Farmakologi Antihipertensi

dr. Imaniar Ranti, M.Sc

Departemen Farmakologi, FKIK UMY

Learning Objective

- Memahami jenis obat antihipertensi
- Memahami farmakokinetik dan farmakodinamika obat antihipertensi
- Mengetahui efek samping obat antihipertensi
- Memahami tatalaksana hipertensi
- Memahami penggunaan obat antihipertensi pada kondisi khusus

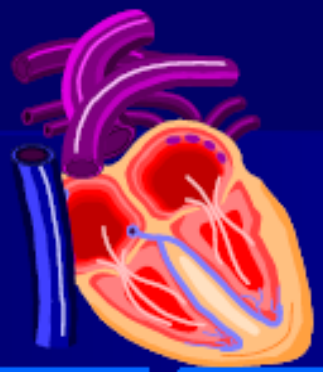
Table 1. Classification of Hypertension Based on Office Blood Pressure (BP) Measurement

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal BP	<130	and	<85
High-normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	≥160	and/or	≥100

TEKANAN DARAH

CURAH JANTUNG

RESISTENSI PERIFER



Denyut Jantung

Isi Sekuncup

Resistensi Pembuluh darah

Viskositas Darah

Kontraktilitas Miokard

Alir Balik Vena

Tonus Arteri & Arteriole

Elastisitas Dinding Pembuluh Darah

Volume Darah

Kapasitas Vena

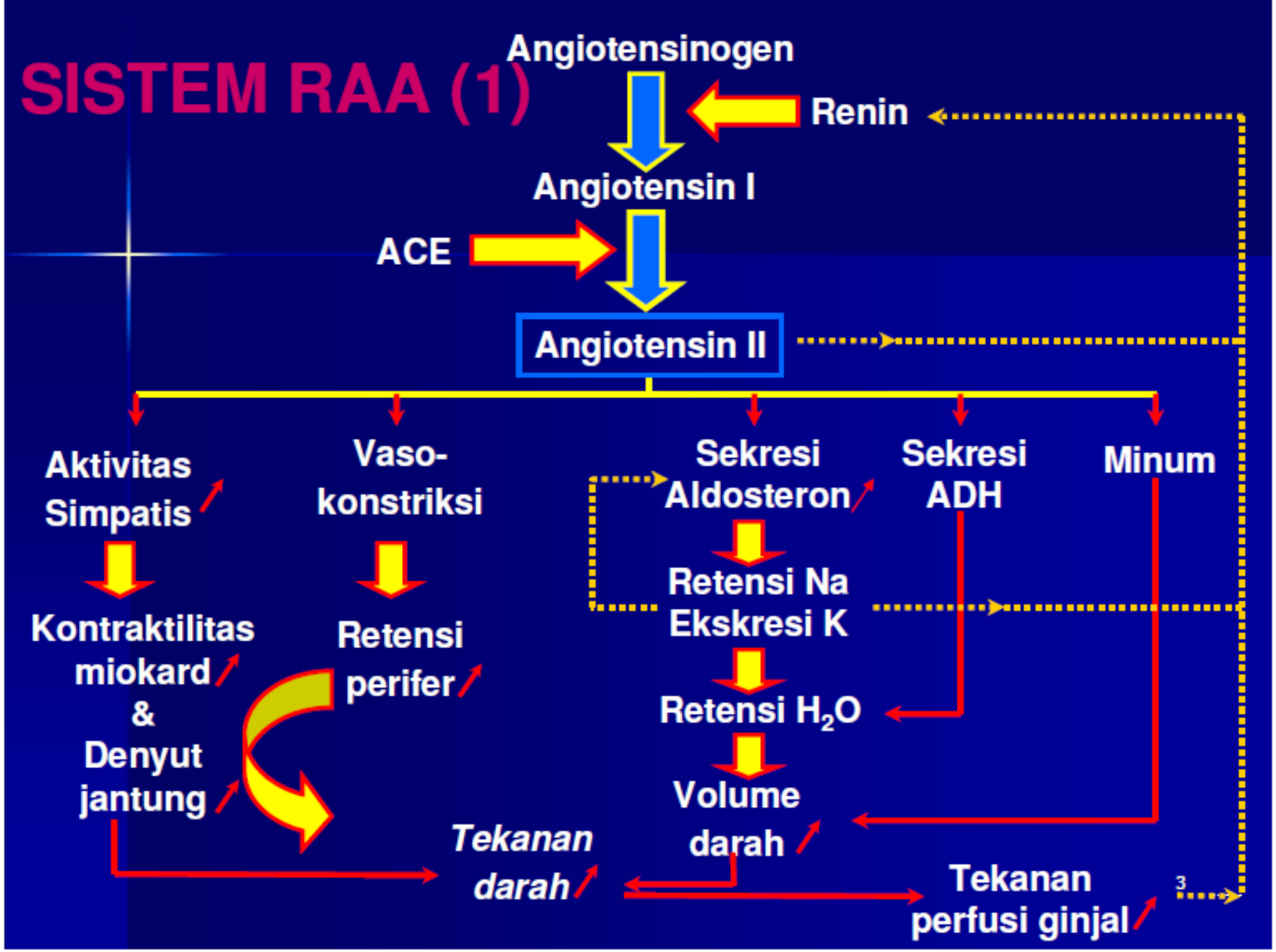
Parasimpatis

RAA

Simpatis

Faktor-Faktor yang Mempengaruhi Tekanan Darah

RAA : Sistem Renin-Angiotensin-Aldosteron


SISTEM RAA (1)
Angiotensinogen
Renin
Angiotensin I
ACE
Angiotensin II
Aktivitas Simpatis
Vaso-konstriksi
Sekresi Aldosteron
Sekresi ADH
Minum
Kontraktilitas miokard & Denyut jantung
Retensi perifer
Retensi Na Ekskresi K
Retensi H_2O
Volume darah
Tekanan darah
Tekanan perfusi ginjal
3

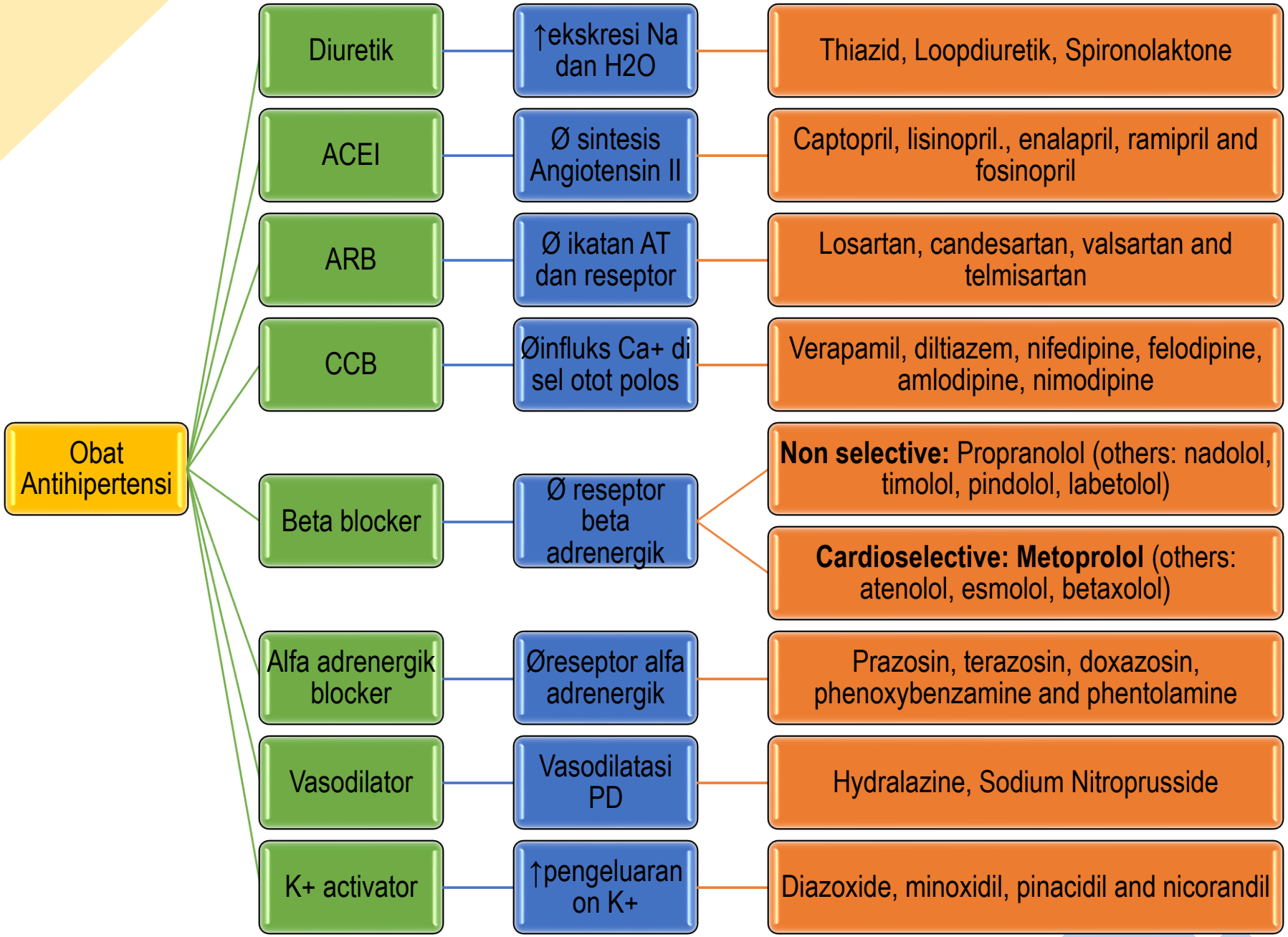
Terapi farmakologis

3 pendekatan utama

- Menurunkan curah jantung
- Menurunkan volume darah
- Menurunkan resistensi perifer

