

ACC Core Curriculum Hypertension

Janet B. Long, MSN, ACNP, CLS, FAHA, FNLA

Objectives

- Discuss various definitions of hypertension
- Discuss Etiology and Pathogenesis of hypertension
- Discuss the clinical approach to assessment and treatment

Hypertension Definitions

- **Hypertension** – Systolic BP of 140 mm Hg or greater and/or a DBP of 90 mm Hg or greater in persons not taking antihypertensive medication. JNC VII
- **Pre-hypertension** – SBP 120-139 mm Hg or DBP 80-89 mm Hg. It is not a disease category. Designation to identify individuals at high risk of developing HTN.
- **Isolated systolic** hypertension (ISH) – primarily in elderly SBP of 140 mm Hg or greater in the presence of a DBP of 90 mg Hg or lower.

Hypertension Definitions

- **Essential, primary, or idiopathic HTN** – High BP due neither to secondary causes nor to a mendelian (monogenetic) disorder, accounts for 90% of all cases.
- **Secondary HTN** – High BP caused by a specific potentially curable disorder
- **Refractory or resistant hypertension** – BP of $\geq 140/90$ mm Hg despite an optimal three drug regimen that includes a diuretic and that has been given at least one month to take effect.

Hypertension Definitions

- **Spurious HTN (pseudohypertension)** – artefactually elevated BP obtained by indirect cuff measurement secondary to reduced arterial compliance.
- **Hypertensive crisis** – DBP >120 mm Hg.
- **Hypertensive emergency** – If the crisis is associated with acute or ongoing target organ damage. If not it is called **Hypertensive urgency**.
- **Malignant HTN** – HTN emergency associated with papilledema.
- **Accelerated HTN** – Hypertensive emergency associated with retinal hemorrhages and exudates (grade 3 retinopathy).

Incidence and Prevalence

- 65% of the population in the 65 to 74 y/o
- SBP increases with advancing age throughout life
- DBP tends to plateau or fall after age 60
- Increased Pulse Pressure (PP) - ↓ DBP in the presence of ↑ SBP – greater CVD risk than SBP alone.

Etiology & Pathogenesis

Etiology & Pathogenesis

Essential HTN – 90% of all cases of HTN

- Families
- Collection of genetically based diseases
- ↑ SNS activity
- ↑ production of sodium retaining hormones and vasoconstrictors (endothelin and thromboxane)
- High sodium intake
- Inadequate intake of dietary potassium and calcium
- ↑ or inappropriate renin secretion
- Deficiencies of vasodilators – prostaglandins and nitric oxide
- Congenital abnormalities of the resistance vessels
- Diabetes Mellitus
- Insulin resistance
- Obesity
- ↑ activity of vascular growth factors
- Altered cellular ion transport

Etiology & Pathogenesis

■ Genetics

- Association HTN and dyslipidemia
- Association HTN and type 2 diabetes (2x as common) even stronger in blacks and Mexican Americans.

■ Inherited CV Risk Factors

- HTN, Insulin resistance, dyslipidemia, obesity associated with microalbuminuria, high uric acid levels, hypercoagulability, and accelerated atherosclerosis.

Etiology & Pathogenesis

■ Sympathetic Nervous System

- ↑ SNS ↑ BP stimulation of heart, peripheral vasculature, and kidneys, ↑ cardiac output, ↑ vascular resistance, and fluid retention
- Autonomic imbalance (↑ sympathetic tone accompanied by ↓parasympathetic tone)
- Cardia Study – association of ↑HR and development of HTN

Etiology & Pathogenesis

Vascular Reactivity

- ↑ sensitivity to norepinephrine
- ↑ peripheral vascular resistance
- ↑ BP

Etiology & Pathogenesis

Vascular Remodeling

- PVR elevated in HTN
 - Alterations in structure
 - Mechanical properties
 - Function of small arteries
- Medications normalize resistance vessel structure
 - ACE
 - ARB
 - CCB
- BB do NOT

Etiology & Pathogenesis

Arterial Stiffness

- SBP and PP ↑ with age
- Endothelial dysfunction
- ↓ NO synthesis ↑ wall thickness of conduit vessels ie: common carotid artery
- Other factors
 - Estrogen deficiency
 - High dietary sodium intake
 - TOB use
 - ↑ homocysteine
 - Diabetes

