



HIPERTENSI

**Integrasi Pedoman Hipertensi
Terkini dalam Praktek Farmasi
Klinis : Fokus pada Individualisasi
Terapi dan Monitoring Terapi**

Apt. Rahmat Hidayat. S.Farm MSc

Hipertensi

Hipertensi Primer (95% Kasus)

Penyebab:

Dipicu oleh gabungan

- faktor genetik (riwayat keluarga) dan
- faktor lingkungan (obesitas, kurang olahraga, konsumsi garam tinggi, merokok, diabetes, atau kolesterol tinggi/dislipidemia).

Hipertensi Sekunder (5% Kasus)

Penyebab:

adanya penyakit lain

- Kerusakan ginjal kronis, gangguan kelenjar adrenal (kelebihan hormon aldosteron), gangguan pernapasan saat tidur atau efek samping dari konsumsi obat-obatan tertentu.

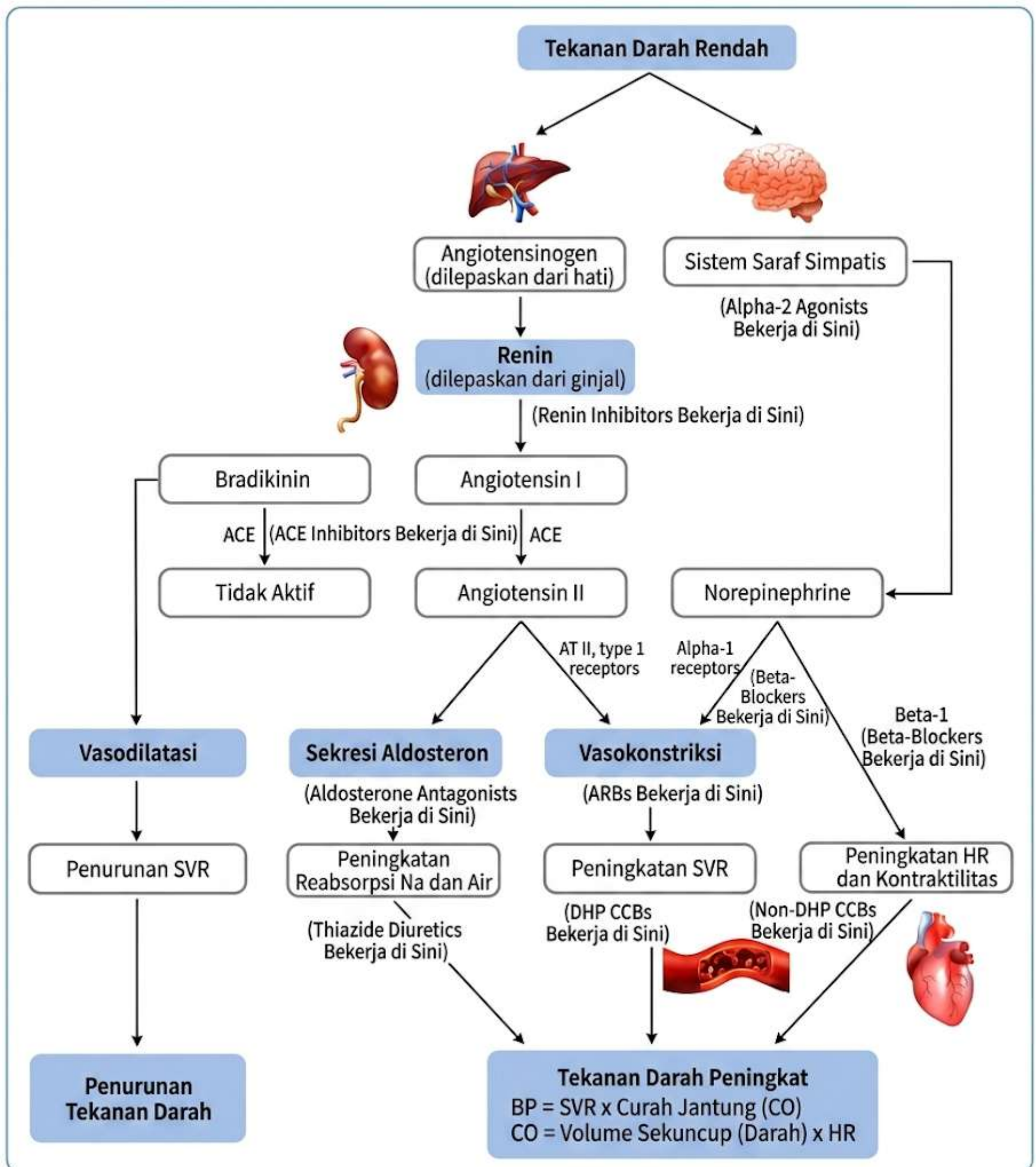
Hipertensi

Saat hipertensi, **Sistem Saraf Simpatis (SNS)** dan **Sistem Renin-Angiotensin-Aldosteron (RAAS)** aktif

norepinefrin, angiotensin II, dan aldosteron

menyebabkan:

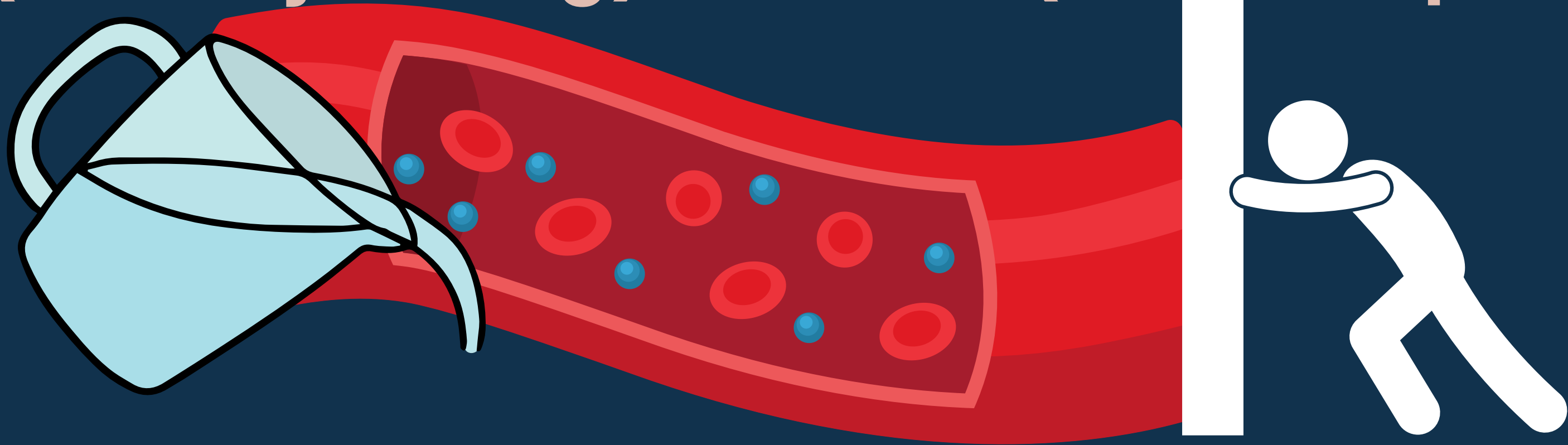
- Penyempitan pembuluh darah (**vasokonstriksi**).
- **Penahanan air** dan garam oleh ginjal.

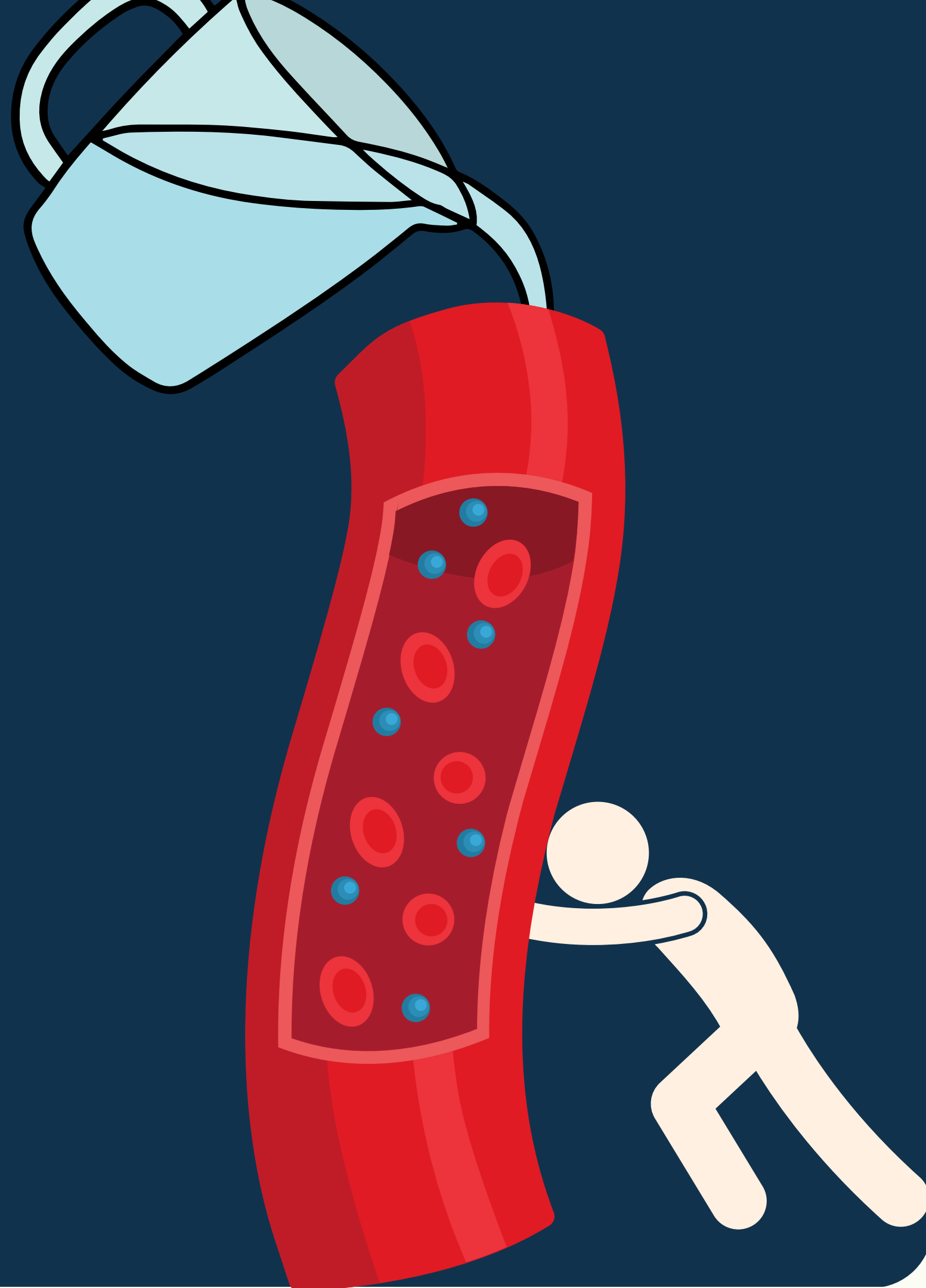


$$(MAP) = CO \times R$$

Tekanan arteri rata2 = (MAP)

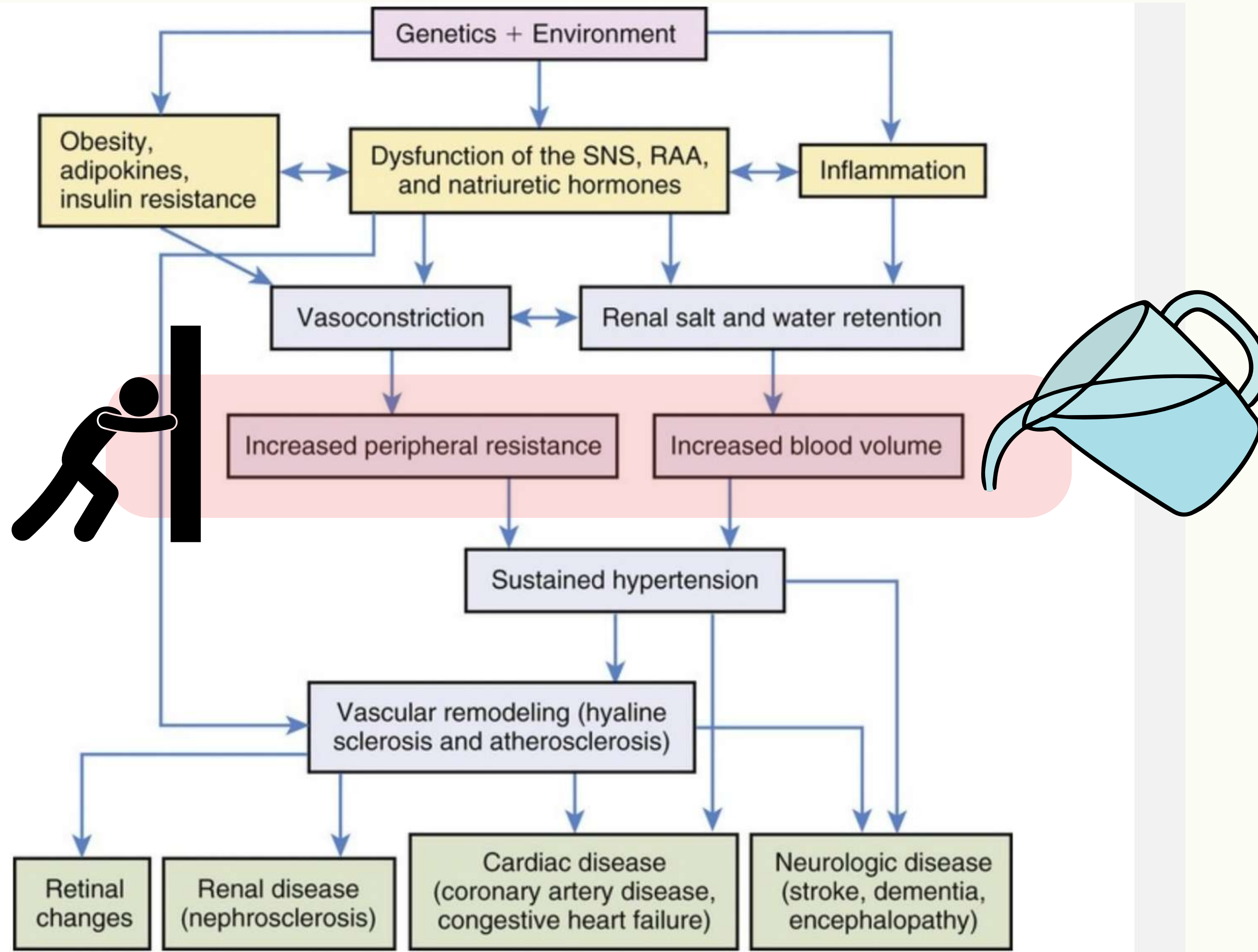
= CO (curah jantung) x R (resisten)
= (Curah jantung) x (tahanan pembuluh)

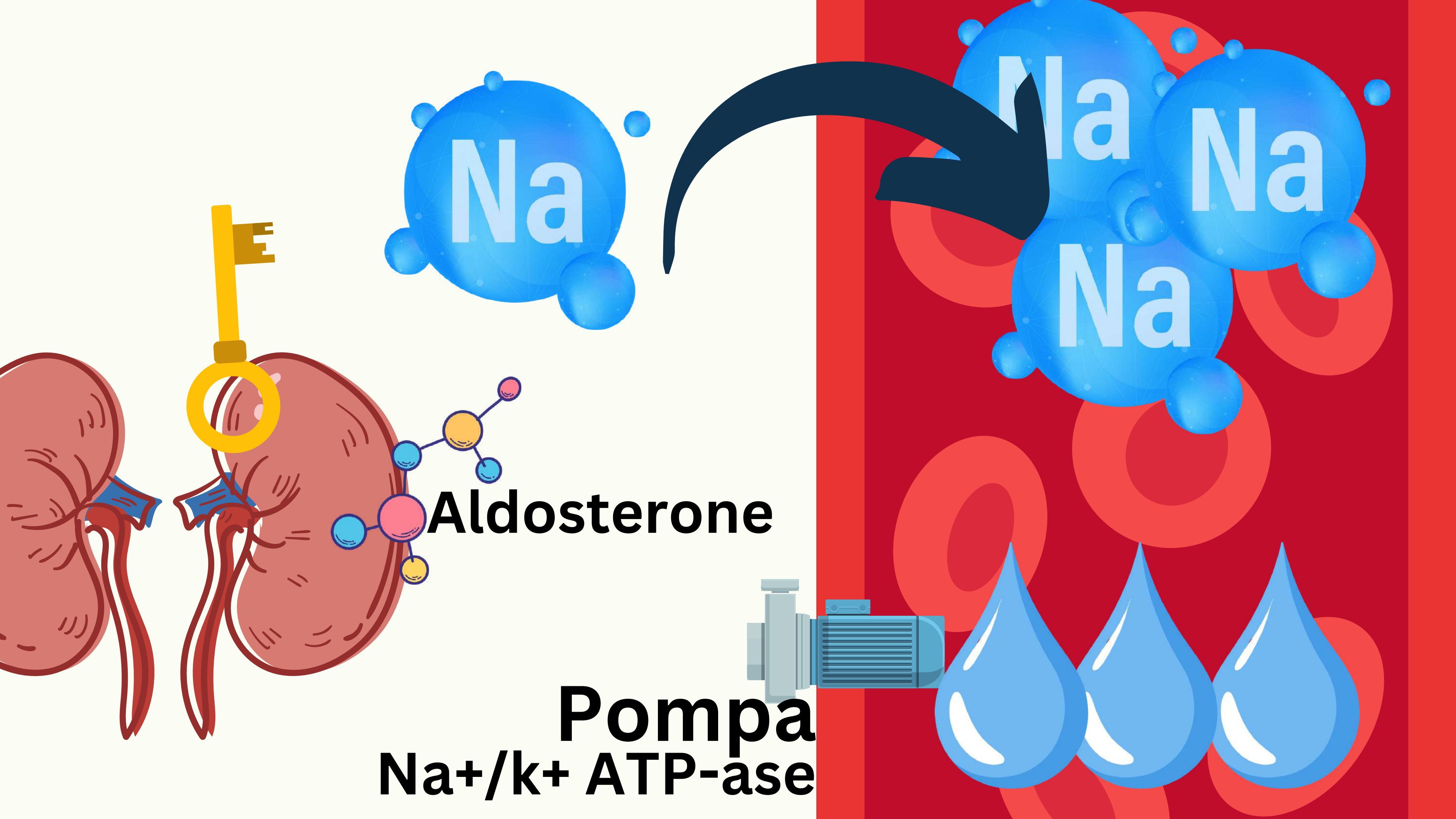




Volume air

Tahanan
pembuluh darah
(diameter)





