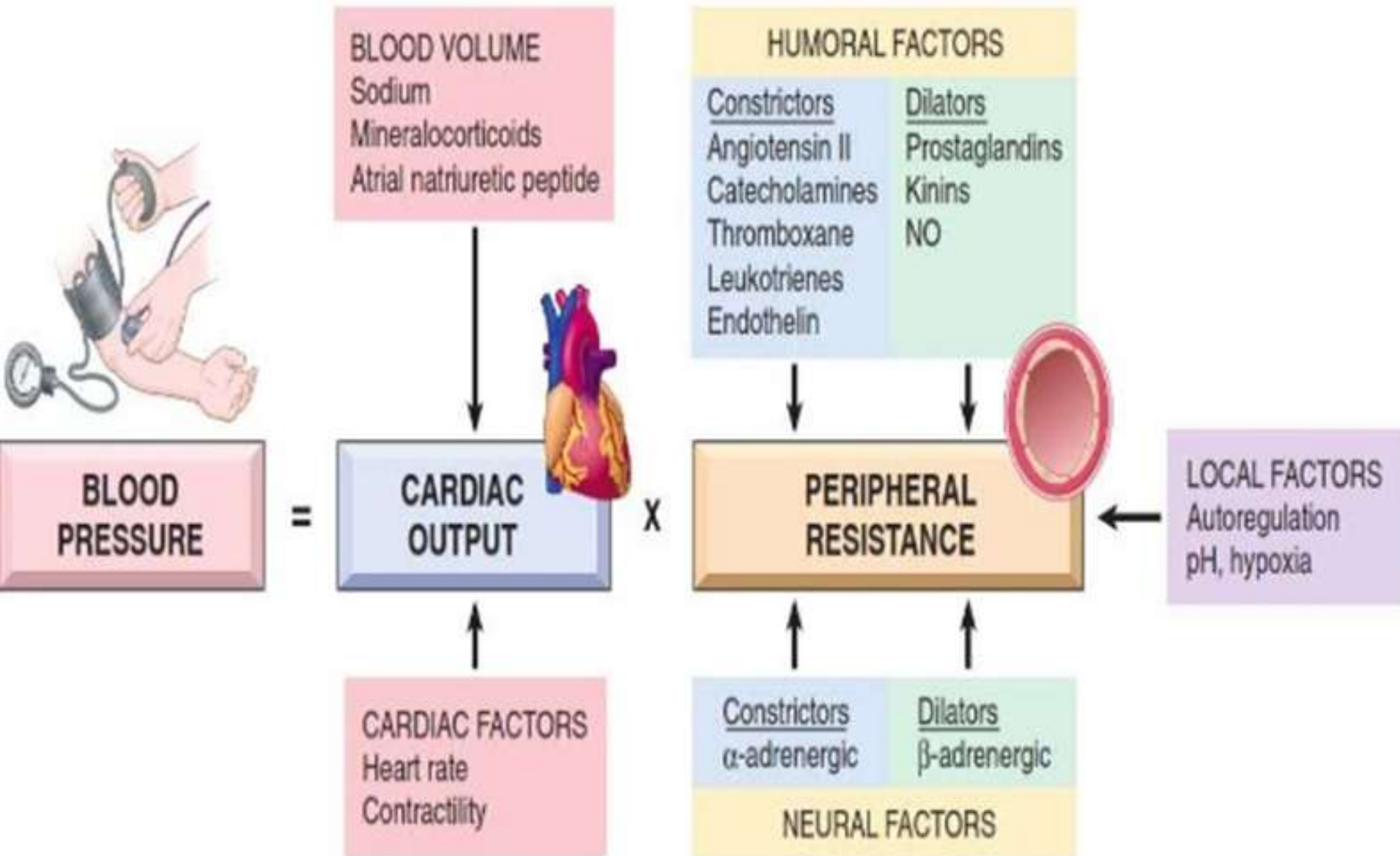


Antihypertensive Drugs

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Blood Pressure Regulation



Antihypertensive Drugs

I. Drugs affecting sympathetic nervous system:

- *beta-blockers;*
- *alpha-blockers;*
- *sympatholytics;*
- *centrally acting drugs;*
- *ganglion blockers.*