Etiology & Pathogenesis

- ↑ arterial stiffness contributes to wide PP
- Pulse wave velocity increased in older persons due to central arterial stiffening.
- Pulse wave reaches aortic valve before closure, leading to higher SBP, PP and afterload and a decreased DBP – may compromise coronary perfusion.
- ↑ SBP ↑ cardiac metabolic requirements – LVH and HF
- PP linked to advanced atherosclerotic disease and CVD events (fatal and nonfatal MI and stroke)
- PP better predictor of CVD risk than SBP or DBP alone

Etiology & Pathogenesis

- Vasodilator drugs ↓ stiffness of peripheral arteries, ↓ pulse wave reflection and augmentation of central aortic and LV systolic pressure
- ACE
- CCB

Etiology & Pathogenesis

Renin-Angiotensin-Aldosterone System

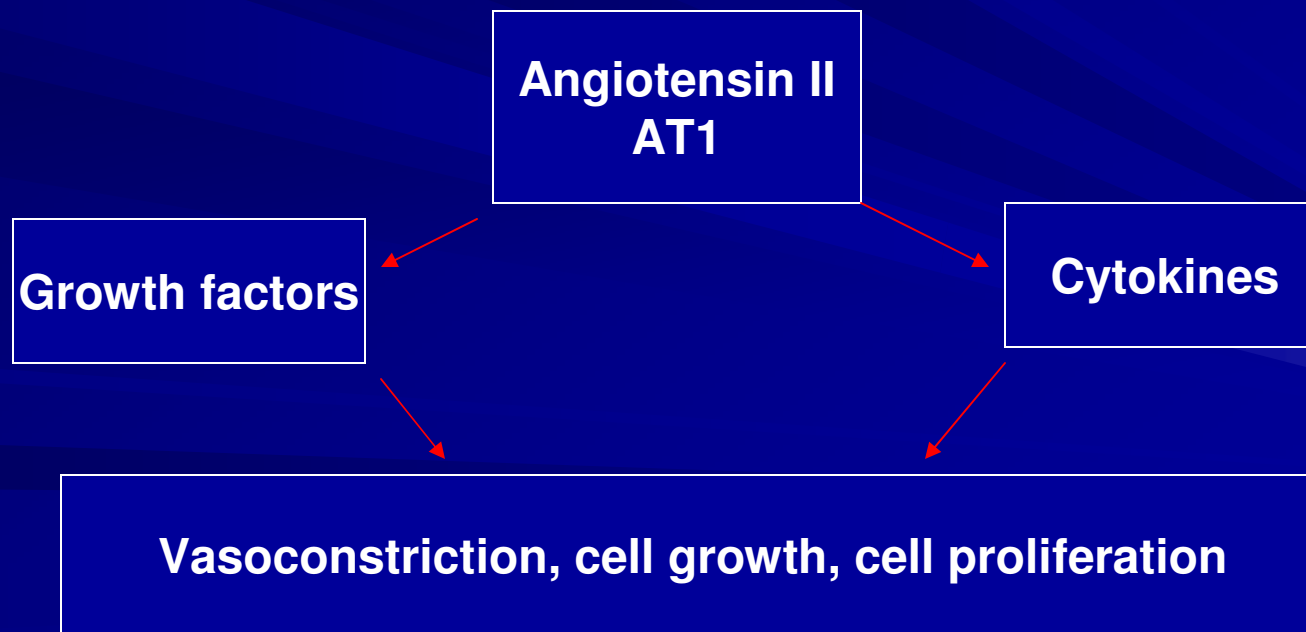
■ Angiotensin II ↑ BP

- Constriction of resistance vessels
- Stimulation of aldosterone synthesis and release and of renal tubular sodium reabsorption (directly and indirectly via aldosterone)
- Stimulation of thirst and release of antidiuretic hormone
- Enhancement of sympathetic outflow from the brain

Etiology & Pathogenesis

Renin Angiotensin Aldosterone System

- Angiotensin II induces cardiac and vascular cell hypertrophy and hyperplasia



Etiology & Pathogenesis

AT 1

- Vasoconstriction, cell growth and cell proliferation
- Antinatriuretic
- Free radicals
- Inhibits PAI-1 and other growth pathways

