Pharmacology
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Drugs used in Cardiovascular disorder

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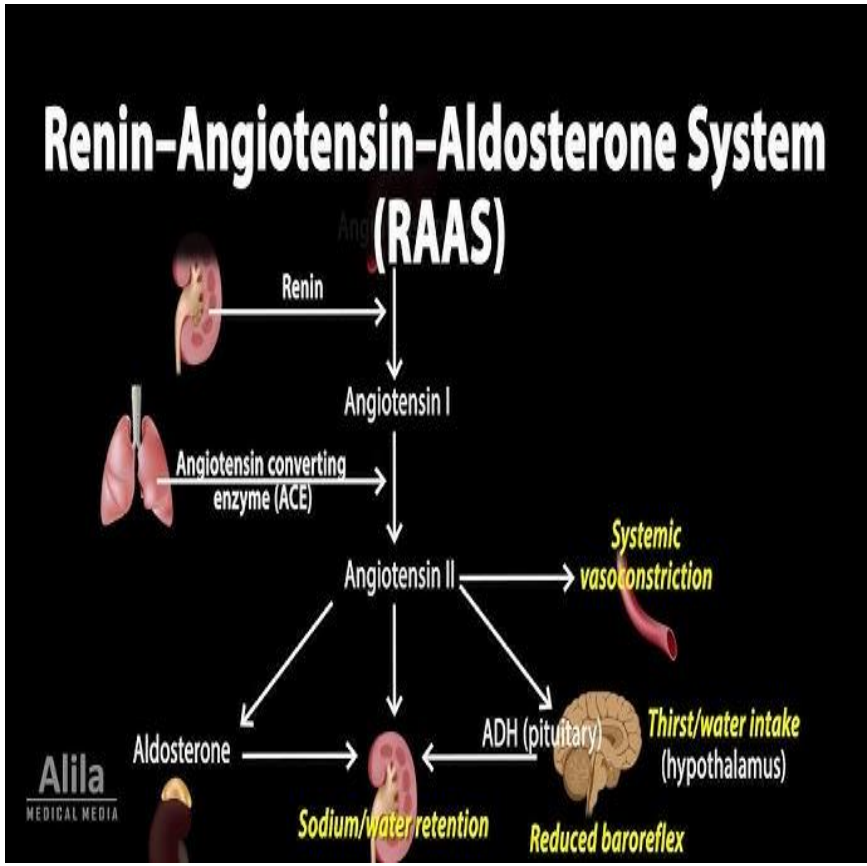
ACE Inhibitors

- There are 2 families of drugs:
  - Angiotensin-converting enzyme (ACE) inhibitors
    - Block the enzyme (ACE) that normally converts angiotensin I to angiotensin II
    - Decrease vasoconstriction & decrease aldosterone production, reducing retention of Na and water



- Used to treat hypertension, heart failure, myocardial infarction, and nephropathy
  - Enalapril
  - Captopril
  - Lisinopril
- Side Effects:
  - Can produce serious first-dose hypotension
  - Cough, due to accumulation of bradykinin
  - Hyperkalaemia, due to inhibition of aldosterone release

•CI: In hypersensitivity to drug

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Agent	Variable (Hr)			
	Peak Onset	Duration of Effect	Elimination Half-life	Usual Dosage Interval
Benazepril	2–4	24	10–11	24
Captopril	1–2	2–12	2	8–12
Enalapril	4–8	12–24	2–6	24
Lisinopril	6	24	11–12	24
Moexipril	1–2	>24	1	24
Perindopril	1–2	10–12	3–10	12–24
Quinapril	1	24	2	24
Ramipril	1	24	13–17	24
Trandolapril	6	72	6–10	24