II. Vasodilators:

- *calcium channel blockers;*
- *potassium channel activators;*
- *donators of nitric oxide (NO);*

III. Drugs affecting renin-angiotensin-aldosterone system (RAAS):

- *renin inhibitors*
- *angiotensin-converting enzyme (ACE) inhibitors;*
- *angiotensin II receptor antagonists (blockers).*

IV. Diuretics:

- *thiazides and thiazide-like diuretics;*
- *loop diuretics;*
- *potassium-sparing diuretics*

Main Classes of Antihypertensive Agents

1. ACE Inhibitors

2. ARA

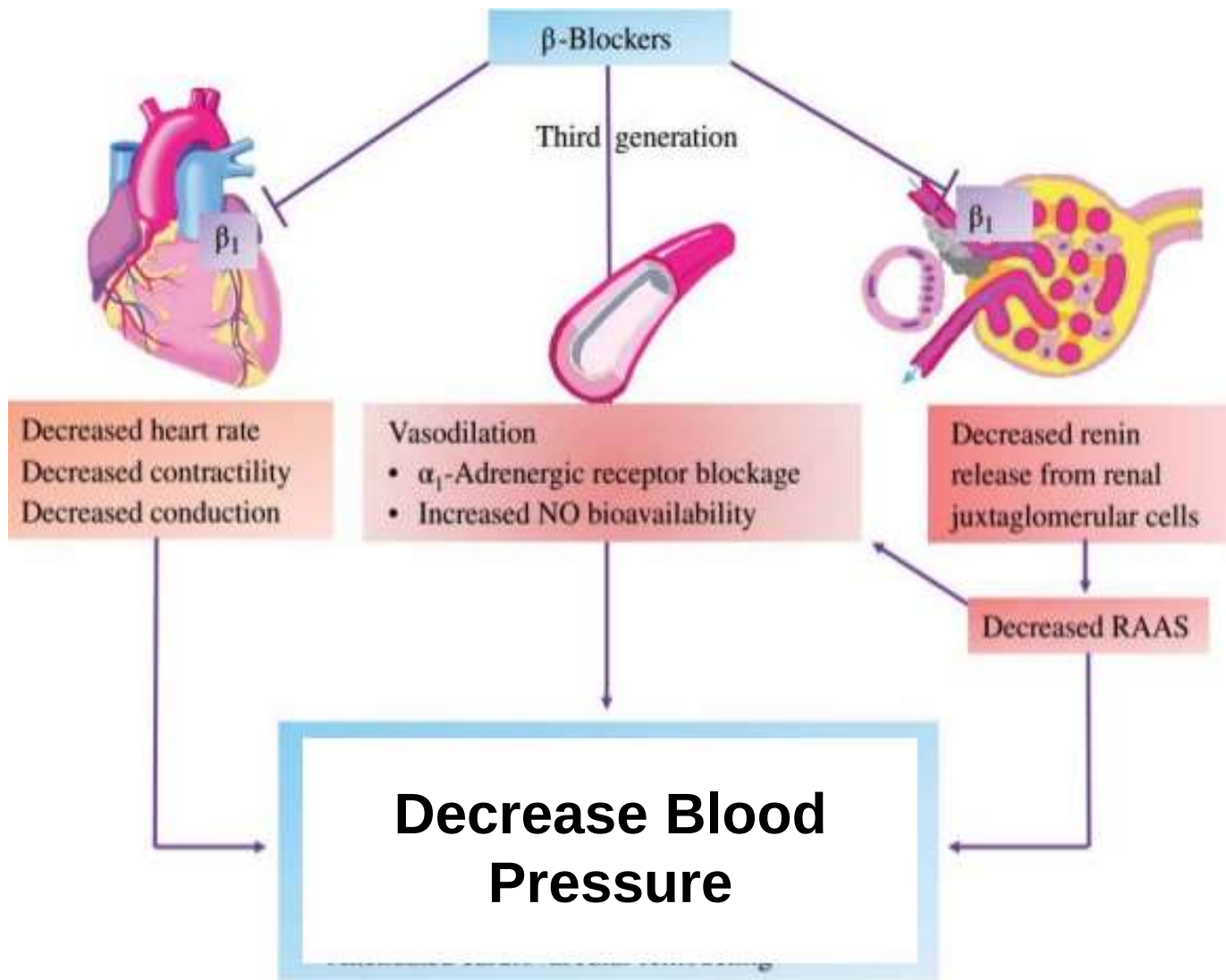
3. Calcium channel blockers

4. β -blockers

5. Diuretics

β -blockers

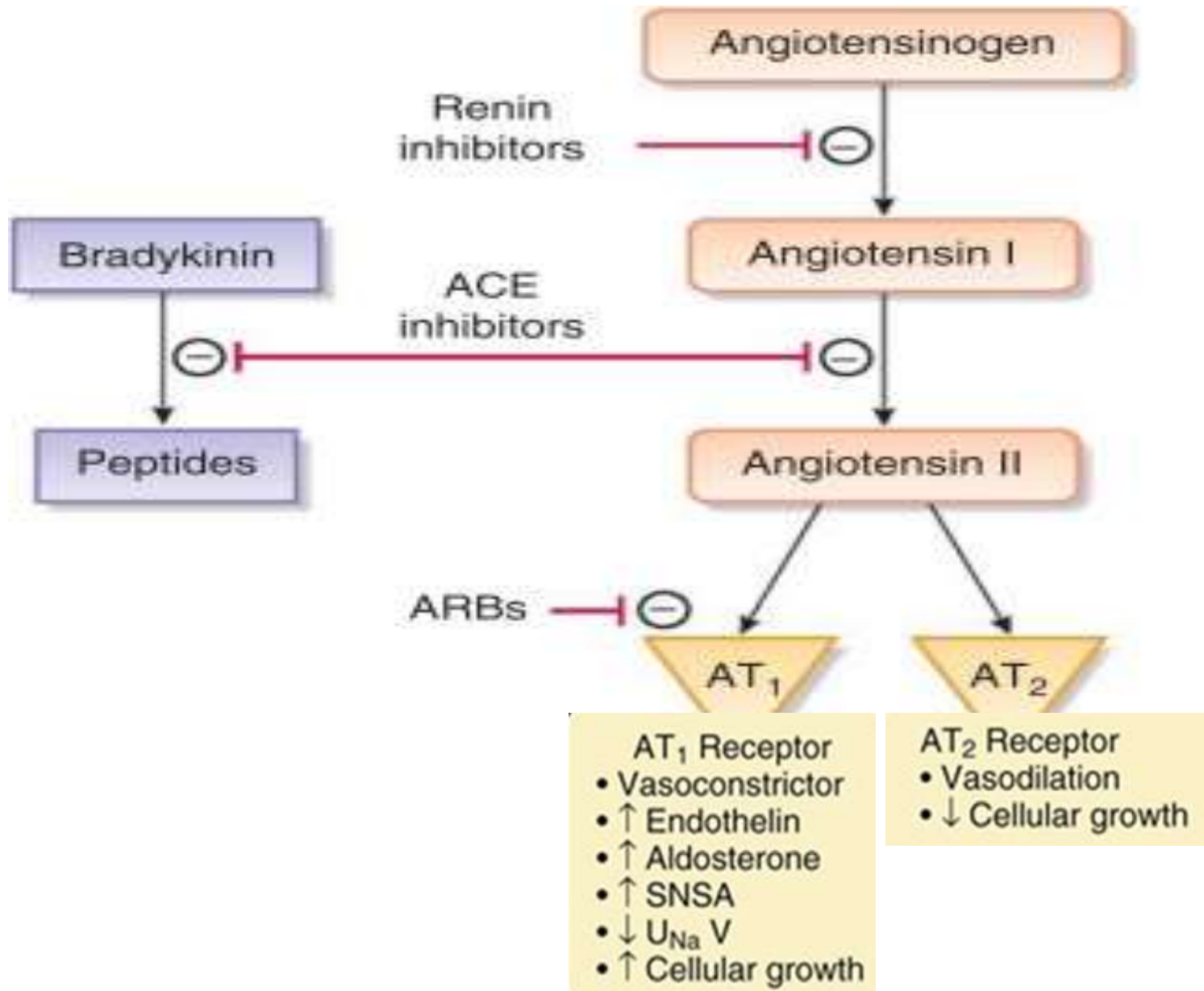
β -blockers: Mechanism of action



β -blockers: properties

- ✓ antiarrhythmic (antifibrillatory) and antianginal action
- ✓ reverse myocardium hypertrophy
- ✓ ↓ mortality of patients with CVD
- ✓ not drugs of choice in patients with obstructive pulmonary disease
- ✓ stop use under the careful control, reducing a dose within 10-14 days

