

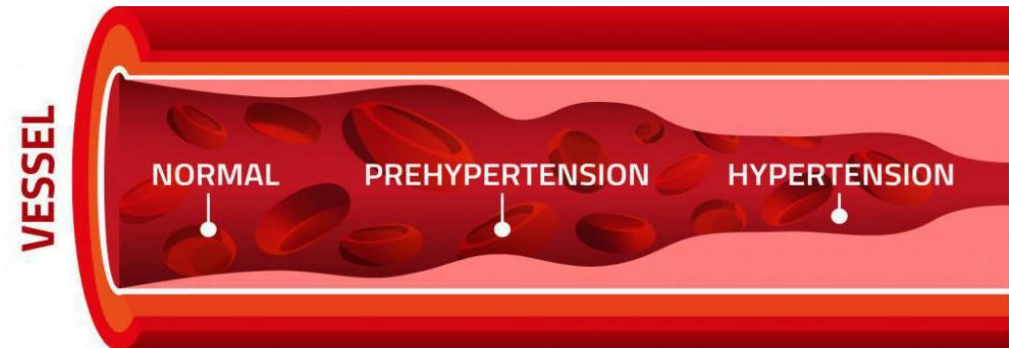
# **Management of Hypertension**

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# High blood pressure (hypertension)

- Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated
- High blood pressure (hypertension) is a common condition in which the long-term force of the blood against your artery walls is high enough that it may eventually cause health problems, such as heart disease.
- Blood pressure is determined both by the amount of blood your heart pumps and the amount of resistance to blood flow in your arteries. The more blood your heart pumps and the narrower your arteries, the higher your blood pressure. A blood pressure reading is given in millimeters of mercury (mm Hg). It has two numbers.



# High blood pressure (hypertension) / classification

- High blood pressure is classified as:
- **primary (essential) hypertension or secondary hypertension.** About 90–95% of cases are **primary**, defined as high blood pressure due to nonspecific lifestyle and genetic factors. Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use.
- The remaining 5–10% of cases are categorized as **secondary high blood pressure**, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.

- **There are two types of high blood pressure.**

- **Primary (essential) hypertension**

- For most adults, there's no identifiable cause of high blood pressure. This type of high blood pressure, called primary (essential) hypertension, tends to develop gradually over many years.

- **Secondary hypertension**

- Some people have high blood pressure caused by an underlying condition. This type of high blood pressure, called secondary hypertension, tends to appear suddenly and cause higher blood pressure than does primary hypertension. Various conditions and medications can lead to secondary hypertension, including:

- Obstructive sleep apnea
- Kidney disease
- Adrenal gland tumors
- Thyroid problems
- Certain defects you're born with (congenital) in blood vessels
- Certain medications, such as birth control pills, cold remedies, decongestants, over-the-counter pain relievers and some prescription drugs
- Illegal drugs, such as cocaine and amphetamines
- Pregnancy
- Obesity
- CKD (Chronic Kidney Disease).

# The Primary/Essential Hypertension

## ➤ The Primary/Essential Hypertension is said to be due to these following mechanisms

- **Sympathetic nervous system hyperactivity.** This is most apparent in younger persons with hypertension, who may exhibit tachycardia and an elevated cardiac output. However, correlations between plasma catecholamines and blood pressure are poor. Insensitivity of the baro-reflexes may play a role in the genesis of adrenergic hyperactivity.
- **Abnormal cardiovascular or renal development** . The normal cardiovascular system develops so that elasticity of the great arteries is matched to the resistance in the periphery to optimize large vessel pressure waves. In this way, myocardial oxygen consumption is minimized and coronary flow maximized. Elevated blood pressure later in life could arise from abnormal development of aortic elasticity or reduced development of the microvascular network. This has been postulated as the sequence of events in low birth weight infants who have an increased risk of hypertension developing in adulthood. Another hypothesis proposes that the association between low birth weight and hypertension arises from reduced nephron number.

## ○ Renin–angiotensin system activity

Renin, a proteolytic enzyme, is secreted by cells surrounding glomerular afferent arterioles in response to a number of stimuli, including:

1. reduced renal perfusion pressure,
2. diminished intravascular volume,
3. circulating catecholamines,
4. increased sympathetic nervous system activity,
5. increased arteriolar stretch, and hypokalemia.

Renin acts on angiotensinogen to cleave off the ten-amino-acid peptide angiotensin I.

This peptide is then acted upon by angiotensin-converting enzyme (ACE) to create the eight-amino-acid peptide angiotensin II, a potent vasoconstrictor and stimulant of aldosterone release from the adrenal glands.

- Despite the role of renin in the regulation of blood pressure, it probably does not play a central role in the pathogenesis of most primary (essential) hypertension; only 10% of patients have high renin activity, whereas 60% have normal levels, and 30% have low levels. Black persons with hypertension and older patients tend to have lower plasma renin activity, which may be associated with expanded intravascular volume.

((Angiotensin is a peptide hormone that causes vasoconstriction and an increase in blood pressure. It is part of the renin–angiotensin system, which regulates blood pressure. Angiotensin also stimulates the release of aldosterone from the adrenal cortex to promote sodium retention by the kidneys.))

## ○ **Defect in natriuresis**

Normal individuals increase their renal sodium excretion in response to elevations in arterial pressure. In hypertensive patients, this pressure-natriuresis relationship is reset so that maintenance of sodium homeostasis requires increased extracellular fluid volume and higher arterial pressure.

## ○ **Intracellular Sodium and Calcium**

Intracellular  $\text{Na}^+$  is elevated in primary (essential) hypertension. An increase in intracellular  $\text{Na}^+$  may lead to increased intracellular  $\text{Ca}^{2+}$  concentration as a result of facilitated exchange and might explain the increase in vascular smooth muscle tone that is characteristic of established hypertension.

## • **What is hypertension?**

Blood pressure is written as two numbers.

- The first (systolic) number represents the pressure in blood vessels when the heart contracts or beats.
- The second (diastolic) number represents the pressure in the vessels when the heart rests between beats.
- If the measurement reads 120 systolic and 80 diastolic, you would say, “120 over 80,” or write, “120/80 mmHg.” (A normal blood pressure level is 120/80 mmHg.)

Hypertension is diagnosed if, when it is measured on two different days, the systolic blood pressure readings on both days is  $\geq 140$  mmHg and/or the diastolic blood pressure readings on both days is  $\geq 90$  mmHg.



