Hypertension for medical student

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Outline

- Epidemiology
- Pathophysiology
- Definitions
- Causes & Risk factor
- Hypertension mediated organ damages
- BP measurement & assessment
- Treatment

Pre-test

- A 50-year-old man, routine check up, has office BP reading of 160/90 mmHg, physical examination is unremarkable as other laboratory investigation. His home blood pressure is 138/80 mmHg.
- What is the diagnosis?

- A) Essential Hypertension
- B) Blood pressure at risk
- C) Isolated systolic hypertension
- D) White coat hypertension
- E) Masked hypertension

Pre-test

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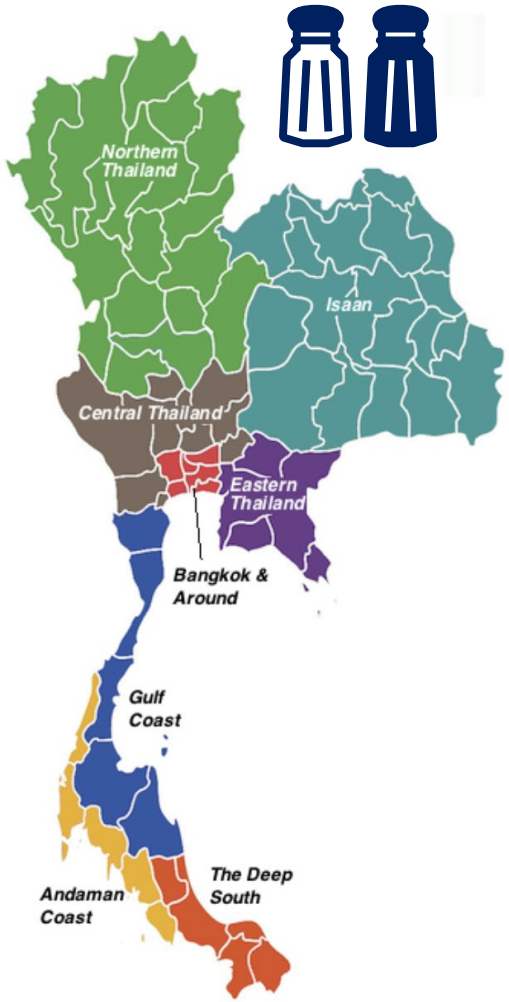
- A 70-year-old man, with history of recurrent hospitalization for heart failure for recent year. Current medications are enalapril, hydrochlorothiazide, amlodipine, all are in maximum dose. Blood pressure is 180/100 mmHg which had been controlled in 5 years of HT diagnosis.
- What is the most appropriate investigation?

- A) Plasma aldosterone, renin activity
- B) Renal doppler ultrasound
- C) Thyroid function test
- D) Polysomnography
- E) 24h-urine fractionated metanephrine

Epidemiology: prevalence of HT



- In Thailand (2024-2025 data)
  - Age ≥15 years, prevalence = 29.5%
  - 3.8% in 15-29 years
  - 76.8% in ≥80 years
  - North-East 33.8%, North 34.2%
  - Undiagnosed 47.8%
  - Well controlled 23.8%

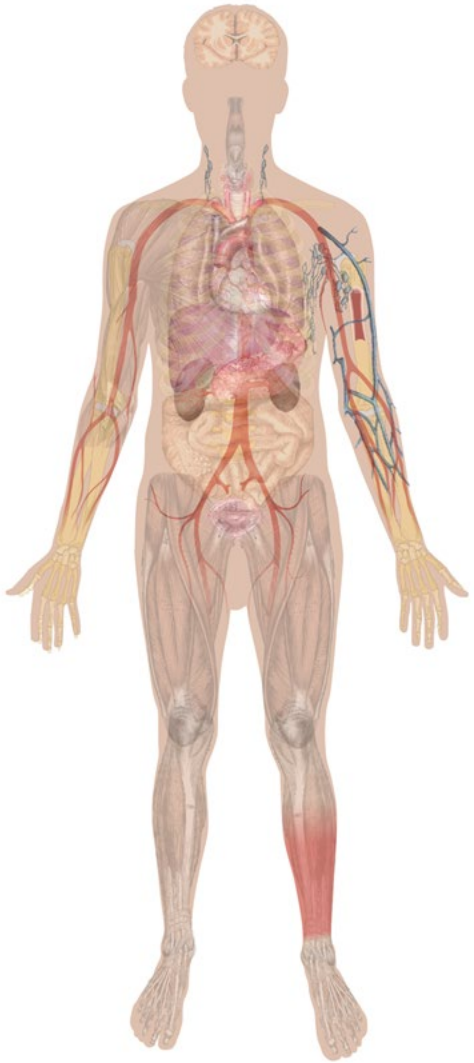
National Health Examination Survey 7th

Epidemiology: outcomes of HT

Every ΔSBP↑20 mmHg
CV death↑33-51%

Major causes of HF, AF, CAD, PAD

Second most common cause of CKD/ESKD



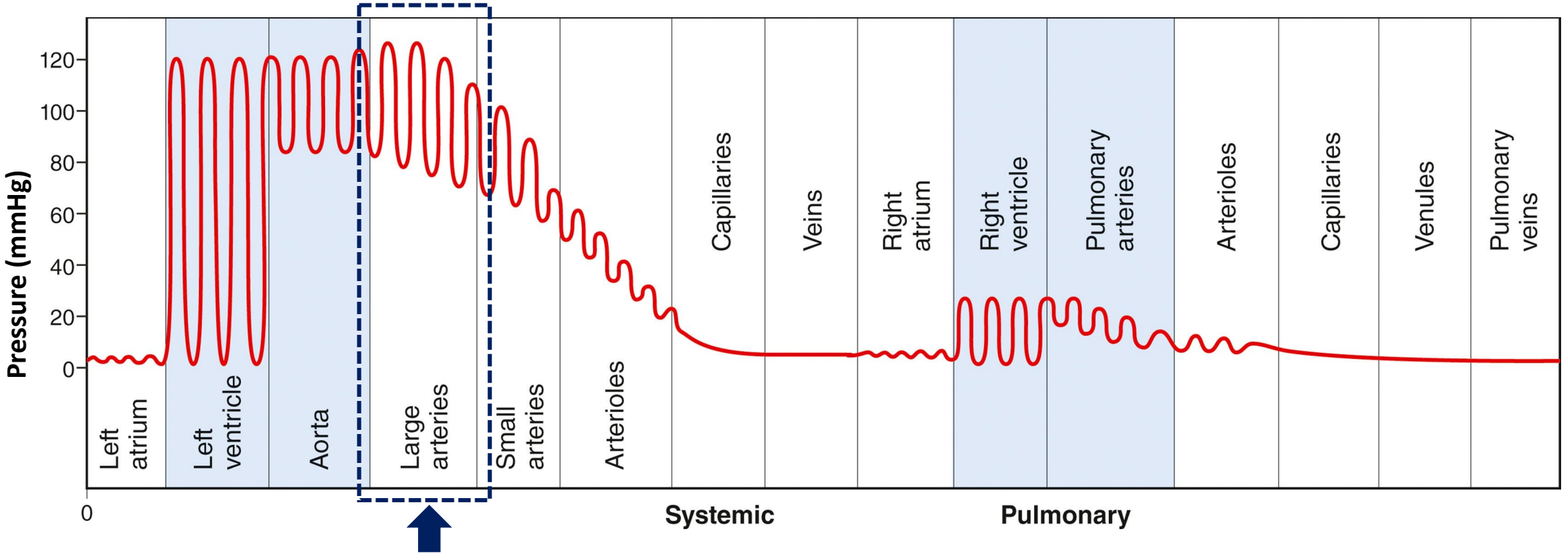
Dominant cause of stroke (77% in 1st diagnosis)

↑Incidence of dementia

Associated with all-cause death 14%

Mills KT, et al. Nat Rev Nephrol. 2020 Apr;16(4):223-237.
Brenner and Rector's the Kidney, 11th edition.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 12th edition.

Blood pressure in vascular beds

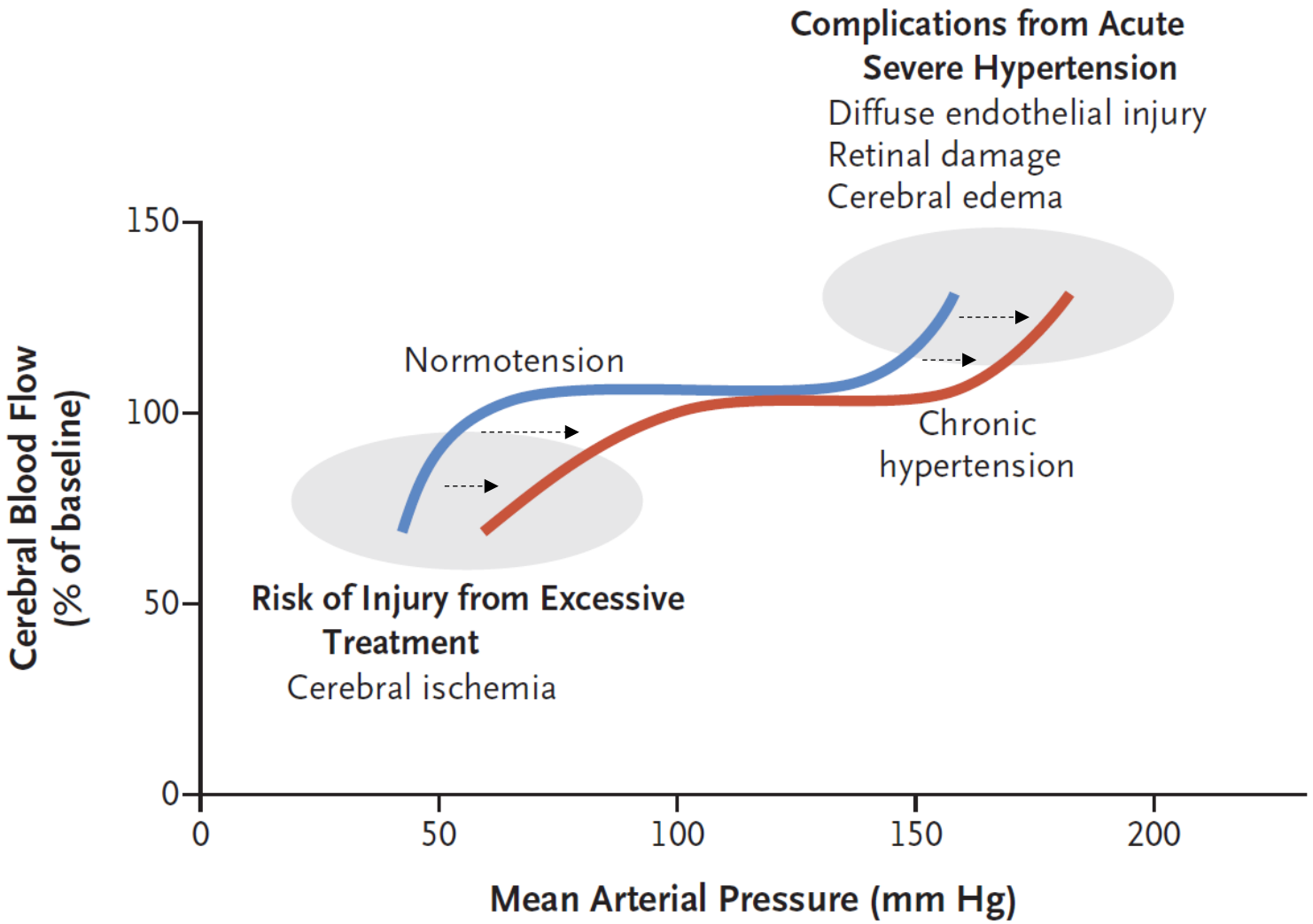


Focusing on *large* arteries pressure
- **Easily measured**
- **Determines organ perfusion**

If too low (shock) → ↓organ perfusion
If too high *(hypertension)* → *acute & chronic damage*

Guyton and Hall physiology textbook, 15th edition.