Klasifikasi Obat

- Menurunkan curah jantung
  - Beta blocker
  - Penghambat syaraf adrenergik
- Menurunkan volume darah
  - diuretik
- Menurunkan resistensi perifer
  - Vasodilator
  - ARB
  - Calsium chanel blocker
  - ACE inhibitor
  - Penghambat reseptor alfa-adrenergik
  - Obat yang bekerja sentral


Obat Antihipertensi
Diuretik
↑ekskresi Na dan H2O
Thiazid, Loopdiuretik, Spironolaktone
ACEI
Ø sintesis Angiotensin II
Captopril, lisinopril., enalapril, ramipril and fosinopril
ARB
Ø ikatan AT dan reseptor
Losartan, candesartan, valsartan and telmisartan
CCB
Øinfluks Ca+ di sel otot polos
Verapamil, diltiazem, nifedipine, felodipine, amlodipine, nimodipine
Beta blocker
Ø reseptor beta adrenergik
Non selective: Propranolol (others: nadolol, timolol, pindolol, labetolol)
Cardioselective: Metoprolol (others: atenolol, esmolol, betaxolol)
Alfa adrenergik blocker
Øreseptor alfa adrenergik
Prazosin, terazosin, doxazosin, phenoxybenzamine and phentolamine
Vasodilator
Vasodilatasi PD
Hydralazine, Sodium Nitroprusside
K+ activator
↑pengeluaran on K+
Diazoxide, minoxidil, pinacidil and nicorandil

Diuretik

- Meningkatkan kecepatan pembentukan urin/ meningkatkan ekskresi air, natrium, klorida --> menurunkan volume darah --> CO ↓ → tekanan darah ↓
- Kadar Na+ tubuh rendah → total peripheral resistance (TPR) turun → resistensi perifer ↓
- Jenis:
  - Thiazide (HCT/hidroklorotiazid)
  - Loop diuretic (furosemid)
  - Diuretika hemat kalium (amilorid, spironolactone)
  - Carbonic anhidrase inhibitor (acetazolamide)
  - Diuretik osmotik (manitol, urea)

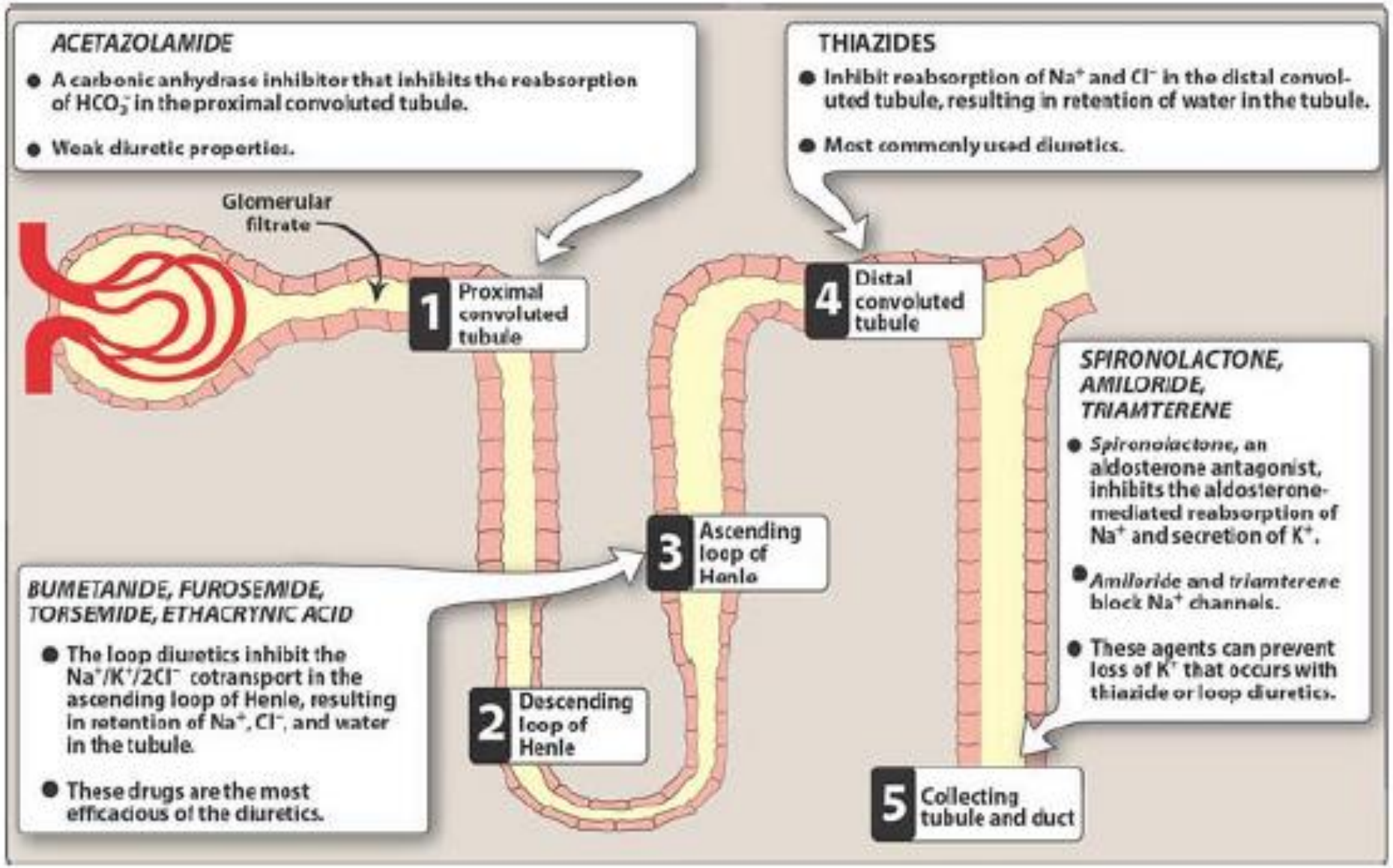
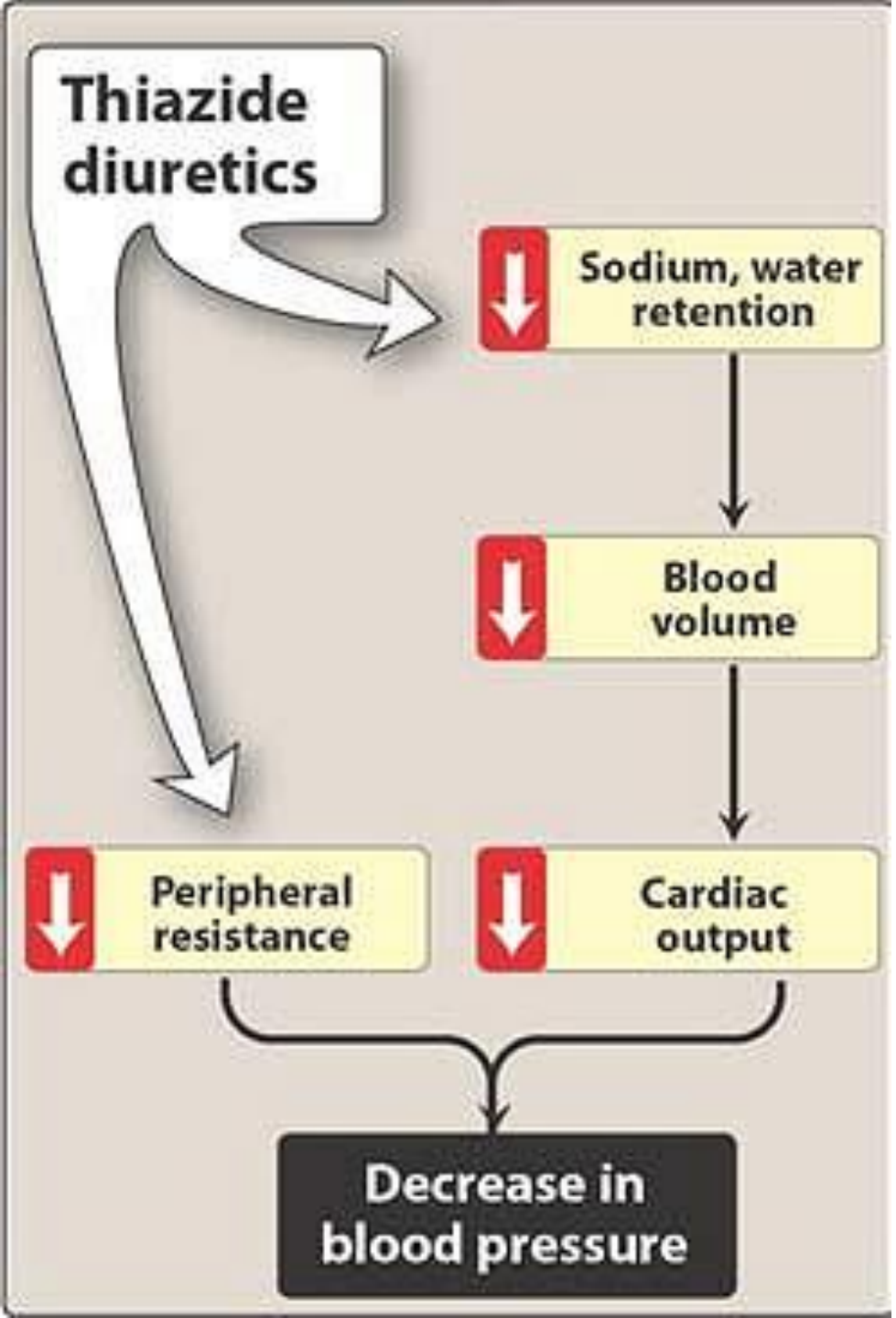