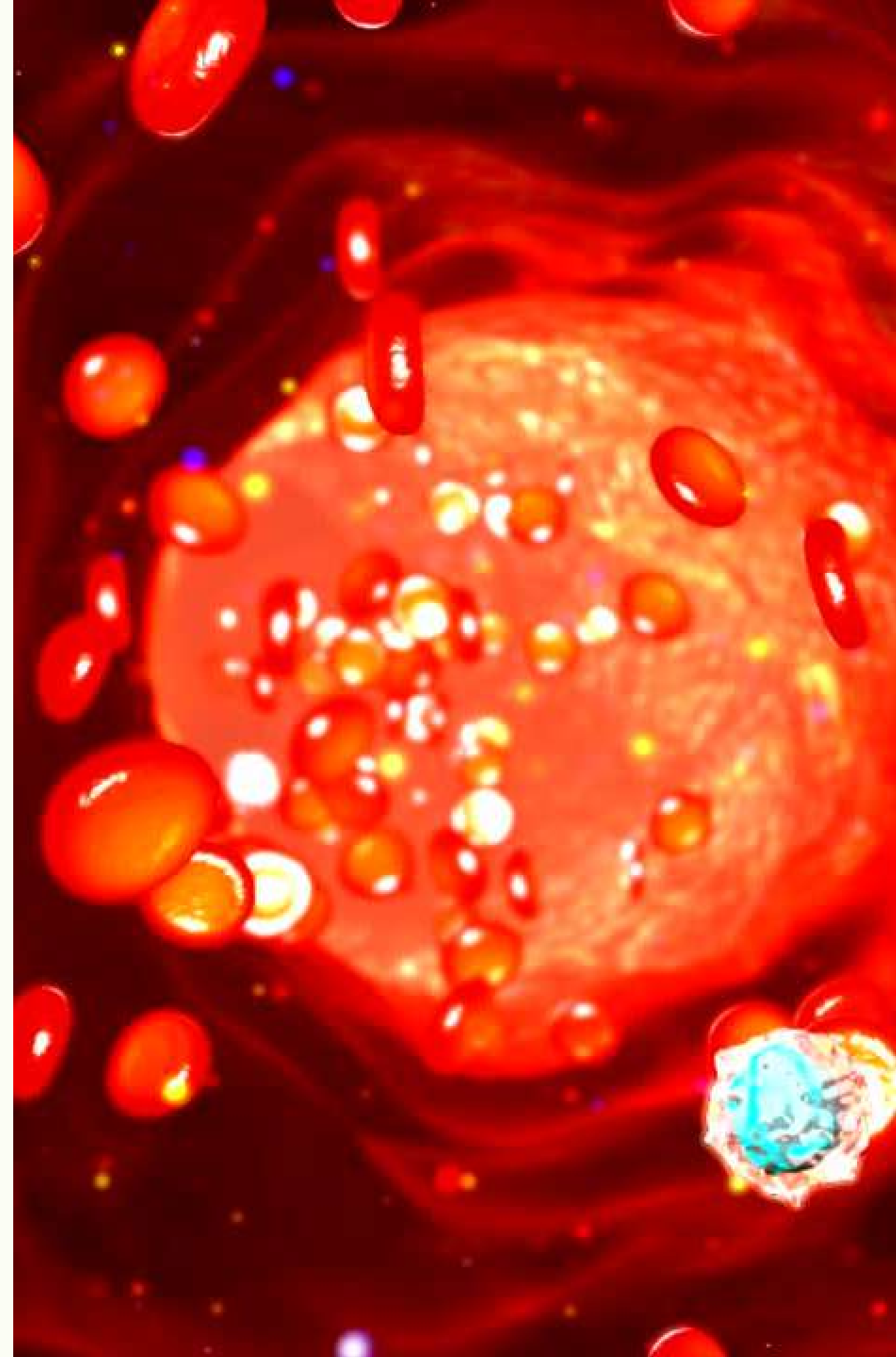
Aldosterone

Pompa
Na⁺/k⁺ ATP-ase

**OOps, aliran darah ke ginjal menurun.
Informasi ini diteruskan ke otak.**

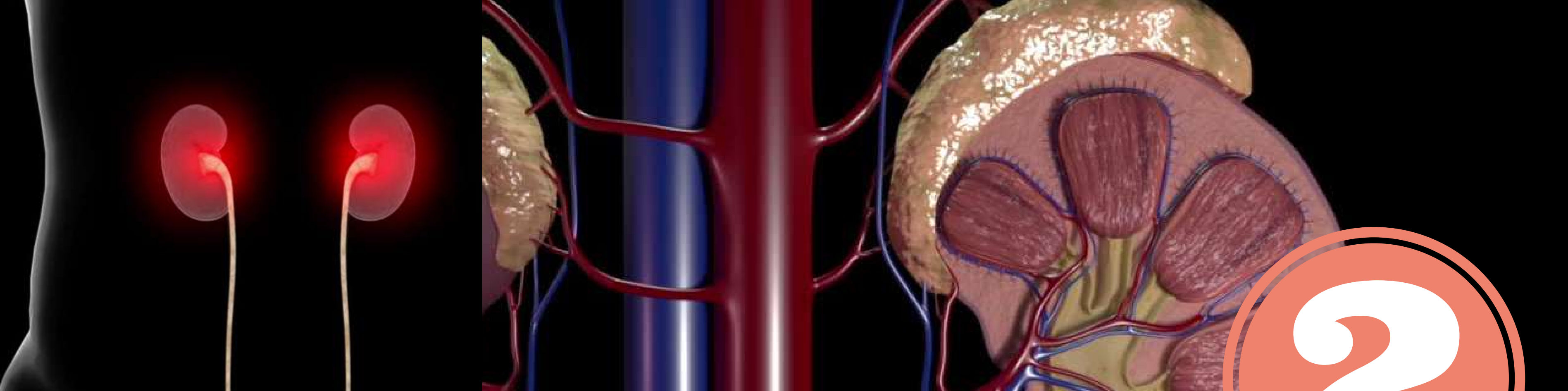
**Otak mengolahnya dan lahirlah 2
tindakan untuk mengompensasi
kondisi ini:**

- 1. **VOLUME DARAH** HARUS DITAMBAH**
- 2. **DARAH HARUS DIPOMPA** LEBIH
BANYAK**



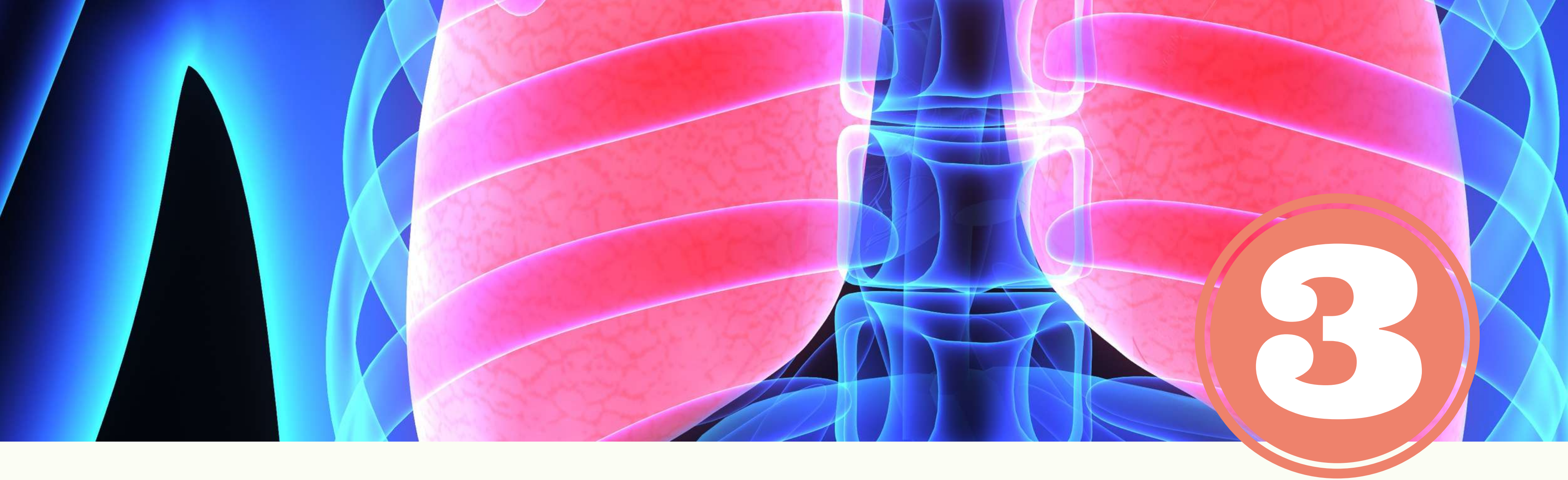


Hati melepaskan protein bernama
ANGIOTENSINOGEN ke dalam darah.

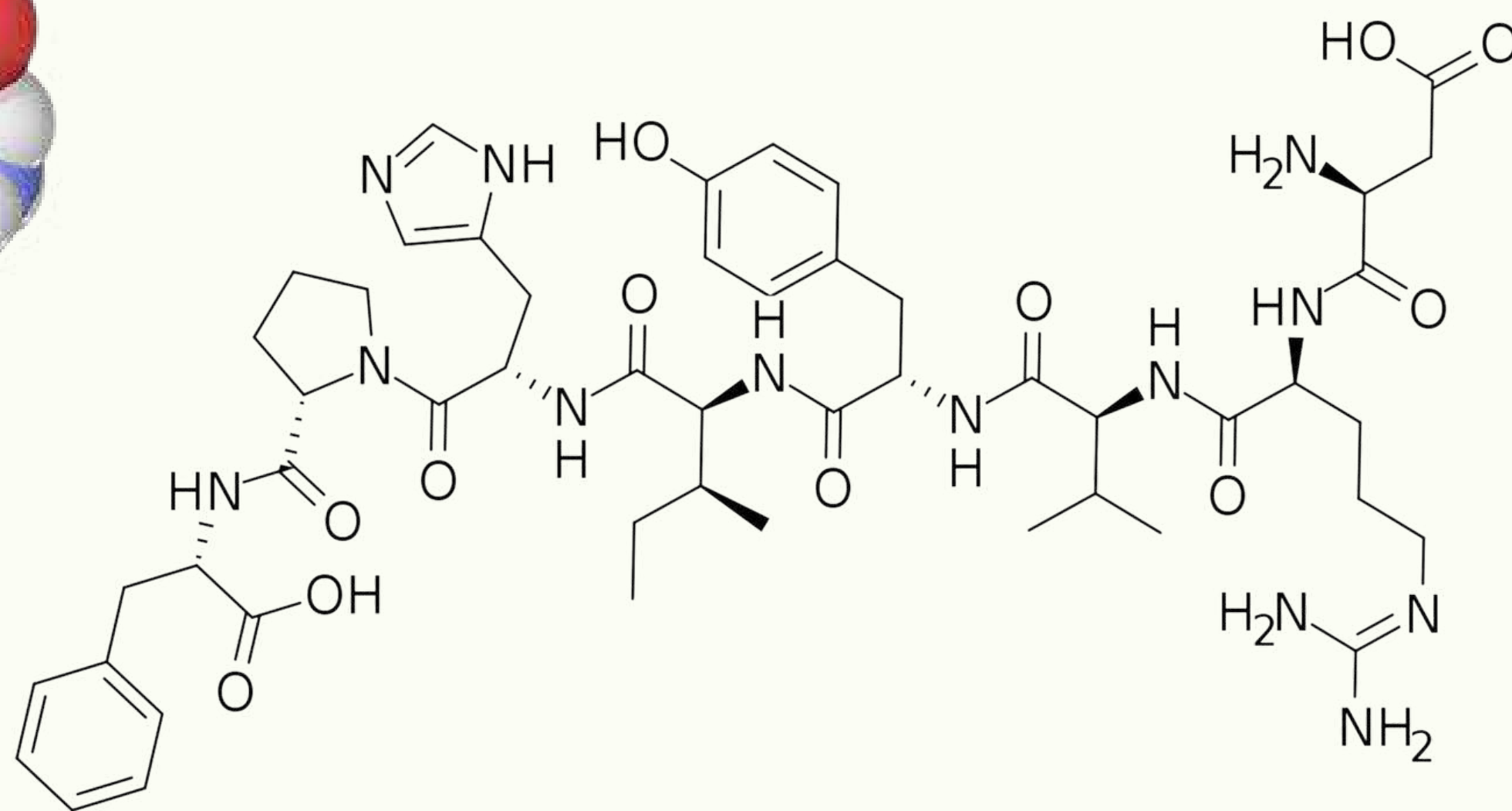
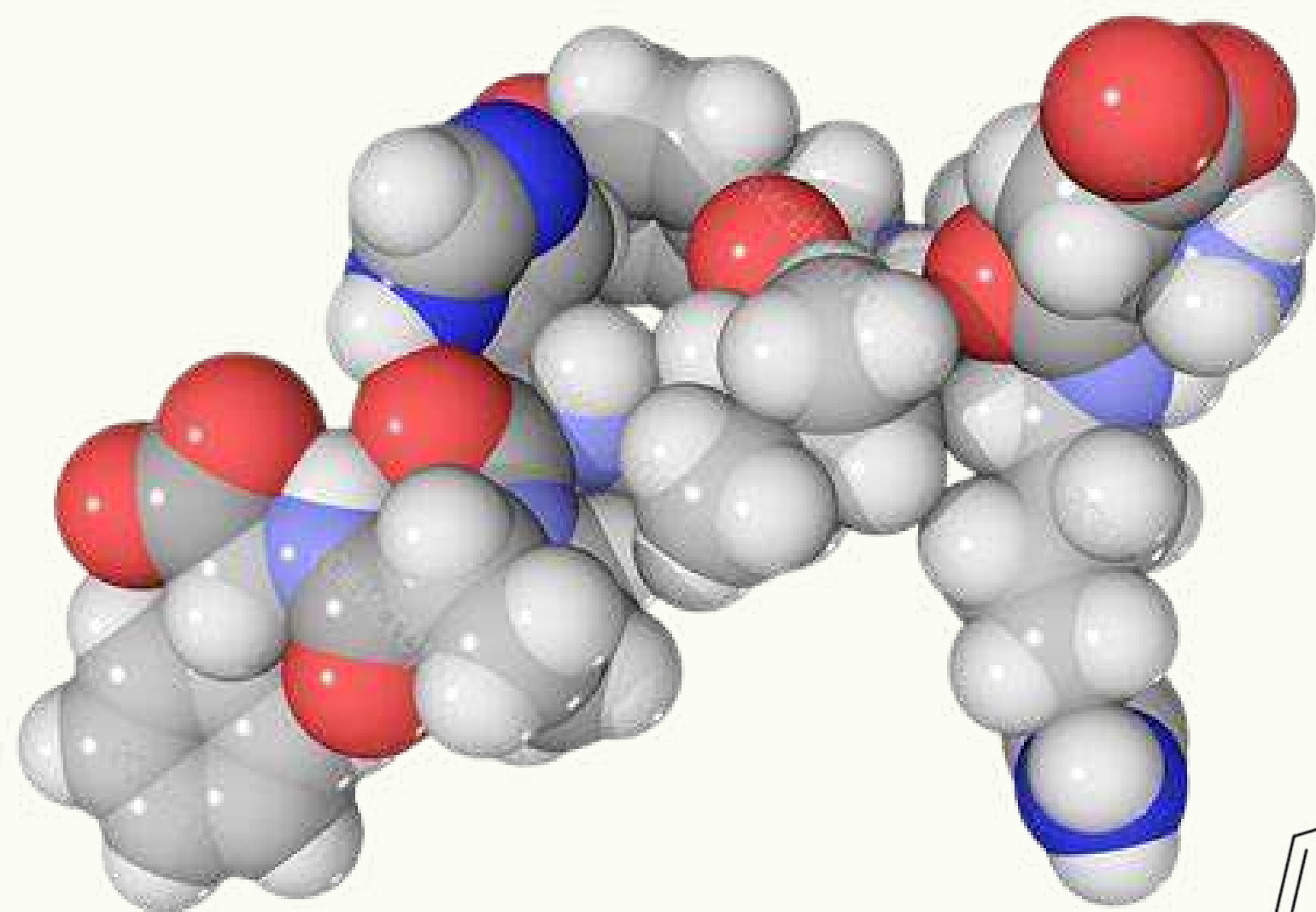


Dia menjalar ke seluruh tubuh.

**Tidak terhindarkan, ANGIOTENSINOGEN
bertemu dengan **Renin diginjal**. Disana,
ANGIOTENSINOGEN **dipotong**, menjadi
ANGIOTENSIN 1.**

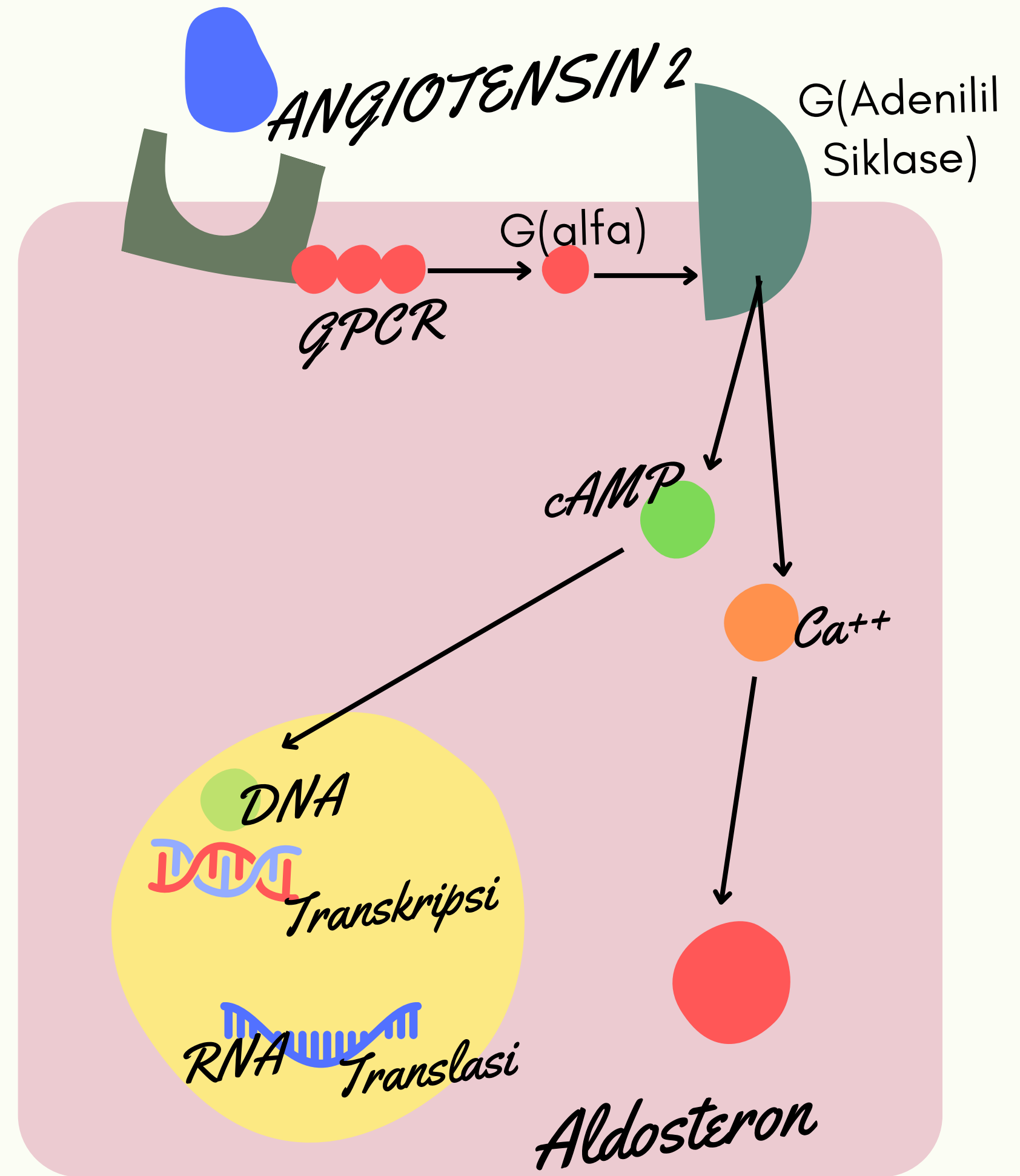
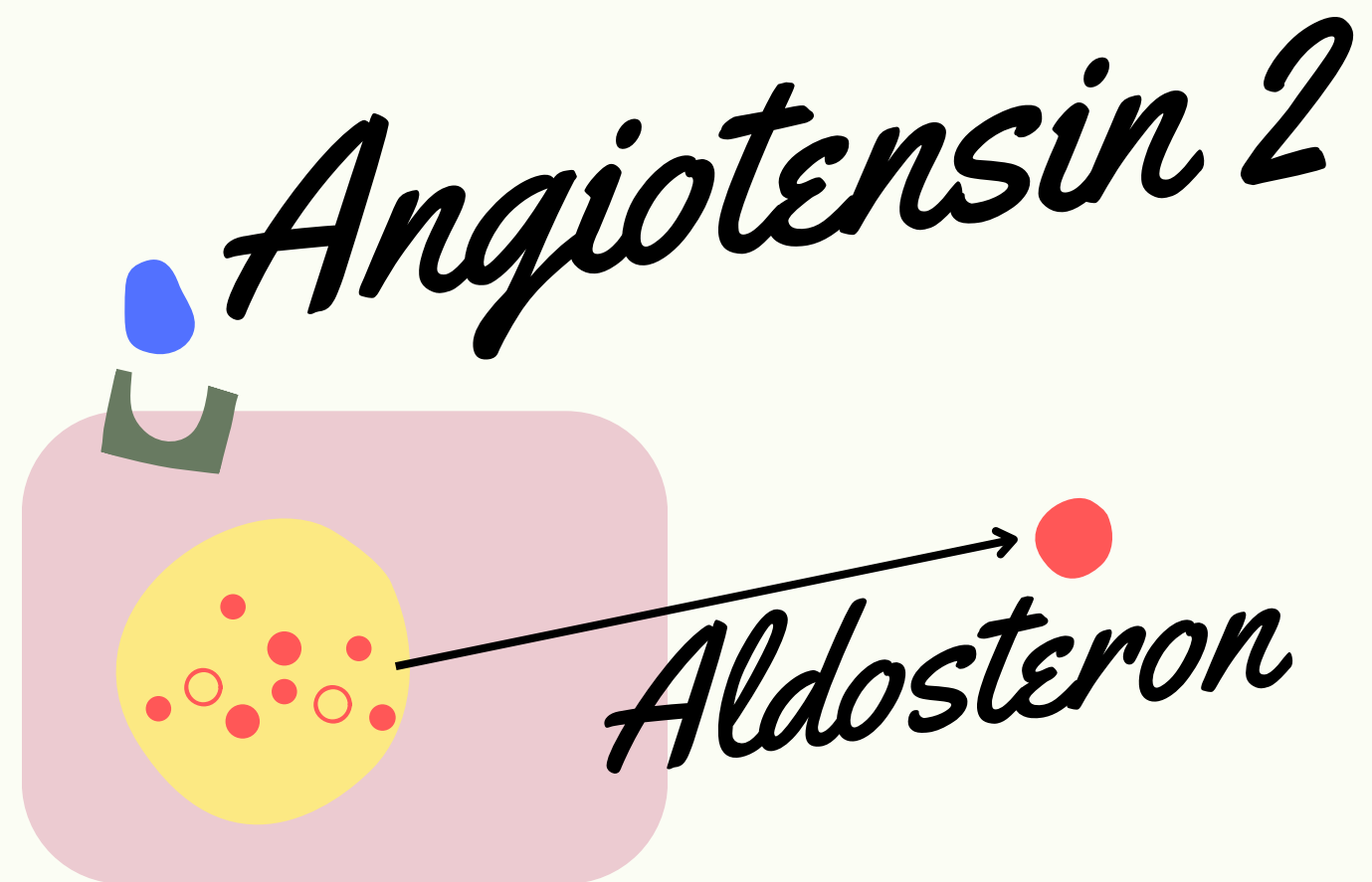


ANGIOTENSIN 1 bertamasya lagi ke seluruh bagiain tubuh. UH OW, dia dicegat di **PARU2**. Disana, sebuah enzim bernama **ANGIOTENSIN CONVERTING ENZYME (ACE)** mengutak atiknya lagi, memotongnya menjadi **ANGIOTENSIN 2**.



