- All diuretic drugs have the same antihypertensive effect.

Diuretics (Saluretics)

- 1st line therapy.
- leads to Na^+ & fluid loss.
- Better in ↓ Coronary heart disease / HF / Stroke & mortality
- Cheap.

→ Early effects:
↳ ↓ systole BP: cuz it ↓ Blood volume (plasma) & cardiac output

→ Lat effects:
→ ↓ blood vessels contractility: due to ↓Na^+ & ↓CL^-
Thus ↓ vasodilation, thus ↓ BP
→ ↑ Plasma renin, thus ↑ angiotensin I & II & aldosterone.
This leads to ↑↑↑↑ BP !! → Tolerance.

SE
→ Diuresis (↑urination)
→ Metabolic side effects: hyperglycemia, hyper uricemia, & hyperlipidemia.

→ Thiazide diuretics:

- Most used.
- uses: Mild & Moderate hypertension. (with normal renal & heart func.).

→ Hydrochlorthiazide
→ Chlorthalidone (long acting).
→ Bendrofluazide
→ Indapamide (Natrilex)
- → vasodilating effects.
- → Lipid-neutral (no lipid abnormalities)
- → Causes regression of left ventricular hypertrophy (LVH).

→ Loop diuretics:

- uses: for Severe hypertension + in renal insufficiency, HF, cirrhosis.
- Very potent

→ Furosemide
- Very potent
- Short acting.

→ Torsemide → Has No metabolic SE.

→ K^+-sparing diuretics:

- They "spare" K^+ from excretion.
- uses: renal insufficiency, HF, cirrhosis.
  ↳ cuz they antagonize aldosterone which is elevated in these diseases.

→ Spironolactone
→ Eplerenone
→ Amiloride
→ Triamterene.

Sympatholytics (Adrenergic blockers):

Non-selective α-adrenergic antagonists

- Phentolamine
- Phenoxybenzamine.
  - → Block both α1 & α2 rec.
  - ⇓ Reflex tachycardia.

There are two types of alpha receptors. Alpha1 are present in the postsynaptic membrane, alpha2 are in presynaptic membrane. Alpha2 receptors inhibit NE release from the vesicle, thus, inhibiting alpha2 receptors alone will increase blood pressure. Inhibiting alpha1 receptors alone will decrease the blood pressure, while inhibiting both causes tachycardia and increase contractility.

  - → Used (only) for pheochromocytoma.

- Used only for pheochromocytoma (a tumor of the adrenal medulla which secretes epinephrine and norepinephrine in large amount, causing hypertension and increasing HR and CO). Therefore, we need a drug that works on both alpha1 and alpha2 receptors.
- EXTRA: in pheochromocytoma we initially give alpha blocker to control the hypertension (even though it causes further increase in HR & CO), then later we give the patient beta blockers to control the heart rate and cardiac output.

α1 blockers

- Prazosin
- Terazosin
- Doxazosin
  - → Used for
    - moderate hypertension
    - benign prostatic hypertrophy
  - → 1st dose phenomenon
    - First-dose phenomenon, similar to ACE inhibitors, a sudden drop in blood pressure that might lead to fainting and tachycardia.
  - → SE:
    - All are free of metabolic effects, but can cause drowsiness, diarrhea, postural hypotension, tachycardia, and tolerance **due to fluid retention**. Similar to short-acting vasodilators.

Non-selective B-blockers:

✱ B-rec. are mainly in heart

- Propranolol (prototype, lipophillic)
- Timolol (lipophillic)
- Nadolol long acting
- Pindolol (ISA)
- Acebutolol (ISA)

B1 blockers

- Esmolol Short half-life.
- Metoprolol
- Atenolol
- Betaxolol
- Bisoprolol

- They ↓ HR / SV / CO
- Can cross BBB → cause central actions in the vasomotor center
- They ↓ renin release & ↓ NE release.
- Monotherapy or combined with vasodilators or ACEIs
- Uses:
  - → high renin hypertension
  - → Ischemic heart diseases IHD
- Doesn't cause postural hypotention (In contrast to vasodilators, CCBs, & diuretics)

SE

- → Bronchospasm.
- → HF
- → CNS effects.
- → Impaired lipids & glucose metabolism.
- → Mask hypoglycemia.
- → Claudication.
- → Withdrawal syndrome.

Side Effects:

- Bronchospasm, especially with the non-selective blockers, because beta2 receptors are found in the lungs and bronchi.
- Heart failure, beta receptors normally stimulate the heart muscle, so blocking these receptors can reduce the activity of the heart. That's why they are not advisable in elderly patients.
  In general, beta blockers are contraindicated in patients with heart problems.
- CNS effects like fatigue, depression, impotence ..etc.
- Impair lipid and glucose metabolism, therefore not used for treatment of hypertensive diabetics.
- Mask hypoglycemia, normally during hypoglycemia sympathetic nervous system gets activated to warn the body, producing severe hunger, increased blood pressure, and increased heart rate. Additionally, you know that beta receptors, in the liver, stimulate gluconeogenesis and glycogenolysis to elevate glucose blood levels. But, if beta receptors are blocked, the body will go into severe hypoglycemia without even noticing.
- Claudication- pain caused by too little blood flow to your leg or arm, due to blockade of beta receptors.

