

## Hypertension

Is the most common of the cardiovascular diseases. Hypertension is defined as either a sustained systolic blood pressure of greater than 140 mm Hg or a sustained diastolic blood pressure of greater than 90 mm Hg.

**There are two types of hypertension:**

### 1-Primary Hypertension

- Age
- weight
- genetics
- race.
- environment

### 2-Secondary Hypertension

- renal disease
- drug-induced factors (e.g. oral contraceptives, corticosteroids).
- pregnancy
- hormonal factors

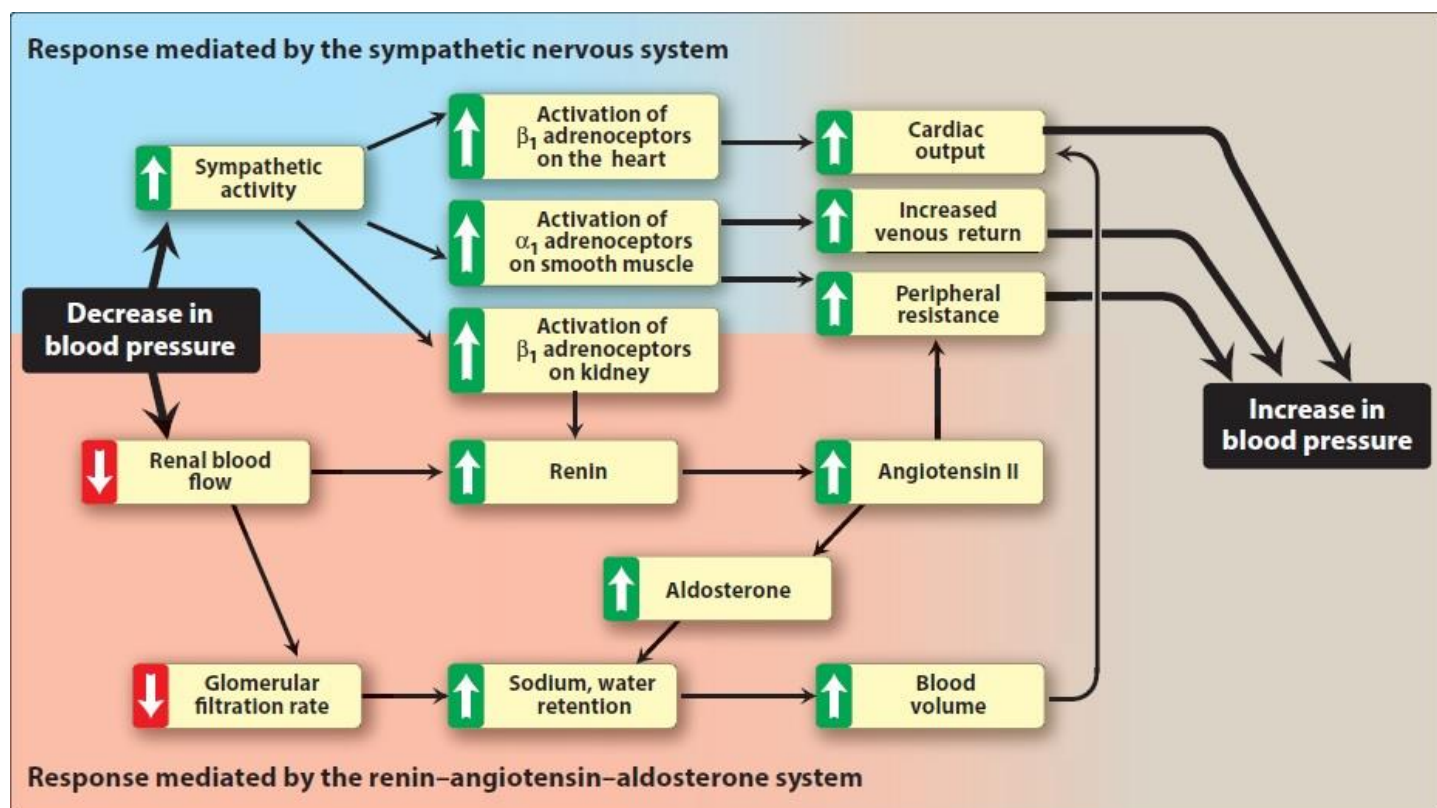
### Factors Responsible for Blood Pressure

- Cardiac output.
  - Peripheral resistance.
  - Blood volume.
- Regulated by:
- A. Baroreceptors and the sympathetic nervous system.
- B. Renin–angiotensin–aldosterone system.

