

Cardio-Vascular Disease

Hypertension

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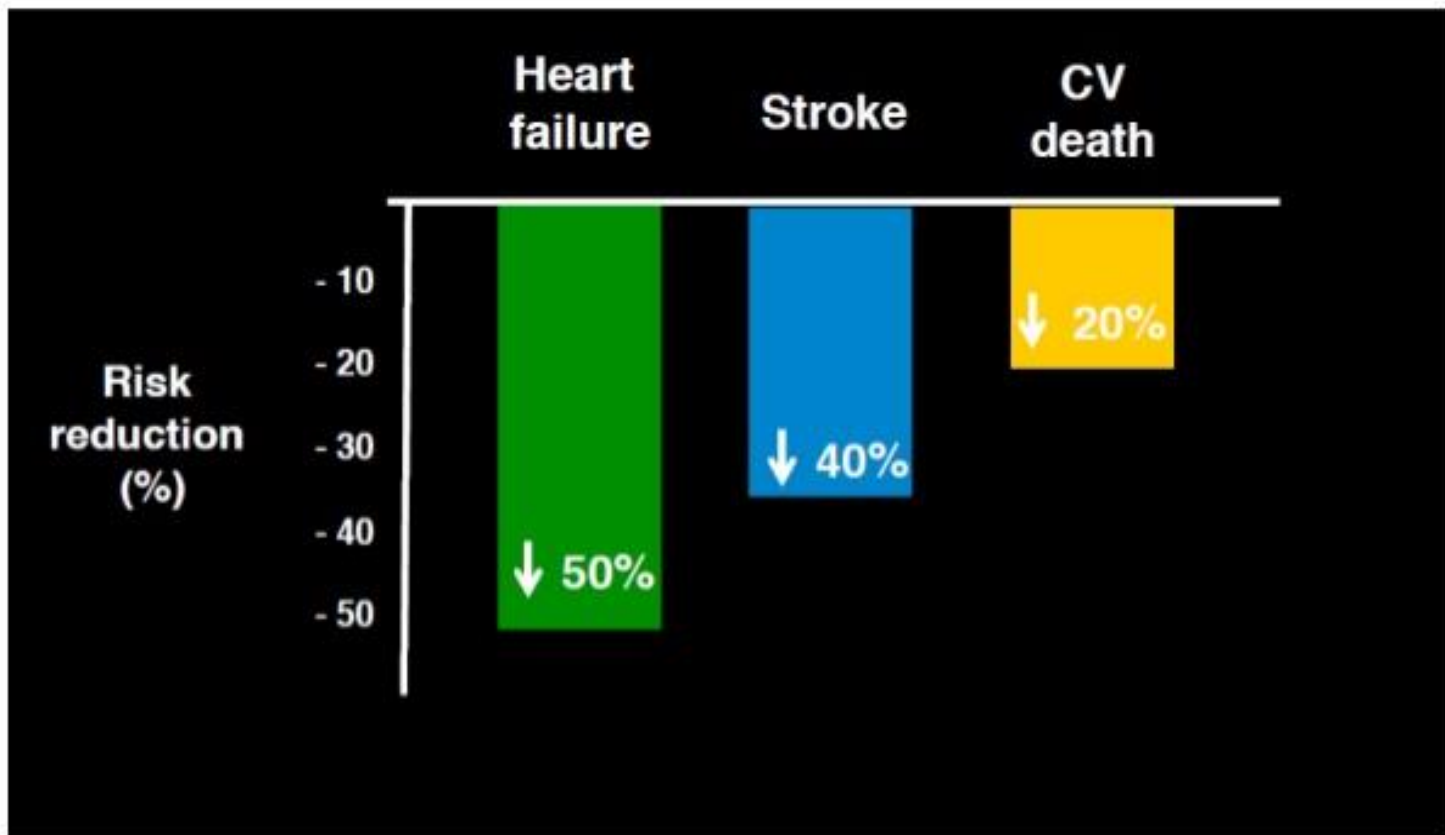




World Health
Organization

- One of the key risk factors for cardiovascular disease is **hypertension** or raised blood pressure.
- Hypertension already affects **1.1 billion** people worldwide (**WHO 2015**), leading to heart attacks and strokes. **By 2025, it is estimated over 1.5 billion** people will have hypertension.
- Researchers have estimated that raised blood pressure currently **kills nine million** people every year.

CV benefits of treating HTN



Hebert et al, Archives Int Med 1993

Risk Reduction (%) for 10 mm Hg fall in SBP – 613,815 patients



**Irrespective of baseline BP
or pre-existing conditions**

Hypertension

- High BP is a trait as opposed to a specific disease.
 - Represents a quantitative rather than a qualitative deviation from the normal.
 - Level of BP at which the benefits of treatment outweigh the costs and hazards.
 - Hypertension is a condition in which arterial BP is chronically elevated.
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Hypertension and Its risk

- leading causes of the global burden of disease.
 - Approximately 7.6 million deaths (13 –15% of the total) and 92 million disability-adjusted life years worldwide (2001)
 - Doubles the risk of cardiovascular diseases
 - often is associated with additional cardiovascular disease risk factors.
 - Antihypertensive therapy clearly reduces the risks of cardiovascular and renal disease
 - But large segments of the hypertensive population are either untreated or inadequately treated.
- 

CVD Risk Factors Common in Patients With Hypertension

Modifiable Risk Factors*	Relatively Fixed Risk Factors†
• Current cigarette smoking, secondhand smoking • Diabetes mellitus • Dyslipidemia/hypercholesterolemia • Overweight/obesity • Physical inactivity/low fitness • Unhealthy diet	• CKD • Family history • Increased age • Low socioeconomic/educational status • Male sex • Obstructive sleep apnea • Psychosocial stress

*Factors that can be changed and, if changed, may reduce CVD risk.

†Factors that are difficult to change (CKD, low socioeconomic/educational status, obstructive sleep apnea, cannot be changed (family history, increased age, male sex), or, if changed through the use of current intervention techniques, may not reduce CVD risk (psychosocial stress).

CKD indicates chronic kidney disease; and CVD, cardiovascular disease.

Most Patients Have Overlapping CV Risk Factors

Overall 23% of individuals without CV comorbidities has HTN

- **HTN was found in:**
- 82% of those with CKD
- 77% of those with DM
- 74% in those with PAD
- 73% of those with CHD
- 71% in those with CHF
- 62% in those with MetS
- 70% in those with stroke
- 52% in those with dyslipidemia

Of all dyslipidaemias:

- 48% have hypertension
- 14% have type 2 diabetes
- 35% are overweight/obese



Of all type 2 diabetes:

- 60% have hypertension
- 60% have hyperlipidemia
- 90% are overweight/obese

Measurement of BP



Selection Criteria for BP Cuff Size for Measurement of BP in Adults

Arm Circumference	Usual Cuff Size
22–26 cm	Small adult
27–34 cm	Adult
35–44 cm	Large adult
45–52 cm	Adult thigh

Clinical indications for HBPM & ABPM

- **Conditions in which white-coat hypertension is more common, e.g.:**
 - Grade I hypertension on office BP measurement
 - Marked office BP elevation without HMOD
- **Conditions in which masked hypertension is more common, e.g.:**
 - High-normal office BP
 - Normal office BP in individuals with HMOD or at high total CV risk
- **When there is considerable variability in the office BP**
- **Evaluation of resistant hypertension**

BP Patterns Based on Office and Out-of-Office Measurements

	Office/Clinic/Healthcare Setting	Home/Nonhealthcare/ABPM Setting
Normotensive	No hypertension	No hypertension
Sustained hypertension	Hypertension	Hypertension
Masked hypertension	No hypertension	Hypertension
White coat hypertension	Hypertension	No hypertension

ABPM indicates ambulatory blood pressure monitoring; and BP, blood pressure.

Etiology

- It may be either
 - **Essential** (90-95 %): Unknown specific cause – multifactorial.
 - **Environmental factors**
 - **Genetic factors**
 - **Fetal factors**
 - **Humoral mechanisms**
 - **Insulin resistance - Metabolic syndrome**
 - **Secondary**: consequence of a specific disease or abnormality leading to sodium retention and/or peripheral vasoconstriction
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Classification of BP

JNC – 8 Classification of BP

Table 3. Classification of Blood Pressure in Adults (age ≥ 18 years)

Classification	Systolic Blood Pressure (mmHg)		Diastolic Blood Pressure (mmHg)
Normal	<120	AND	<80
Prehypertension	120-139	OR	80-89
Stage I HTN	140-159	OR	90-99
Stage 2 HTN	≥ 160	OR	≥ 100

Essential hypertension

- **Genetic factors**

- tends to run in families, by shared environmental influences.
- still largely unidentified genetic component.

- **Fetal factors**

- Low birth weight: May be due to fetal adaptation to intrauterine undernutrition with
 - long-term changes in blood vessel structure
 - Or the function of crucial hormonal systems.