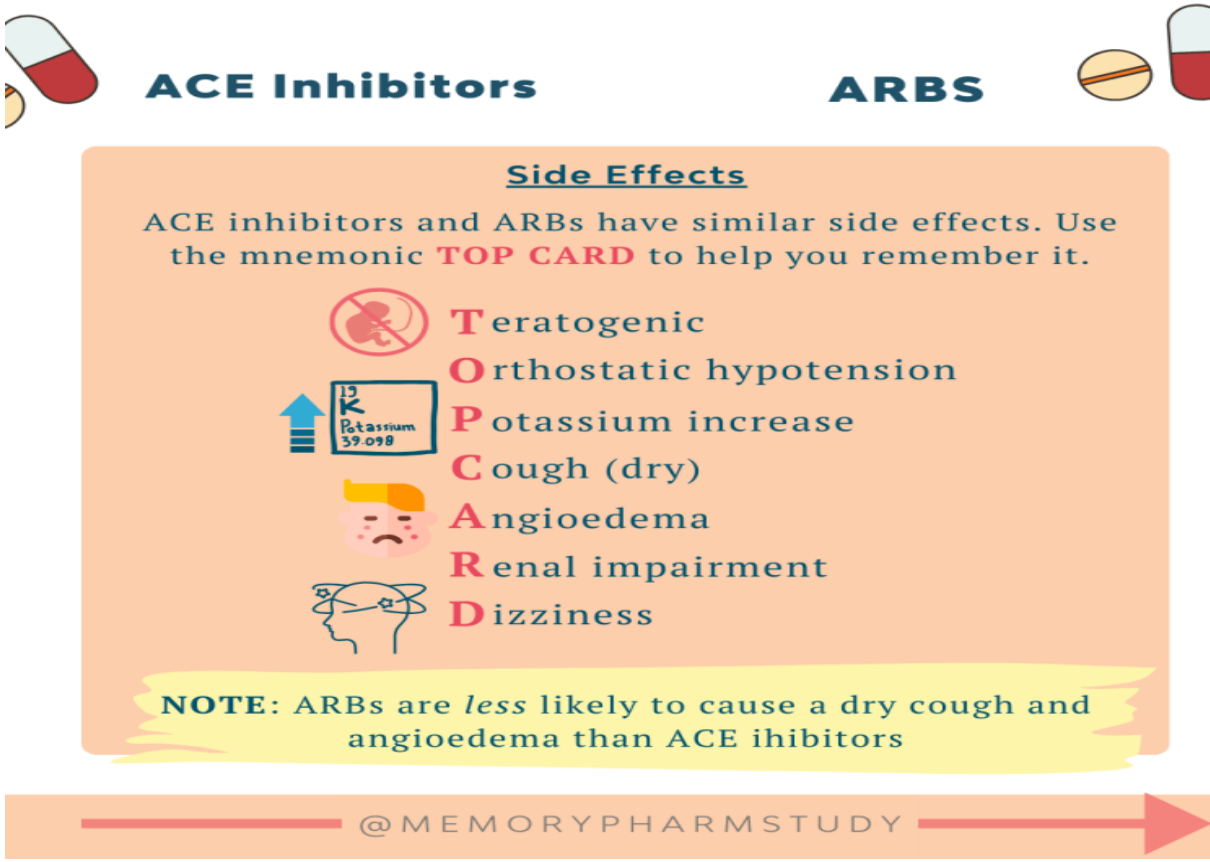
Angiotensin II receptor blockers (ARBs)

- Compete with angiotensin II for tissue binding sites & prevent angiotensin II from combining with its receptors in body tissues
- Used for hypertension, may be used as an alternative to ACE inhibitors in the management of heart failure and diabetic nephropathy.
  - Irbesartan
  - Losartan
  - Valsartan

Key indications and doses in hypertension and heart failure of available ARBs

	Hypertension		Heart failure			
ARB	Starting dose	Maximum dose	Starting dose	Maximum dose	Indicated post-MI?	Indicated for diabetic nephropathy?
Azilsartan	20–40 mg once daily	80 mg once daily	n/a	n/a	No	No
Candesartan	4–8 mg once daily	32 mg once daily	4 mg once daily	32 mg once daily	No	No
Eprosartan	300–600 mg once daily	600 mg once daily	n/a	n/a	No	No
Irbesartan	75–150 mg once daily	300 mg once daily	n/a	n/a	No	Yes – in T2DM
Losartan	25–50 mg once daily	100 mg once daily	12.5 mg once daily	100 mg once daily	No	Yes – in T2DM
Olmesartan	10 mg once daily	40 mg once daily	n/a	n/a	No	No
Telmisartan	2.5–10 mg once daily	80 mg once daily	n/a	n/a	Yes	No
Valsartan	40–80 mg once daily	320 mg once daily	40 mg twice daily	160 mg twice daily	Yes	No