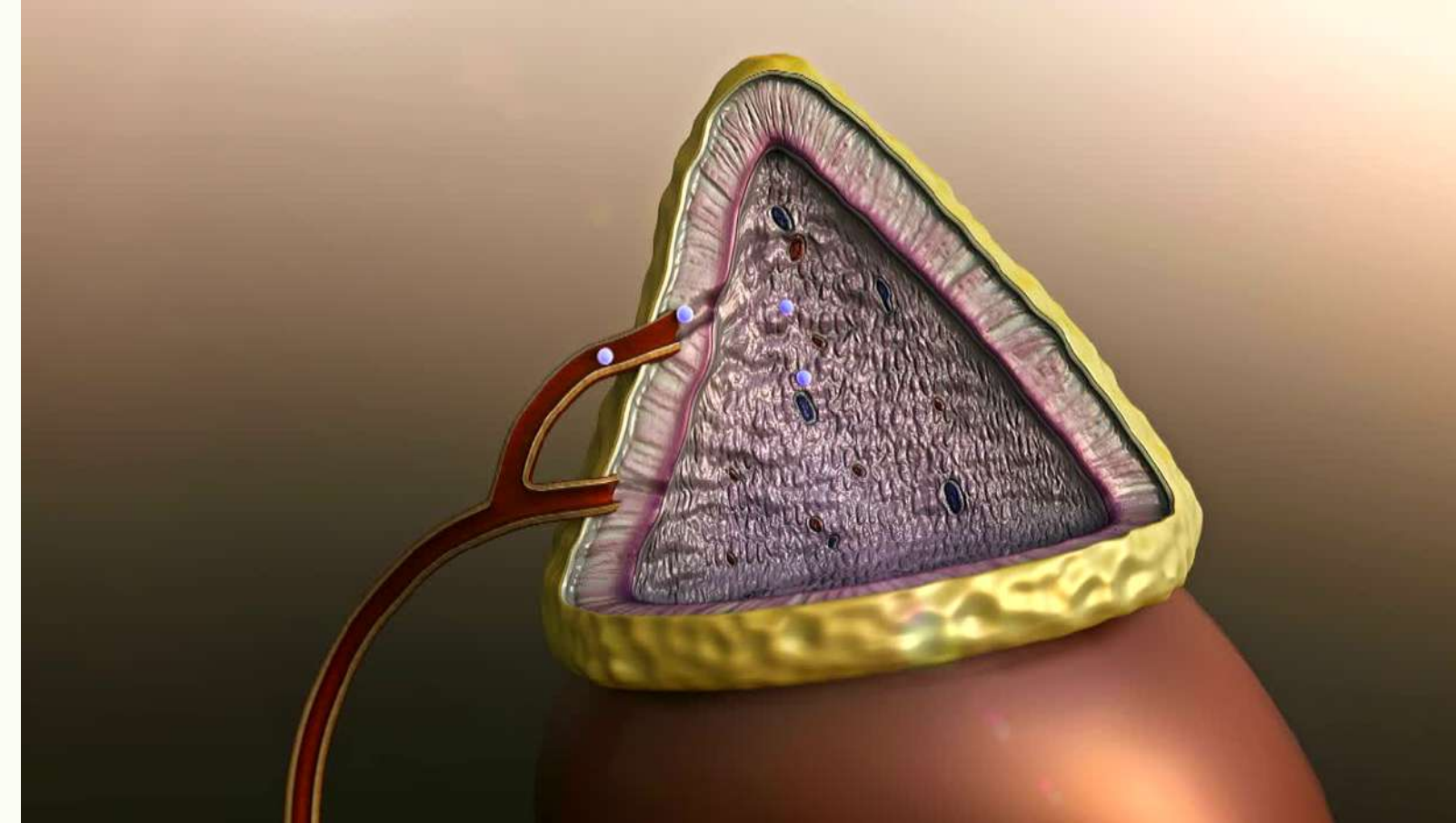
Angiotensin II

PROSES TERJADINYA RESPON SELULAR



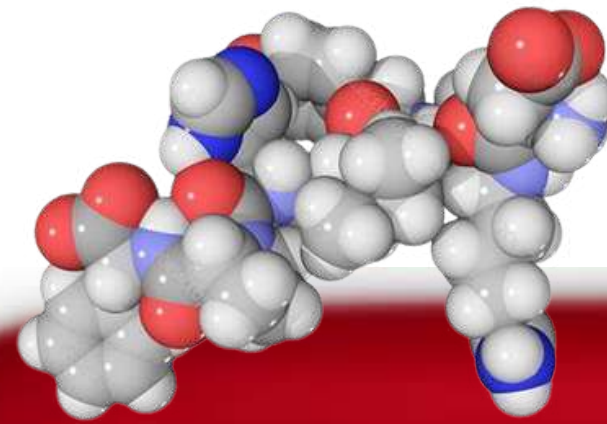
Angiotensin II berikatan pada reseptornya, **lalu meningkatkan keluaran ALDOSTERON (Kortex GINJAL).**

Hormon Aldosteron ini berikatan pula pada reseptornya, **menyebabkan PENGAMBILAN Na^+ (Sodium)** lebih banyak ke dalam aliran darah.



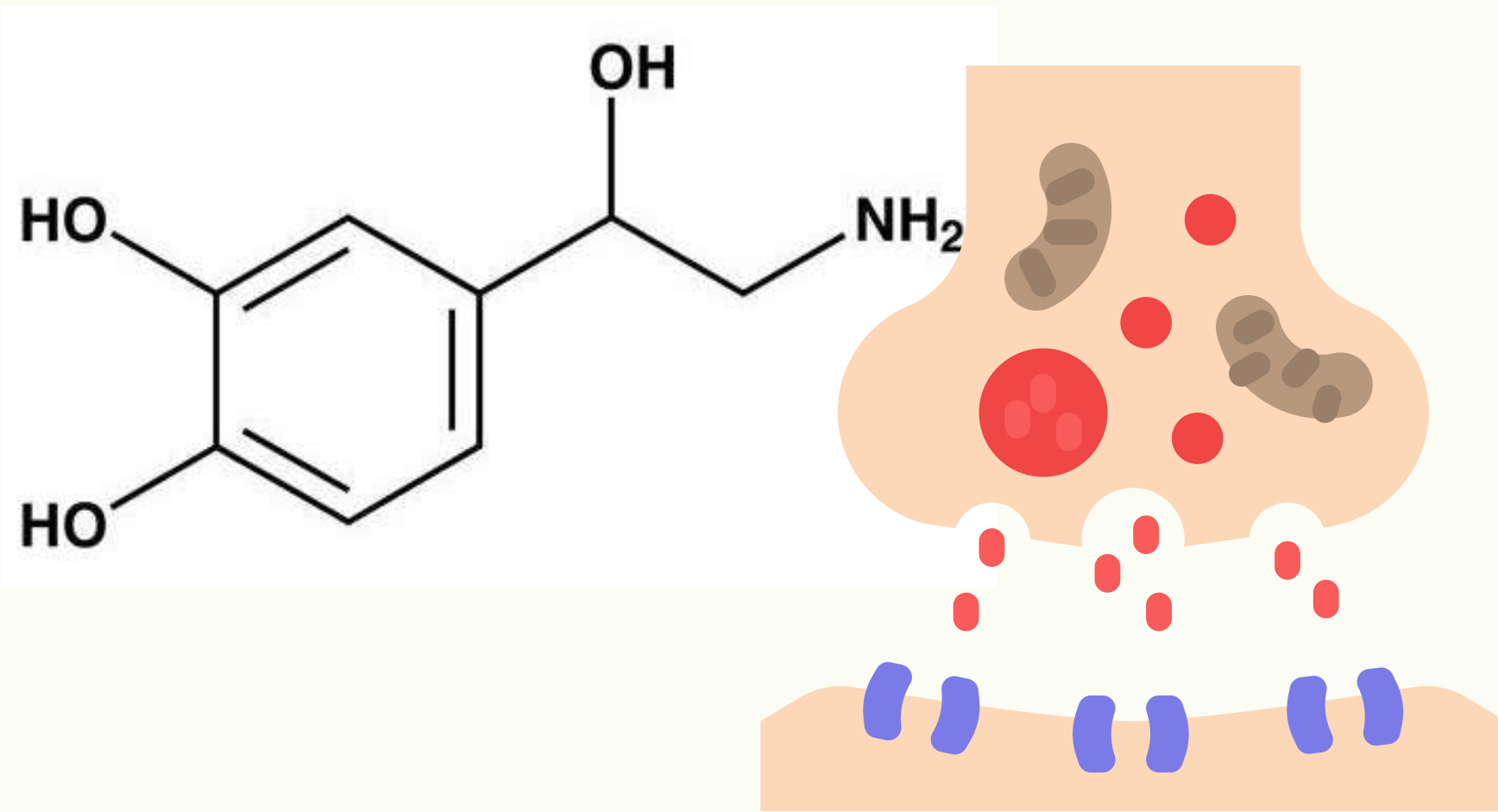
Volume darah meningkat; menyebabkan meningkatnya **tahanan** endotelial pembuluh darah: **TEKANAN DARAH MENINGKAT.**

Angiotensin juga secara langsung **MENCIUTKAN PEMBULUH DARAH** ginjal, menyumbang pada tekanan darah.

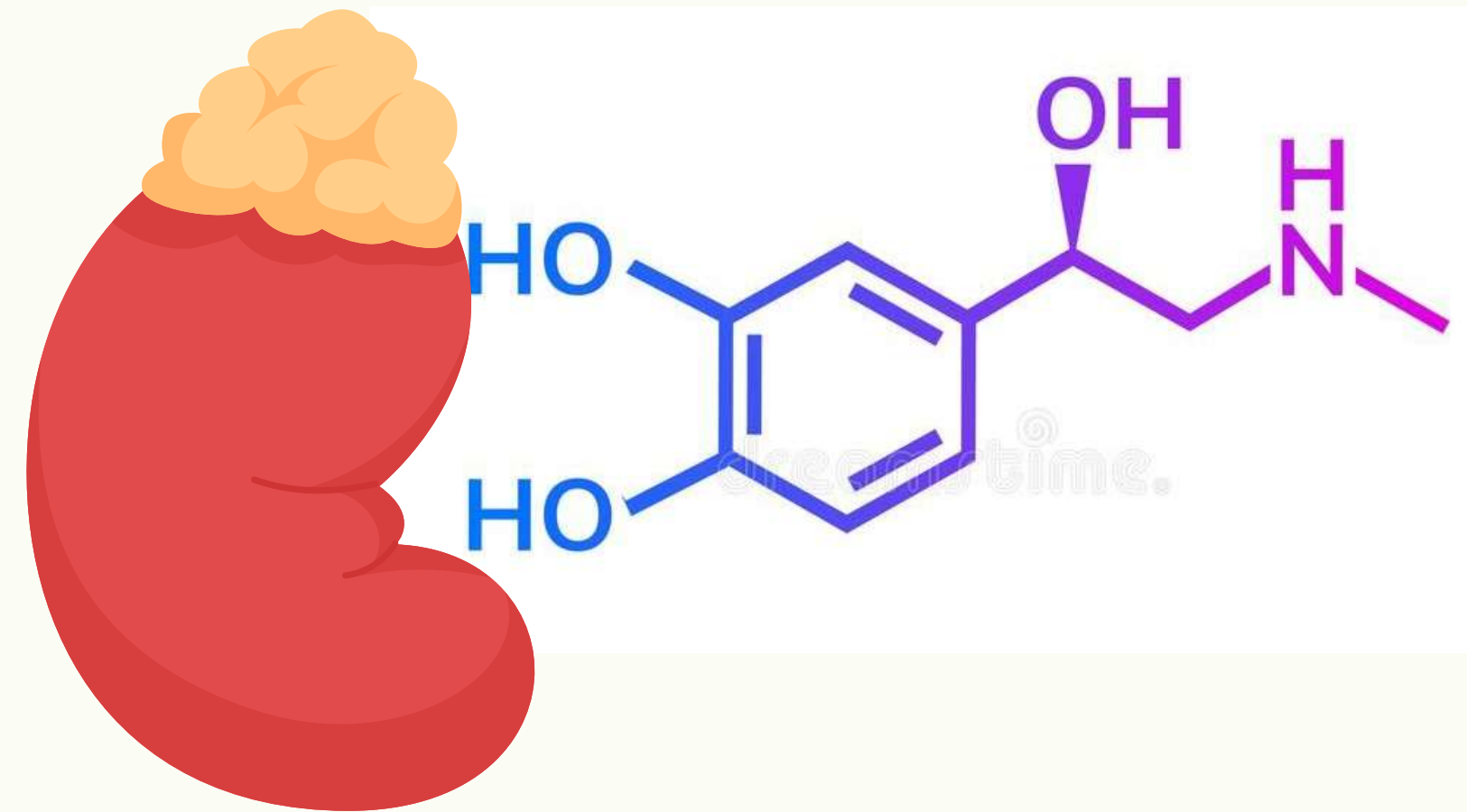


Belum selesai...

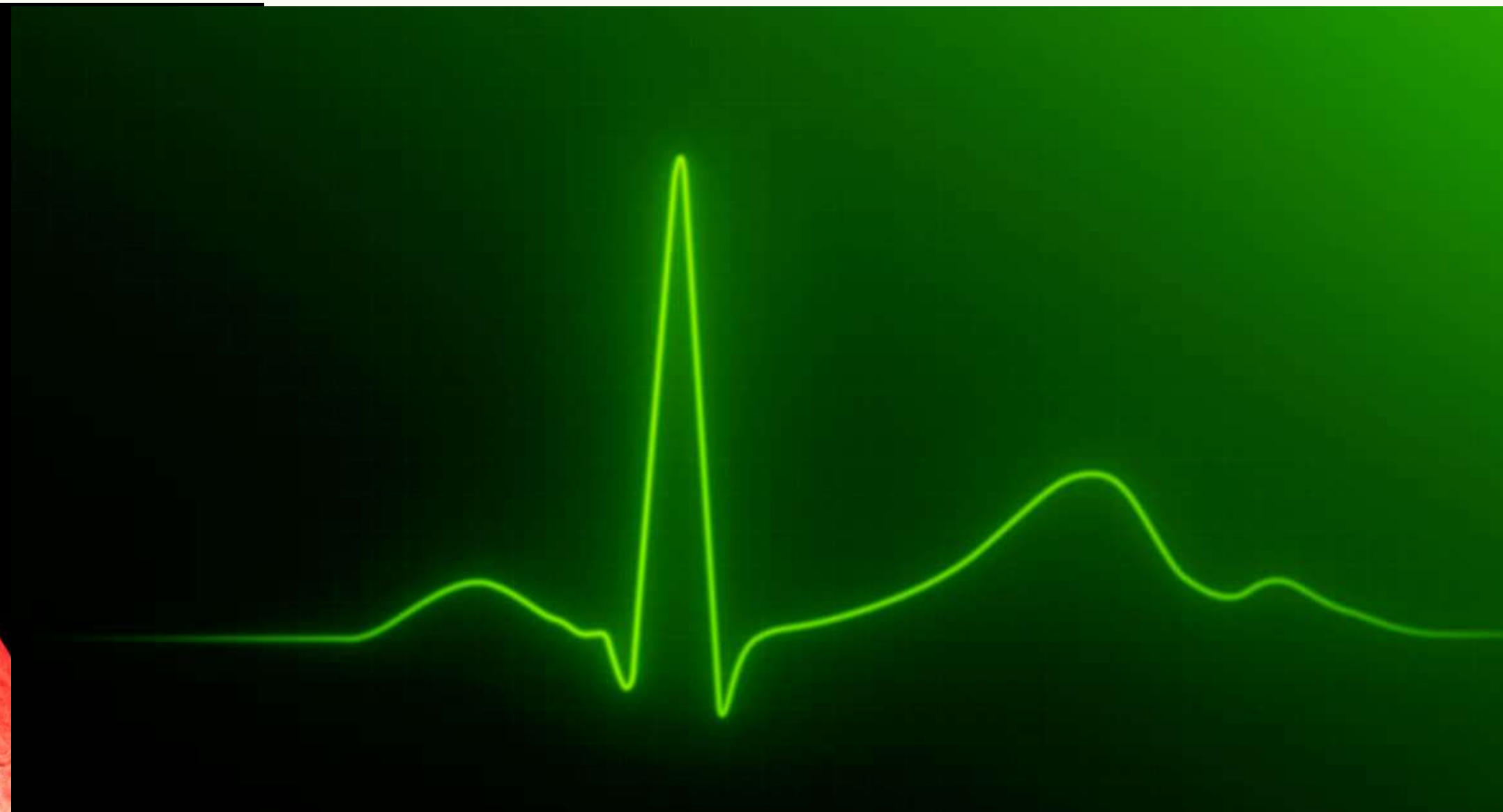
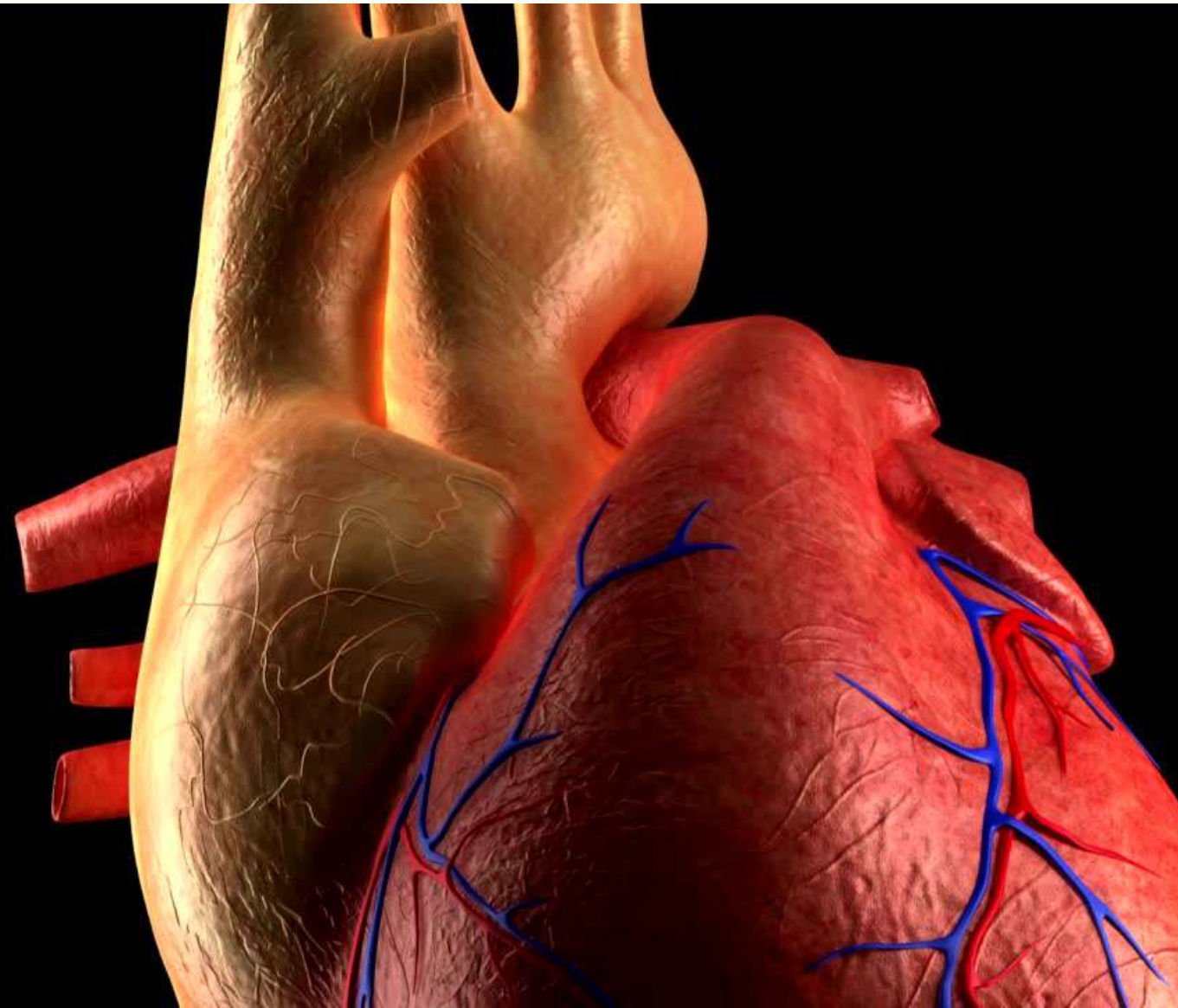
Efinefrin



