Pharmacology 3

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The concept	the notes
ACE Inhibitors • ACE functions 1. cleaves angiotensin I to form the potent vasoconstrictor angiotensin II 2. breakdown bradykinin (endogenous vasodilator).	• **The family**:pril • **recommended** when the preferred first line agents (diuretics or B- blockers) are contraindicated or ineffective. • **Mechanism** :reducing peripheral vascular resistance without reflexively increasing cardiac output. • **side effects**: 1. Dry cough (due to increase level of bradykinin in the pulmonary tree.) 2. Angioedema(may be caused by bradykinin) 3. Potassium level ↑ (spironolactone is contraindicated.) we use **thiazide** to solve the problem 4. first-dose syncope (first administrated under the doctor observation.) **Contraindication**: 1. pregnancy (with ARBs & thiazide) 2. with arbs (same mechanism) • bilateral renal stenosis **Non HTN use :** 1. chronic kidney disease→*diminish proteinuria and stabilize renal function* 2. diabetes 3. heart failure, and after myocardial infarction.
Angiotensin II-receptors antagonists (ARBs) note →alternatives to the ACE Inhibitors	• **The family→** sartan • **prototype →**Losartan • **pharmacologic effects:** 1. vasodilation 2. block aldesterone secretion 3. do not increase the bardykinin levels. • **adverse effect:** →similar to ACE Inhibitor (hyperkalemia)but risks of cough and angioedema are significantly decreased.(**Less side effects)**

ACEI & ARBs combination **we use thiazaide after having hyperkalemia**	• (most cases) = relative contraindication. • can be use in case of **late stages of heart failure.** To block : 1. DIRECT pathway from angiotensinogen to angiotensin II. 2. INDIRECT pathway By blocking 1) non-renin protease/ t-PA/ cathepsin or 2) blocking chymase CAGE .
Calcium channel blockers (CCB)	• effective in patient with **angina and diabetes.** • exerts their antihypertensive effect by their **vasodilation effect.** • The **drug of black people** except in case of (diabetes + hypertension) →ACEI • CCBs are stronger than ACE inhibitors in ter ms of efficacy <u>chemical classes</u> 1. Diphenylalkylamines,ex:Varapamil(arrythmias with hypertension) 2. Bnzothiazepines, ex: Diltiazem 3. Dihydropyridines, ex: Nifedipine (for peripheral arteries) → no orthodtatic hypotension or tachycardia **Mechanism of action :** by antagonists block for the inward movement of calcium by binding to the **L -type calcium channels (fast type)** in the heart and peripheral vasculature. **contraindication** →combination of verapamil or Diltiazem with a beta-blocker #we can use nifedipine with them **see slide 9,10,11,12 the modified**

Centrally acting adrenergic drugs	1. Clonidine 2. Methyldopa
Clonidine	• an alpha 2 agonist hypotensive agent • **MOA:** diminishes central adrenergic outflow. • **the usage :** 1. mild to moderate hypertension that has not responded adequately to treatment with diuretics alone 2. hypertension complicated with renal disease.(Does not decrease renal blood flow) **Side effects:** 1. **s**odium and water retention (usually administered in combination with a diuretics) 2. dry mouth And nasal mucosa. 3. sedation 4. Rebound hypertension following sudden withdrawal 5. (hypertensive crisis): increased sympathetic nervous activity Patients exhibit nervousness, tachycardia, headache, and sweating • **Treatment of the hypertensive crisis →**reinstitution of clonidine therapy or administration of -and -adrenoceptor–blocking agents.
Methyldopa	• Alpha 2 agonist • **MOA:**converted to methylnorepinihrine centrally to diminish the adrenergic outflow from the CNS • **results:** reduce the peripheral resistance and decreased blood pressure. (Cardiac output is not decreased) • **The usage:** **1.** treating hypertension with renal insufficiency. 2. hypertension during pregnancy **side effects: sedation and drowsiness.**

Clonidine and methyldopa	• clonidine lowers heart rate and cardiac output more than does methyldopa.
Selective alpha 1-blockers	• **the family** : sin • Selectively block alpha 1-receptors • Alfuzosin, doxazosin, **prazosin**, terazosin → for patient with prostate hyperplasa and HTN • **Silodosin for:** chronic hypertension and urinary retention in men with benign prostatic hyperplasia. - →FOR PATIENT WITH PROSTATE HYPERPLASIA WITH NO HTN