Antihypertensive Drugs:

- Diuretics
- RAAS inhibitors
- Sympathetic inhibitors
- Ca^{2+} channel blockers
- Vasodilators

Diuretics

Thiazides
- Hydrochloro-thiazide
- Chlorthalidone
- Indapamide

High Ceiling
- Furosemide etc.

Aldosterone Antagonists
- Spironolactone
- Eplerenone

RAAS Inhibitors

ACE-I
- Captopril
- Enalapril
- Lisinopril
- Perindopril
- Ramipril
- Fosinopril
- Trandalopril

ARBs
- Losartan
- Candesartan
- Valsartan
- Telmisartan
- Irbesartan
- Olmesartan

Direct renin Inhibitor
- Aliskiren

Sympathetic Inhibitors

β-adrenergic blockers
- Propranolol
- Metoprolol
- Atenolol
- etc.

α+β adrenergic blockers
- Labetalol
- Carvedilol

α-adrenergic blockers
- Prazosin
- Terazosin
- Doxazosin
- Phentolamine

Central sympatholytics
- Clonidine
- Methyl dopa

Vasodilators

Arteriolar dilator
- Hydralazine
- Minoxidil

Arteriolar + Venodilator
- Sodium nitroprusside

Ca^{2+} Channel Blockers

Phenylalkylamine
- Verapamil

Benzothiazepine
- Diltiazem

Dihydropyridines
- Nifedipine
- Felodipine
- Amlodipine
- Clinidipine
- Lacidipine
- Lercanidipine
- Benidipine
- Nicardipine

Hypertension: meeting ≥ 1 criteria using ambulatory blood pressure monitoring (ABPM):

- 24-hr mean ≥ 125/75 mm Hg
- Daytime (awake) mean ≥ 130/80 mm Hg
- Nighttime (asleep) mean ≥ 110/65 mm Hg

Classification	SBP		DBP
Normal	< 120	+	< 80
Pre-hypertension	120-139	±	80-89
Stage 1 hypertension	140-159	±	90-99
Stage 2 hypertension	≥ 160	±	≥ 100
Isolated systolic hypertension	> 140	+	< 90

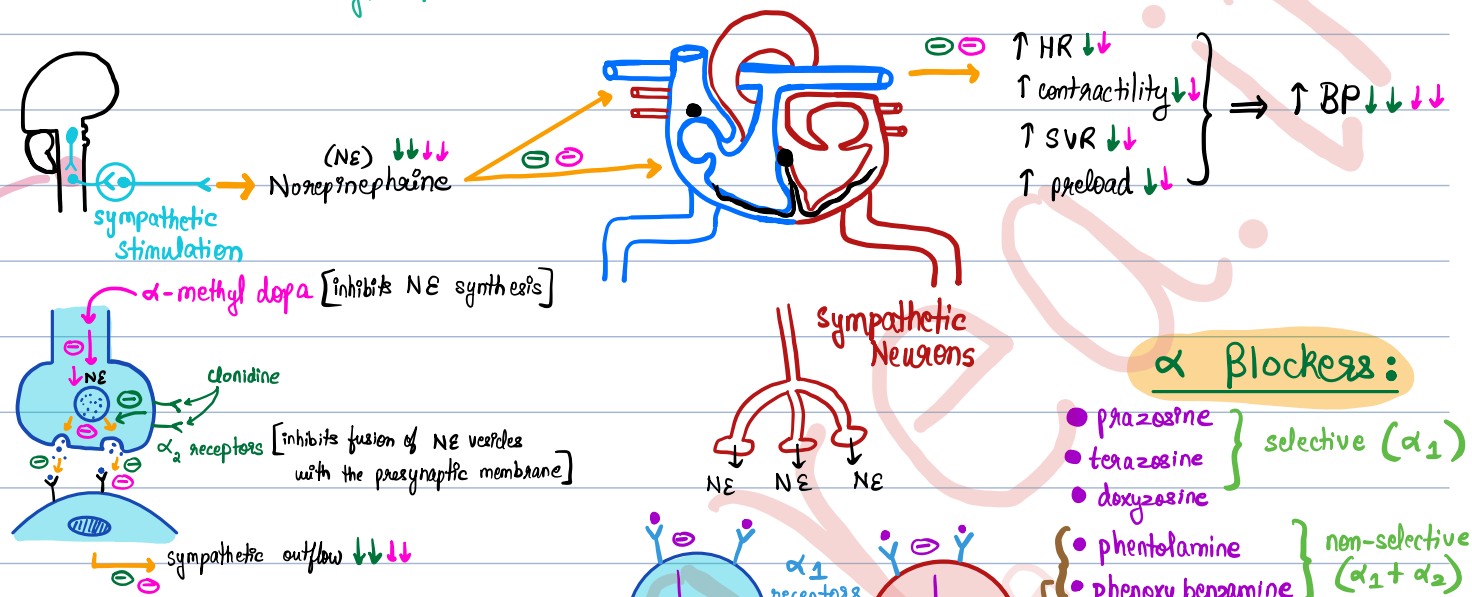
Hypertensive crisis = Hypertensive emergency + Hypertensive urgency

