

Hypertension

Pharmacotherapy I

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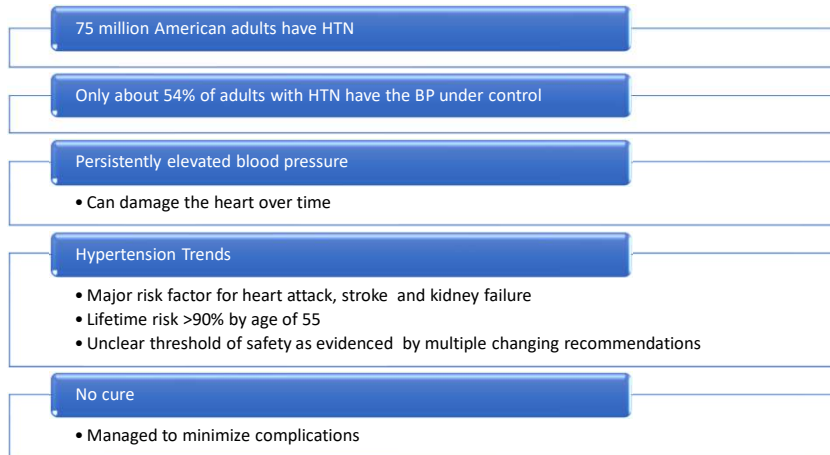
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Learning Objectives

Identify	Identify risk factors and/or diagnostic indicators that may lead to hypertension.
Classify	Classify BP as outlined by ACC/AHA
Explain	Explain the proper way to take a BP.
Define and explain	Define and explain the criteria used to diagnose hypertension.
Identify	Identify first line treatment options for treatment of BP in patients and those with compelling indications according to JNC VIII, ACC/AHA
Explain	Explain the benefits, adverse drug reactions, interactions, contraindications, and monitoring for alternative treatment options for hypertension
Summarize	Summarize counseling points for antihypertensive drug classes.
Explain	Explain the rationale for and determine the appropriateness of combination therapy according to JNC VIII.
Design	Design a treatment and monitoring plan for patients with hypertension

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Overview of HTN



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Fluctuations
in blood
pressure

BP normally follows a circadian rhythm

- Lowest values occur during sleep
- Starts to rise a few hours prior to awakening
- Highest values occur mid-morning

Blood pressure can increase acutely

- Physical activity
- Emotional stress

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Definition of HTN

Hypertension (HTN) or high blood pressure (HBP)

- Patient language:
- Force of your blood moving against the walls of your arteries

Systolic blood pressure (SBP)

- Peak blood pressure achieved during cardiac contraction (systole)
- Patient language:
- Top Number – the pressure in the arteries when the heart beats

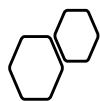
Diastolic blood pressure (DBP)

Minimum pressure achieved in between contractions (diastole)

Patient Language:

- Bottom Number – the pressure measured between heartbeats

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Etiology

Primary HTN

Formally referred to as essential HTN
Unknown cause

Secondary HTN

Known cause
Examples: sleep apnea, CKD, primary aldosteronism

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Primary (essential) hypertension

> 90% of hypertensive patients

Usually results from unknown pathophysiologic etiology

- Several postulated mechanisms

Can't be cured

Genetic factors

- Monogenic and polygenic

Needs to be treated

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Secondary hypertension

< 10% of hypertensive patients

HTN caused by something else

COMMON

- Renovascular disease. Renal parenchymal disease, Primary aldosteronism
- Obstructive sleep apnea. Drug- or alcohol-induced

UNCOMMON

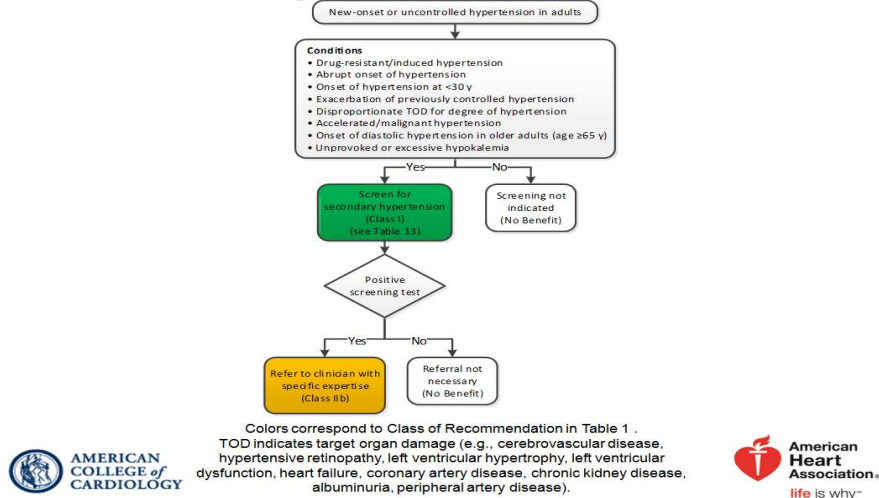
- Pheochromocytoma/ paraganglioma. Cushing's syndrome, Thyroid disease
- Hypo- or Hyperthyroidism
- Coarctation of the aorta (undiagnosed or unrepaired)

Management:

- Treat / correct the underlying comorbid condition!

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Screening for Secondary Hypertension



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Isolated Systolic Hypertension

DBP < 80 mm Hg with SBP ≥ 130

Results from pathophysiologic changes in arterial vasculature consistent with aging

- Decreased compliance of arterial wall

SBP is a strong predictor of CV disease in patients ≥ 50 years old

Pulse pressure = SBP – DBP

- Reflects extent of atherosclerotic disease in elderly
- ↑ pulse pressure, ↑ CV mortality
- Measures arterial stiffness

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↑ BP = ↑ cardiovascular risk

HTN is one of the most significant risk factors for cardiovascular (CV) disease

Strong correlation between BP and cardiovascular (CV) morbidity and mortality

HTN ↑ risk of

Myocardial
infarction
(MI)

Angina

Heart failure

Stroke

Kidney
failure

Early death
from a CV
cause

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Why treat hypertension?

Each 20/10 mm Hg increase over 115/75

Doubles the risk of a death from stroke, heart disease, or other vascular disease

Clinical trials have shown that morbidity and mortality is reduced with antihypertensive drug therapy

↓ stroke incidence
35-40%

↓ myocardial
infarction (MI) 20-25%

↓ heart failure > 50%

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Pathophysiology

Excess Vasoconstrictors

- Angiotensin II, endothelin I

Vasodilator deficiency

- Prostacyclin, bradykinin, nitric oxide

Increased vascular tone

- Natriuretic hormone -Inhibits transport of sodium OUT of arteriolar smooth muscle cells

Vascular smooth muscle growth

- Production of angiotensin peptides by peripheral tissues
- Insulin
 - May increase intracellular calcium, causing ↑ tone

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Pathophysiology

Kidneys

- Maintain BP through volume-pressure adaptive mechanism
 - If BP ↓, kidneys increase sodium and water retention, leading to plasma volume expansion and ↑ BP
 - If BP ↑, kidneys excrete more sodium and water to reduce plasma volume and cardiac output, therefore ↓ BP

RAAS System

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Pathophysiology

Renin

- Stored in juxtaglomerular cell
- Present in afferent arterioles of kidney
- Function as baroreceptor-sensing device
- Released in response to:
 - Intrarenal factors
 - Decreased renal artery pressure/renal blood flow
 - Catecholamine stimulation
 - Extrarenal factors
 - ↓ in sodium and chloride delivered to the distal tubule
 - ↓ serum potassium and/or intracellular calcium
- Catalyzes conversion of angiotensinogen to angiotensin I in the blood

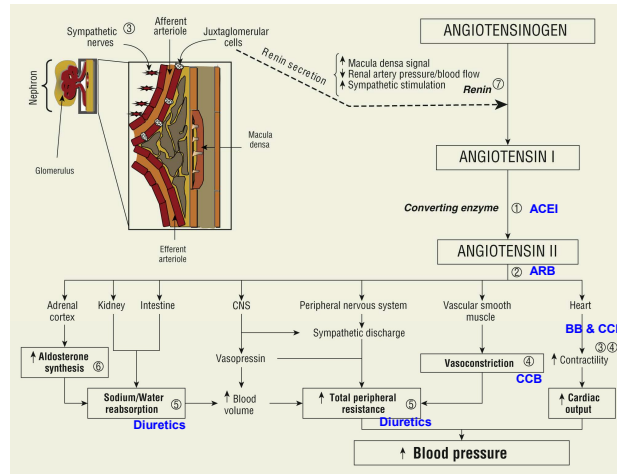
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Pathophysiology

Angiotensin I

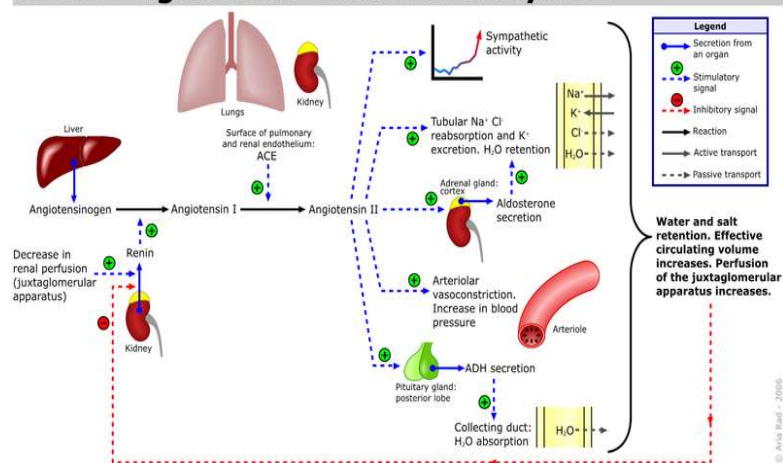
- Vasoconstriction
- Stimulation of catecholamine release
- Centrally mediated increases in sympathetic nervous system activity
- Stimulation of aldosterone synthesis from the adrenal cortex
- Sodium and water reabsorption
- Increases plasma volume, total peripheral resistance, and BP
- Myocardial fibrosis, vascular dysfunction

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Renin-angiotensin-aldosterone system