Autoregulation: local organ regulation



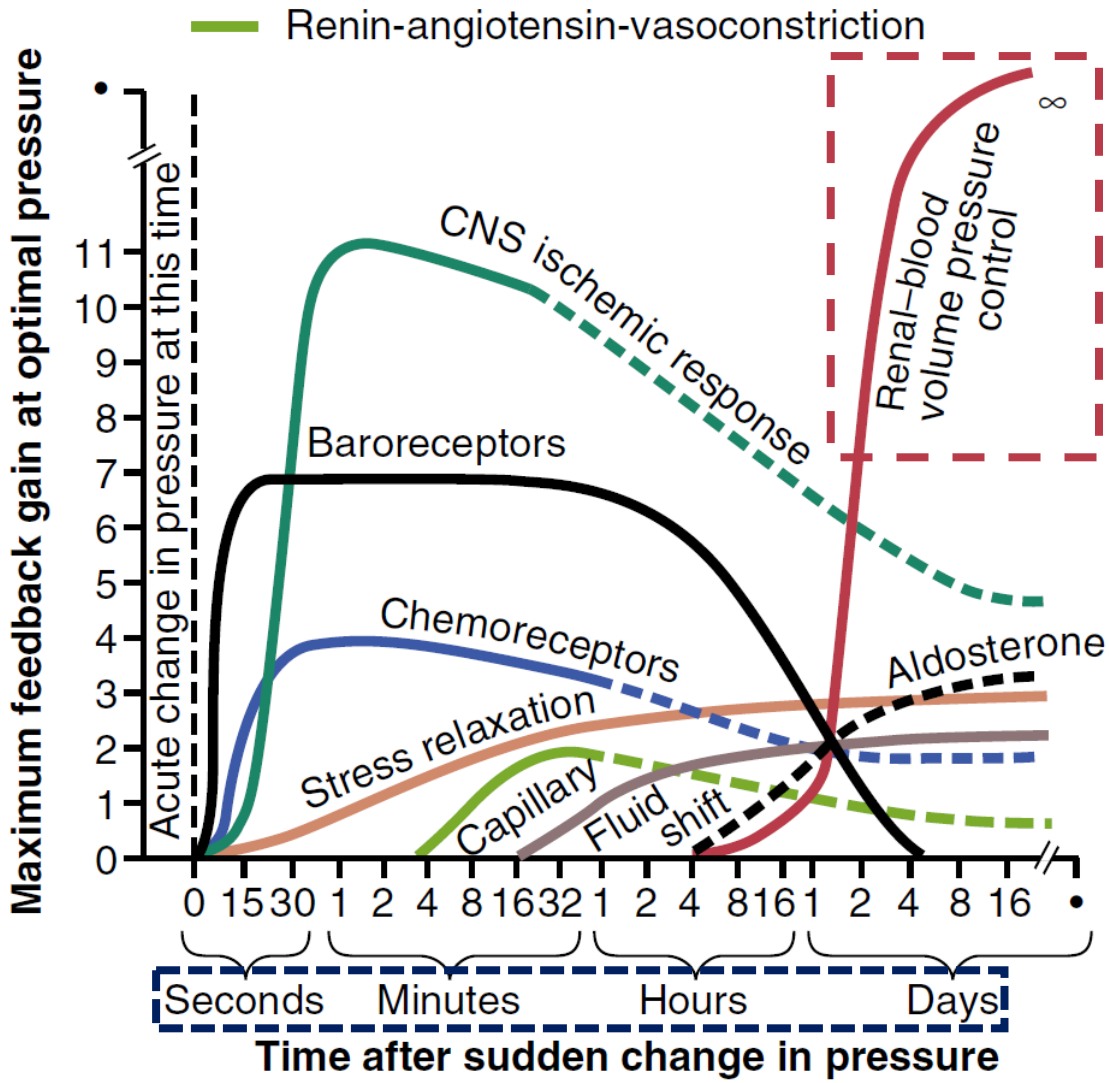
Autoregulation of blood flow

- Organs (i.e., **brain/kidney**) try to maintain **constant blood flow** (perfusion) despite wide range of systemic blood pressure
- **Local** vasodilation if ↓BP
- **Local** vasoconstriction if ↑BP

In ***chronic*** hypertension, graph shifts to the ***right*** to prevent organ injury from intermittent high BP

Peixoto AJ. N Engl J Med. 2019 Nov 7;381(19):1843-1852.

Phases of systemic BP regulation



In short-term (<1 d)

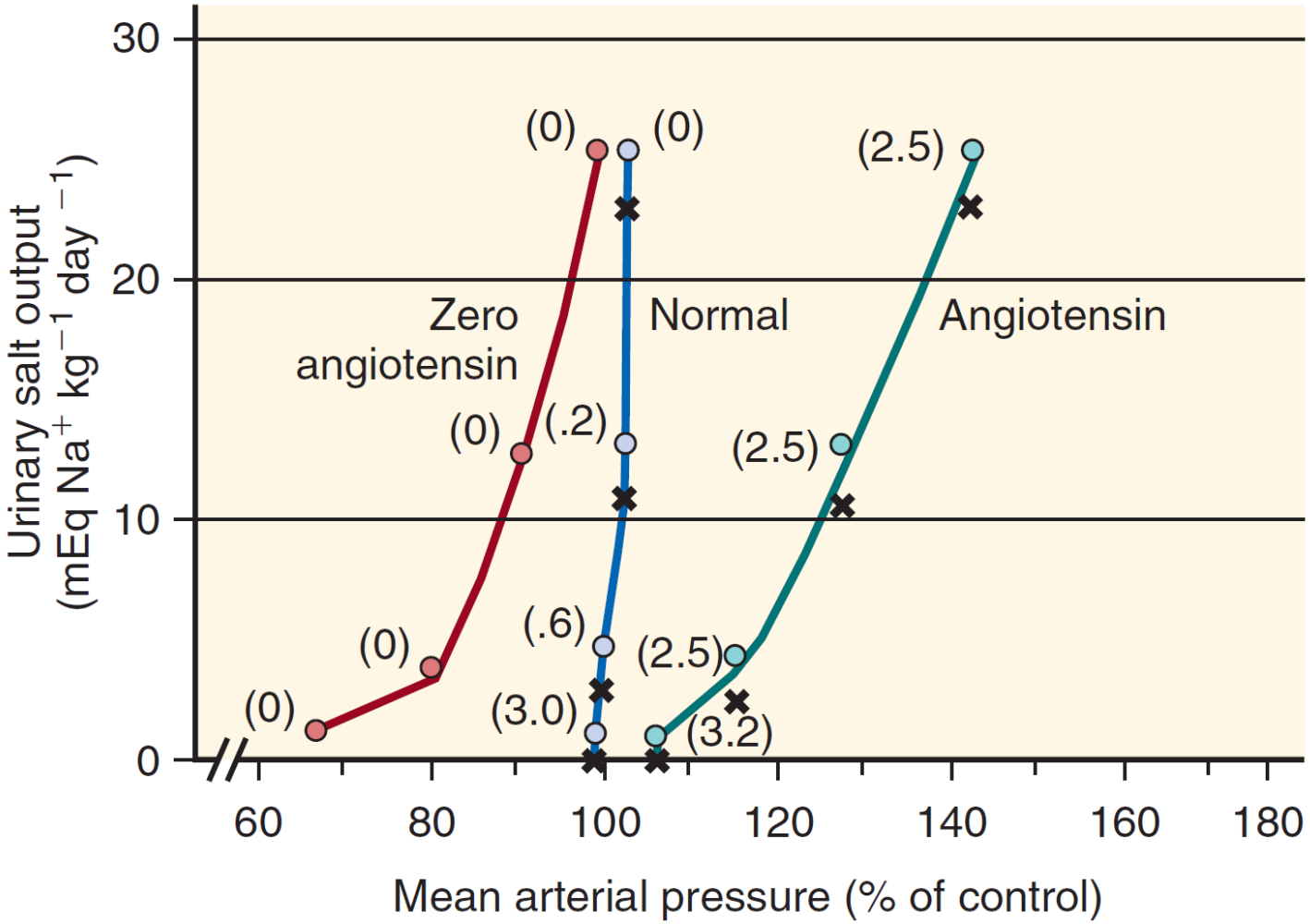
- Baroreceptors, autonomic (SNS & PNS), vasoconstrictors are dominant

In later phase (>1 d)

- **Renal** regulation becomes dominant in determining BP from **volume control** (via **total sodium** regulation mainly)

Guyton and Hall physiology textbook, 15th edition.

Concept of pressure natriuresis



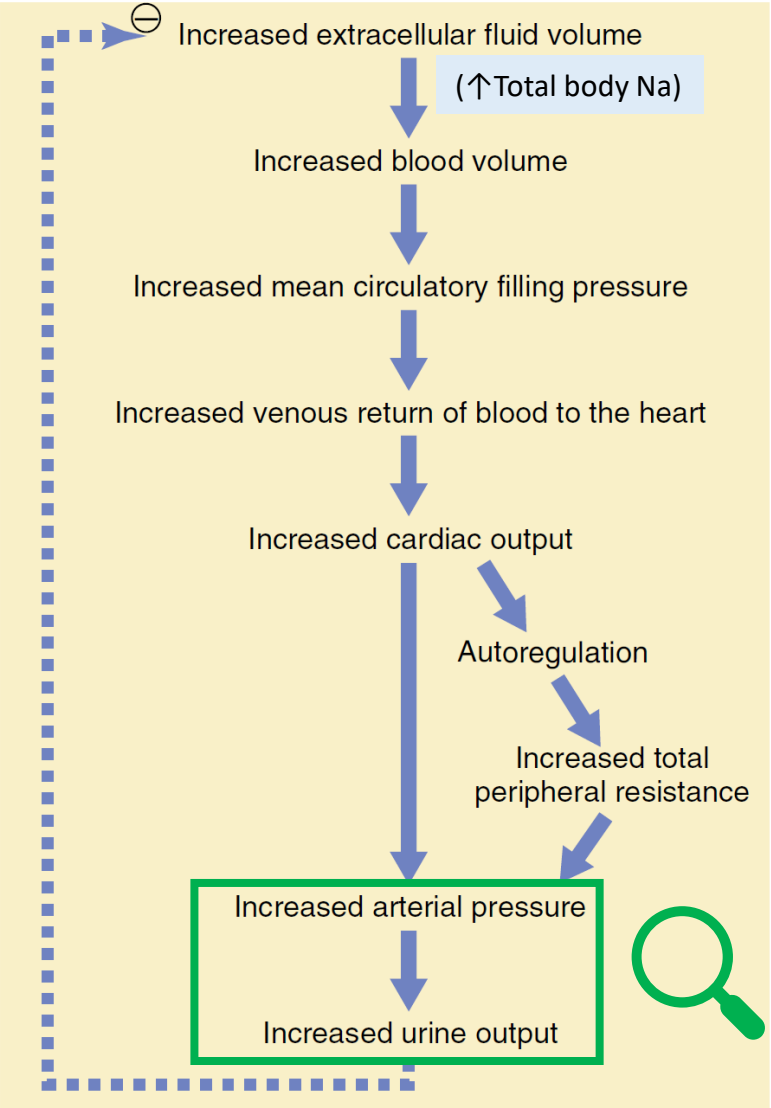
Change in BP in normal status (blue curve) is relatively **constant** despite increased salt intake (measured as urinary salt output)

Kidney can secrete amount of salt in response to increased BP (expanded extracellular volume) and **normalized BP** in long-term phase

To maintain abnormal elevated BP (hypertension), dysfunction of pressure natriuresis system is proposed as a main mechanism

Brenner and Rector's the Kidney, 11th edition.