# Classification of blood pressure in adults

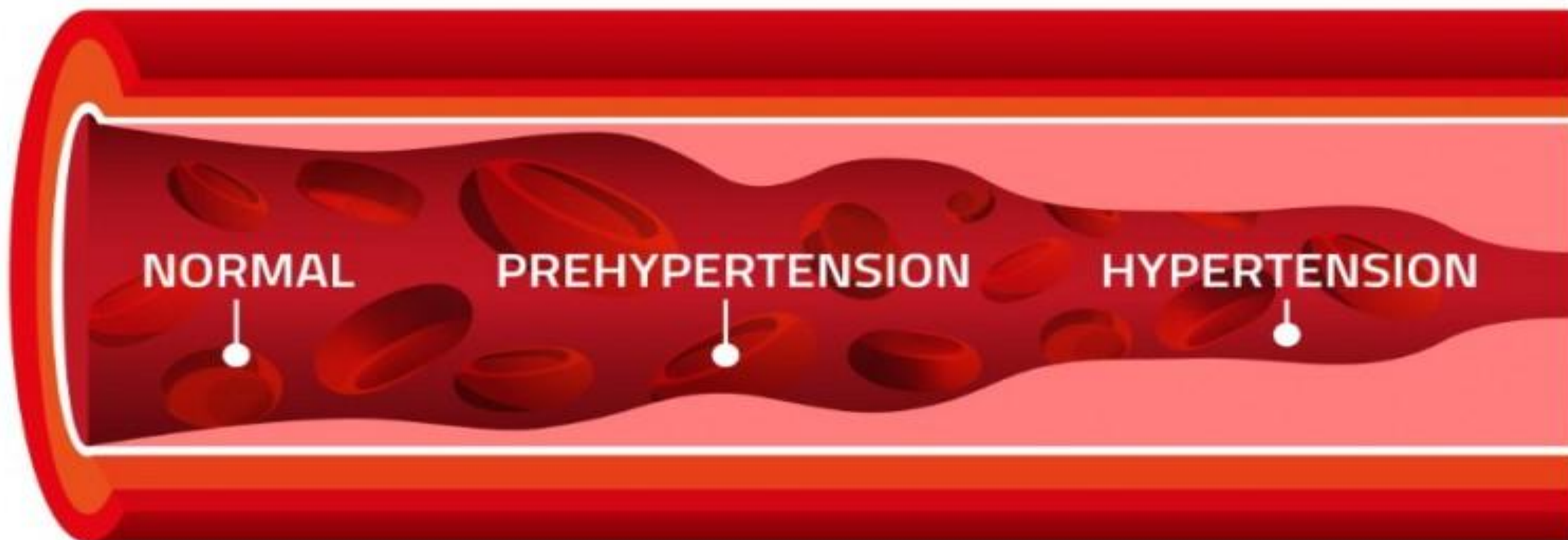
<u>BP classification</u>	<u>SBP (mmHg)</u>	<u>DBP (mmHg)</u>
Normal	< 120	and < 80
Prehypertension	120-139	or 80-89
Stage 1 hypertension	140-159	or 90-99
Stage 2 hypertension	$\geq 160$	or $\geq 100$

**SYSTOLIC PRESSURE**



Is measured between when the heart contracts

**VESSEL**



**DIASTOLIC PRESSURE**



Is measured between beats when the heart relaxes

# What are the risk factors for hypertension?

- **Modifiable risk factors** include unhealthy diets (excessive salt consumption, a diet high in saturated fat and trans fats, low intake of fruits and vegetables), physical inactivity, consumption of tobacco and alcohol, and being overweight or obese.
- **Non-modifiable risk factors** include a family history of hypertension, age over 65 years and co-existing diseases such as diabetes or kidney disease.

# Complications

- Long-term hypertension can cause complications through atherosclerosis, where the formation of plaque results in the narrowing of blood vessels. This makes hypertension worse, as the heart must pump harder to deliver blood to the body.

## Hypertension-related atherosclerosis can lead to:

Heart failure and heart attacks

an aneurysm???, or an abnormal bulge?? in the wall of an artery that can burst, causing severe bleeding and, in some cases, death

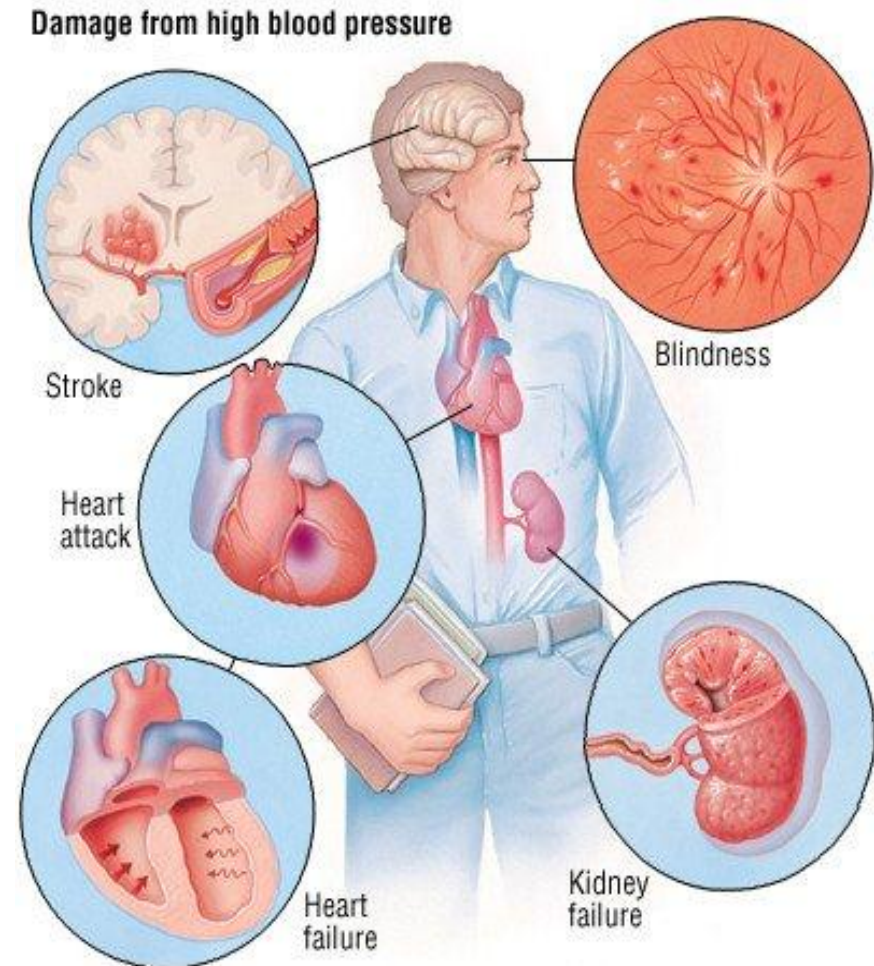
kidney failure

stroke

amputation

hypertensive retinopathies in the eye, which can lead to blindness

Regular blood pressure testing can help people avoid the more severe complications.



# How can the burden of hypertension be reduced?

- Reducing hypertension prevents heart attack, stroke, and kidney damage, as well as other health problems.
- **Prevention**
  - Reducing salt intake (to less than 5g daily).
  - Eating more fruit and vegetables.
  - Being physically active on a regular basis.
  - Avoiding use of tobacco.
  - Reducing alcohol consumption.
  - Limiting the intake of foods high in saturated fats.
  - Eliminating/reducing trans fats in diet.
- **Management**
  - Reducing and managing stress.
  - Regularly checking blood pressure.
  - Treating high blood pressure.
  - Managing other medical conditions.

