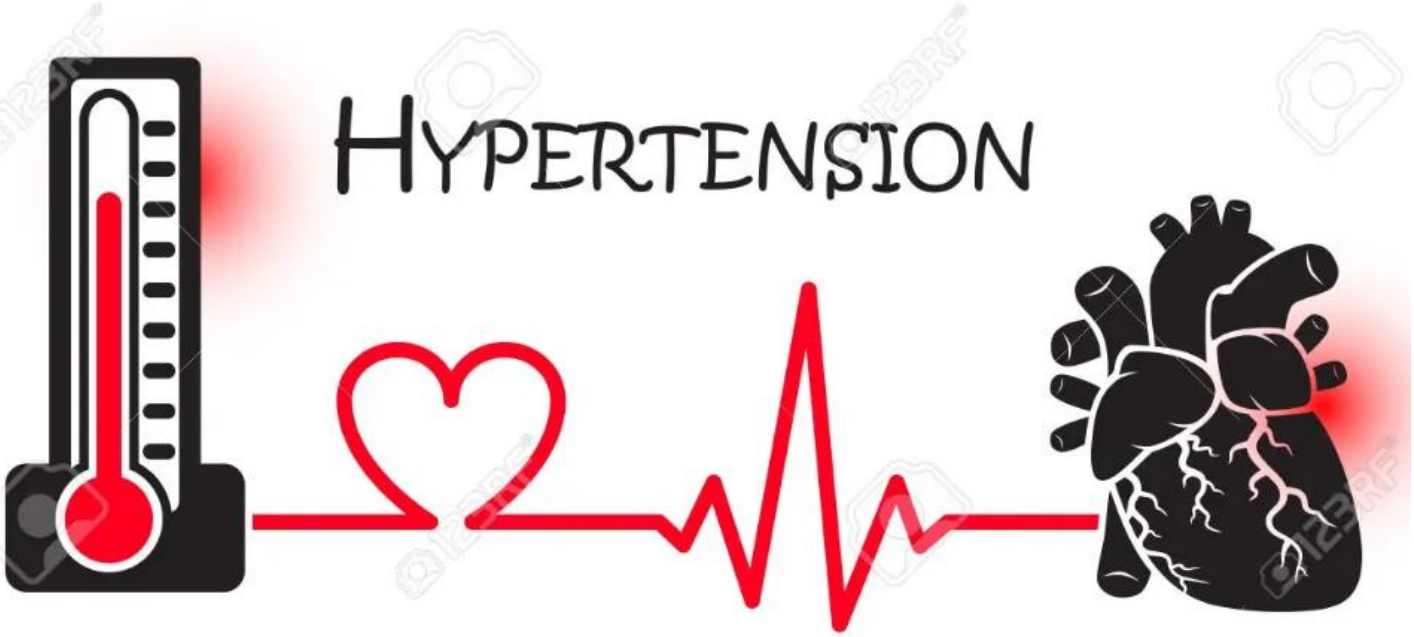
Block CVS-206

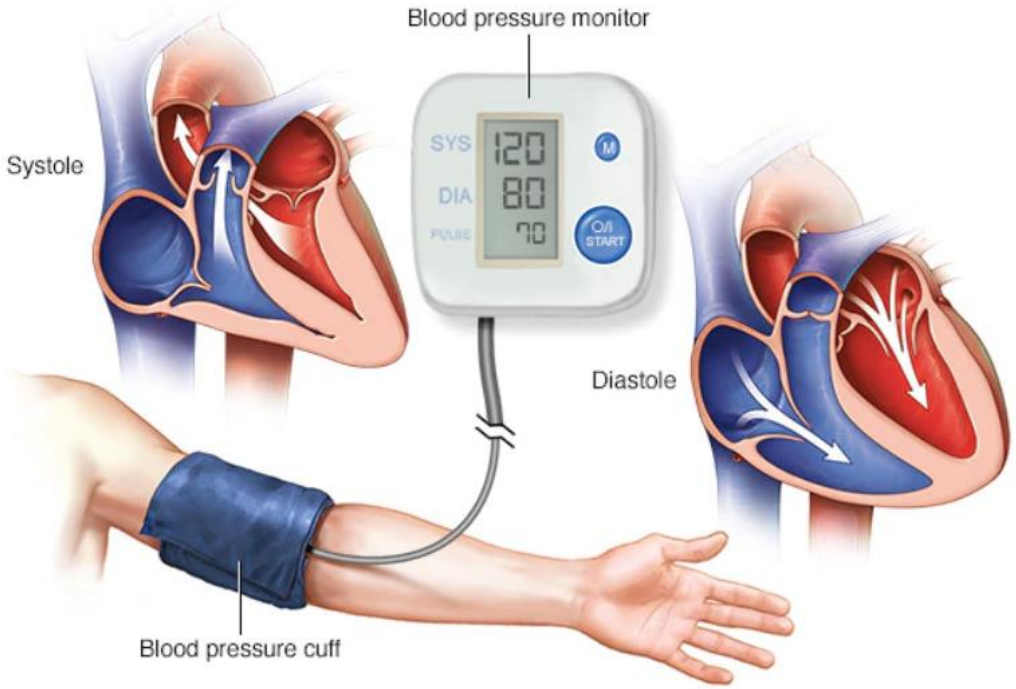
Hypertension



Dr Lobna Aly Abdelzaher

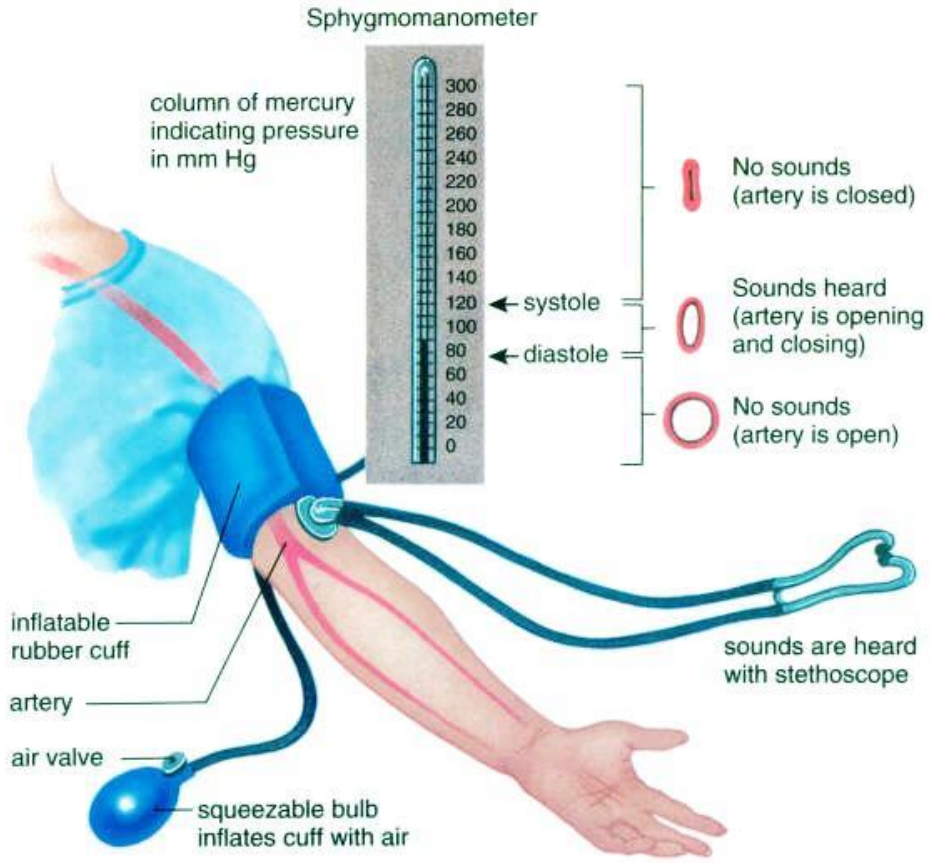
Associate Professor of Pharmacology

Faculty of medicine

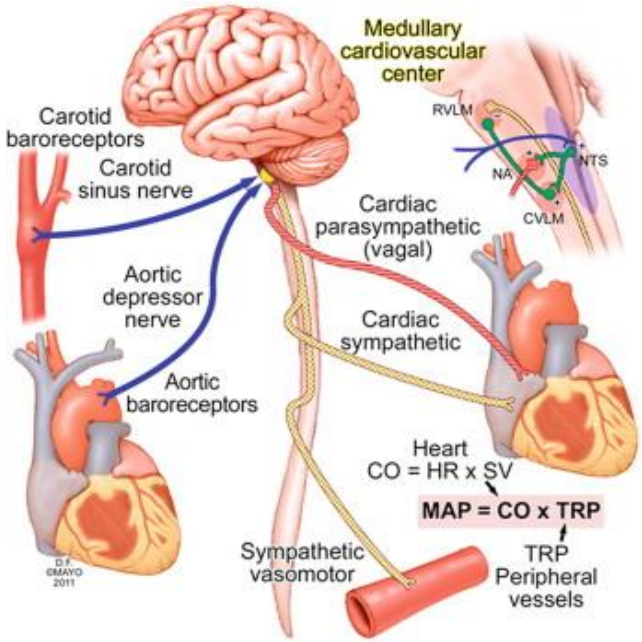


- **Blood pressure (BP)** is the pressure of circulating blood on the walls of the artries.
- Blood pressure is usually expressed in terms of :
  - systolic pressure.
  - diastolic pressure .

How to measure blood pressure



