

HYPERTENSION



Hypertension

- Hypertension: Sustained systolic pressure of greater than 140 mm Hg or sustained diastolic blood pressure greater than 90 mm Hg
- Hypertension is caused by
 - ▣ Increased peripheral vascular arteriolar muscle tone which leads to increased arteriolar resistance

Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

Table 6

- Chronic hypertension can lead to
 - ▣ Cerebrovascular accidents (strokes)
 - ▣ Congestive heart failure
 - ▣ Myocardial infarction
 - ▣ Renal damage
 - ▣ Retinal damage

- The incidence of morbidity and mortality decreases by early diagnosis and treatment of hypertension

□ Causes of hypertension

- 90% of the cases the cause is unknown, essential hypertension, primary hypertension (idiopathic)
- Secondary Hypertension: caused by chronic renal disease (diabetic nephropathy), Pheochromocytoma, stress, aortic coarctation
- Family history of hypertension increases the chances of having higher blood pressure
- More common in middle aged males than females
- Environmental factors such as stress, high sodium diet, and smoking can increase the occurrence of hypertension

Risk Factors for Hypertension




- ❑ Blood relatives with hypertension
- ❑ Men over the age of 55
- ❑ Post-menopausal women
- ❑ Obesity
- ❑ Smoking
- ❑ Diabetes
- ❑ High blood cholesterol

- Arterial blood pressure is regulated within a narrow range to provide adequate tissue perfusion without damaging the vascular system
- Arterial blood pressure is directly proportional to cardiac output (CO) and peripheral resistance
- CO and peripheral resistance are controlled by:
 - Baroreflexes
 - Renin-angiotensin-aldosterone system

Mechanisms for controlling blood pressure

- Most antihypertensive drugs lower blood pressure by:
 - ▣ Reducing cardiac output or/and
 - ▣ Lowering peripheral resistance

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- The goal of hypertension treatment is to reduce cardiovascular and renal morbidity and mortality
 - Mild hypertension can be controlled with one drug but most patients require more than one drug to lower blood pressure
 - Currently therapy is started with a thiazide diuretic with other drugs added if needed

Antihypertensive drugs

- Diuretics
- β -blockers
- ACE inhibitors
- Angiotensin II receptor blockers
- Renin inhibitors
- Calcium channel blockers
- α -blockers
- Other

Diuretics

- First line therapy for hypertension (Thiazide)
- Helps prevent stroke, myocardial infarction and congestive heart failure
- Diuretics classes used for HTN
 - ▣ Thiazide diuretics
 - ▣ Loop diuretics
 - ▣ Potassium sparing diuretics

Thiazide diuretics

- Hydrochlorothiazide
- Mechanism:
 - ▣ Lower blood pressure by increasing sodium and water excretion
 - ▣ This decreases cardiac output and renal blood flow
 - ▣ With long term use peripheral resistance decreases
- Adverse effects
 - ▣ Hypokalemia
 - ▣ Hyperuricemia

Loop diuretics



Furosemide

- Decrease renal vascular resistance and increase renal blood flow
- Produce greater diuresis than thiazide
 - ▣ Used in patients with acute pulmonary edema
- Adverse effects:
 - ▣ Hypokalemia
 - ▣ Hearing loss
 - ▣ Dehydration
 - ▣ Hyperuricemia

Potassium sparing diuretics

- Amiloride inhibit sodium reabsorption in collecting duct
- Spironolactone, aldosterone receptor antagonist
 - ▣ Useful in patients with congestive heart failure
- Side effects:
 - ▣ Hyperkalemia

β -Blockers

- First line therapy for HTN when contaminant disease is present like chronic heart failure, angina, post MI
- Reduce blood pressure by decreasing cardiac output and renin release
- Block sympathetic activity and decrease renin and angiotensin II formation and aldosterone release thereby decreasing peripheral resistance and blood volume

β -Blockers

- Antihypertensive β -blockers
 - ▣ Propranolol (β_1 , β_2 blocker)
 - ▣ Metoprolol (β_1 blocker)
 - ▣ Atenolol (β_1 blocker)
 - ▣ Bisoprolol (β_1 blocker)
- Propranolol is contraindicated in asthma because they block β_2 receptors causing bronchoconstriction

β -Blockers

Adverse effects

- Bradycardia
- Hypotension
- CNS effects insomina, lethargy
- Decrease libido
- Sudden withdrawal can cause myocardial infarction
 - Tapering should be done when the drug needs to be stopped