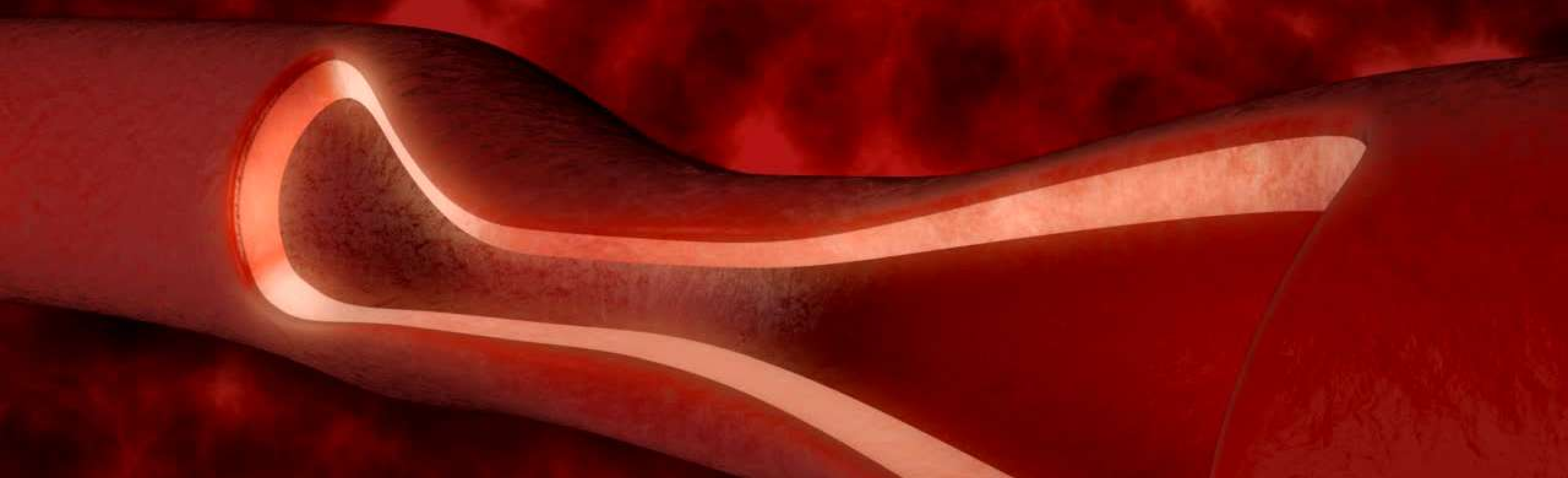
Adrenaline



ANGIOTENSIN pergi ke OTAK. Disana dia melepaskan lebih banyak **NOREFINEFRIN**. Dia juga meminta **MEDULLA** Ginjal melepaskan **ADRENALIN**: SAUDARA KEMBARNYA **EFINEFRIN**.



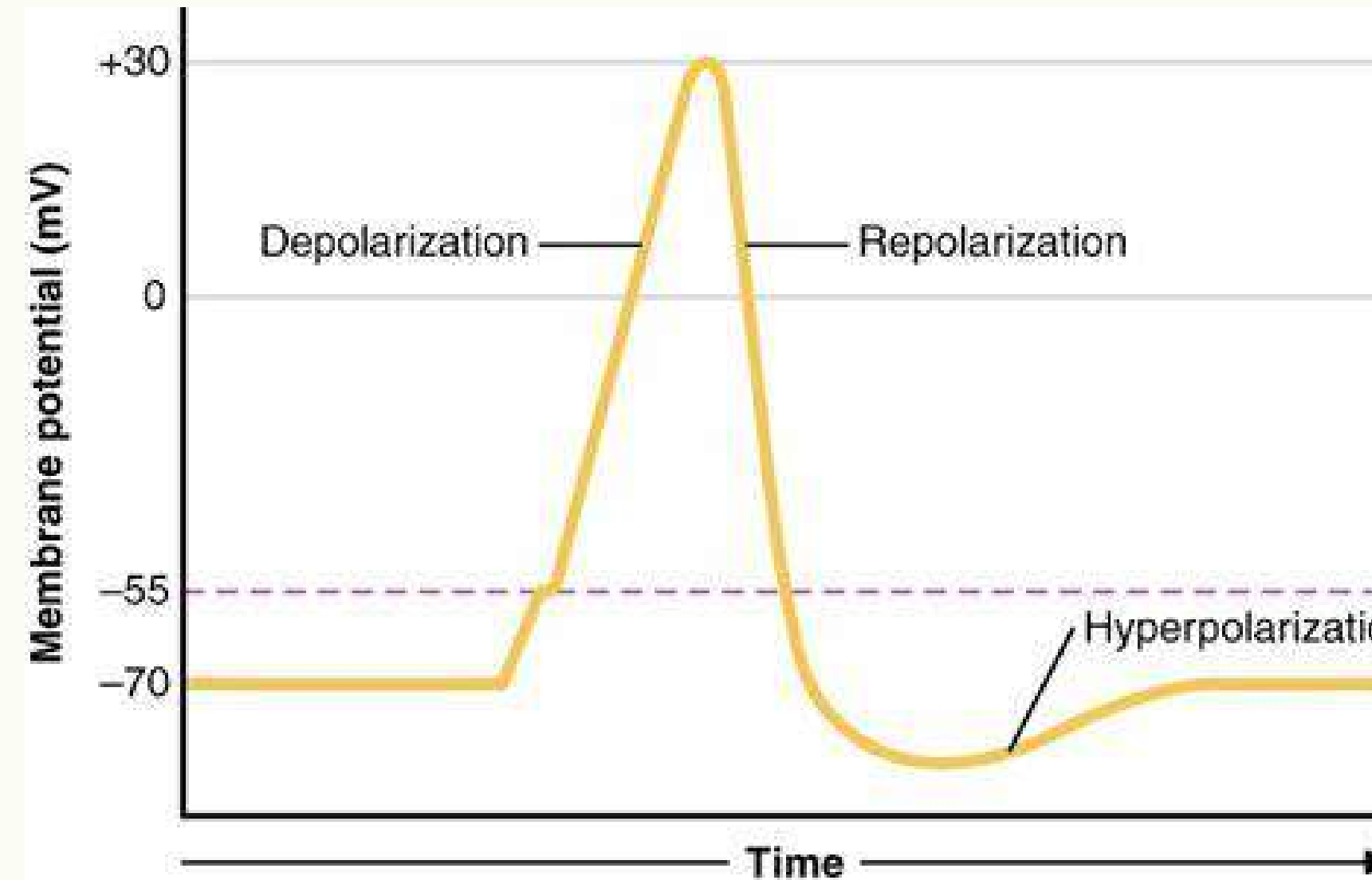
Di jantung, dia melekat pada reseptornya di NODUS SINOATRIAL (beta adrenoseptor), lalu energi listrik menyala; mengakibatkan jantung memompa lebih cepat, denyut nadi meningkat, darah lebih banyak dipompakan..



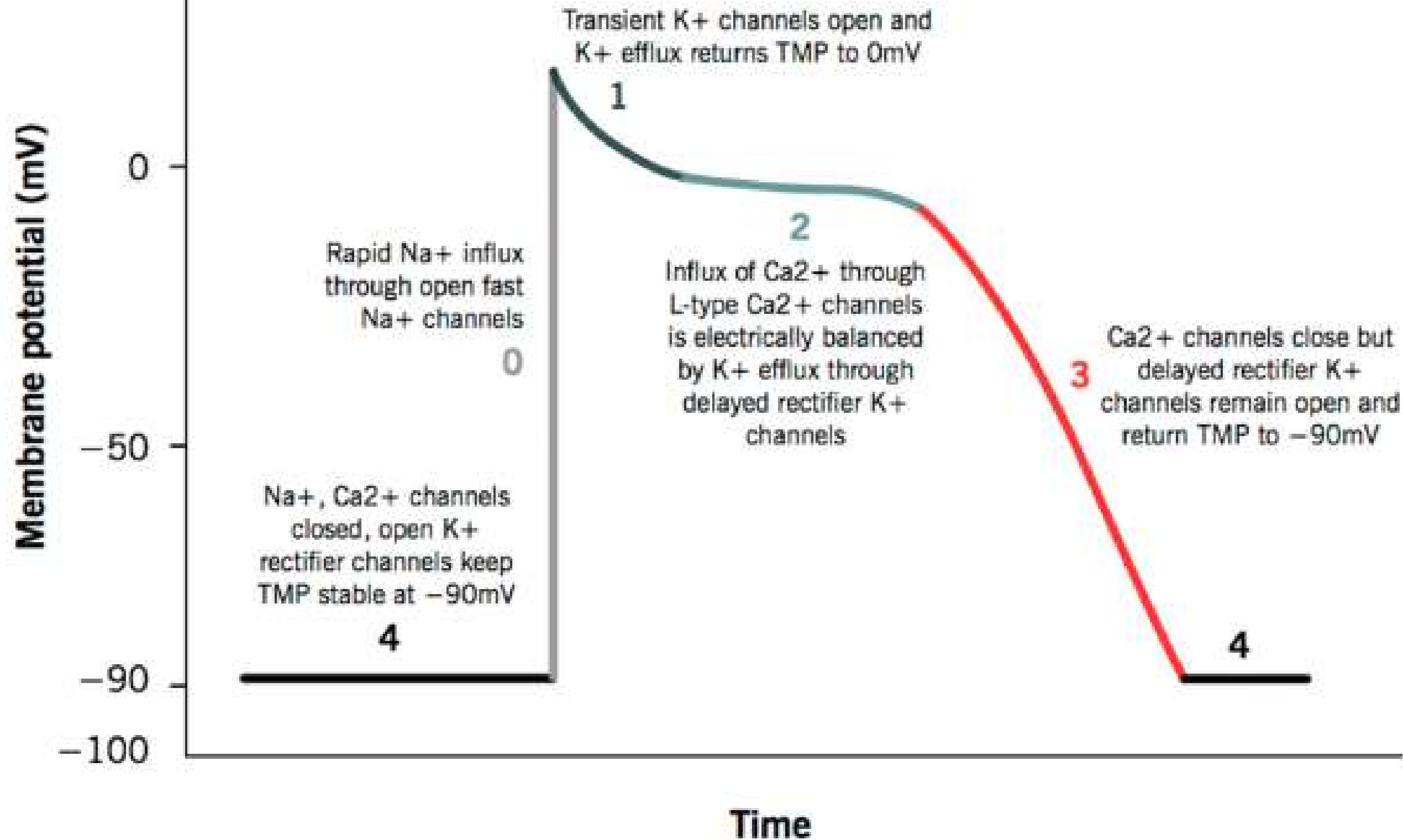
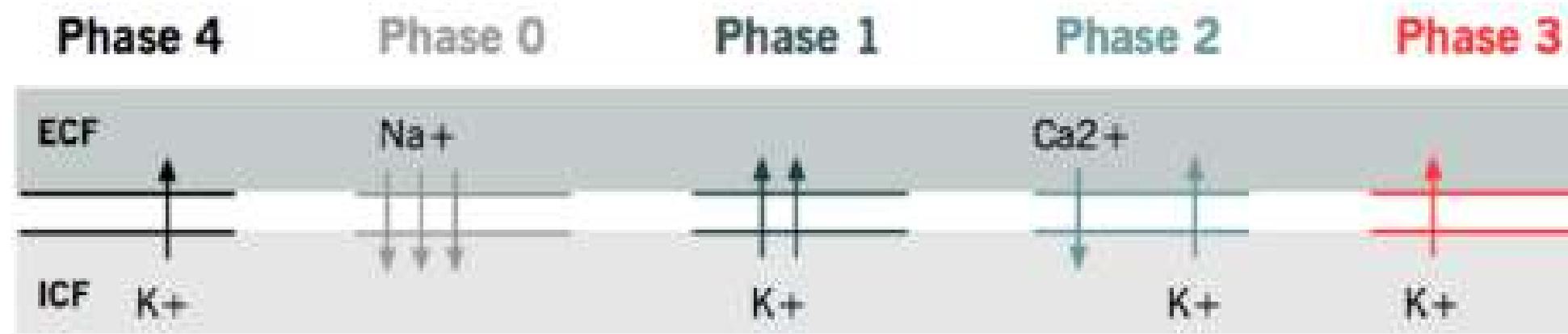
Di pembuluh darah, ikatan EFINEFRIN dan ADRENALIN pada reseptornya menyebabkan PEMBULUH DARAH menciut; meningkatkan tahanan endotelial; tekanan darah meningkat.

Potensial aksi jantung adalah **perubahan tegangan listrik yang singkat** di sepanjang **membran sel** sel jantung.

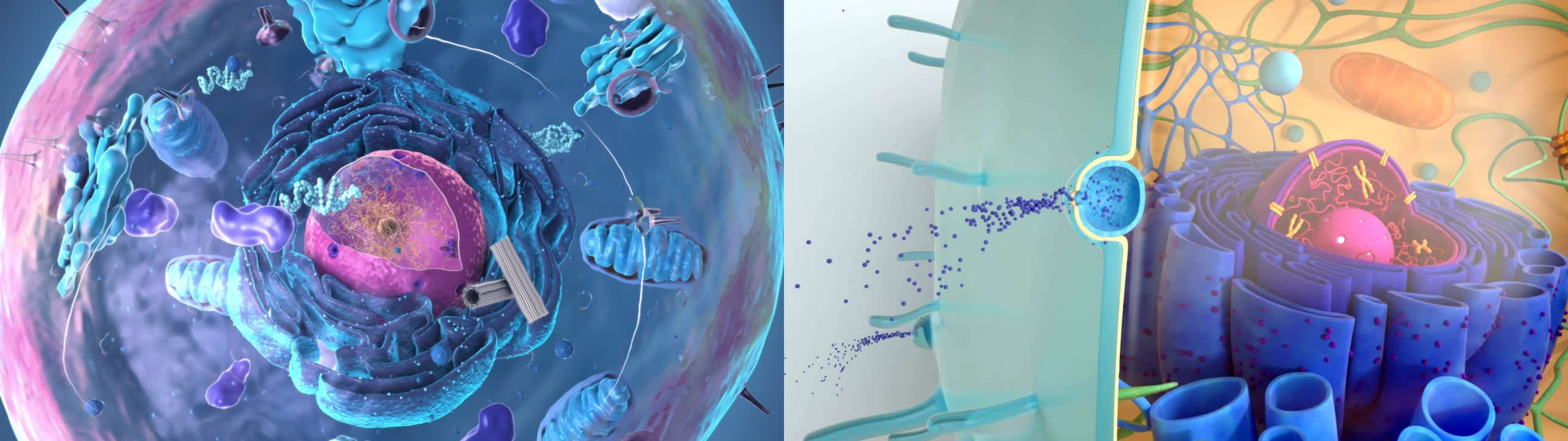
Perubahan ini disebabkan oleh **pergerakan atom bermuatan (ion)** antara **dalam dan luar sel melalui protein yang disebut kanal**.



Ikatan ADRENALIN menyebabkan aliran listrik kan?

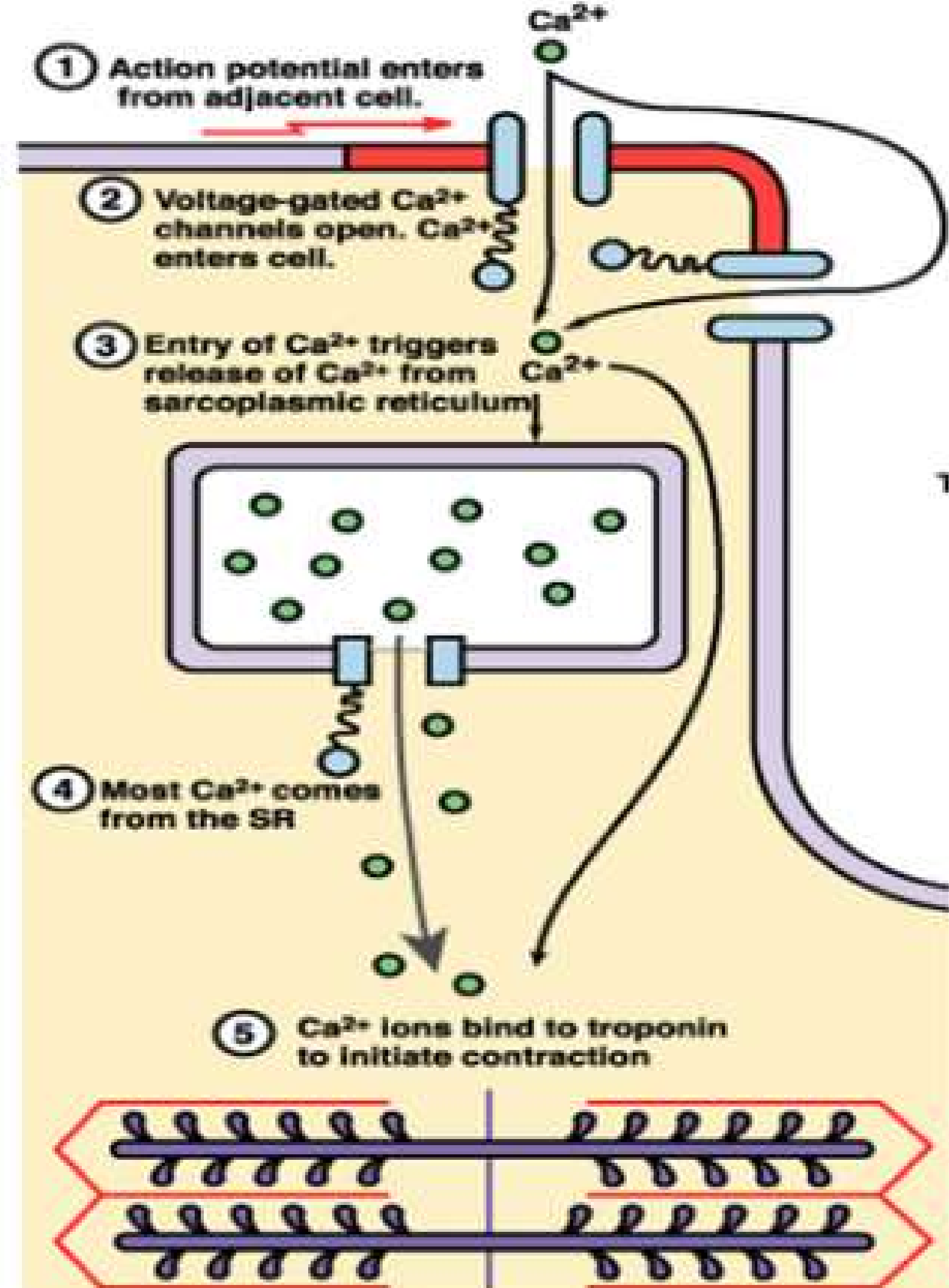


**KONTRAKSI
TERJADI PADA
SAAT KALSIUM
MASUK KE
DALAM SEL....**



Begitu **KALSIUM (Ca^{2+})** masuk ke dalam sel, dia akan berikatan pada reseptornya (**dihidropiridin**) di **RETIKULUM sarkolema**. AKIBATNYA KALSIUM lain yang tersimpan di dalamnya berhamburan keluar.

Apa akibatnya?



Di dalam sel, terdapat protein bernama **AKTIN DAN MIOSIN**.

Saat relaks, **AKTIN DAN MIOSIN** dipisahkan oleh **PROTEIN TROPONIN**.

Begitu ada **KALSIUM**, **TROPONIN BERALIH** mengikatnya sehingga **AKTIN dan MIOSIN TERBEBAS**.