Drugs affecting RAAS



ACE Inhibitors

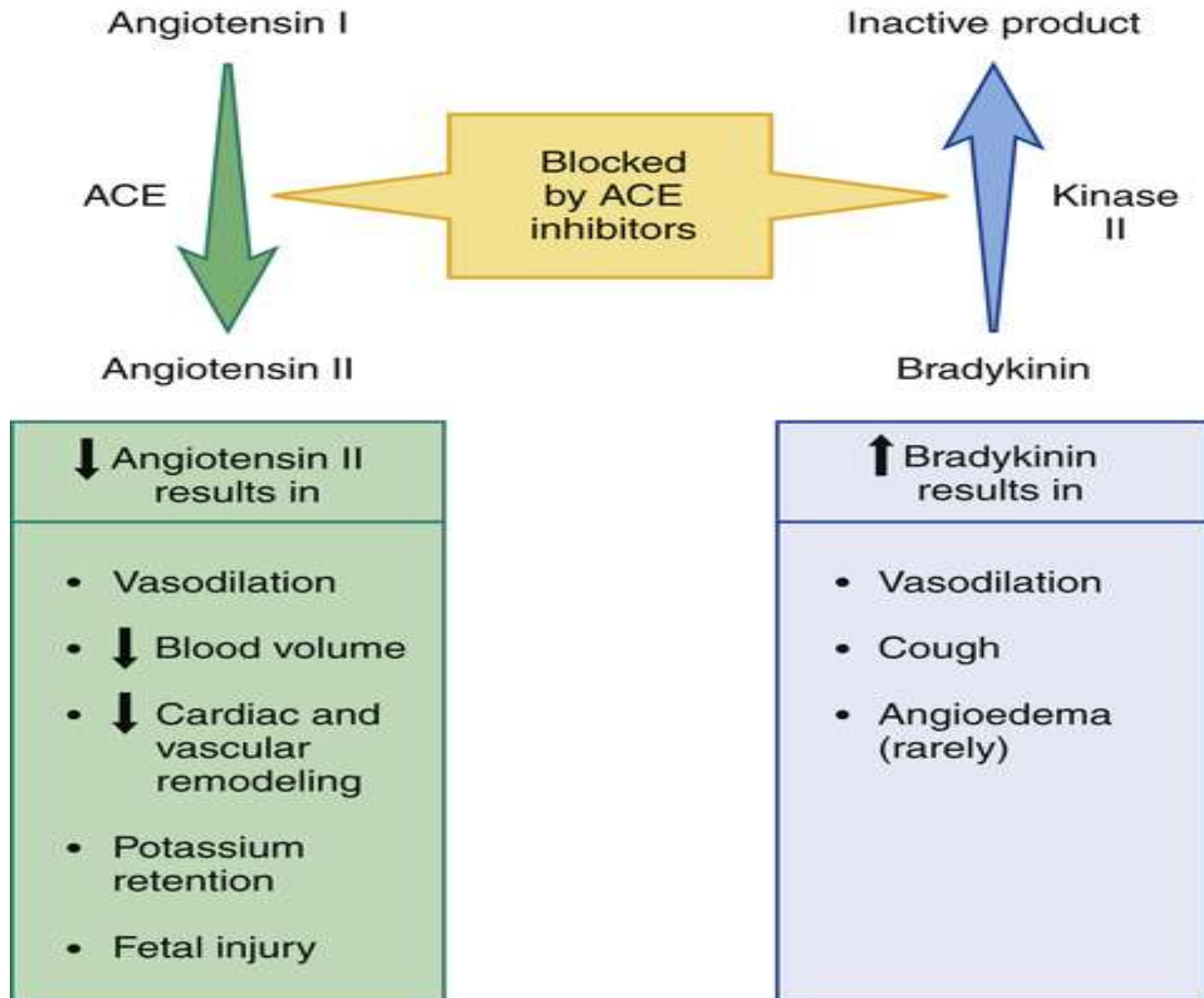
Captopril T 0,025

Enalapril T 0,005; 0,01

Lisinopril

Trandolapril

ACEI: Mechanism of Action



ACEI: Mechanism and Effects

Mechanisms:

- ❑ $\downarrow$ conversion of AT-I into AT-II $\Rightarrow \downarrow$ vascular tone
- ❑ $\downarrow$ aldosterone $\Rightarrow \downarrow$ Na⁺ and H₂O retention , $\uparrow$ K⁺