Essential hypertension

- **Environmental factors**

- **Obesity**

- Fat people have higher blood pressures than thin people.
 - Sleep disordered breathing often seen with obesity may be an additional risk factor

- **Alcohol intake**

- close relationship between the consumption of alcohol and blood pressure level.
 - But small amounts of alcohol seem to be beneficial

- **Sodium intake**

- Directly proportional
 - some evidence that a high **potassium** diet can protect against the effects of a high **sodium** intake

- **Stress**

- Chronic stress – uncertain
 - acute pain or stress can raise blood pressure

Essential hypertension

- **Humoral mechanisms**

- autonomic nervous system, reninangiotensin system, natriuretic peptide and kallikrein-kinin system - short-term changes in blood pressure
- But no convincing evidence - directly involved in the maintenance of hypertension

- **Insulin resistance - Metabolic syndrome**

- hyperinsulinaemia, glucose intolerance, reduced levels of HDL cholesterol, hypertriglyceridaemia and central obesity with hypertension
 - association between diabetes and hypertension has long been recognized
- 

Secondary Hypertension

- **Pregnancy (pre-eclampsia)**
- **Renal disease**
 - Renal vascular disease
 - Parenchymal renal disease, particularly glomerulonephritis
 - Polycystic kidney disease
- **Drugs**
 - Oral contraceptives containing oestrogens
 - Anabolic steroids,
 - Corticosteroids
 - NSAIDs, carbenoxolone,
 - Sympathomimetic agents
- **Coarctation of the aorta**

Secondary Hypertension

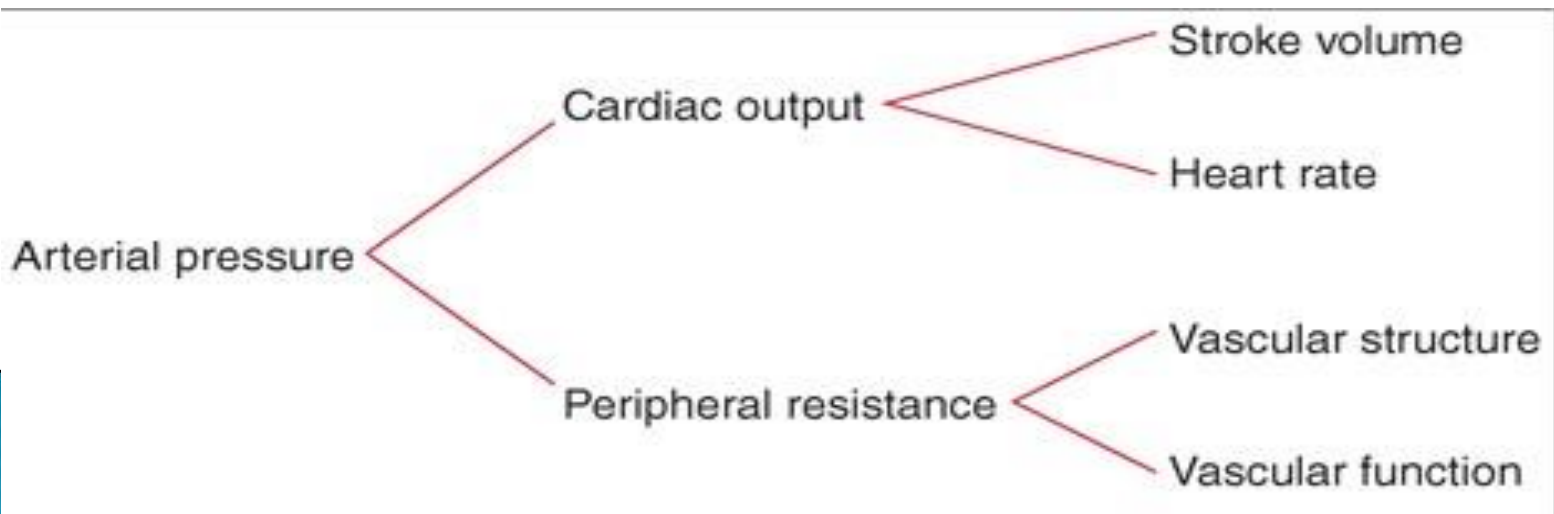
- **Endocrine disease**

- Pheochromocytoma - vascular tumor of the adrenal gland
- Cushing's syndrome – excessive cortisol
- Primary hyperaldosteronism (Conn's syndrome)
- Glucocorticoid-suppressible hyperaldosteronism
- Hyperparathyroidism
- Acromegaly
- Primary hypothyroidism
- Thyrotoxicosis
- Congenital adrenal hyperplasia due to 11- β -hydroxylase or 17 α -hydroxylase deficiency
- Liddle's syndrome
- 11- β -hydroxysteroid dehydrogenase deficiency

Mechanisms of Hypertension

Determinants of arterial pressure:

- **Cardiac output**
 - **Stroke volume:** related to myocardial contractility and to the size of the vascular compartment.
 - **Heart Rate:** neuronal and hormonal control
- **Peripheral resistance:** **functional** and **anatomic** changes in small arteries and arterioles



Mechanisms of Hypertension

- **Intravascular Volume**

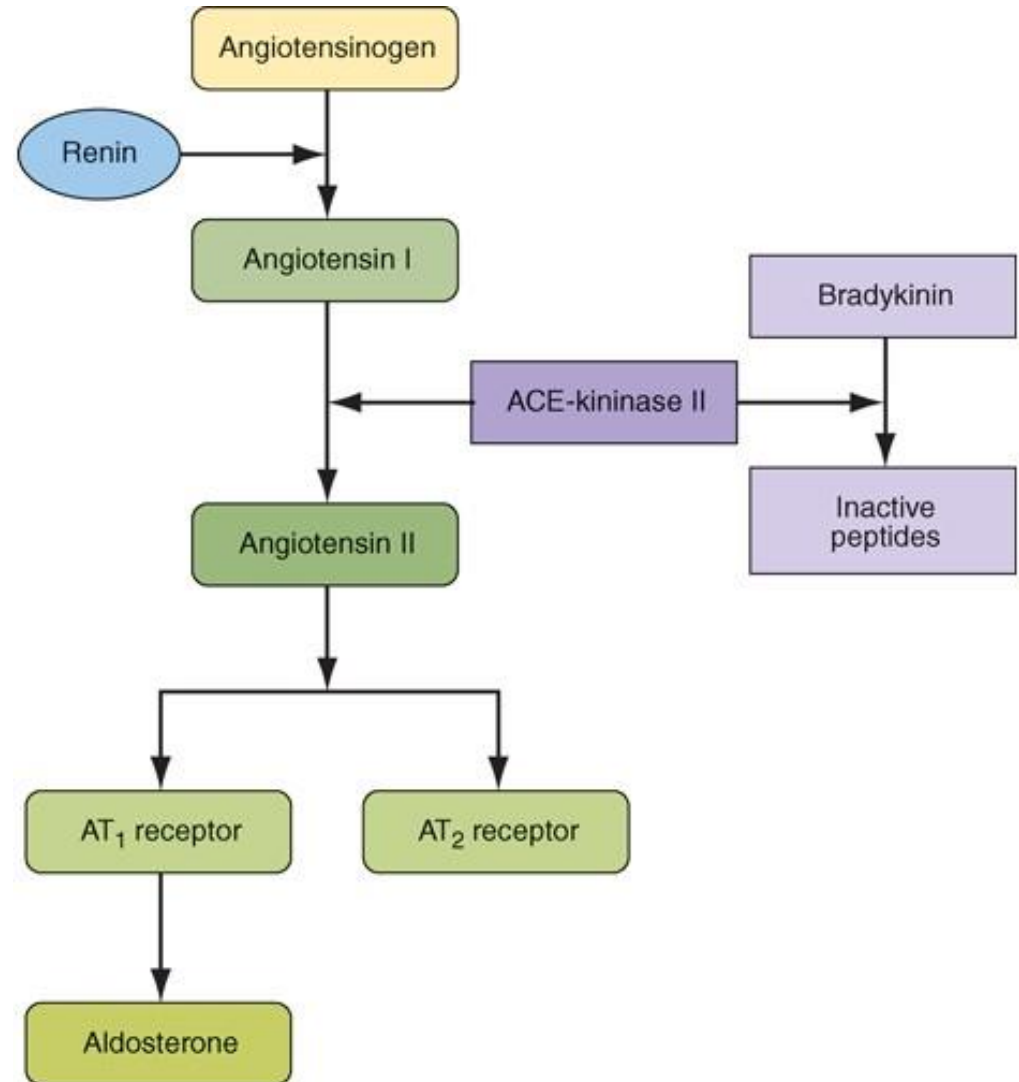
- Sodium is predominantly an **extracellular ion** -primary determinant of the extracellular fluid volume
- When NaCl intake exceeds the capacity of the kidney to excrete sodium
- Vascular volume initially expands and cardiac output increases

- **Autonomic Nervous System**

- homeostasis via **pressure, volume, and chemoreceptor** signals
 - Adrenergic reflexes - **short term,**
 - Adrenergic function, in concert with hormonal and volume-related factors - **long-term regulation**
 - three endogenous catecholamines are **norepinephrine, epinephrine, and dopamine**
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Mechanisms of Hypertension

- **Renin-Angiotensin-Aldosterone**
 - **Vasoconstrictor** properties of **angiotensin II**
 - **Sodium-retaining** properties of **aldosterone**



Mechanisms of Hypertension: Vascular Mechanisms

- **Vascular radius**
 - **Resistance to flow** varies inversely with the **fourth power of the radius**,
 - **Compliance of resistance arteries**
 - **High degree of elasticity**: accommodate an increase of volume with relatively little change in pressure,
 - **Semi-rigid vascular system**: small increment in volume induces a relatively large increment of pressure
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Complications of Hypertension



Atherosclerosis
Aneurysms
Aortic dissections



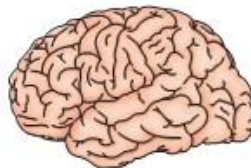
Haematuria
Uraemia
Proteinemia

Chronic kidney disease



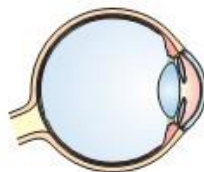
Pulmonary oedema
Myocardial infarction
Left ventricular hypertrophy