Hypertensive urgency:
- BP > 180/120 mm Hg
- no progressive TOD (target organ dysfunction)

Hypertensive emergency:
- BP > 180/120 mm Hg
- impending or progressive TOD

Sympatholytics:

Centrally Acting – • Clonidine [α_2 receptor agonist]
• α methyl dopa



Clonidine: primarily used in treating withdrawal symptoms (which are a result of ↑ sympathetic outflow)

ϕ sedation

α-methyl dopa: used in pregnancy

ϕ +ve coomb's test (in case of anemia testing)

α Blockers:

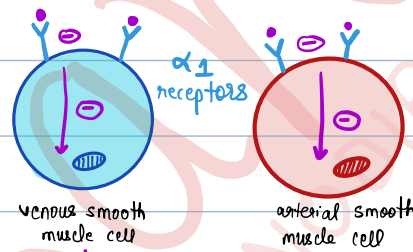
- prazosine
- terazosine
- doxyzosine

} selective (α_1)

- phentolamine
- phenoxy benzamine

} non-selective ($\alpha_1 + \alpha_2$)

given in hypertensive crisis secondary to pheochromocytoma, MAO-I.



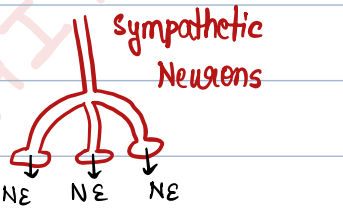
↓ contraction → relaxation ↑ → vasodilation → ↓ SVR → ↓ BP

↓ BP → activation of baroreceptors → medulla → ↑ sympathetic outflow → ↑ HR *

ϕ reflex tachycardia *

relaxation → venodilation → ↓ preload → ↓ CO → ↓ BP

ϕ orthostatic hypotension

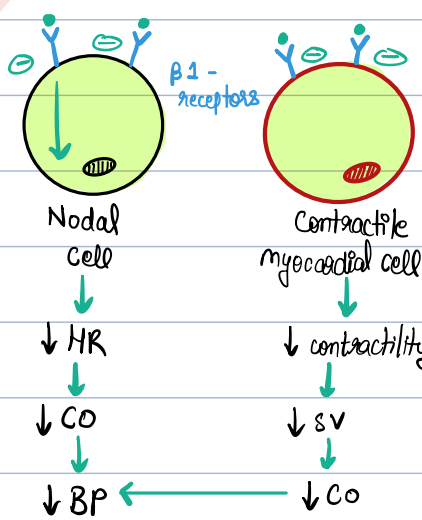


α + β blockers:

- Labetolol
- Carvedilol

} $\alpha_1 + \beta_1 +$ β_2

ϕ Bronchospasm



β1 blockers:

- Atenolol
- Bisoprolol
- Ezmolol
- Metoprolol

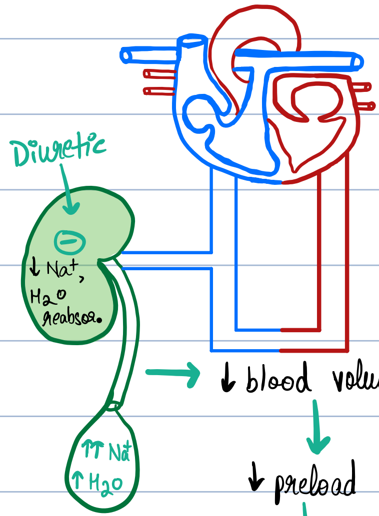
}

ϕ bradycardia

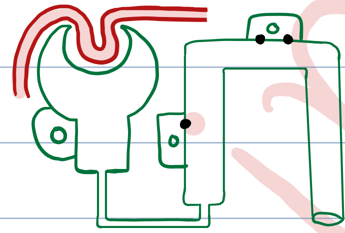
ϕ hypotension leading to cardiogenic shock (in patients with decompensated heart failure)