AT 2

- Vasodilation, antigrowth, cell differentiation
- Natriuretic
- Produces nitric oxide (NO) neutralizes free radicals
- Does not inhibit PAI 1

Mechanisms of Angiotensin II-Oxidant-mediated Vascular Damage

Angiotensin II



Oxidant Stress



Endothelial Dysfunction ↓ NO



PAI 1



Thrombosis



MCP-1, VCAM,
ICAM,
Cytokines



Inflammation



Endothelin
Prostanoids



Vasoconstriction



Growth Factor
Matrix



Vascular Lesion
Formation and
Remodeling

Etiology & Pathogenesis

Aldosterone

Deleterious effects

- Brain, ↑ salt appetite, sympathetic outflow, BP
- Cardiac hypertrophy and fibrosis
- Endothelial dysfunction
- Renal arteriopathy with proteinuria
- Vascular inflammation with extracellular matrix deposition
- Fibrosis and increased stiffness
- All often occur in hypertension
- Low sodium diets ↓ the negative effect on cardiac and vascular pathology

Primary Aldosteronism (PA)

- Results from ↑ production of aldosterone, may account for as many as 5-13% of all cases of HTN – most prevalent form of secondary HTN
- Results in suppressed plasma renin activity, metabolic alkalosis, potassium losing diathesis (sometimes leading to hypokalemia; ≤ 3.5 meq/l) and HTN - variable

Primary Aldosteronism

- All patients with severe or resistant HTN
- Poorly controlled BP on 3 or more meds
- No other obvious secondary causes
- Screen for primary aldosteronism
 - Spontaneous hypokalemia $K \leq 3.5$ meq
 - Or inappropriate hypokalemia $K \leq 3.0$ meq
 - While on conventional doses of diuretics
 - Excessive doses of K replacement
 - Important – Hypokalemia is not always present

Screen for Primary Aldosteronism

When to Consider Screening for Primary Aldosteronism

- HTN and hypokalemia
- Resistant HTN
- Adrenal incidentaloma and HTN
- Whenever considering secondary HTN

Morning blood sample in seated ambulant patient

- Plasma aldosterone concentration (PAC)
- Plasma renin activity (PRA)

↑PAC

↓PRA

PAC/PRA ratio ≥ 20 ng/dl per ng/ml/h

And

PAC ≥ 15 ng/dl

Investigate for

Primary Aldosteronism

Ratio > 70 with PAC of ≥ 15 and a PRA ≤ 1 ng/ml/h diagnostic

Etiology & Pathogenesis

Aldosterone

- Many do not manifest low serum K (not reliable screening test)

Etiology & Pathogenesis

Endothelin

- Potent vasoactive peptide produced by endothelial cells – both vasoconstrictor and vasodilator properties.
- ↑ endothelin levels in some HTN –
 - African Americans
 - Transplant HTN
 - Endothelial tumors
 - Vasculitis

Etiology & Pathogenesis

Endothelin

- Endothelin receptor antagonists reduce BP and PVR in both normotensive and mild to mod essential HTN
- This drug class has been discontinued due to toxicity (teratogenecity, testicular atrophy, and hepatotoxicity)
- They are used to treat pulmonary HTN

ARS Question

- Which of the following system does not contribute to hypertension?
 1. Sympathetic nervous system
 2. Aldosterone
 3. Vasodilation
 4. Renin-angiotension-aldosterone system

Clinical Approach

Diagnostic Work Up

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CV Risk Factors

- Hypertension
- Cigarette smoking
- Obesity (BMI >30)
- Physical inactivity
- Dyslipidemia
- Diabetes Mellitus
- Microalbuminuria or GFR <60 ml/m
- Age (>55 y men, >65 y women)
- Family History of premature CVD (men <55 y/women <65 y)

Target Organ Damage

- Heart
 - LV hypertrophy
 - Angina or prior MI
 - Prior coronary revascularization
- Brain
 - Stroke or TIA
- Chronic Kidney disease
- Peripheral arterial disease
- Retinopathy

Evidence of Secondary HTN

General

- Abrupt onset of HTN
- Onset of HTN in persons <25 y/o or >60 y/o
- Refractory or resistant HTN
- Episodes of hypertensive crisis
- Sudden worsening of BP control
- Specific findings from screening data.
- Resistant HTN