Pressure natriuresis: simplified



Decreased renin and angiotensin

↓

Decreased renal retention of salt and water

↓

Return of extracellular volume almost to normal

↓

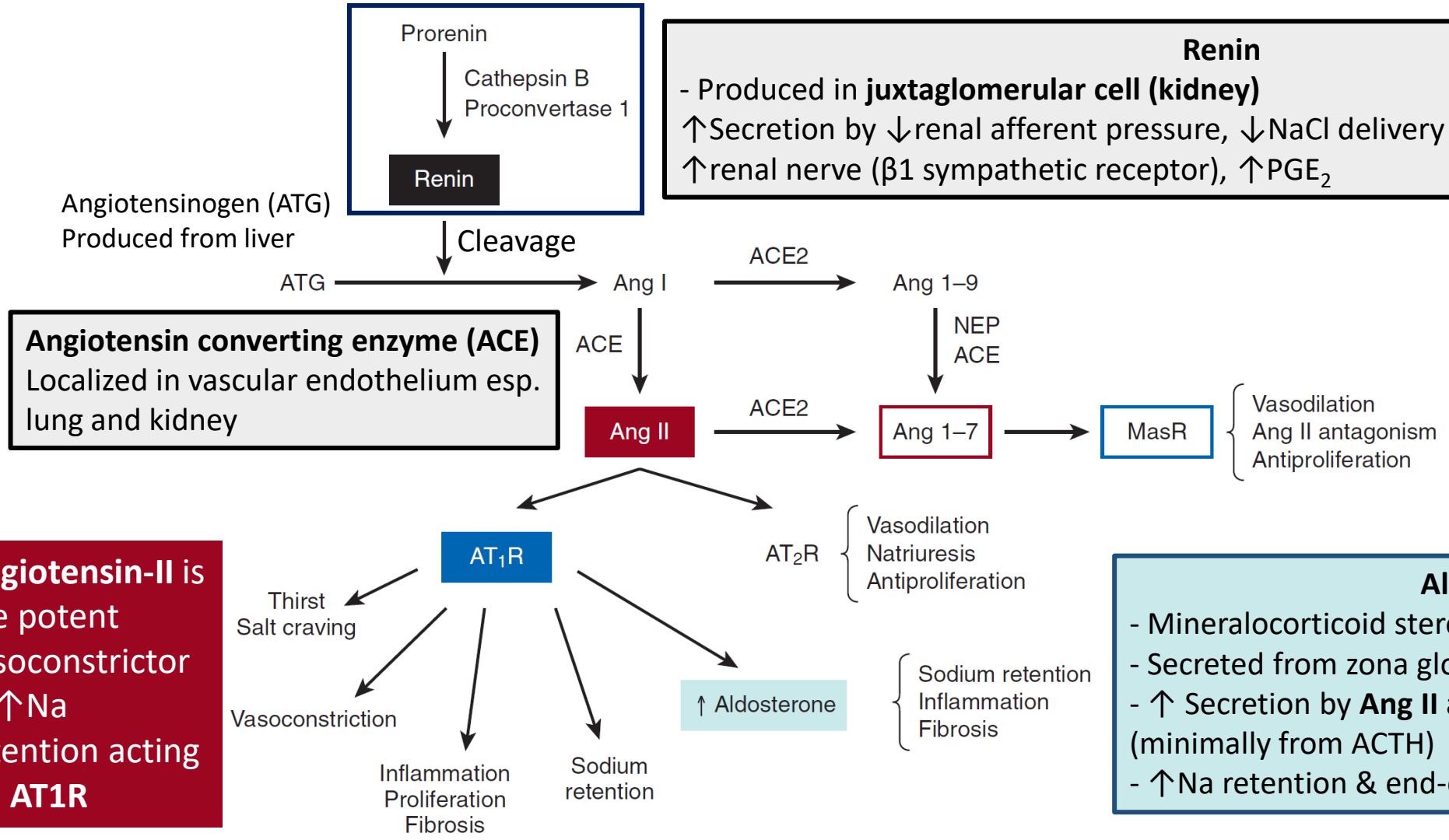
Return of arterial pressure almost to normal

↑Local **kidney** Nitric Oxide (NO) production & ATP
→ ↓Na reabsorption along tubules

↑Natriuretic peptides (from stretched baroreceptors)
→ ↓Na reabsorption along tubules

Guyton and Hall physiology textbook, 15th edition.
Brenner and Rector's the Kidney, 11th edition.

Renin-Angiotensin-Aldosterone



Renin

- Produced in **juxtaglomerular cell (kidney)**

↑Secretion by ↓renal afferent pressure, ↓NaCl delivery to macula densa, ↑renal nerve (β1 sympathetic receptor), ↑PGE_2

Angiotensin converting enzyme (ACE)
Localized in vascular endothelium esp. lung and kidney

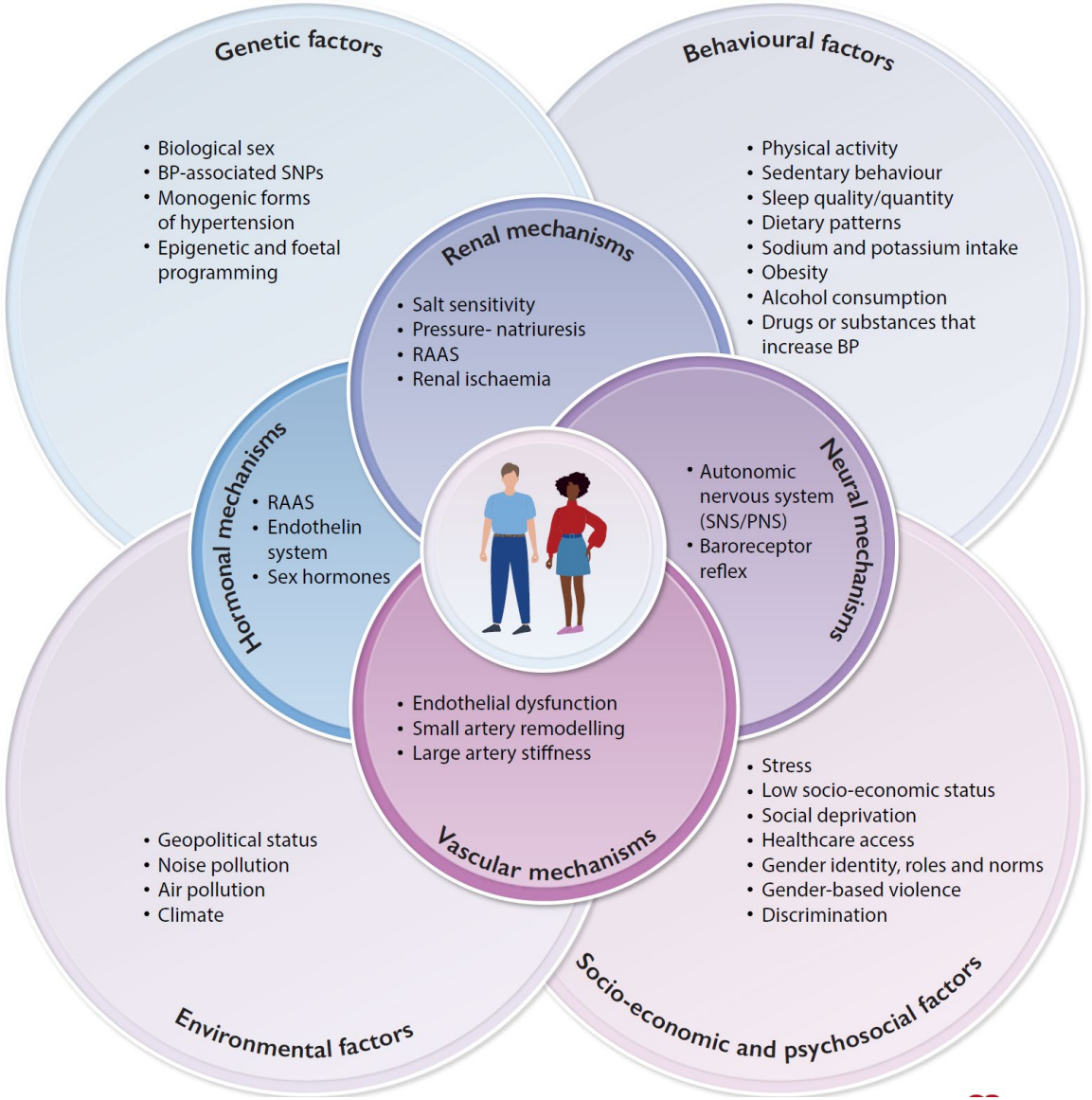
Angiotensin-II is the potent vasoconstrictor & ↑Na retention acting via **AT1R**

Aldosterone

- Mineralocorticoid steroidal hormone
- Secreted from zona glomerulosa of **adrenal cortex**
- ↑ Secretion by **Ang II** acting on AT1R, **hyperkalemia**, (minimally from ACTH)
- ↑Na retention & end-organ inflammation & fibrosis

Brenner and Rector's the Kidney, 11th edition.

Current hypertension mechanisms



Hypertension is a complex condition caused by **genetic** susceptibility and **acquired** conditions (environmental, life-style, socio-economic, aging, drugs/diet)

+

Abnormal body homeostasis (regulations)
- **Renal** (impaired pressure natriuresis)
- **Vascular** (stiffness, endothelial dysfunction)
- **Neuro-hormonal** (**SNS, RAAS**, Sex hormones, endothelin, NO)
- **Immune** (innate + adaptive)

2024 ESC Guidelines for the management of elevated blood pressure and hypertension.
Oparil S, et al. Nat Rev Dis Primers. 2018 Mar 22;4:18014.

What is hypertension?

- **Traditional** (& convenient) **criteria = Persistent office systemic arterial blood pressure *≥140/90 mmHg***
- However, data suggest risk (CV events) ↑ starting from BP ≥115/75 mmHg
- New concept, risk of elevated BP is a continuous data (not dichotomous) and should be based on patient own CV risk (emphasis on individualization)

Lewington S, et al. Lancet. 2002 Dec 14;360(9349):1903-13.
2024 Thai Guidelines on the Treatment of Hypertension.
2024 ESC Guidelines for the management of elevated blood pressure and hypertension.

Causes of hypertension

- Primary (essential) hypertension
- Secondary hypertension (hypertension with *specific* ± correctable cause)
- Genetic hypertension (identified mostly monogenic form of hypertension)
- Drug-induced hypertension

Patient can have >1 causes of hypertension combined

2024 Thai Guidelines on the Treatment of Hypertension.
2024 ESC Guidelines for the management of elevated blood pressure and hypertension.
2025 AHA Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults.

Genetic hypertension

- Hypertension has some genetic predisposing ≈ 30% but **most essential hypertension is "polygenic" and need other risk combined** (environmental, etc.)
- **Genetic hypertension** implies **monogenic** form of hypertension mostly from **abnormal renal sodium reabsorption** which is very rare in population
- Should be suspected in ***pediatrics*** **onset, strong family history & abnormal electrolytes**

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Monogenic hypertension

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Diseases (inheritance)	Mechanisms	Unique features & treatment
Hypertension with hypokalemia		
High PAC, low PRA (1˚ hyperaldosteronism)		
FH type 1 (AD); GRA	Chimeric CYP11B1/CYP11B2, ACTH can stimulate Ald	Hemorrhagic stroke, ↑ 18-hydroxycortisol and 18-oxocortisol, Tx and Dx with Dexa
Low PAC, low PRA		
Liddle syndrome (AD)	Mutation of β/γ subunit of PY motif of **ENaC** (↓ degradation of ENaC by ↓ binding of NEDD4 to PY motif)	No response to spironolactone, Tx: amiloride
AME (AR)	11β-HSD2 dysfunction, ↑ available cortisol to MR (reduced conversion of cortisol to cortisone at kidney)	Urine free Cortisol/cortisone > 5, growth retard, ***nephrocalcinosis & cyst***, CKD, Tx: KT, MRA, Dexa
CAH; 11β-hydroxylase def (AR)	CYP11B1 ↓: ↑deoxycorticosterone (DOC) & androgen	XY: precocious puberty, XX: virilization
CAH; 17α-hydroxylase def (AR)	CYP17A1 ↓: ↑ DOC, ↓ sex steroids (testos, proges)	XY: ambiguous/phenotypic female, XX: 1˚ amen
Geller syndrome (AD)	Overactivity of mineralocorticoid receptors (aggravated by progesterone)	Aggravated by pregnancy & spironolactone, Tx: amiloride
Hypertension with hyperkalemia		
Gordon syndrome (pseudo hypoaldosteronism type 2) (AD)	WNK1, WNK4, KLHL3, CUL3 mutation result in **↑NCC**	**Hyperkalemic**, normal gap metabolic acidosis, hypercalciuria

Brenner and Rector's The Kidney, 11th edition. Williams Textbook of Endocrinology, 15th Edition.

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Secondary hypertension

- Renal cause
  - Renal parenchyma & Renal vascular disease
- Cardiovascular cause
- Endocrine cause
- Miscellaneous
  - OSA (Maybe most common cause)
  - HT in pregnancy (gestational/pre-eclampsia)
  - Obesity (mostly associate with other concomitant risk)

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Williams Textbook of Endocrinology, 15th Edition.