Keseluruhan PROSES INI MENGAKIBATKAN: VOLUME darah meningkat, meningkatkan tahanan ENDOTELIUM, MENINGKATKAN POMPAAN JANTUNG, DAN MENCIUTKAN PEMBULUH DARAH:

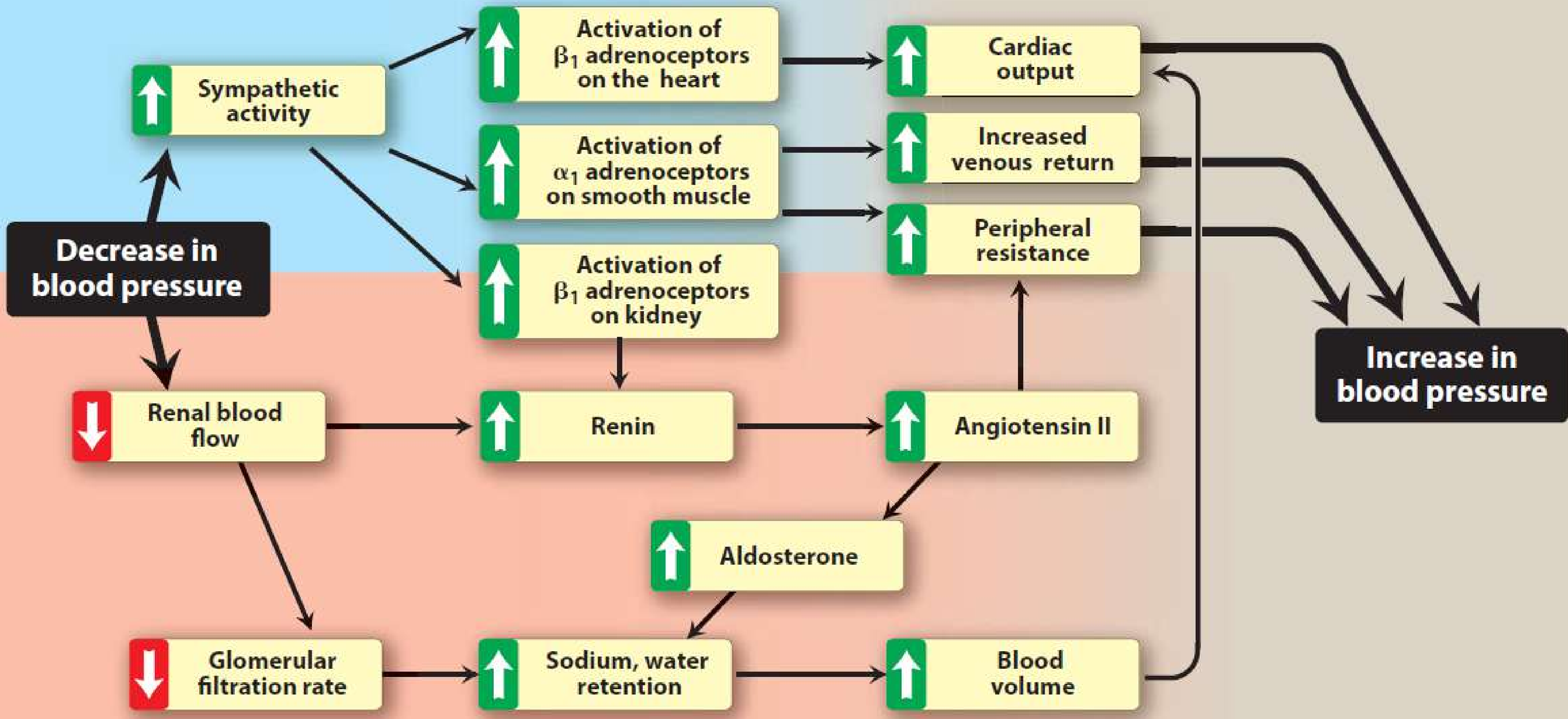
TEKANAN DARAH MENINGKAT: HIPERTENSI..

Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Response mediated by the sympathetic nervous system



Response mediated by the renin-angiotensin-aldosterone system

TENTU SAJA MENCEGAH
terbentuknya ANGIOTENSIN 2, lalu
menghambat aksinya pada resptor.
Lalu mencegah aksi RENIN

ACE inhibitor (ACEi)



Renin inhibitor

Angiotensin Receptor Blocker (ARB)

Di ginjal

Angiotensinogen

Renin



ALISKIREN

Renin inhibitor

Di Paru2



Angiotensin 1

ACE



Kaptopril,
Lisinopril, Enalapril

Angiotensin
Converting Enzyme
inhibitor

ACEi

Angiotensin 2



Losartan
Valsartan,
Candesartan

Angiotensin 2
Receptor blocker

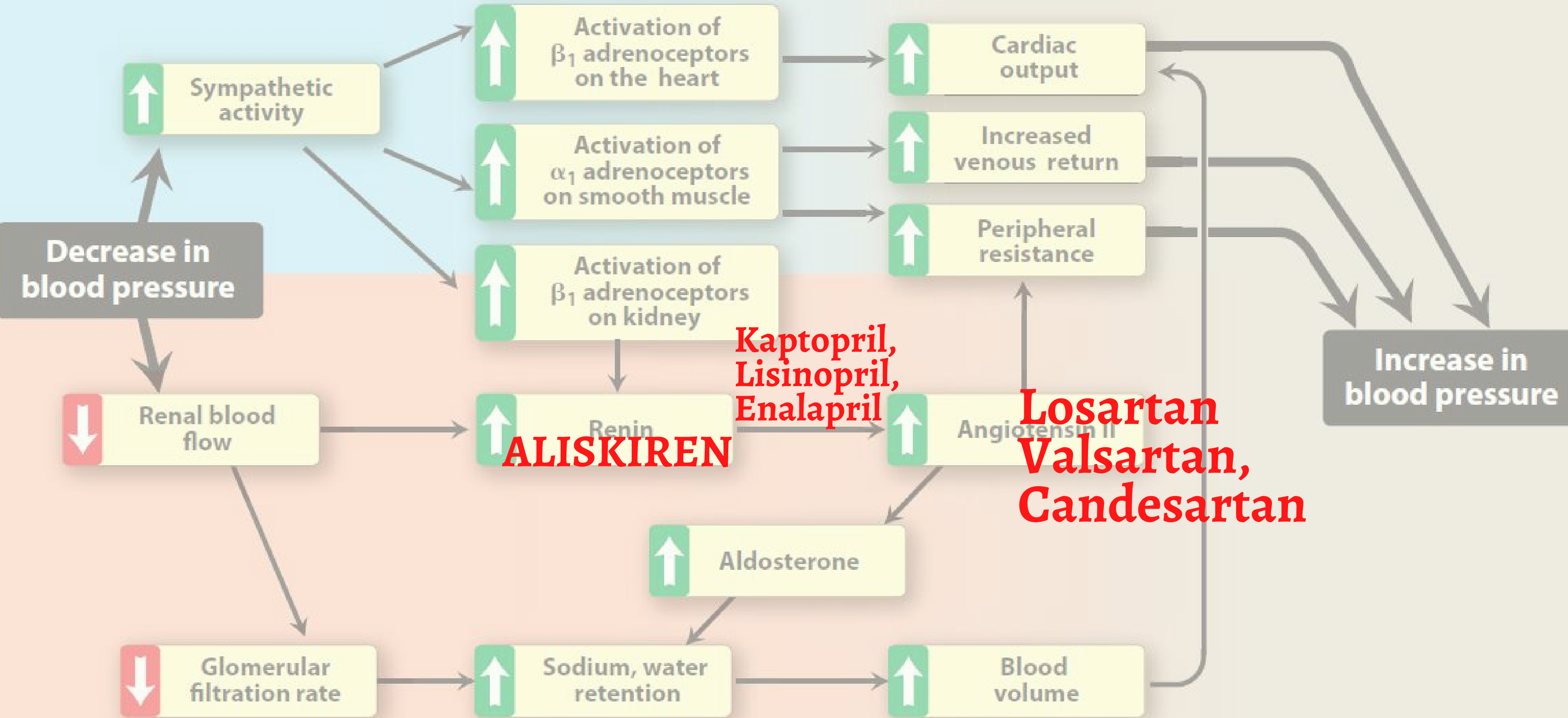
ARB

Di Ginjal



Aldosterone

Response mediated by the sympathetic nervous system



Response mediated by the renin-angiotensin-aldosterone system

ACE inhibitor (ACEi)

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Benazepril (Lotensin)	5-40 mg daily	BOXED WARNINGS Can cause <u>injury and death to the developing fetus</u> when used in the 2nd and 3rd trimesters; <u>discontinue as soon as pregnancy is detected</u> CONTRAINDICATIONS <u>Do not use</u> with history of <u>angioedema</u> <u>Do not use</u> <u>within 36 hrs</u> of <u>sacubitril/valsartan (Entresto)</u> <u>Do not use</u> with aliskiren in diabetes WARNINGS <u>Angioedema, hyperkalemia, hypotension, renal impairment, bilateral renal artery stenosis (avoid use)</u> SIDE EFFECTS Generally well-tolerated, can cause <u>cough, hyperkalemia, ↑ SCr, hypotension/dizziness</u> [↑ risk if volume-depleted (e.g., with concurrent diuretic)], headache MONITORING <u>BP, K, renal function, s/sx of angioedema</u> NOTES Once-daily drugs can be used BID if needed
Enalapril (Vasotec, Epaned powder for oral solution) Enalaprilat (Vasotec IV)	PO: 5-20 mg daily or BID IV (enalaprilat): 0.625-5 mg Q6H	
Lisinopril (Prinivil, Zestril, Qbrelis oral solution)	5-40 mg daily	
Quinapril (Accupril)	5-40 mg daily	
Ramipril (Altace)	2.5-20 mg daily	
Captopril	12.5 mg BID-50 mg <u>TID</u>	
Fosinopril	10-40 mg daily	
Moexipril	3.75-30 mg daily	
Perindopril	4-16 mg daily	
Trandolapril	1-8 mg daily	

Angiotensin Receptor Blocker (ARB)

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Irbesartan (Avapro)	75-300 mg daily	Same as ACE inhibitors except: <u>Less</u> cough <u>Less</u> angioedema <u>No washout period required</u> with sacubitril/valsartan (<i>Entresto</i>)
Losartan (Cozaar)	25-100 mg daily in 1-2 divided doses	
Olmesartan (Benicar)	10-40 mg daily	
Valsartan (Diovan)	80-320 mg daily	Additional safety issues unique to ARBs include: WARNINGS <u>Olmesartan: sprue-like enteropathy</u> – severe, chronic diarrhea with substantial weight loss; can occur months to years after drug initiation NOTES Azilsartan: keep in original container to protect from light and moisture
Azilsartan (<i>Edarbi</i>)	40-80 mg daily	
Candesartan (<i>Atacand</i>)	8-32 mg daily in 1-2 divided doses	
Eprosartan	400-800 mg daily in 1-2 divided doses	
Telmisartan (<i>Micardis</i>)	20-80 mg daily	

Sesudah itu, **TURUNKAN KONTRAKSI**
JANTUNG dan **PEMBULUH** darah, dengan
menghambat KANAL KALSIUM. Mulai
dulu dari ujung, agar efek sampingnya
tidak besar.

SO, PILIHAN KEDUA IALAH: CALCIUM
CHANNEL BLOCKER

3

**Calcium Channel Blocker
(CCB)**

Calcium Channel Blocker (CCB)

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Amlodipine (Norvasc, Katerzia) Tablet, suspension	2.5-10 mg daily	CONTRAINDICATIONS Nicardipine should not be used in advanced aortic stenosis WARNINGS <u>Hypotension</u> (especially with severe aortic stenosis), worsening angina and/or MI, severe hepatic impairment, use caution in heart failure (see Notes) <u>Nifedipine IR: do not use for chronic hypertension or acute BP reduction in non-pregnant adults (profound hypotension, MI and/or death has occurred)</u> SIDE EFFECTS Generally well-tolerated, can cause <u>peripheral edema/headache/flushing/palpitations/reflex tachycardia/fatigue</u> (worse with nifedipine IR), nausea, <u>gingival hyperplasia</u> (more gingival hyperplasia with non-DHPs) MONITORING <u>Peripheral edema</u> , BP, HR NOTES <u>Amlodipine</u> is considered the <u>safest</u> if a CCB must be used to lower BP in <u>heart failure</u> with reduced ejection fraction <u>Nifedipine ER</u> is a <u>drug of choice in pregnancy</u> DHP CCBs (e.g., <u>nifedipine ER</u>) are used to prevent peripheral vasoconstriction in <u>Raynaud's</u> (i.e., cold/ <u>blue fingers</u>) <i>Adalat CC</i> and <i>Procardia XL</i> : OROS/gel matrix formulations (see Drug Formulations and Patient Counseling chapter) can leave a ghost tablet (empty shell) in the stool
Nicardipine IV (Cardene IV) Nicardipine IR Capsule, injection	IV: 5 mg/hr, ↑ by 2.5 mg/hr every 5-15 mins to max dose of 15 mg/hr IR: 20-40 mg TID	
Nifedipine ER (Adalat CC, Procardia XL) Nifedipine IR (<i>Procardia</i>)	30-90 mg daily	
Felodipine ER	2.5-10 mg daily	
Isradipine	2.5-10 mg BID	
Nisoldipine ER (<i>Sular</i>)	8.5-34 mg daily	
Nisoldipine ER (original formulation)	10-60 mg daily	

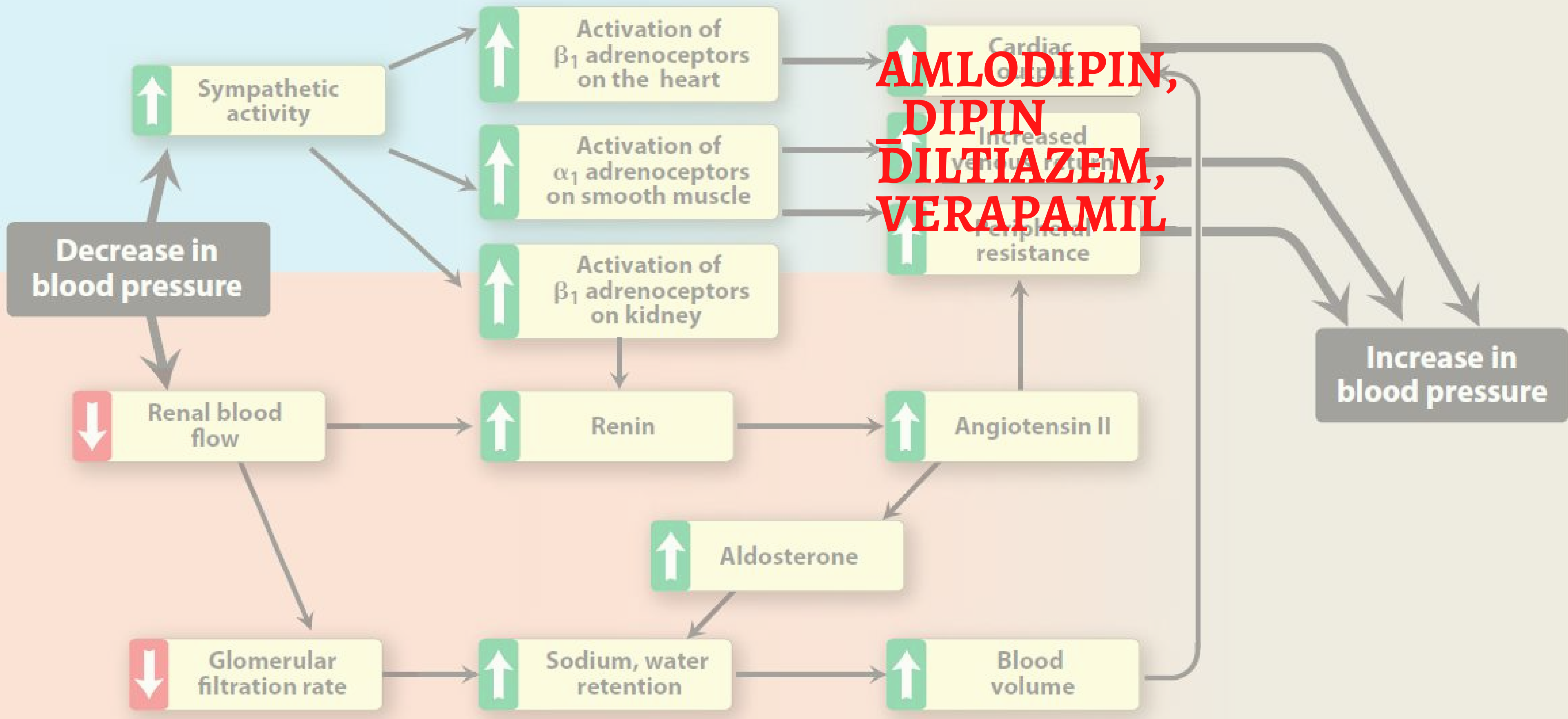
Calcium Channel Blocker (CCB)

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Clevidipine (Cleviprex) Injection	1-21 mg/hr	CONTRAINDICATIONS <u>Allergy to soybeans, soy products or eggs</u>; defective lipid metabolism (e.g., lipoid nephrosis, hyperlipidemia with acute pancreatitis); severe aortic stenosis WARNINGS <u>Hypotension, reflex tachycardia, infections</u> (see Notes) SIDE EFFECTS <u>Hypertriglyceridemia</u>, headache, atrial fibrillation, nausea MONITORING BP, HR NOTES A <u>lipid emulsion</u> (provides 2 kcal/mL); it is <u>milky-white</u> in color Use <u>strict aseptic technique</u> due to infection risk; maximum time of use after vial puncture is <u>12 hrs</u>

Calcium Channel Blocker (CCB)

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Diltiazem (<i>Cardizem, Tiazac, Cardizem CD, Cardizem LA, Cartia XT, others</i>) IR tablet, ER tablet (24-HR), ER capsule (12-HR), ER capsule (24-HR), injection	120-360 mg daily; max dose varies with product IR tablet: daily dose given in 4 divided doses ER capsule (12-HR): daily dose given in 2 divided doses	CONTRAINDICATIONS Hypotension (SBP < 90 mmHg) or cardiogenic shock; 2 nd or 3 rd degree AV block or sick sinus syndrome (unless has a functioning artificial ventricular pacemaker), acute MI and pulmonary congestion (diltiazem), severe left ventricular dysfunction (verapamil), atrial flutter or atrial fibrillation and an accessory bypass tract (verapamil) WARNINGS <u>Heart failure (may worsen symptoms), bradycardia, hypotension, acute liver injury/↑ LFTs, cardiac conduction abnormalities (diltiazem), hypertrophic cardiomyopathy (verapamil)</u> SIDE EFFECTS <u>Edema, constipation (more with verapamil), gingival hyperplasia, headache, dizziness</u> MONITORING BP, HR, ECG, LFTs NOTES IV:PO dose conversions are not 1:1 Non-DHP CCBs are used to reduce rapid heart rate in atrial fibrillation
Verapamil (<i>Calan SR, Verelan, Verelan PM</i>) IR tablet, ER tablet, ER capsule (24-HR), injection	240-480 mg daily IR tablet: daily dose given in 3 divided doses <i>Calan SR</i> : daily dose can be given in 2 divided doses (QAM and QPM) <i>Verelan PM</i> : daily dose given QHS	

Response mediated by the sympathetic nervous system



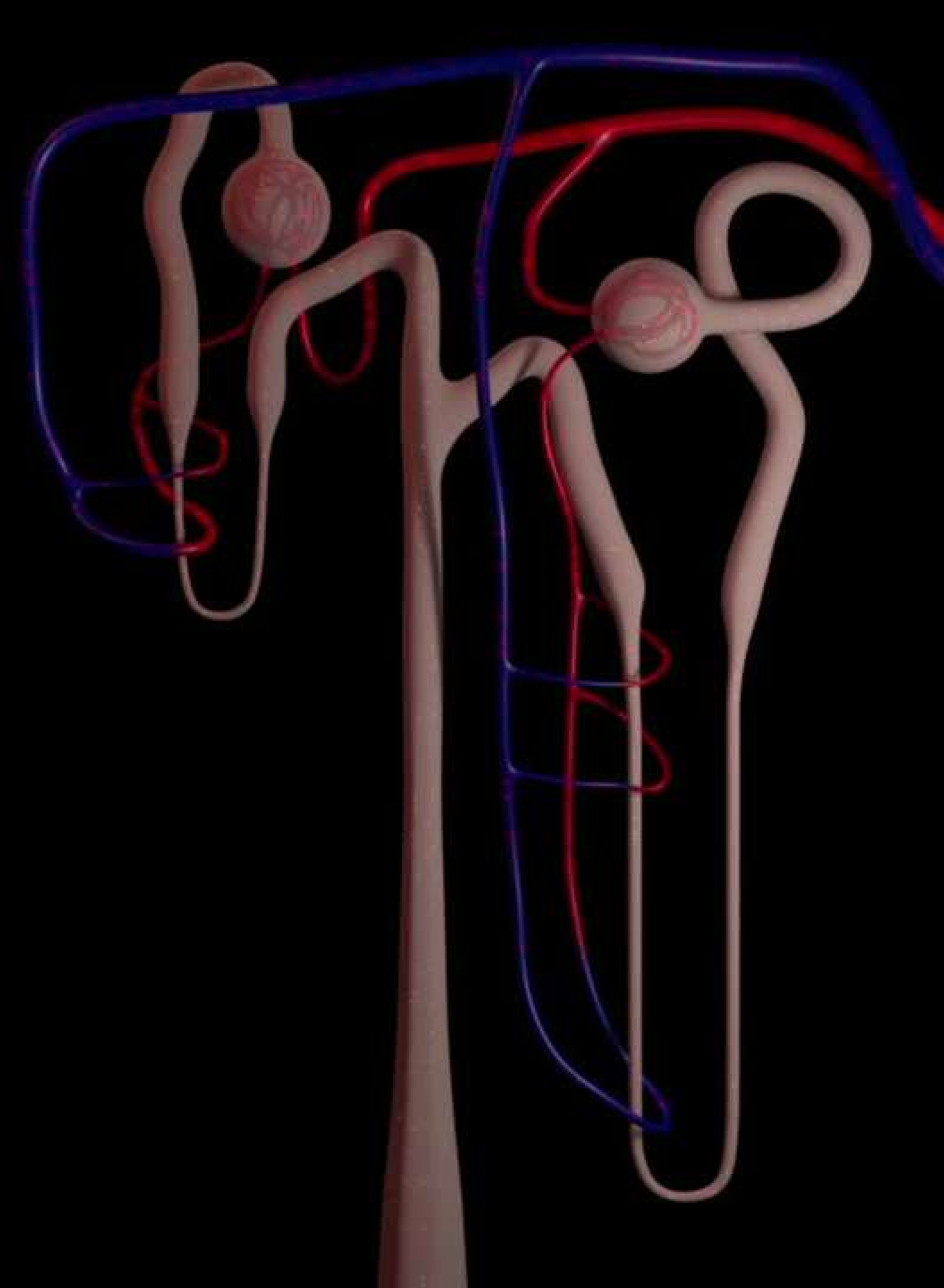
Response mediated by the renin-angiotensin-aldosterone system

Diuretik tiazid



Selanjutnya, **cegah supaya SODIUM (Na)** sedikit masuk ke dalam aliran darah; volume plasma darah menurun, tekanan darah menurun.

