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

- 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 (β1, β2 blocker)
  - Metoprolol (β1 blocker)
  - Atenolol (β1 blocker)
  - Bisoprolol (β1 blocker)
- Propranolol is contraindicated in asthma because they block β2 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^+ andCl^-
  - 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 $Na^+/K^+/2Cl^-$ 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