# Management and Treatment

- Lifestyle adjustments are the standard, first-line treatment for hypertension. Some recommendations are as follows:
- **Regular physical exercise**
- Current guidelines recommend that all people, including those with hypertension, engage in at least [150 minutes Trusted Source](#) of moderate-intensity, aerobic exercise every week, or 75 minutes per week of high-intensity exercise.
- Alongside 150 minutes of exercise, most adults will benefit from engaging in strength training at least [twice per week](#).
- People should exercise at least 5 days every week.
- Examples of suitable activities are:
  - walking
  - jogging
  - cycling
  - swimming

# Stress Reduction

- ❑ Avoiding or learning to manage stress can help a person control blood pressure.
- ❑ A few relaxation techniques that can help **relieve stress** are:
  - ✓ meditation
  - ✓ warm baths
  - ✓ yoga
  - ✓ going on long walks
- People should avoid consuming **alcohol** and **recreational drugs** to cope with stress, as these can contribute to elevated blood pressure and the complications of hypertension.
- **Smoking** can also increase blood pressure. Avoiding or quitting smoking reduces the risk of hypertension, serious heart conditions, and other health issues.

# Diet

- People can prevent high blood pressure by following a heart-healthy diet.
- Reducing salt intake : High sodium consumption contributes Trusted Source to high blood pressure. The main source of sodium in the diet is salt
- Moderating alcohol consumption : Moderate to excessive alcohol consumption can increase blood pressure.
- Managing body weight : Excess body weight can contribute Trusted Source to hypertension. A fall in blood pressure usually follows weight loss, as the heart does not have to work so hard to pump blood around the body.



# Medication / When do you need hypertension drugs?

- Suggest a hypertension drug if:
- Your blood pressure remains at 160/100 mmHg or more after following [lifestyle guidelines for hypertension](#).
- Your blood pressure remains at 140/90 mmHg or more additionally having [diabetes](#) or [cholesterol](#) or having a cardiovascular disease after following lifestyle guidelines for hypertension.
- People whose blood pressure remains at 130/80 mmHg or more additionally have certain diseases - have had a recent heart attack, stroke, TIA (transient ischemic attack) or chronic kidney diseases. Follow lifestyle guidelines for hypertension along with the medication to avoid further risks.

# Medication

- Eventually, people with hypertension may need to combine [two or more Trusted Source](#) drugs to manage their blood pressure.
- **Medications for hypertension include:**
  - diuretics, including thiazides, chlorthalidone, and indapamide
  - beta-blockers and alpha-blockers
  - calcium-channel blockers
  - central agonists
  - peripheral adrenergic inhibitor
  - vasodilators
  - angiotensin-converting enzyme (ACE) inhibitors
  - angiotensin receptor blockers
- **The choice of medication depends on the individual and any underlying medical conditions they may experience.**
- Anyone taking antihypertensive medications should carefully read the labels of any over-the-counter (OTC) drugs they may also take, such as decongestants. These OTC drugs may interact with the medications they are taking to lower their blood pressure.



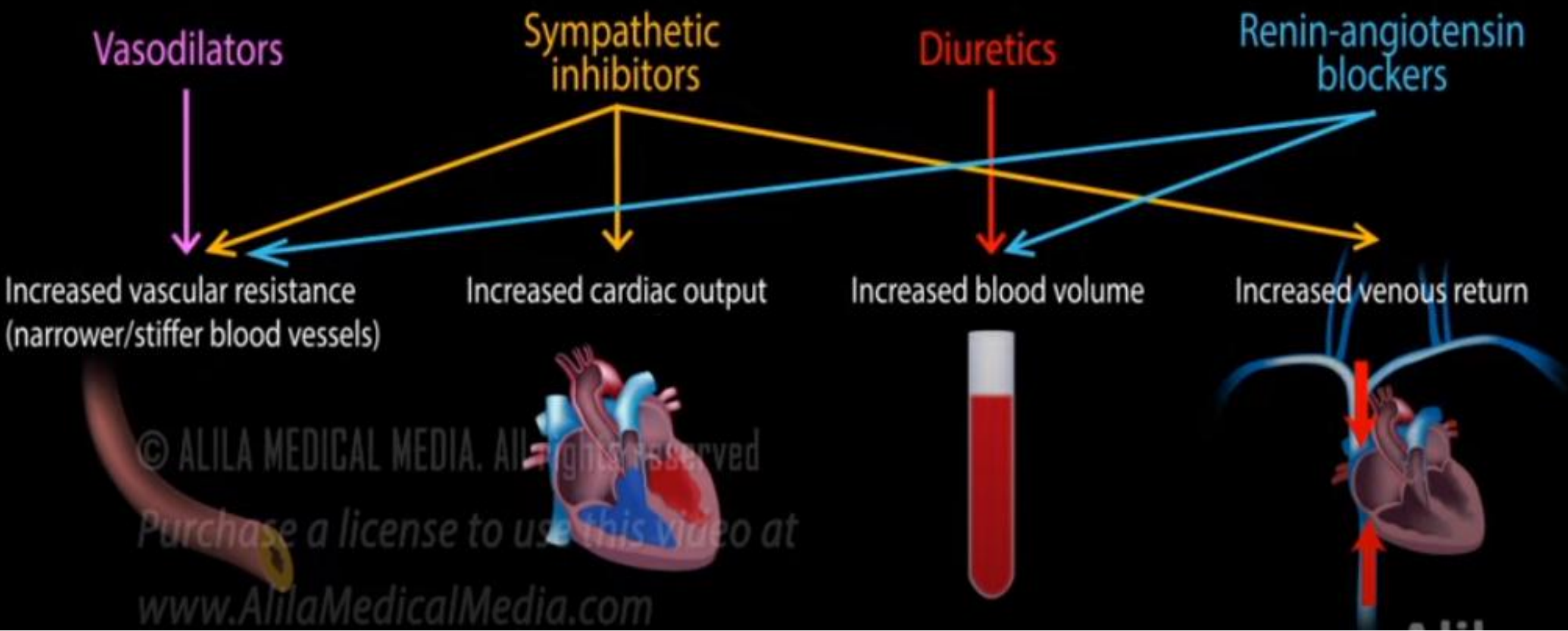
# Different classes of hypertension medication

- Blood pressure medications also known as antihypertensive are to lower your blood pressure available on prescription. The classes of blood pressure medications include:
- [\*Diuretics\*](#) - Diuretics get rid of excess sodium and water from your body and help control blood pressure. Mostly used in combination with other medication.
- [\*ACE inhibitors\*](#) - Angiotensin is a chemical in your kidney and throughout the body causes the arteries to narrow. Angiotensin-converting enzyme (ACE) inhibitors allow the body produce less angiotensin, which helps the blood vessels to relax, which lowers blood pressure.
- [\*ARBs\*](#) - Angiotensin II receptor blockers blocks angiotensin, a chemical causes the arteries to narrow. Angiotensin needs a receptor to bind with to constrict the blood vessel. Angiotensin receptor blocker (ARBs) block the receptors so fails to constrict the blood vessel. Blood vessels stay relaxed and thus blood pressure reduced.
- [\*Beta-blockers\*](#) - Beta-blockers reduces your heart rate, heart's workload and heart's output, which lowers your blood pressure.
- [\*Calcium channel blockers\*](#) - It prevents calcium from entering the smooth muscle cells of the heart and arteries, which lowered normal heart's contraction. Calcium channel blockers relax blood vessels, reduce heart rate and lower blood pressure.