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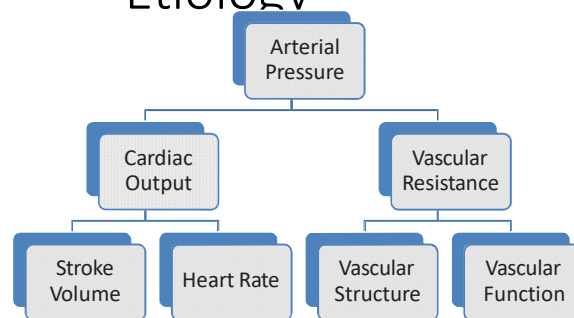
Pathophysiology of HTN

- $BP = CO \times TPR$
 - Cardiac Output = $HR \times \text{Stroke volume}$
 - Major determinant of SBP
 - Total peripheral resistance (TPR)
 - Major determinant of DBP
- Drugs decrease BP by decreasing CO, TPR or both



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Hypertension Etiology



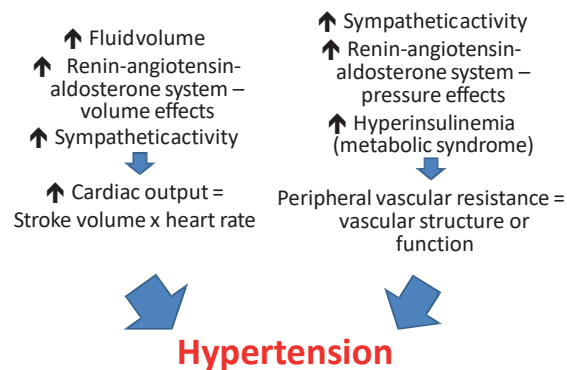
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Hypertension Determinants

Stroke volume	Heart Rate	Vascular Structure	Vascular Function
• ↑ aldosterone or antidiuretic hormone/ vasopressin. • Renal artery stenosis Renal disease. • Pregnancy/ preeclampsia. • High sodium intake	• Elevated EPI or norEPI levels → RAAS activation. • Obesity, sleep apnea, hyperthyroidism.	• Age/Genetics AKA "PRIMARY HTN". • Atherosclerosis. • Diabetes, sleep apnea, obesity	• Age/Genetics. • Elevated EPI or norEPI levels → RAAS activation. • Stress • Diabetes, hyperthyroidism, sleep apnea, obesity

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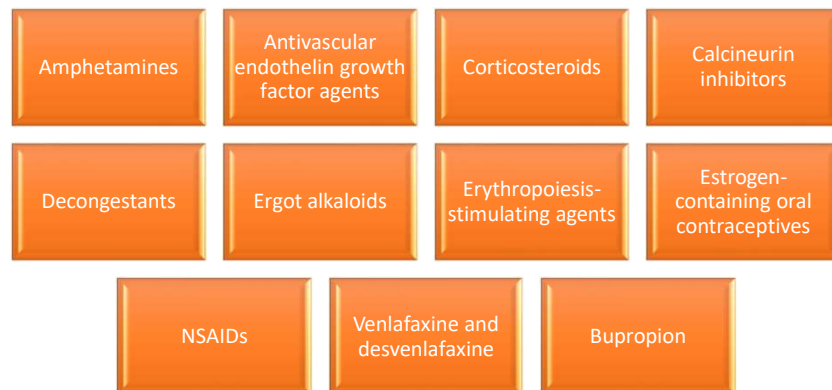
Summary of mechanisms causing HTN



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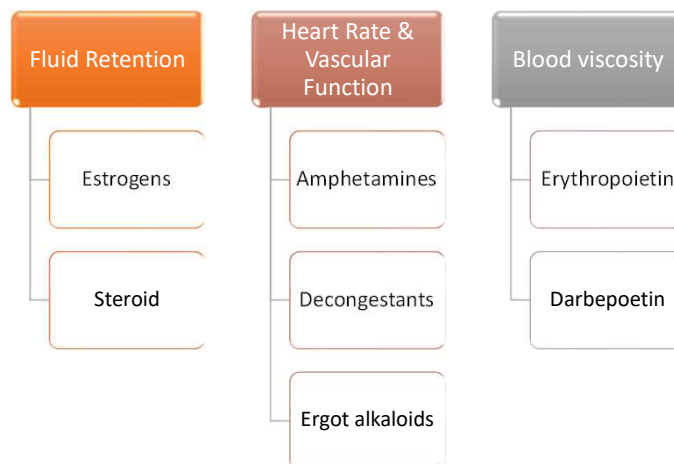
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Medications Associated with HTN



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Drug Induced Hypertension



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Drug Inducted Hypertension

Heart Rate & Vascular Function (Foods)	heart Rate & Vascular Function (Herbal/recreational drugs)	Cardiac Output, Heart Rate or Vascular Structure/Function
• Sodium, licorice, ethanol, caffeine, smoking • Tyramine containing foods such as wine or cheese	• Cocaine and cocaine withdrawal • Ma huang and ephedra	• Nonsteroidal anti-inflammatory agents • Cyclosporine, tacrolimus • Bupropion, venlafaxine, desvenlafaxine • Bevacizumab, sorafenib, sunitinib • Nicotine and narcotic withdrawal; NRT • St. John's wort; weight loss supplements such as caffeine • Rapid d/c of beta-blocker or central alpha2 agonist

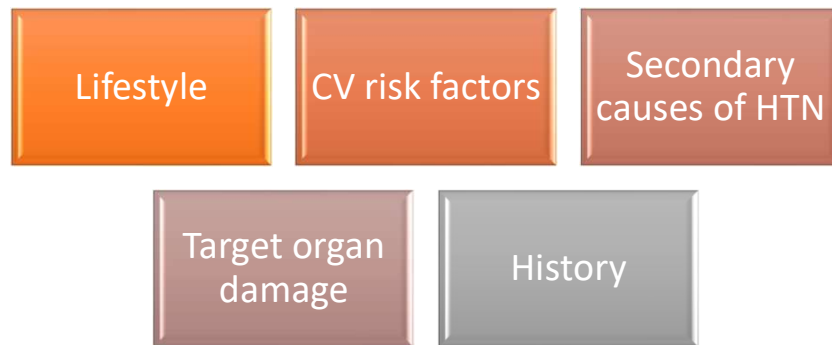
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Diseases Associated with HTN

CKD	Cushing's syndrome	Coarctation of the aorta
Obstructive sleep apnea	Parathyroid disease	Pheochromocytoma
Primary aldosteronism	Renovascular disease	Thyroid disease

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Patient Evaluation



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Metabolic Syndrome

Associated with HTN & metabolic abnormalities such as ↑ serum insulin levels

Metabolic syndrome is diagnosed if 3 of the 5 following are present:

- abdominal obesity (>40" men; >35" women)
- HTN ($\geq 130/\geq 85$ or taking antihypertensives)
- elevated fasting glucose (≥ 100 mg/dL or on diabetes meds)
- elevated TG (≥ 150 mg/dL or on lipid meds)
- low HDL (<40 mg/dL men; <50 mg/dL women)

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CVD Risk Factors Common in Patients With Hypertension

Modifiable Risk Factors

- Current cigarette smoking, secondhand smoking
- Diabetes mellitus
- Dyslipidemia/hypercholesterolemia
- Overweight/obesity
- Physical inactivity/low fitness
- Unhealthy diet

Relatively Fixed Risk Factors

- CKD
- Family history
- Increased age
- Low socioeconomic/educational status
- Male sex
- Obstructive sleep apnea
- Psychosocial stress

<https://www.acc.org/-/media/Non-Clinical/Files/PDFs-Excel-MS-Word-etc/Guidelines/2017/2017-Blood-Pressure-Guideline.ppt>

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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.

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Measurments

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How is blood pressure measured?

Sphygmomanometer and stethoscope

Measured in millimeters of mercury (mm Hg)

Systolic blood pressure (SBP)

- Top number; peak value
- Measured during cardiac contraction

Diastolic blood pressure (DBP)

- Bottom number; nadir value
- Measured after contraction when the cardiac chambers are filling

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Different Readings

Appropriate measurement!

In office readings

Home readings

Ambulatory monitoring

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Out of Office Monitoring

Ambulatory

- Document BP at frequent time intervals over 8 -24h
- Useful to determine nighttime high BP readings

Home

- Measurements collected by patients – average home BP over 1 week
- Check AM and HS
- Arm cuffs more accurate than wrist or finger
- FABRICATED readings!
- Accurate if within 5mmHg of in-office reading – wait 1 minute between readings

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Blood Pressure Measurement

- Steps for Proper BP Measurement
 - Step 1: Prepare the patient
 - Step 2: User proper technique for BP measurement
 - Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/HTN
 - Step 4: Properly document accurate BP readings
 - Step 5: Average the readings
 - Step 6: Provide BP readings to the patient

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Step 1: Properly prepare the patient

- Have the pt relax, sitting in a chair (feet on floor, back supported) for > 5 min.
- Avoid caffeine, exercise, and smoking for at least 30 minutes before measurement
- Ensure the pt has emptied his/her bladder
- Neither the patient nor the observer should talk during the rest period or during the measurement
- Remove all clothing covering the location of cuff placement
- Note: Measurements made while pt is sitting/lying on examining table do not fulfill these criteria

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Step 2: Use proper technique

- Use a BP measurement device that has been validated, and ensure the device is calibrated periodically
- Support the patient's arm (ex: rest on a desk)
- Position the middle of the cuff on the pt's upper arm at the level of the right atrium (midpoint of the sternum)
- Use the correct cuff size (bladder encircles 80% of the arm).
- Note if larger or smaller than normal cuff size is used
- Either the stethoscope diaphragm or bell may be used for auscultatory readings

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Step 3: Take proper measurements

- At first visit, record BP in both arms, Use the arm that gives higher reading for subsequent readings
- Separate repeated measurements by 1-2 min
- For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20-30 mmHg above this level for an auscultatory determination of the BP level (more info in notes)
- For auscultatory readings, deflate the cuff pressure by 2 mmHg per second, and listen for Korotkoff sounds

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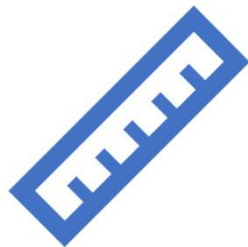


Step 4: Properly document accurate BP readings

- Record SBP and DBP
- If using auscultatory technique, record SBP and DBP as the onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number
- Note the time and most recent BP medication taken before measurements

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Step 5: Average the readings

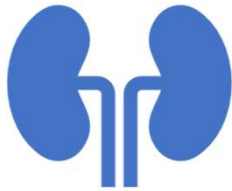


- Use an average of ≥ 2 readings obtained on $\geq$ occasions to estimate the individual's level of BP

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Step 6: Provide BP readings to patient



- Provide the patient the SBP/DBP readings both verbally and in writing

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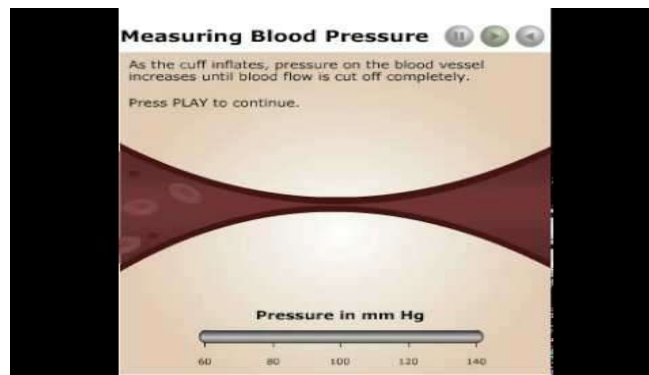
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https://www.youtube.com/watch?v=u6saTO8_o2g

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Counseling the Patient: Monitoring Blood Pressure

Accurate monitoring

- Proper cuff technique
- Proper preparation
 - Relaxed in chair for 5 minutes
 - No exercise, smoking, or caffeine before

How often?