Norepinephrine will overly activate alpha receptors causing vasoconstriction of peripheral blood vessels, usually in upper and lower limbs leading to cold extremities, cold and cyanotic nose and ear lobes, especially in winter.

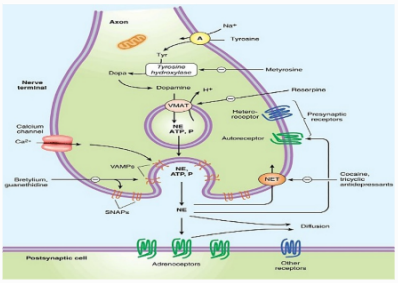
- Withdrawal syndrome due to up-regulation of these receptors. This might happen upon sudden stop of using beta blockers.
  Over-activity of sympathetic systems happens which leads to stimulation of the heart, and increase in blood pressure to levels above that of pretreatment. So beta blockers should be stopped gradually over a two to three days.

Vasodilating B-blockers:

- Labetalol
  - → B & α1 (weak) antagonist.
  - → B2 partial agonist → vasodilation.
  - → Uses: pheochromocytoma & emergencies.
- Carvedilol → B & α1 (weak) antagonist.
- Esmolol → B1 selective, short half life.
- Nebivolol
  - → B1 selective
  - → Nitric oxide potentiating vasodilatory effects.

Adrenergic neuron blockers:

- Guanethidine
- Bethanedine
- Debrisoquin
- Guanadrel
- Reserpine



- → hydrophilic
- → Blocks NE release, they displace NE from intracellular vesicles, then the free NE inside the cell will be metabolized by monoamine oxidase (MAO).
  - ↓ NE depletion from peripheral nerve endings.

- → From "Rauwolfia" alkaloid plant.
- → lipophilic
- → Binds to symp. intracellular vesicles & prevents dopamine (DA) uptake by them.
- → Amines are metabolized by MAO.

- It depletes NE, 5HT (serotonin), ACTH, & DA.
- Slow, cheap.
- SE: depression, suicide (crosses BBB, lipophilic), & concinogenic effects.

Ganglionic blockers:

- Trimthoprim
- Pentolinium
- Mecamylamine

SE

Organ	Predominate System	Results
Cardiovascular System		
Heart	Parasympathetic	Tachycardia
Arterioles	Sympathetic	Vasodilatation
Veins	Sympathetic	Dilation
Eye		
Iris	Parasympathetic	Mydriasis
Ciliary Muscle	Parasympathetic	Cycloplegia
GI Tract	Parasympathetic	Relaxation (constipation)
Urinary Bladder	Parasympathetic	Urinary retention
Salivary Glands	Parasympathetic	Dry Mouth
Sweat Glands	Sympathetic	Anhidrosis

- Block transmission in both symp. / parasymp. systems.
- Act immediatly
- Are very efficacious
- Used for Short-term control of BP (Intraoperatively & in emergencies)

  Because the effect of ganglionic blockers can be rapidly reversed.

Notes from Sheets:

Systolic/Diastolic pressure (mm Hg)	Category
< 120/80	Normal
120-135 / 80-89	Prehypertension
>= 140/90	hypertension
140-159 / 90-99	Stage 1
>= 160/100	Stage 2

	HEART RATE	CARDIAC OUTPUT	TOTAL PERIPHERAL RESISTANCE	PLASMA VOLUME	PLASMA RENIN ACTIVITY
Diuretics	↔	↔	↓	↓	↑
Sympatholytic agents					
Centrally acting	↓	↓	↓	↑	↓
Adrenergic neuron blockers	↓	↓	↓	↑	↑
α receptor antagonists	↑	↑	↓	↑	↔
β receptor antagonists					
No ISA	↓	↓	↓	↑	↓
ISA	↔	↔	↓	↑	↓
Arteriolar vasodilators	↑	↑	↓	↑	↑
Ca^{2+} channel blockers	↓ or ↑	↓ or ↑	↓	↑	↑
ACE inhibitors	↔	↔	↓	↔	↑
AT_1 receptor antagonists	↔	↔	↓	↔	↑
Renin inhibitor	↔	↔	↓	↔	↓ (but [renin] ↑)

- Neural control of BP:
1. Baroreceptors in carotid sinuses detect changes in BP and send signals to the brain.
2. Activation of vasomotor center.
3. The vasomotor center then sends signals back to the blood vessels and heart through the sympathetic and parasympathetic systems.
- Also, the nervous system can control the kidneys.

- دعواتكم ♥
- غلا الأحدب