Causes of Secondary HTN

Systolic and Diastolic

- **Pregnancy-induced HTN**
- **Sleep Apnea**
- **Coactation of the Aorta**
- **Neurologic Disorders**
 - **Dysautonomia**
 - **Increased Intracranial pressure**
 - **Obstructive Sleep Apnea**
 - **Quadriplegia**
 - **Lead Poisoning**
 - **Guillain-Barré Syndrome**
- **Postoperative HTN**
- **Drugs and Chemicals**
 - **Cyclosporine**
 - **Ethanol**
 - **Oral Contraceptives**
 - **Glucocorticoids**
 - **Mineralocorticoids, including Licorice and Carbenoxolone**
 - **Sympathomimetics**
 - **Tyramine and Monoamine Oxidase Inhibitors**
 - **Erythropoietin**
 - **Antidepressants**
 - **Appetite Suppressants**
 - **Nonsteroidal Anti-inflammatory agents**
 - **Nasal Decongestants**
 - **Phenothiazines**

Causes of Secondary HTN

Systolic and Diastolic HTN

Renal

- Renal Parenchymal Ds.
 - Chronic Nephritis
 - Polycystic Ds.
 - Collagen Vascular Ds
 - Diabetic Nephropathy
 - Hydronephrosis
- Renal Vascular Ds
- Renal Transplantation
- Renin Secreting Tumors

Endocrine

- Adrenal
 - Primary aldosteronism
 - Overproduction of 11-deoxycorticosterone (DOC), 18-hydroxy-DOC, and other Mineralocorticoids
 - Congenital Adrenal Hyperplasia
 - Cushing Syndrome
 - Pheochromocytoma
 - Extra Adrenal Chromaffin Tumors
 - Hyperparathyroidism
 - Acromegaly

Causes of Secondary HTN

Isolated Systolic HTN

- Aging, with associated Aortic Rigidity
- Increased Cardiac Output
 - Thyrotoxicosis
 - Anemia
 - Aortic Valvular insufficiency
- Decreased Peripheral Vascular Resistance
 - Arteriovenous shunts
 - Paget disease of bone
 - Beriberi

Identifiable Causes of Secondary HTN

| Diagnosis | Diagnostic Test |
|---|--|
| Chronic Kidney Ds | Estimated GFR |
| Coarctation of the aorta | CT angiography |
| Cushing syndrome and other glucocorticoid excess states including chronic steroid therapy | History/dexamethasone suppression test |
| Drug induced/related | History; drug screening |
| Pheochromocytoma | 24 hr urine metanephrine, normetanephrine and plasma metanephrine |
| Primary aldosteronism- other mineralcorticoid excess states | 24 hr. urine aldosterone level or specific measurements of ther mineralocorticoids |
| Renovascular HTN | Doppler flow study; magnetic resonance angiography |
| Sleep apnea | Sleep study with O2 saturation |
| Throid/parathyroid ds. | TSH; serum PTH |

Evaluation of Patient with Elevated BP

Key Historical Features

- Duration and severity of elevated BP
- Past experiences with antihypertensive medications
- Symptoms and signs of vascular disease
- Weight changes
- Other CV risk factors
- Current and past medications
- Dietary and exercise habits
- Use of tobacco, alcohol, drugs
- Psychosocial background
- Family history of HTN, diabetes, CVD and other disorders

In office BP Measurement

- Except in extreme BP elevation (SBP >210 mmHg, DBP >120 mm Hg or both) or elevated BP with evidence of ongoing target organ damage, HTN diagnosed when at least 2 separate readings obtained at least 1-2 weeks apart average $\geq 140/90$ mm Hg.

JNC VII Guidelines for Measurement of BP

Method

Brief Description

In-office



Two readings, 5 minutes apart, sitting in chair. Confirm elevated reading in contralateral arm.

Ambulatory BP monitoring

Indicated for evaluation of “white-coat” HTN. Absence of 10–20% BP decrease during sleep indicates increased CVD risk.

Self-measurement

Provides information on response to Rx. May help improve adherence to Rx and evaluate “white-coat” HTN.