- Daily
 - Average of 2 readings 1 minute apart
 - Before medications in the morning
 - Before supper in the evening

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	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

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA
Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

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Diagnosis

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Making the Diagnosis

AA is a 57 YO obese BF (5'4", 210 lbs.) that was newly diagnosed with HTN referred by PCP for HTN management and education.

Her BP is 149/85mmHg, which is around her readings for the last 2 months.

She has been trying lifestyle modification for the last two months, but her BP has not changed. She is not taking any medications for HTN. What stage HTN does AA have?

You have identified a need for additional medication. Which of the following is the most appropriate initial pharmacotherapy for AA?

What if The blood pressure was 164/94 mmHg? What if she is a Diabetic?

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Making the Diagnosis

2 or more consecutive elevated arterial blood pressure readings from 2 or more encounters

Higher of the 2 values (SBP/DBP) determines the diagnosis

Elevated SBP strong predictor of CV mortality $\geq$ 50 yo

Elevated DBP strong predictor of CV mortality < 50yo

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Classification of BP / HTN

Classification	SBP (mm Hg)		DBP (mm Hg)
Normal	< 120	and	< 80
Elevated	120-129	and	<80
Stage 1 HTN	130-139	or	80-89
Stage 2 HTN	≥ 140	or	≥ 90
HTN Crisis	> 180	or	> 120

- Adults (≥ age 18 years)
- Diagnosis based on the *average* of two or more properly measured seated BP measurements from two or more clinical encounters
 - At least 2 elevated readings on at least 2 visits

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GOALS OF TREATMENT

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Secondary Goals

1

Treating to a desired BP goal

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Starting at 115/75, risk of CV event doubles with every 20/10 mmHg increase

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Risks vs benefits

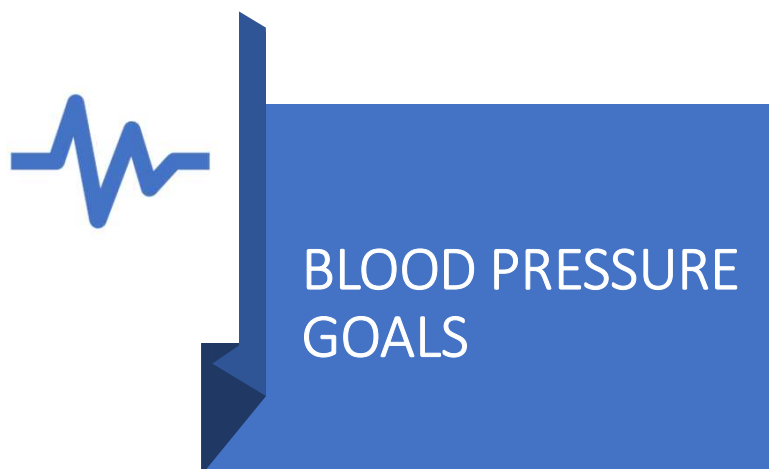
Target organ damage

- Heart disease – angina, MI, HF
- Cerebrovascular disease – stroke, TIA
- Kidney disease
- Retinopathy
- Peripheral arterial disease

Benefits of controlling BP

- Reduction in target organ damage
- Reduction in stroke risk
- Reduction in MI risk
- Reduction in HF risk

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Comparison of BP Target Recommendations

BP Target		BP Categories		
JNC 8, 2014	< 150/90 mm Hg for patients ≥ 60 < 140/90 mm Hg for patients < 60, diabetes, and chronic kidney disease		SBP	DBP
		Normal	< 120	< 80
		Prehypertension	120–139	80–89
		Stage 1 hypertension	140–159	90–99
		Stage 2 hypertension	≥ 160	≥ 100
ACC/AHA 2017	≤ 130/80 mm Hg		SBP	DBP
		Normal	< 120	< 80
		Elevated	120–129	< 80
		Stage 1 hypertension	130–139	80–89
		Stage 2 hypertension	≥ 140	≥ 90

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Sprint Trial

Population included ≥ 50 yrs, baseline SBP ≥ 130 , elevated CV risk but not diabetes or stroke

- Elevated risk = CKD, 10-year Framingham risk score $\geq 15\%$, ≥ 75 yrs
- Target BP < 140 vs. < 120

Mean SBP 121 mmHg vs. 136 after 1 year

Primary composite outcomes (myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes) better with lower BPs

All-cause mortality was also significantly lower in the intensive-treatment group

Rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls, were higher in the intensive-treatment group than in the standard-treatment group

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None Pharmacological treatment

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Nonpharmacological Treatment

Diet	Exercise	Unhealthy Habits
• DASH Diet • Decreased sodium • Increased Potassium	• Weight loss • Increased physical activity	• Alcohol moderation • Smoking Cessation

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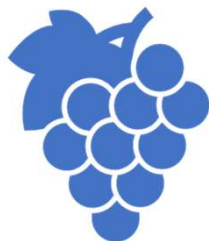
Nonpharmacological Treatment

	Nonpharmacologic Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Weight loss	Weight/body fat	Ideal body weight is best goal but at least 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	Diet rich in fruits, vegetables, whole grains, and low-fat dairy products with reduced content of saturated and trans fat	-11 mm Hg	-3 mm Hg
Reduced intake of dietary sodium	Dietary sodium	<1,500 mg/d is optimal goal but at least 1,000 mg/d reduction in most adults	-5/6 mm Hg	-2/3 mm Hg
Enhanced intake of dietary potassium	Dietary potassium	3,500-5,000 mg/d, preferably by consumption of a diet rich in potassium	-4/5 mm Hg	-2 mm Hg
Physical activity	Aerobic	• 120-150 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 x 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 Hg

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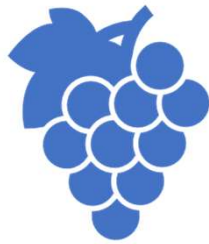
DASH Diet



- Dietary Approaches to Stop Hypertension
 - Vegetables, fruits, whole grains
 - Fat-free or low-fat dairy products
 - Poultry, beans, nuts, vegetable oils
 - Limit food high in saturated fat – fatty meats, full-fat dairy products, tropical oils
 - Limit sugar-sweetened beverages and sweets

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DASH Diet



- Grains (6-8 servings/day)
- Fruit (4-5 servings/day)
- Sodium (2,300mg or less per day)
- If daily sodium intake is 1,500mg or less, BP is lowered even further
- Vegetables (4-5 servings/day)
- Meats, Poultry, Fish (6 or less/day)
- Fats and Oils (2-3 servings/day)
- Low-fat or fat-free dairy (2-3 servings/day)

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Exercise

- American Heart Association Recommendations:
 - Aim for 90-150 minutes of aerobic and/or dynamic resistance exercises per week
 - Get the equivalent of 150 minutes per week of moderate- intensity physical activity (such as brisk walking)
 - Perform physical activity in at least 10-minute intervals and
 - spread throughout the week
 - Include flexibility and stretching
 - Include muscle-strengthening activity at least twice per week



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Patient Counseling

Encourage physical activity

Consult with doctor regarding best way to begin a routine

Mix up the activity

- Walking, stair-climbing
- Bicycling, rowing, swimming
- Dancing, gardening
- Household chores

Pace yourself

Practice breath control

Warm up and cool down

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Smoking Cessation

- Counsel on benefits of quitting as often as possible
- Medications + support = improved quit rates
- Offer encouragement as it often takes more than one try to quit



American Heart Association. Why Quit Smoking?
http://www.heart.org/HEARTORG/GettingHealthy/QuitSmoking/QuittingSmoking/Why-Quit-Smoking_UCM_307847_Article.jsp

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Resources for Patients



- CardioSmart.org – American College of Cardiology
 - Patient Handout Fact-Sheets
 - <https://www.cardiosmart.org/Heart-Conditions/Fact-Sheets>
 - Treatment and Medication Information
 - <https://www.cardiosmart.org/Drugs-and-Treatments/Treatments>

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MEDICATION THERAPY

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Treatment Recommendations

Initiation of antihypertensive drug therapy, first line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs

Stage 1 HTN and goal BP <130/80 – initiation of antihypertensive drug therapy with a single antihypertensive drug is reasonable with dosage titration and sequential addition of other agents to achieve the BP target

Stage 2 HTN and an average BP more than 20/10 mmHG above BP target – initiation of antihypertensive drug therapy with 2 first-line agents of different classes is recommended