Cardiac failure



Haemorrhage / infarction
Seizures
Vascular dementia

Stroke / TIA



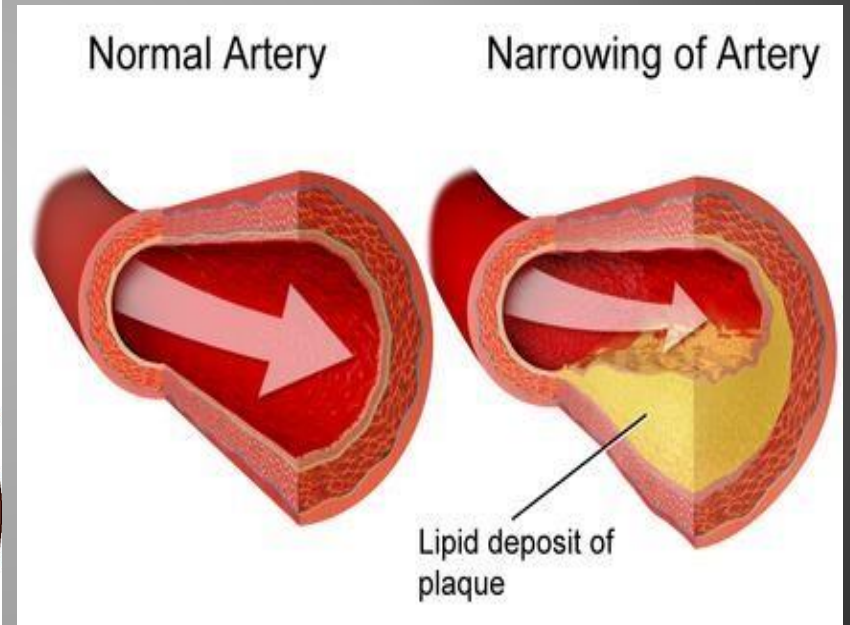
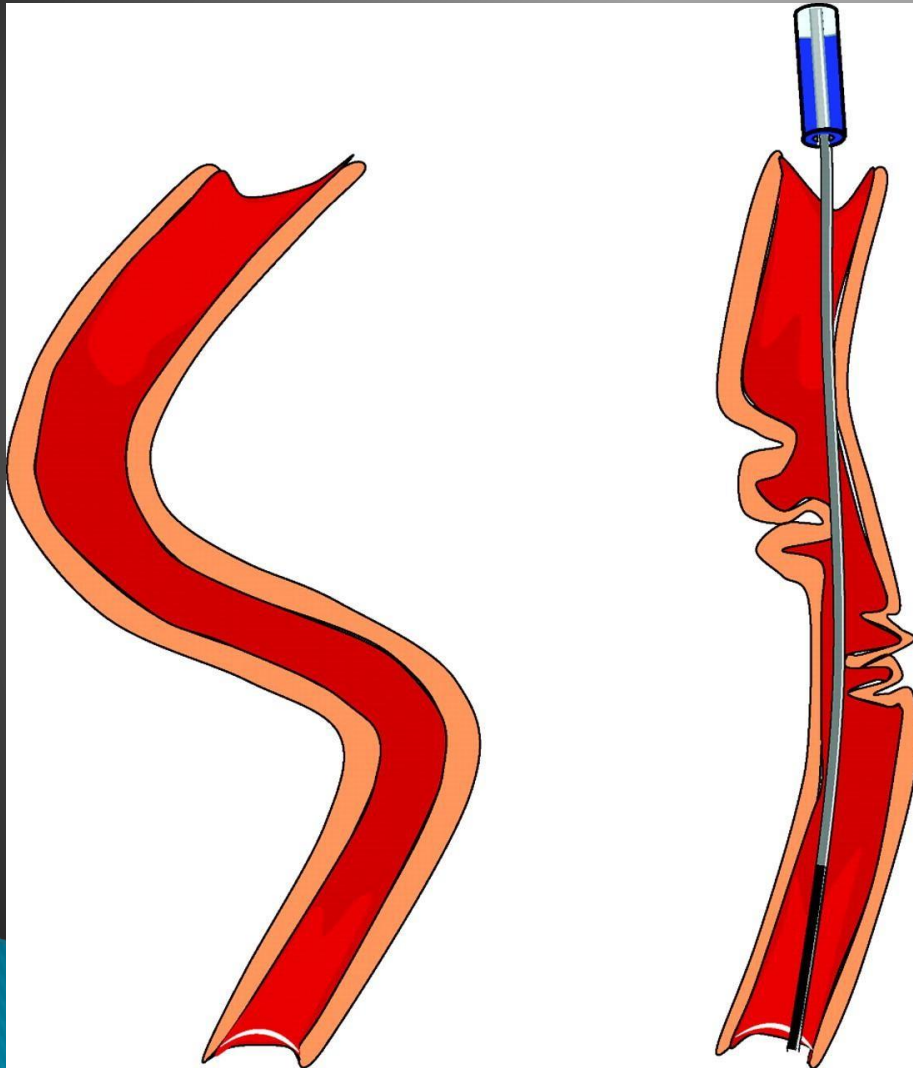
Haemorrhages
Exudates
A-V nipping
Papilloedema

Blindness

Complications: Blood Vessels

- Larger arteries ($> 1\text{ mm}$)
 - Internal elastic lamina is **thickened**, smooth muscle is
 - ▶ hypertrophied and fibrous tissue is deposited
 - The vessels **dilate** and become **tortuous**, and their walls become
 - ▶ less compliant.
- Smaller arteries ($< 1\text{ mm}$)
 - hyaline arteriosclerosis
 - lumen narrows and aneurysms
 - **Atheroma** develops : coronary and cerebrovascular disease
 - **Risk factor**: smoking, hyperlipidaemia, diabetes
- This changes in the vasculature often **perpetuate** and
 - ▶ **aggravate** hypertension
 - Increasing peripheral vascular resistance
 - Reducing renal blood flow

Complications: Blood Vessels

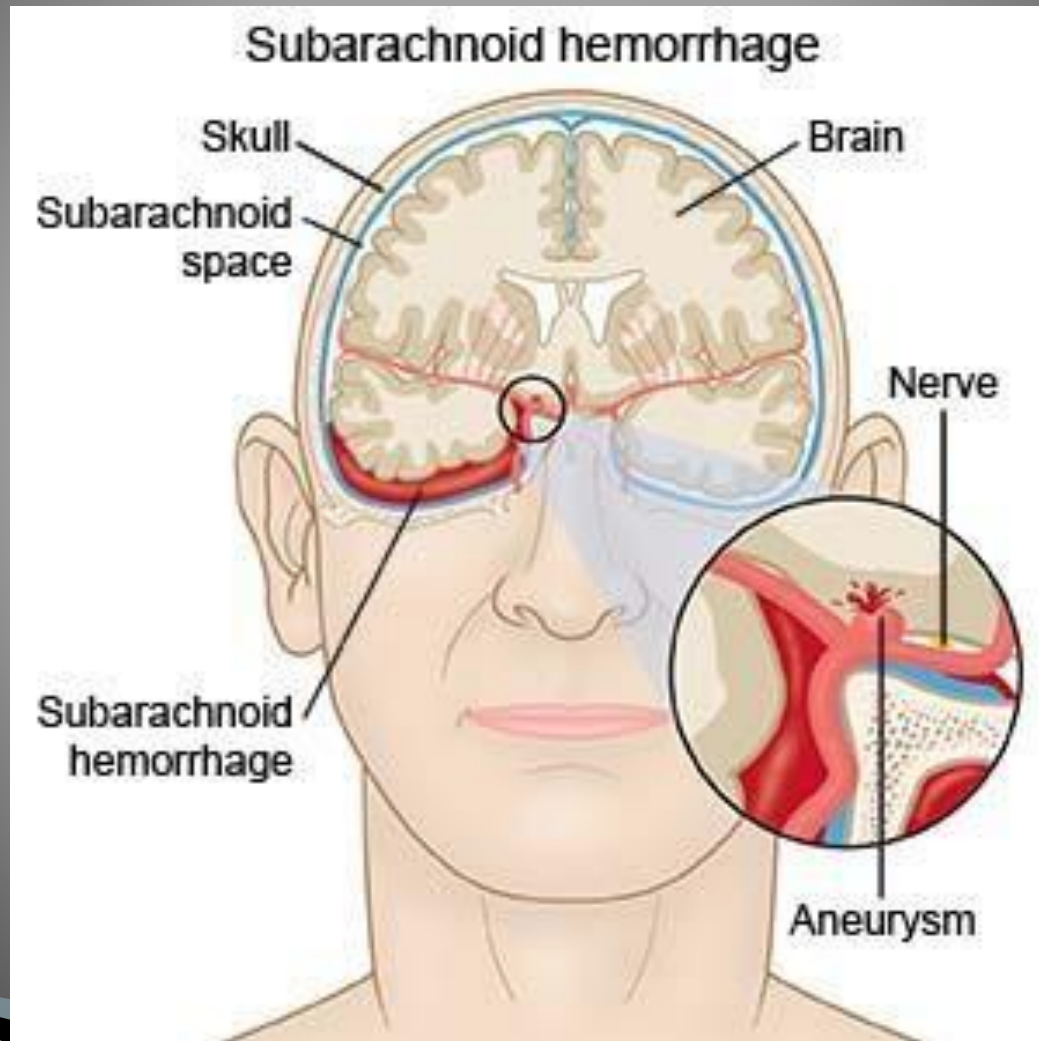


Complications:

Central nervous system

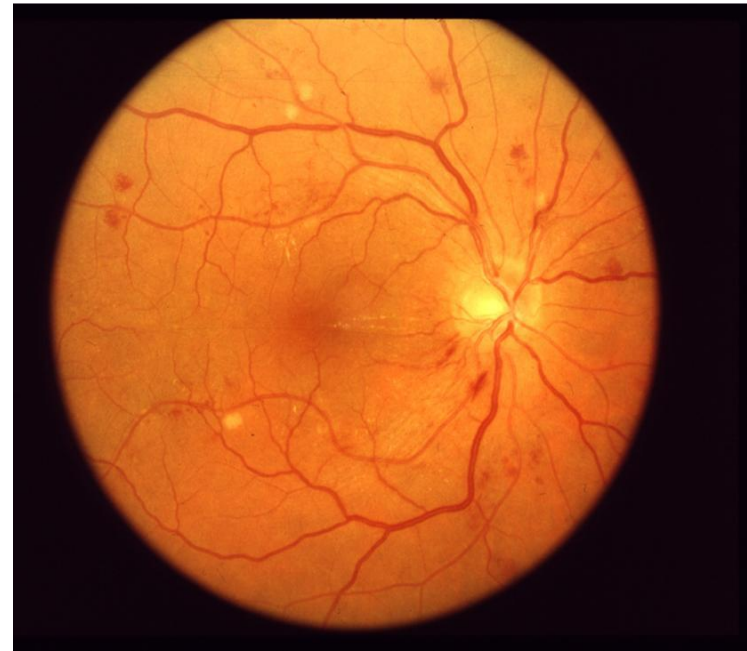
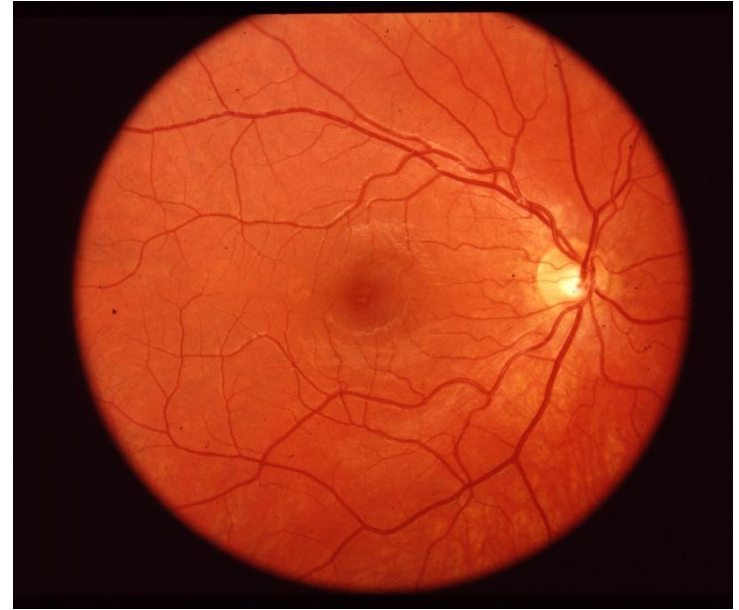
- **Stroke** most common complication
 - Cerebral haemorrhage or infarction
 - **Subarachnoid haemorrhage**
 - **Hypertensive encephalopathy** – rare conditions
 - High BP
 - **Neurological symptoms:** transient disturbances of speech or vision, paraesthesiae, disorientation, fits and loss of consciousness.
 - **Neurological deficit** - usually reversible if the hypertension is properly controlled
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Complications: Central nervous system

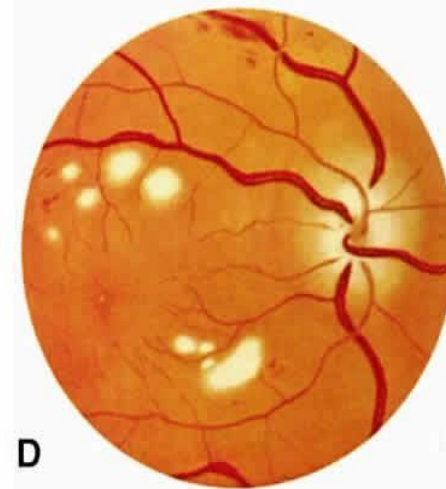
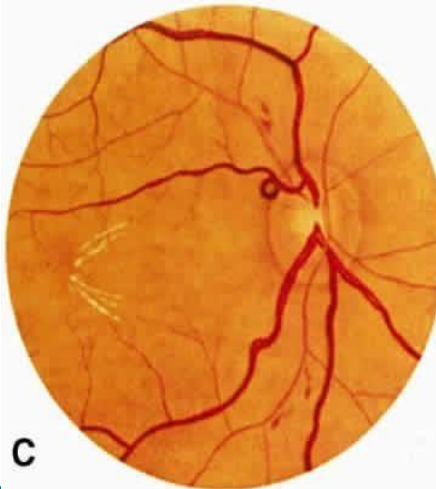
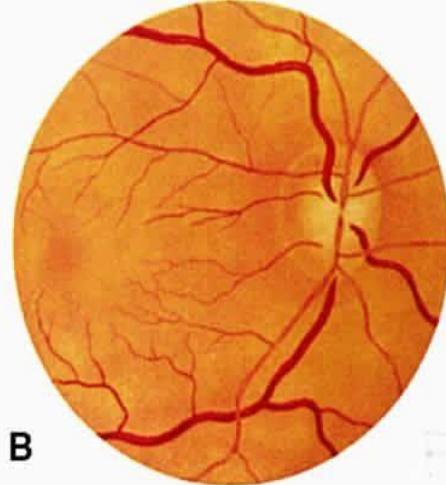
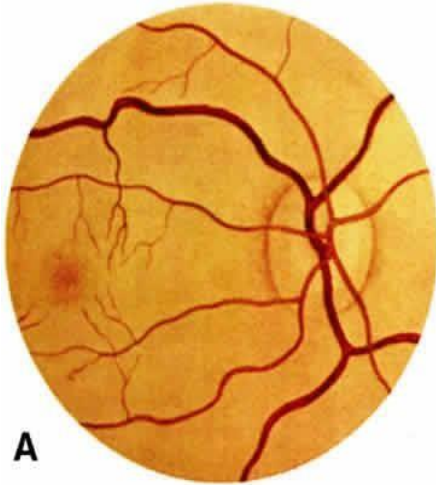


Complications: Retina

- **Optic fundi** - gradation of changes linked to the severity of hypertension
- **Cotton wool** exudates
 - Associated with retinal ischaemia or infarction
 - Fade in a few weeks
- **Hard exudates**
 - Associated with diabetic retinopathy
 - small, white, dense deposits of lipid
 - microaneurysms ('dot' haemorrhages)



Complications: Retina



- **Grade 1**
 - Arteriolar thickening
 - Tortuosity
 - Increased reflectiveness - **silver wiring**
- **Grade 2**
 - Grade 1
 - Constriction of veins at arterial crossings - **arteriovenous nicking**
- **Grade 3**
 - Grade 2
 - **Retinal ischaemia** - flame-shaped or blot haemorrhages and '**cotton wool**' exudates
- **Grade 4**
 - Grade 3
 - **papilloedema**

Complications: Heart

- **Coronary artery disease**
 - Very high incidence
 - Pressure load on the heart
 - may lead to left ventricular hypertrophy
 - forceful apex beat and fourth heart sound
- **Atrial fibrillation**
 - diastolic dysfunction caused by left ventricular hypertrophy
 - Or the effects of coronary artery disease.
- **Left ventricular failure - severe hypertension**
 - Absence of coronary artery disease
 - **Risk factor: impaired** renal function, and therefore sodium retention

Complications: Kidneys

- Major risk factor for renal injury and **end-stage renal disease**
- **Atherosclerotic**, hypertension-related vascular lesions - **preglomerular arterioles**
 - Resulting in **ischemic changes** in the glomeruli and postglomerular structures
 - This leads to **reduced GFR** and, finally, a reduction in **Na** and **water excretion**
 - activation of the renin-angiotensin system
- May cause proteinuria (>3 g/24 h) or if untreated it may cause **Progressive renal failure**

Basic and Optional Laboratory Tests for Primary Hypertension

Basic testing	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR*
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
	Urinalysis
	Electrocardiogram
Optional testing	Echocardiogram
	Uric acid
	Urinary albumin to creatinine ratio

*May be included in a comprehensive metabolic panel.
eGFR indicates estimated glomerular filtration rate.