- Side-effects
  - Hypotension
  - Less likely to cause cough and
  - hyperkalaemia than ACE inhibitors



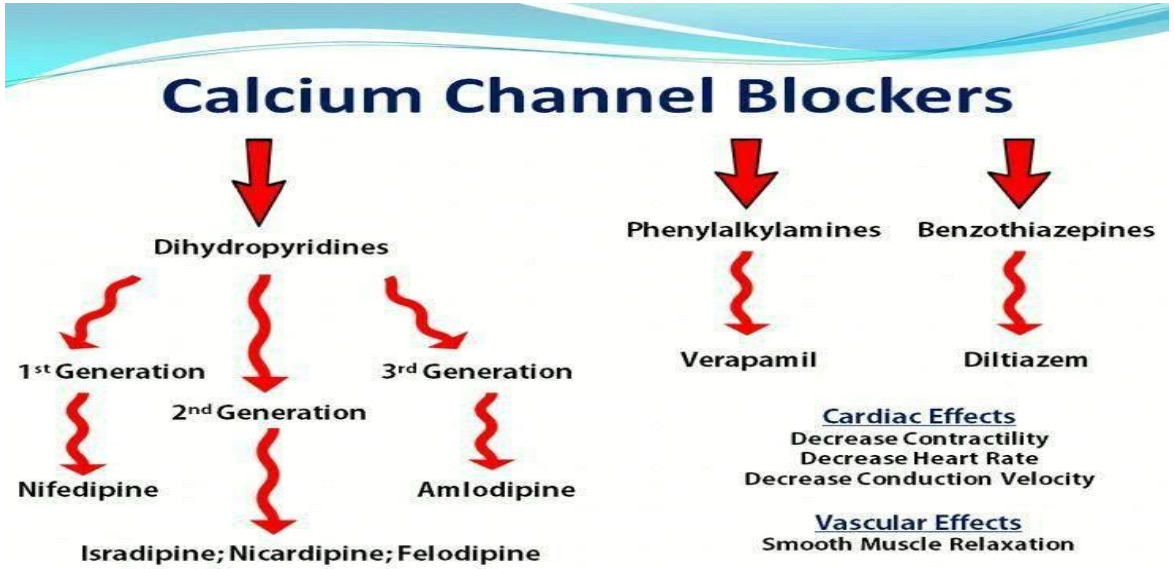
ACE inhbitors and Angiotensin II receptor antagonists may cause **first dose hypotension**

Calcium Channel Blockers

Drugs the prevent calcium ions from entering cells

Vascular Smooth Muscle:

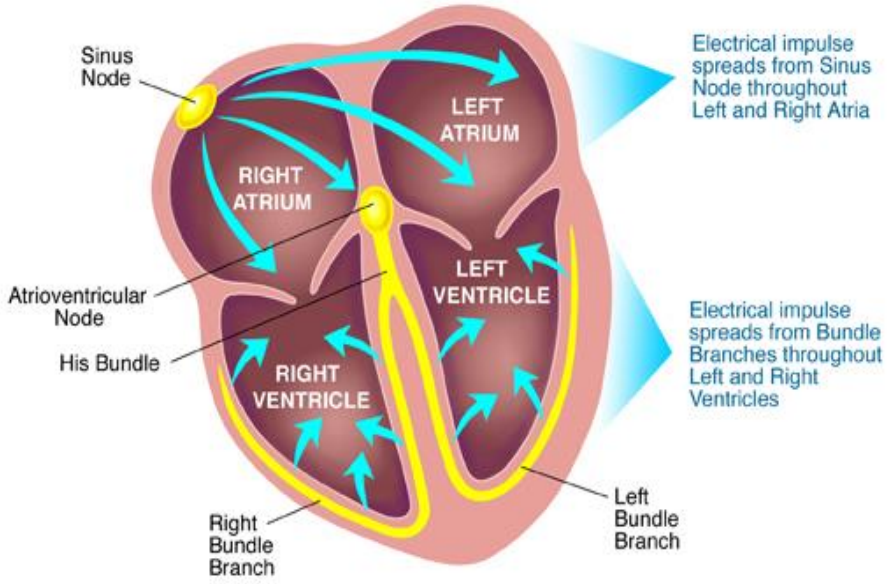
- Calcium channels regulate contraction
- If channels are blocked, contraction will be prevented and vasodilation will result
- Act selectively on peripheral arterioles and arteries and arterioles of the heart (no effect on veins)