BP=Blood pressure, CVD=Cardiovascular disease,
HTN=Hypertension

Chobanian AV et al. *JAMA*. 2003;289:2560-2572

Office BP Measurement

- Patients should be seated with back supported and arm bared and supported.
- The cuff should be at the level of the patient's heart
- Patients should refrain from smoking or ingesting caffeine for 30 minutes prior to measurement
- The patient should be allowed to rest in a quiet room for five minutes prior to measurement
- Appropriate cuff size (the bladder within the cuff should encircle at least 90% of the patient's arm) and calibrated equipment should be used.
- Record both systolic and diastolic BP's
- Two or more readings separated by at least two minutes should be averaged
- Measure the BP in both arms on the first visit if there is evidence of peripheral vascular disease
- Measure the BP in the standing and seated positions in elderly individuals, diabetics, and others in whom orthostatic hypotension is common.
- ACC SAP Book 4

When to Treat

- Presence of CV risk factors
- Elevated BP first office visit common – reassess
- Target organ damage – long standing – poorly controlled BP
- Hypertensive crisis SBP > 210 mmHg, DBP > 120 mm Hg or both)

Elderly

- Accuracy difficult in elderly –stiffening of arterial walls – falsely elevated
- Suspect pseudohypertension if no evidence of target organ damage is present
- Osler's maneuver – inflate BP above the SBP – if radial or brachial artery remains palpable – stiffening may be falsely elevating BP measurement

Laboratory Tests and Other Diagnostic Procedures

- ECG
- Urinalysis
- Blood glucose
- Hematocrit
- Potassium
- Creatinine
- Calcium
- Fasting Blood lipid profile (T.Chol, Trig, HDL, LDL)
- Optional
 - Urinary albumin excretion or albumin/creatinine ratio

Resistant HTN

- 10% of cases
- Defined as BP \geq 140/90 mmHg in the presence of 2 drug regimen that has been in effect for 4 weeks or more
- Up to 50% caused by non-adherence
- Clues
 - Missed appointments
 - Failure to manifest expected biological effects of medication such as decreased HR with BB tx.

Causes of Resistant HTN

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Drug Induced or Other causes

- Nonadherence
- Inadequate doses
- Inappropriate combinations
- NSAIDs; cyclo-oxygenase 2 inhibitors
- Cocaine, amphetamines, other illicit drugs
- Sympathomimetics (decongestants, anorectics)
- Oral contraceptives
- Adrenal steroids
- Cyclosporine and tacrolimus
- Erythropoietin
- Licorice (including some chewing tobacco)
- Selected over the counter dietary supplements (ephedra, ma huang, bitter orange)

■ Improper BP Measurement

■ Volume Overload and Pseudotolerance

- Excess Sodium intake
- Volume retention from kidney disease or heart failure
- Inadequate diuretic therapy

■ Associated Conditions

- Obesity
- Excessive alcohol intake

Treatment

JNC VII Guidelines for Management and Rx

| BP classification | SBP* mmHg | DBP* mmHg | Lifestyle modification | Initial drug therapy | |
|----------------------|-----------|-----------|------------------------|---|---|
| | | | | Without compelling indication | With compelling indications |
| Normal | <120 | and <80 | Encourage | | |
| Prehypertension | 120–139 | or 80–89 | Yes | No antihypertensive drug indicated. | Drug(s) for compelling indications. † |
| Stage 1 Hypertension | 140–159 | or 90–99 | Yes | Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination. | Drug(s) for the compelling indications. ‡ |
| Stage 2 Hypertension | ≥160 | or ≥100 | Yes | 2-drug combination for most† (usually thiazide-type diuretic and ACEI or ARB or BB or CCB). | Other antihypertensive drugs (as needed. |

