Management of Hypertension

Yasmin Grace, B.S., Pharm.D.
Professor of Pharmacy Practice
Palm Beach Atlantic University
Gregory School of Pharmacy
West Palm Beach, Florida

1

Objectives

Upon completion of this activity, the pharmacist will be able to:

- List factors contributing to the etiology of primary and secondary hypertension.
- Describe the diagnosis of hypertension and the purpose of ambulatory blood pressure monitoring
- Recommend lifestyle modifications for the management of hypertension and describe the effectiveness of these modifications.
- Describe the current approach to the management of hypertension.
- Compare and contrast the characteristics of antihypertensive drug classes including place in therapy, adverse effects, drug interactions, contraindications, and monitoring.
- Design individualized antihypertensive treatment regimens for different patient populations.

2

Objectives

Upon completion of this activity, the pharmacy technician will be able to:

- Describe factors contributing to the etiology of primary and secondary hypertension.
- Review the diagnosis of hypertension and the purpose of ambulatory blood pressure monitoring.
- Recommend lifestyle modifications for the management of hypertension and describe the effectiveness of these modifications.
- Review the current approach to the management of hypertension.
- Compare and contrast the characteristics of antihypertensive drug classes including place in therapy, adverse effects, drug interactions, contraindications, and monitoring.
- Review individualized antihypertensive treatment regimens in different patient populations.

3

Hypertension

- Most significant risk factor for cardiovascular disease (CVD) and stroke.
- In 2020, >670,000 deaths were due to high BP
- 47% of US adults have HTN (>130/80 mmHg)
- 24% of adults have controlled hypertension
- 45% of those with uncontrolled blood pressure have a BP of ≥140/90 mmHg
- Costs $131 billion US dollars each year

U.S. Department of Health and Human Services; 2021. Centers for Disease Control and Prevention; 2022. *Hypertension*. 2018;71(19):e13–115. *J Am Heart Assoc*. 2018;7:e008731.

4

Epidemiology

2018 (American Heart Association heart disease and stroke statistics update)→ 32% of US adults had HTN

2017 American college of Cardiology/American Heart Association (ACC/AHA) with lower BP thresholds estimate → 46% prevalence of hypertension in U.S. adults

Circulation. 2017;135:e146-603. *Hypertension*. 2018;71(19):e13–115

5

Epidemiology

Prevalence based on age	Ages 20-44 years: men 30%, women 19%
	Ages 65-74 years: men 77%, women 75%
Prevalence varies with ethnicity & sex	Black: men 59% and women 56%
	White: men 47%, women 41%
	Asian: men 45%, women 36%
	Hispanic: men 44%, women 42%

Hypertension. 2018;71(19):e13–115.

6

Systolic/Diastolic Blood Pressure (mmHg)	Hypertension Stage
<120 and <80	Normal
120 - 129 and <80	Elevated (Pre-hypertension)
130 - 139 or 80-89	Stage 1 Hypertension
≥ 140 or ≥ 90	Stage 2 Hypertension

Hypertension Classifications

Hypertension. 2018;71(19):e13–115.

7

What Stage is this BP?

135/85	Stage 1 HTN
132/92	Stage 2 HTN
124/81	Stage 1 HTN

8

Primary Hypertension

- Diet
- Low Physical Activity
- Family History
- Alcohol consumption
- Smoking
- Obesity

Hypertension with an unknown cause

Hypertension. 2018;71(19):e13–115.

9

Secondary Hypertension

- Chronic Kidney Disease
- Coarctation of the Aorta
- Cushing Syndrome
- Pheochromocytoma
- Primary aldosteronism or mineralocorticoid excess
- Renovascular hypertension
- Sleep apnea
- Thyroid and parathyroid disease

Hypertension with an identifiable cause

Hypertension. 2018;71(19):e13–115.