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Follow-up Recommendations

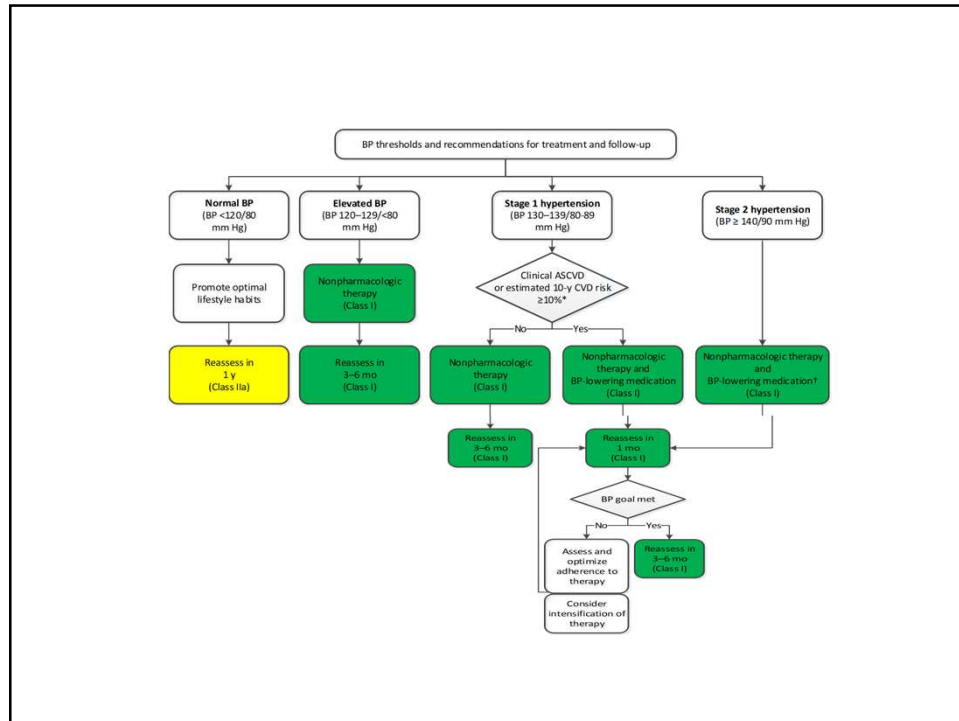
After initial BP elevation

- Elevated BP or Stage 1 HTN with 10-year ASCVD risk less than 10% - nonpharmacological therapy and repeat BP evaluation in 3-6 months
- Stage 1 HTN with 10-year ASCVD risk of 10% or greater – nonpharmacological therapy AND antihypertensive treatment and follow-up in 1 month
- Stage 2 HTN – evaluated by or referred to PCP within 1 month of initial diagnosis
 - nonpharmacological therapy AND 2 antihypertensive drug therapies and follow-up in 1 month

After initiating antihypertensive drug therapy

- Initiating a new or adjusted drug regimen for HTN should have follow-up evaluation of adherence and response at monthly intervals until goal is reached

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Pharmacotherapy Options

First Line

- Thiazides
- ACEIs
- ARBs
- Calcium Channel Blockers
- Beta-1 Blockers **

Second Line

- Potassium Sparing Diuretics (possibly loop diuretics in CKD and HF)
- Aldosterone Antagonists
- Direct Renin Inhibitors
- Direct Vasodilators
- Centrally Acting Alpha-2 Antagonists
- Peripheral Adrenergic Inhibitors
- Alpha-1 Agonists

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Thiazide

MOA	Contraindications	Drug interactions
• ↑ excretion of Na, Cl, H₂O • Inhibit Na ion transport across renal tubular epithelium • Inhibit active Cl reabsorption at distal ascending limb or distal tubule • Decrease SV and CO • Reduce TPR	• Cross-sensitivity with other thiazides or sulfonamides, anuria, renal decompensation, hemodialysis • Drug interactions • Lithium, dofetilide, NSAIDs	• Lithium, dofetilide, NSAIDs

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Thiazide

Cautions	Monitoring parameters
• Lose effectiveness when CrCl < 30 ml/min • Metolazone can still be used • Use caution in patients with sulfonamide allergy • May precipitate gout (especially if not on uric acid-lowering therapy), systemic lupus erythematosus, and change in glucose control	• -SCr/BUN, Electrolytes, uric acid, Glucose, lipids, Blood pressure, dizziness • Assess weight, Intake & Output (I&O) reports daily to determine fluid loss

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Thiazide Diuretics/Adverse reactions

Hypo

- Hypokalemia
- Hyponatremia
- Hypomagnesemia
- Hypochloremia

HYPER-

- Hypercalcemia
- Hyperuricemia
- Hyperglycemia
- Hyperlipidemia

Photosensitivity

Higher risk of new onset diabetes (vs ACEI, ARBs, CCB, BB)

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Thiazide Diuretics

Clinical Pearls

- Chlorthalidone preferred based on prolonged half-life and proven trial reduction of CVD
- Dose in morning and early afternoon if 2nd dose is needed
- Use in caution with patients with history of acute gout unless on uric acid lowering therapy
- Check electrolytes at baseline and as clinically necessary
- Cautions
 - Lose effectiveness when CrCl < 30 ml/min
 - Metolazone can still be used
 - Use caution in patients with sulfonamide allergy
 - May precipitate gout (especially if not on uric acid-lowering therapy), systemic lupus erythematosus, and change in glucose control

Commonly prescribed

- Hydrochlorothiazide 12.5 – 25 mg
- -Chlorthalidone 12.5 – 50mg
- -Indapamide 1.25 – 5mg

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Loop & Potassium Sparing Diuretics

Major Use	MOA	ADRs (dose-related)	Contraindication
- Loops for CKD & heart failure; fluid management - K sparing as "add on" to other diuretics; weak diuretics	- Loops - natriuresis & diuresis at loop of Henle, ↑ renal PG synthesis - K sparing – natriuresis & diuresis at DCT - Chronically decreased PVR due to decrease intracellular fluid in vessel walls → widening vessel lumen	- Loops - electrolyte disturbances, elevated uric acid, dehydration, Ototoxicity - Sulfonamide allergy Exception: ethacrynic acid (Edecrin®) - K sparing – hyperkalemia	- Loops – volume depletion, hypotension, Anuria, severe electrolyte imbalances - K sparing – hyperkalemia

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Loop & Potassium Sparing Diuretics

Monitoring	Clinical Pearls	Commonly prescribed
SCr/BUN, -Electrolytes, uric acid, -Blood pressure, dizziness, -Hearing	- Dose early in the day. Loops often require K supplementation; - Loops may precipitate gout attacks in gout-prone patients	- Loops – furosemide 20 – 80mg, bumetanide 0.5 – 4 mg, torsemide 5 – 10mg - K Sparing – triamterene/HCTZ 37.5-75/25-50 mg

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Loop Diuretics/Adverse reactions

Hypo

- Hypokalemia
- Hypomagnesemia
- Hyponatremia
- Hypochloremia
- Hypocalcemia

HYPER

- Hyperuricemia
- Dizziness
- Impaired glucose test
- ↑ cholesterol and triglyceride levels

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ACE-Inhibitor

Major Use

- First line for all ages with or without CKD or diabetes

MOA

- Blocks angiotensin converting enzyme (ACE) → prevents the conversion of angiotensin I to angiotensin II
- Block bradykinin degradation
- Stimulate synthesis of prostaglandin E2 & prostacyclin - vasodilators
- Prevent or regress left ventricular hypertrophy

ADRs

- Hyperkalemia, increased SCr, Angioedema, Cough, Hypotension

DI

- NSAIDs, cyclosporine, antacids, lithium, K supplements

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ACE-Inhibitors

Contraindications

- Angioedema related to previous treatment with ACE-inhibitor
- Idiopathic or hereditary angioedema
- Pregnancy
- Do NOT use with ARBs or direct renin inhibitor

Cautions

- Aortic stenosis
- Renal artery stenosis (unstented unilateral OR bilateral) or renal impairment → could cause acute renal failure

Clinical Pearls

- Shown to work better in Caucasians than AA
- Acute kidney failure – adjust dose or d/c if > 35% increase in SCr from baseline
- Dose increase slowly; can decrease or stop quickly
- Do not use in combination with ARB or DRI
- Usually once daily dosing, Twice daily dosing may be needed to maintain 24-hour BP control

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ACE-Inhibitors

Generic	Brand	Usual Daily Dose (mg)
Benazepril	Lotensin®	10 - 40 1 or 2 doses per day
Captopril	Capoten®	25 - 150 2 or 3 doses per day
Enalapril	Vasotec®	5 - 40 1 or 2 doses per day
Fosinopril	Monopril®	10 - 40 Daily
Lisinopril	Prinivil®, Zestril®	10 - 40 Daily

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ACE-Inhibitors

Generic	Brand	Usual Daily Dose (mg)
Moexipril	Univasc®	7.5 - 30 1 or 2 doses per day
Perindopril	Aceon®	4 - 16 1 or 2 doses per day
Quinapril	Accupril®	10 - 80 Daily
Ramipril	Altace	2.5 - 20 Daily
Trandolapril	Mavik	1 - 4 Daily

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Angiotensin Receptor Blockers

Major Use

- First line in all ages with or without CKD or diabetes
- More data to support renoprotective effects

MOI

- Binds to the AT1 angiotensin II receptor, which prevents angiotensin II from binding to the receptor
- Blocks the vasoconstriction and aldosterone secreting effects of angiotensin

Contraindications

- Angioedema related to previous treatment with ARB
- If angioedema with ACEI, can receive ARB 6 weeks after ACEI is discontinued
- Pregnancy
- Do NOT use with ACEI or direct renin inhibitor

Cautions

- Aortic/mitral stenosis, unstented unilateral or bilateral renal artery stenosis, renal impairment

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Angiotensin Receptor Blockers

Adverse reactions

- Angioedema, Dyspepsia, Dyspnea
- Hyperglycemia, Hyperkalemia, Hypertriglyceridemia, Hyperuricemia
- ↑ in serum creatinine

Drug interactions Lithium, NSAIDs

Monitoring parameters Potassium, renal function, blood pressure, Scr.