**(Blood pressure= Cardiac output × Systemic vascular resistance)**

**\*\* Most antihypertensive drugs lower blood pressure by reducing cardiac output and/or decreasing peripheral resistance.**

**Cardiac output:** The volume of blood pumped per minute. The higher the cardiac output, the higher the blood pressure. Determined by **heart rate** and **stroke volume:** is the amount of blood pumped by a ventricle in one contraction.



(Response of the autonomic nervous system and the renin–angiotensin–aldosterone system to a decrease in blood pressure)

## - Anti-Hypertensive Drugs

### 1. Diuretics:

Diuretics are often the first-line medications for hypertension because they have few side effects and can control minor to moderate hypertension. also used to treat heart failure and kidney disorders. Used alone or in combination with other antihypertensive drugs.

\*\*\* **Mechanism of Action:** Regardless of class, the initial mechanism of action of diuretics is based upon decreasing blood volume through the increase of urinary excretion of water and electrolytes (such as sodium (Na<sup>+</sup>), calcium (Ca<sup>2+</sup>), chloride (Cl<sup>-</sup>), and potassium (K<sup>+</sup>) which ultimately leads to decreased blood pressure.

#### A. Thiazide diuretics

lower blood pressure initially by increasing sodium and water excretion. This causes a decrease in blood volume, resulting in a decrease in cardiac output and renal blood flow.

- E.g. hydrochlorothiazide
- thiazide diuretics are not effective in patients with inadequate kidney function.

- Thiazides are useful in combination therapy with a variety of other antihypertensive agents, including  $\beta$ -blockers.
- **Side effect:** Thiazide diuretics can induce hypokalemia, hyperuricemia and, to a lesser extent, hyperglycemia in some patients.
- **hydrochlorothiazide (monozide)** is B pregnancy category.

### B. Loop diuretics

- **E.g.** furosemide (**Lasix**), bumetanide
- act by blocking  $\text{Na}^+$  and  $\text{Cl}^-$  reabsorption in the kidneys, thus causing decreased renal vascular resistance and increased renal blood flow.
- can be used in patients with poor renal function or those who have not responded to thiazide diuretics.
- they can cause hypokalemia. And loop diuretics increase the  $\text{Ca}^{2+}$  content of urine.
- **Side effects:** Loop diuretics are ototoxic

### C. $\text{K}^+$ -sparing diuretics:

- E.g. Spironolactone, amiloride.
- Used to treat hypertension.
- Potassium-sparing diuretics are sometimes used in combination with loop diuretics and thiazides to reduce the amount of potassium loss induced by these diuretics.
- Clients should avoid excess potassium in their diet and salts that contain potassium.

## 2. Angiotensin converting enzyme inhibitors (ACEI):

- **E.g.** (captopril, enalapril , lisinopril , Ramipril)
- **Mechanism of action:** Block or inhibition the **Angiotensin converting enzyme** that convert angiotensin I to angiotensin II (potent vasoconstrictor), thus causes the vasodilation (lowering peripheral resistance) and decrease aldosterone production (decreasing blood volume).
- **Indication:**
  - a. Enalapril, Lisinopril: used for hypertensive patients with heart failure.
  - b. Enalapril is pregnancy category D.
  - c. Enalapril has a prolonged half-life (once or twice daily)

