Introduction:

> most common CVS disease

> elevated arterial BP damages vessels in renal, heart and brain

Complications:	Renal failure, Coronary disease, Heart failure, Stroke, Diamentia

Classification:

Classification:	Systolic BP	Diastolic BP:
Normal:	<120	<80
Pre-hypertension:	120-139	80-89
Stage 1 HTN:	140-159	90-99
Stage 2 HTN:	>= 160	>=100

Types of Hypertension:

Essential Hypertension (85-90%):	Primary hypertension, no identifiable cause (genetic), can't be cured, can be controlled
Secondary Hypertension (10-15%):	Specific identified cause (comorbid disease or drug), can be cured when cause is eliminated

Secondary Causes of HTN:

> Genetic factors

> Psychological stress

> Environmental and Dietary Factors:	high salt diet, decreased calcium and phosphate intake, sedentary lifestyle
> Diseases:	renal, endocrine, vascular, renal diseases
> Drugs:	sympathomimetic amines, amphetamines, oral decongestants (eg. pseudoehedrine), corticosteroids, osteogens (C0Cs), NSAIDs, COX-2 inhibitors

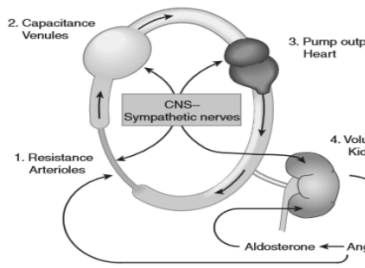
Clinical presentation:

- Often incidental finding

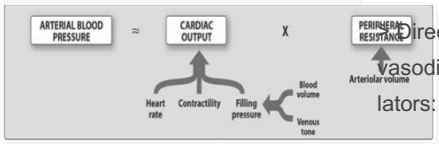
- Adults should get BP checks once a year

- Severe cases:	**Headaches**, visual disturbances, target organ damage (stroke, ischemic heart disease, renal failure)

Normal regulation of BP:



Factors Influencing BP:

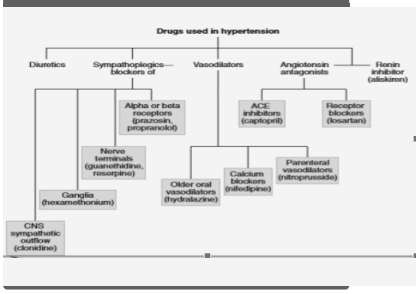


Potential Mechanisms of Pathogenesis:

BP= CO x PVR

Increased Cardiac output:	Increased fluid volume from excessive sodium intake or renal sodium retention Venous constriction: due to excess stimulation of RAAS
Increased Peripheral resistance:	Excess stimulation of RAAS Sympathetic nervous system over-activity

Antihypertensive Drugs:



Classes of Antihypertensive Agents:

Diuretics:	Reduce blood volume=Depletes the body of sodium, Venodilation
> Sympathoplegic agents:	Reduce peripheral vascular resistance, Inhibit cardiac function, Increase venous pooling capacitance vessels
> Direct vasodilators:	Reduce peripheral vascular resistance, Increase venous pooling capacitance vessels
> Angiotensin antagonists:	Reduce peripheral vascular resistance, Reduce blood volume

Diuretics:

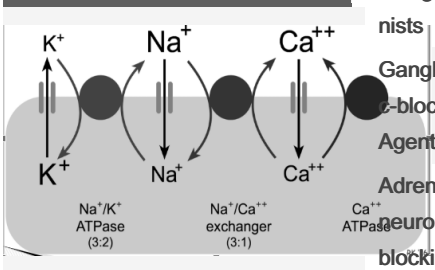
- Reduce blood volume and cardiac output

- Cardiac output returns to normal	But peripheral vascular resistance declines
- Sodium	Contributes to vascular resistance = Increase vessel stiffness

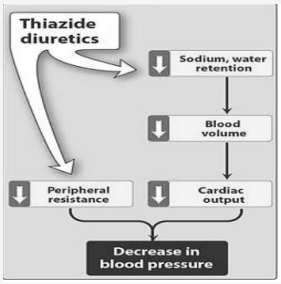
Diuretics: (cont)

- Venodilation	Altered sodium-sodium calcium exchange

Vasodilation mechanism by Diuretics:



Thiazide Diuretics:



Use of Diuretics:

> Lower BP by 10-15 mmHg in most patients

> Thiazide diuretics –mild to moderate HTN

> Loop diuretics – severe HTN and hypertensive emergencies

Adverse Effects (Thiazide Diuretics):

Potassium depletion – hypokalemia

Magnesium depletion

Hyperuricemia- gouty attacks

Glucose intolerance

Increase serum lipid concentrations

Sympathoplegic Drugs:

Centrally-acting Drugs:	Methyldopa, clonidine
Adreno-ceptor antago-nists	Beta-blockers, alpha-1 blockers
Ganglioni-c-blocking Agents:	No longer used clinically ; hexamethonium
Adrenergic neuron blocking agents:	Block the release of noradrenaline, Reserpine, guanethidine, debrisoquin, Not/rarely used clinically

Centrally-Acting Drugs:

- Methyl-dopa, clonidine	rarely used except clondine
- Reduces sympathetic outflow	
- Compen-satory response mechanism:	salt retention
- **Clonidine**, guanabenz, guanfacine	Stimulate central alpha-2 adreno-ceptors
- Methyldopa – anologue of L-dopa	Results in the synthesis of a false neurotran-smitter