Normal regulation of blood pressure



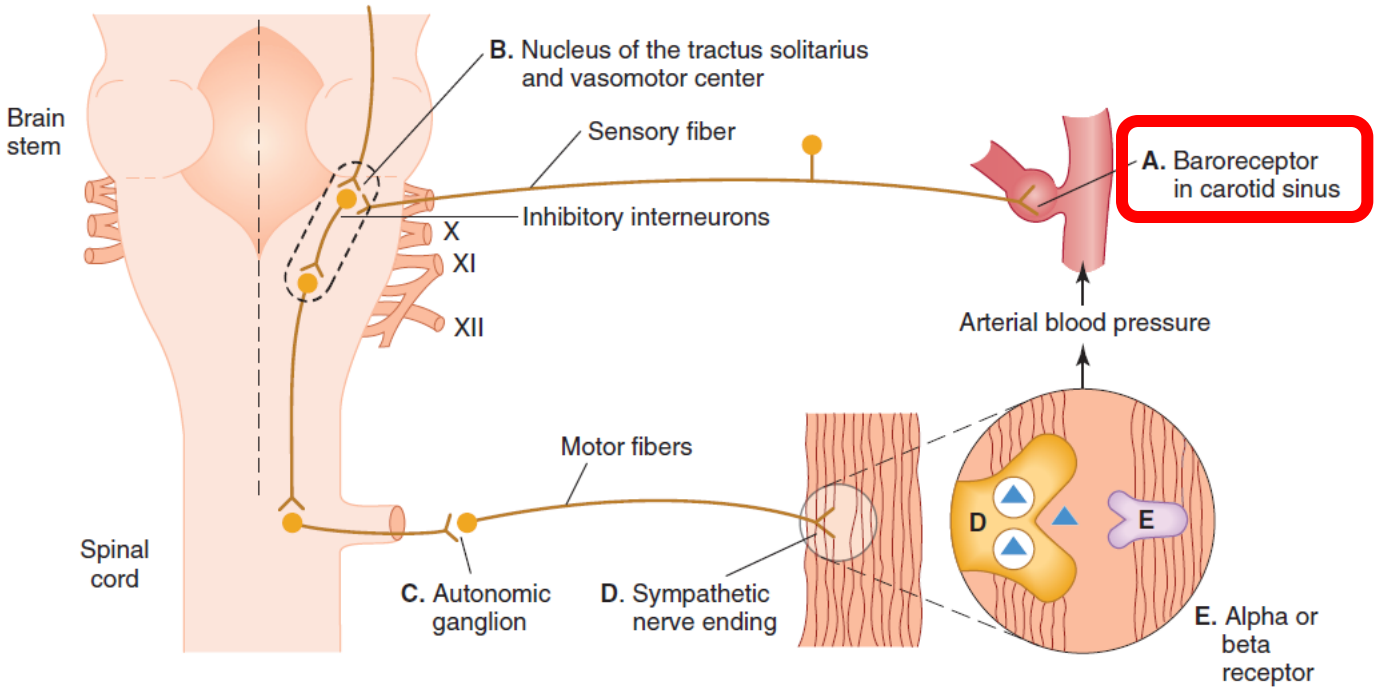
BP = Cardiac Output (CO) X Peripheral Vascular Resistance (PVR)

- **Cardiac Output (CO)**: **CO** = Stroke Volume (**SV**) **X** Heart Rate (**HR**)
- **Stroke Volume (SV)**: is the volume of blood pumped from the left ventricle of the heart per beat.
- **Heart Rate (HR)**: is the speed of the heartbeat measured by the number of poundings of the heart per unit of time (typically beats per minute).