Clinical Pearls

- ACE/ARB combination therapy only with severe nephrotic syndrome
- Combination ACE/ARB therapy not recommended for HTN
- Alternative for ACEI-induced cough
- Lower risk of angioedema; not recommended
- If angioedema with ACEi, patient can start on ARB 6 weeks after discontinuation of ACEi
- Dose increase slowly; can decrease or stop quickly

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Angiotensin Receptor Blockers

Generic	Brand	Usual Daily Dose (mg)
Azilsartan	Edarbi™	40 - 80 Daily
Candesartan	Atacand®	8 - 32 Daily
Eprosartan	Teveten®	400 - 800 1 or 2 doses per day
Irbesartan	Avapro®	150 - 300 Daily
Losartan	Cozaar®	25 - 100 1 or 2 doses per day
Olmesartan	Benicar®	20 - 40 Daily
Telmisartan	Micardis®	20 - 80 Daily
Valsartan	Diovan®	80 - 320 1 or 2 doses per day

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Calcium Channel Blockers

Inhibits calcium ion from entering the “slow channels” (select voltage-sensitive areas of vascular smooth muscle and myocardium during depolarization)

Produces a relaxation of coronary vascular smooth muscle and coronary vasodilation

Increases myocardial oxygen delivery in patients with vasospastic angina

Non-dihydropyridines ONLY slow automaticity and conduction of AV node

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Calcium Channel Blockers

Contraindications

- Non-dihydropyridines
 - Severe LV dysfunction, cardiogenic shock, sick sinus syndrome, 2nd or 3rd degree AV block
- Dihydropyridines
 - Hypersensitivity, advanced aortic stenosis

Cautions

- Avoid in heart failure with reduced ejection fraction (amlodipine or felodipine may be used if needed)
- Hepatic impairment, hypertrophic cardiomyopathy, renal impairment
- Avoid routine use of non-dihydropyridines with BB due to risk of bradycardia and heart block

Adverse reactions

- Non-dihydropyridines
 - Edema, HA, 1st degree AV block, hypotension, flushing, rash, gout, constipation (more so with verapamil), diarrhea, myalgias, dyspnea, gingival hyperplasia (verapamil)
- Dihydropyridines
 - Peripheral edema, HA, somnolence, male sexual dysfunction, abdominal pain, dyspepsia, gingival hyperplasia, muscle cramps

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Calcium Channel Blockers

Major use:

- first line for all ages with or without diabetes
- NDHP – rate control in atrial fibrillation, CHF (diastolic, EF preserved)

Non-dihydropyridines D/I

- CYP 3A4 inducers and inhibitors
- Amiodarone, azole antifungals, benzodiazepines, carbamazepine, dabigatran, digoxin, dronedarone, seizure medications, macrolide antibiotics, protease inhibitors, ranolazine, risperidone, conivaptan, tolvaptan

Dihydropyridines D/I

- Azole antifungals, barbiturates, clopidogrel, conivaptan, fosphenytoin, macrolide antibiotics, seizure medications, neuromuscular blockers, protease inhibitors, CYP3A4 and 1A2 inducers and inhibitors
- grapefruit ↑ serum concentration of DHP (but you have to drink LOTS of it)

Monitoring parameters

- HR, BP, peripheral edema & dyspnea (worsening CHF)

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Calcium Channel Blockers

- Non-dihydropyridines

Generic	Brand	Usual Daily Dose (mg)
Diltiazem extended release (capsule)	Cardizem CD®, Dilacor XR®, Tiazac	180 - 420 Daily
Diltiazem extended release (tablet)	Cardizem LA	120 - 540 Daily
Verapamil immediate release	Calan®, Isoptin®	80 - 320 Split in 2 doses
Verapamil extended release (tablet)	Calan SR®, Isoptin SR®	120 - 480 1 or 2 doses per day
Verapamil extended release (capsule)	Covera-HS®, Verelan PM®	120 - 480 Daily (at bedtime) 100 - 400 Daily (at bedtime)

Both diltiazem and verapamil available as IV

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Calcium Channel Blockers

Dihydropyridines

Generic	Brand	Usual Daily Dose (mg)
Amlodipine	Norvasc®	2.5 - 10 Daily
Felodipine	Plendil®	2.5 - 20 Daily
Isradipine	Dynacirc®	2.5 - 10 Split in 2 doses
Nicardipine sustained release	Cardene SR®	60 - 120 Split in 2 doses
Nifedipine long-acting	Adalat CC®, Procardia XL®	30 - 90 Daily
Nisoldipine	Sular®	10 - 40 Daily

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β – blockers Mechanism of Action

Competitively block beta adrenergic receptors

Effect is dependent on type of receptor

- Beta₁ blockade
 - ↓HR, contractility, cardiac output
- Beta₂ blockade
 - Vasoconstriction
 - Bronchoconstriction

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β - blockers

Contraindications

- Sinus bradycardia, second- or third-degree heart block, cardiogenic shock, overt heart failure, sick sinus syndrome, uncompensated heart failure, pulmonary edema

Cautions

- Should NOT be withdrawn abruptly
 - Taper over 1-2 weeks
- Bronchospastic disease (non-selective BB should be avoided), DM, heart failure

Adverse reactions

- Hypotension. Bradycardia, Dizziness, Fatigue, Insomnia, nightmares
- Decreased libido or impotence, Bronchospasm, Depression

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β - blockers

Drug interactions

- Digoxin, theophylline, sulfonylureas, dronedarone

Monitoring parameters

- HR, BP

Potentially favorable effects:

- Useful for atrial tachyarrhythmias/fibrillation, migraine, thyrotoxicosis (short term), essential tremor, perioperative hypertension

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β – blockers/Lipid Solubility

High

- Largely metabolized by the liver
- Penetrate CNS
- Provide better effects for non-CV conditions
 - Migraine headache prevention, essential tremor, thyrotoxicosis

Low

- Excreted unchanged by kidneys

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β – blockers (BB)

Non-selective beta blockers (1st generation)

- Bind to β_1 and β_2 receptors

Cardioselective beta blockers ♥ (2nd Generation)

- Bind to β_1 receptors
- Can bind to β_2 at higher doses

BB with vasodilatory properties

- α -adrenergic blockade
- Direct vasodilation

BB with intrinsic sympathomimetic activity (ISA)

- Act as both agonist and antagonist at beta receptors

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β - blockers

Combined *alpha* and beta blockers

- Carvedilol (Coreg®, Coreg CR®)
- Labetalol (Normodyne®, Trandate®)

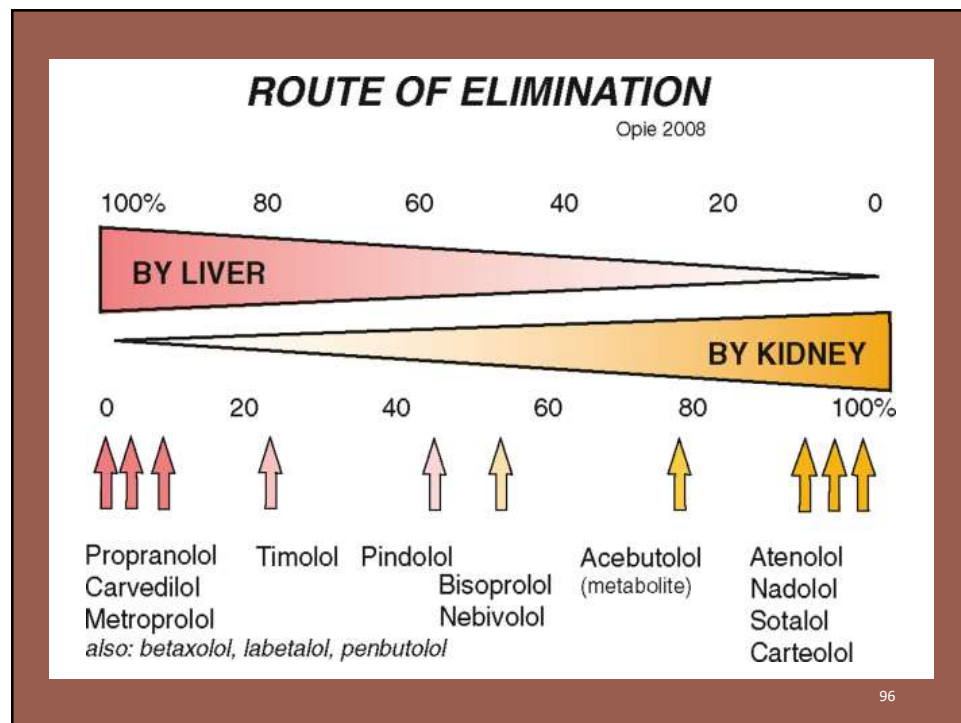
Vasodilators

- Nebivolol (Bystolic®)

Intrinsic Sympathomimetic (AVOID)

- Acebutolol (Sectral®) ♥
- Penbutolol (LevatoI®)
- Pindolol
- Carteolol

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β - blockers

♥ =
cardioselective

Generic	Brand	Usual Daily Dose (mg)
Atenolol ♥	Tenormin®	25 - 100 Daily
Betaxolol ♥	Kerlone®	5 - 20 Daily
Bisoprolol ♥	Zebeta	2.5 - 10 Daily
Esmolol ♥	Brevibloc®	IV only – bolus then continuous infusion
Metoprolol tartrate ♥	Lopressor®	50 - 400 2 or 3 doses per day
Metoprolol succinate ♥	Toprol XL®	50 - 200 Daily
Nadolol	Corgard®	40 - 120 Daily
Propranolol	Inderal	80 - 640 Split in 2 doses
Propranolol (long-acting)	Inderal LA®	60 - 180 Daily

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♥ =
cardioselective



Carvedilol (α and β)	Coreg	12.5 - 50 Split in 2 doses
Labetolol (α and β)	Normodyne®, Trandate®	200 - 800 Split in 2 doses
Nebivolol ♥ plus vasodilation	Bystolic®	5 - 40 Daily

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"Other" β -
blockers
(rarely used)

Generic	Brand	Usual Daily Dose (mg)
Timolol	Blocodren	20 - 40 Split in 2 doses
<u>A</u>cebutolol ISA	Sectral®	200 - 800 Split in 2 doses
<u>P</u>indolol ISA	Visken	10 - 40 Split in 2 doses
<u>P</u>enbutolol ISA	Levatol	10 - 40 Daily
<u>C</u>arteolol ISA	Cartrol	2.5 - 10 Daily

Act as both agonist and antagonist at beta receptors

♥ =
cardioselective

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SECOND LINE MEDICATION THERAPY

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Alternative Agents

Direct arterial vasodilator

- Hydralazine – is commonly used

Alpha blockers

- Doxazosin (Cardura®), Prazosin (Minipress®), Terazosin (Hytrin®)

Direct renin inhibitor

- Aliskiren (Tekturna®)

Centrally acting antihypertensives

- Clonidine
- Methyldopa (drug of choice in pregnancy!)