Secondary hypertension

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Causes	Characteristics
Renal causes	
Renal parenchyma*	Edema, proteinuria, hematuria, azotemia (IgAN, LN, ADPKD, etc.)
Renal vascular disease	Abdominal bruit, flash pulmonary edema, intolerant to RASi (FMD, Atherosclerosis)
Cardiovascular cause	
Coarctation of aorta	Arm BP > leg BP 20mmHg (±interarm difference), radio-femoral pulse delay (Turner)
Endocrine causes	
Primary aldosteronism*	Hypokalemia, resistant hypertension, adrenal incidentaloma, AF, OSA
Thyroid dysfunction	Isolated systolic HT in hyperthyroid, isolated diastolic HT in hypothyroid
1˚ Hyperparathyroidism	Hypercalcemia, unexplained osteoporosis, renal stones
Acromegaly	Enlarge nose, lips, tongue, hands, jaws, prognathism, OSA
Cushing syndrome	Cushingoid facies, proximal muscle weakness, thin skin, purplish striae
Pheochromocytoma	Paroxysm (spells of palpitation, sweating, headache), Orthostatic hypotension
Miscellaneous	
Obstructive sleep apnea*	Loud snoring/apnea/gasping, daytime sleepiness, crowded oropharynx

*Common causes

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Secondary hypertension

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Causes	Investigation
Renal causes	
Renal parenchyma*	Kidney biopsy, Imaging (ADPKD), specific serology test
Renal vascular disease	Doppler ultrasonography of renal artery, CTA/MRA, Catheter angiography
Cardiovascular cause	
Coarctation of aorta	CXR, Echocardiography, CTA
Endocrine causes	
Primary aldosteronism*	Plasma aldosterone concentration & Plasma renin activity
Thyroid dysfunction	Thyroid function test, specific thyroid antibody
1˚ Hyperparathyroidism	Calcium, Phosphate, intact Parathyroid, Film bone
Acromegaly	Serum IGF-1, GH level after OGTT
Cushing syndrome	24h-urinary free cortisol, low-dose dexamethasone suppression test, salivary cortisol
Pheochromocytoma	24h-urine fractionated metanephrine, plasma-free metanephrine
Miscellaneous	
Obstructive sleep apnea*	Screening: STOP-BANG/Berlin questionnaire, Diagnosis: Polysomnography

*Common causes

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Williams Textbook of Endocrinology, 15th Edition.

Drug-induced (exacerbating) HT

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Drugs	Characteristics
NSAIDs*	Hyperkalemia, edema, hyponatremia, azotemia, ↓RASi efficacy
Acetaminophen	If taking >4 g/d
Contraceptive drugs*	Mostly from estrogen containing (>50 ug) pill
Corticosteroids	Low BP effect in low mineralocorticoids activity (dexamethasone, budesonide)
Performance enhancing drug	Testosterone, growth hormone, erythropoietin
Herbs	Licorice (>50 g in 2 weeks)
Sympathomimetics*	Weight loss drug, ADHD treatment, amphetamine, cocaine, ecstasy, decongestants
Immunosuppression	Calcineurin inhibitors (Cyclosporin A > Tacrolimus)
Anti-Cancer therapy	Anti-VEGF, TKIs, Gemcitabine
Anti-migraine	Ergots, Triptans
Anti-depressants/psychiatric	SSNRIs, MAOIs, lithium, carbamazepine, clozapine
Miscellaneous	Anti-retroviral drugs (PIs), caffeinated drinks

*Common drugs

2024 ESC Guidelines for the management of elevated blood pressure and hypertension.

Definitions

- **Hypertension**: persistent (standard) ***office*** BP **≥140/90** mmHg (adult), pediatrics (1-13y): ≥95th percentile + 12 mmHg or ≥130/80 mmHg
- **Out-of-office BP**
  - **Ambulatory BP monitoring (ABPM):** ≥24h period (q20-30 mins)
  - **Home blood pressure monitoring (HBPM):** patient self-BP measurement from validated machine
- **White coat effect, White coat hypertension:** office BP>out-of-office BP (white coat HT = met criteria for office BP but not out-of-office BP)
- **Masked hypertension:** normal criteria for office BP but met criteria for "out-of-office" BP
- **Orthostatic hypotension:** BP after supine 5 mins then stand up then BP at 1 and 3 mins if BP ↓≥20/10 mmHg (stand up from sitting is acceptable)

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Hypertension mediated organ damages

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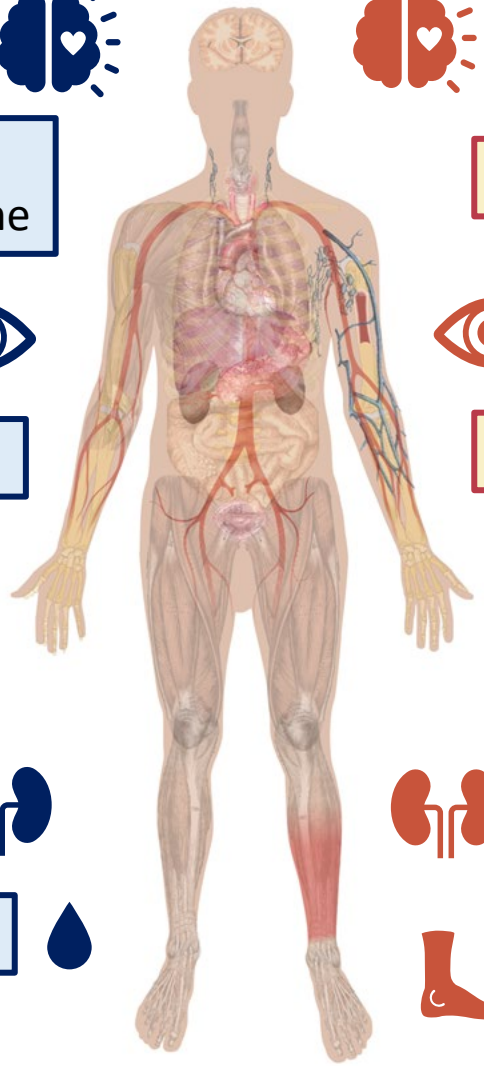
Acute (hypertensive emergency)

- Acute Stroke (ischemic/hemorrhage)
- Hypertensive encephalopathy
  Posterior Reversible Encephalopathy Syndrome
- Hypertensive retinopathy gr III, IV
- Acute heart failure/Flash pulmonary edema
- Acute coronary syndrome
- Aortic dissection
- AKI (Malignant HT induced TMA)
- Microangiopathic hemolytic anemia (MAHA)



Chronic

- Dementia, vascular dementia
- Hypertensive retinopathy gr I, II
- Carotid stenosis
- Left ventricular hypertrophy
- Diastolic heart failure
- Chronic coronary syndrome
- Hypertensive nephrosclerosis (CKD)
- Peripheral arterial disease

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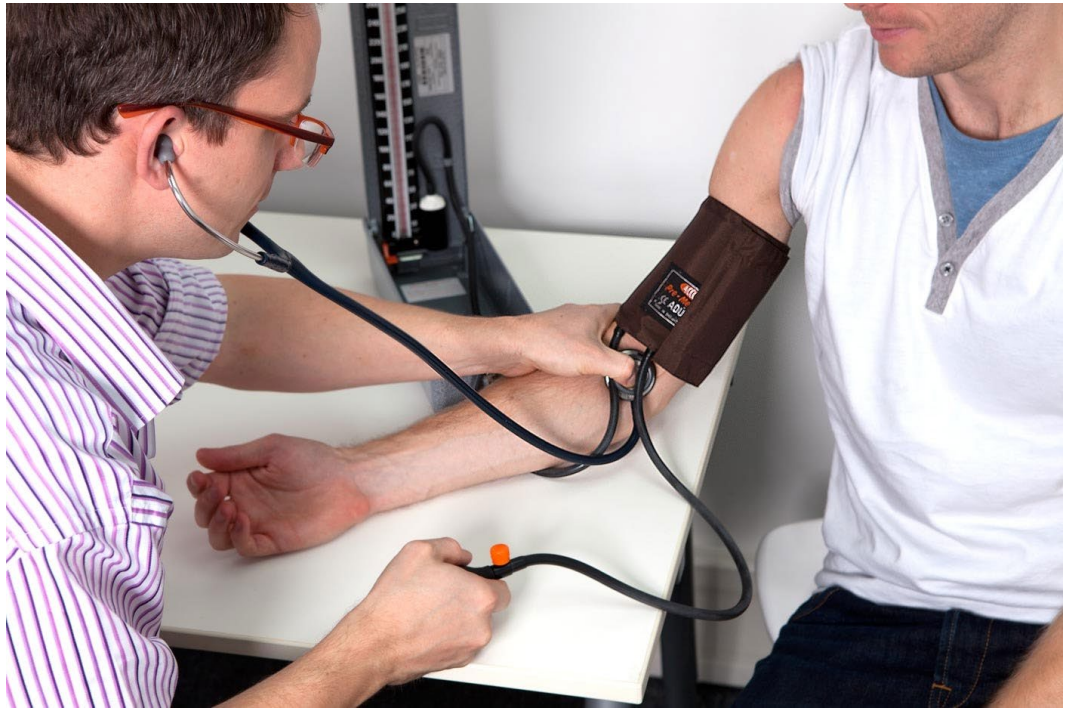
Blood pressure measurements (office)

- ***Standard*** **office blood pressure**
  - Recommended method to **lessen white coat effect**
  - Auscultatory (mercury/aneroid) vs Automated (oscillometric)
- **Unattended standard office blood pressure**
  - Automated BP measurement ***without physician*** in the same room (< standard office BP ≈ 5-10 mmHg approximates daytime ambulatory BP)
  - Inconvenient in usual practice (only in clinical trial)

In nowadays, *automated* standard office blood pressure is favored but should be validated + avoid in patient with atrial fibrillation

Ott C, Schmieder RE. Kidney Int. 2022 Jan;101(1):36-46.
2024 Thai Guidelines on the Treatment of Hypertension.

Standard measurement



Auscultatory (manual) BP measurement (Mercury sphygmomanometer)

Preparation

- Patient avoid coffee/alcohol/smoking >30 mins
- Empty bladder
- Quiet environment, no talking (physician & patient)
- Rest (sit) for 5 minutes, back & arm support
- Both feet flat on the ground, avoid leg crossed
- Cuff at the same level of patient heart
- No cloth covered between cuff (avoid rolling up sleeves)
- Avoid muscle tensing/hand clenching

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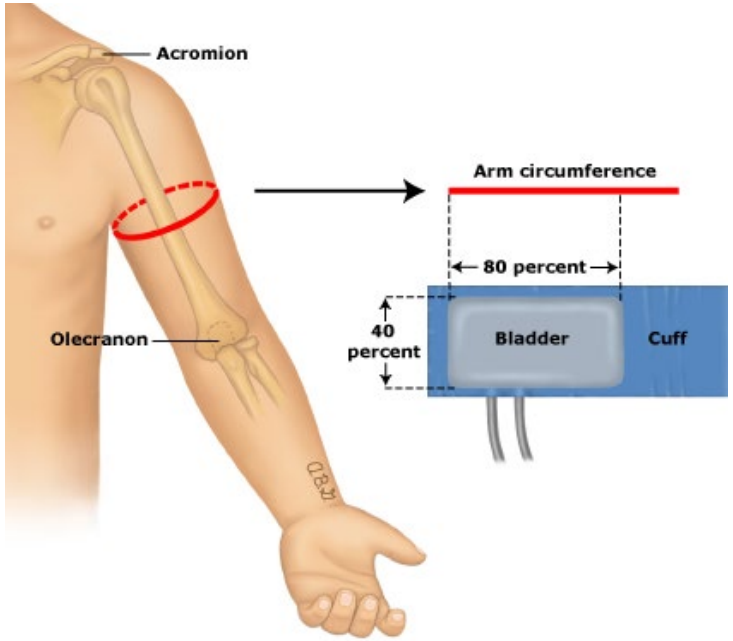
Standard measurement



ARM CIRCUMFERENCE (CM)	USUAL CUFF SIZE
22–26	Small adult
27–34	Adult
35–44	Large adult
45–52	Adult thigh

If cuff too small = falsely elevated BP and vice versa

Cuff size & place

- Bladder length is 80% of arm circumference & 40% width of arm circumference
- Place around upper arm (2 cm lower border above cubital fossa)
- Avoid same side of AV access & history of lymphedema post surgery
- First time measuring: both arms and choose the **higher one** for further measurement
- If interarm difference >20/10 mmHg, highly suspect of vasculopathy
- Remove the air in bladder (flatten) before blowing cuff