Figure 22.2 Major locations of ion and water exchange in the nephron, showing sites of action of the diuretic drugs.

Diuretics

- Rekomendasi JNC :
  - Thiazide dosis rendah (12.5 – 25 mg per day) pada hipertensi essential
  - Lansia → diuretik hemat kalium (first choice)
  - Gagal → pilih jenis antihipertensi lainnya, bukan meningkatkan dosis thiazide
  - Loop diuretics → severe hypertension with retention of body fluids (CHF, CRF)



Diuretik Thiazid

- Bekerja pada tubulus distal → menghambat kotransporter Na+/Cl- pada membran lumen tubulus distal → reabsorbsi Na+ terganggu
- Jika ada penurunan fungsi ginjal menjadi kurang efektif
- Tidak mengganggu keseimbangan asam basa

Diuretik Thiazid

Pharmacokinetics:

- Absorbsi baik secara oral
- Waktu paruh biologi lama (40 jam)
- Diekskresikan oleh sistem sekresi asam organik ginjal

Thiazide diuretics

- ESO:
  - Hipokalemia – nyeri otot dan lelah, bahkan henti jantung (tosades de pointes) → tx: diet tinggi kalium, suplementasi K
  - Hiperglikemia: menghambat perubahan proinsulin mjd insulin → DM
  - Hiperlipidemia: peningkatan total LDL → stroke
  - Hiperurisemia: menghambat ekskresi asam urat
  - Jika pemberian dosis tinggi 50 – 100 mg per day → gangguan metabolik

Loop diuretics

- Memiliki aktifitas diuretik tertinggi dibanding golongan diuretik lain
- Mekanisme → menghambat kotranspor Na+/K+/2Cl- pada membran lumen ansa henle pars asenden
- Bisa diberikan pada pasien dgn fungsi ginjal buruk

Loop diuretics

Pharmacokinetics:

- Diberikan oral atau parenteral, bekerja cepat
- Diekskresi melalui urine

Adverse effects:

- Ototoxicity: meningkat jika digunakan bersama aminoglycoside antibiotics.
- Hyperuricemia
- Acute hypovolemia
- Hipomagnesemia
- Hipokalemia

Potassium-Sparing Diuretics (Diuretik hemat kalium)

- Steroid sintesis
- Antagonis aldosteron pada reseptor sitoplasmik intraseluler → ikatan kompleks reseptor dengan DNA terganggu → menghambat produksi protein mediator untuk pertukaran Na+/K+ → menghambat reabsorbsi Na+ dan ekskresi K+ pada tubulus koligens ginjal
- Contoh: Spironolacton

Potassium-Sparing Diuretics (hemat kaliun)

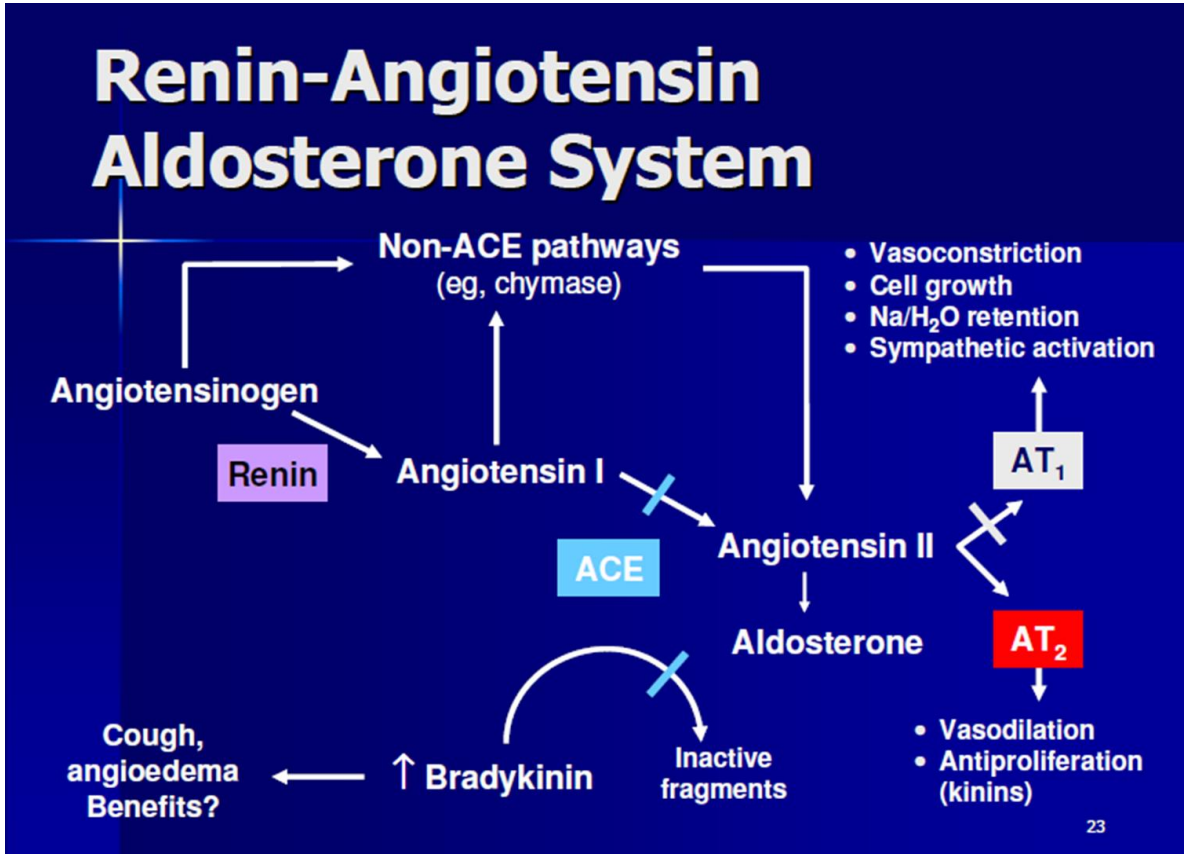
Pharmacokinetics:

- Diabsorbsi baik secara oral
- Dimetabolisme secara cepat menjadi Cancrenone

Adverse effects

- Gangguan lambung → ulkus peptikum
- Ginekomastia
- Gangguan menstruasi

ACE inhibitors



- Mekanisme aksi : menghambat pembentukan angiotensin II dari angiotensin I
- Captopril, lisinopril, enalapril, ramipril and fosinopril etc.
- Efek samping: batuk kering, angioedema, hiperkalemia, rash, leukopeni, gangguan pengecapan

Captopril

- Menurunkan TPR dalam jangka panjang → dilatasi arteriol → TD ↓
- Pharmacokinetics:
  - Available only orally,
  - 70% - 75% is absorbed
  - Food interferes with its absorption
  - Partly excreted unchanged in urine
  - Half life: 2 Hrs, but action stays for 6-12 Hrs

Captopril

- Hyperkalemia in renal failure patients with K+ sparing diuretics, NSAID and beta blockers (routine check of K+ level)
- Hypotension – sharp fall may occur – 1st dose
- Angioedema: swelling of lips, mouth, nose etc.
- Rashes, urticaria etc
- Dysgeusia: loss or alteration of taste
- Foetopathic: hypoplasia of organs, growth retardation etc
- Neutropenia
- Contraindications: Pregnancy, bilateral renal artery stenosis, hypersensitivity and hyperkalaemia

Enalapril

- a prodrug – diubah menjadi Enalaprilate
- Advantages over captopril:
  - Longer half life – OD (5-20 mg OD)
  - Absorption not affected by food
  - Rash and loss of taste are less frequent
  - Longer duration of action
  - Less side effects