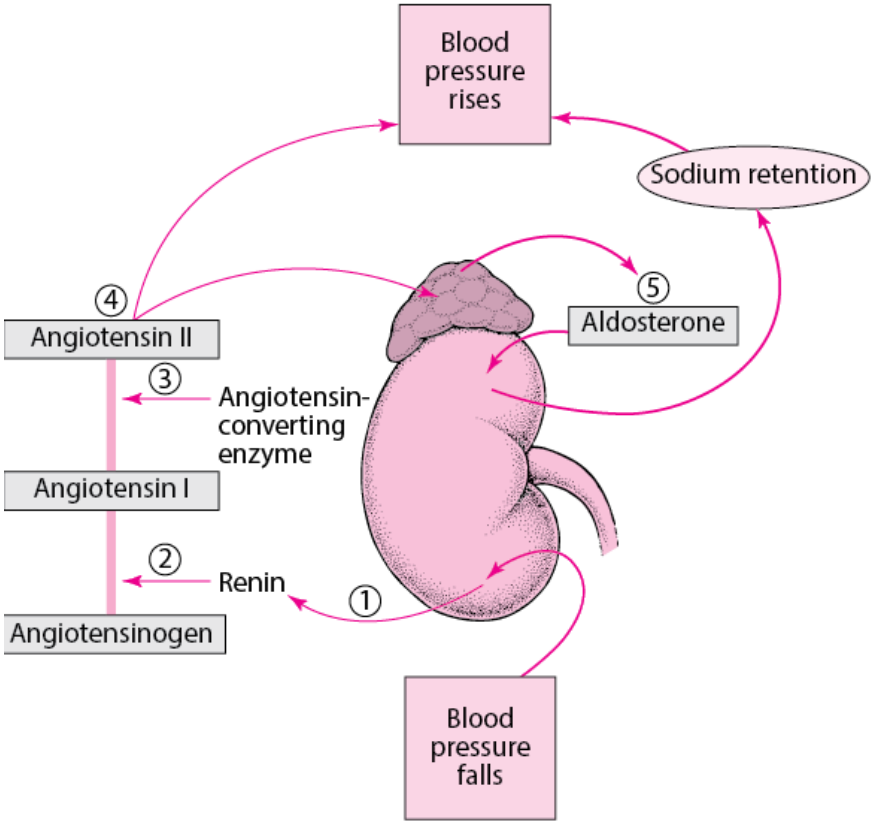
  - ***Increase*** CO or PVR, or both ⇨ ***Increase*** BP.
  - ***Decrease*** CO or PVR, or both ⇨ ***Decrease*** BP.

- **Mean BP** is 1/3 of systolic + 2/3 of diastolic pressure.
- **Pulse pressure** is the systolic – diastolic pressure.
- **BP** = cardiac output (COP) X peripheral resistance (PR).
- Systolic BP depends mainly on COP while diastolic depends on PR.

Baroreceptor Reflex



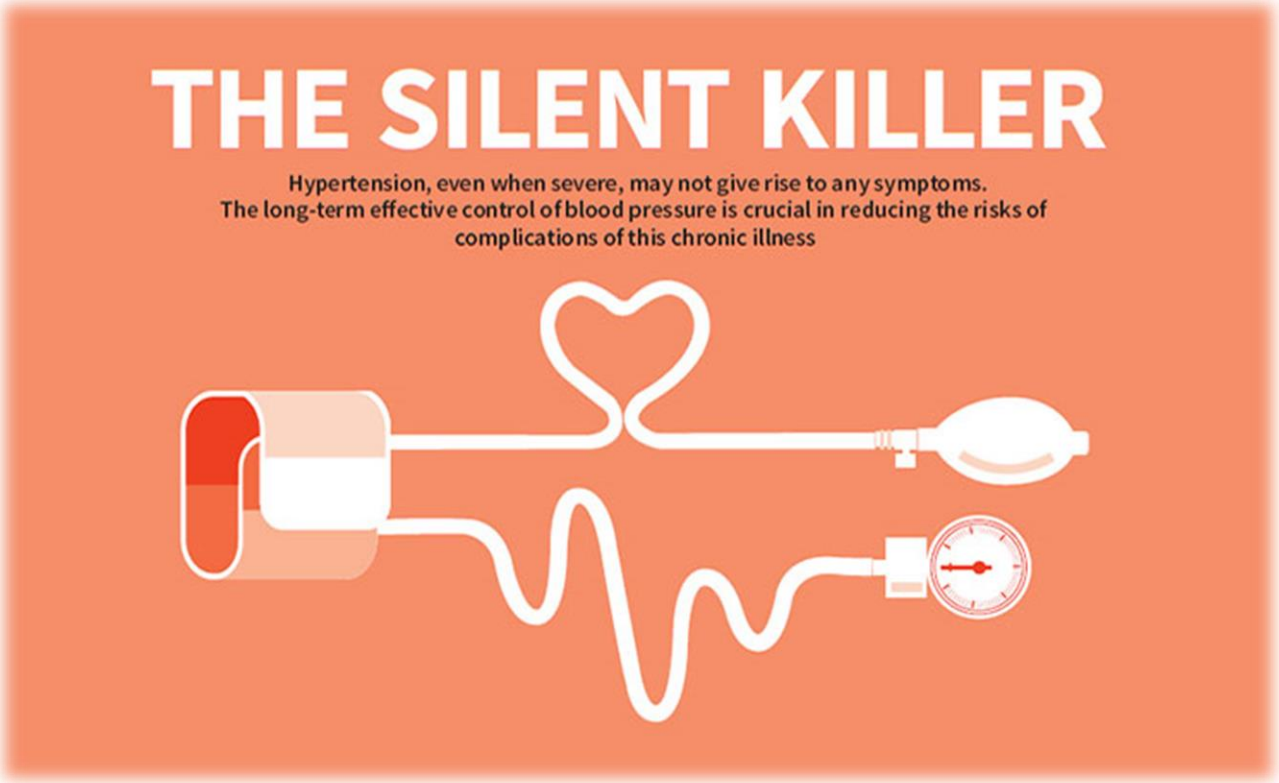
The Renin-Angiotensin-Aldosterone System