So, kita perlu **DIURETIK TIAZID**.



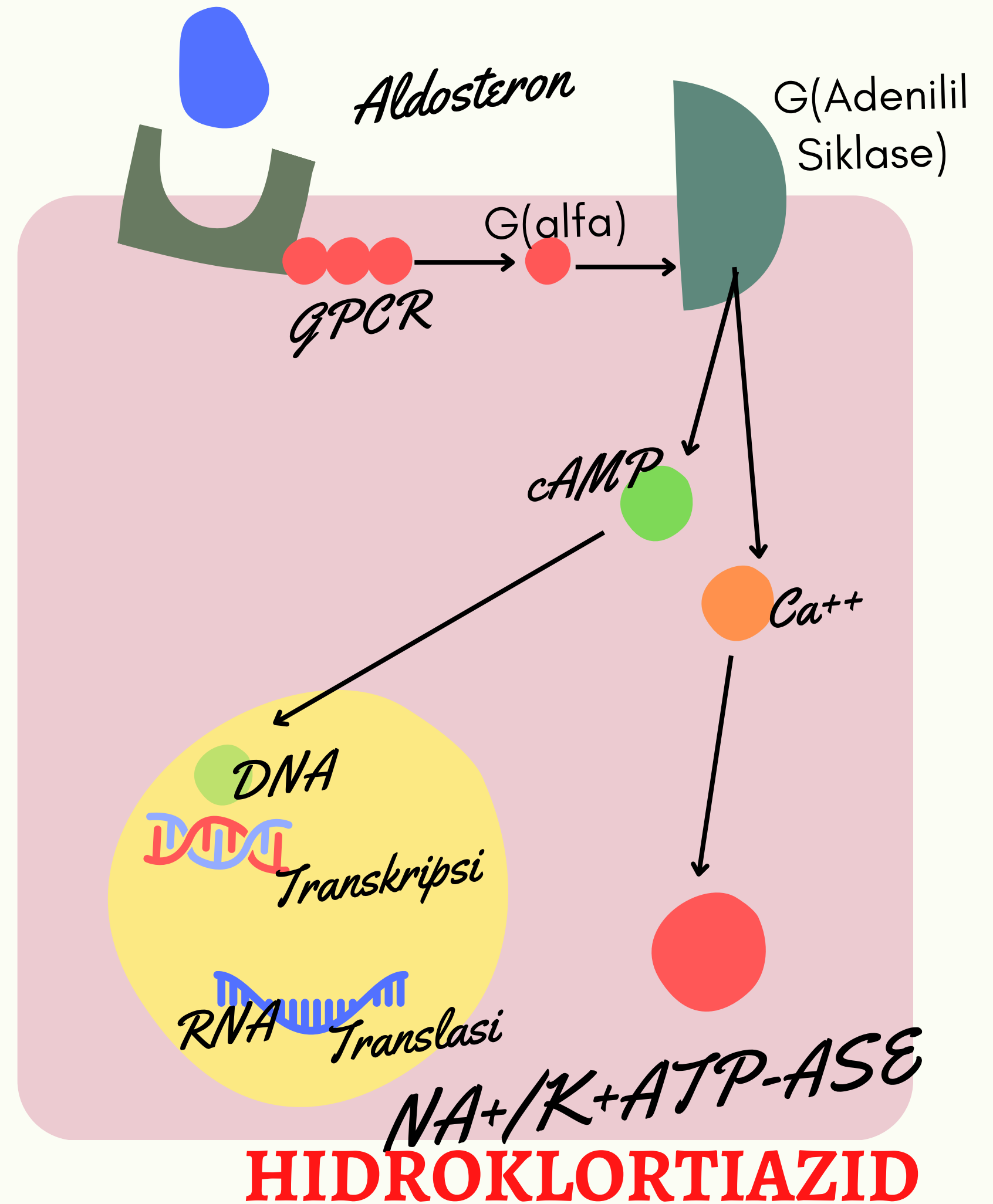
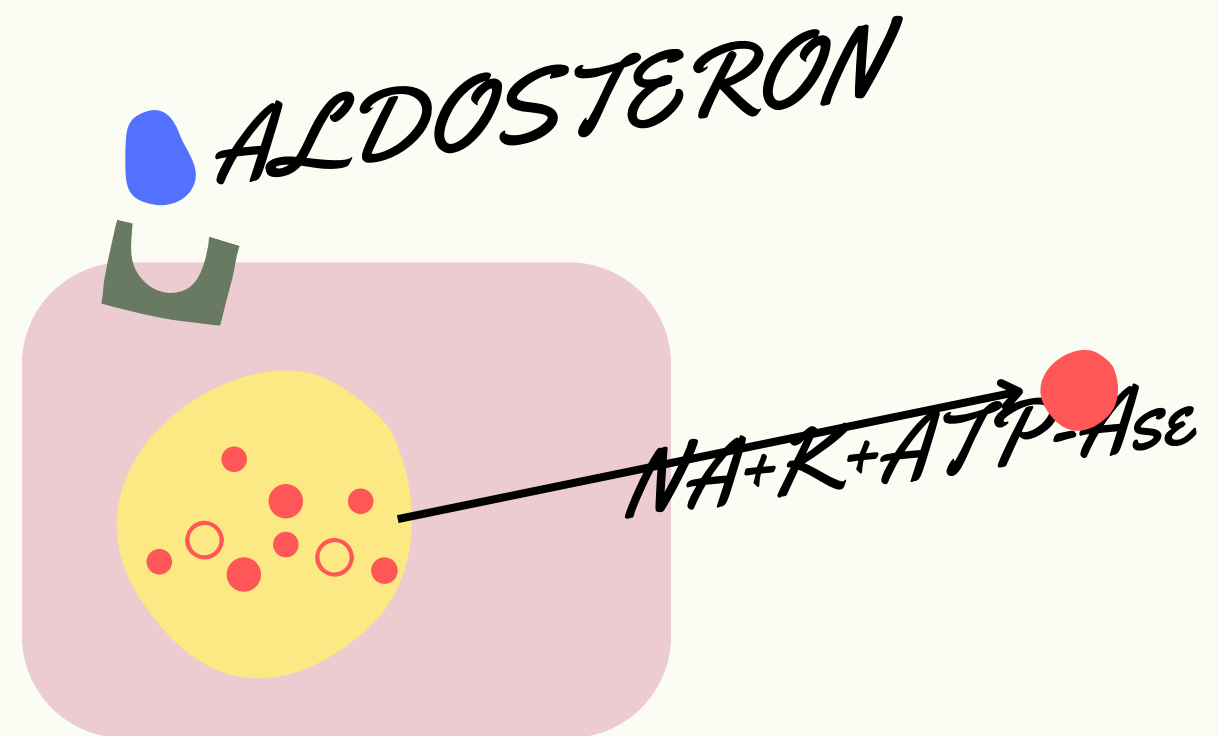
**Diuretik TIAZID
menghamabt**

**NA/K⁺-ATPase di
tubulus Proksimal.**



NA/K-ATP Ase

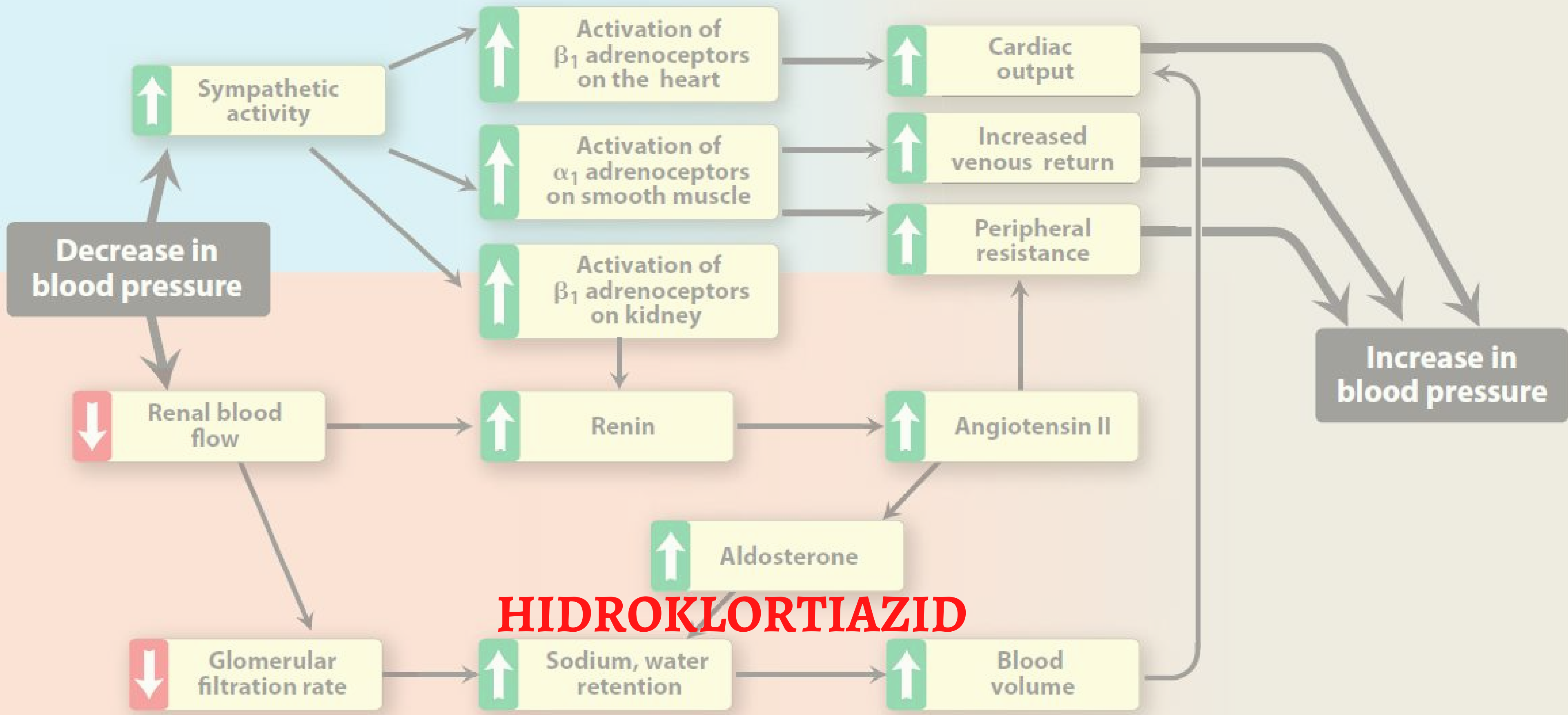




Diuretik tiazid

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Chlorthalidone Tablet	<u>12.5-25 mg daily</u> (max dose is 100 mg daily but doses > 25 mg/day have limited clinical benefit)	CONTRAINDICATIONS <u>Hypersensitivity to sulfonamide-derived drugs</u> (not likely to cross-react – see Drug Allergies & Adverse Drug Reactions chapter); anuria WARNINGS Severe renal disease (can precipitate azotemia), progressive liver disease (fluid and electrolyte changes can precipitate hepatic coma), can precipitate or exacerbate conditions such as systemic lupus erythematosus (SLE), gout and diabetes, transient myopia or acute angle-closure glaucoma (hydrochlorothiazide)
Hydrochlorothiazide (Microzide*) Tablet, capsule	<u>12.5-50 mg daily</u> (max dose is 100 mg daily but doses > 50 mg/day have limited clinical benefit and ↑ risk of adverse effects)	SIDE EFFECTS <u>↓ electrolytes: K, Mg, Na</u> <u>↑ electrolytes/labs: Ca, UA, LDL, TG, BG</u> <u>Photosensitivity</u> (including a small ↑ risk of non-melanoma skin cancer), <u>impotence</u> , dizziness, rash
Chlorothiazide (<i>Diuril</i> , <i>Sodium Diuril</i>) Tablet, oral suspension, injection	500-2,000 mg daily in 1-2 divided doses	MONITORING <u>Electrolytes, renal function</u> , BP, fluid status (input and output, weight), BG (in diabetes)
Indapamide Tablet	1.25-5 mg daily	NOTES <u>Thiazides are not effective when CrCl < 30 mL/min</u> (except metolazone, which may work with reduced renal function or diuretic resistance) <u>Take early</u> in the day to <u>avoid nocturia</u> <u>Chlorothiazide</u> is the only medication in this class <u>available IV</u>
Metolazone Tablet	2.5-5 mg daily	Chlorthalidone may be preferred over hydrochlorothiazide due to longer duration (if a patient is doing well on hydrochlorothiazide, no need to switch) Hypokalemia can be avoided with regular intake of potassium-rich foods or potassium supplements

Response mediated by the sympathetic nervous system



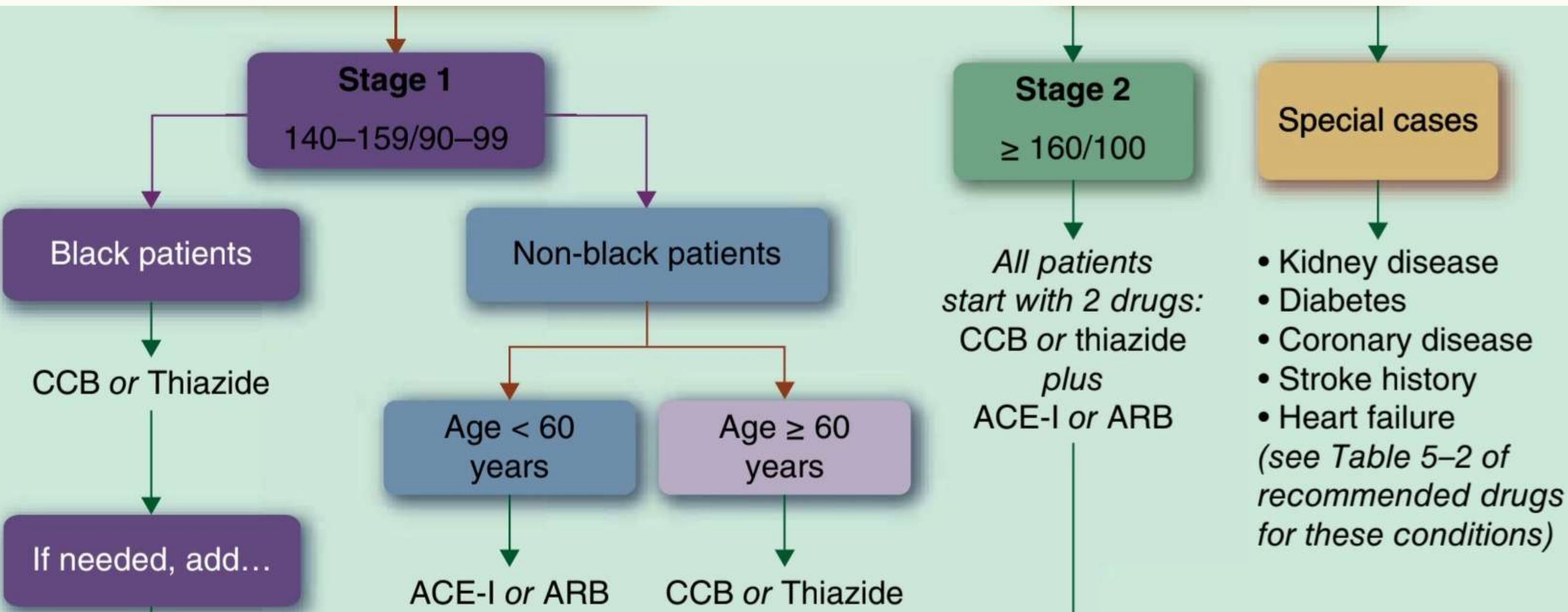
Response mediated by the renin-angiotensin-aldosterone system

Tekanan darah $\geq 140/90$ dewasa >18 th (>80 th td $\geq 150/90$, atau $140/90$ resiko tinggi (diabetes, ginjal))

Mulai dri perubahan gaya hidup (turunkan BB, kurangi asupan garam, berhenti merokok)

**Terapi
obat**

**Terapi
obat**



↓
ACE-I *or* ARB
or
combine
CCB *plus* Thiazide

If needed...

↓
If needed, add...

↓
CCB *or* Thiazide

If needed...

↓
If needed, add...

↓
ACE-I *or* ARB

If needed...

↓
If needed...

→ CCB, Thiazide, *plus* ACE-I *or* ARB ←

* In stage 1 patients without other cardiovascular risk factors or abnormal findings, some months of regularly monitored lifestyle management without drugs can be considered.