Calcium Channel Blockers

Heart:

- Regulate function of myocardium, SA & AV nodes.
- Myocardium
  - Positive inotropic effect (increases force of contraction)
  - Calcium is blocked, contractile force will diminish



- SA Node:
  - Pacemaker activity regulated by calcium influx
  - Calcium is blocked, heart rate is reduced
- AV Node:
  - Excitability of AV nodal cells is regulated by calcium entry
  - Calcium is blocked, discharge of Av nodal cells is suppressed (decreases the velocity of conduction through the AV node).

Calcium Channel Blockers

Three chemical families in CCB's

Verapamil:

- Blocks calcium channels in blood vessels and in the heart
- Used for:
  - Angina Pectoris (vasodilation)
  - Hypertension
  - Cardiac dysrhythmias
- Careful administration/contraindications:
  - Cardiac failure, AV block, sick sinus syndrome

Diltiazem: similar to Verapamil

Nifidipine

- Relaxes vascular smooth muscle and dilates coronary and peripheral arteries
- More effect on vessels less on myocardium
  - Used for:
    - Prophylaxis of Angina Pectoris (vasodilation)
    - Hypertension

- Careful administration/contraindications:
  - Cardiac shock, advanced aortic stenosis, within one month of MI, acute attack of angina

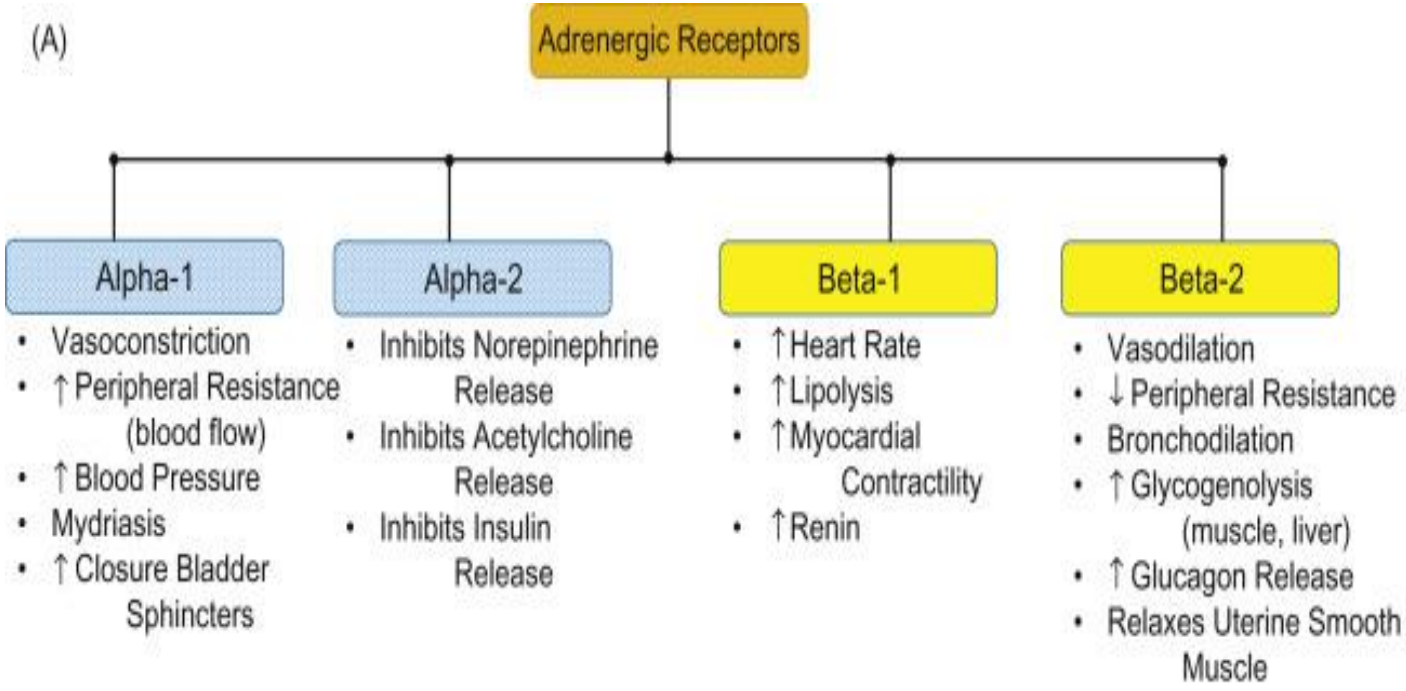
Sympatholytics (Adrenergic Antagonists)