Investigation: All patients

- Urinalysis for blood, protein and glucose
 - Blood urea, electrolytes and creatinine
 - Blood glucose
 - Serum total and HDL cholesterol
 - 12-lead ECG - left ventricular hypertrophy, coronary artery disease
- 

Investigation: Selected patients

- **Chest X-ray:** cardiomegaly, heart failure, coarctation of the aorta
 - **Ambulatory BP recording:** assess borderline or 'white coat' hypertension
 - **Echocardiogram:** detect or quantify left ventricular hypertrophy
 - **Renal ultrasound:** to detect possible renal disease
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Investigation: Selected patients

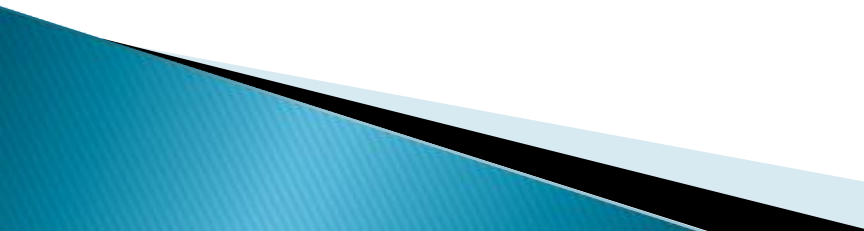
- **Renal angiography:** detect or confirm presence of renal artery stenosis
 - **Urinary catecholamines:** possible phaeochromocytoma
 - **Urinary cortisol and dexamethasone suppression test:** possible Cushing's syndrome
 - **Plasma renin activity and aldosterone:** possible primary aldosteronism
- 

Hypertension and CV Risk Assessment

10-y CV Risk Categories

Very high risk	Subjects with any of the following: ▪ CVD ▪ Type 2 diabetes, or type 1 diabetes & target organ damage ▪ Patients with moderate to severe CKD (GFR <60mL/min/1.73m²) ▪ SCORE ≥10%
High risk	Subjects with: ▪ Markedly elevated single risk factors such as: – Familial dyslipidaemias – Severe hypertension. ▪ SCORE ≥ 5% and <10%
Moderate risk	SCORE is ≥1 and <5% at 10 years, further modulated by: ▪ family history of premature CAD ▪ abdominal obesity ▪ physical activity pattern ▪ HDL-C ▪ TG ▪ hsCRP ▪ social class  ESC European Society of Cardiology  ESH European Society of Hypertension
Low risk	SCORE less than 1% and free of qualifiers

Management

- Initially there should be complete **assessment** with **repeated BP measurements** for 6 months until its not severe.
 - **Advice** and **non-pharmacological measures (Life-style changes)** should be given prior to the initiation of drug therapy.
 - A target of **~140 mm Hg** systolic and **≈85 mm Hg** diastolic blood pressure is recommended.
 - Diabetes, renal impairment or established CVS disease **≈130/80 mmHg** is recommended
- 

Hypertension and Total CV Risk Assessment

- There is also emerging evidence that increased serum uric acid to levels lower than those typically associated with gout (6.5-7 mg/dl) is independently associated with increased CV risk in both the general population and hypertensive patients.

2017 Hypertension Guideline

Nonpharmacological Interventions



Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mm Hg	-3 mm Hg
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5/6 mm Hg	-2/3 mm Hg
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.

DASH indicates Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

Resources: Your Guide to Lowering Your Blood Pressure With DASH—How Do I Make the DASH?

Available at: <https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to>.

Top 10 Dash Diet Tips. Available at: http://dashdiet.org/dash_diet_tips.asp



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Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension* (cont.)

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Physical activity	Aerobic	● 90–150 min/wk ● 65%–75% heart rate reserve	-5/8 mm Hg	-2/4 mm Hg
	Dynamic resistance	● 90–150 min/wk ● 50%–80% 1 rep maximum ● 6 exercises, 3 sets/exercise, 10 repetitions/set	-4 mm Hg	-2 mm Hg
	Isometric resistance	● 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ● 8–10 wk	-5 mm Hg	-4 mm Hg
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: ● Men: ≤2 drinks daily ● Women: ≤1 drink daily	-4 mm Hg	-3 mm

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.

†In the United States, one "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).

Pharmacological Management

- Decision to commence specific drug therapy - only after a careful period of assessment with lifestyle changes, of up to 6 months.
 - Unless its not having end organ damage or other hyperetensive complications
 - Aim, plan and side effect of drug treatment - carefully explained to the patient.
 - Patient compliance is very essential for efficacy of drugs – long term results.
- 

Drugs for the treatment of Hypertension

- In previous guidelines 5 major drug classes (ACEIs, ARBs, BBs, CCBs, Ds) were recommended based on
 - Proven ability to reduce BP
 - CV event reduction in placebo-controlled studies
 - Broad equivalence in overall CV morbidity/mortality
 - Conclusion that benefit predominantly derives from BP lowering
- These conclusions have since been confirmed by recent meta-analyses
- These guidelines thus recommend that the same 5 major classes of drugs should form the basis of antihypertensive therapy

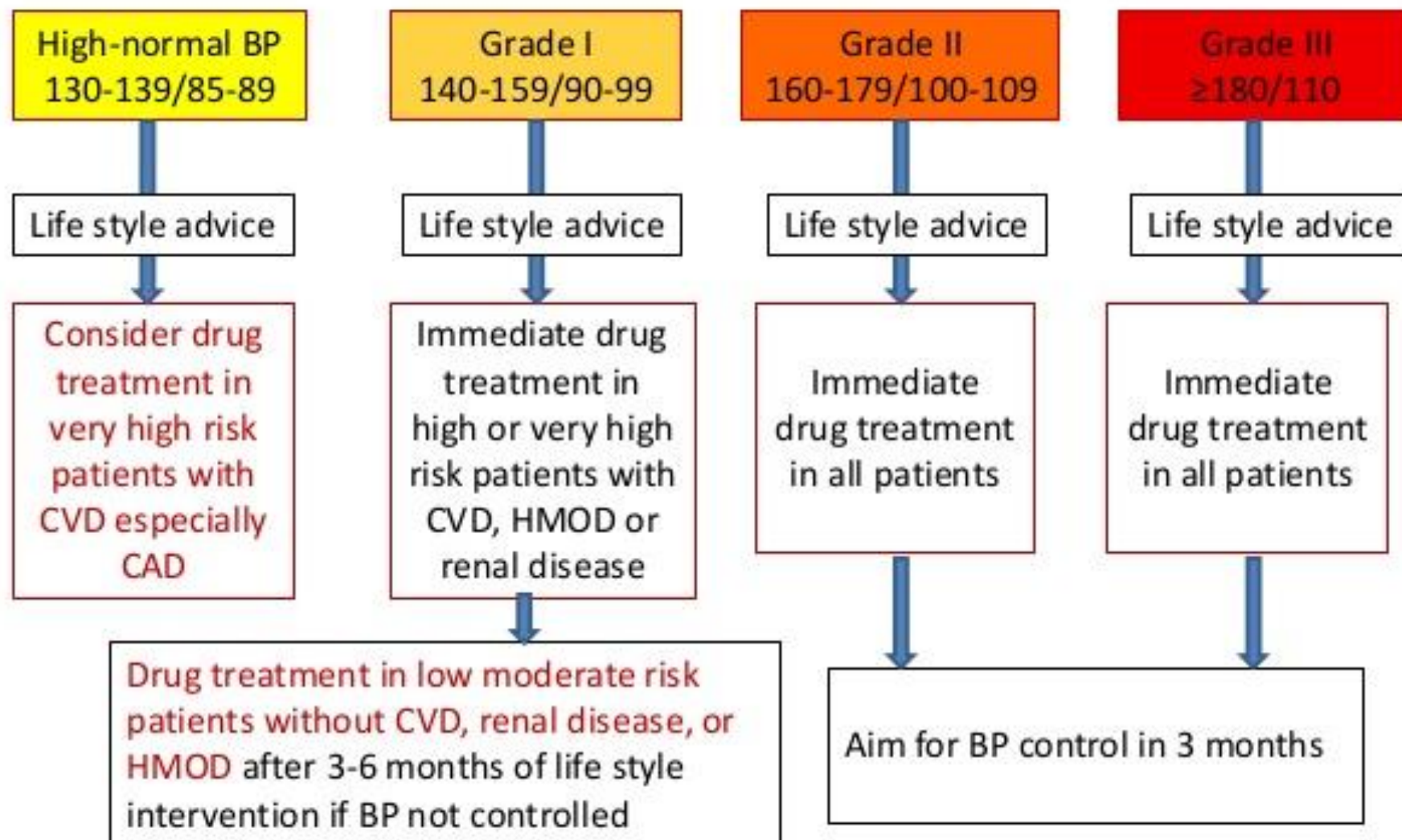
Major Novelties on antihypertensive treatment

- Increasing dose of initial monotherapy.
- Monotherapy substitution.
- “Stepped - care” approach (monotherapy with subsequent addition of other drugs).
- Initial two drug combination treatment.
- Use of single pill combinations.