10

Medications that can Elevate Blood Pressure

Alcohol	• Limit alcohol to ≤1 drink daily for women and ≤2 drinks for men
Amphetamines (e.g., amphetamine, methylphenidate dexmethylphenidate, dextroamphetamine)	• Discontinue or decrease dose • Consider behavioral therapies for ADHD
Antidepressants (e.g., MAOIs, SNRIs, TCAs)	• Consider alternative agents (e.g., SSRIs) depending on indication • Avoid tyramine-containing foods with MAOIs
Atypical antipsychotics (e.g., clozapine, olanzapine)	• Discontinue or limit use when possible • Consider behavior therapy where appropriate • Recommend lifestyle modification • Consider alternative agents associated with lower risk of weight gain, diabetes mellitus, and dyslipidemia (e.g., aripiprazole, ziprasidone)
Caffeine	• Generally, limit caffeine intake to <300 mg/d • Avoid use in patients with uncontrolled hypertension • Coffee use in patients with hypertension is associated with acute increases in BP; long-term use is not associated with increased BP or CVD
Decongestants (e.g., phenylephrine, pseudoephedrine)	• Use for shortest duration possible, and avoid in severe or uncontrolled hypertension • Consider alternative therapies (e.g., nasal saline, intranasal corticosteroids, antihistamines)

Hypertension. 2018;71(19):e13–115.

11

Medications that can Elevate Blood Pressure

Herbal supplements (e.g., Ma Huang [ephedra], St. John's wort [with MAO inhibitors, yohimbine])	• Avoid use
Immunosuppressants (e.g., cyclosporine)	• Consider converting to tacrolimus, which may be associated with fewer effects on BP
Oral contraceptives	• Use low-dose (e.g., 20–30 mcg ethinyl estradiol) agents or a progestin-only form of contraception • Consider alternative forms of birth control where appropriate (e.g., barrier, abstinence, IUD) • Avoid use in women with uncontrolled HTN
NSAIDs	• Avoid systemic NSAIDs when possible • Consider alternative analgesics (e.g., acetaminophen, tramadol, topical NSAIDs), depending on indication and risk
Recreational drugs (e.g., "bath salts" [MDPV], cocaine, methamphetamine, etc.)	• Discontinue or avoid use
Systemic corticosteroids (e.g., dexamethasone, fludrocortisone, methylprednisolone, prednisone, prednisolone)	• Avoid or limit use when possible • Consider alternative modes of administration (e.g., inhaled, topical)
Angiogenesis inhibitor (e.g., bevacizumab) and tyrosine kinase inhibitors (e.g., sunitinib, sorafenif)	• Initiate or intensify antihypertensive therapy

12

Regular Acetaminophen Use and Blood Pressure in People with Hypertension

Circulation. 2022;145(6):416-423.

13

Is Tylenol Safe in Hypertension?

Design: Single-center, randomized, double-blind, placebo-controlled, crossover study, funded by the British Heart Foundation

Aim → assess BP effects of regular APAP use in patients with HTN

Inclusion: Adults either taking anti-hypertensive treatment with an average daytime ABPM < 150/95 mmHg or had untreated HTN with an average daytime ABPM ≥135/85 mmHg but <150/95 mmHg

Exclusion: Liver disease, Kidney disease, Weight < 55 kg, APAP, NSAIDs, corticosteroids, or oral anticoagulants use

Treatment: APAP 1 gram or a matching placebo by mouth 4 times daily for 14 days, followed by a 14-day washout period, and then crossed over to the alternate treatment regimen for 14 days.

Circulation. 2022;145(6):416-423.

14

PATH TRIAL – TYLENOL

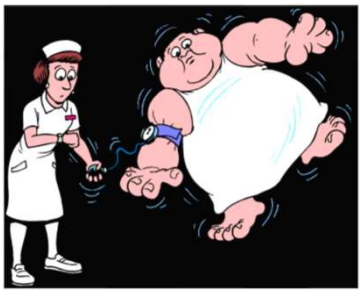
	APAP		Placebo			
	Baseline	**Mean change baseline to day 14**	Baseline	**Mean change baseline to day 14**	Difference	*P* value
Daytime systolic BP	132.8	**3.7 ± 7.4**	133.9	**-1.4 ± 7.6**	4.7 (2.9-6.6)	< 0.0001
24-h systolic BP	126.5	**3.5 ± 7.1**	127.4	**-1.0 ± 7.3**	4.2 (2.4-6.0)	< 0.0001
Daytime diastolic BP	81.2	**0.9 ± 4.2**	81.7	**-0.8 ± 4.4**	1.6 (0.5-2.7)	0.005
24-h diastolic BP	76.8	**0.9 ± 4.2**	77.3	**-0.5 ± 4.3**	1.4 (0.2-2.5)	0.017
Clinic systolic BP	137.4	**3.15 ± 10.3**	136.6	**-1.1 ± 9.2**	4.6 (2.4-6.7)	< 0.0001
Clinic diastolic BP	85.9	**0.6 ± 6.6**	85.7	**-0.9 ± 6.1**	1.6 (-0.1-3.1)	0.031

Circulation. 2022;145(6):416-423.