- d. Captopril (Capoten): is indicated for malignant hypertension.
- **Side effects:** hyperkalemia, persistent cough.
- 3. Angiotensin II Receptor Blockers (ARBs):**
- **E.g.** (candesartan, losartan, valsartan, telmisartan).
  - **Mechanism of action:** block receptors for angiotensin II in arteriolar smooth muscle and in the adrenal gland, thus causing blood pressure to fall. produce arteriolar and venous dilation and block aldosterone secretion, thus lowering blood pressure and decreasing salt and water retention ARBs do not increase bradykinin levels. Thus effects are more specific on angiotensin II, and ARBs do not increase bradykinin levels.
  - **Indication**  
**Losartan:** beneficial in patients with hypertension and diabetic nephropathy.
  - **Side effect:** The most common side effects of ARBs are cough, hyperkalemia dizziness, headache, drowsiness, diarrhea.
- 4. Antiadrenergic drugs or adrenergic blocking agent ( $\alpha$  and  $\beta$  Antagonist):**
- Mechanism of action: Inhibit activity of the sympathetic nervous system by block or interrupt beta-adrenergic and alpha-adrenergic receptors, so that inhibit the stimulation of beta-adrenergic fibers, which in turn decreasing heart rate, force of myocardial contraction, cardiac output, also vasodilation and decrease blood pressure
  - **Classification:**  
**A. Alpha 1 adrenergic receptor blocking agents**  
**NOTE:**  $\alpha$ 1-receptor occur in the arterioles
  - **E.g.** tetrazosin, doxazosin, prazosin
  - **Mechanism of action:** They block alpha1 adrenergic receptors **causing vasodilation and** decrease peripheral vascular resistance.
  - These drugs are also used to treat benign prostatic hyperplasia (BPH) and urinary obstruction because they relax smooth muscle in the prostate and bladder neck.

**B. Alpha 2 adrenergic receptor blocking agents:**

- **e.g:** (clonidine, methyldopa)
- **M.O.A:** Act centrally sympatholytics stimulate presynaptic in the brain.

**C. Selective Beta-Adrenergic blocking drugs**

- **E.g:** atenolol (Tenormin), metoprolol, bisoprolol
- **Mechanism of action:** block Beta1-receptors (in the heart). selective beta1 blockers decrease heart rate and affect myocardial conduction and contractility.
- **Indications: Atenolol (Tenormin):** used to treat hypertension (for adult, children and neonates). Also used for treatment and prophylaxis of angina.

**D. Non-selective Beta-Adrenergic blocking drugs**

- **E.g:** propranolol (Inderal), timolol:
- **Mechanism of action:** blockade of both beta1 and beta2 receptors, produce the same effects but also act on the respiratory system and the blood vessels, producing vasoconstriction and bronchoconstriction.
- **Indication:** hypertension, arrhythmias, chronic angina, migraines and Myocardial infarction.
- **Side effects:** producing vasoconstriction and bronchoconstriction. But occur at high doses.

**E. Alpha/Beta-Adrenergic blocking drugs**

- E.g: Labetalol and carvedilol
- Mechanism of action: act by dual antihypertensive action of reduction in heart rate (beta1 receptor blockade) and vasodilation (alpha1 receptor blockade).
- Indications:
  - a. **Carvedilol:** is taken orally, and used to treat mild to moderate heart failure.
  - b. **Labetalol** is used in the management of hypertensive emergencies.

**5. Calcium Channel Blocking Agents (CCBs)**

- **E.g:** Amlodipine, nifedipine, diltiazem
- **Mechanism of action:** Contraction of muscle is regulated by the amount of calcium ion inside the cell. When calcium enters the cell through channels in the plasma membrane, muscular contraction is