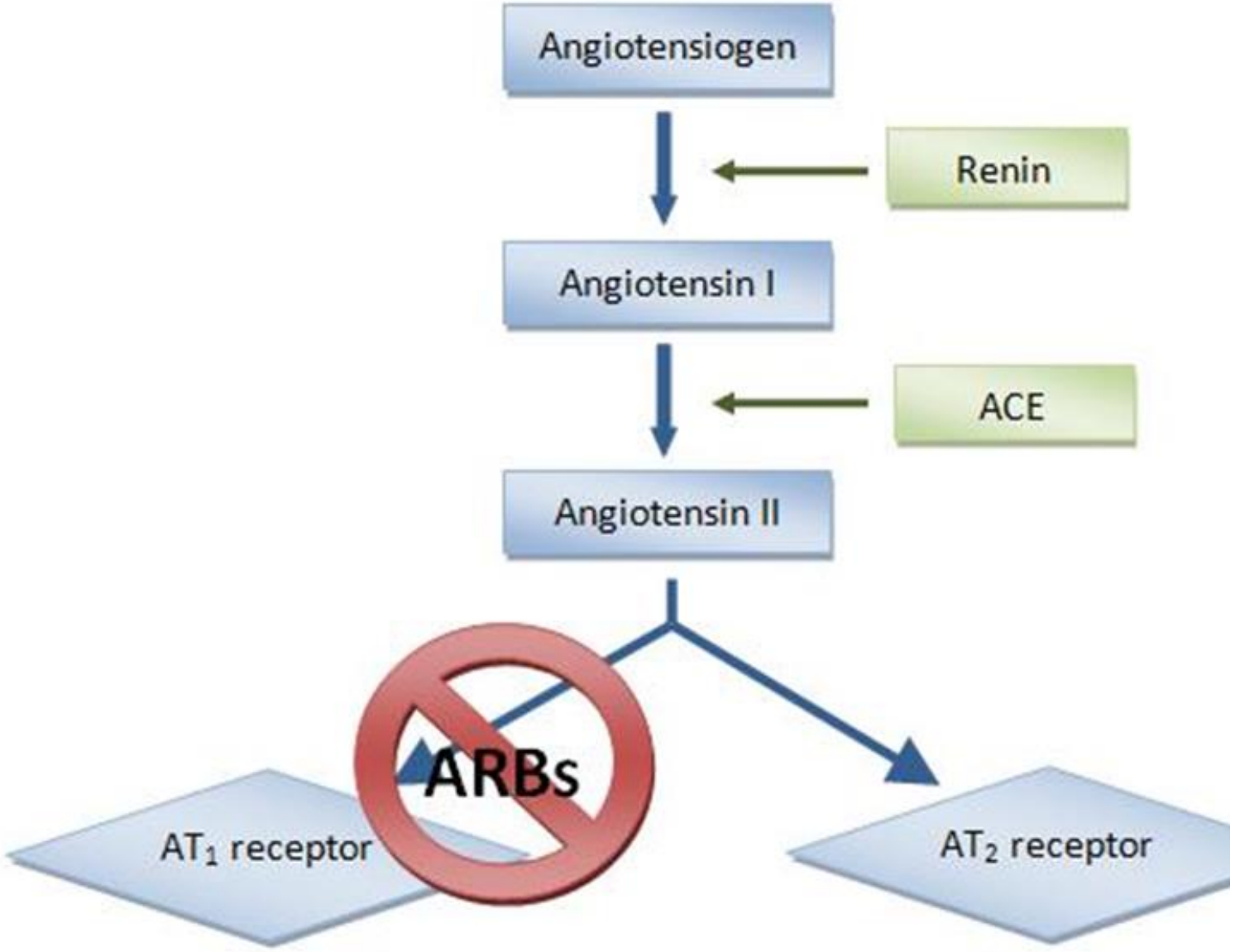
ACE inhibitors – Ramipril

- It’s a popular ACEI now
- It is also a prodrug with long half life
- *Tissue specific* – Protective of heart and kidney
- Uses: Diabetes with hypertension, CHF, AMI and cardio protective in angina pectoris
- Blacks in USA are resistant to Ramipril – addition of diuretics help
- Dose: Start with low dose; 2.5 to 10 mg daily

ACE inhibitors and hypertension

- 1st line of Drug:
  - No postural hypotension or electrolyte imbalance (no fatigue or weakness)
  - Safe in asthmatics and diabetics
  - Prevention of secondary hyperaldosteronism and K+ loss
  - Renal perfusion well maintained
  - Reverse the ventricular hypertrophy and increase in lumen size of vessel
  - No hyperuraecemia or deleterious effect on plasma lipid profile
  - No rebound hypertension
  - Minimal worsening of quality of life – general wellbeing, sleep and work performance etc.

Angiotensin Receptor Blockers (ARBs)



Angiotensin Receptor Blockers (ARBs)

Angiotensin Receptors:

- Specific angiotensin receptors have been discovered, grouped and abbreviated as – AT1 and AT2
- They are present on the surface of the target cells
- Most of the physiological actions of angiotensin are mediated via AT1 receptor
- Blocks all the actions of A-II - vasoconstriction, sympathetic stimulation, aldosterone release and renal actions of salt and water reabsorption

Losartan

- Theoretical superiority over ACEIs:
  - Cough is rare – no interference with bradykinin and other ACE substrates
  - Complete inhibition of AT1 – alternative remains with ACEs
  - Result in indirect activation of AT2 – vasodilatation (additional benefit)
  - Clinical benefit of ARBs over ACEIs – not known
- However, losartan decreases BP in hypertensive which is for long period (24 Hrs)
  - heart rate remains unchanged and cvs reflexes are not interfered
  - no significant effect in plasma lipid profile, insulin sensitivity and carbohydrate tolerance etc
  - Mild uricosuric effect

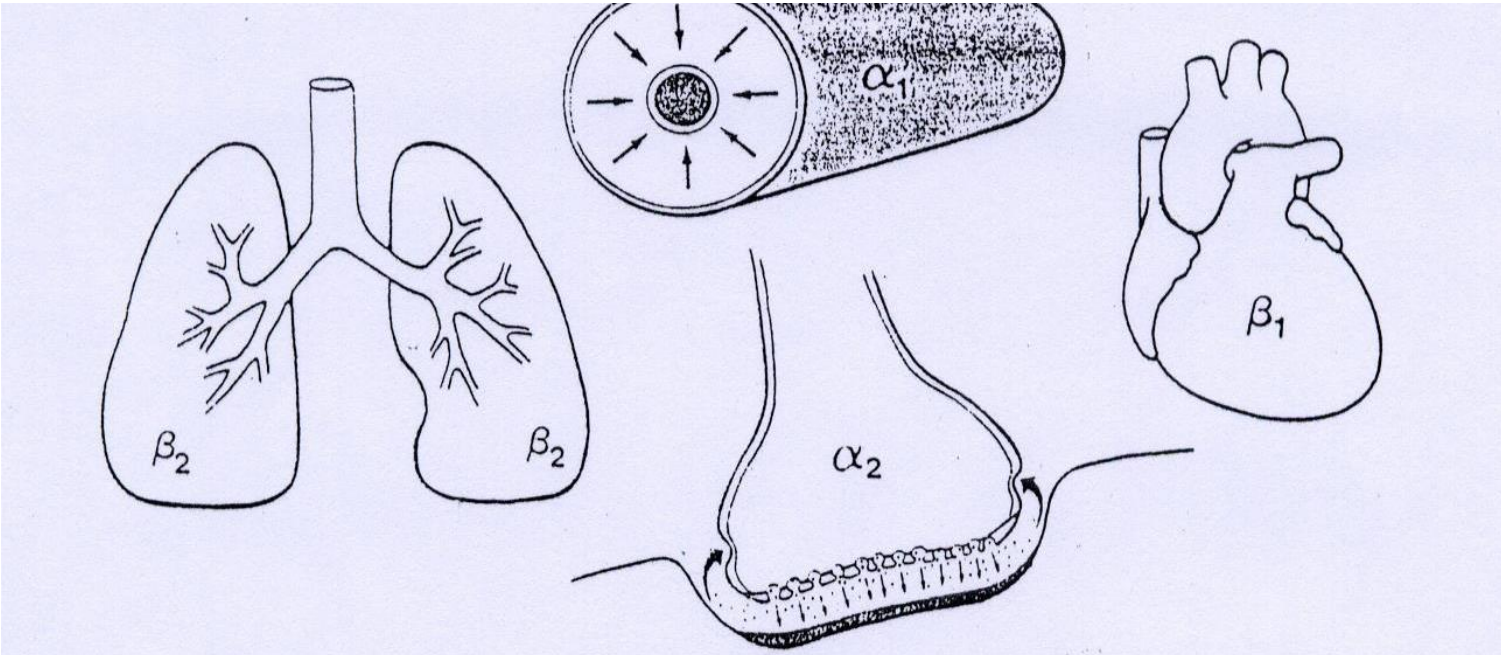
Losartan

- Pharmacokinetic:
  - Absorption not affected by food but unlike ACEIs its bioavailability is low
  - High first pass metabolism
  - Carboxylated to active metabolite E3174
  - Highly bound to plasma protein
  - Do not enter brain
- Adverse effects:
  - Foetopathic like ACEIs – not to be administered in pregnancy
  - Rare 1st dose effect hypotension
  - Low dysgeusia and dry cough
  - Lower incidence of angioedema
- Available as 25 and 50 mg tablets

