.

Classification of $\alpha+\beta$ blockers

- ✓ Labetalol
- ✓ Carvedilol

$\alpha+\beta$ blockers.....

Mechanism of action

- ✓ Labetalol produces vasodilatation by blocking α_1 and β_1 receptors
- ✓ Carvedilol produces vasodilatation by blocking α_1 , β_1 and β_2 receptors

Adverse effects

- Drowsiness
- Fatigue
- Insomnia
- Orthostatic hypotension

$\alpha+\beta$ blockers

Therapeutic uses

- ❖ They are mainly used for controlling hypertension in Pheochromocytoma.
- ❖ Carvedilol due to its antioxidant and antimitogenic property is also useful in CHF

8.) Central Sympatholytics

Classification of Central Sympatholytics

- ✓ Clonidine
- ✓ Methyl dopa

Central Sympatholytics.....

Clonidine-Agonist of alpha 2 receptor

Mechanism of action

- It acts centrally as an alpha 2 agonist to produce inhibition of sympathetic vasomotor centers, decreasing sympathetic outflow to the periphery.
- This leads to reduced total peripheral resistance and decreased blood pressure

Central Sympatholytics.....

Clonidine-Agonist of alpha 2 receptor

Adverse effects:

- ✓ Dryness of mouth & eyes
- ✓ Sedation
- ✓ Depression
- ✓ Bradycardia
- ✓ Dizziness
- ✓ Postural hypotension

Therapeutic uses:

Clonidine is used to treat withdrawal symptoms in opioid and alcohol addicts.

Central Sympatholytics.....

α Methyldopa

Mechanism of action

Alpha Methyldopa gets converted to Alpha methyl noradrenaline which acts on alpha 2 receptors in brain and causes inhibition of adrenergic discharge-fall in BP

Adverse effects:

- ✓ Dryness of mouth
- ✓ Sedation
- ✓ Depression
- ✓ Bradycardia
- ✓ Headache

Therapeutic uses:

Methyldopa is the drug of choice for hypertension during pregnancy

9.) VASODILATORS

Vasodilators reduces blood pressure by acting directly on arteriolar and venous smooth muscle.

Classification of Vasodilators

✓ Arteriolar dilators

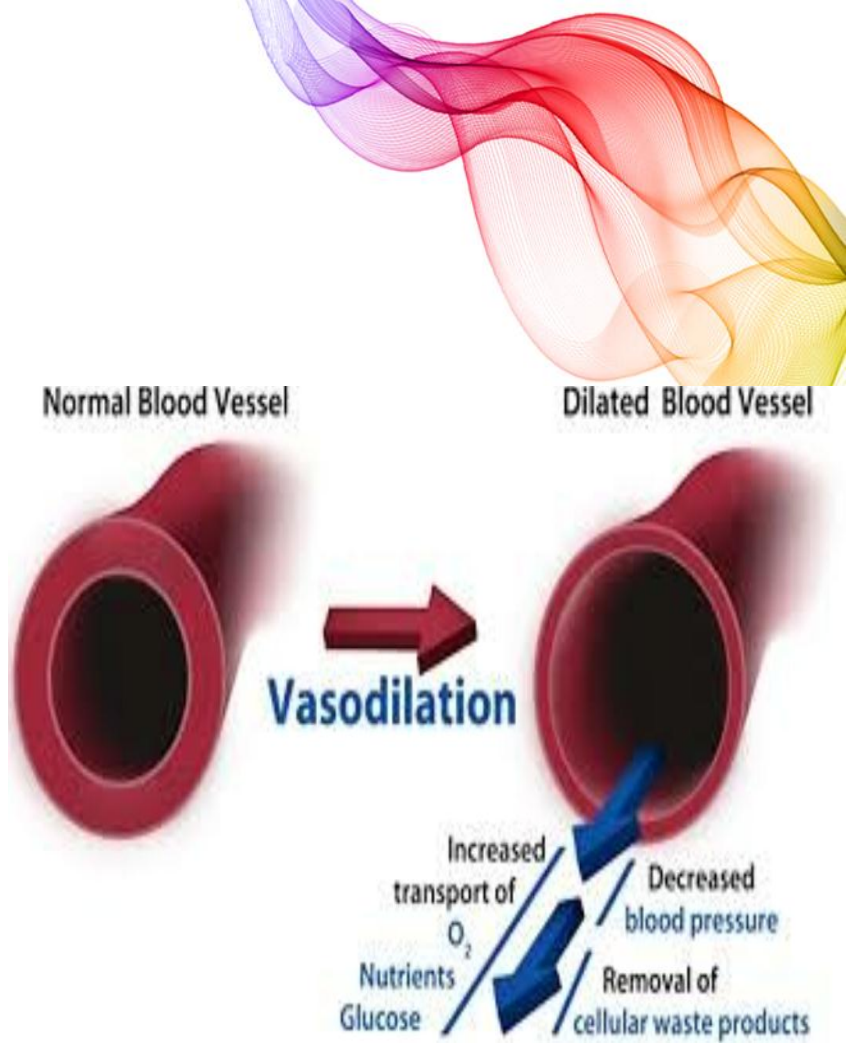
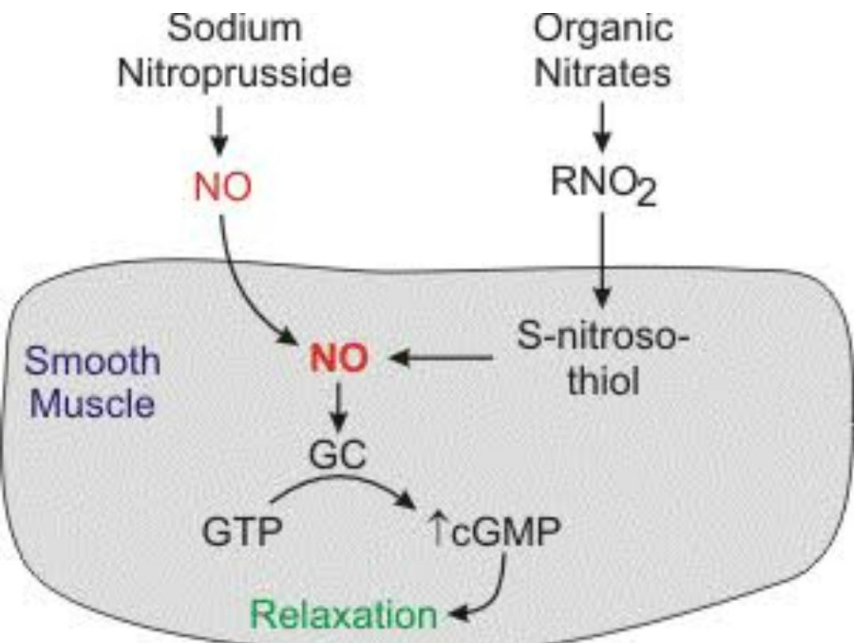
- Hydralazine
- Minoxidil
- Diazoxide

✓ Arteriolar + Venous dilators

- Sodium nitroprusside

Vasodilators.....

Mechanism of action




Vasodilators.....



Adverse effects:

- ✓ Hyperglycemia
- ✓ Anorexia
- ✓ Nausea, vomiting
- ✓ Fatigue
- ✓ Palpitation
- ✓ Flushing
- ✓ Tachycardia

Therapeutic uses:

- Minoxidil used to promote hair growth in Alopecia(baldness in male)
 - Sodium nitroprusside is the drug of choice for hypertension during pregnancy
- 

Thank