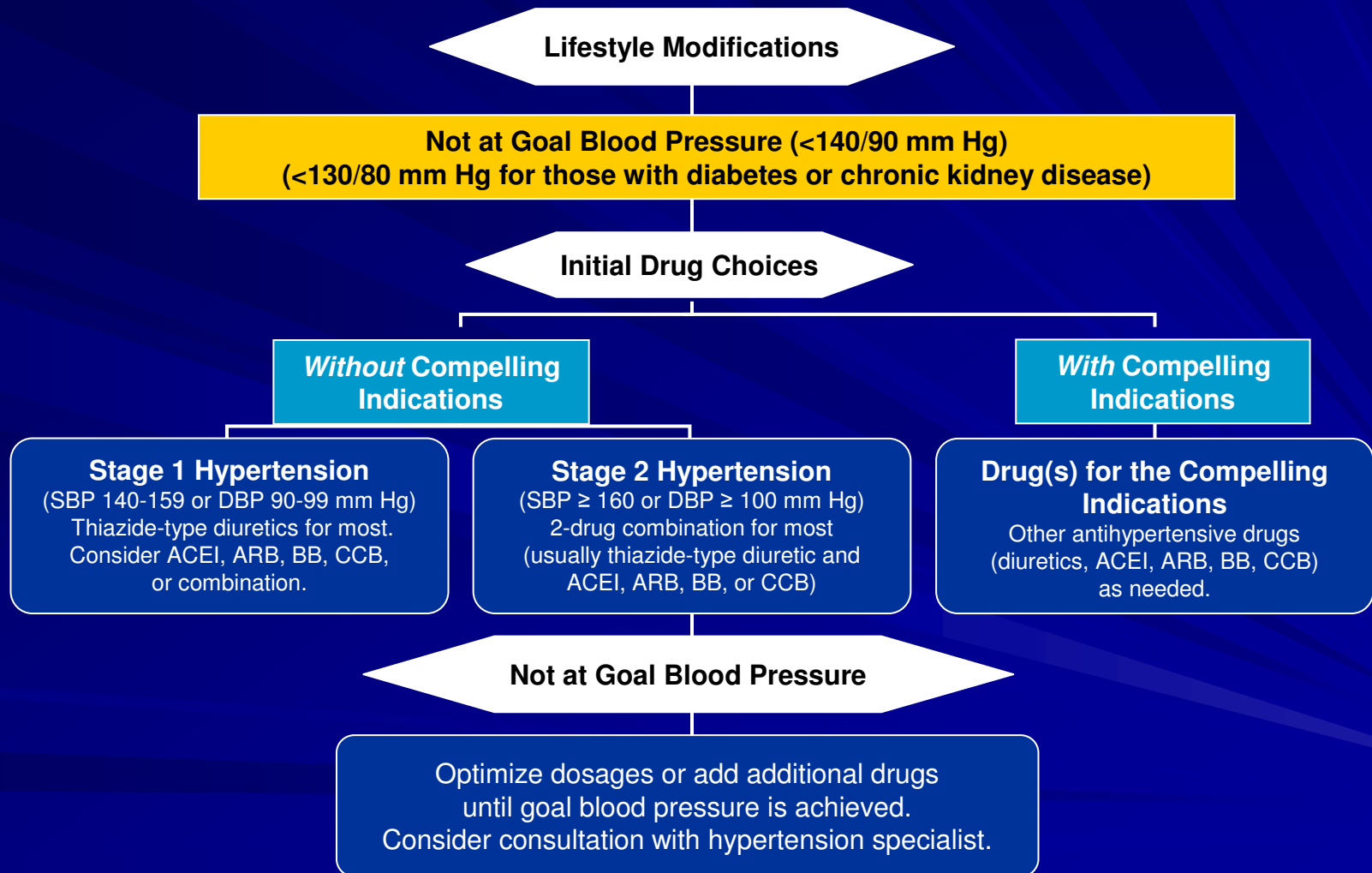
ACEI=Angiotensin converting enzyme inhibitor, ARB=Angiotensin receptor blocker, BB=β-blocker, BP=Blood pressure, CCB=Calcium channel blocker, DBP=Diastolic blood pressure, SBP=Systolic blood pressure

*Treatment determined by highest blood pressure category.

†Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

‡Treat patients with chronic kidney disease or diabetes mellitus to blood pressure goal of <130/80 mmHg.