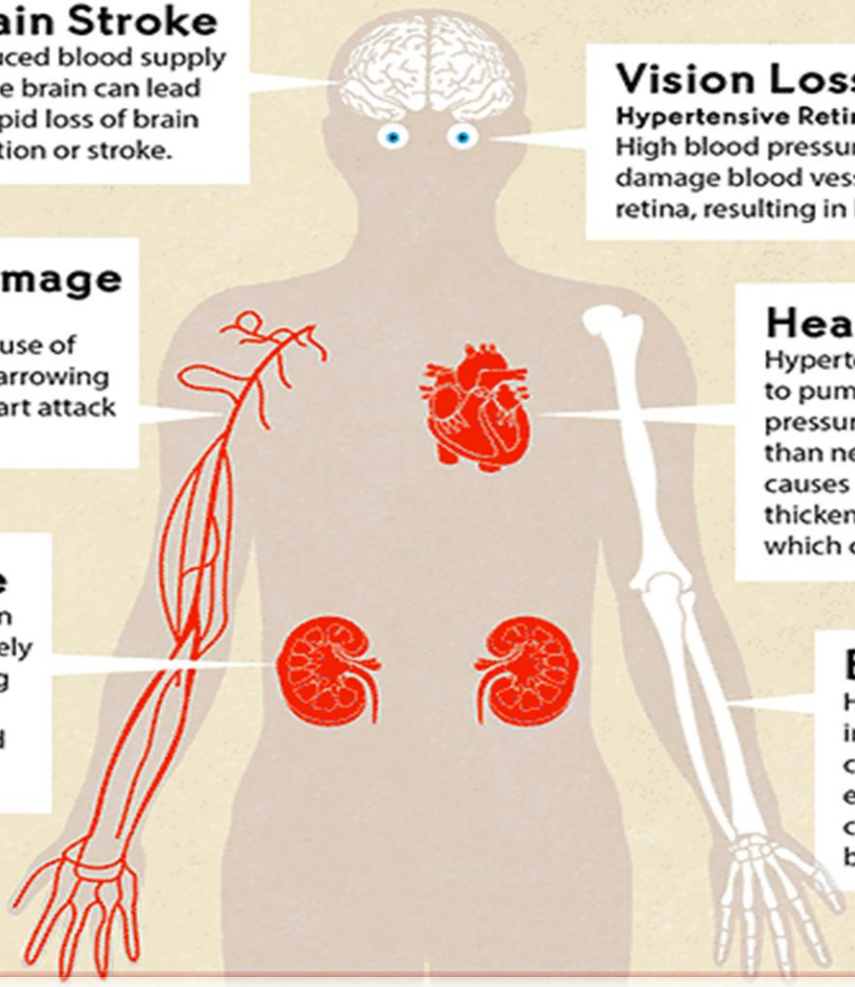
Hypertension

- **Sustained elevation of blood pressure ≥ 140/90 mm Hg.**
- Sustained increased blood pressure **damages blood vessels in kidney, heart, and brain leading to increased incidence of renal failure, coronary disease, heart failure, stroke and dementia**.
- It is **asymptomatic** disease.

Hypertension is **asymptomatic** in most cases



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).

Classification

- **According to the etiology:**
  - **Primary (essential hypertension)**:
    - **90% of** the cases.
    - **no cause** for hypertension.
    - Drug treatment to control but not cure hypertension.
  - **Secondary hypertension**:
    - **10% of** the cases.
    - They have **specific causes** (e.g. renovascular disease, cushing syndrome and pheochromocytoma).
    - The treatment of the cause can lead to cure from hypertension.
- **According to the degree of rise in BP:**

Category	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Mild	140- 159	90 – 99
Moderate	160-179	100 – 109
Severe	≥ 180	110 - 130
Crisis		≥ 130

* **Isolated systolic hypertension**: systolic BP above 140-160 mmHg while diastolic BP is normal below 90 mm Hg. It is usually encountered in elderly patients above 60 years old.

- **JNC classification of hypertension:**

Systolic/diastolic BP (mm Hg)	Category
< 120/80	Normal
120-135/80-89	Prehypertension
≥ 140/90	Hypertension
140-159/90-99	Stage 1
≥ 160/100	Stage 2

➢ **Hypertensive Crises :-**

- *Hypertensive crisis*; patients with blood pressures (BP) ≥ 180/110 mm Hg.
  - This condition has been classified as hypertensive emergencies and hypertensive urgencies;
    - **Hypertensive urgency**;
      - Elevations in BP (≥ 180/110 mm Hg) without progressive target-organ damage.
      - May or may not experience one or more of these symptoms: severe headache, shortness of breath, nosebleeds and severe anxiety.
    - **Hypertensive emergency**;
      - Severe elevations in BP (≥ 180/110 mm Hg) with the presence of acute or ongoing target-organ damage.
      - Acute target-organ damage can include; hypertensive encephalopathy, intracranial hemorrhage, acute myocardial infarction, acute heart failure, pulmonary edema (shortness of breath), aortic dissection, retinopathy or papilledema, decreased urine output or acute renal failure and eclampsia.

Risk Factors

Hypertension Risk Factors :-

- **Risk factors that can be controlled are:**
  - High cholesterol level.
  - Tobacco use (Smoking).
  - Diabetes mellitus.
  - Overweight and obesity.
  - Physical inactivity.
  - High salt intake.
  - Coarctation of the aorta.
  - Sleep apnea.
- **Risk factors beyond our control are:**
  - Age.
  - Family history of heart disease.

Diagnosis

- Hypertension is diagnosed by measurement of the BP using **sphygmomanometer at three different times**.
- **Lab tests** to detect complications:
  - Renal function tests and urine analysis.
  - Fundus examination.
  - ECG.
  - Fasting blood glucose.
  - Serum lipids.
  - Serum potassium.
  - Investigations to detect secondary causes of hypertension.

Treatment

- **Aim of treatment:**
  - To achieve blood pressure lowering below 140 / 90 mmHg in general population, below 130/85 mmHg in diabetic patients and below 125 / 75 mm Hg in patient with renal disease.
- **Antihypertensive therapy** includes
  - Non-pharmacological therapy and
  - Drug therapy.

Non-pharmacological treatment

- *Weight reduction*,
- *Reduce salt intake*,
- *Intake of potassium rich diet* (K+ increase excretion of Na+ and decreases renin secretion).
- *Stop smoking*,
- Avoid stress,
- *Aerobic physical activity* (30-45 minutes per day).
- *Reduce intake of cholesterol and saturated fat in diet*.

Drug therapy

- Since arterial blood pressure = COP x PVR, drugs used in hypertension act to decrease:

a) COP

- by decreasing myocardial contractility,
- venodilators or
- diuretics.

b) PVR

- by arterial vasodilation through interfering with the activity of systems that produce constriction of blood vessels as:
  - sympathetic nervous system and
  - renin-angiotensin aldosterone system.

c) Both CO and PVR.

- **First line drugs**:
  - ***Diuretics***,
  - ***β-blockers***,
  - ***Drugs affecting renin-angiotensin-aldosterone system:***
    - *Angiotensin converting enzyme inhibitors (**ACEIs**),*
    - *Angiotensin receptor blockers (**ARBs**),*
    - ***Renin inhibitors** and aldosterone antagonists*
  - ***Calcium channel blockers (CCBs)***.
- **Second line drugs:**
  - ***Sympatholytics** **except β-blockers***,
  - ***Direct vasodilators*** are alternatively used when the first line drugs failed to control hypertension.

