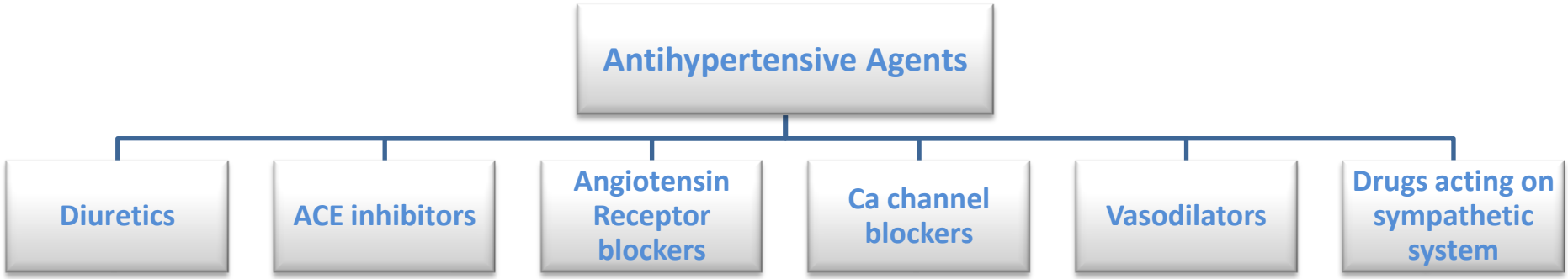
Treatment of Hypertension



Diuretics	**e.g. hydrochlorothiazide, furosemide**
M.O.A	**cause sodium and water loss ⟶ decrease blood volume ⟶ decrease C.O ⟶ lower B.P**
Uses	Mild to moderate hyper tension

ACE inhibitors	**e.g. captopril, enalapril, ramipril**
M.O.A	**Vasodilatation by** - Inhibiting ACE - Inactivating Bradyknin - ↓ aldosterone production
Pharmacokinetics	- GIT absorption after oral dose - Prodrugs converted to active metabolite in liver (Enalaprilat is the active metabolite of enalapril given by I.V in ER) - Long $t_{1/2}$ (given once daily)
Uses	- **Renovascular hypertension** (hypertension results from excess rennin production) - hypertension in patients with **chronic renal disease, ischemic heart disease, diabetes** - **heart failure**
Adverse effects	- **Acute renal failure** (patient with renal artery stenosis) - **Hyperkalemia** (patient with renal insufficiency or diabetes) - **Severe hypotension** (hypovolemic patients) - **Dry cough, wheezing, Angioneurotic edema** in nose, throat, tongue and larynx (caused **by inhibition of bradykinin metabolism**, which accumulate in bronchial mucosa) - **Dysgeusia, skin rash, fever, Proteinuria, neutropenia** (just in Captopril because it contains **sulfhydryl grp.**)
Contraindication	- During the second and third trimesters of pregnancy - Renal artery stenosis
Drug interaction	- **potassium-sparing diuretics** - **NSAIDs** (impair their hypotensive effects by blocking bradykinin-mediated vasodilatation)

Angiotensin receptor blockers	**e.g. Losartan, Valsartan**
M.O.A	- **Selective block of AT_1 receptors** (no effects on Bradykinin) - **complete inhibition of angiotensin** (they inhibit the process from the beginning)
Pharmacokinetics	- Orally - Long $t_{1/2}$ (given once daily) - Losartan is a potent active metabolite - Valsartan doesn't have an active metabolite - Don't cross BBB
Uses	As ACEI
Adverse Effects	AS ACEI except: - **Dry cough, wheezing, Angioneurotic edema** (they don't affect Bradykinin metabolism)

Ca channel blockers	**Dihydropyridine group (Nifedipine, Nicardipine)**	**Verapamil**	**Diltiazem**
Main effects	**act mainly on smooth muscle and used as vasodilators**	**act more on the myocardium and used as antiarrhythmic drug**	**intermediate effect**
M.O.A	**Block Ca influx resulting into: - Peripheral vasodilatation - Decrease cardiac contractility**		
Pharmacokinetics	- **Orally** (1/2 to 2hrs onset of action) and **I.V.**(1-3min onset of action) - Absorbed in GIT - **Highly bound to plasma proteins** (nifedipine and Verapamil >90%) , (Diltiazem <70-80%) - verapamil and diltiazem have active metabolites - nifedipine doesn't have active metabolites		
Uses	- **Treatment of chronic hypertension with oral preparation** - **I.V. Nicardipine used in hypertensive emergency**		
Adverse Effects	- Headache , Flushing , Hypotension - Peripheral edema (ankle edema) - Tachycardia	- Headache , Flushing , Hypotension - Peripheral edema (ankle edema) - Bradycardia (Cardiac depression A-V block) - Constipation	- Headache , Flushing , Hypotension - Peripheral edema (ankle edema) - Bradycardia (Cardiac depression A-V block)

Vasodilators	**Hdralazine**	**Minoxidil**	**Diazoxide**	**Sodium nitropruside**
Site of action	Arteriodilator	Arteriodilator	Arteriodilator	Arterio & venodilator
M.O.A	Direct	Opening of K channels in smooth ms. membranes by minoxidil sulfate (active metabolite)	Opening of K channels	Release of nitric oxide (NO)
Route of admin.	Oral	Oral	Rapid intravenous	Intravenous infusion
Uses	**1.Moderate -severe hypertension** (In combination with diuretic & β-blockers) **2.Hypertensive pregnant woman**	**1.Moderate -severe hypertension** (In combination with diuretic & β-blockers) **2. baldness**	**1.Hypertensive emergency** (In combination with diuretic & β-blockers) **2. Hypoglycemia due to insulinoma**	**1.Hypertensive emergency** (In combination with diuretic & β-blockers) **2.Severe heart failure**
Adverse Effects	Hypotension, reflex tachycardia, palpitation, angina, salt and water retention (edema)			Severe hypotension *more in original slides*
Specific adverse effects	- lupus erythematosus like syndrome	- Hypertrichosis (excessive growth of hair) *Contraindicated in females	- Inhibit insulin release from β cells of the pancreas causing hyperglycemia *Contraindicated in diabetics	- Methemoglobin during infusion - Cyanide toxicity - Thiocyanate toxicity

Drugs acting on sympathetic system	**β-blockers**	**α-blockers**	**Centrally Acting Adrenergic Drugs α_2 - agonist**	
e.g.	**Propranolol, atenolol**	**prazosin**	**Clonidine**	**α - methyl dopa**
M.O.A	**They lower blood pressure by :** - **decreasing C.O.** - **inhibiting the release of renin**	**- Block α- receptors in arterioles and venules** **- Decrease both afterload & preload**	**- diminishes central adrenergic outflow** **- doesn't decrease renal blood flow**	**- converted to methyl NE centrally to diminish the adrenergic outflow** **- Decrease peripheral resistance**
Uses	- **mild to moderate hypertension.** - **In severe cases used in combination with other drugs**		- **hypertension complicated by renal disease**	