Simpatolitik (penghambat adrenergik)

- Beta-Blocker (propanolol, metoprolol)
- Alpha-Blocker (prazosin, fentolamin)
- Bekerja sentral (metildopa, klonidin)
- Penghambat saraf adrenergik (reserpin, guanetidin)
- Penghambat reseptor alfa dan beta(labetolol)
- Penghambat ganglion simpatis (trimetafan)

Lokasi reseptor adrenergik



β1—Jantung: Miokardium, *SA node*; Ginjal: sel juxtaglomerular.
β2—Paru-paru: otot polos bronkus (dan vaskuler)
α1—Otot polos vaskuler
α2—axon terminal

Aspek klinis reseptor adrenergik

Gambar 11.3—Reseptor Adrenergik

Tipe Reseptor	Lokasi	Respon	Efek dari Perangsangan
α1	◆ otot polos arteriol ◆ otot polos vena	◆ vasokonstriksi ◆ vasokonstriksi	◆ tahanan arteriol meningkat ◆ venous return meningkat
α2	◆ ujung saraf adrenergik	◆ umpan balik menghambat pelepasan noradrenalin	◆ mencegah stimulasi yang berlebihan terhadap jaringan
β1	◆ pacemaker jantung (SA node) ◆ miokardium ◆ korteks ginjal	◆ denyut jantung meningkat ◆ kontraktilitas meningkat ◆ sekresi renin meningkat	◆ output jantung meningkat ◆ stroke volume meingkat ◆ variable
β2	◆ otot polos vaskuler ◆ otot polos bronkus	◆ vasodilatasi ◆ bronkodilatasi	◆ dapat diabaikan ◆ aliran udara meningkat

Beta-adrenergic blockers

- **Non selective: Propranolol** (others: nadolol, timolol, *pindolol*, labetolol)
- **Cardioselective: Metoprolol** (others: atenolol, esmolol, betaxolol)
- Advantages:
  - No postural hypotension
  - No salt and water retention
  - Low incidence of side effects
  - Low cost
  - Once a day regimen

- Drawbacks (side effects):
  - Fatigue, lethargy
  - Loss of libido – impotence
  - Cognitive defects – forgetfulness
  - Therefore cardio-selective drugs are preferred now

Beta-adrenergic blockers

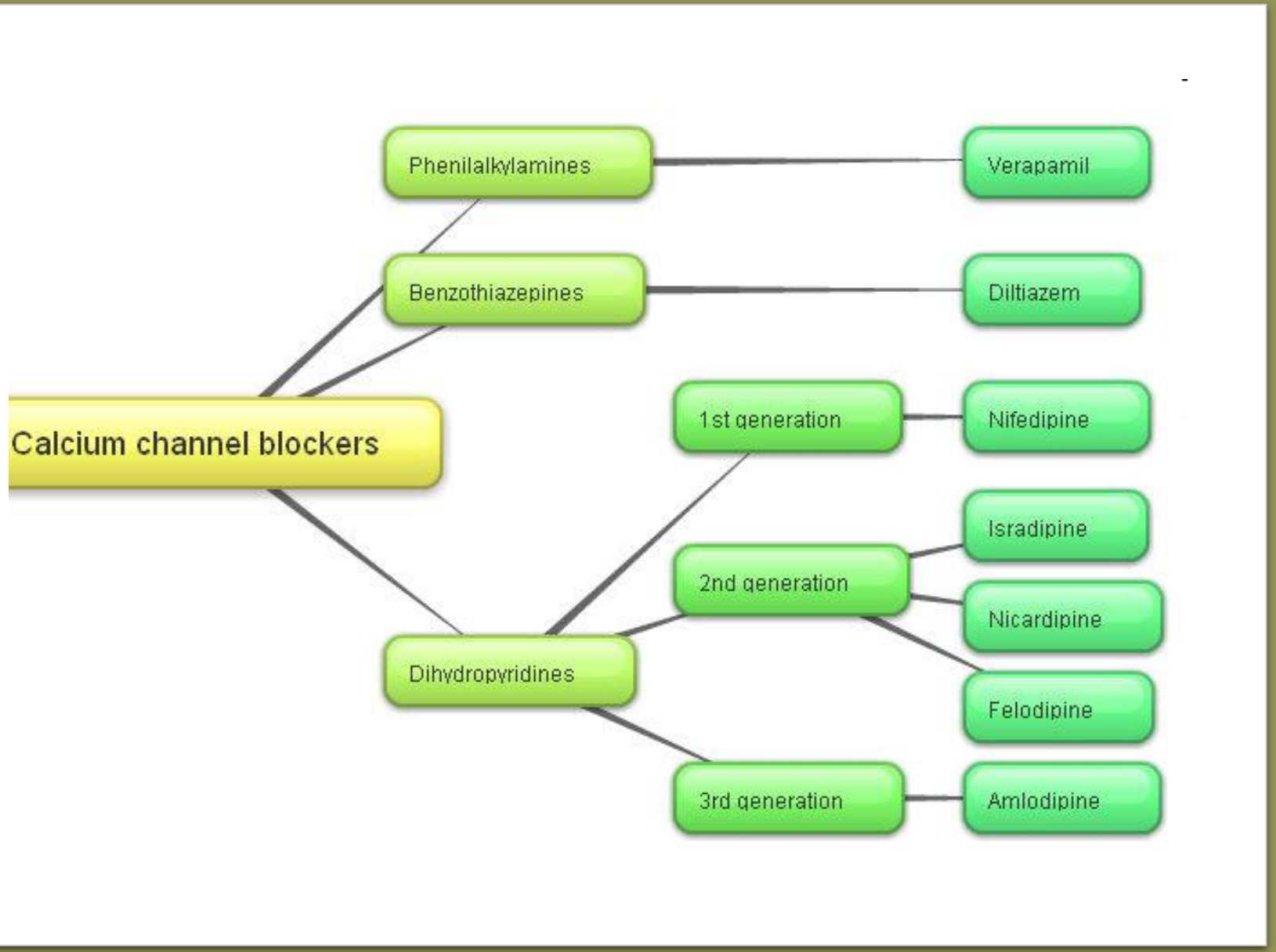
- Advantages of cardio-selective over non-selective:
  - In asthma
  - In diabetes mellitus
  - In peripheral vascular disease
- Current status:
  - JNC 7 recommends - 1st line of antihypertensive along with diuretics and ACEIs
  - Preferred in young non-obese hypertensive
  - Angina pectoris and post angina patients
  - Post MI patients – useful in preventing mortality
  - In old persons, carvedilol – vasodilatory action can be given

Alpha-adrenergic blockers

- Non selective alpha blockers are not used in chronic essential hypertension (phenoxybenzamine, phentolamine), only used sometimes as in phaechromocytoma
- Specific alpha-1 blockers like prazosin, terazosin and doxazosine are used
- PRAZOSIN is the prototype of the alpha-blockers
- Reduction in t.p.r and mean BP – also reduction in venomotor tone and pooling of blood – reduction in CO
- Does not produce tachycardia as presynaptic auto (alpha-2) receptors are not inhibited – autoregulation of NA release remains intact

Alpha-adrenergic blockers.

- Adverse effects:
  - Prazosin causes postural hypotension – start 0.5 mg at bedtime with increasing dose and up to 10 mg daily
  - Fluid retention in monotherapy
  - Headache, dry mouth, weakness, dry mouth, blurred vision, rash, drowsiness and failure of ejaculation in males
- Current status:
  - Several advantages – improvement of carbohydrate metabolism – diabetics, lowers LDL and increases HDL
  - But not used as first line agent, used in addition with other conventional drugs which are failing – diuretic or beta blocker
- Doses: Available as 0.5 mg, 1 mg, 2.5 mg, 5 mg etc. dose:1-4 mg twice daily (Minipress/Prazopress)



Calcium Channel Blockers - Classification

Calcium Channel Blockers

- Three types Ca+ channels in smooth muscles – Voltage sensitive, receptor operated and leak channel
- Voltage sensitive are again 3 types – L-Type, T-Type and N-Type
- Normally, L-Type of channels admit Ca+ and causes depolarization – excitation - contraction coupling through phosphorylation of myosin light chain – contraction of vascular smooth muscle – elevation of BP
- CCBs block L-Type channel:
  - Smooth Muscle relaxation
  - Negative chronotropic and ionotropic effects in heart
- DHPs have highest smooth muscle relaxation and vasodilator action followed by verapamil and diltiazem
- Other actions: DHPs have diuretic action

Calcium Channel Blockers

- Advantages:
  - Unlike diuretics no adverse metabolic effects but mild adverse effects like – dizziness, fatigue etc.
  - No sedation or CNS effect
  - Can be given to asthma, angina and PVD patients
  - No renal and male sexual function impairment
  - No adverse fetal effects and can be given in pregnancy
  - Minimal effect on quality of life

Calcium Channel Blockers

- Contraindications:
  - Unstable angina
  - Heart failure
  - Hypotension
  - Post infarct cases
  - Severe aortic stenosis
- Preparation and dosage:
  - Amlodipine – 2.5, 5 and 10 mg tablets (5-10 mg OD) – Stamlo, Amlopres, Amlopin etc.
  - Nimodipine – 30 mg tab and 10 mg/50 ml injection – Vasotop, Nimodip, Nimotide etc.