ϕ Hypoglycemia unawareness [in DM patients]

Diuretics: ⇒ ↓↓ Na^+, H_2O retention



→ ↓ blood volume
↓
↓ preload
↓
↓ CO
↓
↓ BP



∴ Indicated in volume overload
- ↳ congestive heart failure
- → iatrogenic volume overload

ϕ hyponatremia
ϕ hypokalemia
ϕ metabolic alkalosis
ϕ hyperuricemia (gout)
ϕ ottotoxicity

[I] Thiazides: [inhibit Na^+/Cl^- exchanger in early DCT]

First Line Agents [for HTN]

- Hydrochlorothiazide
- Chlorthalidone
- Metolazone

[II] Loop Diuretics [inhibit $Na^+/K^+/2Cl^-$ cotransporter in ascending limb of LOH]

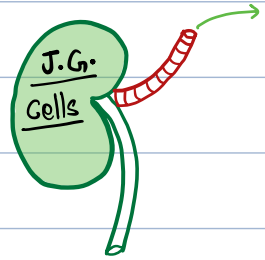
- Furosemide
- Bumetanide
- Torsemide

[III] Aldosterone Antagonists: [inhibit aldosterone receptors & ∴ synthesis of ENaC in late DCT]

ϕ hyperkalemia

- Eplerenone
- Amiloride
- Spironolactone → ϕ gynecomastia

RAAS Inhibitors:

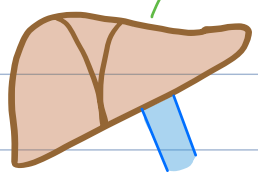


↓ blood flow through renal artery

↓

stimulates JG cells to secrete renin

synthesized by

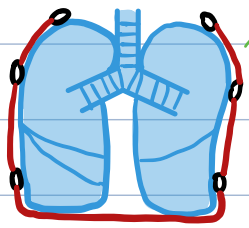


Angiotensinogen

↓ renin

Angiotensin I (A.T-I)

present in alveoli



angiotensin converting enzyme (ACE)

↓

AT-II

(very potent vasoconstrictor)

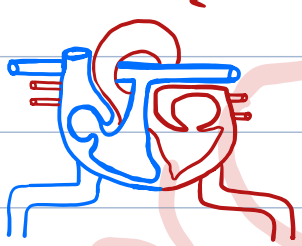
AT-II binds to AT-II receptors on efferent arteriole → efferent arteriolar vasoconstriction

↑ glomerular BP

↑ GFR ↑ proteinuria

↑ thickening of glomerular basement membrane

↑ risk of CKD



AT-II Receptors are found on the vascular smooth muscles

↓

Smooth muscle contraction

↓

Vasoconstriction

↓

increase in total peripheral resistance

↓

increase BP

AT-II stimulates the Posterior pituitary

↓

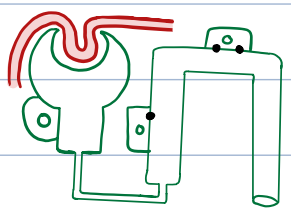
Posterior pituitary releases ADH

↓

ADH acts on the Kidney (collecting duct) to increase water reabsorption

↓

increased blood volume



AT-II stimulates the zona glomerulosa cells on adrenal cortex

↓

release of aldosterone

↓

aldosterone acts at the DCT of Kidneys

↓

increases water reabsorption by increasing Na^+ reabsorption

↓

increased blood volume

[I] ACE-I:

- Captopril
- Lisinopril
- Enalapril
- Benzopril
- Ramipril

[II] ARBs:

- Losartan
- Valsartan
- Candesartan
- Telmisartan

Adverse Effects:

1. Hyperkalemia
2. Hypotension
3. Angioedema & dry cough (severe reaction to ACE-I)
4. First-dose hypotension
5. Dysguesia (altered taste sensation)
6. Granulocytopenia

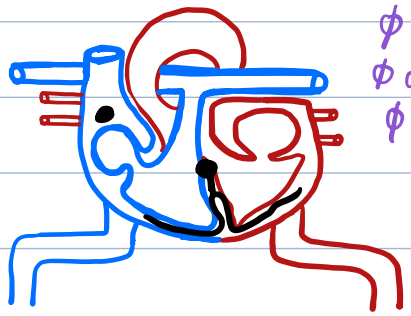
Contraindications:

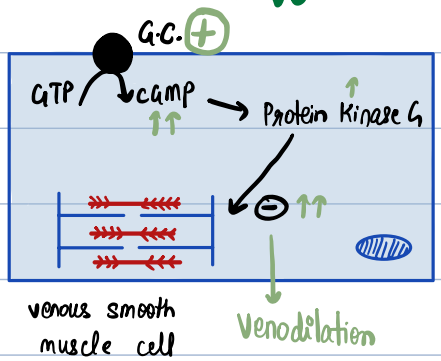
- C1E-I deficiency
- Angioedema
- Pregnancy (teratogenic)
- Bilateral renal artery stenosis
- Severe CKD
- Serum creatinine > 3.5 mg/dL

Vasodilators:

ARTERY ⊖ vasoconstriction → ↑SVR → TBP ↓↓

VEIN ⊖ venoconstriction → ↑preload → ↑CO → ↑BP ↓↓





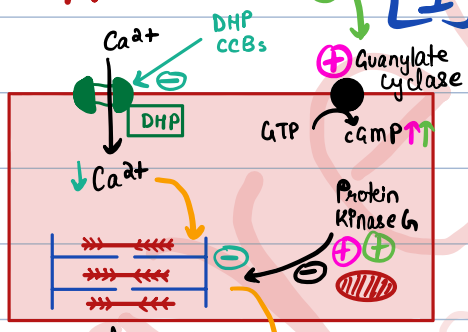
[III] ⊕ Guanylyl Cyclase
[Direct Acting Vasodilators]

- Hydralazine — action on arteries >>> veins
  - ϕ reflex tachycardia
  - ϕ drug-induced SLE
  - ϕ orthostatic hypotension
- Minoxidil

[IV] ↑↑ NO (Nitrodilators)

- Sodium nitroprusside
  - ϕ cyanide poisoning
  - ϕ lactic acidosis
  - ϕ coronary steal syndrome
- NTG → veins >>> arteries — ↑↑↑ doses

↑↑ NO ⊕



[I] Dihydropyridine CCBs

- Nifedipine
- Amlodipine
- Nicardipine
- Nimodipine
- Clevidipine

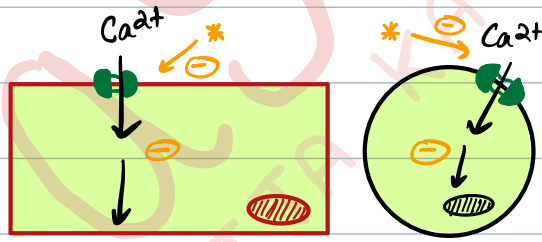
no effect on cardiomyocytes

↓↓ vasoconstriction ↓↓ → ↓SVR → ↓BP ↓↓↓↓

- ϕ reflex tachycardia
- ϕ orthostatic hypotension (due to mild venodilation effect)

Venodilators:

- NTG (low dose) — ϕ orthostatic hypotension, ϕ R.V. MI, ϕ PDE-5 I, ϕ α-Blockers
- Isosorbide dinitrate
  - ↳ indicated in H.F. + african-american + already on hydralazine



CONTRACTILE CELL → contraction ↓ → ↓↑contractility → ↓CO → ↓BP

NODAL CELL → ↑HR ↓ → ↓CO → ↓BP

[II] Non-DHP CCBs:

(present only in myocardial cells)

- Verapamil
- Diltiazem

*

- ϕ Bradycardia
- ϕ ↓↓↓BP progressing to cardiogenic shock (in patients with decompensated heart failure)

small vasodilatory effect

Arteriolar Dilators: I, II, III, IV