# Different classes of hypertension medication

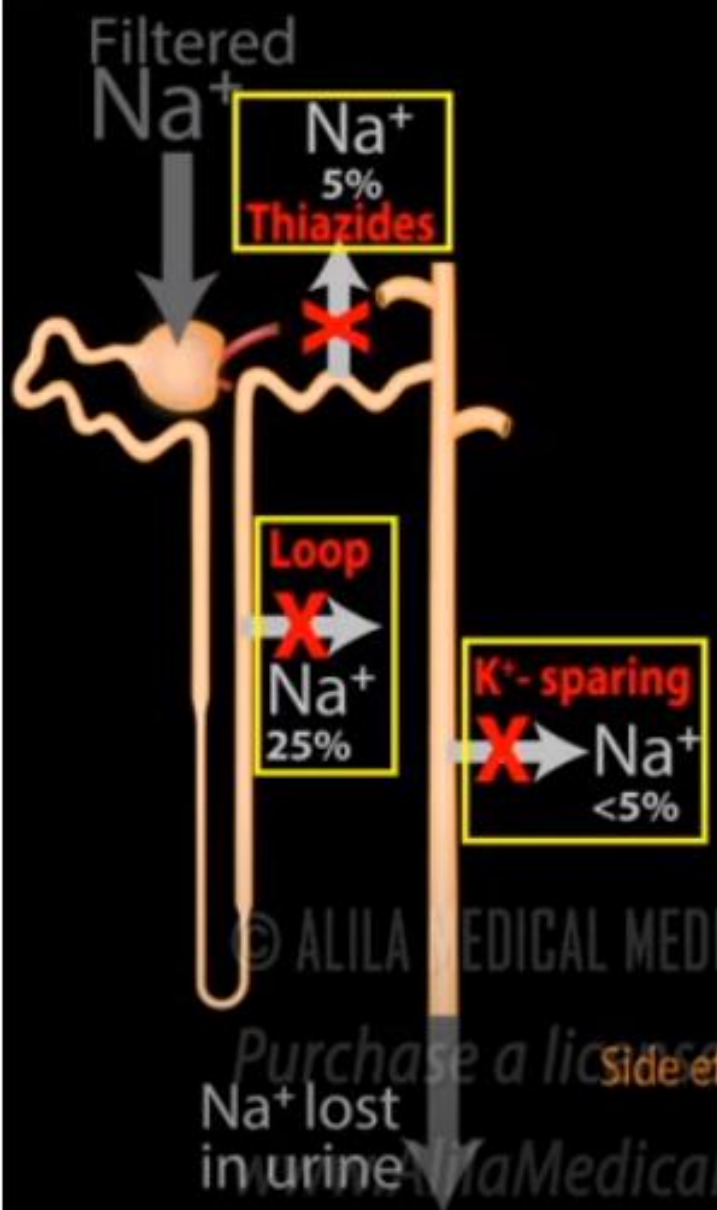
- [Renin inhibitors](#) - Renin is an enzyme produced by your kidneys that start a chain of chemical steps that constrict blood vessels thus increases blood pressure. Renin inhibitors reduce the production of renin and lowering its ability to begin this process. Thus relaxes the blood vessels and lower the blood pressure.
- [Alpha blockers](#) - It reduce the arteries resistance, relax muscle tone of the vascular walls.
- [Alpha-beta blockers](#) – It is used as an IV drip for patients under hypertensive crisis and prescribed for hypertensive outpatient at risk for heart failure. Alpha-beta blockers include carvedilol (Coreg) and labetalol (Trandate).
- [Central agonists](#) - It works in the central nervous system rather than work directly on the cardiovascular system, thus may cause drowsiness.
- [Peripheral adrenergic inhibitors](#) - It blocks brain signal that messages blood vessels to constrict. This medication is rarely used when others failed to help.
- [Blood vessel dilator or vasodilators](#) - It causes the blood vessel muscles to relax, allowing it to dilate (widen).
- [Antihypertensive combination medicine](#) - It is a combination of 2 different type of hypertension medicine to get the benefit of both for effective blood pressure control.