Vasodilators - Hydralazine

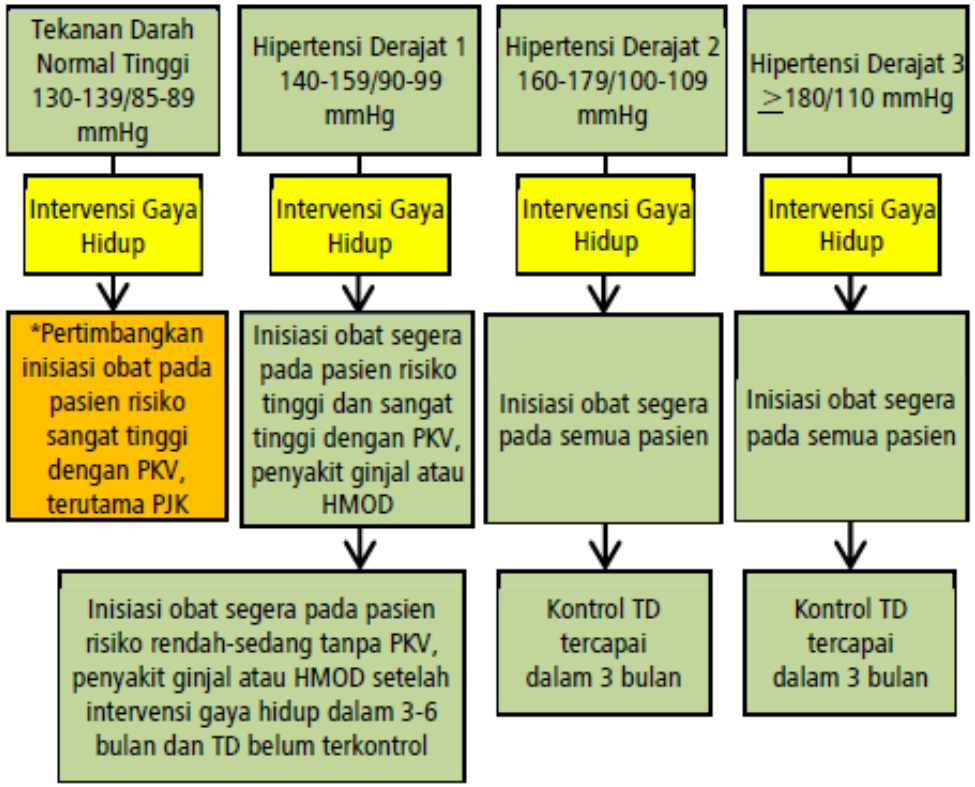
- Directly acting vasodilator
- MOA: hydralazine molecules combine with receptors in the endothelium of arterioles – NO release – relaxation of vascular smooth muscle – fall in BP
- Subsequenly fall in BP – stimulation of adrenergic system leading to
  - Cardiac stimulation producing palpitation and rise in CO even in IHD and patients – anginal attack
  - Tachycardia
  - Increased Renin secretion – Na+ retention
  - These effects are countered by administration of beta blockers and diuretics
- Uses: 1) Moderate hypertension when 1st line fails – with beta-blockers and diuretics 2) Hypertension in Pregnancy, Dose 25-50 mg OD

Vasodilators - Minoxidil

- Powerful vasodilator, mainly 2 major uses – antihypertensive and alopecia
- Prodrug and converted to an active metabolite which acts by hyperpolarization of smooth muscles and thereby relaxation of SM – leading to hydralazine like effects
- Rarely indicated in hypertension especially in life threatening ones
- More often in alopecia to promote hair growth
- Orally not used any more
- Topically as 2-5% lotion/gel and takes months to get effects
- MOA of hair growth:
  - Enhanced microcirculation around hair follicles and also by direct stimulation of follicles
  - Alteration of androgen effect of hair follicles

Centrally acting Drugs

- Alpha-Methyldopa: a prodrug
  - Precursor of Dopamine and NA
  - MOA: Converted to alpha methyl noradrenaline which acts on alpha-2 receptors in brain and causes inhibition of adrenergic discharge in medulla – fall in PVR and fall in BP
  - Various adverse effects – cognitive impairment, postural hypotension, positive coomb`s test etc. – Not used therapeutically now except in Hypertension during pregnancy
- Clonidine: Imidazoline derivative, partial agonist of central alpha-2 receptor
  - Not frequently used now because of tolerance and withdrawal hypertension



Gambar 3. Alur Panduan Inisiasi Terapi Obat Sesuai dengan Klasifikasi Hipertensi

HMOD=*hypertension-mediated organ* damage; PJK=penyakit jantung koroner; PKV=penyakit kardiovaskular; TD=tekanan darah.

*Inisiasi terapi obat pada kelompok pasien ini disarankan untuk dikonsultasikan kepada spesialis dengan target tatalaksana disesuaikan dengan panduan penyakit spesifik.

Diadaptasi dari *2018 ESC/ESH Hypertension Guidelines.*

Tabel 9. Kontraindikasi Pemberian Obat Antihipertensi

Obat	Kontraindikasi	
	Tidak dianjurkan	Relatif
Diuretik (tiazid/*thiazide- like*, misalnya chlorthalidone dan indapamide)	Gout	Sindrom metabolik Intoleransi glukosa Kehamilan Hiperkalsemia Hipokalsemia
Beta bloker	Asma Setiap blok sinoatrial atau atrioventrikular derajat tinggi Bradikardi (denyut jantung <60 kali per menit)	Sindrom metabolik Intoleransi glukosa Atlit dan individu yang aktif secara fisik
Calcium Channel Blocker (Dihidropiridin)		Takiaritmia Gagal jantung (HFrEF kelas III atau IV) Terdapat edema tungkai berat
Calcium Channel Blocker (Non-Dihidropiridin)	Setiap bloksinoatrial atau atrioventrikular derajat tinggi Gangguan ventrikel kiri berat (fraksi ejeksi ventrikel kiri<40%) Bradikardia (denyut jantung <60 kali per menit)	Konstipasi
ACE Inhibitor	Kehamilan Riwayat angioedema Hiperkalemia (kalium >5,5 meq/L) Stenosis arteri renalis bilateral	Perempuan usia subur tanpa kontrasepsi
Angiotensin Receptor Blocker	Kehamilan Hiperkalemia (kalium >5,5 meq/L) Stenosis arteri renalis bilateral	Perempuan usia subur tanpa kontrasepsi

ACE=*angiotensin converting enzyme*; HFrEF= *heart failure reduced ejection fraction.*