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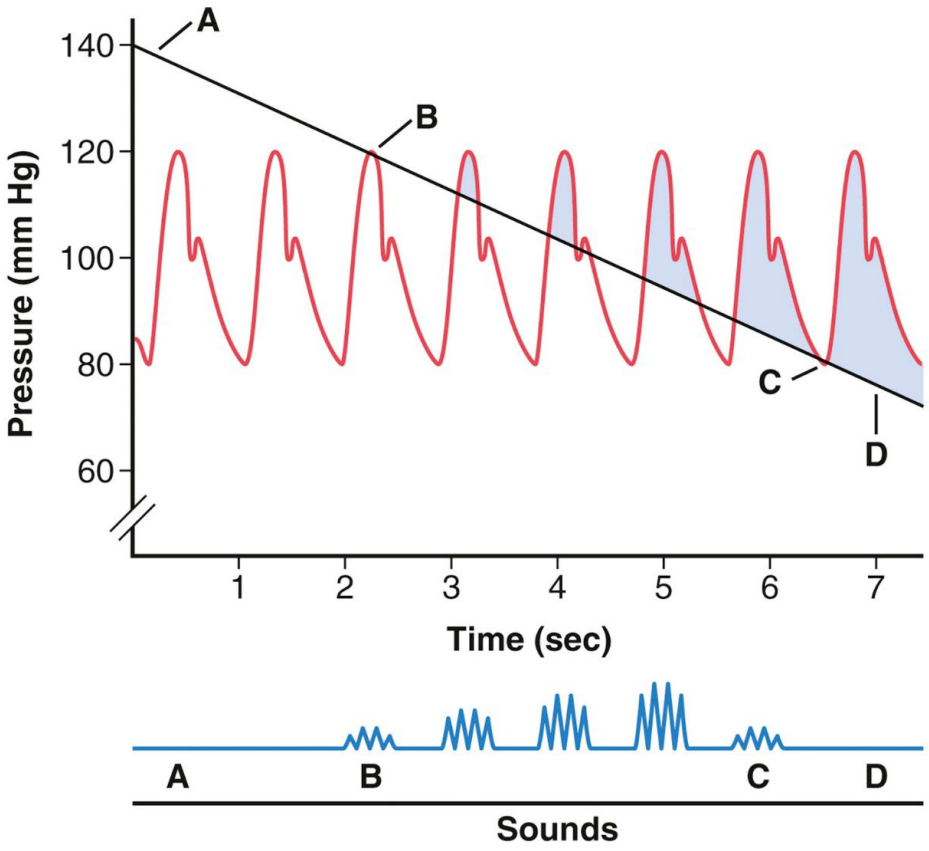
Standard measurement



Korotkoff 1 Korotkoff 5

Measurement steps

- Blow the cuff while palpating the brachial pulse for approximate the systolic BP (BP when pulse disappeared) then wait for 1 minute
- Place stethoscope on brachial artery (not between the cuff and skin)
- Blow the cuff higher 20 mmHg than the approximated BP
- Then slowly deflate the cuff 2-3 mmHg/sec
- The first sound appearing = Korotkoff 1 = SBP
- Deflating until the sound disappear = Korotkoff 5 = Diastolic blood pressure
- Repeat the entire procedure next 1 minute
- At least 3 times use the average of the last 2 only if the BP difference is <10 mmHg

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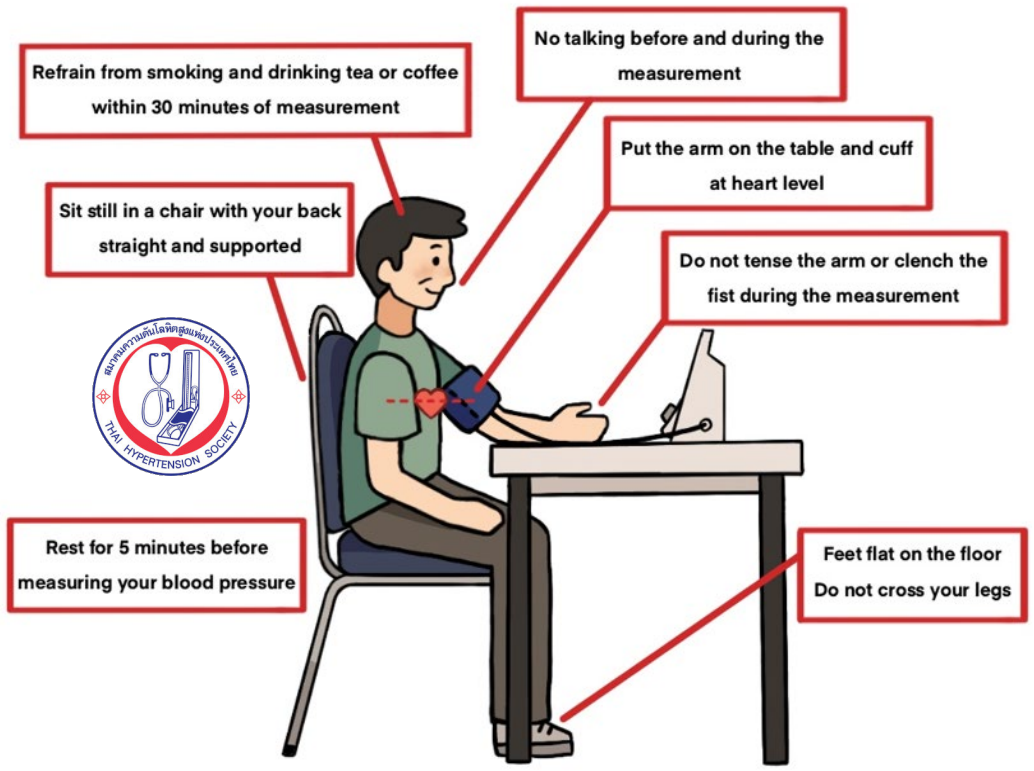
Standard measurement (automated)



Automated method

- Validated upper arm automated device
- The oscillometric method will measure **mean arterial pressure** but the machine will **calculate SBP & DBP**
- Cuff selection as auscultatory method
- Same patient preparation
- If atrial fibrillation (irregular rhythm), auscultatory method is preferred

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Out-of-office BP monitoring

Home BP

- **Validated** BP device (www.validatebp.org)
- **Morning** (prior to breakfast and medicine) 2 measures and **bedtime** 2 measures for 7 days before doctor visit, use the average BP
- Same method as office BP

Ambulatory BP

- Device **automatically** measured q 20 min during **daytime** and 30 min during **night-time** for ≥24h
- Can detect night-time BP and dipping status
- Gold standard but not widely available

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When to consider “out-of-office BP”

- **Currently, should always be done initially to confirm hypertension** (office BP prone to error from white coat effect and correlate better with outcomes)
- Diagnosis of white coat HT & masked HT
- Improve patient adherence & participance (Home BP)
- Night-time reading (Ambulatory BP)
- Detect dipping status (poor outcome in non-dipper)

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Criteria of various BP measurement

	Office BP (mmHg)[a]	Home BP (mmHg)	Daytime ABPM (mmHg)	24 h ABPM (mmHg)	Night-time ABPM (mmHg)
Reference					
Non-elevated BP	<120/70	<120/70	<120/70	<115/65	<110/60
Elevated BP	120/70–<140/90	120/70–<135/85	120/70–<135/85	115/65–<130/80	110/60–<120/70
Hypertension	≥140/90	≥135/85	≥135/85	≥130/80	≥120/70

For hypertension diagnosis comparing with office BP,
HBPM ↓*5 mmHg*, ABPM ↓*10 mmHg* due to elimination of white coat effect

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Criteria & severity of hypertension

Diagnosis	Cut off BP (mmHg)	
	SBP	DBP
Optimal	<120	<80
Normal	120-129	<80
BP at risk	130-139	80-89
Hypertension grade 1	140-159	90-99
Hypertension grade 2	160-179	100-109
Hypertension grade 3	≥180	≥110
Isolated systolic hypertension	≥140	<90
Isolated diastolic hypertension	<140	≥90

Office BP **measurement is the reference for severity grading**

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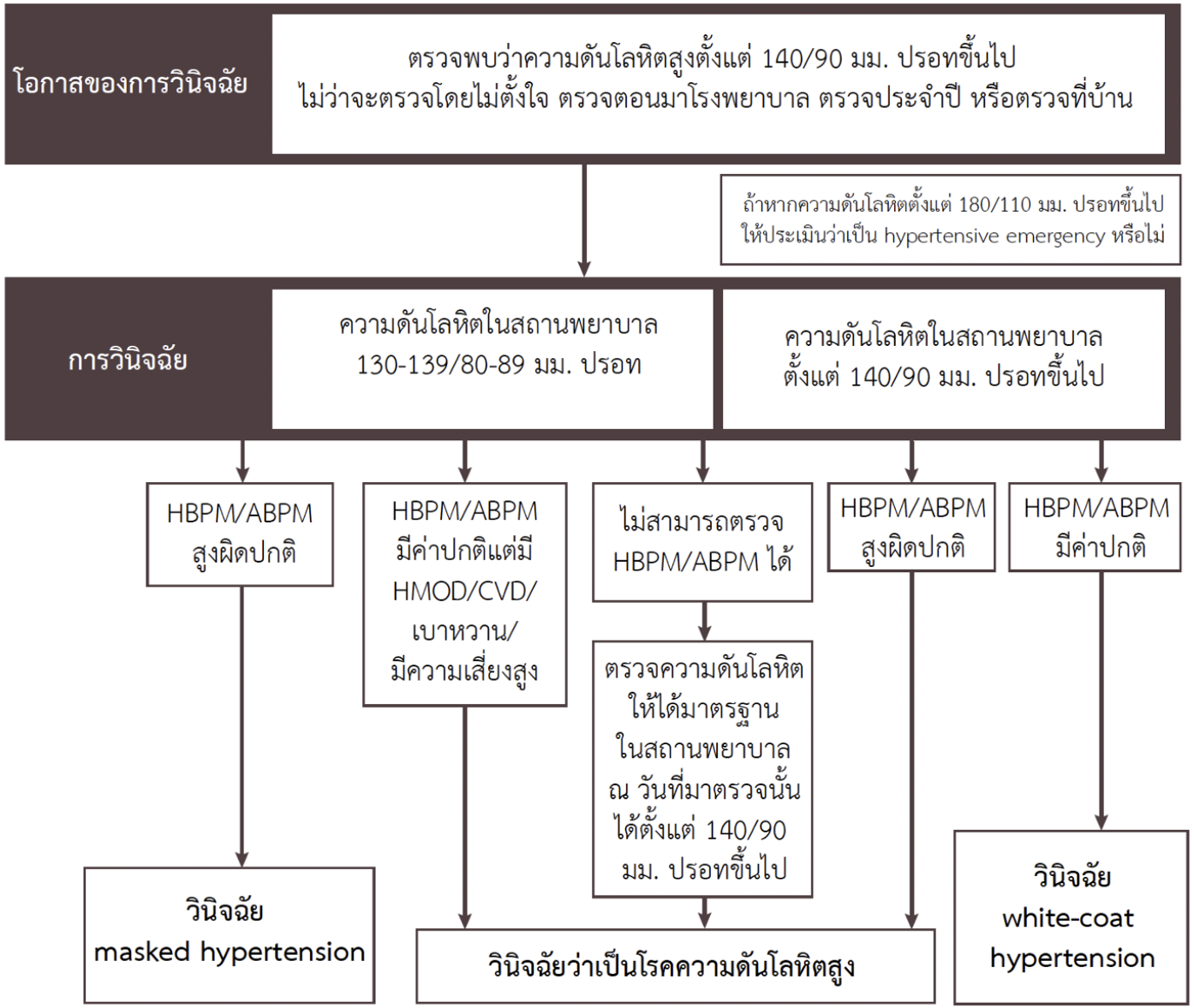
Diagnostic approach for hypertension



1) If grade 3 hypertension = diagnosis
2) If BP at risk (office) check HMOD, CVD, T2D, 10-year CV risk >10% = diagnosis
3) If office BP ≥130/80 mmHg and not compatible with 1,2 then confirm with “out-of-office BP” if not available then repeat standard office BP
4) If discordance of “office” and “out-of-office” BP use out-of-office BP

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Principle of hypertension assessment*

1) Confirmation of BP for correct diagnosis
2) Clinical features of specific cause of HT (2˚HT)
3) Identify comorbid (↑CV risk or affect treatment)
4) Patient preferences & life-style factor
5) Evaluation of hypertension mediated organ damage
6) Shared decision making of treatment plan

*Assessment including comprehensive history taking, physical examination, and investigation

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Clinical assessment: history

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- **Age of onset, previous measurement, treatment, and control**
- **Clues of 2˚HT (**thyroid dysfunction, cramp/proximal muscle weakness (hypokalemia), tinnitus (FMD), paroxysm, etc.)
- **HMODs: ASCVD symptoms** (stroke, HF, CAD, PAD)**, CKD** (previous renal function, nocturia, edema, etc.), **AF** (syncope/palpitation)
- **Family history**, **medication** (current drug & drug allergy)
- **Comorbid**, **personal history** (life-style; alcohol, smoking, recreational drug, salt intake, physical activity, obstetric history, LMP if reproductive age), **past-history**
- **Health coverage, occupation, domicile**

Brenner and Rector's the Kidney, 11th edition.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 12th edition.

Clinical assessment: physical examination

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- **Standard BP measurement** (if initial evaluation include both arms and legs)**, BP supine + upright** (look for orthostatic hypotension in initial evaluation or history of syncope upon standing)**, pulse** (regularity, look for atrial fibrillation)
- **Weight & height** (BMI) + **waist circumference** (metabolic syndrome/obesity)
- **Clues of 2˚ HT** (thyroid gland enlargement, signs of hypo/hyperthyroid, neck circumference (OSA), cushingoid appearance, abdominal bruit (renal artery stenosis), proximal muscle weakness (hypokalemia), bimanual palpation (ADPKD))

Brenner and Rector's the Kidney, 11th edition.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 12th edition.