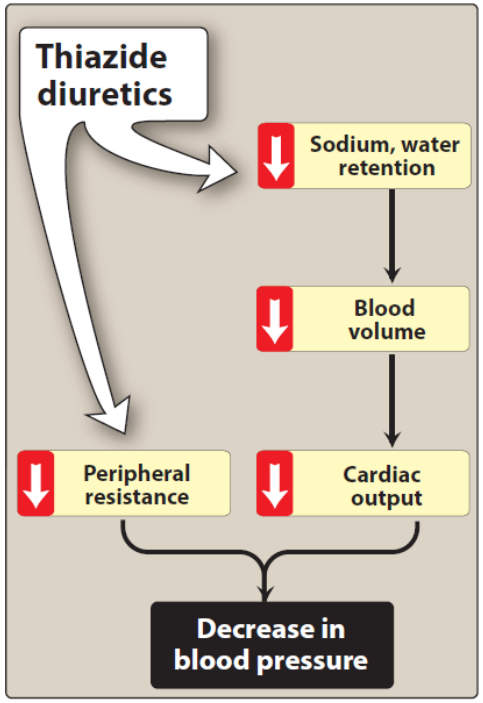
- The choice of antihypertensive drugs for individual patients is complex and generally **empirical**.

Antihypertensive Drugs

Antihypertensive drugs are classified into 5 groups:

1. **Diuretics**
2. **β –blockers**
3. **Drugs affecting renin-angiotensin aldosterone systems**
4. **Calcium channel blockers**
5. **Sympatholytics (except β –blockers)**
6. **Direct vasodilators**

1-Diuretics



Actions of thiazide diuretics

- **Initially**, they decrease plasma volume by **suppressing tubular re-absorption of sodium**.
- **With chronic therapy**, they **reduce the peripheral vascular resistance**.

Clinical Application

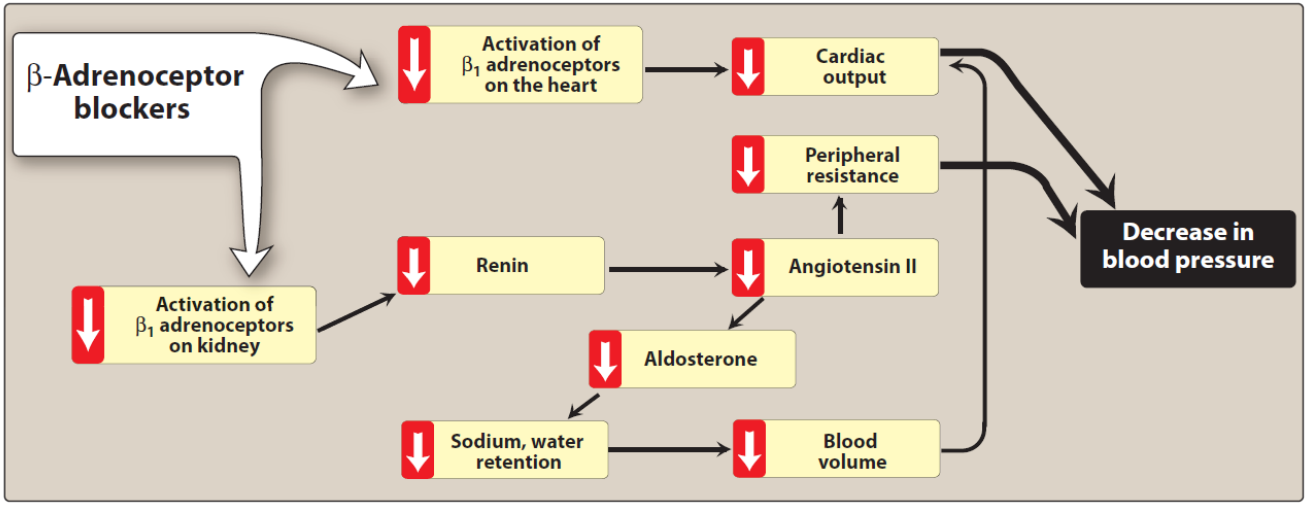
1. ***Thiazides:*** are frequently used in **mild-moderate** HTN (normal renal function is mandatory).
   - **Not suitable in cases of emergency & severe renal dysfunction**.
   - Not used in diabetics, gout, hyperlipidemia and hypokalemia.

2. ***Loop diuretics:*** due to rapid onset and short duration, preferred to be used in:
   a. **Hypertensive emergencies** (I.V.) & severe hypertension (orally).
   b. **All grades of hypertension** if patients with renal dysfunction (when glomerular filtration rate is less than 30 or 40 mL/min).
   c. **Hypertensive patients with pulmonary edema**.

3. ***K-sparing diuretics*** are **weak antihypertensive** but often used to **compensate hypokalemia of K-depleting diuretics**.

2-β-adrenergic blocking agents

- ***Propranolol, Metoprolol, Bisoprolol, Labetalol, Nebivolol*** and ***Carvedilol***.
- β-blockers lower BP by the following suggested mechanisms:
  - ***a) Blocking β1 receptors in heart***
  - ***b) Blocking β1 receptors in the kidneys*** (decreasing renin release).
  - **c) Central effects** (decrease sympathetic discharge).



Therapeutic applications:

- Effective therapy for all grades of hypertension.
- the ***elderly*** and ***blacks*** tend to have less antihypertensive response to β-blocking agents.
- Highly preferred drugs for hypertensive patients with ***MI, cardiac ischemia, congestive heart failure (carvedilol or metoprolol)*** or ***SVT***.
- **Cardio-selective β- blockers** are preferred in patients with **bronchial asthma, diabetes mellitus, and peripheral vascular diseases**.
- **Vasodilator β- blockers** *are used as the following:*
  - ***a) Labetalol*** (mixed α1+β-antagonist) is given IV in **hypertensive emergencies**.
  - ***b) Carvedilol*** (mixed α1+β-antagonist) has been approved for the treatment of **hypertension with symptomatic heart failure**.
  - ***c) Nebivolol*** (β1 selective blocker + NO releasing agent) is useful in **hypertensive patients with erectile dysfunctions.**

Precautions of β- Blockers:

- Used **cautiously in:**
  - Patients with **diabetes mellitus**
  - Patients with **bronchial asthma or COPD.**

- **Avoid sudden cessation of BBs to avoid rebound tachycardia and/or hypertension**.

3- OTHER SYMPATHOLYTICS

α1-receptors blockers:

- ***Prazosin***, ***Terazosin***, and ***Doxazosin***.
- α1-receptor antagonists are **not recommended as monotherapy** for hypertensive patients but used primarily in conjunction **with diuretics and β blockers.**
- α1-receptor blockers are attractive drugs for ***hypertensive patients with benign prostatic hyperplasia***.
- May cause ***first dose hypotension***, so it is better to used at bed time.

Methyldopa:

- *Methyldopa* is a **centrally acting antihypertensive agent**.
- It **decreases central sympathetic outflow to the blood vessels causing vasodilation and decrease in PVR**.
- Methyldopa is a preferred drug for treatment of **hypertension with pregnancy**.