Dikutip dari *ESC/ESH 2018 Hypertension Guidelines.*

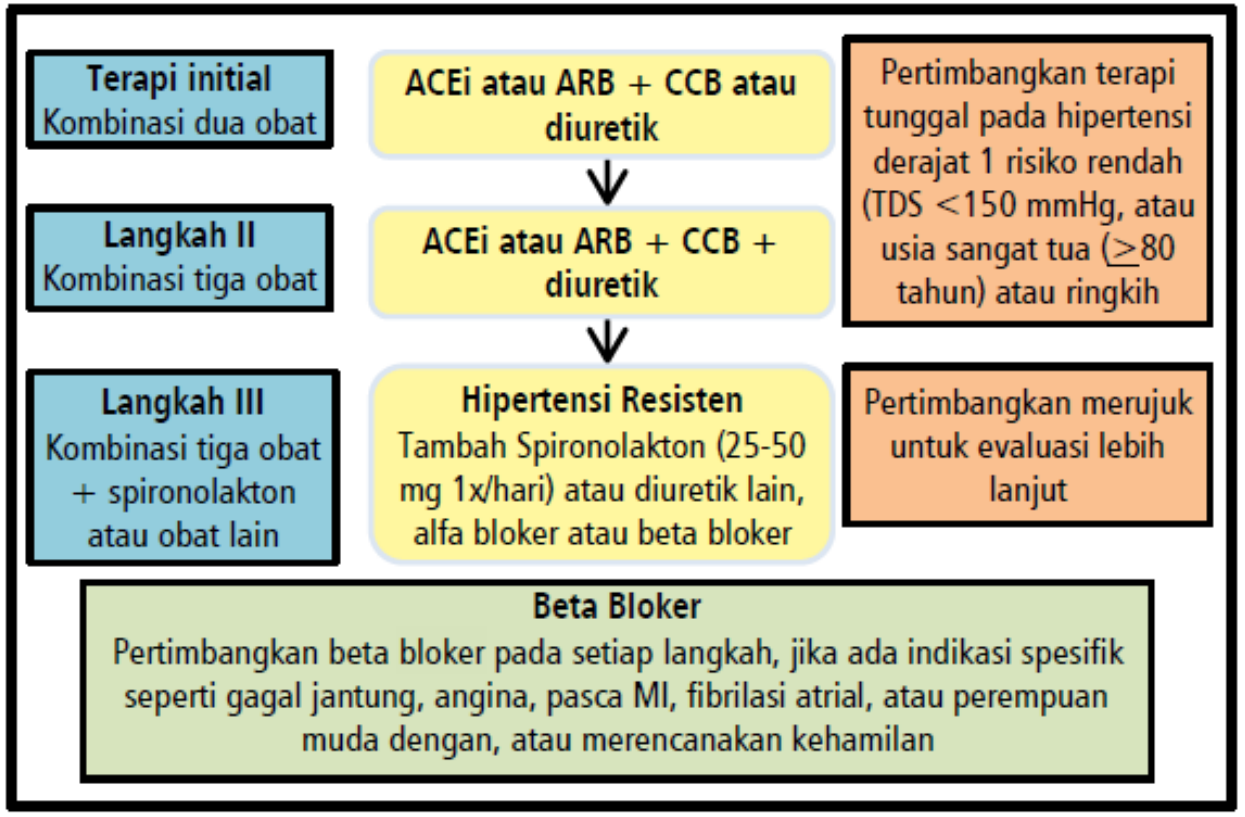
Tabel 10. Obat Antihipertensi Oral

Kelas	Obat	Dosis (mg/hari)	Frekuensi per hari
Obat-obat Lini Utama			
Tiazid atau *thiazide-type diuretics*	Hidroklorothiazid	25 – 50	1
	Indapamide	1,25 – 2,5	1
ACE inhibitor	Captopril	12,5 – 150	2 atau 3
	Enalapril	5 – 40	1 atau 2
	Lisinopril	10 – 40	1
	Perindopril	5 – 10	1
	Ramipril	2,5 – 10	1 atau 2
ARB	Candesartan	8 – 32	1
	Eprosartan	600	1
	Irbesartan	150 – 300	1
	Losartan	50 – 100	1 atau 2
	Olmesartan	20 – 40	1
	Telmisartan	20 – 80	1
	Valsartan	80 – 320	1
CCB - dihidropiridin	Amlodipin	2,5 – 10	1
	Felodipin	5 – 10	1
	Nifedipin OROS	30 – 90	1
	Lercanidipin	10 – 20	1
CCB – nondihidropiridin	Diltiazem SR	180 – 360	2
	Diltiazem CD	100 – 200	1
	Verapamil SR	120 – 480	1 atau 2
Obat-obat Lini Kedua			
Diuretik loop	Furosemid	20 – 80	2
	Torsemid	5 – 10	1
Diuretik hemat kalium	Amilorid	5 – 10	1 atau 2
	Triamteren	50 – 100	1 atau 2
Diuretik antagonis aldosteron	Eplerenon	50 – 100	1 atau 2
	Spironolakton	25 – 100	1
Beta bloker - kardioselektif	Atenolol	25 – 100	1 atau 2
	Bisoprolol	2,5 – 10	1
	Metoprolol tartrate	100 - 400	2
Beta bloker – kardioselektif dan vasodilator	Nebivolol	5 – 40	1
Beta bloker – non kardioselektif	Propanolol IR	160 – 480	2
	Propanolol LA	80 – 320	1
Beta bloker – kombinasi reseptor alfa dan beta	Carvedilol	12,5 – 50	2
Alfa-1 bloker	Doxazosin	1 – 8	1
	Prazosin	2 – 20	2 atau 3
	Terazosin	1 – 20	1 atau 2
Sentral alfa-1 agonis dan obat sentral lainnya	Metildopa	250 – 1000	2
	Klonidin	0,1 – 0,8	2
Direct vasodilator	Hidralazin	25 - 200	2 atau 3
	Minoxidil	5 – 100	1 – 3

ACE=*angiotensin-converting enzyme*; ARB=*angiotensin receptor blocker*; CCB=*calcium channel blocker*; OROS=*osmotic-controlled release oral delivery system*; IR=*immediate release*; LA=*long-acting*; SR=*sustained release*.

Dikutip dari ACC/AHA Guideline of Hypertension 2017.

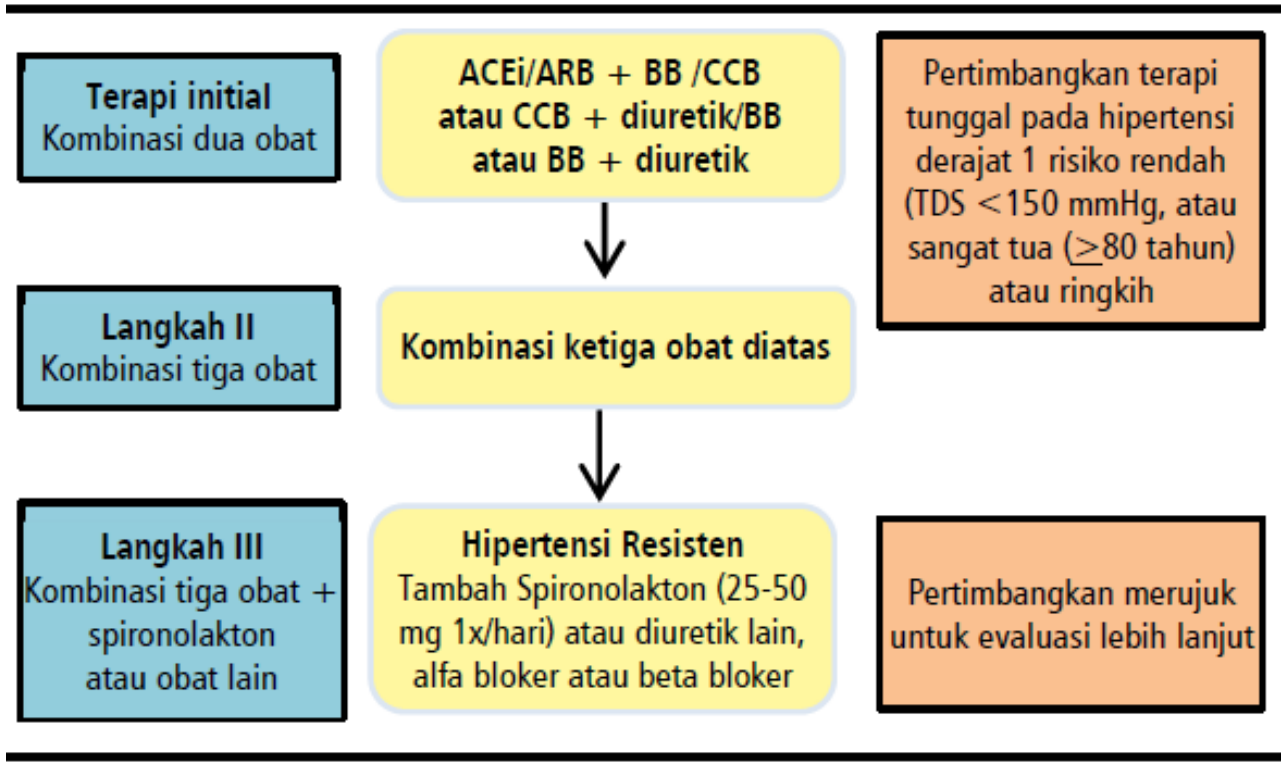
Algoritma tatalaksana hipertensi



Gambar 4. Strategi Penatalaksanaan Hipertensi Tanpa Komplikasi

ACEi = *angiotensin-converting enzyme* inhibitor; ARB = *angiotensin receptor blocker*; CCB = *calcium channel blocker*; MI = *myocardial infarction*.