JNC 7 Hypertension Treatment Algorithm



JNC VII Lifestyle Modifications for BP Control

| Modification | Recommendation | Approximate SBP Reduction Range |
|-------------------------------|--|--|
| Weight reduction | Maintain normal body weight (BMI=18.5-25) | 5-20 mmHg/10 kg weight lost |
| DASH eating plan | Diet rich in fruits, vegetables, low fat dairy and reduced in fat | 8-14 mmHg |
| Restrict sodium intake | <2.4 grams of sodium per day | 2-8 mmHg |
| Physical activity | Regular aerobic exercise for at least 30 min. most days of the week | 4-10 mmHg |
| Moderate alcohol | ≤2 drinks/day for men and ≤1 drink/day for women | 2-4 mmHg |

BMI=Body mass index, SBP=Systolic blood pressure

Chobanian AV et al. *JAMA*. 2003;289:2560-2572

Hypertension Therapies: JNC VII

| | |
|------------------------------------|--|
| Thiazide diuretics | Use with caution in patients with gout or hyponatremia |
| β-blockers | Avoid in patients with: <ul style="list-style-type: none">■ Asthma■ Reactive airways disease■ 2° or 3° heart block |
| ACEIs, ARBs | Contraindications <ul style="list-style-type: none">■ Pregnancy■ Women likely to become pregnant |
| ACEIs | Avoid in patients with history of angioedema |
| Aldosterone antagonists | Avoid in patients with serum potassium >5.0 mEq/L while not taking medication |

JNC VII Compelling Indications for Drug Classes

| Compelling Indication | Initial Therapy Options | Clinical-Trial Basis |
|-----------------------------|-----------------------------------|--|
| Heart Failure | Diuretic, BB, ACEI, ARB, Aldo ANT | MERIT-HF, COPERNICUS, CIBIS, SOLVD, AIRE, TRACE, Val-HeFT, RALES |
| Post-MI | BB, ACEI, Aldo ANT | ACC/AHA Post-MI Guideline, BHAT, SAVE, Capricorn, EPHEBUS |
| High CAD Risk | Diuretic, BB, ACEI, CCB | ALLHAT, HOPE, ANBP2, LIFE, CONVINCENCE |
| Diabetes Mellitus | Diuretic, BB, ACEI, ARB, CCB | NKF-ADA Guideline, UKPDS, ALLHAT |
| Chronic Kidney Disease | ACEI, ARB | NKF Guideline, Captopril Trial, RENAAL, IDNT, REIN, AASK |
| Recurrent Stroke Prevention | Diuretic, ACEI | PROGRESS |

ACEI=Angiotensin converting enzyme inhibitor, Aldo ANT=Aldosterone antagonist, ARB=Angiotensin receptor blocker, BB=b-blocker, CAD=Coronary artery disease, CCB=Calcium channel blocker, MI=Myocardial Infarction

Combination Therapy JNCVII

- Most patients require ≥ 2 drugs to achieve goals
- If blood pressure $>20/10$ mm Hg above goal, consider initiating treatment with 2 drugs
 - Separate prescriptions, or fixed-dose combinations
 - Using lower-than-standard doses of ≥ 2 drugs may improve efficacy and reduce adverse effects
- Use caution in patients at risk for orthostatic hypotension
 - Diabetes
 - Autonomic dysfunction
 - Older patients

Chobanian AV, et al. *JAMA*. 2003;289:2560-2572.

Law MR, et al. *BMJ*. 2003;326:1427-1434.

Follow Up and Monitoring JNC VII

- Repeat monthly visits until BP goal achieved
- More frequent visits
 - Stage 2 hypertension
 - Comorbid conditions
- Monitor serum potassium, creatinine
1-2 times/year
- When BP is at goal and stable, follow-up visits Q 3-6 months
 - More frequent visits for patients with chronic heart failure, diabetes, etc

ISHIB

Blood Pressure Goals

| Condition | mm Hg |
|---|---------|
| Diabetes | <130/80 |
| Nondiabetic kidney disease (proteinuria <1 g/d) | <140/90 |
| Nondiabetic kidney disease (proteinuria \geq 1 g/d) | <130/80 |
| High-risk* hypertensives | <130/80 |

***Beware of overemphasizing race as a criterion
for blood pressure control methods –
these goals are applicable to patients of all races***

*History of CVD event, stroke, TIA, evidence of target-organ damage (eg, LVH, microalbuminuria), CHD, or high-risk for CHD (eg, metabolic syndrome)

Adapted from Douglas JG, et al. *Arch Intern Med.* 2003;163:525-541.