Trimethaphan:

- It acts by **blocking of the sympathetic and parasympathetic ganglia**.
- It is used by I.V. infusion in **hypertensive emergency** as the last choice because of undesirable responses.

Reserpine:

- In **combination with diuretics**, it is used in the treatment of hypertension, especially in the elderly.
- It has both central and peripheral effects. **It depletes storage of catecholamines in the peripheral nerve endings**.

4- CALCIUM CHANNEL-BLOCKERS (CCBs)

Classification:

*1- **Dihydropyridine derivatives:***

- ***e.g.,*** Nifedipine and Amlodipine.
- They produce vasodilation with reflex tachycardia.

*2- **Non-dihydropyridine:***

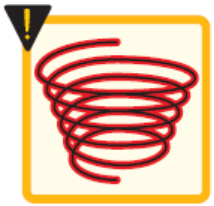
- ***e.g.,*** Diltiazem and Verapamil
- They cause vasodilation with –ve chronotropic & -ve inotropic effects.

Mode of antihypertensive action:

Blocking Ca2+ channels (L-type voltage-sensitive type) causing decrease of intracellular Ca2+ **causing vasodilation of arterial beds with reduction in peripheral vascular resistance and BP**.

Uses:

- **Stage 1 and stage 2 hypertension** as a monotherapy.
- **Isolated systolic hypertension**: in elderly Patients (e.g., amlodipine) with thiazide diuretics.



Adverse effects:

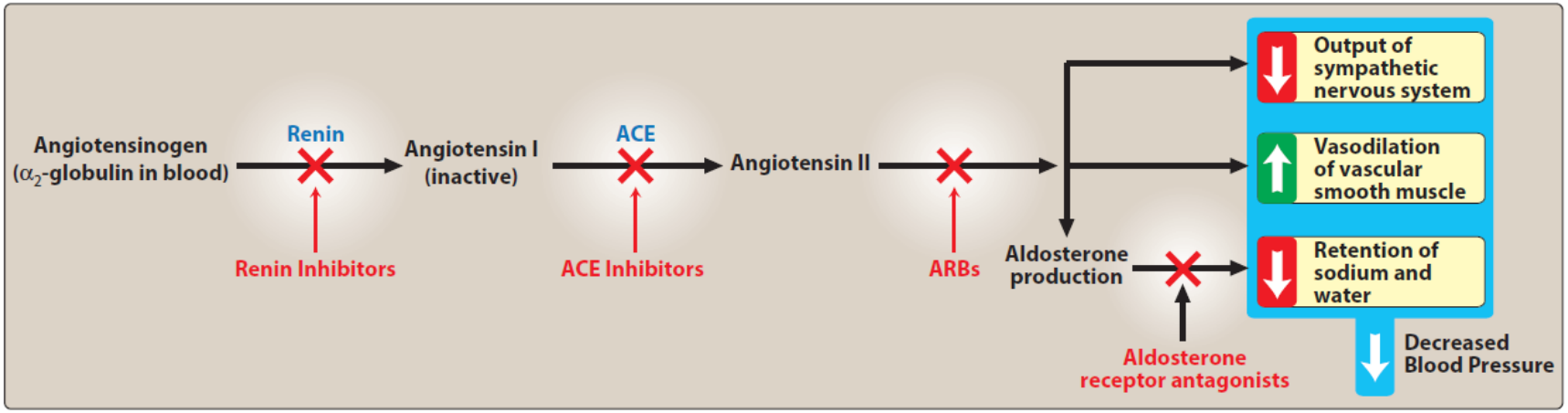
- ***Cardiac failure:*** with verapamil & diltiazem (if used I.V. and in patients recently treated with beta-blockers).
- ***Bradycardia*** and ***transient asystole***: with verapamil and diltiazem and ***heart block***.
- **Reflex tachycardia:** only with dihydropyridines.
- ***Flushing, headache, dizziness and nausea.***
- ***Ankle swelling and peripheral edema:*** common with dihydropyridine, uncommon with verapamil.
- ***Constipation:*** frequently with Verapamil.
- ***Hypotension:*** may occur especially with dihydropyridines due to excessive VD.
- **Gastroesophageal reflux:** due to relaxation of lower esophageal sphincter.
- **Aggravation of myocardial ischemia** due to excessive hypotension by large dose.

5-DRUGS AFFECTING RENIN-ANGIOTENSIN ALDOSTERONE SYSTEM

A. Angiotensin Converting Enzyme Inhibitors (ACE inhibitors)

B. Angiotensin Receptor Blockers (ARBs OR SARTANS)

C. Renin Inhibitors (Aliskiren)

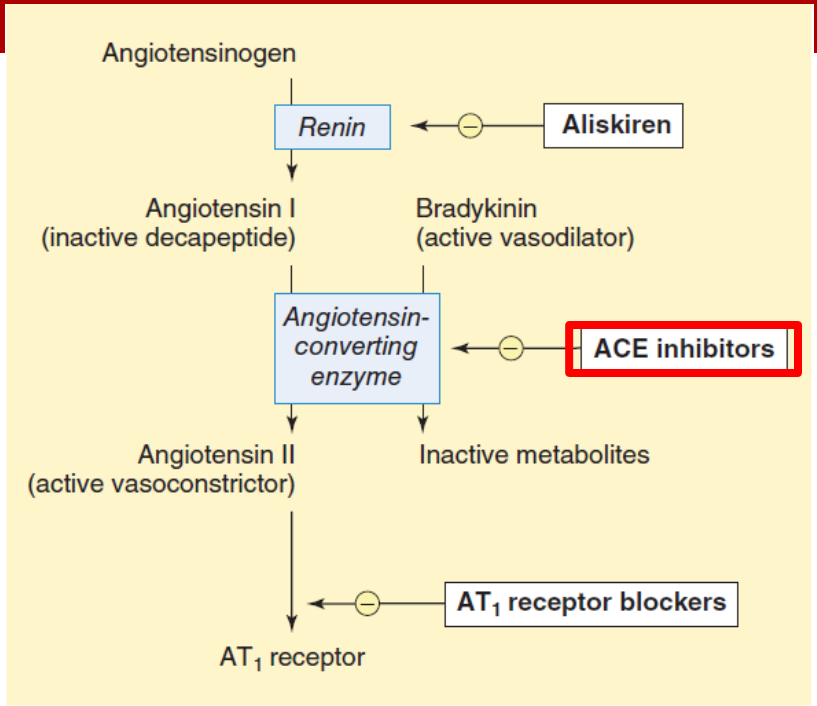


Dr Lobna Aly Abdelzaher

2025-2026

A-Angiotensin Converting Enzyme Inhibitors (ACEIs)

- ***Captopril***.
- ***Enalapril*** is an oral prodrug metabolized to enalaprilat, with effects similar to short acting captopril but with longer duration of action.
- ***Lisinopril***, ***ramipril***, ***fosinopril***, ***benazepril***, ***moexipril***, ***perindopril***, ***quinapril***, ***ramipril***, ***and trandolapril*** are long-acting members of this class become available.
- These drugs have proven to be very **useful for the treatment of hypertension** because of their **efficacy** and their very **favorable profile of adverse effects**, which enhances patient adherence.