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Renin Inhibitor

MOI:

- Directly inhibits renin, Inhibits conversion of angiotensinogen to Angiotensin I
- Results in decreased production of Angiotensin II

ADRs: Angioedema rarely, Hyperkalemia

Contraindications: Pregnancy Category D

Clinical Pearls

- Alternative or combination therapy
- Once daily dosing only
- Taken with high fat meals will reduce absorption
- No CV risk benefits
- Avoid combination of ACEI/ARB + K

Common Names: Aliskiren, Tekturna

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Alpha Antagonists

MOA: Antagonize post-synaptic α_1 receptors, Result in peripheral vasodilation

ADRs: First-dose effect, Orthostatic hypotension, Dizziness

Contraindications

- Severe orthostatic hypotension

Clinical Pearls

- Start at low dose and titrate slowly
- No CVD risk benefit
- Benefit for use in patients with BPH
- Use in combination with other therapies

Common Names ("zosins") Doxazosin (Cardura)/Prazosin (Minipress)/Terazosin (Hytrin)

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Aldosterone Antagonism

MOA

- Diuresis secondary to aldosterone receptor blockage
- Inhibits effects of aldosterone on distal renal tubules
- Enhances Na, Cl, and H₂O excretion
- Reduces excretion of K, ammonium, and phosphate

ADRs

- Hyperkalemia
- Gynecomastia – spironolactone
- Dehydration, volume depletion
- Sexual dysfunction

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Aldosterone Antagonism

Contraindications

- Acute renal insufficiency
- Hyperkalemia

Clinical Pearls & Monitoring

- Heart failure & resistant hypertension
- Preferred in primary aldosteronism
- CKD – monitor serum creatinine & K carefully
- Caution when combined with ACEI/ARB, if K > 4.5 mEq/dL and GFR < 60 mL/min
- Administer in the AM
- eplerenone is metabolized by CYP3A4

Common Names

- Spironolactone 25 mg to 100mg daily
- Eplerenone

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Central Alpha-2 Agonists

MOA

- Stimulate α_2 receptors in brain
- Reduce sympathetic outflow
- Results in decreased HR, CO, TPR

ADRs

- Somnolence, confusion, dizziness, falls, headache
- Sedation, dry mouth, orthostasis
- Anticholinergic effects (clonidine)
- Hemolytic anemia, hepatitis, Na/H₂O retention (methyldopa)

Contraindications

- Avoid in the elderly

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Central Alpha-2 Agonists

Clinical Pearls & Monitoring

- Ambulation, alertness
- Concurrent diuretic
- Hepatic function, WBC (methyldopa)
- Avoid abrupt discontinuation
- Must be tapered
- Methyldopa – can be used in pregnancy
- Generally last line therapy due to CNS effects

Common Medications

- Methyldopa 750mg to 3000mg/day BID to TID
- Clonidine 0.1mg to 0.3mg TID
- Guanfacine (Tenex)

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Peripheral Vasodilators

MOA

- Arterial smooth muscle vasodilation, NO formation (hydralazine) and K⁺ channel mediated (hydralazine and minoxidil)
- Directly relax smooth muscle in arterioles
- Results in peripheral vasodilation

ADRs

- Reflex tachycardia, Headache, worsening angina
- Sodium and water retention, edema
- Lupus (hydralazine) immune disorder
- Hirsutism (minoxidil)

Contraindications

- SLE, CAD

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Peripheral Vasodilators

Clinical Pearls & Monitoring

- Muscle weakness (hydralazine)
- Admin w/diuretic and β receptor antagonist, rarely used alone.
- Minoxidil requires a loop diuretic and can cause pericardial effusion
- Third-line or later

Common Medications

- Minoxidil 5mg to 40mg/day in divided doses
- Hydralazine 40mg to 300mg/day in divided doses

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Classification of BP / HTN

Classification	SBP (mm Hg)		DBP (mm Hg)
Normal	< 120	and	< 80
Elevated	120-129	and	<80
Stage 1 HTN	130-139	or	80-89
Stage 2 HTN	≥ 140	or	≥ 90
HTN Crisis	> 180	or	> 120

- Adults (≥ age 18 years)
- Diagnosis based on the *average* of two or more properly measured seated BP measurements from two or more clinical encounters
 - At least 2 elevated readings on at least 2 visits

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Normal BP



SBP < 120 and DBP < 80



Promote optimal lifestyle habits



Re-assess every year

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Stage 1 Hypertension/
SBP 130-139 or DBP 80-89

Non-pharmacologic (lifestyle
modifications) for both groups

Assess presence of Clinical CVD

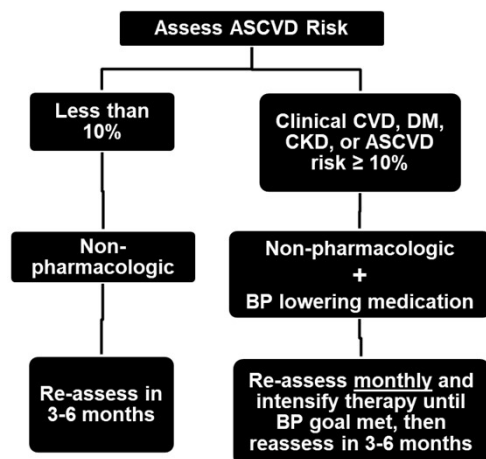
- Coronary heart disease (CHD/CAD), congestive heart failure, or stroke

If no clinical CVD, assess ASCVD (10-year
risk for heart disease and stroke)

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Stage 1
Hypertension



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ASCVD Risk Calculator

(atherosclerotic cardiovascular disease)

AMERICAN COLLEGE of CARDIOLOGY ASCVD Risk Estimator Plus

Estimate Risk provided for exam impact

App intended for primary prevention patients (without ASCVD) who have LDL-C < 190 mg/dL (4.921 mmol/L)

Current Age Sex ☐ Male ☐ Female Race ☐ White ☐ African American ☐ Other

Systolic Blood Pressure (mm Hg) Diastolic Blood Pressure (mm Hg)

Total Cholesterol (mg/dL) HDL Cholesterol (mg/dL) LDL Cholesterol (mg/dL)

History of Diabetes? ☐ Yes ☐ No Smoker: ☐ Yes ☐ Former ☐ No

On Hypertension Treatment? ☐ Yes ☐ No On a Statin? ☐ Yes ☐ No On Aspirin Therapy? ☐ Yes ☐ No

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Stage 2 Hypertension

SBP $\geq$ 140 or DBP $\geq$ 90

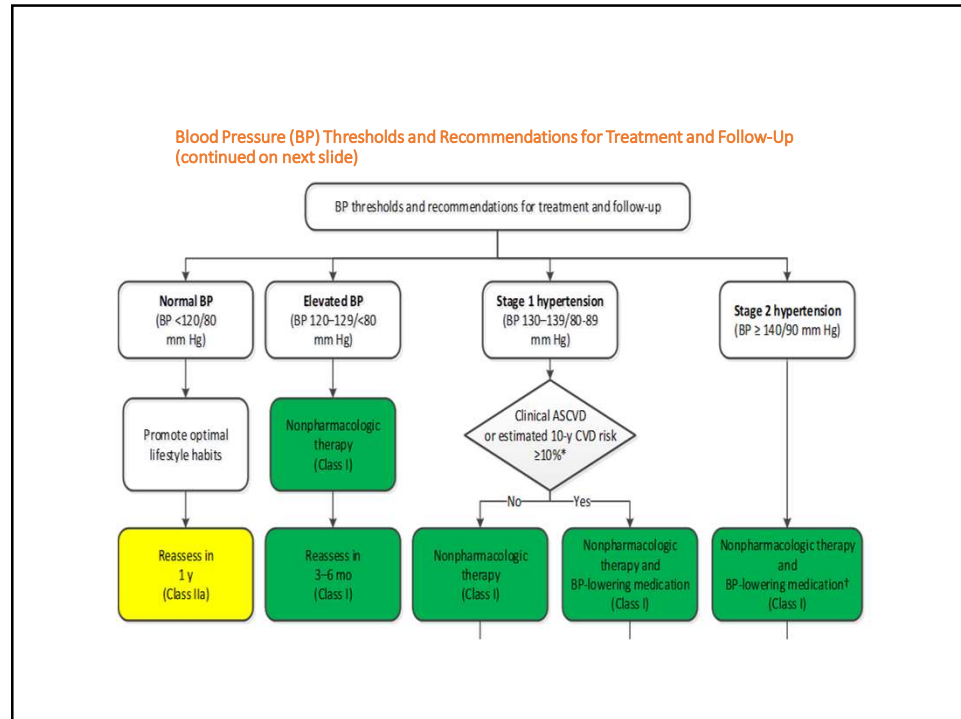
Non-pharmacologic therapy (lifestyle modifications)

Plus

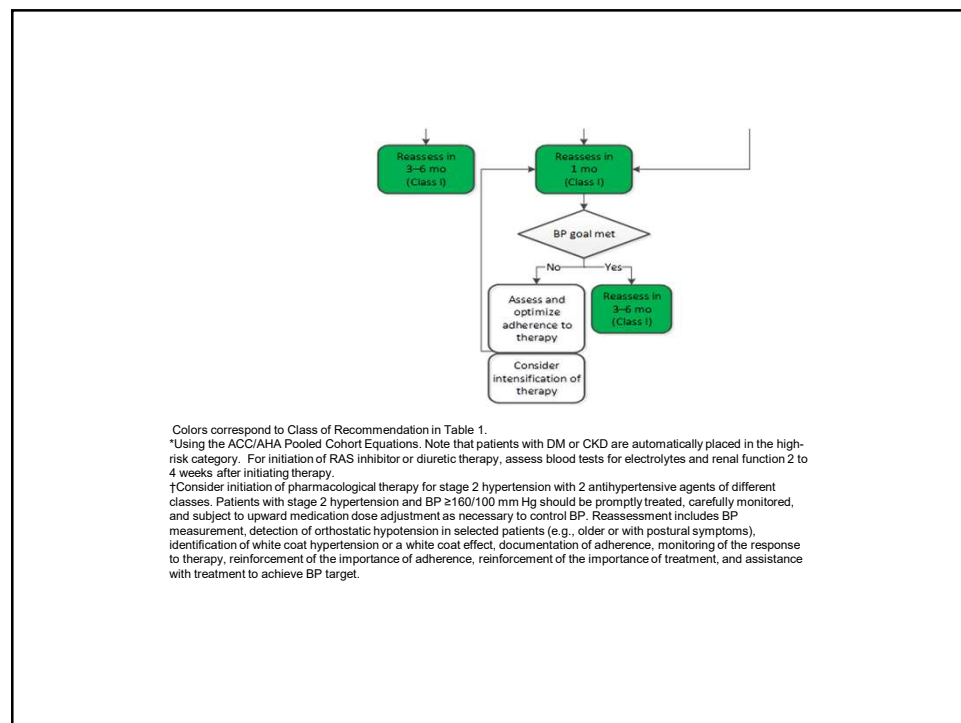
2 BP lowering medications (from 2 different classes)