Centrally-Acting Drugs: (cont)

Alpha-methylnoradrenaline = Stimulates central alpha-2 adrenoceptors

Clonidine:

Reduces cardiac output, PVR, relaxation of capacitance vessels

Rarely causes postural hypotension

Adverse effects:

- Dry mouth
- Sedation

Contraindication: Patients with depression

Caution: Abrupt discontinuation can lead to hypertensive crisis

Adrenoceptor antagonists: Beta-blockers

Non-selective: Propranolol

Beta-1 selective: “BBEAM”	Betaxolol, bisopr-olol, esoprolol, **atenolol, metoprolol**, Cardioselective
Vasodi-lator beta-b-lockers	Also block alpha-1 receptors,Labetolol, carvidelol, nebivolol

Decrease cardiac output

Decrease peripheral vascular resistance

Inhibit stimulation of renin production by catecholamines

Adverse effects= Heart block, bronchoconstriction, diabetes, vivid dreams

Alpha-1 blockers:

Prazosin, terazosin, doxazosin

Block alpha-1 receptors in arterioles and veins

Vasodilation	Reduce peripheral resistance
Compen-satory mechanism:	salt and water retention

More effective when used with other drugs

Calcium Channel Blockers:

> Dihydr opy-ridines	amlodipine, isradipine, nicardipine, nimodi-pine, felodipine, nisold-ipine, lacidipine
> Non-dihyd-ropyri-dines	Verapamil, diltiazem, hydralazine
	Benzothiazepine (dilti-azem)

Mechanism of action:

- Inhibit calcium influx through voltage-dependent L-type calcium channels
- Relax arteriolar smooth muscle, reduce peripheral vascular resistance
- Cause coronary and peripheral vasodilation

CCB: Mechanisms of Action:

Dihydr opy-ridine CCBs	Primary vasodilators (reduce PVR), All decrease cardiac contractility except amlodipine and felodipine

CCB: Mechanisms of Action: (cont)

Non-dihydropyridines (diltiazem, verapamil)	directly block the AV node, decrease heart rate,decrease cardiac contraction

Adverse effects: 1. **Flushing, peripheral oedema, tachycardia, bradycardia, heartblock**

2. **Headache**, flushing, dizziness, palpitations, hypotension occur within a few hours of dosing, Associated w high initial doses or rapid increase in dose, Common with short-acting preparations

3. Ankle oedema: Due to a rise in intracapillary pressure as a result of selective dilatation of precapillary arterioles, NOT due to sodium retention, Relieved by bed rest

4. **Gum Hypertrophy:** dihydropyridines

5. GIT: constipation (verapamil), nausea, and vomiting

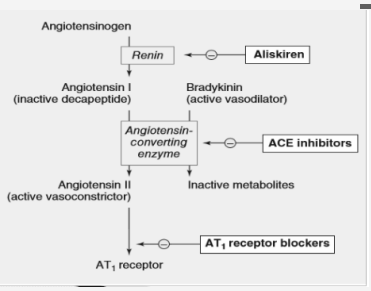
Inhibitors of Angiotensin:

Angiotensin converting enzyme inhibitors (ACEIs)	Captopril, enalapril, Ramipril, fosinopril, trandopril

Inhibitors of Angiotensin: (cont)

Angiotensin receptor blockers (ARBs)	Losartan, valsartan, telmisartan, irbesartan, candesartan
Renin-inhibitors	Aliskiren

Inhibitors of Angiotensin:



Adverse Effects

ACEIs =

Dry cough

Can cause hyperkalemia – potassium monitoring essential

Angioedema (substance P?)

ARBs =

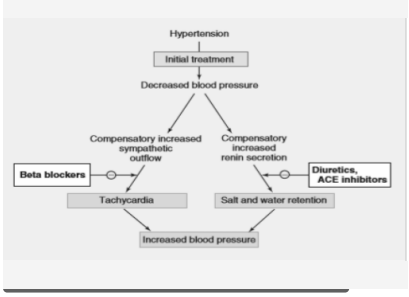
No dry cough

Hyperkalemia

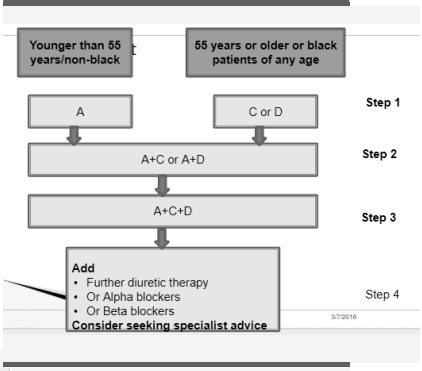
Angiodema is less common than ACEIs

Contraindicated in pregnancy

Combination Treatment: Vasodilators:



Management Approach:



First-line agents: "ACD" drugs:

- A: ACEIs and ARBs
- C: Calcium channel antagonists
- D: Diuretics (Thiazides)

Second-line agents:

- **Beta-adrenoceptor blockers**
- Aldosterone antagonists (spironolactone, eplerenone)
- Alpha-blockers (doxazosin, prazosin, terazosin)
- Loop diuretics (frusemide, torsemide)
- Direct vasodilators (hydralazine, minoxidil) [last-line of therapy]
- Central α-2 agonists (clonidine)
- Adrenergic antagonists (reserpine)