- ❑ $\uparrow$ bradykinin $\Rightarrow \uparrow$ synthesis of PG $\Rightarrow \downarrow$ vascular tone

Pharmacological effects:

- ❑ $\downarrow$ peripheral vascular resistance
- ❑ $\downarrow$ myocardium preload and postload
- ❑ $\downarrow$ cardiomyocyte hypertrophy
- ❑ $\downarrow$ progression of heart failure and risk of sudden death

ACEI: Side Effects



Hypotension



Dry cough



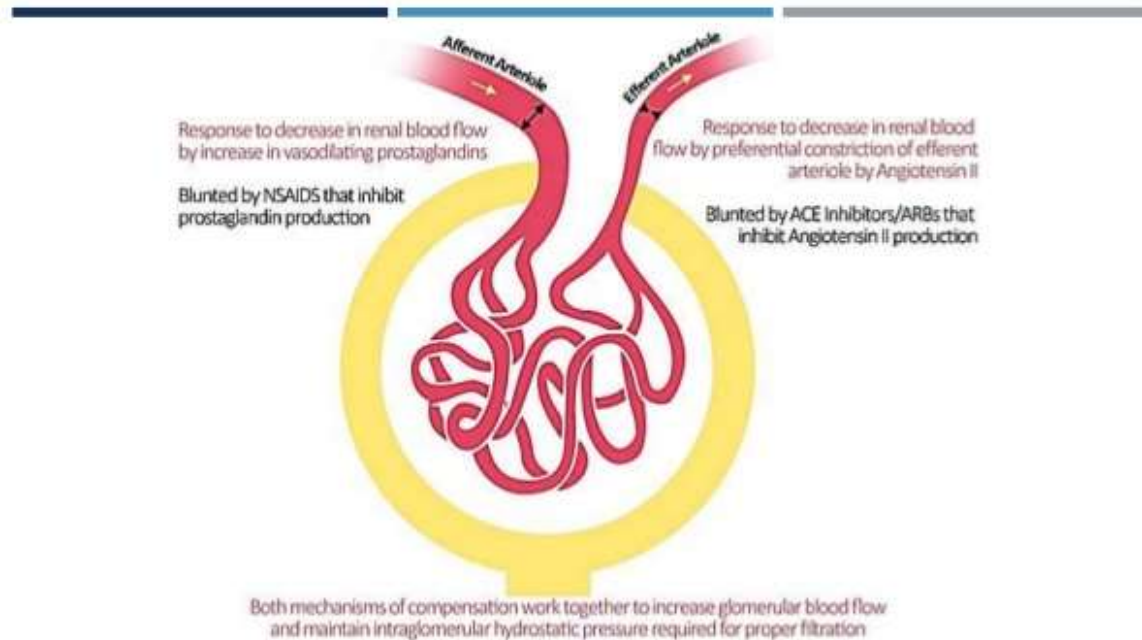
Allergic reactions (skin rashes, itching, angioedema)