# Antihypertensives



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# Diuretics



## Loop

- Furosemide
- Bumetanide
- Torsemide

Not recommended as first-line drugs

## Thiazides

- Hydrochlorothiazide
- Chlorthalidone

First-line drugs for uncomplicated hypertension

## $\text{K}^+$ -sparing

- Spironolactone
- Amiloride
- Triamterene

Can correct  $\text{K}^+$  loss  
Use with thiazide or loop diuretics



- Hypokalemia
- Alkalosis

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# Sympatholytics

$\alpha_2$  receptor

Central sympatholytics

Mixed  $\alpha$  &  $\beta$  blockers

$\beta$  receptor

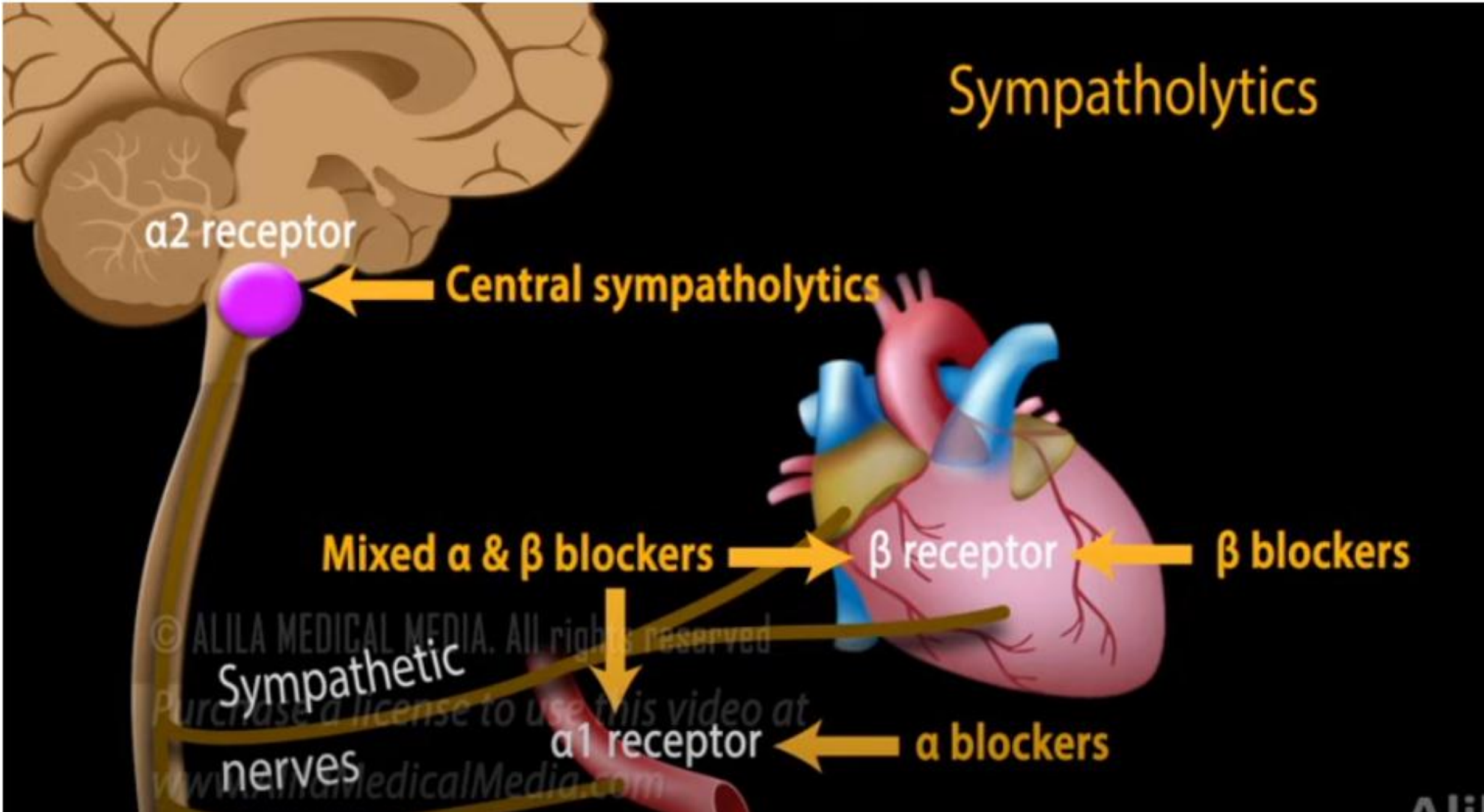
$\beta$  blockers

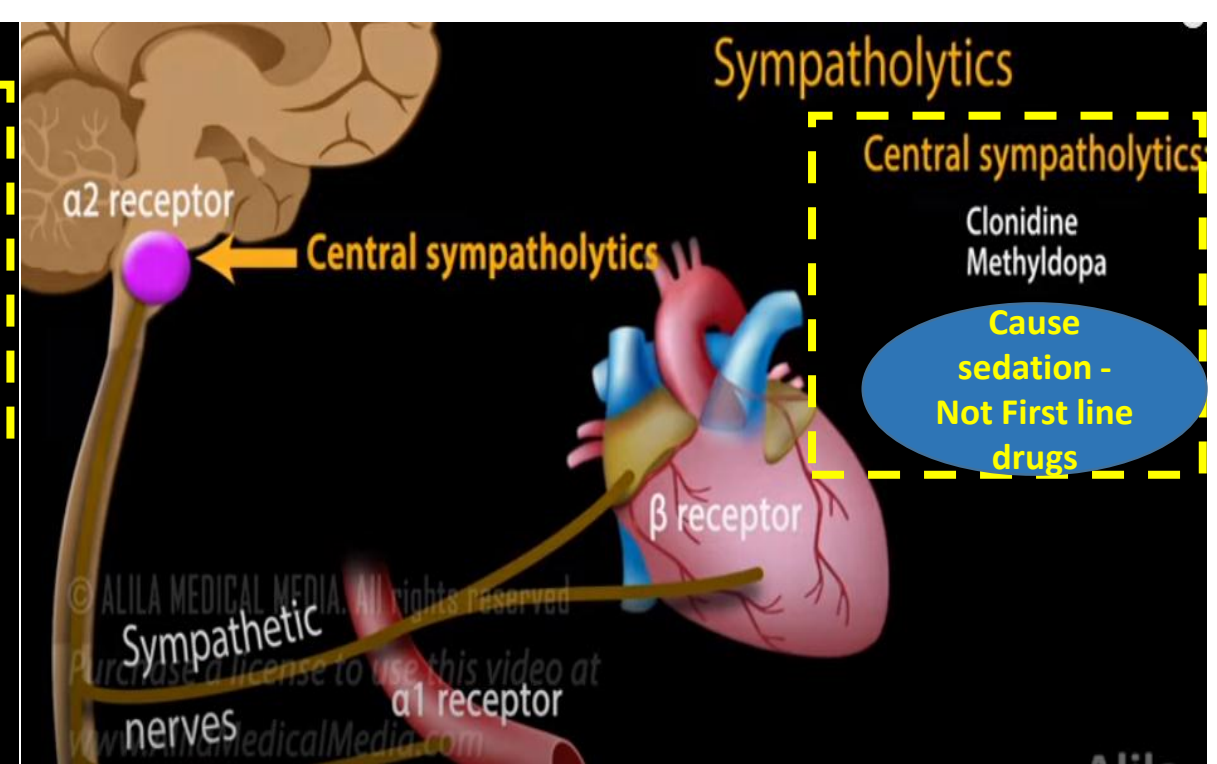
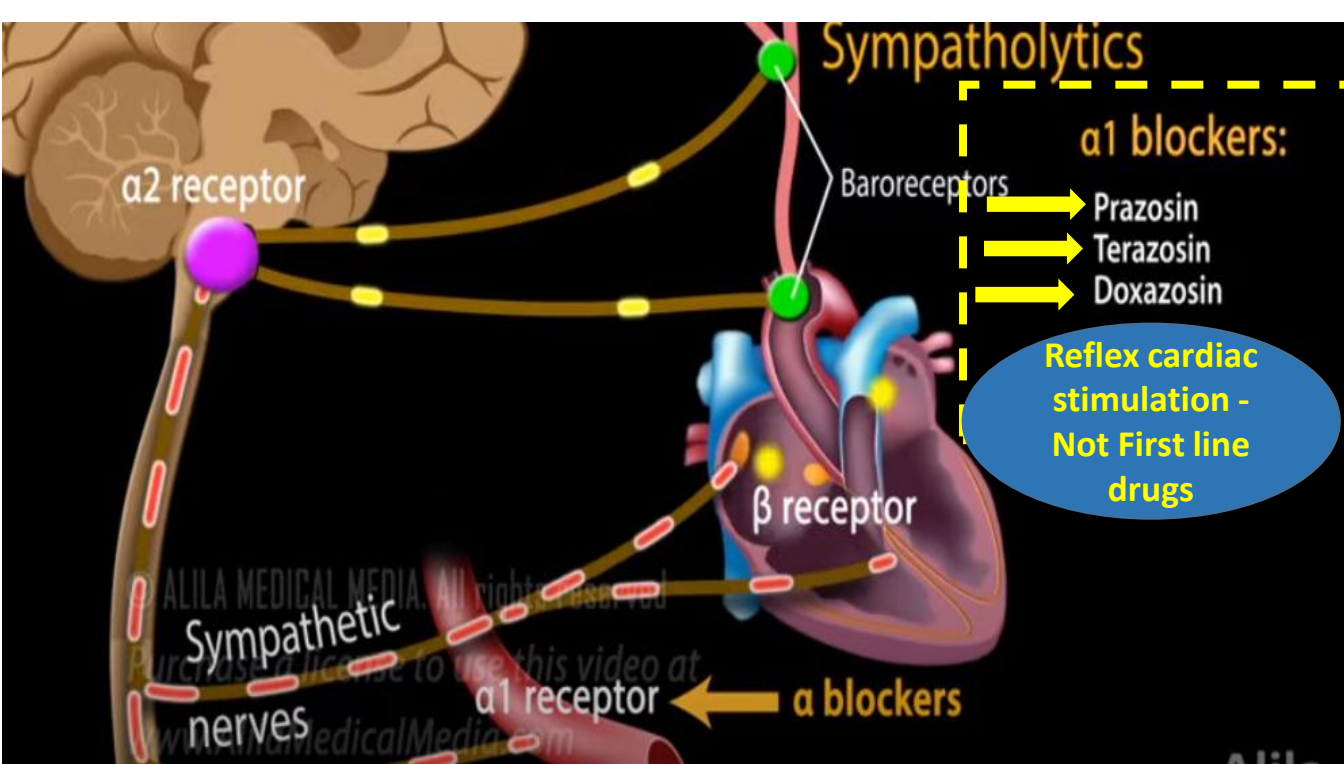
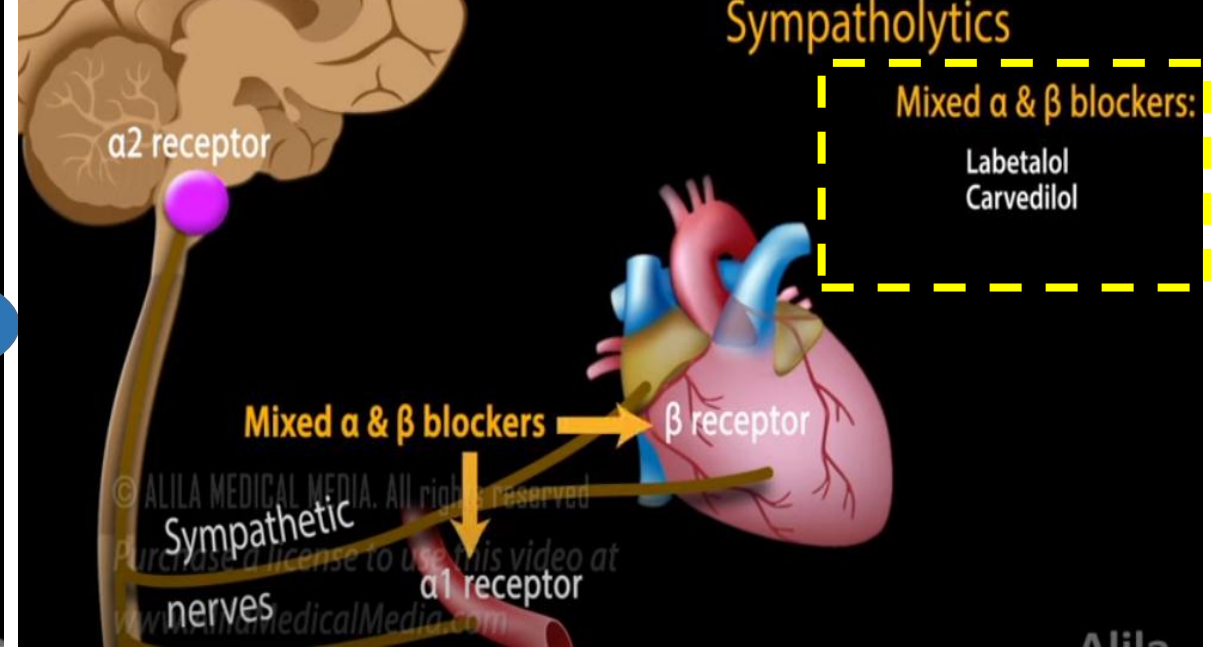
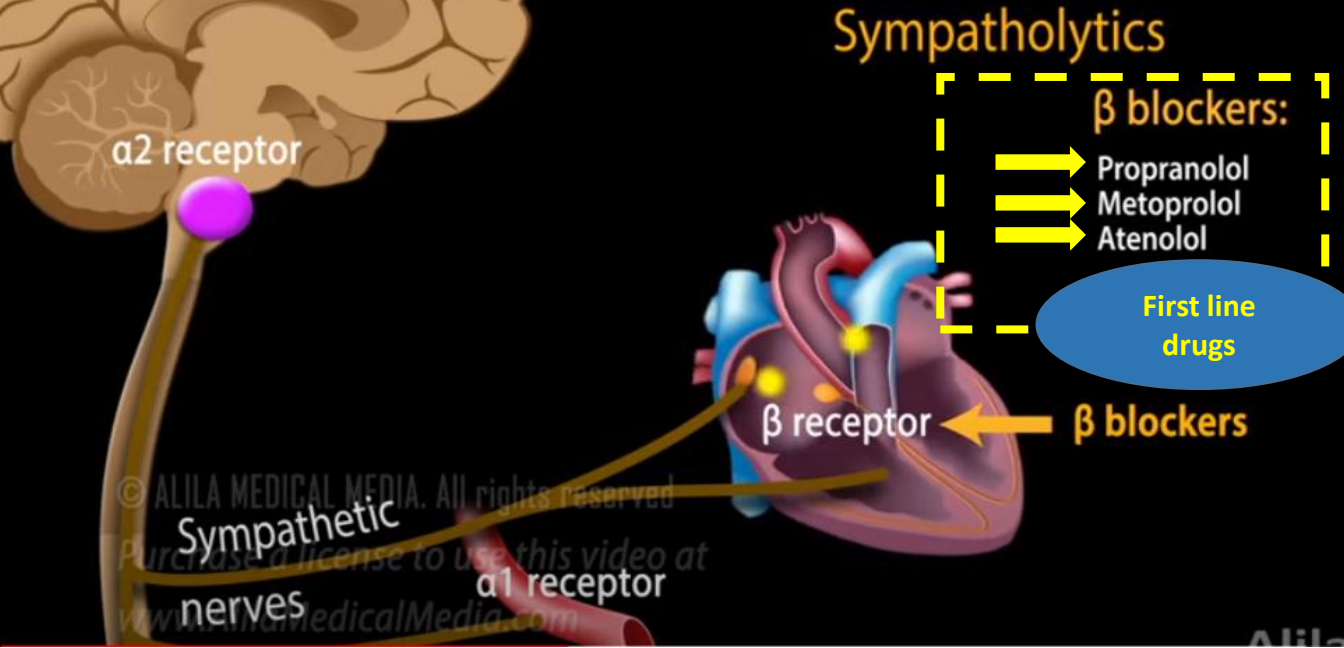
Sympathetic nerves