Suppress the influence of the sympathetic nervous system on the heart, blood vessels, and other structures

Five Subcategories:

- Beta blockers
- Alpha$_1$ blockers
- Alpha/beta blockers
- Centrally acting antihypertensives
- Adrenergic neuron blockers

(A)



(B)

Alpha-1	Alpha-2	Beta-1	Beta-2
NE > E	E > NE	E = NE	E >> NE
NE = Norepinephrine; E = Epinephrine			

Beta-Adrenergic Blockers

Most widely used antihypertensive drugs

Four useful actions in hypertension:

- Blockade of cardiac beta$_1$ receptors
  - Decreases heart rate and contractility (decreases cardiac output)
  - Suppress reflex tachycardia caused by vasodilators in the regimen

- Blockade of beta$_1$ receptors on juxtaglomerular cells of kidney reduce release of renin
  - Reduces Angiotensin II vasoconstriction, aldosterone mediated volume expansion
- Long term use reduces peripheral vascular resistance

- Adverse effects:
  - Bradycardia, decreased AV conduction, reduced contractility
- Contraindicated:
  - Sick sinus syndrome/ AV blocks/ asthma (bronchoconstrictive effects)

Non selective Beta blockers

Propranolol hydrochloride

Sotalol

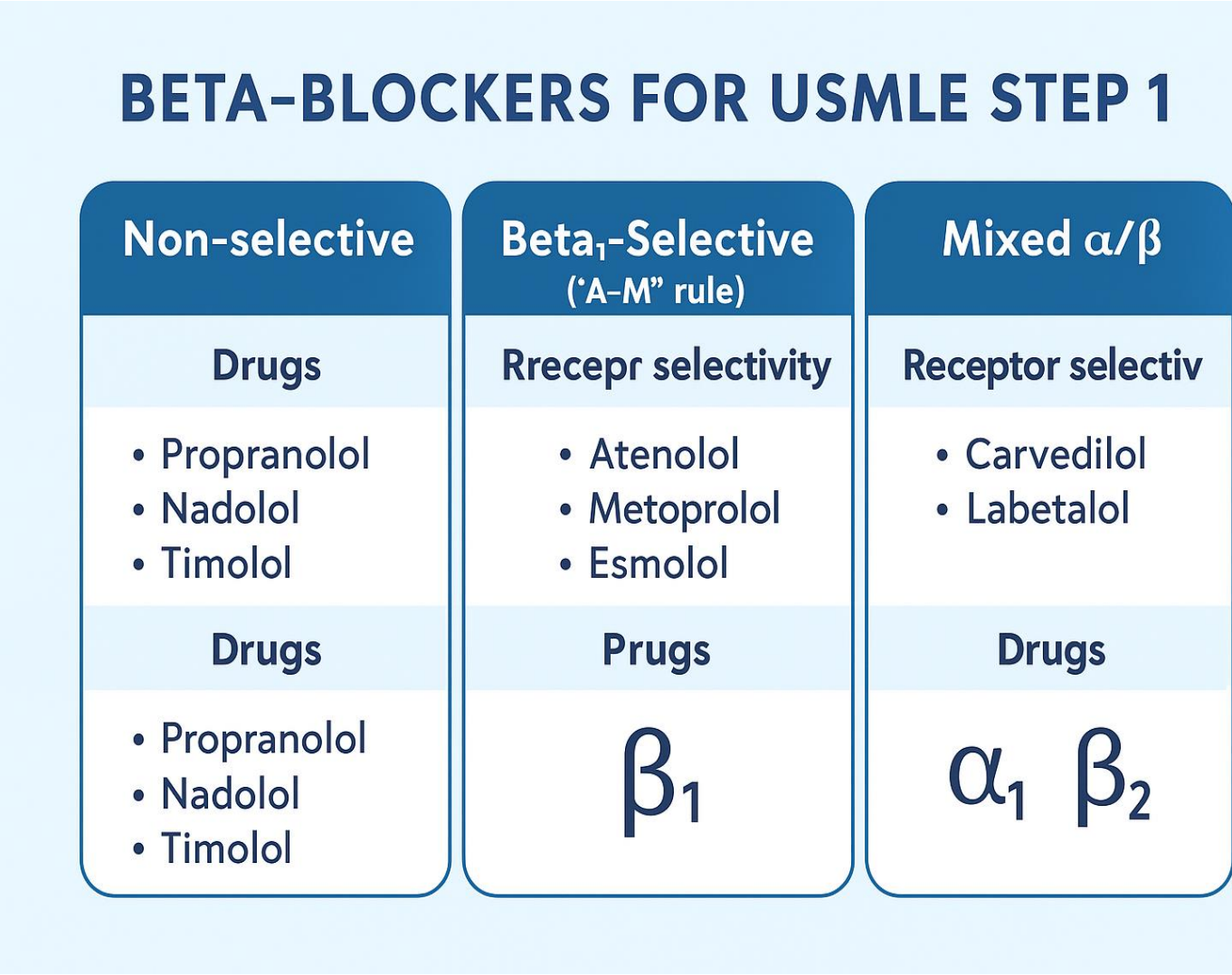
Timolol

Pindolol

Levobunolol

Nadolol

Metipranolol



Cardioselective Beta blockers

Atenolol

Acebutolol

Metoprolol

Bisoprolol

Esmolol

Betaxolol

Nebivolol

Alpha$_1$ Blockers