Mechanism of antihypertensive action:

a) They **decrease angiotensin II formation** (which is a potent vasoconstrictor, and stimulator for sympathetic and aldosterone secretion) leading to **vasodilation**, **decrease Na+/water retention** with **subsequent decrease in BP**.

b) **Reduce metabolism** of vasodilator **bradykinin** with subsequent increase in its level.

c) **Increase the synthesis of vasodilator prostaglandins** (PGI2 and PGE).

d) They **decrease vascular and cardiac smooth muscle proliferation and hence decrease remodeling**.

Pharmacokinetics:

1. Oral bioavailability of captopril is 65 %, and decreased to 30-40 % in presence of food.
2. **t½** of captopril is **3 hours**, but other drugs are long acting **t½:11-13 hours**.
3. All ACEIs (except captopril and lisinopril) are **prodrugs**, so they have slow onset of action.
4. Enalapril is **more potent** and **longer duration** of action than captopril (but has **slow onset**).
5. Enlapril is rapidly absorbed orally and absorption is less affected by food as captopril.

Therapeutic indications:

1- Hypertension:

- Young and middle-aged white patients have a higher probability of responding to ACE inhibitors; while, **elderly and black patients are more resistant** to the hypotensive effect of these drugs.

  Advantages of ACE inhibitors in hypertension:

  a) Unlike direct sympatholyic drugs, **the cardiovascular reflexes are retained** and **do not cause postural hypotension**.

  b) Unlike β-blockers, they are **not contraindicated in bronchial asthma** and **diabetes**.

  c) Unlike thiazides diuretics, they **do not cause hypokalemia, hyperglycemia**, **hyperuricemia** or **hyperlipidemia**.

  d) Do **not impair quality of life**, as they **rarely cause impotence** or fatigue.

2- Diabetic nephropathy:

- ACEIs were found to retard significantly the development of renal failure.

a) **Reduction of glomerular capillary pressure** (which induces glomerular injury).

b) **Decrease in mesangial cell growth and matrix production**, which are increased in diabetic nephropathy by reducing angiotensin II formation.

3- Heart failure:

- ACE inhibitors are first line therapy in the treatment of heart failure as they decrease preload, afterload and have antiremodeling effect).

4- Post - myocardial infarction.

5-Reduce the incidence of diabetes in patients with high cardiovascular risk: recent approval.

Side effects:

1- First dose phenomenon avoided by beginning with small dose, giving first dose at bed time, correcting any salt depletion, and stop diuretics few days before administering these drugs.

2- Chronic dry cough (bradykinin).

3- Angioedema: rare but dangerous (especially laryngeal edema) due to accumulation of bradykinin.

4- Skin rash and alteration in taste sensation (dysgeusia): with captopril only (as it contains sulfhydryl group).

5- Proteinuria and neutropenia (bone marrow suppression).

6- Hyperkalemia especially if the patient uses K-sparing diuretics, B-blockers, NSAIDs, K-supplements or in renal insufficiency.

7- Acute renal failure in patients with bilateral renal artery stenosis, heart failure or dehydration.

8- Fetopathic potential if given during the second or third trimester.

9- With chronic use, compensatory *increase in renin secretion*.

Drug interactions:

1. If used with potassium supplements or potassium-sparing diuretics, can result in hyperkalemia.
2. Nonsteroidal anti-inflammatory drugs may impair the hypotensive effects of ACEIs by blocking bradykinin mediated vasodilation, which is mediated by prostaglandins.

B. Angiotensin Receptor Blockers (ARBs)

Members:

- **Losartan**, **valsartan**, **candesartan**, **irbesartan** and **telmisartan.**

Mechanism of action:

• **Competitive antagonists of angiotensin II at AT1 receptors** leading to:

- Vascular dilatation (antihypertensive).
- Increase in renal salt and water excretion.
- Reduction in plasma volume.
- Decrease cellular hypertrophy with antiremodeling effect.

Uses:

a) They provide benefits similar to those of ACE inhibitors in patients with **heart failure, hypertension and chronic kidney disease**.

b) They are also effective in patients with **portal hypertension**.

Side effects:

a) Similar to those of ACEIs as hypotension, hyperkalemia and fetopathic potential

b) Unlike ACEIs, ARBs ***do not cause cough or angioedema*** as they do not increase the level of bradykinin (advantages over ACEIs).

C. Renin Inhibitors (Aliskiren)

Mechanism and pharmacological actions:

- It acts by **inhibition of renin activity**, so it inhibits the first and rate-limiting step in renin angiotensin system i.e., ***aliskiren*** decreases plasma renin activity.
- **It can completely inhibit renin angiotensin system** (ACEIs and ARBs cause incomplete inhibition due to presence of alternative pathways and compensatory feedback mechanism which can cause increase in plasma renin activity).

Advantages:

1. It causes **complete inhibition of renin-angiotensin system activity**.
2. It does not affect bradykinin metabolism, so it does not cause cough or angioedema.
3. **Can be used orally once / day** (t ½ is 24 h.) and effective in controlling blood pressure in mild to moderate hypertension regarding the age or the gender.
4. **No rebound hypertension after discontinuation** of the therapy.
5. **Well tolerated by most of patients.**
6. It shows **additive effect when used with other antihypertensive drugs**.

Therapeutic uses:

- Treatment of mild to moderate hypertension and CHF.

Adverse effects: Headache, dizziness and diarrhea.

6- DIRECT VASODILATORS

- They cause relaxation of smooth muscles of arterioles only **except** Na+ nitroprusside which dilates also veins, so they decrease the peripheral resistance and BP.
- They include:
  - ***a) Oral direct vasodilators***: e.g., hydralazine and minoxidil (hydralazine is used also I.V. and I.M.). They are used for long-term therapy orally.
  - ***b) Parenteral direct vasodilators:*** e.g., Na+ nitroprusside, diazoxide and fenoldopam, they are used to treat hypertensive emergency.

A) HYDRALAZINE

Mechanism of action:

- It acts by **direct relaxation of arteriolar smooth muscle** by unknown mechanism, so it decreases peripheral vascular resistance (PVR) and BP.
- The vasodilation is associated with:
  - a) **Reflex tachycardia**.
  - b) Increase in plasma renin activity associated with **Na+ and water retention**.
- Reflex tachycardia and Na+/water retention cause increase in the BP leading to rapid decrease in its antihypertensive effect (***tachyphylaxis***).
- To avoid this tachyphylaxis effect, hydralazine must be combined with β-blockers and diuretics.