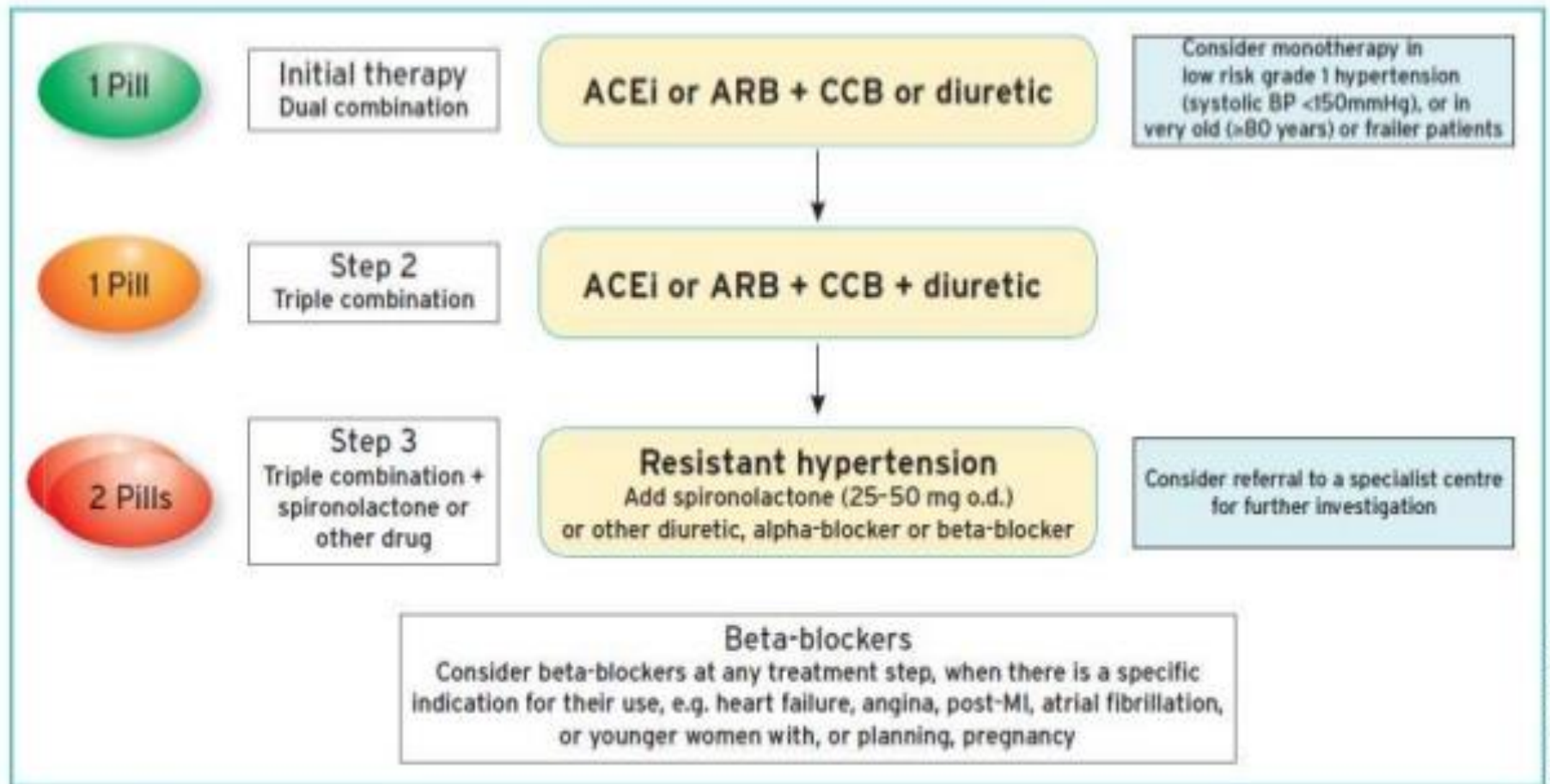
Rationale for initial two drug-combination therapy in most patients

- Greater BP reduction even vs maximum dose monotherapy.
- Reduced heterogeneity of the BP response to initial therapy.
- Steeper dose-response relationship with treatment up-titration.
- No/small increase in risk of hypotensive episodes (even in grade I hypertension).
- More frequent BP control after 1 year
 - Better adherence to treatment
 - Reduced therapeutic inertia
- Reduce CV events (grade I hypertension, HOPE-3)

Initiation of BP Lowering Treatment (Life style changes and medications) at different initial office BP levels



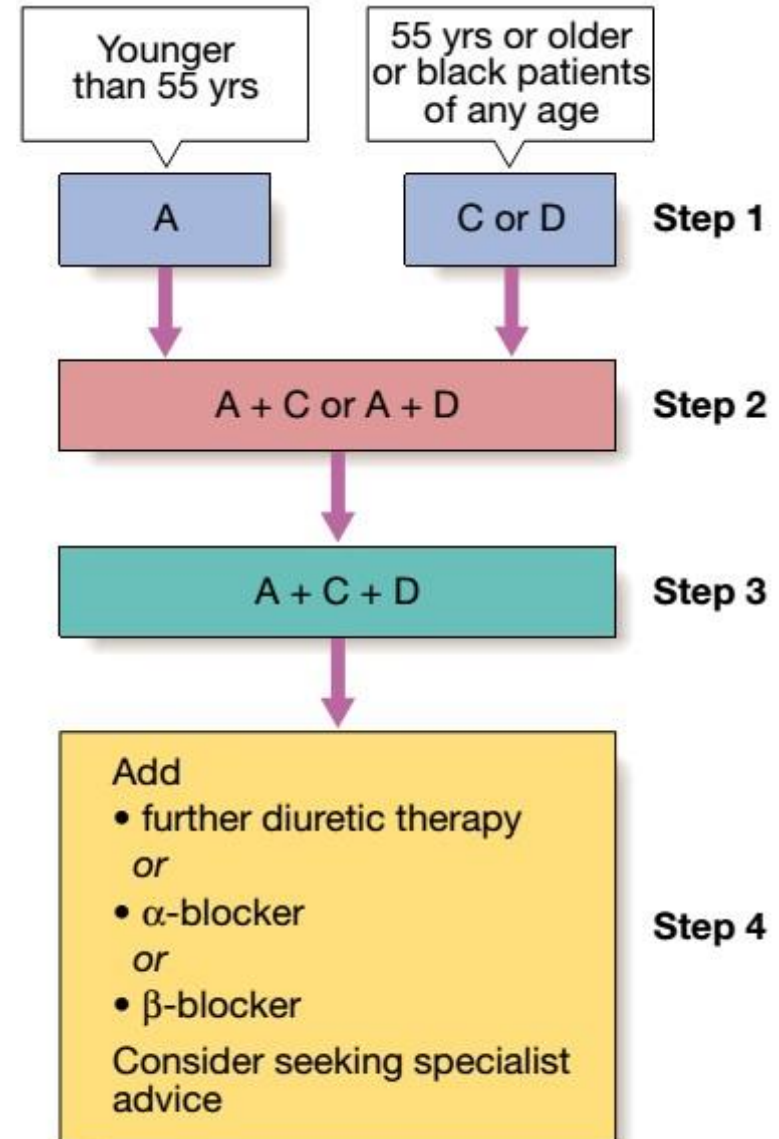
Core drug treatment strategy for uncomplicated hypertension



The core algorithm is also appropriate for most patients with HMOD, CVA, DM, or PAD

Pharmacological Management

- The drugs commonly used to treat HT are
 - **Alpha-blockers**
 - **Aldosterone antagonists**
 - **Angiotensin-converting enzyme inhibitors**
 - **Angiotensin II receptor blockers**
 - **Beta-blockers**
 - **Calcium channel blockers**
 - **Centrally acting**
 - **Diuretics**
 - **Renin inhibitors**
 - **Vasodilators**



Pharmacological Management

Drug	Dose	Conditions favouring use	Cautions/contraindications
Alpha-blockers			
Doxazosin	1.0–16 mg daily	Benign prostatic hypertrophy	Postural hypotension, urinary incontinence
Indoramin	25–100 mg x2 daily		
Phenoxybenzamine	1 mg/kg i.v. over >2 h	Phaeochromocytoma crisis	Profound hypotension
Phentolamine	2.0–5.0 mg i.v.		
Aldosterone antagonists			
Spironolactone	50–400 mg daily	Primary hyperaldosteronism, heart failure	Hyperkalaemia
Eplerenone	50–100 mg daily		
Angiotensin-converting enzyme inhibitors			
Enalapril	5.0–40 mg daily	<55 years old, Caucasian, heart failure or left ventricular dysfunction, myocardial infarction or cardiovascular disease, diabetic nephropathy, chronic renal disease, stroke secondary prevention	Renal failure (monitor electrolytes), peripheral vascular disease (if renovascular disease), pregnancy
Lisinopril	2.5–40 mg daily		
Perindopril	2.0–8.0 mg daily		
Ramipril	1.25–10 mg daily		