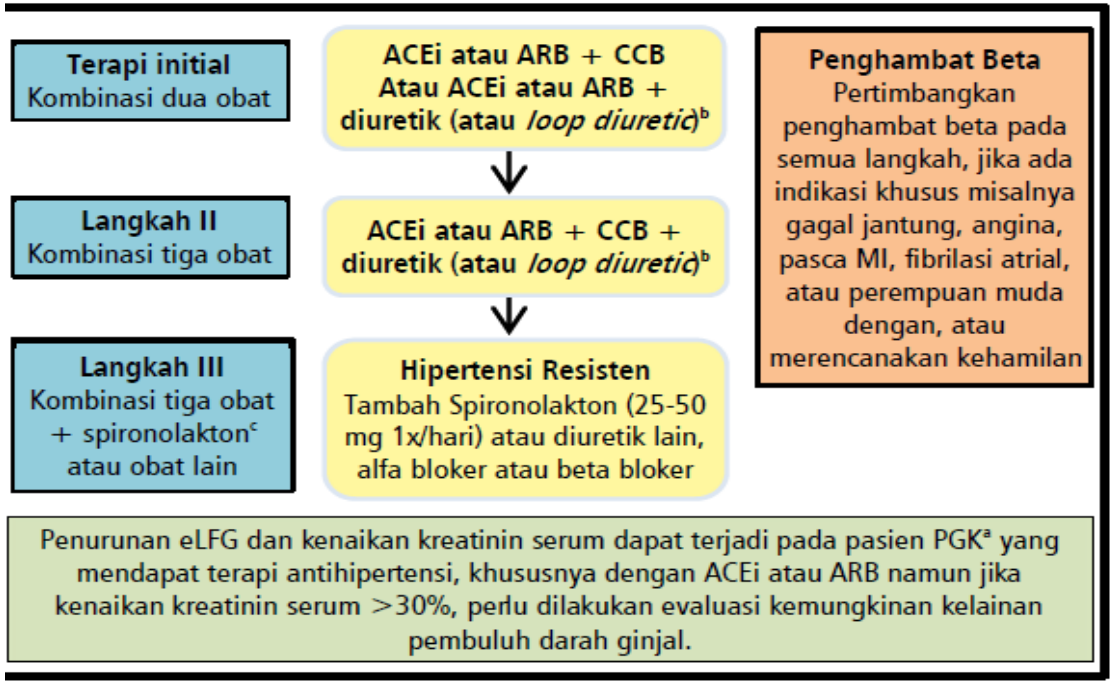
Algoritma tatalaksana hipertensi



Gambar 5. Strategi Pengobatan pada Hipertensi dan Penyakit Arteri Koroner

ACEi= *angiotensin-converting enzyme* inhibitor; ARB = *angiotensin receptor blocker*; CCB = *calcium channel blocker*; CVD = *cardiovascular disease*; MI = *myocardial infarction, BB=beta bloker*

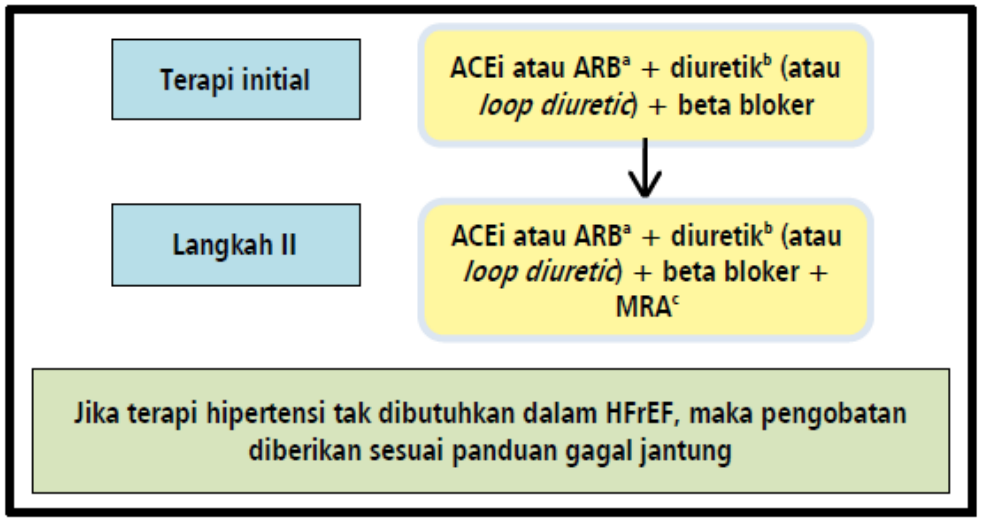
Algoritma tatalaksana hipertensi



Gambar 6. Strategi Pengobatan pada Hipertensi dan PGK

ACEi = *angiotensin-converting enzyme* inhibitor;
ARB = *angiotensin receptor blocker*; CCB = *calcium channel blocker*; MI = *myocardial infarction*.
[a]PGK didefinisikan sebagai eLFG <60 ml/menit/1,72 m^2 dengan atau tanpa proteinuria.
[b]Gunakan *loop diuretic* jika eLFG <30/ml/menit/1,72 m^2, karena thiazide/*thiazide-like diuretic* efektivitasnya lebih rendah/tidak efektif pada eLFG yang serendah ini.
[c]Peringatan: risiko hiperkalemia dengan spironolakton, terutama jika eLFG <45 ml/menit/1,72 m^2 atau nilai awal $K^+ \geq 4,5$ meq/L.

Algoritma tatalaksana hipertensi



Gambar 7. Strategi Pengobatan Hipertensi dan Gagal Jantung dengan Fraksi Ejeksi Menurun

Jangan menggunakan CCB non-dihidropiridin (yaitu verapamil atau diltiazem).

ACEi = *angiotensin-converting enzyme* inhibitor;

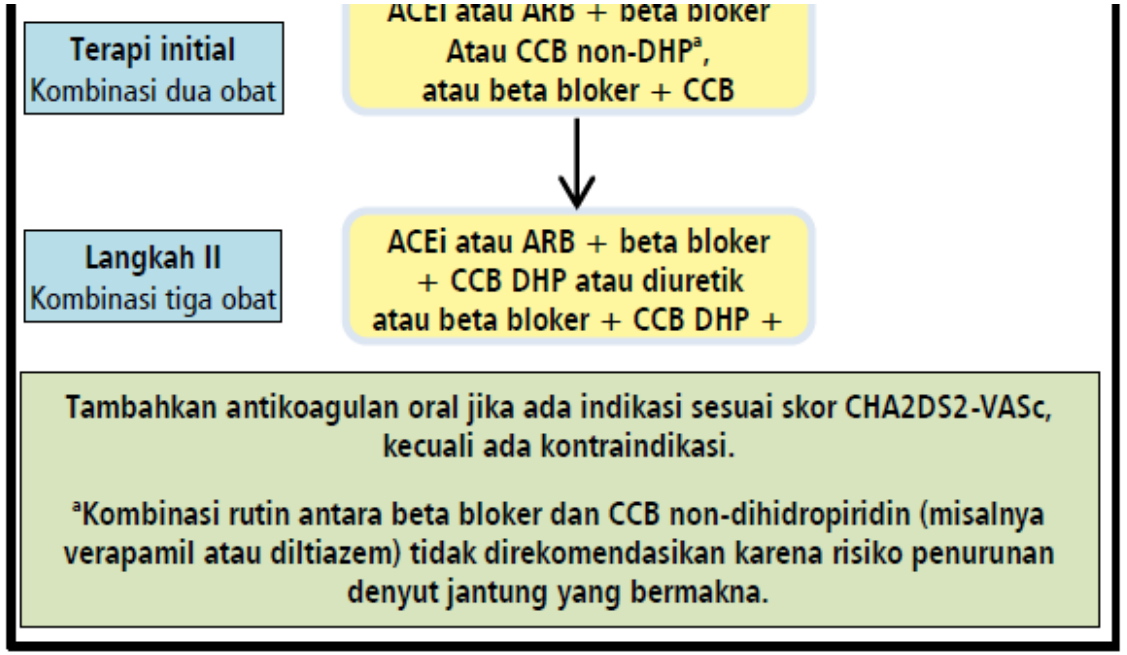
ARB = *angiotensin receptor blocker*; CCB = *calcium channel blocker*; MRA = *mineralocorticoid receptorantagonist*.

[a]Pertimbangkan *angiotensin receptor/neprilysin inhibitor* daripada ACEi atau ARB sesuai *ESC Heart Failure Guidelines*.

[b]Diuretik yang dimaksud adalah *thiazide/thiazide-like diuretic*. Pertimbangkan *loop diuretic* sebagai obat pilihan lain pada pasien edema.

[c]MRA (spironolakton atau eplerenon).

Algoritma tatalaksana hipertensi



Gambar 8. Strategi Pengobatan Hipertensi dan Fibrilasi Atrial

ACEi=*angiotensin-converting enzyme* inhibitor; ARB=*angiotensin receptor blocker*; CCB=*calcium channel blocker*; CHA2DS2-VASc=*Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled) – Vascular disease, Age 65 – 74 and Sex category (Female);* DHP = dihidropiridin.

Table 12. Hypertensive Emergencies Requiring Immediate BP Lowering

Clinical Presentation	Timeline and Target BP	First Line Treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP –20% to –25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP –20% to –25%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke and SBP >220 mm Hg or DBP >120 mm Hg	1 h, MAP –15%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke with indication for thrombolytic therapy and SBP >185 mm Hg or DBP >110 mm Hg	1 h, MAP –15%	Labetalol Nicardipine	Nitroprusside
Acute hemorrhagic stroke and SBP >180 mm Hg	Immediate, 130<SBP<180 mm Hg	Labetalol Nicardipine	Urapidil
Acute coronary event	Immediate, SBP <140 mm Hg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediate, SBP <140 mm Hg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic disease	Immediate, SBP <120 mm Hg and heart rate <60 bpm	Esmolol and nitroprusside or nitroglycerine or nicardipine	Labetalol or metoprolol
Eclampsia and severe preeclampsia/ HELLP	Immediate, SBP <160 mm Hg and DBP <105 mm Hg	Labetalol or nicardipine and magnesium sulphate	

Adapted from van den Born et al.[127]

Terima Kasih