Clinical assessment: physical examination

- **HMODs: fundoscopy**, **carotid bruit**, **signs of HF** (elevated JVP, crepitation, edema, S3/S4 gallop), **LV heaving**/Apical displacement, **ABI** (ankle-brachial index; ↓ if PAD), focal **neurological deficit** (previous stroke)
- **Comorbid:** acanthosis nigricans (insulin resistance), nutrition status (malnutrition), frailty (elderly patient), reactive airway disease (contra-indication for non-selective beta blockers)

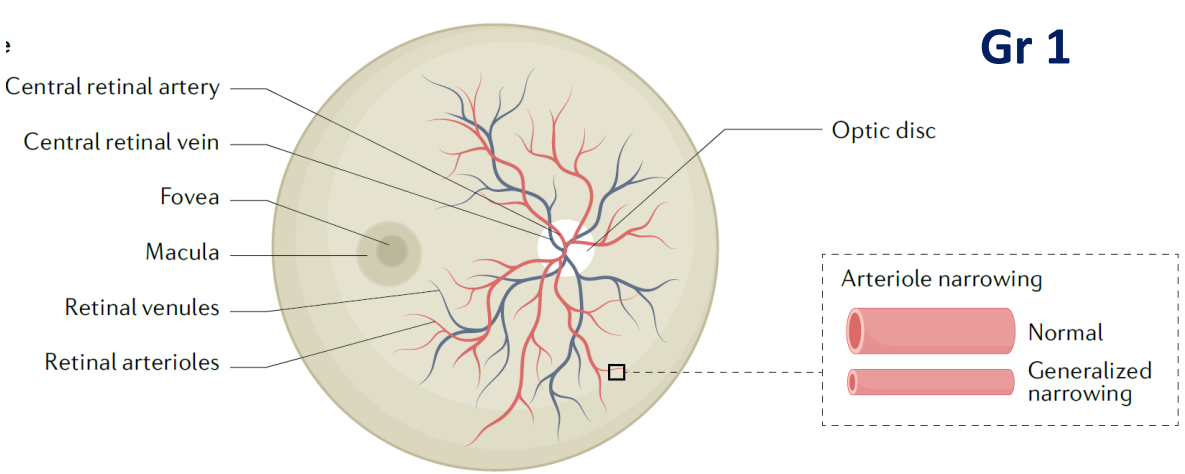
Brenner and Rector's the Kidney, 11th edition.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 12th edition.

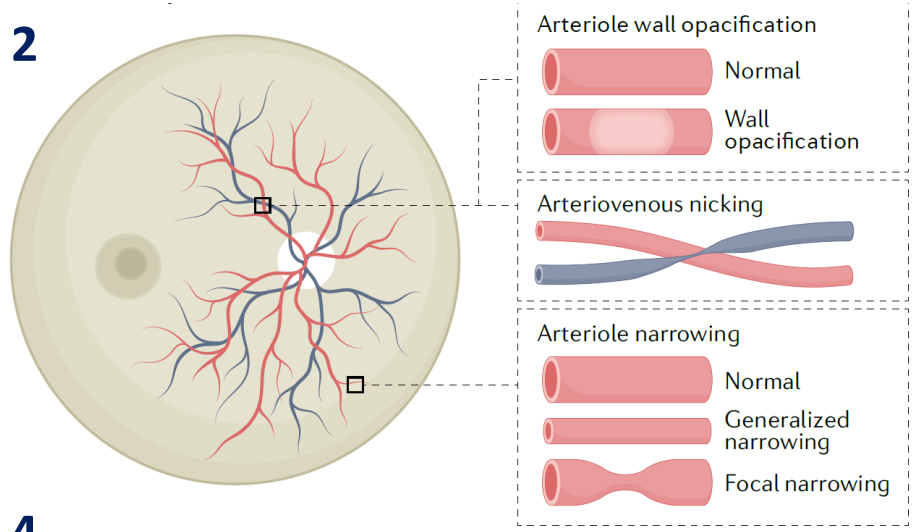
Hypertensive retinopathy

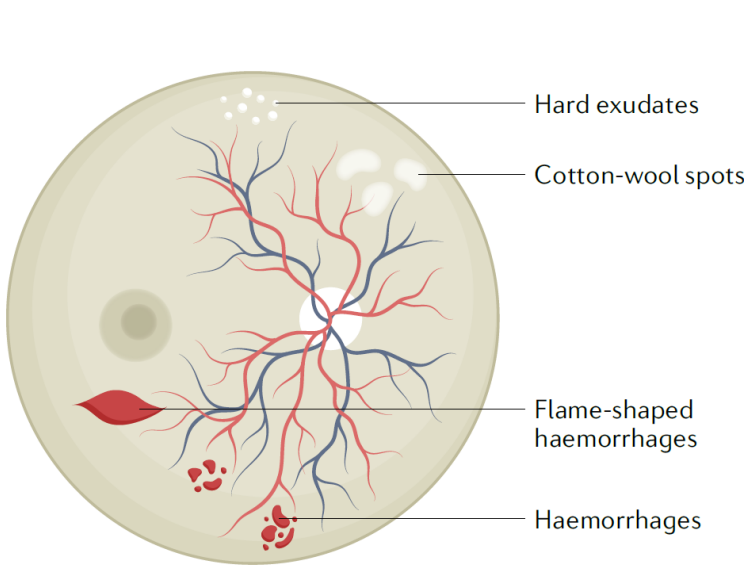
Keith–Wagener–Baker system (1939)[121]		Mitchell-Wong system (2004)[155]		Key pathophysiological changes and signs	
Grade	**Clinical features**	**Grade**	**Clinical features**		
1	Mild to moderate narrowing or sclerosis of the arterioles	Mild	Generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacification of the arteriolar wall (silver or copper wiring), or a combination of these signs	Retinal vascular re-modelling and retinal arteriolar wall signs	Chronic
2	Moderate to marked narrowing of the arterioles, local and/or generalized narrowing of arterioles, exaggeration of the light reflex, arteriovenous crossing changes or nicking				
3	Retinal arteriolar narrowing and focal constriction, retinal oedema, cotton-wool patches, retinal haemorrhages, hard exudates	Moderate	Signs of mild retinopathy plus retinal haemorrhages (blot, dot or flame-shaped), microaneurysms, cotton-wool spots, hard exudates, or a combination of these signs	Retinal tissue damage with breakdown of the blood–retina barrier and retinal microvascular signs	Acute & Severe
4	Grade 3 plus optic disc swelling	Malignant	Signs of moderate retinopathy plus optic disc oedema, in the presence of severely elevated blood pressure	Ischaemia, raised intracranial pressure, hypertensive encephalopathy and bilateral optic disc swelling	

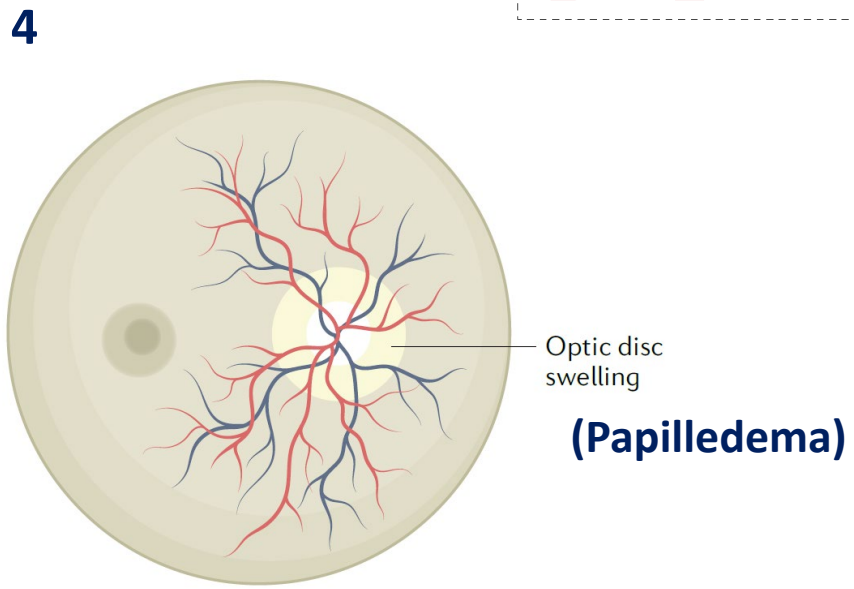
Cheung CY, et al. Nat Rev Dis Primers. 2022 Mar 10;8(1):14.

Hypertensive retinopathy









Cheung CY, et al. Nat Rev Dis Primers. 2022 Mar 10;8(1):14.

Clinical assessment: *routine* investigation

Investigation	Details
Serum Cr (eGFR), UA, ACR	Assessment of HMODs to kidney, Renal parenchyma as a 2˚ HT
Electrolytes	Hypernatremia (r/o 1˚ aldosteronism), Hyponatremia (r/o thiazide diuretics effect), Hypokalemic metabolic alkalosis (hyperaldosteronism or apparent mineralocorticoid excess), Hyperkalemia (S/E of RASi or Gordon disease)
Serum calcium	Hypercalcemia if 1˚ hyperparathyroidism
Hb/HCT	Erythrocytosis (severe OSA/smoking)
ECG	LVH (HMODs), Atrial fibrillation
TSH	Thyroid dysfunction as a cause of 2˚ HT
FPG, HbA1C	Metabolic syndrome or diabetes mellitus
Lipid profile	Dyslipidemia & calculate CV risk

ACR; urine Albumin-creatinine ratio, HMODs; hypertensive mediated organ damages, LVH; left ventricular hypertrophy

2024 Thai Guidelines on the Treatment of Hypertension.

Management of hypertension: principle

- **Treat "specific" causes** a.k.a. 2˚ hypertension including drug-induced HT
- **Set goal of treatment** (BP goal) based on age, frailty (≈life expectancy), **CV risk**, side effect or tolerability
- Treatment should always ***combine*** **life-style** modification & **pharmacologic** treatment
- **Patient aspect** (adherence & side effect) should be monitored regularly
- Most important goal is to **↑Survival & ↓CV events** more than just blood pressure reduction

2024 Thai Guidelines on the Treatment of Hypertension.

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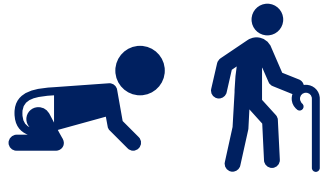
When to consider secondary hypertension



Extreme age of onset
Pediatrics: genetic HT
Elderly: renal artery stenosis (atherosclerosis)

Difficult/Severe case
Resistant hypertension
Severe hypertension
Disproportionated BP and HMODs
Abruptly worsening

Abnormal unusual findings
Hypokalemia (with/without diuretics)
Severe Obesity (obstructive sleep apnea)
Paroxysm (palpitation, sweating, headache): pheochromocytoma
Abnormal physical examinations
(cushingoid, hypo/hyperthyroid, acromegaly, abdominal bruit)

Brenner and Rector's the Kidney, 11th edition.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 12th edition.