Hyperkalemia (in combination with potassium-sparing diuretics, NSAIDs, potassium salts)

ACEI: Contraindications

❑ renal artery stenosis ($\downarrow$ *glomerular filtration*)



❑ pregnancy (*fetal abnormalities, growth retardation and fetal death*)

Angiotensin II receptor antagonists (ARA)

Losartan T 0,05

Valsartan T 0,32

ARA: Mechanism of Action

- ❑ **Selective blocking of AT-II receptor type 1**
- ❑ ↓ vascular tone
- ❑ ↓ aldosterone $\Rightarrow$ ↓ Na^+ and H_2O retention , ↑ K^+
- ❑ ↑ renin and AT II $\Rightarrow$ activation of AT-II receptor type 2
- ❑ Do not affect the metabolism of bradykinin

ARA: Side Effects

- ☐ hypotension
- ☐ Hyperkalemia
- ☐ Decrease renal function in renal artery stenosis
- ☐ Hepatotoxicity

ARA: Contraindications

- ☐ **renal artery stenosis** (*↓ glomerular filtration*)
- ☐ **pregnancy** (*fetal abnormalities, growth retardation and fetal death*)

Calcium channel blockers

Nifedipine

Amlodipine

Verapamil

Diltiazem

Calcium channels

Type	Location	Blockers
L (long acting)	Lm – heart, smooth muscle Ln – neurons	nifedipine amlodipine verapamil diltiazem
T (transient)	CNS neurons	ethosuximide
N (neuronal)	Neurons	-

Calcium channel blockers: Mechanism of Action

- ❑ **↓ peripheral vascular resistance**
blockade of potential-dependent Ca^{++} channels $\Rightarrow$
 $\downarrow \text{Ca}^{++}$ in smooth muscle of arterioles $\Rightarrow \downarrow$ vascular tone
 - ❑ **↓ heart rate and cardiac output** – negative inotropic and chronotropic effects (*for verapamil and diltiazem*)
- NB!** Combination of verapamil / diltiazem with beta-blockers is contraindicated!

Calcium channel blockers:

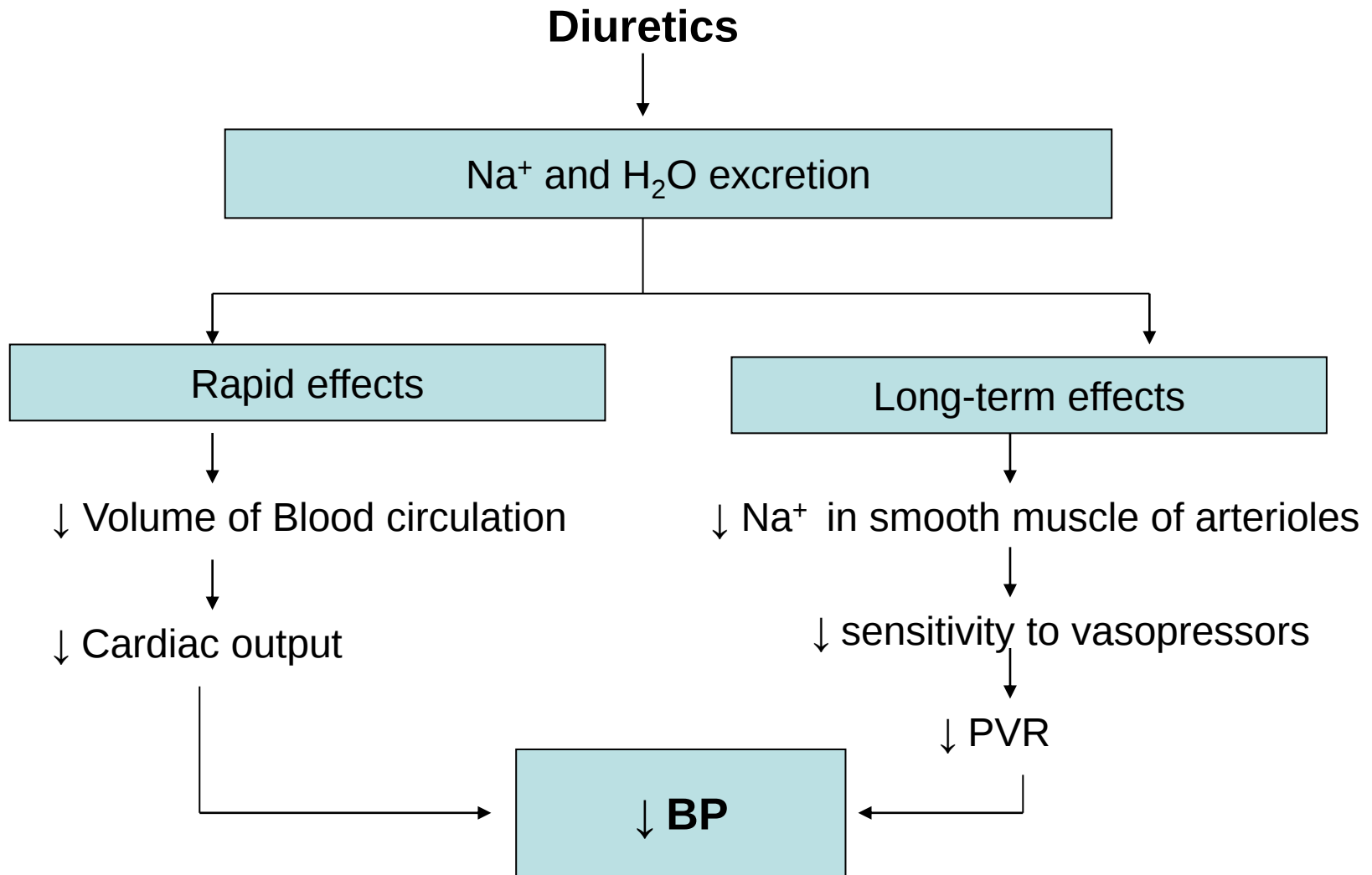
Side Effects

- Bradycardia, AV-blockad (*verapamil and diltiazem*)
- Reflex tachycardia (*nifedipine*)
- Hypotension
- Headache, dizziness
- Ankle edema
- Constipation (*verapamil*)

Diuretics

Thiazide and thiazide-like diuretics are the drugs of choice for long-term treatment of hypertension