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Pharmacologic Therapy/First line agents



Thiazide diuretics



Calcium channel blockers



ACE-inhibitors



Angiotensin II receptor blocker

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Pharmacologic Therapy



Most patients with Stage I HTN should receive a thiazide diuretic, ACE-inhibitor, angiotensin receptor blocker, or calcium channel blocker



Patients with Stage II hypertension generally require combination regimen

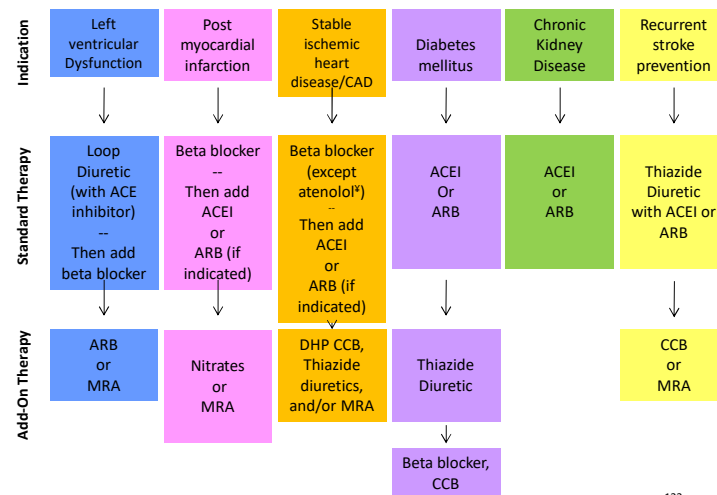


Two drugs also likely needed if BP is > 20/10 mmHg above the goal

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Preferred medication classes for comorbidities/compelling indications

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Heart Failure

Diuretics

- Thiazides better for BP lowering
- Loops better for volume control for LVD and may be necessary if volume overload is a problem

ACEI/ARBs

B-Blockers

- Improved outcomes with 3 specific agents:
- Carvedilol, metoprolol succinate, bisoprolol

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Heart Failure

Mineralocorticoid receptor antagonists (MRA)

- Spironolactone or eplerenone
- Class II-IV HF with LVD (Class II, EF<35%; Class III-IV EF<40%)

Drugs to avoid in HF pts with HTN:

- Non-dihydropyridines
 - Verapamil, diltiazem
- Clonidine
- Minoxidil

Only use alpha-blockers if other drugs are inadequate to achieve BP control

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Post Myocardial Infarction

β -Blockers

- Start with a short acting B1 selective without intrinsic sympathomimetic activity
- Given with nitrates in acute MI

Using non-dihydropyridine CCB

- If BB is CI and there is no LVD
- If pt has supraventricular tachycardia
- Do NOT use if bradyarrhythmia or impaired LV function

CCB – dihydropyridine

- Long acting

Note CCB can $\uparrow$ mortality if LVD &/or pulmonary edema

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Post Myocardial Infarction

ACEI

- Use in pts with anterior MI (when stable) and persistent HTN, LVD, HF, or DM
- Benefit if infarct is large (STEMI) &/or history of previous infarction or HF
- ARB can also be used, but lower level of evidence

Mineralocorticoid receptor antagonists (MRA)

- Spironolactone or eplerenone
- Use in STEMI with LVD & HF

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Stable ischemic heart disease/CAD

β-Blocker

ACEI or ARB

- Especially if DM &/or LVD (systolic), but consider for all

Thiazide diuretic

CCB – non-dihydropyridines

- If BB contraindicated
- Do NOT use if LVD

CCB – dihydropyridine

- Long acting

Mineralocorticoid receptor antagonist

- Spironolactone or eplerenone

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Diabetes

ACEI or ARB

- Slow nephropathy & reduce macroalbuminuria

Diuretic

CCB or BB

All reduce CVD and stroke in diabetic pts

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Chronic Kidney Disease (CKD)

ACEI or ARB

- CKD 3 or higher
- Preferred *if albuminuria present* in stage 1 & 2 CKD
- ≥ 300 mg/day or ≥ 300 mg/g creatinine
- Delay progression of renal disease
- Rise in serum creatinine (SCr) up to 35% above baseline is acceptable
- Do not hold therapy unless hyperkalemia develops

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Chronic Kidney Disease (CKD)

In absence of albuminuria, CCB or thiazide diuretics can be used

Loop diuretics are usually needed with advanced renal disease to control volume status (in combination with other medications)

After kidney transplant, it's reasonable to use CCB

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Recurrent Stroke Prevention

Thiazide diuretic, ACE or ARB

Thiazide Diuretic + ACEI (or ARB)

- Combination of diuretic and ACEI reduces rates of recurrent stroke

After first line, BP reduction appears to be more important than agent choice

- May add CCB or mineralocorticoid receptor antagonists (MRA)

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For patients without compelling indications

Non-black patients with HTN/Initial therapy

- Thiazide-type diuretics
 - Thiazides, chlorthalidone, indapamide
- Calcium channel blockers (CCB)
- Angiotensin converting enzyme inhibitors (ACEI)
- Angiotensin receptor blockers (ARB)

Black patients with HTN

- Thiazide-type diuretics
 - Thiazides, chlorthalidone, indapamide
- CCB

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Chronic Kidney Disease and HTN

Regardless of race or diabetic status, ACEI or ARB should be used to improve kidney outcomes

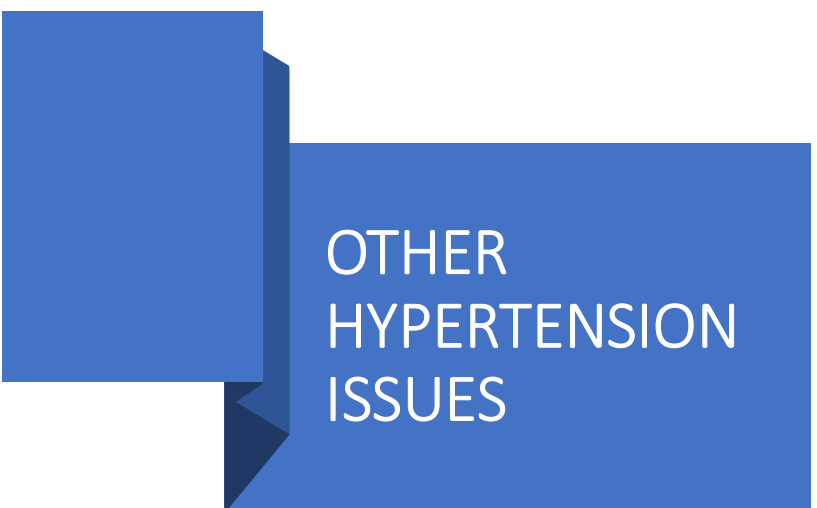
Initial therapy ACEI or ARB

May use ACEI/ARB as add on therapy **Do not use ACEI and ARB together**

Clinical pearls

- If CKD and proteinuria initial therapy should include ACEI or ARB
- Higher likelihood of progression to end stage renal disease (ESRD)
- If ACEI/ARB not used as initial therapy, it can be added as second-line drug if necessary, to achieve goal BP
- Most patients with CKD and HTN require more than one drug to reach goal BP
- ACEI/ARB with thiazide-type diuretic or CCB

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OTHER
HYPERTENSION
ISSUES

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Orthostatic Hypotension

- Orthostatic hypotension ↓ 20 mmHg SBP or 10 mmHg DBP with standing
 - Diabetes
 - Dehydration
 - ↓ baroreceptor activity (age)
 - Autonomic insufficiency (CKD)
 - Venodilators (α -blockers, mixed α/β -blockers, nitrates, phosphodiesterase inhibitors)

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Resistant Hypertension

Definition	Causes
• Failure to achieve BP goal despite 3 or more BP medications on optimum doses	• Drugs – inadequate doses, inappropriate choices, BP-elevating agents • Fluid overload • Nonadherence • Obesity, alcohol, sleep apnea, excess dietary sodium • Poor blood pressure measurement technique • White coat/pseudohypertension

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Resistant Hypertension

Treatment

- Remove/treat secondary causes – see earlier slides
- Maximize diuretic therapy
- Add a mineralocorticoid receptor antagonist
- Add other agents with different MOAs
- Use loop diuretics in patients with CKD and/or patients receiving potent vasodilators (minoxidil)
- Identify and correct barriers to adherence
- Weight loss, limit alcohol, sodium restriction
- Potassium supplementation
- Home/ambulatory monitoring, Osler's sign

Refer to specialist

- Refer to specialist for known or suspected secondary cause(s) of HTN
- Refer to HTN specialist if BP remains uncontrolled after 6 mon of treatment

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Pregnancy

Preferred meds

- Methyldopa
- Nifedipine
- Labetalol

Hydralazine may also be used

ACEIs and ARBS should NOT be used

- Potential for fetal defects
- Should be avoided in women likely to become pregnant also¹³⁸

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HTN Pearls in the Elderly

Drug	Disadvantages – how to monitor
Thiazide/Loop diuretics	Urinary Frequency – take earlier in the day Electrolyte abnormalities – K, Na; monitor more frequently Worsening of gout – monitor uric acid
ACEI/ARB	Acute renal failure – avoid if Scr rises > 35% Hyperkalemia – low potassium diet Profound BP lowering w/volume depletion – dose low, go slow
CCBs	Peripheral edema – elevate legs, avoid excess Na Reflex tachycardia – consider combined use with BBs Profound BP lowering – dose low, go slow Bradycardia (nonDHPs) – avoid use with BBs Constipation – laxatives, fiber, fluids Isolated systolic hypertension - preferred
BBs (beta1 preferred)	Bradycardia – avoid use with nonDHP CCBs
Clonidine	Anticholinergic effects - depression, urinary retention, sedation, falls, confusion, vivid dreams, third- or fourth-line agent
α - Antagonists	Orthostasis, dizziness – take at bedtime, dose slowly, use generally for benign prostatic hypertrophy symptoms; little CV benefit