Prevent stimulation of alpha1 receptors on arterioles and veins, thereby preventing sympathetically mediated vasoconstriction.

Resultant vasodilation results in lowered blood pressure

Blockade of Alpha$_1$ receptors can cause orthostatic hypotension, reflex tachycardia.

- 1% of patients lose consciousness 30-60 minutes after receiving their first dose
- NOT be used as first line therapy for hypertension.

Alpha$_1$ Blockers

Prazocin

Doxazosin

Indoramin

Terazosin

Examples of non-selective α-adrenergic blockers include:
Phenoxybenzamine
Phentolamine

Selective α1-adrenergic blockers include:
Prazosin
Doxazosin
Tamsulosin
Terazosin

Selective α2-adrenergic blockers include:
Mirtazapine
Yohimbine

The agents carvedilol and labetalol are both α- and β-blockers.

Alpha/Beta Blockers

Block $Alpha_1$ and Beta receptors

Blood pressure drops:

- $Alpha_1$ blockade promotes dilation of arterioles/veins
- Blockade of cardiac $beta_1$ receptors reduced heart rate and contractility
- Blockage of $beta_1$ receptors on juxtaglomerular cells suppresses release of renin
- Reduce peripheral vascular resistance

Watch for:

- Bradycardia, AV heart block, asthma, postural hypotension

Prototypes: Carvedilol, Labetalol

Adverse effects

- Postural hypotension
- Tachycardia
- Sedation
- Nasal stuffiness
- Miosis
- Impotence (inhibits ejaculation)
- Exercise care in hypovolemic patients


Thank you