Side effects:

1- ***Excessive vasodilation*****:** headache, dizziness, flushing, nausea and vomiting. In severe cases, it may cause ***hypotension***.

2- ***Reflex tachycardia*** which may induce anginal attacks in ischemic heart.

3- ***Salt and water retention***.

4- ***Lupus erythematosus -like syndrome*** due to immunological reaction:

- It occurs with ***chronic use*** of ***large dose*** in ***slow acetylators.***
- Manifestations are fever, arthralgia, myalgia and skin rash.

5- ***Peripheral neuropathy*** as the drug binds to pyridoxine to form hydrazone.

B) MINOXIDIL

Mechanism of action:

- Minoxidil is prodrug, metabolized **by hepatic** "sulfotransferase" into minoxidil sulphate (active form) which causes direct vasodilation.
- It acts by **increasing the K+ efflux through BV membrane (K+ channels opener) causing hyperpolarization and smooth muscle relaxation**.
- As hydralazine, it causes increase in sympathetic outflow, Na/water retention and increase in renin secretion. It is preferred to be used in **combination** with beta blockers and diuretics.

Therapeutic uses:

1- ***Orally:*** in severe hypertension or CHF in combination with B-blockers and diuretics.

2- ***Topically:*** to stimulate hair growth in male baldness and alopecia.

Side effects:

a) ***Excessive vasodilation***: headache, dizziness, flushing, nausea and vomiting.

b) In severe cases, it may cause ***hypotension***.

c) ***Reflex tachycardia***.

d) ***Salt and water retention***.

e) ***Hypertrichosis*** (increase hair growth) may due to K+-channel activation.

C) DIAZOXIDE

Mechanism of action:

- It acts by direct dilation of arteries by opening of K+ channels (similar to minoxedil).

Therapeutic uses:

1. ***Hypertensive emergencies*** (it is used by rapid I.V. injection), may combined with B-blockers.
2. Treatment of ***hypoglycemia due to hyperinsulinoma*** because it decreases insulin release.

Side effects:

1. **Excessive vasodilation**: headache, dizziness, flushing, nausea and vomiting.
2. In severe cases, it may cause **hypotension** and **reflex tachycardia.**
3. **Salt and water retention** but usually it is not a problem as the drug is used as a short term treatment.
4. **Hyperglycemia** due to decrease in insulin secretion by stimulation of K+-channels.

D) FENOLDOPAM

- It is a **peripheral arteriolar dilator**; acts as agonist on D1-receptors causing dilatation of the arteries and natriuresis.
- It is used by **continuous I.V. infusion in the treatment of hypertensive emergency** and **postoperative hypertension**.
- Excessive vasodilatation & increases IOP are side effects.

E) SODIUM NITROPRUSSIDE

Mechanism of action:

- It dilates both **arteries and veins**. It acts by activation of guanylate cyclase enzyme (either by the drug or its metabolite i.e. nitric oxide, so it increases cGMP which causes relaxation of vascular smooth muscles and reduces BP.

Therapeutic uses:

i. ***Hypertensive emergencies*** (IV infusion as a short term treatment). It is the drug of choice due to rapid, strong and controllable effect.

ii. ***Severe cardiac failure*** (as a short term treatment) as it decreases preload & afterload.

iii. ***To induce controlled hypotension during anesthesia***: as it decreases bleeding.

Side effects:

1. ***Excessive vasodilation:*** headache, dizziness, flushing, nausea and vomiting.
2. ***Hypotension and reflex tachycardia:*** in severe cases.
3. ***Accumulation of cyanide***

TREATMENT OF HYPERTENSIVE EMERGENCIES & URGENCIES

Hypertensive crisis: critical rise in diastolic BP (>130 mmHg):

a) **HTN emergency:** HTN crisis with end organ damage as heart failure, renal failure, hypertensive encephalopathy.
b) **HTN urgency:** HTN crisis without end organ damage.

HTN Emergency

- Parenteral therapy in ICU with rapid lowering of BP (within a few hours) provided that diastolic must be lowered to only 100-110 mm Hg) not less because excessive fall of BP may lead to hypoperfusion of vital organs that may results in stroke & MI (Rapid normalization of blood pressure may lead to cerebral hypoperfusion and brain injury). When diastolic BP being 110 mm Hg, patients is switched into oral medications at home. Drugs used include:
  i- ***Sodium nitroprusside*** (by I.V. infusion pump) is first choice.
  ii- Other parenteral drugs ***nitroglycerin, furosemide, labetalol, trimethaphan, diazoxide, hydralazine, enalaprilate, fenoldopam*** are alternatives.
  iii- ***I.V. Esmolol*** is used in intra-and post-operative hypertension (short duration).

HTN Urgency

- Need prompt medical treatment, BUT, lowering BP can be achieved within 24-48 h by **vigorous oral therapy at home**. Oral captopril or clonidine can be used.

CHOICE OF THE DRUG FOR TREATMENT OF HYPERTENSION

1. **Begin by single drug: (one of the following drugs)**
   - **a) Thiazides diuretics:**
     - First choice, less expensive
     - Better in elder, obese and in presence of CHF or edema
     - Not used in diabetics, gout, hyperlipidemia and hypokalemia
   - **b) β-adrenergic blockers:**
     - Better in young, in presence of angina or arrhythmia, but not used in acute HF.
     - Non-selective blocker should be avoided in D.M., bronchial asthma and vasospastic angina.
   - **c) Ca++ channel blockers:**
     - Used if patient cannot tolerate diuretics or B-blockers
     - Used in elder, black, asthma, left ventricular hypertrophy, arrhythmia, D.M. and gout, but not used in CHF.
   - **d) ACE inhibitors:**
     - Used if patient cannot tolerate diuretics or B-blockers.
     - Used in CHF, D.M., asthma, arrhythmia, gout, hypokalemia and in young adult males
2. **If no response to the initial monotherapy, switch to multiple drug therapy**

MULTIDRUG THERAPY OF HYPERTENSION

- The use of more than one drug in the treatment of hypertension.

Aim:

- To **increase the antihypertensive effect**, especially if there is less response to single drug.
- To **control severe hypertension** or **hypertensive crisis.**
- To **counteract adverse effects of a second drug**.
- To **improve potency and efficacy of drugs**.
- To **decrease the dose-related side effects**.

Examples:

1. **To decrease the side effects:**
   - Loop or thiazides diuretics + K-sparing diuretics to control the hypokalemia.
   - Thiazides + ACEIs (or ARBs) to control the effect on serum K+
2. **To increase the antihypertensive effect:** e.g., multiple drugs.


Thank
You