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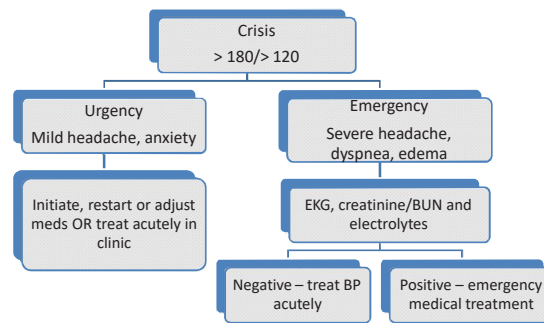
Hypertensive Emergencies

- Causes
 - Vascular sclerosis
 - Renal parenchymal disease
 - Cocaine, amphetamine or stimulant abuse
 - Rapid clonidine withdrawal
 - Endocrine disease – pheochromocytoma, hyperaldosteronism, Cushing's
 - CNS trauma, Guillain-Barré syndrome
 - Coarctation of aorta
 - Pre-eclampsia
 - Postoperative

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Hypertensive Crisis



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Hypertensive Crises

Hypertensive Urgency

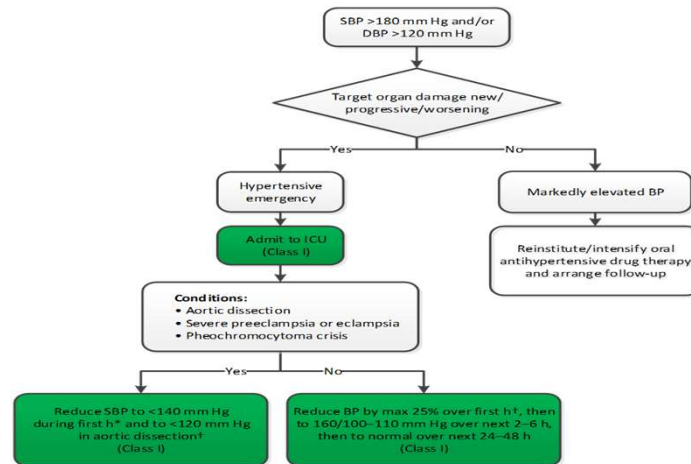
- SBP>180, DBP >120 without acute end organ damage
- Reinstitute or intensify antihypertensive drug therapy and treat anxiety (if applicable)
- Reduce BP in 24-48 hrs with oral antihypertensives
- Rapid reduction may cause morbidity & mortality

Hypertensive Emergency

- SBP > 180, DBP > 120 with new or worsening target organ damage
- Hypertensive encephalopathy, intracranial hemorrhage, acute ischemic stroke, acute MI, acute LV failure with pulmonary edema, unstable angina, dissecting aortic aneurysm, acute renal failure, or eclampsia

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Hypertensive Crisis



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Hypertensive Emergency

Admit to ICU

Use parenteral antihypertensives

Aortic dissection

- In first hour, reduce SBP to < 120

Severe preeclampsia/eclampsia or pheochromocytoma crisis

- In first hour, reduce SBP to < 140

None of the above:

- In first hour, reduce BP by max of 25%
- If stable, to 160/100 in next 2-6 hours
- Then cautiously to normal during following 24-48 hrs

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Hypertensive Emergency

Acute Intracerebral hemorrhage

- Continuous IV antihypertensive infusion with close BP monitoring
- Immediate reduction of SBP to < 140 can be harmful

Acute ischemic stroke

- IV thrombolysis candidates
 - Lower SBP to < 185 and DBP to < 110 *before* initiating thrombolysis
 - Maintain BP $< 180/105$ for first 24 hrs after thrombolysis
- Non-thrombolysis candidates
 - If BP $> 220/110$, lower BP 15% during first 24 hours
 - If BP $\leq 220/110$, no benefit of treating HTN in first 48-72 hrs

Start/resume antihypertensives ≥ 72 hrs from symptom onset with stable neurological status if SBP is ≥ 140 or DBP is ≥ 90

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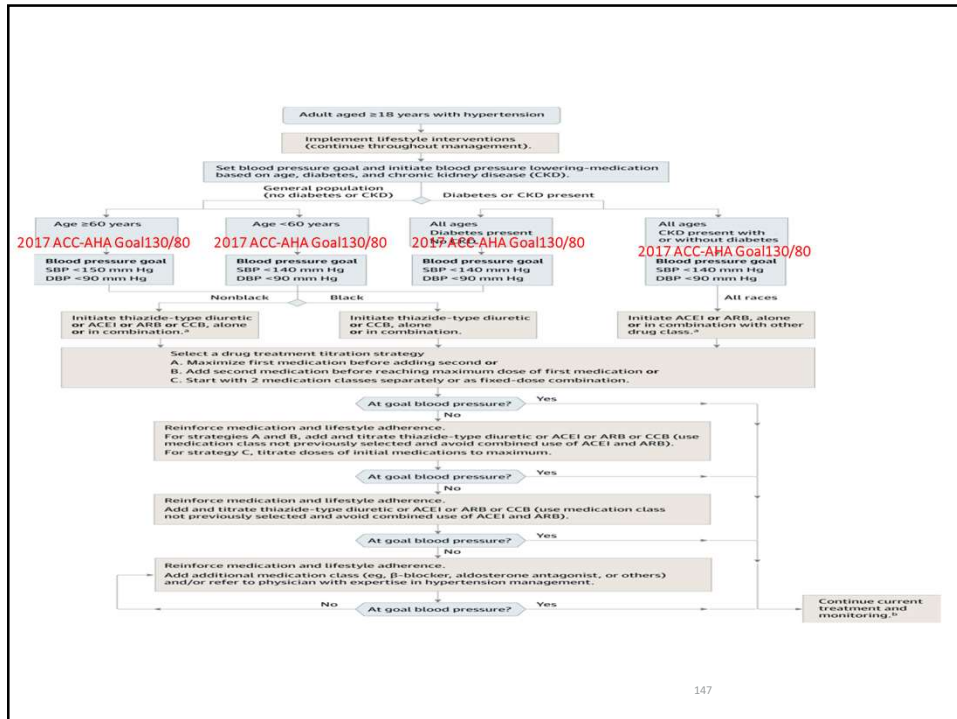
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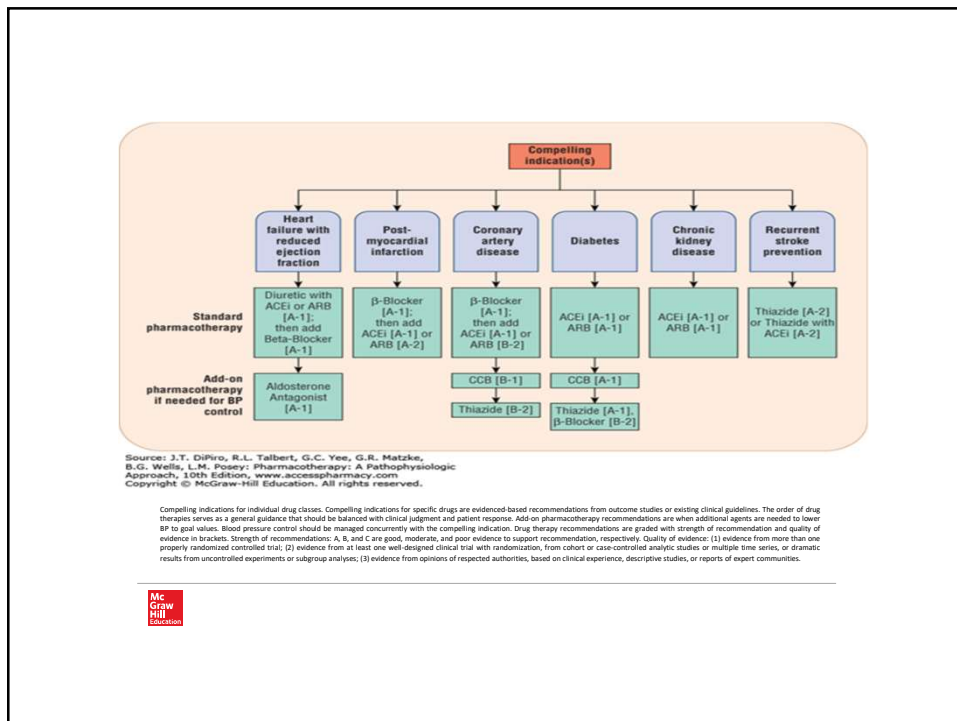
LET'S PUT IT
ALL
TOGETHER

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Attaining and Maintain goal BP



- Main objective – Attain & maintain goal BP
 - If goal BP not reached in ≤ 1 month – add 2nd drug
 - if goal not reached with 2 drugs – add 3rd drug
 - Do not combine ACEI and ARB
 - If goal BP can't be reached using the recommended drugs because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensives from other classes may be used
- Refer to HTN specialist when above strategy fails to achieve goal

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CLINICAL MONITORING

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Monitoring Parameters

BP monitoring

- 2 to 4 weeks after changing or initiating therapy
- 6 to 12 months when controlled or stable
- Home or more frequent monitoring if uncontrolled or suspect organ damage

Organ disease progression

- Signs: EKG, SCr, proteinuria, retinal exam
- Symptoms: ischemic chest pain (or pressure), palpitations, dizziness, dyspnea, orthopnea, headache, sudden change in vision, one-sided weakness, slurred speech, and loss of balance

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ADHERENCE

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Adherence

Identify

- Identify any drug therapy problems – indication, safety, efficacy, adherence!

Simplify

- Simplify medication regimen
- Drug combinations, sustained release formulations

Empower

- Empower informed patients
- Explicit instruction, good counseling techniques, teach back, literacy issues
- Pill boxes
- Phone or email reminders of refills, phone/office appointments

Maintain

- Maintain follow-up with patient, home blood pressure monitoring

Team

- Team-base, collaborative models of care

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Summary

Hypertension increases risk for cardiovascular morbidity and mortality

Lifestyle modifications should be encouraged for all patients,

Stage I and II HTN typically require pharmacologic therapy

- Stage II often requires more than one agent

Specific treatment recommendations are defined for compelling indications, ischemic heart disease, African Americans, and elderly pts

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