Diuretics: Optimal Utilization

- Virtually indispensable when >2 nondiuretic drugs have been prescribed
- Monitor potassium closely if potassium-sparing diuretics are used in persons taking ACEI, ARBs, potassium supplements
- Must know kidney function level
 - EGFR $<$ mid 40s: use loop diuretic or metolazone
 - If furosemide used, dose at least twice daily
 - Conventional thiazide doses are likely to be ineffective, though higher doses 50-100 mg/d may work
 - EGFR $>$ mid 40s: use thiazide diuretic (can use metolazone)
 - Loop diuretics not as effective as thiazides in this setting

Aldosterone

Aldosterone

- Non-selective aldosterone antagonist
 - Spironolactone ↓ proinflammatory cytokines, chemokines
- Selective mineralcorticoid receptor antagonist
 - Eplerenone ↓ proinflammatory cytokines, chemokines
 - Prevents the ↑ aortic stiffness and pulse pressure widening

Angiotensin-Converting Enzyme Inhibitors

Advantages

- Proven renoprotective in type 1 diabetes and nondiabetic CKD
- Profoundly antiproteinuric
- Morbidity and mortality and symptomatic improvement in CHF patients
- Ventricular remodeling and mortality post-MI
- Risk of micro- and macrovascular disease in DM and vascular disease
- Risk of diabetes
- Tx for CCB-induced edema

Disadvantages

- Cough (~9%-20+%)
- Angioedema, more common in African-Americans
- Rare hyperkalemia
- Higher dose requirements in African-American, women, and/or obese persons
- BP-lowering effect very sensitive to level of dietary sodium intake
- ↑ Serum creatinine
- Rise in creatinine reflects ACEI MOA; consider lowering dose or stopping if creatinine increases >30%

Angiotensin II Receptor blockers ARB

Advantages

- Most renoprotective drug class in type 2 diabetes with nephropathy
- Profoundly antiproteinuric
- Excellent long-term tolerability
- ↓ Morbidity and mortality in CHF (similar to ACEI)
- No cough
- Can substitute for ACEI when the latter aren't tolerated
- Less hyperkalemia than with ACEI

Disadvantages

- Rare angioedema (less than ACEI)
- Infrequent hyperkalemia
- Higher dose requirements in some African-Americans
- ↑ Serum creatinine, though less than with ACEI
- Rise in creatinine reflects ACEI MOA; consider lowering dose or stopping if creatinine increases >30%

Calcium Antagonists

Advantages

- Highly effective BP lowering efficacy in African-Americans, diabetics, elderly
- Superior stroke risk reduction
- Useful in diastolic dysfunction (rate-lowering)
- Metabolically neutral
- Minimal erectile dysfunction
- BP-lowering effect is robust in setting of high dietary sodium intake
- BP-lowering effect not attenuated by NSAIDs

Disadvantages

- Immediately post-MI or during unstable angina (short-acting dihydropyridines) may increase CHD risk
- Rate-lowering CCBs can worsen CHF and mortality in patients with systolic heart failure
- Side effect profile varies—
verapamil: constipation
dihydropyridines: pedal edema and vasodilatory symptoms
- Avoid DHP CCB without RAS blocker in CKD
- Avoid rate-lowering CCB and beta-blocker combination

Alpha₁ Antagonists

Advantages

- Positive effect on all lipoprotein fractions
- Improved insulin sensitivity
- Unchanged or improved sexual function in men
- Blunts thiazide-induced rise in cholesterol
- Improves maximum urine flow and prostatic obstruction symptoms

Disadvantages

- Orthostatic hypotension (particularly in the elderly, in those with autonomic dysfunction, in combination with other vasodilators, and in volume depleted patients)
- Asthenia
- Slightly higher doses needed in African-Americans
- Less effective in ↓ heart failure risk than diuretics

Direct Vasodilators

Advantages

- Relatively inexpensive
- Effective in severe hypertension (minoxidil > hydralazine)

Disadvantages

- Best suited for adjunctive therapy
- Salt and water retention necessitate use of loop diuretics or metolazone
- Reflex tachycardia necessitates use of rate-limiting CCB or beta-blocker
- Do not regress LVH
- Lupus-like syndrome (>200 mg/d of hydralazine)
- Hirsutism (minoxidil)
- Edema (minoxidil)

ARS Question

- Which drug is not used to treat systemic hypertension?
 1. CCB
 2. ACE inhibitor
 3. ARB
 4. Endothelin receptor antagonist

JNCVIII

- Expected Update of Hypertension Guidelines JNC VIII Summer 2010