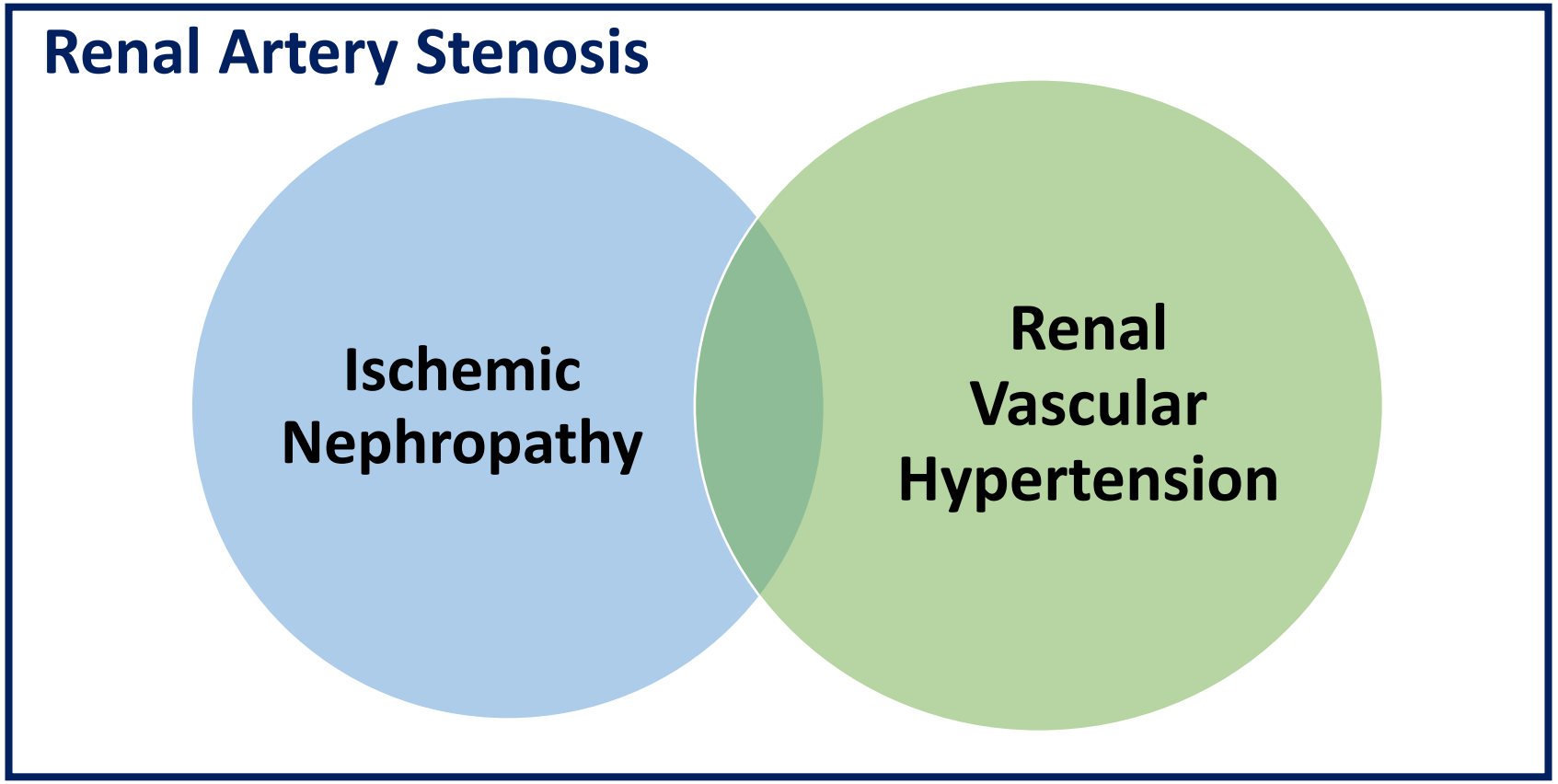
Cause-specific treatment (example)

- Withdrawal of drug-induced HT
- Anti-thyroid drugs if hyperthyroidism
- Termination of pregnancy if severe pre-eclampsia
- Unilateral laparoscopic adrenalectomy of aldosterone producing adenoma

Correction of hypertension causes substantially improves BP and disease specific morbidity (but not always cure HT)

Harrison's Principles of Internal Medicine, 22nd Edition.

Renovascular disease: definitions



RVH: ***arterial hypertension*** induced by *significantly* reduced renal perfusion

Ischemic Nephropathy: ***Kidney dysfunction*** from significant reduced renal perfusion

*Not all renal artery stenosis results in RVH/Ischemic nephropathy

Brenner and Rector's The Kidney, 11th edition. Comprehensive Clinical Nephrology, 7th edition.

Etiology

Causes of renal artery stenosis
Atherosclerosis renal artery stenosis (80-90%)
Fibromuscular disease (10%)
Coarctation of Aorta
Systemic vasculitis (Takayasu arteritis, **polyarteritis nodosa**)
Renal compression (tumor, Page kidney)
Covering of origin of RA by aortic stent graft
Arteriovenous fistula
Renal artery embolism/infarction
NF-1, TSC, Ehlers–Danlos syndrome, Marfan syndrome, Turner syndrome

Brenner and Rector's The Kidney, 11th edition.
Comprehensive Clinical Nephrology, 7th edition.
Plouin PF, Bax L. Nat Rev Nephrol. 2010;6(3):151-159.

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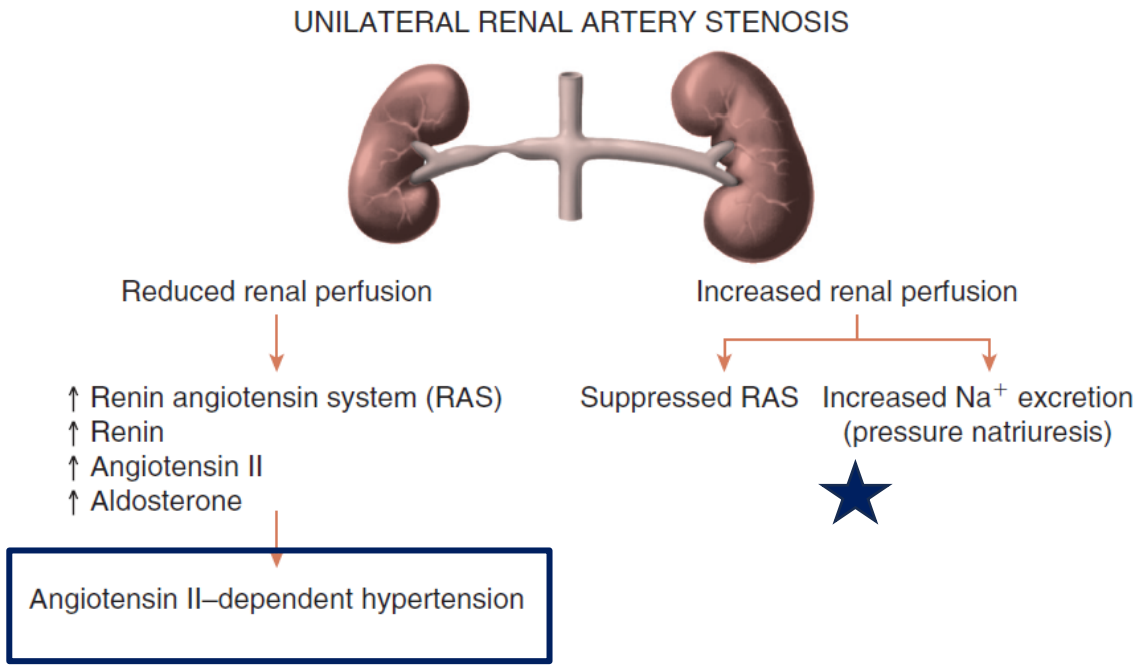
Atherosclerosis-RVD vs FMD

Characteristics	ARVD	FMD
Age	**> 60 years**	**< 40 years**
Sex	Either	**Female**
Atherosclerosis risk	**High**	Normal
Extra-renal	***HF**/MI/PAD	**Pulsatile tinnitus 33%**/headache 70% (migraine 30%)/stroke/SCAD
Lateralization	Uni/bilateral	**Mostly unilateral**
Renal function	**Impaired**	Preserved
Prognosis after revas.	+/- & may recurrent	**Good & low recurrent**
Lesion location	**Ostium/proximal part**	Middle to distal
Progression	Probably	**Usually no** (except dissection/aneurysm)

Dworkin LD, Cooper CJ. N Engl J Med. 2009;361(20):1972-1978.
Brenner and Rector's The Kidney, 11th edition.

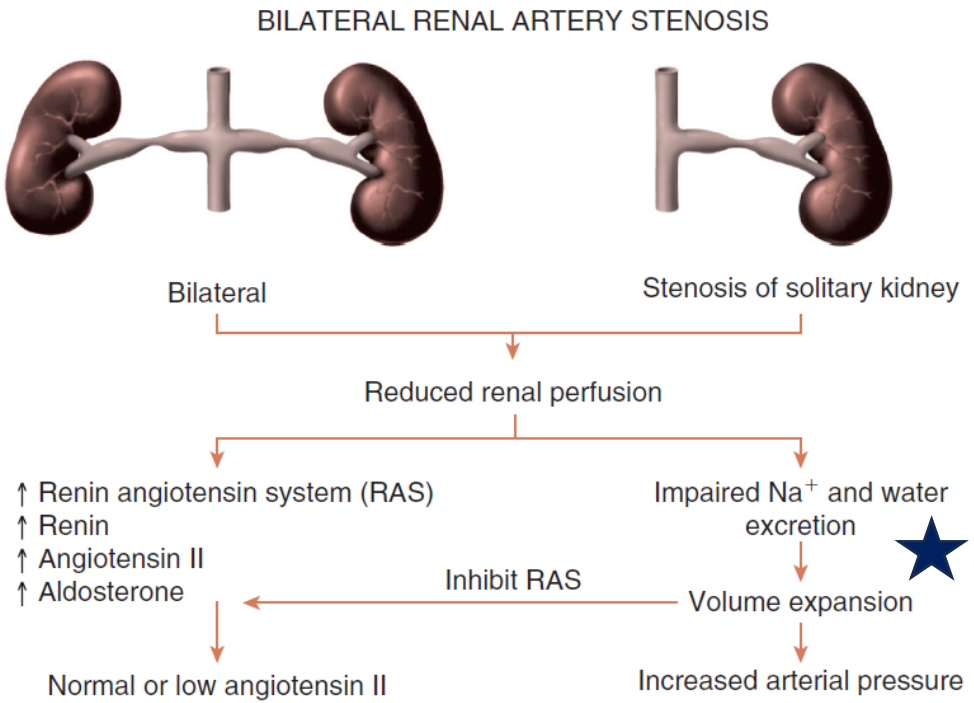
Pathophysiology of hypertension

One clip two kidneys



Preserved GFR
High renin activity
Angiotensin dependent HT

One clip one kidney



Reduced GFR
Normal/low renin
Salt-sensitive HT

Brenner and Rector's The Kidney, 11th edition.

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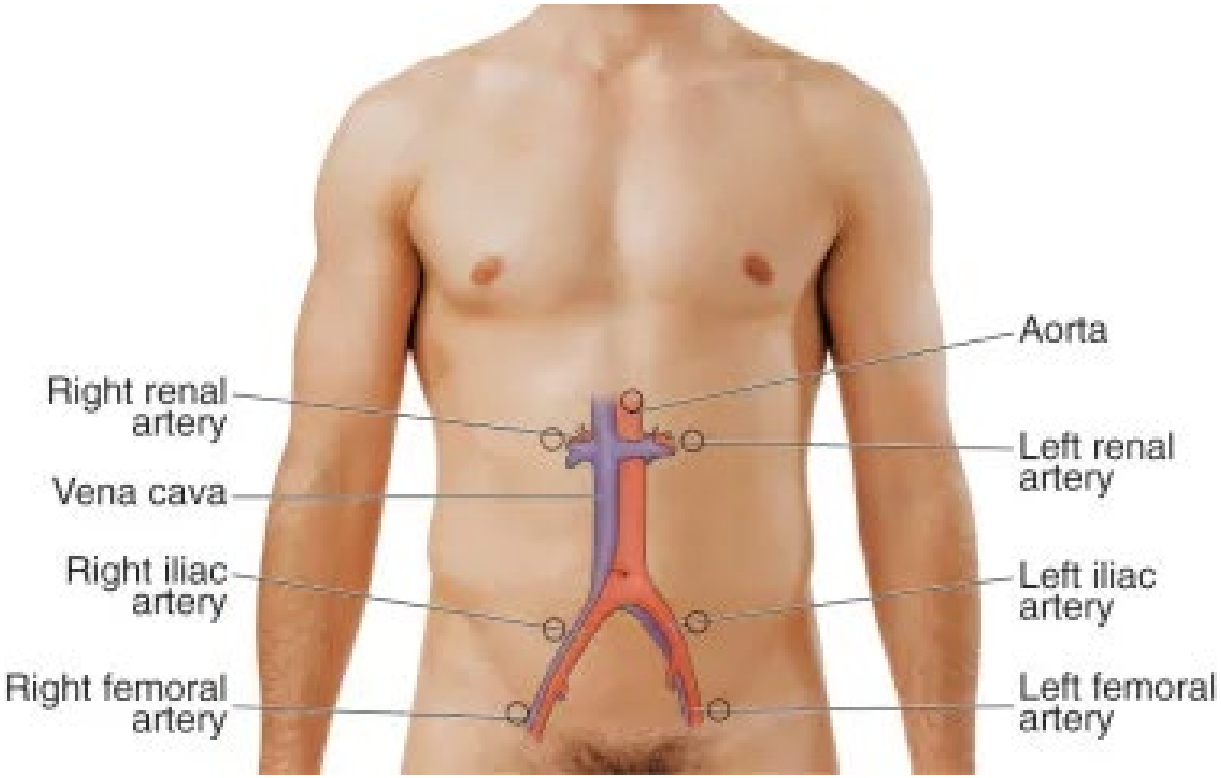
Clinical manifestation

When to suspect renovascular disease (signs and symptoms)
Early (< 30 years) or late (> 60 years) onset hypertension, in FMD and ARVD respectively
Uncontrolled/severe resistant hypertension (40%)
Accelerated HT of previous controlled HT within a year (24%)
Flash pulmonary edema (Pickering syndrome)* (up to 40%)
Refractory heart failure (preserved EF + LVH; diastolic dysfunction)*
Pulsatile tinnitus & migraine headache (FMD)
Abdominal bruit (46%)
Angina without significant coronary artery disease in hypertensive patients

***Bilateral disease/unilateral in solitary functioning kidney**

Hicks CW, et al. *Am J Kidney Dis*. 2022;79(2):289-301.
Brenner and Rector's The Kidney, 11th edition.
Braunwald's Heart Disease, a Textbook of Cardiovascular Medicine, 12th edition.
Plouin PF, Bax L. Nat Rev Nephrol. 2010;6(3):151-159.