α -Blockers

- Prazosin
- Terazosin

- Block α -1 receptors decreasing peripheral resistance and blood pressure by relaxing the arterial and venous smooth muscle
- Side effects
 - ▣ Orthostatic hypotension
 - ▣ Reflex tachycardia

α_1 -/ β - Blockers

- Labetolol
 - ▣ Can be used in emergency hypertension
- Carvedilol

- Mainly used for heart failure
- Side effects:
 - ▣ Bradycardia
 - ▣ Bronchoconstriction
 - ▣ Postural hypotension

α_2 -Agonists

- Clonidine
- Methyldopa (can be used in pregnant patients)

Decrease the sympathetic nervous system activity

- Side effects:
 - Abrupt discontinuation can cause rebound hypertension
 - Tapering should be done when the drug needs to be stopped

ACE inhibitors

- Enalapril
- Captopril

- Used when diuretics and β -blockers are ineffective or contraindicated

- Can be used in combination with a diuretic

- Mechanism
 - ▣ Lower blood pressure by inhibiting angiotensin converting enzyme, and reducing peripheral resistance
 - ▣ Reduce cardiac preload and afterload

ACE inhibitors

- Used in hypertensive patients with congestive heart failure, and patients with chronic renal disease and hypertension
- Adverse effects
 - ▣ Dry cough
(reversible upon discontinuation of the drug)
 - ▣ Hyperkalemia
 - ▣ Rash
 - ▣ Hypotension
 - ▣ Angioedema
- Contraindicated in pregnancy

Angiotensin II receptor blockers

- Losartan
- Valsartan
- Block angiotensin II binding to its receptors
- Mechanism: Lower blood pressure by causing arteriolar and venous dilation and block aldosterone secretion
- Adverse effects: similar to ACE inhibitors with less chance of dry cough and angioedema
- Contraindicated in pregnancy

Calcium channel blockers

Affect the heart and arterioles

- Verapamil
- Diltiazem

Mainly cause dilation of the arterioles

- Nifedipine
- Amlodipine

- Mechanism of action: Affect cardiac and smooth muscles by blocking calcium entry to cells, relaxing the vascular smooth muscles, dilating the arterioles and decreasing blood pressure

Calcium channel blockers

- Adverse effects
 - ▣ Hypotension
 - ▣ Constipation
 - ▣ Fatigue
 - ▣ Reflex tachycardia (Nifedipine, amlodipine)
 - ▣ Verapamil and diltiazem should be avoided in patients with chronic heart failure due to its negative inotropic effect

Vasodilators

- Hydralazine
- Smooth muscle relaxant, causes vasodilation, decreases peripheral resistance
- Can be used in pregnant hypertensive patients
- Adverse effects
 - ▣ Reflex tachycardia
 - ▣ SLE like reaction (rare)
- Sodium nitroprusside can be used in hypertension emergencies

Hypertensive emergency

- BP > 210/150
- IV administration of antihypertensive drugs
- Example:
 - Labetolol (α -/ β - blocker)
 - Sodium nitroprusside (vasodilator)

DIURETICS



Diuretics

- Diuretics: Drugs inducing a state of increased urine flow
- Used for
 - ▣ Edema (abnormal fluid retention)
 - ▣ Heart failure (decrease pulmonary and peripheral edema, and reduce the preload and afterload)
 - ▣ Hypertension (diuretics lower blood volume and decrease peripheral resistance)

Thiazide diuretics

- Most commonly used diuretics
- Hydrochlorothiazide
- Mechanism of action: Decrease Na^+ reabsorption by inhibiting Na^+/Cl^- co-transporter
- Effects
 - ▣ Increase excretion of Na^+ and Cl^-
 - ▣ Loss of K^+
 - ▣ Reduce peripheral resistance

Thiazide diuretics

□ Uses

▣ Hypertension

- Reduce systolic and diastolic blood pressure
- Reduce peripheral resistance

▣ Heart failure

□ Adverse effects

- ▣ Hypokalemia (K^+ supplements can be added)
- ▣ Volume depletion, can cause orthostatic hypotension

Loop diuretics

- Furosemide (Trade name: Lasix®)
- Torsemide
- Mechanism of action: inhibit the cotransport of $\text{Na}^+/\text{K}^+/2\text{Cl}^-$ in the loop of Henle
- Uses
 - Drug of choice for reducing pulmonary edema in heart failure
 - Useful in emergency situations like acute pulmonary edema

Loop diuretics

- Adverse effects
 - ▣ Ototoxicity (damage to the ear)
 - ▣ Acute hypovolemia, severe and rapid reduction in blood volume with the possibility of hypotension, shock and cardiac arrhythmias
 - ▣ Hyperuricemia
 - ▣ Hypokalemia