$\alpha_1$  receptor

$\alpha$  blockers

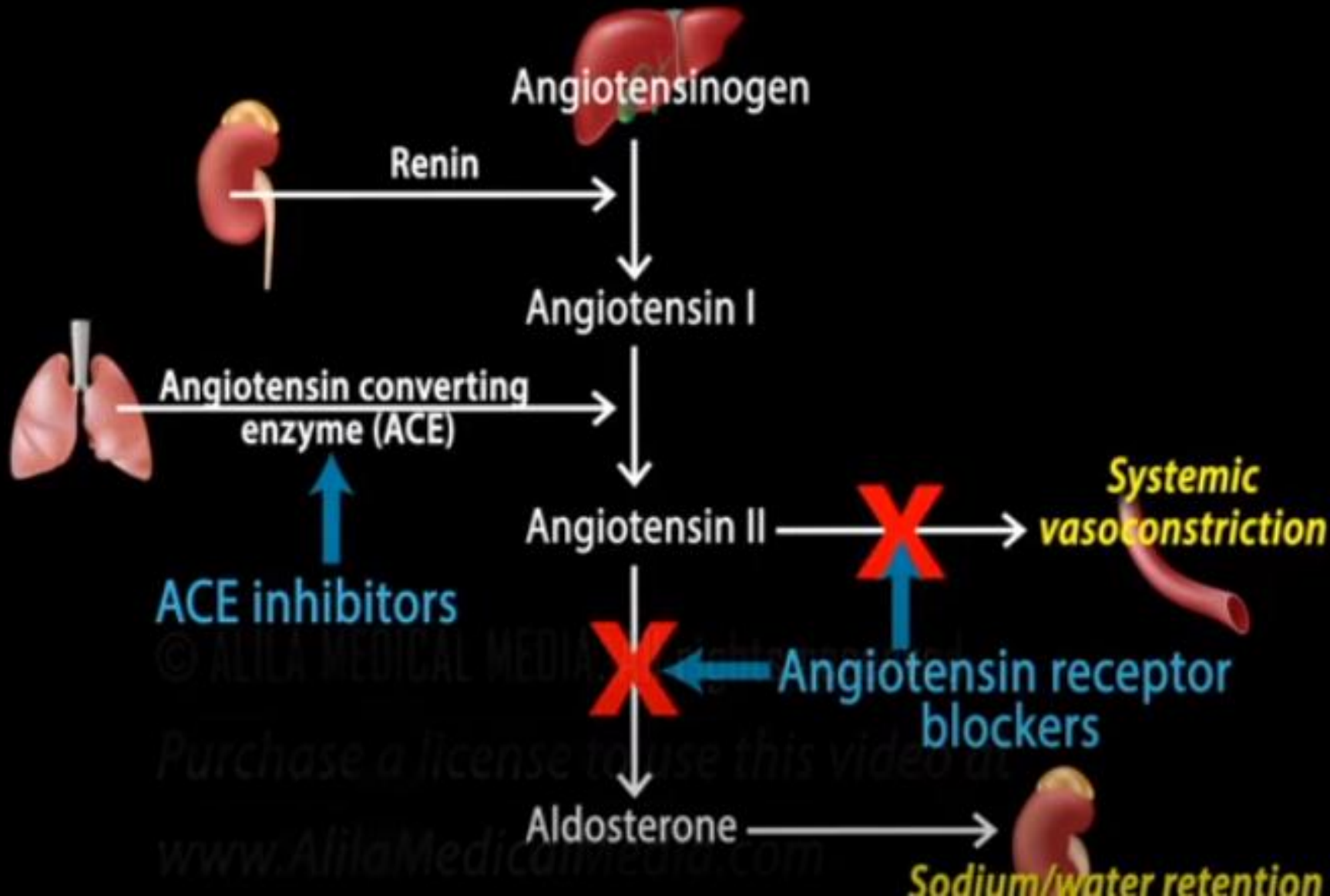
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# Renin-angiotensin system blockers



## ACE inhibitors:

Captopril  
Enalapril  
Lisinopril

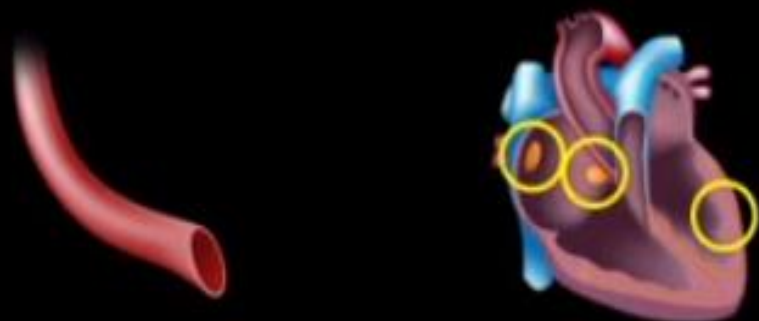
First line - drugs

## Angiotensin receptor blockers:

Losartan  
Valsartan

# Vasodilators

## Ca<sup>++</sup> channel blockers



Dihydropyridine:  
**Nifedipine**  
**Amlodipine**

Non-Dihydropyridine:  
**Verapamil**  
**Diltiazem**

Reflex cardiac  
stimulation

No reflex cardiac stimulation

Not for systolic heart failure

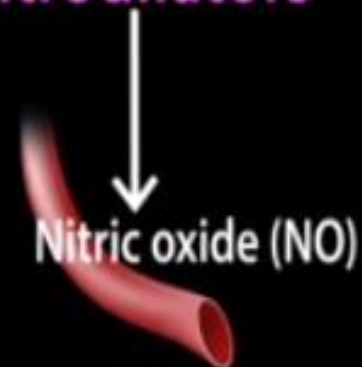
## Direct arterial vasodilators



**Minoxidil**  
**Hydralazine**

Reflex cardiac stimulation  
Only for short-term treatment of  
refractory hypertension

## Nitrodilators



**Sodium nitroprusside**  
**Nitroglycerine**

For acute hypertensive crises  
and to control blood pressure  
during surgery

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# Medication

- **Diuretics** : Diuretics help the body get rid of excess sodium (salt) and water and help control blood pressure. They are often used in combination with additional prescription therapies.
- **Thiazide and thiazide-like diuretics** have been a mainstay of the therapy of primary hypertension. The most popular agent in this class, hydrochlorothiazide, was traditionally used in doses of 50 to 100 mg/day. These doses were associated with metabolic and electrolyte complications. Low-dose therapy has since been demonstrated to be efficacious and to have a much lower incidence of side effects.
- **Chlorthalidone and indapamide**, both thiazide-like diuretics, have been shown to provide greater antihypertensive efficacy and, more importantly, to reduce cardiovascular events and mortality compared with hydrochlorothiazide (a thiazide-type diuretic).