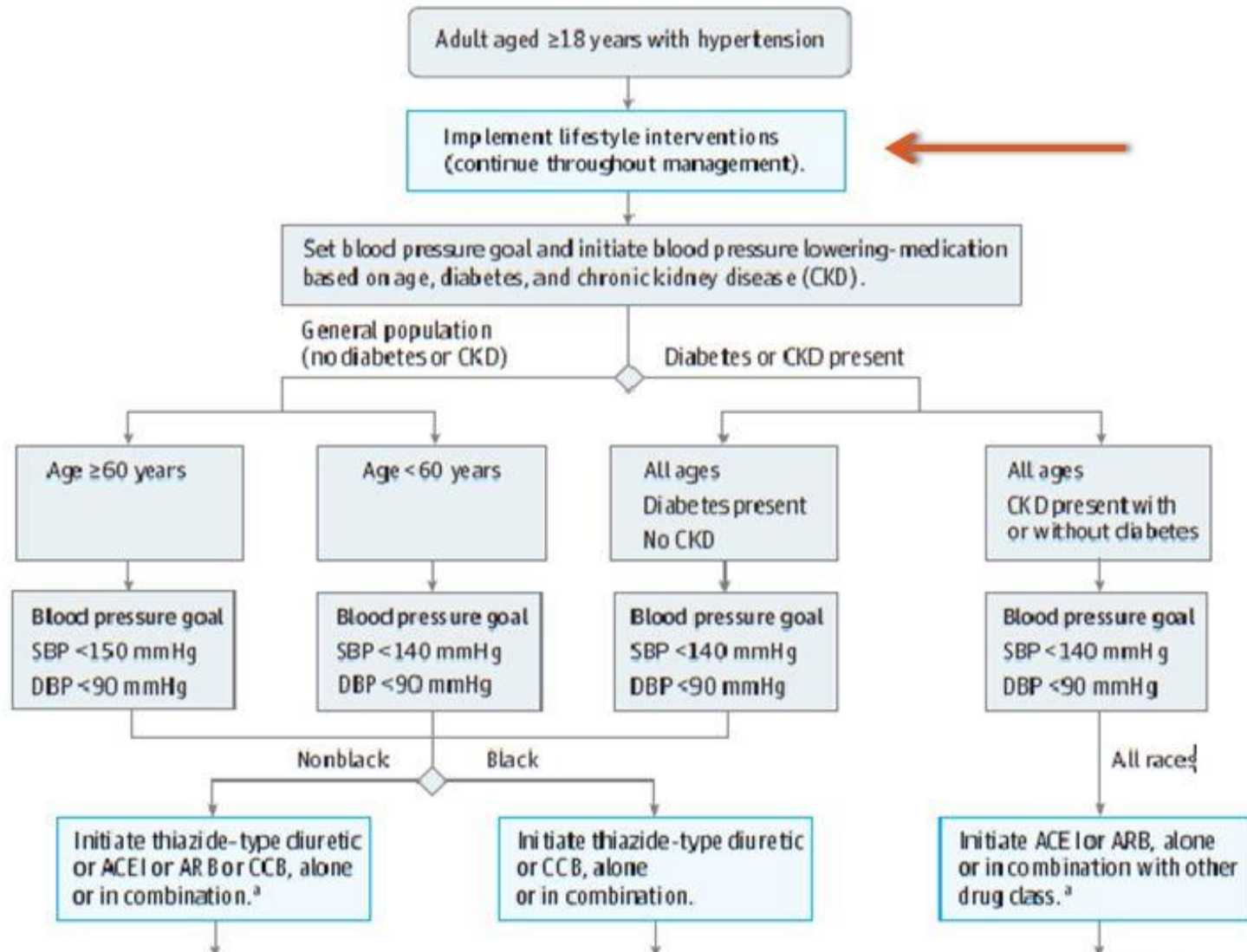
Pharmacological Management

Drug	Dose	Conditions favouring use	Cautions/contraindications
Angiotensin II receptor blockers			
Losartan	50–100 mg daily	ACE inhibitor intolerant, <55 years old, Caucasian, hypertension with LVH, heart failure or left ventricular dysfunction, myocardial infarction, diabetic nephropathy, chronic renal disease	Renal failure (monitor electrolytes), peripheral vascular disease (if renovascular disease), pregnancy
Candesartan	2.0–32 mg daily		
Valsartan	40–320 mg daily		
Olmesartan	10–40 mg daily		
Telmisartan	40 mg daily		
Beta-blockers			
Atenolol	25–100 mg daily	Coronary heart disease (post myocardial infarction or angina), heart failure (bisoprolol and carvedilol)	Diabetes, peripheral vascular disease, asthma/COPD, heart block, unstable heart failure
Bisoprolol	1.25–20 mg daily		
Carvedilol	12.5–50 mg daily		
Labetalol	100–200 mg ×2 daily (max. 2.4 g/day)	Hypertension in pregnancy	
Calcium channel blockers			
Amlodipine	5.0–10 mg daily	>55 years, black patients, angina	Bradycardia, heart block, heart failure, beta-blockers (verapamil)
Nifedipine (long acting)	20–90 mg daily		
Diltiazem (long acting)	90–180 mg ×2 daily		
Verapamil	120–240 mg ×2 daily		

Pharmacological Management

Drug	Dose	Conditions favouring use	Cautions/contraindications
Centrally acting			
Methyldopa	250 mg–1 g ×3 daily	Hypertension in pregnancy, breastfeeding	Monitor blood counts and liver function tests
Moxonidine	200–600 µg daily	Resistant hypertension, insulin resistance	Renal or heart failure, glaucoma, angioedema, bradycardia
Diuretics			
Bendroflumethiazide	2.5 mg daily	>55 years, black patients, heart failure, stroke secondary prevention	Gout, diabetes, hypokalaemia
Chlortalidone	25 mg daily		
Furosemide	40–80 mg daily	Heart failure, renal dysfunction	Hypokalaemia
Renin inhibitors			
Aliskiren	150–300 mg daily	Resistant hypertension	Renal failure, pregnancy
Vasodilators			
Hydralazine	25–50 mg ×2 daily	Black patients, heart failure (when combined with nitrates)	SLE
Minoxidil	5.0–50 mg daily	Severe hypertension (with a diuretic and beta-blocker)	Pregnancy
Sodium nitroprusside	0.3–5 µg/kg per min i.v.	Hypertensive crisis	Needs intra-arterial BP monitoring, avoid prolonged use

JNC 8: Treatment Algorithm



What is the best effective evidence-based treatment strategy to improve BP control

- Use combination treatment in most patients, especially in the context of lower BP targets
- Use single-pill-combination therapy in most patients to improve adherence to treatment
- Above treatment algorithm, that is simple, applies extensively and is pragmatic.
- Exceptions: BP in the high normal range and in frail older patients

Hypertensive Crisis: Emergency vs Urgency

- Hypertensive emergency^{1,2}
 - Evidence of end-organ damage
 - Kidney
 - Retina
 - Heart
 - Brain
 - About 500,000 cases annually in US due to high prevalence of HTN
- Hypertensive urgency^{1,2}
 - No evidence of end-organ damage
 - BP reduction over several hours to days
 - Usually treated with oral antihypertensives

1. Mansoor GA, Frishman WH. *Heart Dis.* 2002;4:358-371.

2. Varon J, Marik PE. *Chest.* 2000;118:214-227.

Definitions

- **Hypertensive crisis**
 - A hypertensive urgency or emergency
- **Hypertensive emergency**
 - Characterized by severe elevations in BP ($>180/120$) complicated by evidence of impending or progressive *target organ dysfunction*
- **Hypertensive urgency**
 - Severe elevations in BP without progressive *target organ dysfunction*
- **Malignant hypertension**
 - Old term, varying definitions, unlikely to find in recent guidelines
 - Severely elevated blood pressure with retinal hemorrhages or papilledema vs. encephalopathy or acute nephropathy

DEFINITIONS

- **HYPERTENSIVE EMERGENCY**

BP elevation is associated with ongoing
neurological, myocardial, hematological or renal
TARGET ORGAN DISEASE (TOD)

- **HYPERTENSIVE URGENCY**

- potential for TOD is great & likely to occur if BP is not controlled.

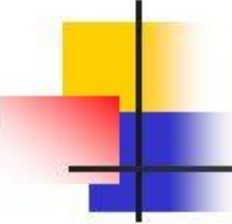
- occurs on chronic stable complication

- . Stable angina

- . Old MI

- . CCF, CRF

- . TIA, old CVA



Urgency vs. Emergency

■ **Urgency**

- No need to acutely lower blood pressure
- May be harmful to rapidly lower blood pressure
- Death **not** imminent

■ **Emergency**

- Immediate control of BP essential
- Irreversible end organ damage or death within hours

HTN CRISIS: TREATMENT

HTN URGENCY

OUTPATIENT or

SAME-DAY OBSERVATION

Oral antihypertensives

**GOAL: no more than
25% MAP reduction in
1st 24 hours**

HTN EMERGENCY

INPATIENT or

INTENSIVE CARE

Parenteral drugs

**GOAL: 10% MAP
reduction in 1st hour;
15% reduction in next
2-3 hours**

TREATMENT FOR HYPERTENSIVE EMERGENCIES

Goal:

- Lower MAP no greater than 20-25% in a few hours
- Maintain DBP 100-110 mmHg
- Too rapid or too much → *cerebral hypoperfusion*

Continuous BP monitoring

IV Vasodilators

Sodium Nitroprusside

Nicardipine

Nitroglycerin

Enalaprilat

Fenoldopam

Hydralazine

IV Adrenergic Inhibitors

Labetalol

Esmolol

Phentolamine

Approach to: **possible hypertensive emergency**

Specific condition causing/associated with hypertension?

- Pregnancy
- Aortic dissection
- SCAPE (sympathetic crashing acute pulmonary edema)
- Type-I myocardial infarction (plaque rupture MI)
- Cerebrovascular accident (CVA)
- Scleroderma renal crisis
- Sympathomimetic intoxication (e.g. cocaine)
- Pheochromocytoma
- HTN due to uncontrolled pain/anxiety (e.g. post-intubation HTN)

Yes

Secondary hypertension

Evaluate & treat using *specific* strategies unique to the underlying condition (covered in other chapters)

No

Meets criteria for hypertensive emergency?

[1] Target organ damage

- Acute kidney injury
- Type-II myocardial infarction
- Hypertensive encephalopathy
- Pulmonary edema

[2] Severe hypertension

- MAP at least over ~135 mm (varies, depending on patient's baseline Bp & acuity of Bp rise)
- Among patients with chronic hypertension, the Bp should be well *above* the patient's baseline

Yes

Primary hypertensive emergency

- Immediate Bp control required using IV antihypertensives (e.g. nicardipine infusion).

No

Not a hypertensive emergency

- No need for immediate Bp management.
- If the patient is having concerning symptoms, then look for an alternative explanation.