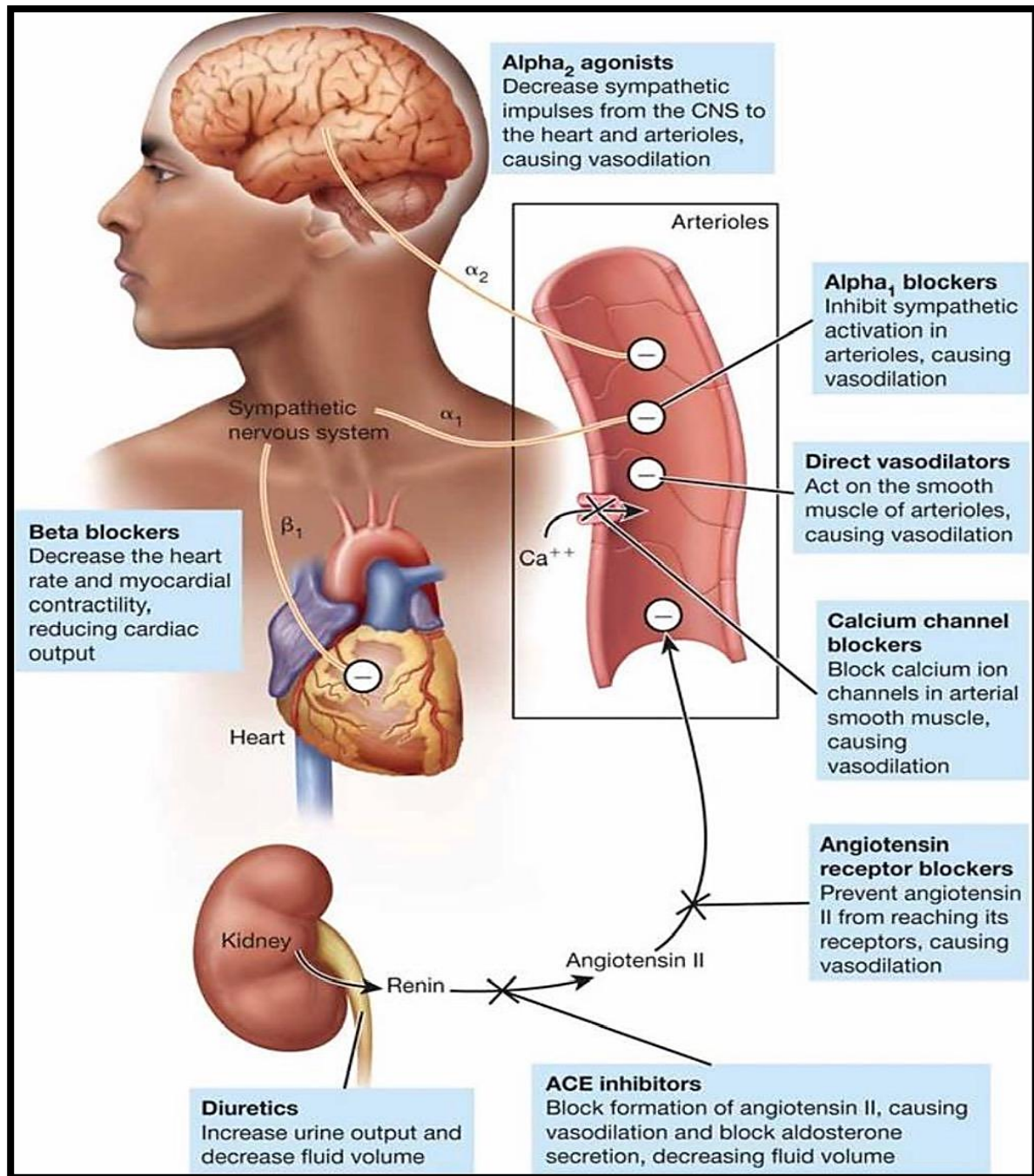
initiated. **CCBs block these channels and inhibit calcium from entering the cell, limiting muscular contraction leading to relaxation of smooth muscle in arterioles, lowering peripheral resistance and decreasing blood pressure.**

- **Indications:** Treat hypertension, treatment of angina and dysrhythmias.

#### **6. Vasodilators:**

- **E.g:** (Hydralazine, Minoxidil, nitroprusside)
- **Mechanism of action:** (The direct-acting smooth muscle relaxants), act by producing relaxation of vascular smooth muscle, primarily in arteries and arterioles. This results in decreased peripheral resistance and, therefore decrease blood pressure.
- **Indication: Hydralazine:** is less commonly used now, available as injectable forms to treat hypertensive emergencies.  
**Nitroprusside:** to treat hypertension by intravenous infusion for emergencies.
- **Side effects:** Tachycardia, palpitation, angina, it is common, Excessive hypotension.





**Mechanism of action of antihypertensive agents**