Potassium sparing diuretics

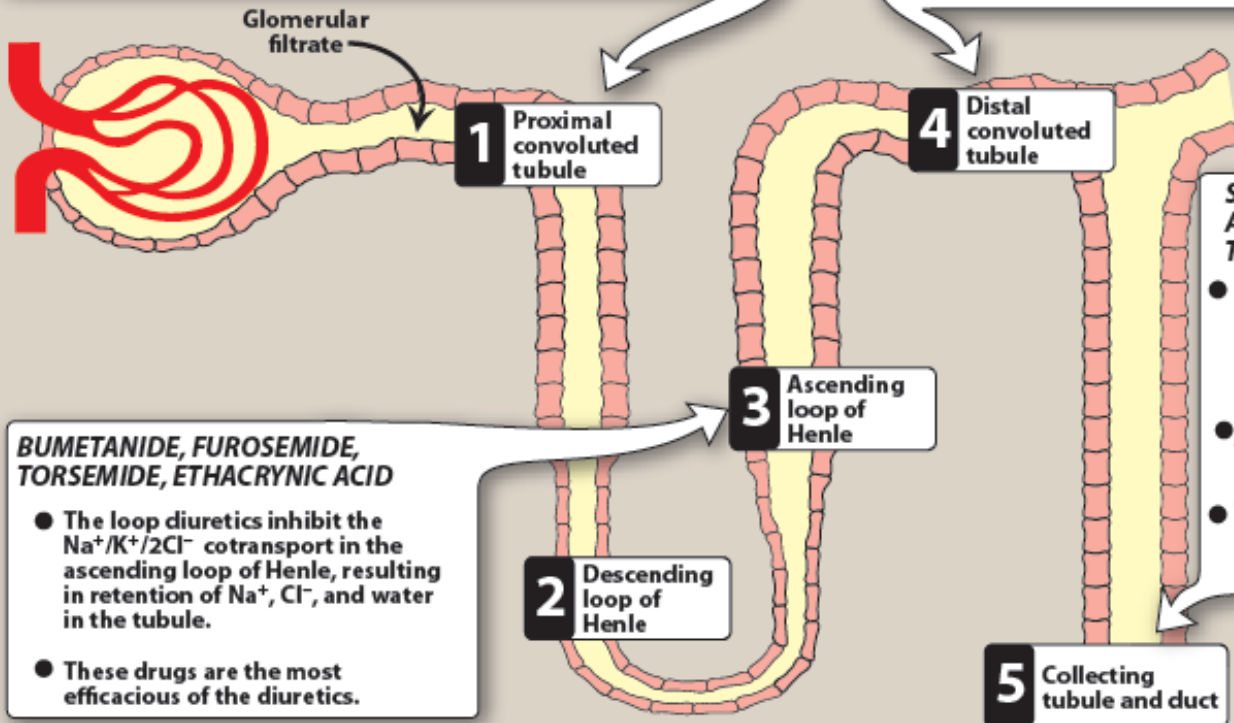
- Spironolactone
 - ▣ Mechanism: Aldosterone antagonist, prevents Na^+ reabsorption
 - ▣ Used in heart failure
 - ▣ Hyperaldosteronism
- Amiloride
 - ▣ Mechanism: Block Na^+ transport channels resulting in a decrease in Na^+/K^+ exchange
- Adverse effects
 - ▣ Hyperkalemia

ACETAZOLAMIDE

- A carbonic anhydrase inhibitor that inhibits the reabsorption of HCO_3^- in the proximal convoluted tubule.
- Weak diuretic properties.

THIAZIDES

- Inhibit reabsorption of Na^+ and Cl^- in the distal convoluted tubule, resulting in retention of water in the tubule.
- Most commonly used diuretic for the treatment of hypertension.



BUMETANIDE, FUROSEMIDE, TORSEMIDE, ETHACRYNIC ACID

- The loop diuretics inhibit the $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransport in the ascending loop of Henle, resulting in retention of Na^+ , Cl^- , and water in the tubule.
- These drugs are the most efficacious of the diuretics.

SPIRONOLACTONE, AMILORIDE, TRIAMTERENE

- *Spironolactone*, an aldosterone antagonist, inhibits the aldosterone-mediated reabsorption of Na^+ and secretion of K^+ .
- *Amiloride* and *triamterene* block Na^+ channels.
- These agents can prevent loss of K^+ that occurs with thiazide or loop diuretics.