Goals of Tx: Hypertensive Emergency

- Altered auto-regulation is present
- End-organ damage is already present
- Excessive correction can worsen damage
- Use IV infusion of a short acting, titratable medication
- Use intra-arterial BP monitoring if severe clinical manifestations or labile BP
- Goal: ↓DBP 15-20% or to about 110mmHg over 1-2hr
 - If dissection: this should be done in 5-10 minutes

Parenteral Drugs for Treatment of Hypertensive Emergencies based on JNC 7

Drugs	Dose	Onset	Duration of Action
Sodium nitroprusside	0.25-10 μ g/kg/min	Immediate	1-2 minutes after infusion stopped
Nitroglycerin	5-500 μ g/min	1-3 minutes	5-10 minutes
Labetolol HCl	20-80 mg every 10-15 min or 0.5-2 mg/min	5-10 minutes	3-6 minutes
Fenoldopan HCl	0.1-0.3 μ g/kg/min	<5 minutes	30-60 minutes
Nicardipine HCl	5-15 mg/h	5-10 minutes	15-90 minutes
Esmolol HCl	250-500 μ g/kg/min IV bolus, then 50-100 μ g/kg/min by infusion; may repeat bolus after 5 minutes or increase infusion to 300 μ g/min	1-2 minutes	10-30 minutes

Parameter	Severe hypertension (Urgency)		Hypertension emergency
	Asymptomatic	Symptomatic	
Blood pressure	> 180/110 mmHg	> 180/110 mmHg	Usually $\geq$ 220/140 mmHg
Symptoms	Headache, anxiety, often asymptomatic	Severe headache, shortness of breath, nose bleeding	Shortness of breath, chest discomfort, nocturia, dysarthria, weakness, altered consciousness
Examination	No TOD, no clinical cardiovascular disease	TOD; clinical cardiovascular disease present, stable	Encephalopathy, pulmonary edema, renal insufficiency, cerebrovascular accident, cardiac ischemia
Therapy	Observe 1-3 hours, initiate or resume medication, increase dosage of inadequate agent	Observe 3-6 hours, lower BP with short-acting oral agent, adjust current therapy	Baseline laboratory tests, intravenous line, monitor BP, may initiate parenteral therapy in emergency room
Plan	Arrange follow-up within 3-7 days	Arrange follow-up evaluation in less than 72 hours	Immediate admission to critical care unit, treat to initial goal BP, additional diagnostic studies

TOD: Target organ damage

Order Treatment

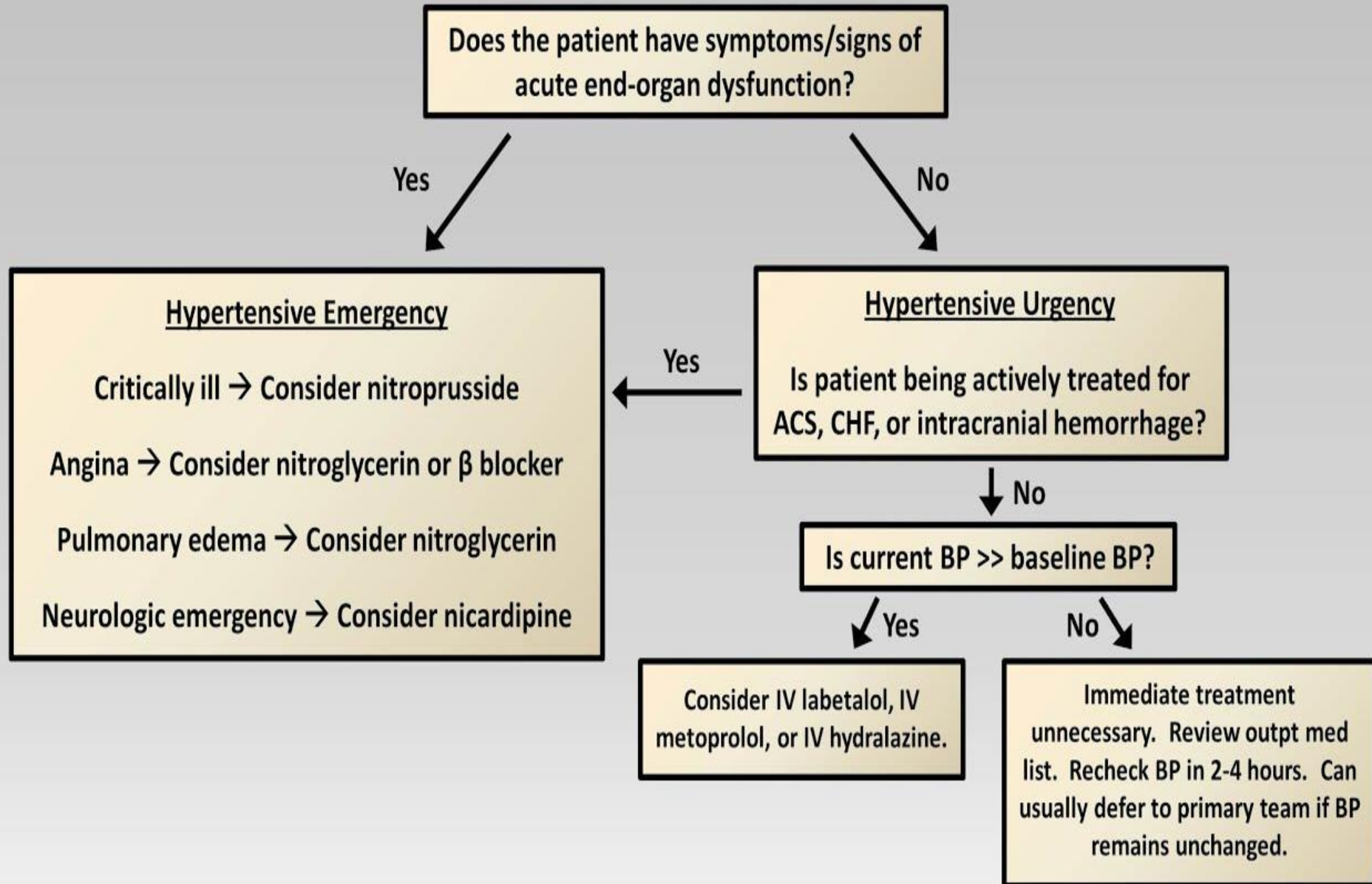


Table 2. Symptoms Associated with Hypertension

Hypertensive Emergency	Blood Pressure Target	Treatment
Aortic Dissection	Reduce SBP to 100–120 mmHg Lower heart rate to <60 bpm	1. Labetalol or Esmolol 2. Nitroprusside or nicardipine after beta-blocker
Acute Myocardial Infarction	Reduce BP < 160 mmHg	Nitroglycerin Labetalol or metoprolol (if no heart failure)
Acute Pulmonary Edema	Reduce BP by 20%–30%	Nitroglycerin sublingual/topical/IV or Nitroprusside IV or Nicardipine IV and Furosemide if volume overloaded
Acute Renal Failure	Acute reduction in BP by < 20%	Nicardipine IV or Clevidipine IV
Hypertensive Encephalopathy	Reduce BP 20–25% in first hour	Nicardipine IV or Clevidipine IV or Labetalol IV
Subarachnoid Hemorrhage	Reduce SBP to <160 mmHg	
Intracerebral hemorrhage	SBP goal 140–180 mmHg	
Acute Ischemic Stroke	Receiving tPA: Reduce <185 mmHg with goal 140–150 mmHg No tPA: Reduce to <220/120 mmHg	

Malignant hypertension

- Patient should be hospitalized immediately in case of
 - severe hypertension (diastolic pressure >140 mmHg),
 - malignant hypertension (grades 3 or 4 retinopathy),
 - hypertensive encephalopathy
 - Or with severe hypertensive complications, such as cardiac failure,
- BP should **not be reduced too rapidly** - cerebral, renal, retinal or myocardial infarction
- Reduce the diastolic blood pressure to **100–110 mmHg** over 24–48 hours.
 - Achieved with oral medication, e.g. **amlodipine**.
- Then BP can be normalized over the next 2–3 days.
- When rapid control of blood pressure is required (e.g. in an aortic dissection), the agent of choice is IV sodium nitroprusside or labetalol
- The infusion dosage must be titrated against the blood pressure response.

Treatment Continued

■ Hypertensive Emergency:

- Goal: Lower Diastolic BP to approximately 100-105 over 2-6 hours; max initial fall not to exceed 25%
 - More aggressive decrease can lead to ischemic stroke and myocardial ischemia
- If focal neurological sx present → obtain MRI to r/o acute stroke (rapid BP correction contraindicated)
- Parenteral antihypertensives (IV Drip) recommended over oral agents in hypertensive emergency

Hypertension in Pregnancy

- There are three types of hypertension seen in pregnant women:
 - Chronic or pre-existing hypertension
 - Gestational hypertension
 - Pre-eclampsia and eclampsia
- 1st line therapy: **Methyldopa** (no adverse effects on the fetus)
- 2nd line agents: **Nifedipine and labetalol**.
- The target blood pressure should be <150/100 mmHg
- **Gestational hypertension:** >140/90 mmHg in the **2nd trimester** in a previously normotensive woman.
 - risk of developing **pre-eclampsia**

Pre-eclampsia

- Multi-system disorder that occurs after 20 weeks' gestation consisting of:
 - Hypertension
 - Oedema
 - Proteinuria (>0.3 g/24 hours).
- These patients should be admitted and treated for hypertension with regular
 - BP measurements (4 times daily)
 - blood tests 2–3/week.
 - close fetal monitoring due to the risks of placental insufficiency and intrauterine growth retardation.
- Patients who progress to **eclampsia (convulsions)** and/or **HELLP** (haemolysis, elevated liver enzymes, low platelet count) syndrome should be admitted to a critical care unit (CCU)
 - intravenous hydralazine, labetalol, and magnesium sulphate (for convulsions)
 - Prompt delivery.

Prognosis

- Depends on a number of features:
 - Level of blood pressure
 - Presence of target-organ changes (retinal, renal, cardiac or vascular)
 - Co-existing risk factors for cardiovascular disease, such as hyperlipidaemia, diabetes, smoking, obesity, male sex
 - Age at presentation.
 - Several studies have confirmed that the treatment of hypertension, even mild hypertension, will reduce the risk not only of stroke but of coronary artery disease as well.
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Thank You