# Diuretics

Generic name	Common brand names
<b>Thiazide diuretics</b>	
chlorthalidone	Hygroton
chlorothiazide	Diuril
hydrochlorothiazide	Esidrix, Hydrodiuril, Microzide
indapamide	Lozol
metolazone	Mykrox, Zaroxolyn
<b>Potassium-sparing diuretics</b>	
amiloride hydrochloride	Midamar
spironolactone	Aldactone
triamterene	Dyrenium

<b>Thiazide-Type Diuretic</b>	<b>Equipotent Dose, mg</b>	<b>Maximum Daily Dose, mg</b>	<b>Duration of Action</b>
Bendroflumethiazide*	2.5	20	12–24 h (up to 48 h)†
Chlorothiazide	250	1,000	6–12 h (up to 24 h)†
Chlorthalidone	12.5	100	24–72 h†
Hydrochlorothiazide	25	200	6–12 h (up to 24 h)†
Indapamide	2.5	5	36 h
Methylclothiazide	2.5	20	24 h
Metolazone	2.5	20	12–24 h (up to 48 h)†
Quinethazone*	25	200	12–24 h†

# Diuretics

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## Loop diuretic

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furosemide

Lasix

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bumetanide

Bumex

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## Combination diuretics

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amiloride hydrochloride + hydrochlorothiazide    Moduretic

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spironolactone + hydrochlorothiazide    Aldactazide

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triamterene + hydrochlorothiazide    Dyazide, Maxzide

# Beta-blockers

Beta-blockers reduce the heart rate, the heart's workload and the heart's output of blood, which lowers blood pressure.

<b>Generic name</b>	<b>Common brand names</b>
acebutolol	Sectral
atenolol	Tenormin
betaxolol	Kerlone
bisoprolol fumarate	Zebeta
carteolol hydrochloride	Cartrol
metoprolol tartrate	Lopressor
metoprolol succinate	Toprol-XL
nadolol	Corgard
penbutolol sulfate	Levatol
pindolol*	Visken
propranolol hydrochloride*	Inderal
solotol hydrochloride	Betapace
timolol maleate*	Blocadren
<b>Combination beta-blocker/diuretic</b>	
hydrochlorothiazide and bisoprolol	Ziac

# ACE inhibitors (Angiotensin-converting enzymes inhibitors (ACE Inhibitors))

**Angiotensin :** is a protein hormone that causes blood vessels to become narrower. It helps to maintain blood pressure and fluid balance in the body. Angiotensin is a chemical that causes the arteries to become narrow, especially in the kidneys but also throughout the body. ACE stands for Angiotensin-converting enzyme. ACE inhibitors help the body produce less angiotensin, which helps the blood vessels relax and open up, which, in turn, lowers blood pressure.

<b>Generic name</b>	<b>Common brand names</b>
benazepril hydrochloride	Lotensin
captopril	Capoten
enalapril maleate	Vasotec
fosinopril sodium	Monopril
lisinopril	Prinivel, Zestril
moexipril	Univasc
perindopril	Aceon
quinapril hydrochloride	Accupril
ramipril	Altace
trandolapril	Mavik



# Angiotensin II receptor blockers

- These drugs block the effects of angiotensin, a chemical that causes the arteries to become narrow. Angiotensin needs a receptor- like a chemical "slot" to fit into or bind with- in order to constrict the blood vessel. ARBs block the receptors so the angiotensin fails to constrict the blood vessel. This means blood vessels stay open and blood pressure is reduced.

## Pharmacokinetics

Route	Onset	Peak	Duration
Oral	Varies	1-3 h	24 h

T1/2: 2 h

Metabolism: liver

Excretion: urine and feces

Generic name	Common brand names
candesartan	Atacand
eprosartan mesylate	Teveten
irbesartan	Avapro
losartan potassium	Cozaar
telmisartan	Micardis
valsartan	Diovan

# Calcium channel blockers

- This drug prevents calcium from entering the smooth muscle cells of the heart and arteries. When calcium enters these cells, it causes a stronger and harder contraction, so by decreasing the calcium, the hearts' contraction is not as forceful. Calcium channel blockers relax and open up narrowed blood vessels, reduce heart rate and lower blood pressure.

Route	Onset	Peak	Duration
Oral and extended release	30-60 min	6-11 h	12 h
T1/2: 5-7 h Metabolism: liver . Excretion: urine			

Generic name	Common brand names
amlodipine besylate	Norvasc, Lotrel
bepidil	Vasocor
diltiazem hydrochloride	Cardizem CD, Cardizem SR, Dilacor XR, Tiazac
felodipine	Plendil
isradipine	DynaCirc, DynaCirc CR
nicardipine	Cardene SR
nifedipine	Adalat CC*, Procardia XL
nisoldipine	Sular

# Alpha blockers

- These drugs reduce the arteries' resistance, relaxing the muscle tone of the vascular walls.

<b>Generic name</b>	<b>Common brand names</b>
doxazosin mesylate	Cardura
prazosin hydrochloride	Minipress
terazosin hydrochloride	Hytrin

# Alpha-2 Receptor Agonists

- These drugs reduce blood pressure by decreasing the activity of the sympathetic (adrenaline-producing) portion of the involuntary nervous system. Methyldopa is considered a first line antihypertensive during pregnancy because adverse effects are infrequent for the pregnant woman or the developing fetus.

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**Generic name**

methyldopa

**Common brand names**

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Some noted possible side effects of Alpha-2 Receptor Agonists:

- Methyldopa can cause drowsiness or dizziness

# Central agonists

- Central agonists also help decrease the blood vessels' ability to tense up or contract. The central agonists follow a different nerve pathway than the alpha and beta-blockers, but accomplish the same goal of blood pressure reduction.

<b>Generic name</b>	<b>Common brand names</b>
alpha methyldopa	Aldomet
clonidine hydrochloride	Catapres
guanabenz acetate	Wytensin
guanfacine hydrochloride	Tenex

- These medications reduce blood pressure by blocking neurotransmitters in the brain. This blocks the smooth muscles from getting the "message" to constrict. These drugs are rarely used unless other medications don't help.

<b>Generic name</b>	<b>Common brand names</b>
guanadrel	Hylorel
guanethidine monosulfate	Ismelin
reserpine	Serpasil

# Blood vessel dilators (vasodilators)

- Blood vessel dilators, or vasodilators, can cause the muscle in the walls of the blood vessels (especially the arterioles) to relax, allowing the vessel to dilate (widen). This allows blood to flow through better.

## Pharmacokinetics

Route	Onset	Peak	Duration
IV	1-2 min	Rapid	1-10 min
T1/2: 2 min Metabolism: liver Excretion: urine			

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### Generic name

hydralazine hydrochloride

minoxidil

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### Common brand names

Apresoline

Loniten

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Medication	Initial Dosing	Maximum Dosing
<b>ACE inhibitors</b>		
Lisinopril	10 mg once daily	40 mg once daily
Enalapril	5 mg once daily	40 mg once daily
Captopril	50 mg twice daily	150 mg three times daily
<b>ARB</b>		
Losartan	50 mg once daily	100 mg once daily
Valsartan	40 mg once daily	320 mg once daily
Irbesartan	75 mg once daily	300 mg once daily
<b><math>\beta</math>-blockers</b>		
Atenolol	25 mg once daily	100 mg once daily
Metoprolol	50 mg twice daily	450 mg total daily dose
<b>Calcium channel blockers</b>		
Amlodipine	5 mg once daily	10 mg once daily
Diltiazem (extended release)	120 mg once daily	480 mg once daily
<b>Thiazide diuretics</b>		
Hydrochlorothiazide	25 mg once daily	50 mg once daily
Chlorthalidone	12.5 mg once daily	100 mg once daily