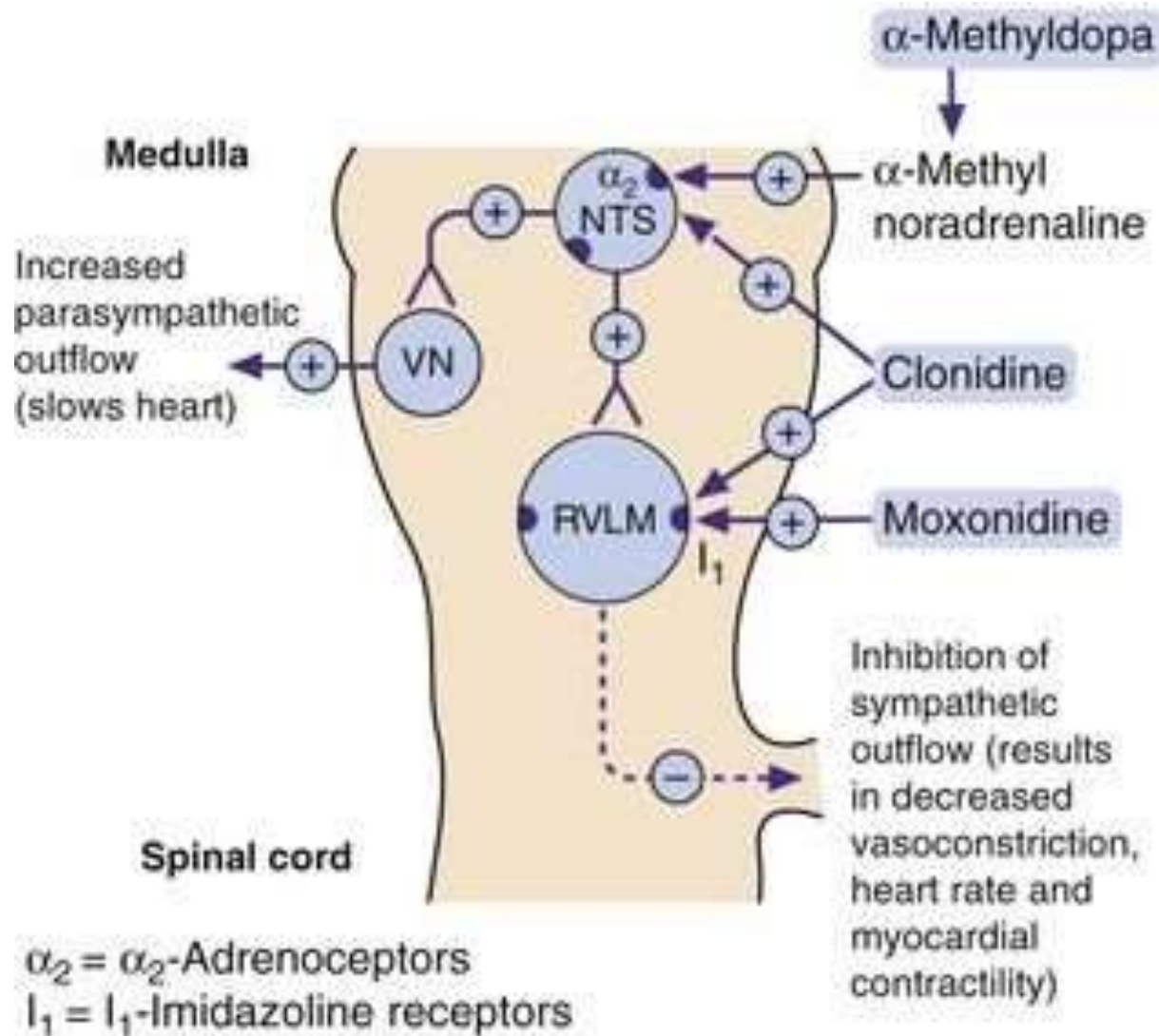
Diuretics: Mechanism of Action



Centrally acting drugs

Drugs	Receptors in medulla	Applications
Methyldopa T 0,25	✓ converted to methylnorepinephrine ✓ $\uparrow \alpha_2$	management of hypertension in pregnancy
Clonidine	$\uparrow \alpha_2$ $\uparrow I_1$ - imidazoline receptors	hypertensive emergency
Moxonidine T 0,002; 0,004	$\uparrow I_1$ ($\uparrow I_1 \gg \alpha_2$)	management of hypertension

Centrally acting drugs: Mechanism of action



- ✓ Inhibit of sympathetic vasomotor centers
- ✓ decreasing sympathetic outflow to the periphery
- ✓ reduce peripheral vascular resistance and heart work

Clonidine: Side Effects

- Sedation, potentiate of the ethanol effects on CNS
- Dry mouth
- Bradycardia
- Orthostatic hypotension
- Edema (Na^+ and H_2O retention)
- Constipation
- Withdrawal syndrome (headache, anxiety, tremor, tachycardia, **rebound hypertension** occurs following abrupt withdrawal. It *should* be withdrawn slowly)

The main indication is a hypertensive crisis.

Thanks for attention!