If needed, add other drugs, eg, spironolactone; centrally acting agents; β -blockers

If needed, refer to a Hypertension Specialist

Terapi LINI PERTAMA

Pencegahan
utama



MONOTERAPI

1

- ACEI
- ARB
- CCB
- DIURETIK TIAZID



KOMBINASI DUA OBAT

2

- ACEI / ARB +
 - CCB
-
- ACEI / ARB +
 - Diuretik Tiazid

Terapi LANJUTAN

KOMBINASI TIGA OBAT

- ACEI / ARB +
- Diuretik Tiazid +
- CCB

- ACEI / ARB +
- Diuretik Tiazid +
- BETA1-Blocker

- ACEI / ARB +
- CCB +
- BETA1-Blocker



Terapi LANJUTAN



4

KOMBINASI EMPAT OBAT

- ACEI / ARB +
- Diuretik Tiazid +
- CCB +
- BETA1-Blocker

- Pertimbangkan KLORTALIDONE daripada HCTZ

- Pertimbangkan SPIRONOLAKTON

- Pertimbangkan ALTERNATIF lain

Terapi LANJUTAN



4

KOMBINASI EMPAT OBAT

- **ALTERNATIF lain**

Agen alternatif:

VASODIALTOR: HIDRALAZINE

MINOXIDIL

SO. NITROPRUSID

ADRENERGIK ANTAGONIS

METILDOPA

KLONIDIN

RESERPIN

Terapi pendukung lainnya:

Diuretik hemat kalium

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Spironolactone (Aldactone, CaroSpir oral suspension)	25-100 mg daily in 1-2 divided doses	BOXED WARNINGS Amiloride and triamterene: <u>hyperkalemia (K > 5.5 mEq/L)</u> – more likely in patients with diabetes, renal impairment, or elderly patients CONTRAINDICATIONS Do not use if <u>hyperkalemia, severe renal impairment, Addison's disease (spironolactone) or taking strong CYP3A4 inhibitors (eplerenone)</u> SIDE EFFECTS <u>Hyperkalemia, ↑ SCr, dizziness, hyperchloremic metabolic acidosis (rare)</u> Spironolactone: <u>gynecomastia, breast tenderness, impotence, irregular menses, amenorrhea</u> Eplerenone: ↑ TGs MONITORING <u>BP, K, renal function, fluid status, s/sx of HF</u> NOTES CaroSpir suspension (also approved for use in heart failure and edema due to cirrhosis) is not therapeutically equivalent to Aldactone and dosing recommendations differ; doses > 100 mg can cause unexpectedly high concentrations; use a different formulation in this case
Triamterene (Dyrenium) + HCTZ (Dyazide*, Maxzide, Maxzide-25)	100-300 mg daily in 1-2 divided doses + HCTZ: 37.5 mg/25 mg daily or BID + HCTZ: 75 mg/50 mg daily	
Amiloride	5-20 mg daily	
Eplerenone (Inspra)	50 mg daily or BID	

Beta-blocker

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Beta-1 Selective Blockers		
Atenolol (Tenormin)	25-100 mg daily	BOXED WARNINGS Do not discontinue abruptly (particularly in patients with CAD/IHD); gradually <u>taper dose</u> over 1-2 weeks to avoid acute tachycardia, hypertension, and/or ischemia CONTRAINDICATIONS Severe bradycardia; 2nd or 3rd degree AV block or sick sinus syndrome (unless a permanent pacemaker is in place); overt cardiac failure or cardiogenic shock Esmolol: pulmonary hypertension; use of IV non-DHP CCBs WARNINGS Use <u>caution</u> in patients with <u>diabetes</u>: can worsen <u>hyperglycemia</u> or <u>hypoglycemia</u> and <u>mask hypoglycemic symptoms</u> (see Diabetes chapter) Use <u>caution</u> with bronchospastic diseases (e.g., <u>asthma, COPD</u>), <u>beta-1 selective preferred</u> Use caution with <u>Raynaud's</u>/other peripheral vascular diseases, pheochromocytoma and heart failure (slow dose titration required if used in these conditions) Can mask signs of hyperthyroidism (e.g., tachycardia), can worsen CNS depression SIDE EFFECTS <u>Bradycardia, fatigue, hypotension, dizziness, depression, impotence</u> (less than thiazides), cold extremities (can <u>exacerbate Raynaud's</u>) MONITORING HR (↓ dose if HR < 55 BPM), BP NOTES Oral drugs: titrate doses every 1-2 weeks (as tolerated), take without regard to meals (except <u>Lopressor and Toprol XL should be taken with or immediately following food</u>) <u>Metoprolol tartrate IV is not equivalent to PO (IV:PO ratio is 1:2.5)</u> When switching from metoprolol tartrate to metoprolol succinate, the same total daily dose of metoprolol should be used <i>Kapspargo Sprinkle</i> should be swallowed whole; for patients with difficulty swallowing, the capsule can be opened and the contents sprinkled on 1 teaspoonful of soft food (e.g., applesauce, yogurt or pudding) – the mixture must be swallowed within 60 mins <i>Toprol XL</i> can be split in half For beta-1 selective drugs, remember: "AMEBBA" – <u>A</u>tenolol, <u>M</u>etoprolol, <u>E</u>smolol, <u>B</u>isoprolol, <u>B</u>etaxolol, <u>A</u>cebutolol
Esmolol (Brevibloc) <u>Injection</u>	0.5-1 mg/kg IV bolus followed by 50-150 mcg/kg/min via continuous IV infusion, titrate as needed to a maximum of 300 mcg/kg/min	
Metoprolol tartrate (Lopressor) Tablet, injection Metoprolol succinate extended release (Toprol XL, Kapspargo Sprinkle) Tablet, capsule sprinkle	IR: 100-450 mg daily in 2-3 divided doses XL: 25-100 mg daily; max dose is 400 mg daily	
Acebutolol	200-800 mg daily in 1-2 divided doses	
Betaxolol <i>Betoptic S</i> – ophthalmic solution	5-20 mg daily	
Bisoprolol	2.5-20 mg daily	

Beta-blocker

Beta-1 Selective Blocker with Nitric Oxide-Dependent Vasodilation		
Nebivolol (Bystolic)	5-40 mg daily CrCl < 30 mL/min or moderate liver impairment, start at 2.5 mg daily	Same as above plus: CONTRAINDICATIONS Severe liver impairment (Child-Pugh > class B) SIDE EFFECTS Fatigue, nausea, ↑ TGs, ↓ HDL NOTES Nitric oxide causes peripheral vasodilation
DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Beta-1 and Beta-2 Blockers (Non-Selective)		
Propranolol (Inderal LA, Inderal XL, InnoPran XL, Hemangeol) Tablet, ER capsule, oral solution, injection	IR: 80-160 mg BID, max dose is 640 mg daily LA: 80-160 mg daily, same max dose as IR XL: 80 mg daily; max dose is 120 mg daily	Same as for beta-1 selective blockers plus: NOTES <u>Propranolol has high lipid solubility</u> (lipophilic) and crosses the blood-brain barrier; it is associated with <u>more CNS side effects</u> , but this makes it <u>useful</u> for other conditions (e.g., <u>migraine prophylaxis</u> , essential tremor) <u>Non-selective beta-blockers</u> are used in <u>portal hypertension</u> (see Hepatitis & Liver Disease chapter)
Nadolol (Corgard)	40-320 mg daily	
Pindolol	5-30 mg BID	
Timolol Timoptic – ophthalmic solution	10-30 mg BID	

Beta-blocker

Non-Selective Beta-Blocker and Alpha-1 Blockers		
Carvedilol (Coreg, Coreg CR) Tablet, ER capsule	IR: 6.25-25 mg BID CR: 20-80 mg daily	Same as for beta-1 selective and non-selective blockers plus: CONTRAINDICATIONS Severe hepatic impairment WARNINGS Intraoperative floppy iris syndrome has occurred in cataract surgery patients who were on or were previously treated with an alpha-1 blocker SIDE EFFECTS Edema, weight gain NOTES <u>Take all forms of carvedilol with food</u> to ↓ the rate of absorption and the risk of orthostatic hypotension Carvedilol CR has less bioavailability than carvedilol IR; <u>dosing conversions are not 1:1</u> (e.g., Coreg 3.125 mg BID = Coreg CR 10 mg daily)
Labetalol Tablet, injection	PO: 100-1,200 mg BID	Same as above for carvedilol plus: SIDE EFFECTS <u>Dizziness</u>, fatigue, nausea NOTES <u>Drug of choice in pregnancy</u> Injection is commonly used in the hospital setting and can be administered by repeated IV push or slow continuous infusion

CENTRALLY-ACTING ALPHA-2 ADRENERGIC AGONISTS

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Clonidine (Catapres*, Catapres-TTS patch, Duraclon inj) Kapvay – for ADHD Tablet, patch, injection	0.1-0.2 mg PO BID, max dose is 2.4 mg daily Weekly patch Catapres-TTS-1 = 0.1 mg/24 hr Catapres-TTS-2 = 0.2 mg/24 hr Catapres-TTS-3 = 0.3 mg/24 hr	CONTRAINDICATIONS <u>Methyldopa: concurrent use with MAO inhibitors and active liver disease</u> WARNINGS <u>Do not discontinue abruptly</u> (can cause <u>rebound hypertension</u> , sweating, anxiety, tremors); <u>must taper</u> gradually over 2-4 days <u>Methyldopa: risk for hemolytic anemia</u> (detected by a positive Coombs test), hepatic necrosis SIDE EFFECTS <u>Dry mouth, somnolence, fatigue, dizziness, constipation, ↓ HR, hypotension, impotence, headache, depression, behavioral changes (irritability, confusion, anxiety, nightmares)</u> <u>Clonidine patch: skin rash, pruritus, erythema</u> <u>Methyldopa: hypersensitivity reactions [e.g., drug-induced lupus erythematosus (DILE)], edema or weight gain (control with diuretics), ↑ prolactin levels</u> MONITORING BP, HR, mental status NOTES <u>Clonidine patch: apply weekly</u> to a clean, dry and hairless area of skin on the upper outer arm or upper chest; <u>remove before MRI</u> ; can apply the adhesive cover over the patch if it loosens <u>Methyldopa is a preferred drug in pregnancy</u>
Guanfacine IR (<i>Tenex*</i>) Guanfacine ER (Intuniv) – for ADHD	1-2 mg QHS	
Methyldopa Tablet, injection	250 mg BID-TID; max dose is 3 grams daily	

DIRECT VASODILATORS

DRUG	DOSING	SAFETY/SIDE EFFECTS/MONITORING
Hydralazine Tablet, injection	PO: 10-50 mg QID, max dose is 300 mg daily IM, IV: 10-20 mg Q4-6H PRN	CONTRAINDICATIONS Mitral valvular rheumatic heart disease, CAD WARNINGS <u>Drug-induced lupus erythematosus</u> (DILE – dose and duration related), peripheral neuritis, blood dyscrasias, hypotension SIDE EFFECTS <u>Peripheral edema/headache/flushing/palpitations/reflex tachycardia, nausea/vomiting</u> MONITORING HR, BP, ANA titer
Minoxidil <i>Men's Rogaine,</i> <i>Women's Rogaine</i> – <u>OTC topical for hair growth</u>	5-40 mg daily in 1-2 divided doses, max dose is 100 mg daily	BOXED WARNING <u>Potent antihypertensive</u> – can cause pericardial effusion and angina exacerbations; administer with a beta-blocker and loop diuretic CONTRAINDICATION Pheochromocytoma SIDE EFFECTS <u>Fluid retention, tachycardia, hair growth</u>

**Bagaimana jika pasien
memiliki kondisi
patologis lain?**

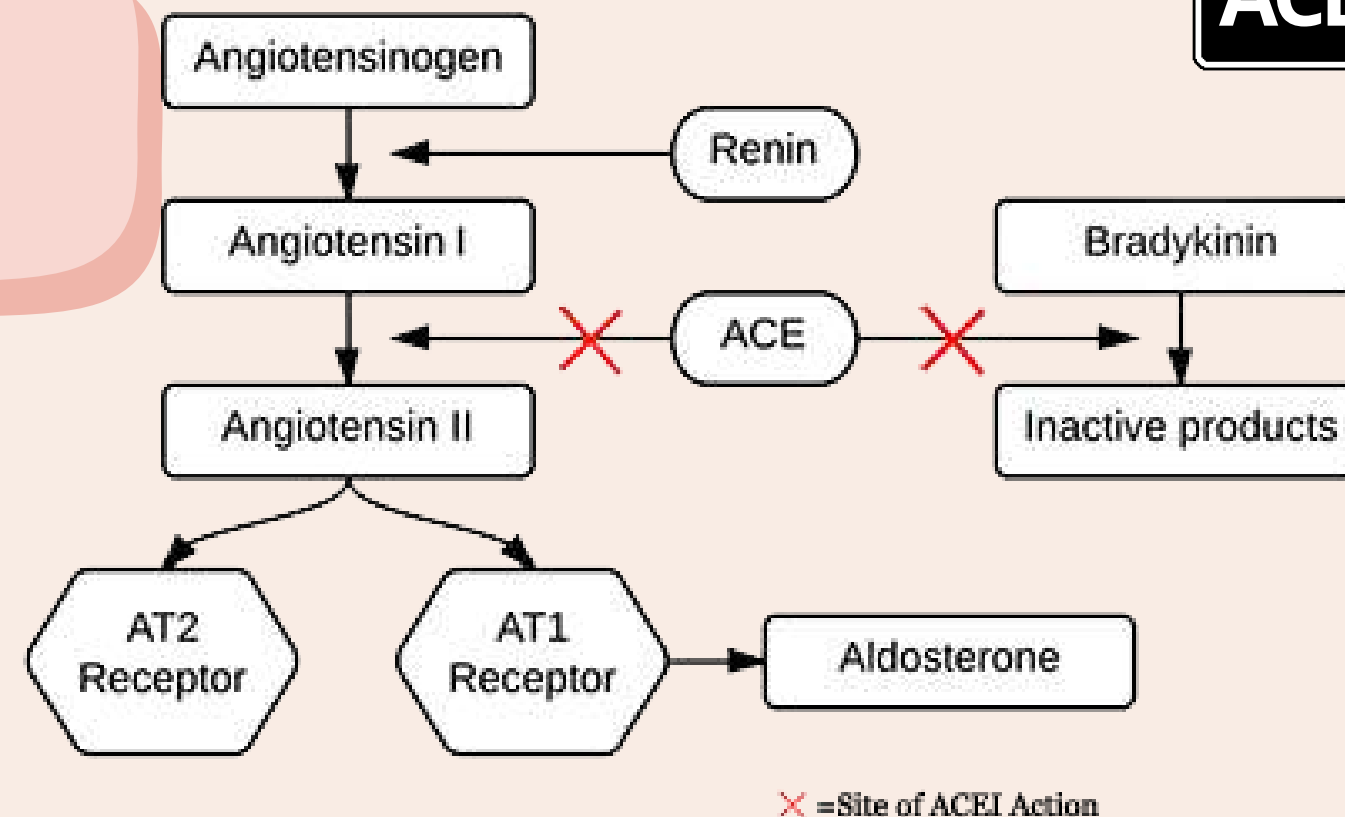
Hipertensi + asma/PPOK

Obat yang dihindari:

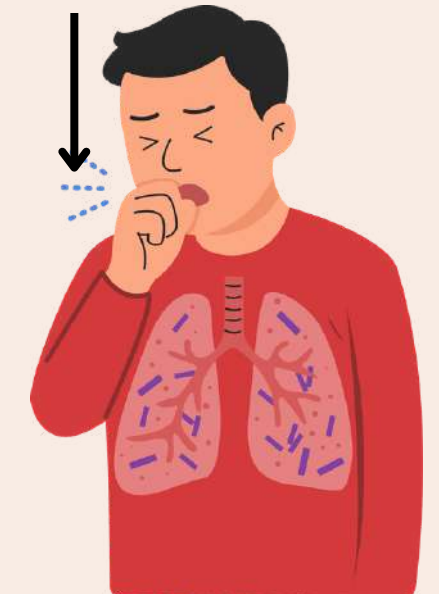
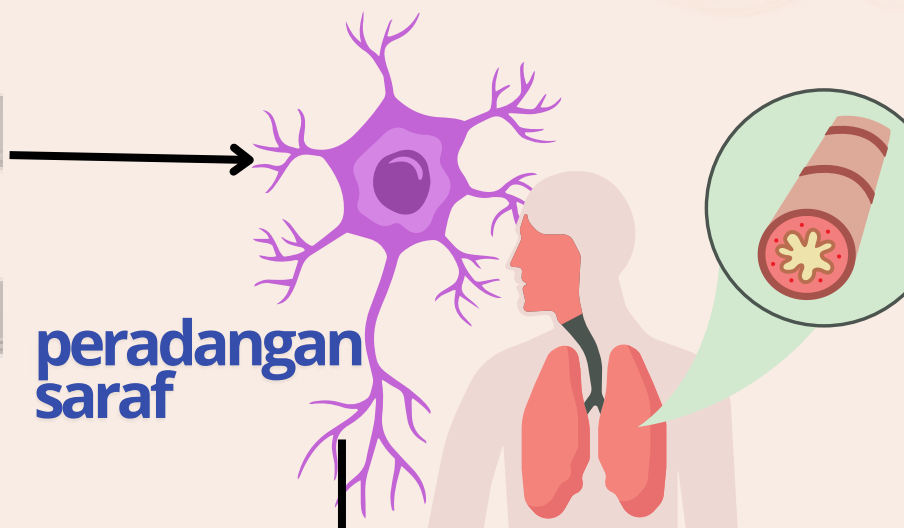
1. ACE inhibitor
2. Beta-blocker

Yang dipilih:

1. ARB,
2. CCB
3. Diuretik



ACE inhibitor dihindari

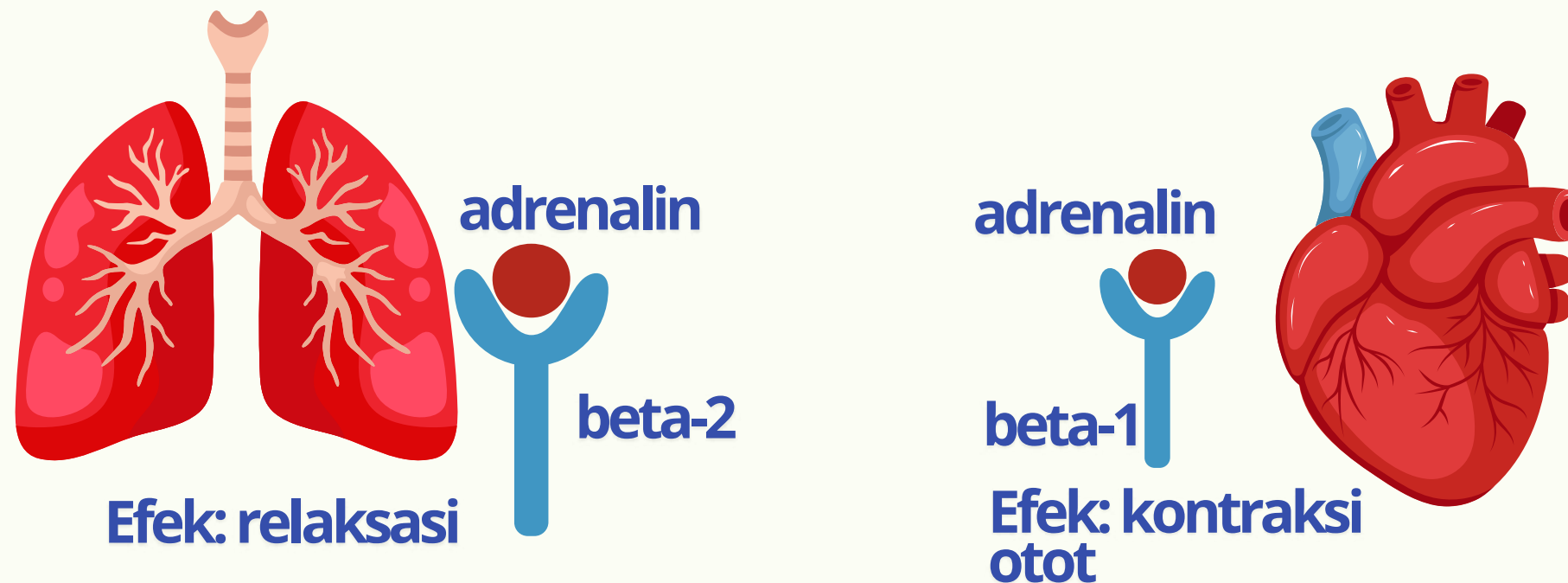


ACE inhibitor tidak hanya menghambat pembentukan ang II, tapi juga mengurangi penguraian bradikinin menjadi bentuk tidak aktif: akibatnya **BRADIKIN menumpuk**

Sebagai mediator radang, bradikinin mengiritasi saraf dan memperburuk **gejala asma/ PPOK**

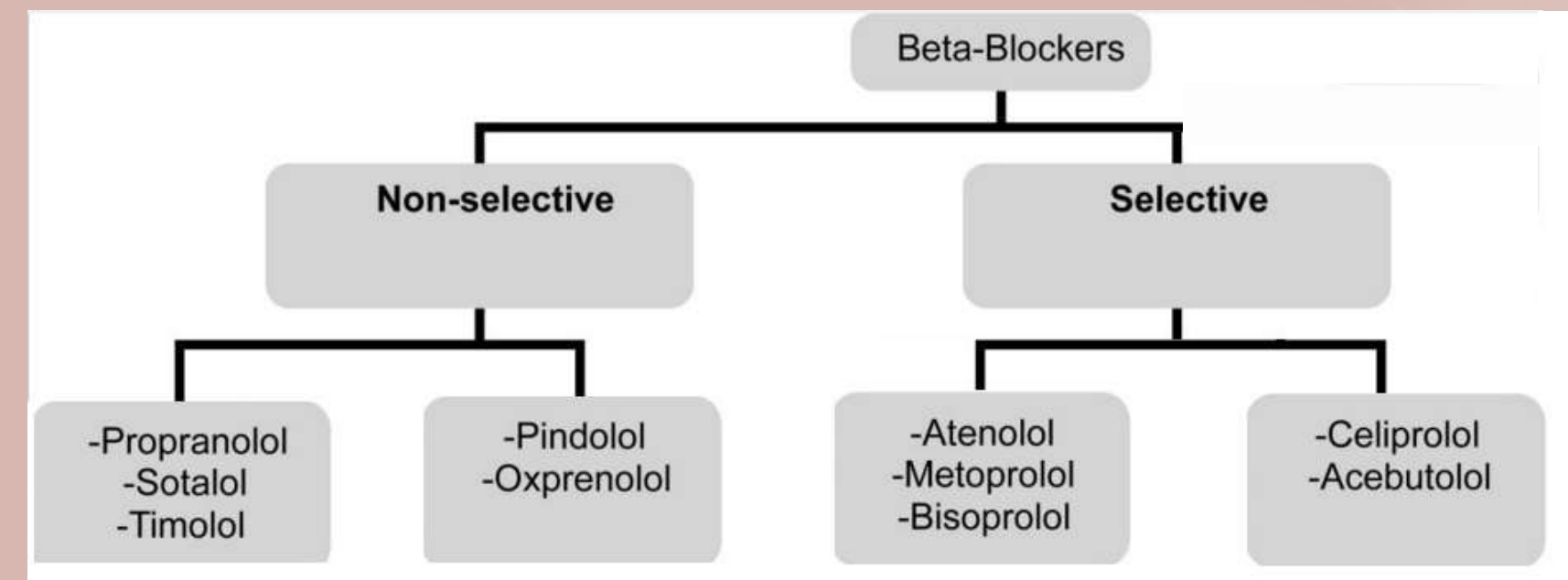
Hipertensi + asma/PPOK

Beta blocker dihindari



Beta bloker tidak selektif, terutama, akan bikin efek yang **berlawanan** pada jantung dan paru-paru.