Abdominal bruits



- **Listen before palpation**
- **Aorta = Midline** (level between umbilicus and xyphoid process)
- **Renal artery** = **2 cm** from midline (level between umbilicus and xyphoid process)
- **Bruits** in both systole and diastole indicate **stenosis**

However, absence of bruit does not exclude renal artery stenosis

Bates' Guide to Physical Examination and History Taking, 12th edition.

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Clinical manifestation

When to suspect renovascular disease (investigation)
Hypokalemia (16%)
Acute renal failure during treatment of hypertension
Progressive renal failure (unexplained-subnephrotic bland sediment)*
Renal asymmetry >1.5 cm
Increased in serum creatinine > 20-30% after RAASi within 1-2 weeks (up to 70%)*
± High renin-high aldosterone (multiple-confounding)

***Bilateral disease/unilateral in solitary functioning kidney**

Hicks CW, et al. *Am J Kidney Dis*. 2022;79(2):289-301.
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Plouin PF, Bax L. Nat Rev Nephrol. 2010;6(3):151-159.

Diagnosis & Treatment

- **Doppler ultrasonography** of renal artery is the 1st line screening test
- Confirmation test is "**catheter angiography**" which demonstrates significant renal artery stenosis
- **Revascularization** for significant stenosis in patient with refractory HT, recurrent HF, progressive GFR decline, bilateral disease (or solitary kidney)
- Anti-hypertensive of choice = **ACEI/ARBs** but with closed monitoring

Mazzolai L, et al. Eur Heart J. 2024;45(36):3538-3700.
Brenner and Rector's The Kidney, 11th edition.
Braunwald's Heart Disease, a Textbook of Cardiovascular Medicine, 12th edition.

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General management of hypertension

- **High cardiovascular risk =** Established ASCVD, Diabetes, Moderate-advance CKD, 10-year CVD risk >10%, Familial hypercholesterolemia
- **Moderate risk =** 10-year CVD risk 5-10%
- **Risk modifiers =** Autoimmune disease (SLE, Rheumatoid arthritis, etc.), HIV, Family history of premature ASCVD (male <55 y, female <65y), history of GDM/gestational HT

ASCVD; Atherosclerotic Cardiovascular Disease

Those with High CV risk or moderate risk + risk modifiers may benefit from "more aggressive BP management"

2024 ESC Guidelines for the management of elevated blood pressure and hypertension.

Threshold of pharmacologic treatment

- Those with high CV risk: start anti-hypertensive agents if “office” **BP ≥130/80 mmHg**
- Those without risk: start anti-hypertensive agents if “office” **BP ≥140/90 mmHg**

2024 Thai Guidelines on the Treatment of Hypertension.

Goal of treatment

Age (y)	*Office* BP goal (mmHg)	*Home* BP goal (mmHg)
18-79	<130/80	<125/75 if high risk or age<65 y
65-79 with isolated systolic HT	SBP 130-139 (if tolerated)	<135/85 or history of stroke
≥80	SBP 130-139 (if tolerated)	<140/80

Standard office BP <120/70 mmHg should be avoided
If goal BP is intolerable, BP should be set as low as patient can get

2024 Thai Guidelines on the Treatment of Hypertension.

Life-style modification

Categories	Details
Sodium intake	Limit Na <2 g/d (NaCl <5 g/d) ≈ 1 tablespoon of salt
Potassium intake	Moderate potassium intake 3.5-5 g/d (avoid if Hx of hyperkalemia or advanced CKD)
Healthy diet	DASH diet (diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat)
Physical activity	Moderate intensity exercise 150 min/week, avoid sedentary lifestyle
Optimize weight	Maintain healthy BMI (18.5-22.9 kg/m^2)
Smoking	Avoid smoking or e-cigarette
Alcohol	Avoid excessive alcohol (≤2 drinks in male, ≤ drink in female)
Stress control	Meditation, breath control, avoid pollution (noise & air)

DASH diet; Dietary Approaches to Stop Hypertension

2024 Thai Guidelines on the Treatment of Hypertension.
2024 ESC Guidelines for the management of elevated blood pressure and hypertension.
2025 AHA Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults.

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Pharmacologic treatment of hypertension

- Selecting anti-hypertensive agents should be based on **“compelling indication”** first
- If no preference of specific drug, then selecting class of medication in the **“first-line”** anti-hypertensive agents **(ACEIs, ARBs, DHP-CCBs, Thiazides)**
- **Avoid** combining ACEIs & ARBs
- Most patients need ≥2 classes of drugs, most effective method is **“single-pill combination”**

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Compelling indication

Conditions	Specific anti-hypertensive agents
Chronic stable angina	Beta-blockers, calcium channel blockers
Post-MI	Beta-blockers
Atrial fibrillation	Beta-blockers, non-DHP CCBs
Heart failure (reduced EF)	Beta-blockers, ACEIs/ARBs, MRAs
CKD with albuminuria	ACEIs/ARBs
T2D (esp. CKD)	ACEIs/ARBs
Pregnancy	Methyldopa, nifedipine, labetalol, hydralazine

MRAs; mineralocorticoid receptor antagonists (spironolactone)

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Braunwald's Heart Disease, a Textbook of Cardiovascular Medicine, 12th edition.

Anti-hypertensive agents

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Medication class	Examples	Indications	Contra-indications	Adverse effect	Pregnancy
Angiotensin converting enzyme inhibitors (ACEIs)	Enalapril, -pril	Albuminuric CKD, HFrEF	Uncontrolled hyperkalemia, AKI	Hyperkalemia, GFR↓, cough, angioedema	X
Angiotensin II receptor blockers (ARBs)	Losartan, -sartan	Albuminuric CKD, HFrEF	Uncontrolled hyperkalemia, AKI	Hyperkalemia, GFR↓	X
Dihydropyridine calcium channel blockers	Amlodipine, -dipine	Chronic stable angina	HFrEF	Edema, gum hyperplasia	Nifedipine✓
Thiazide/Thiazide-like	Hydrochlorothiazide	Renal stones from hypercalciuria	Hyponatremia, hypokalemia	Hyponatremia, ↑Uric, ↑FPG, hypokalemia	X
Beta blockers	Carvedilol, -lol	HFrEF, AF, angina, post-MI	Reactive airway disease (non-specific)	Bradycardia	Labetalol✓
Mineralocorticoid receptor antagonists	Spironolactone	Resistant HT, Primary aldosteronism	Uncontrolled hyperkalemia, advanced CKD	Hyperkalemia, gynecomastia, ↓libido	X
Alpha blockers	Doxazosin, -osin	BPH, pheochromocytoma	-	Orthostatic hypotension	X

Brenner and Rector's The Kidney, 11th edition.
Braunwald's Heart Disease, a Textbook of Cardiovascular Medicine, 12th edition.

Resistant hypertension: definition

ESC European Society of Cardiology

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- Hypertension that after treatment strategy including appropriate lifestyle measures and treatment with *maximum or maximally tolerated* doses of a ***diuretic*** (thiazide or thiazide-like), a **RAS blocker**, and **a calcium channel blocker** fail to lower office BP <140/90 mmHg which is **confirmed by "out-of-office"** BP measurement

Pseudo-resistant HT should be excluded (non-adherence)
If advanced CKD (GFR <30 ml/min), adequate loop diuretics dose should be attempted

*Refractory HT = BP not in target despite ≥5 medications, including spironolactone, long-acting thiazide like diuretics

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2024 Thai Guidelines on the Treatment of Hypertension.

Resistant hypertension management

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- **Confirm** out-of-office BP & adherence
- R/O **drug**-induced HT & **secondary** HT
- **Refer** to specialist (cardiologist or nephrologist)
- If GFR**>30** mL/min add **spironolactone**
- If GFR**<30** mL/min add **long-acting thiazide-like** diuretic

If BP goal not met

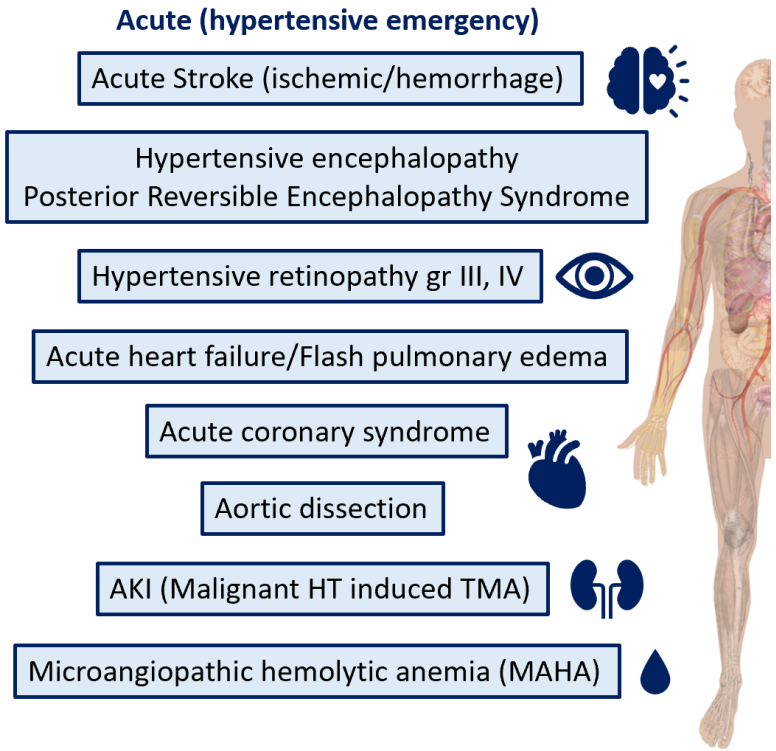
Add Beta blockers, convert RAS blockers to ARNI*
If GFR>30 mL/min, consider renal denervation

*ARNI, Angiotensin Receptor-Neprilysin Inhibitors

2024 ESC Guidelines for the management of elevated blood pressure and hypertension.
2024 Thai Guidelines on the Treatment of Hypertension.

Hypertensive emergency: evaluation

- **Hypertensive emergency = severe HT (mostly grade III; ≥180/110 mmHg) *with acute* hypertension mediated organ damage**



Causes

- **Poor adherence (mostly essential HT)**
- **2˚ HT should be look for**

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2024 Thai Guidelines on the Treatment of Hypertension.

Hypertensive emergency: management

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- **Admit ICU + invasive BP monitoring + IV short-acting anti-hypertensive agents**
- **Target BP lowering & class of drug depends on organ involvement**
- **Consult specialists + organ support**

Organ involvement	Target BP (mmHg)	Anti-hypertensive agents
ACS/acute HF	SBP <140 as fast as possible	**Nitroglycerine**, furosemide (if HF)
Aortic dissection	SBP <120, pulse<60/min as fast as possible	**Labetalol, esmolol**, nicardipine
Ischemic stroke	If re-perfusion treatment: <180/105 for 1 d If no re-perfusion: <220/110, ↓15% in 1d	**Nicardipine**, labetalol
Hemorrhagic stroke	SBP 140-160 within 6 h of symptoms	**Nicardipine**, labetalol
Malignant HT (hypertensive retinopathy gr III/IV), TMA	SBP↓25% within the 1st h then <160/100 in next 2-6h then SBP 130-140 in next 1-2 d	**Nicardipine**, labetalol, nitroprusside (avoid if AKI)
Severe pre-eclampsia/eclampsia	<160/105 within 150-180 min	**Labetalol**, nifedipine, methyldopa

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Take home message

- Hypertension is very common and remains the most important systemic disease involving multiple organs
- Screening and making correct diagnosis by standard BP measurement is the essential step
- Comprehensive assessment is crucial
- Always identify treatable causes
- Treatment including life-style modification + drugs

Thank you for your attention