Di jantung, beta bloker akan mengurangi kontraksi, dan di paru, ia akan menyempitkan: **memperburuk gejala** asma/PPOK.



Beta blocker dipilih

CCB, dan diuretik tidak mengganggu fungsi paru.

ARB, walaupun memiliki mekanisme kerja yang mirip dengan ACE inhibitor, **tidak menyebabkan iritasi pada saluran nafas** (tidak menyebabkan penimbunan bradikinin).

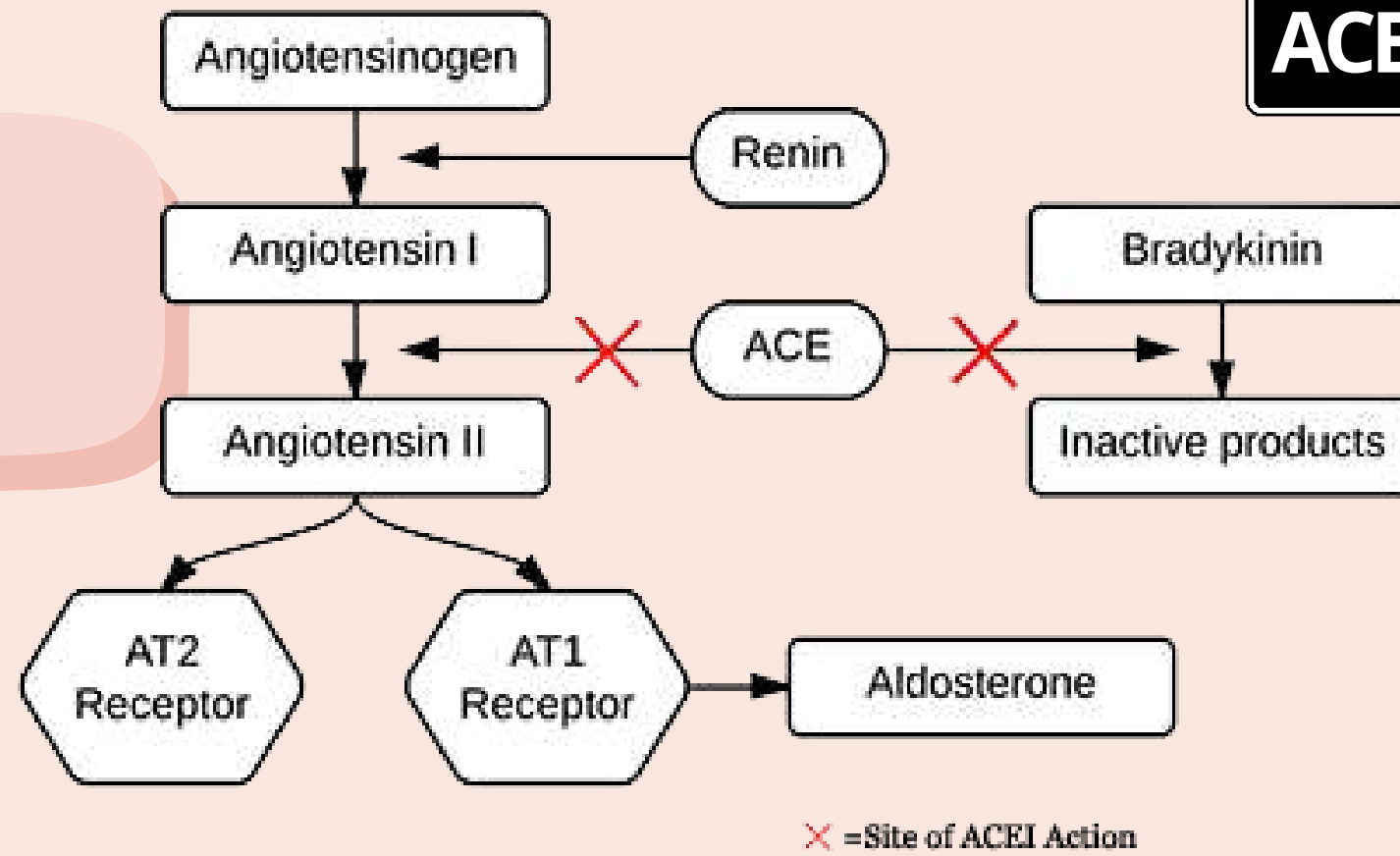
Hipertensi + asma/PPOK

Obat yang dihindari:

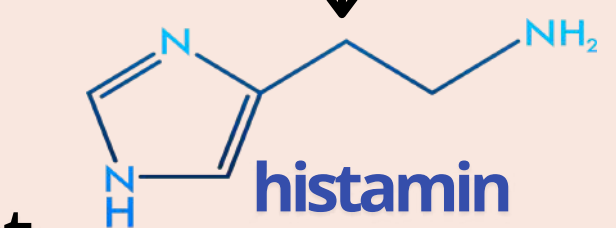
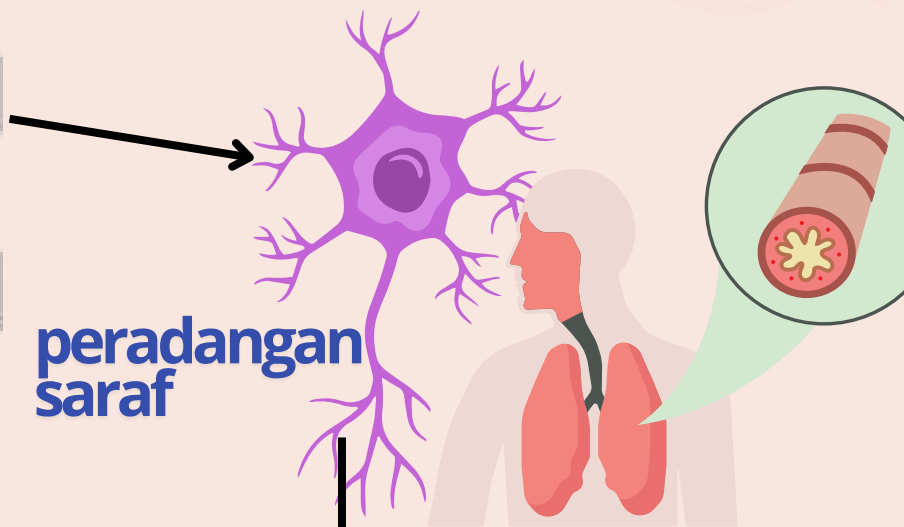
1. ACE inhibitor
2. Beta-blocker

Yang dipilih:

1. ARB,
2. CCB
3. Diuretik



ACE inhibitor dihindari



ACE inhibitor tidak hanya menghambat pembentukan ang II, tapi juga mengurangi penguraian bradikinin menjadi bentuk tidak aktif. akibatnya **BRADIKIN menumpuk**

Sebagai mediator radang, bradikinin mengiritasi saraf dan memperburuk **gejala asma/ PPOK**

Hipertensi (lansia)

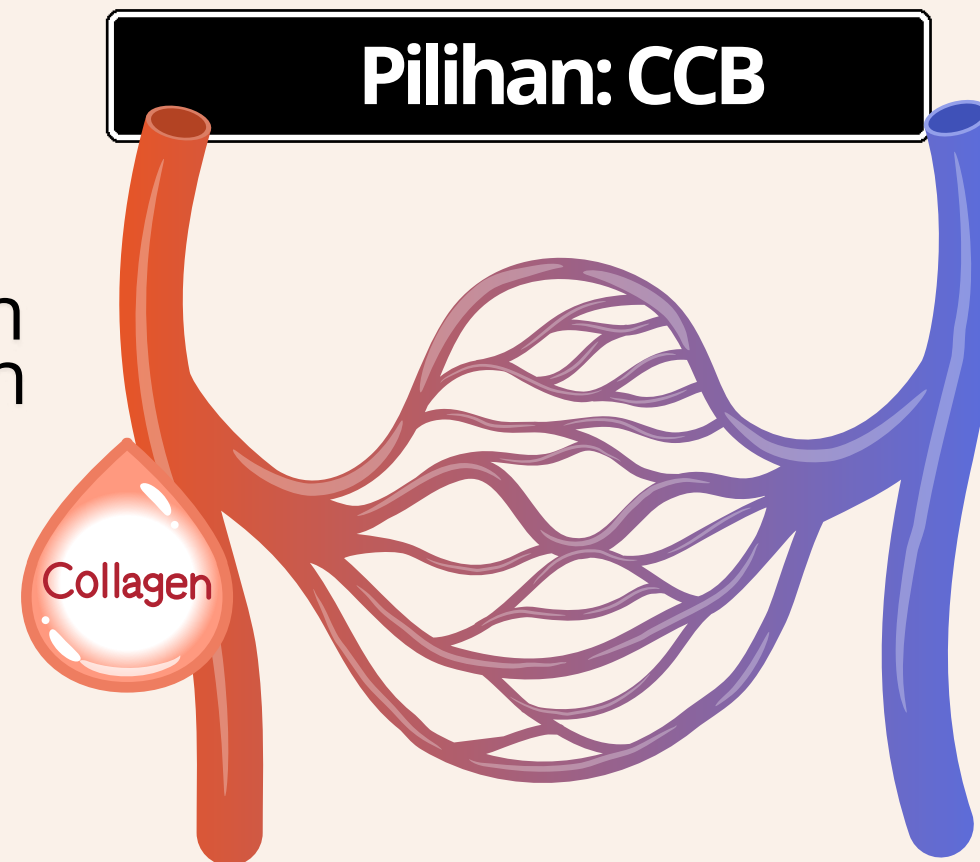
Obat pilihan:

1. **CCB**
2. **diuretik tiazid**

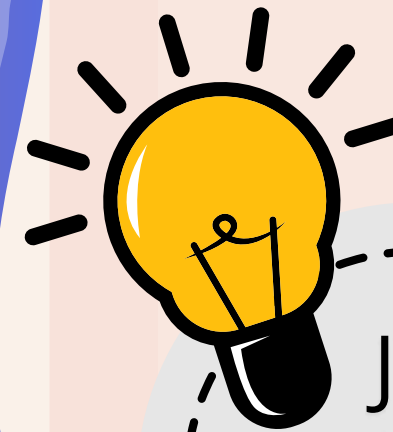
Pada lansia, pembuluh darah arteri cenderung kaku; elastin di dalamnya berkurang dan kolagen meningkat.

Akibatnya: sistolik, rentan tinggi- namun diastolik tetap atau rendah.

CCB adalah pilihan yang paling baik untuk lansia, karena ia bekerja pada arteri. Arteri memiliki otot polos sedangkan vena tidak.



Itulah kenapa CCB menyebabkan bengkak di awal penggunaan. Ia melebarkan arteri, namun tidak vena. Aliran darah meningkat pada arteri perifer, namun tidak vena. Tekanan meningkat, dan cairan merembes.



Jika bengkak terjadi, diuretik bukan solusi. CCB sebaiknya diganti dengan ACEi/ARB yang bekerja pada arteri dan vena; tidak hanya arteri.

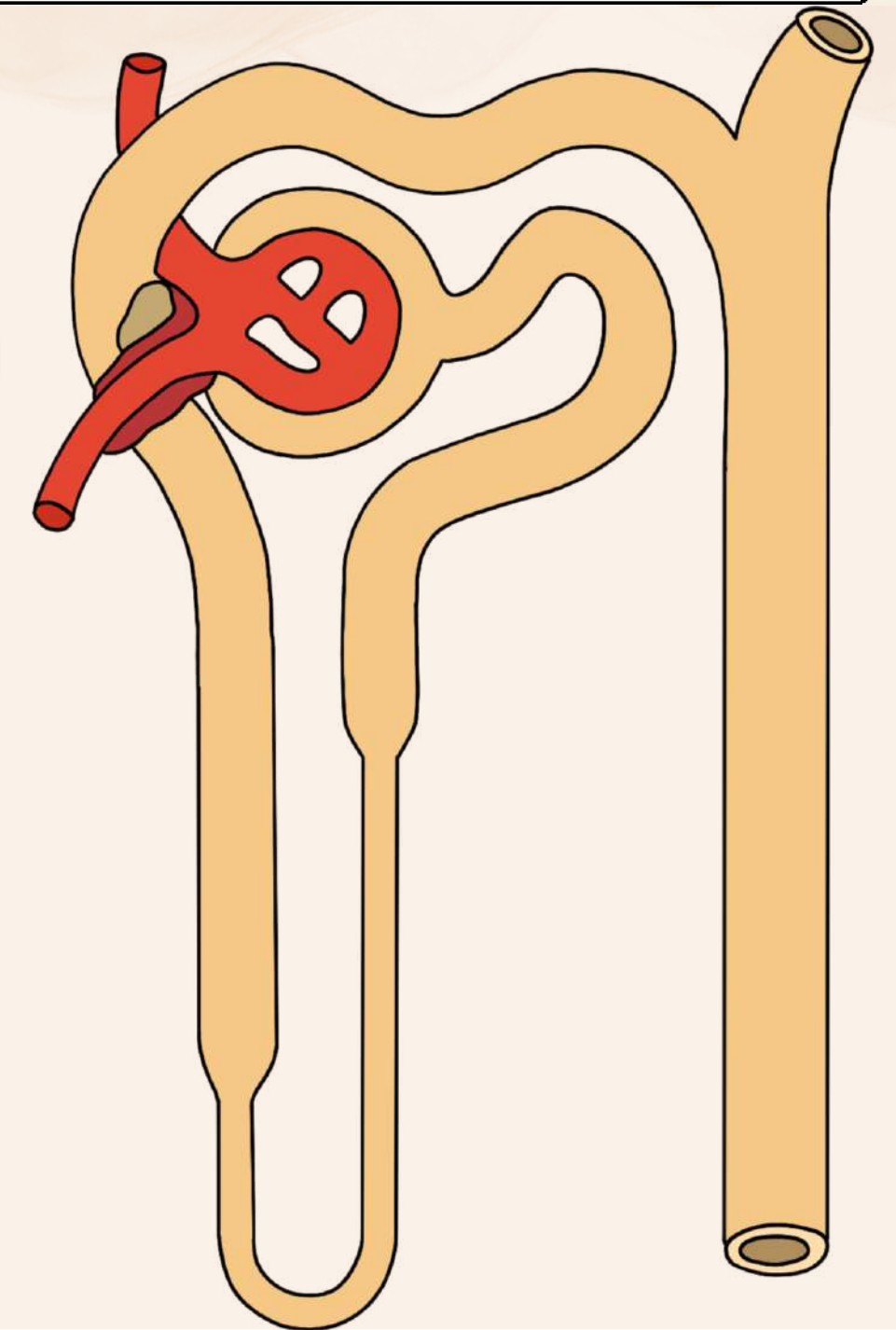
Hipertensi (lansia)

Pilihan: diuretik tiazid

Diuretik tiazid menghambat penyerapan **kembali natrium** di ginjal. Karena natrium menarik air, otomatis **volume cairan** di dalam pembuluh darah **berkurang**, menurunkan **tekanan darah**.

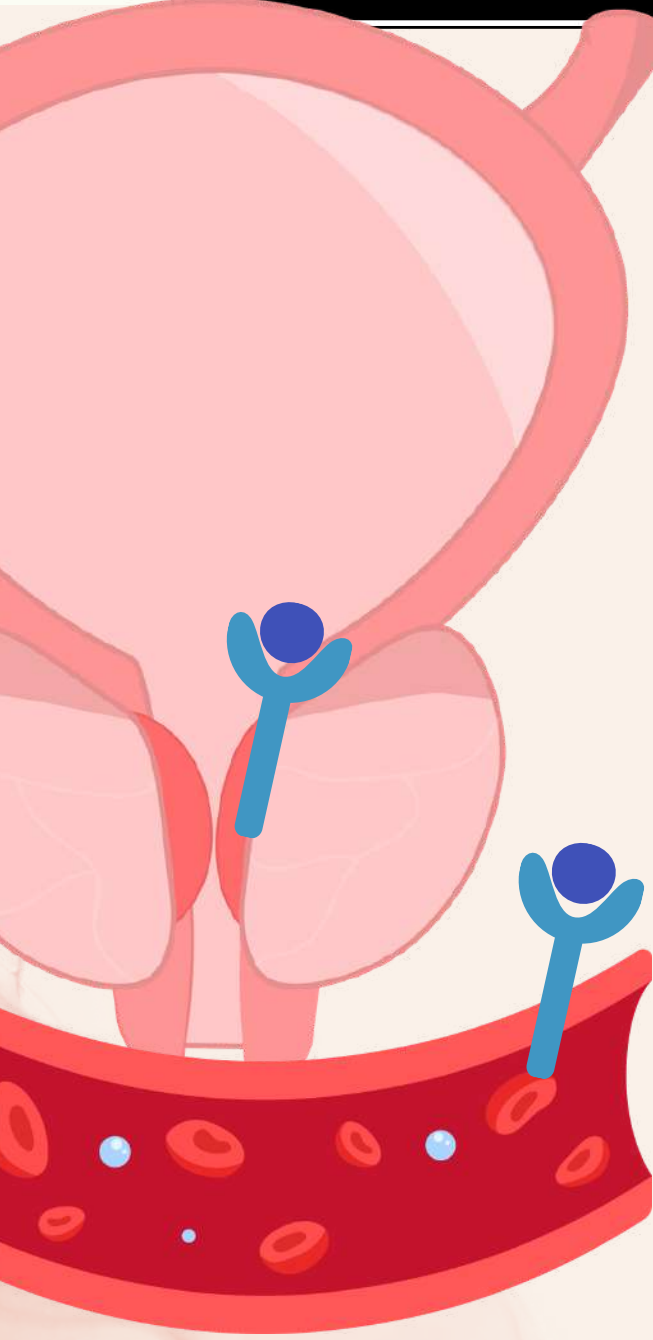


Karena garam menyebabkan pembuluh darah, kaku; kehilangan natrium melenturkan pembuluh darah jangka panjang.



Hipertensi + perbesaran prostat

Pilihan: alfa-1 blocker



Noradrenalin terikat pada receptornya: **alfa 1** di otot halus uretra- menyebabkan kontraksi yg merintangi aliran urin dari kandung kemih ke ureter.

Noradrenalin juga terikat pada reseptornya di otot pembuluh darah.



Dengan kata lain, alfa-1 bloker yang merintangi noradrenalin terikat pada reseptor alfa; akan mengurangi kontraksi uretra dan mengurangi tekanan darah.

Selective α 1-adrenergic blockers include:

Prazosin
Doxazosin
Tamsulosin
Terazosin

Hipertensi + perbesaran prostat



Dihindari: CCB

Pembuluh darah pasien hipertensi berkontraksi, *right?*

Untuk urin bisa di"pompa" keluar, otot polos dinding kandung kemih (detrusor), harus bisa berkontraksi.

Jadi situasinya TERBALIK. Kita ingin pembuluh darah lemas, dan dinding kantung berkontraksi.



CCB melebarkan pembuluh darah, tapi mengurangi kontraksi dinding otot detrusor; mengurangi kemampuan kandung kemih "memompa" urin.

Jadi, pilihan pada hipertensi+ perbesaran prostat: alfa-1 bloker, dan CCB dihindari.

Hipertensi + Diabetes Melitus

Standar
Terapi

ACEi atau
ARB

Terapi
tambahan

CCB

Tiazid,
B-Blocker

PENYAKIT GINJAL KRONIS

Standar
Terapi

ACEi atau
ARB

Penyakit Jantung Koroner

Standar
Terapi

B-Blocker
+
ACEi
atau ARB

Terapi
tambahan

CCB

Diuretik Tiazid

Gagal jantung dengan EF yg menurun

Standar
Terapi

Diuretik
+
ACEi atau ARB
+ Beta-blocker

Terapi
tambahan

Antagonis
Aldosteron

Pencegahan Strok berulang

Standar
Terapi

Tiazid
atau Tiazid +ACEi

Referensi:

- **2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/P CNA guideline for the prevention, detection, evaluation, and management of high blood pressure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018;71:e 13-e115 .**
- **Management of Stage 1 Hypertension in Adults With a Low 10-Year Risk for Cardiovascular Disease: Filling a Guidance Gap: A Scientific Statement From the American Heart Association, Hypertension 2021;77(6):e58-e67.**