15

Diagnosis

- Average of ≥ 2 BP measurements taken during ≥ 2 clinical encounters
- Measure BP in both arms
  - Use higher value



Hypertension. 2018;71(19):e13–115.

16

Tips for Proper Blood Pressure Monitoring

Blood pressure should be measured after the patient has emptied their bladder and has been seated for five minutes with back supported and legs resting on the ground (not crossed).

Rest arm used for measurement on a table, at heart-level.

Use a stethoscope or automated electronic device with the correct size arm cuff.

Take two readings one to two minutes apart and average the readings.

Measure blood pressure in both arms at initial evaluation then use the higher reading for measurements thereafter.

Hypertension. 2018;71(19):e13–115.

17

Does Cuff Size Matter?

Effects of Cuff Size on the Accuracy of Blood Pressure Readings: The Cuff(SZ) Randomized Crossover Trial

- Primary outcome: difference in mean SBP and DBP obtained using a regular BP cuff compared with an appropriately sized BP cuff.
- 195 participants
- Mean age of 54 years
- 68% were Black
- 66% were female
- Average body mass index (BMI) was 28.8 kg/m2

JAMA Intern Med. 2023;183(10):1061-1068

18

Mean Difference in BP When a Regular BP Cuff Was Used Regardless of Appropriate BP Cuff Size

		SBP		DBP	
Appropriate Cuff Size	**BP Cuff Used**	**BP Difference mmHg (95% CI)**	**P value**	**BP Difference mmHg (95% CI)**	**P value**
Small (n=35)	1 size too large	**-3.6 (-5.6 to –1.7)**	< .001	**-1.3 (-2.4 to –0.2)**	.02
Regular (n=54)	Correct cuff size	**0**	N/A	**0**	N/A
Large (n=65)	1 size too small	**4.8 (3.0 to 6.6)**	< .001	**1.8 (1.1 to 2.6)**	< .001
Extra large (n=40)	2 sizes too small	**19.5 (16.1 to 22.9)**	< .001	**7.4 (5.7 to 9.1)**	< .001

JAMA Intern Med. 2023;183(10):1061-1068

19

White Coat & Masked Hypertension

White Coat Hypertension

- Elevated office blood pressure and normal out-office blood pressure
- Prevalence ranges from 10-20%
- More common in children, older adults, women and pts with office BP closer to thresholds

Masked Hypertension

- Office blood pressure is normal and elevated out-of-office blood pressure
- Prevalence ranges from 10-30%
- More common in men, African Americans, Diabetes, CKD, OSA
- Associated with higher CV risk

Hypertension. 2018;71(19):e13–115.

20

Out of Office BP Monitoring

Home blood pressure monitoring (HBPM)

- Self-monitoring tool patients can incorporate at home
- Improves BP control, diagnosis of white-coat and masked HTN & prediction of CV risk
- Less expensive and more convenient than ABPM
- Allows patients to be more involved in HTN management
- Detects BP variability

Ambulatory blood pressure monitoring (ABPM)

- BP readings over a continuous period
- Taken every 20-30 minutes during the day and at night
- Measures changes in BP and HR
- BP distribution pattern according to daily activities and sleep patterns
- Can determine effects of antihypertensives on BP
  - Allows for dose adjustments or time for medication administration
  - Predictor for cardiovascular and cerebrovascular disease
  - Detects target organ damage

Hypertension. 2018;71(19):e13–115.

21

Definition of HTN According to Office, Ambulatory, and Home BP

Office	HBPM	Daytime ABPM	Nighttime ABPM	24-hr ABPM
≥130/80	≥130/80	≥130/80	≥110/65	≥125/75

Hypertension. 2018;71(19):e13–115.

22

Patient Evaluation

Objectives:

1. Assess lifestyle and identify other CV risk factors or concomitant disorders that affects prognosis and guides treatment.
2. Identify causes of hypertension.
3. Assess the presence or absence of target organ damage and CVD.

23

Cardiovascular Risk Factors

Age (>55 men, >65 women)
Family history of premature CVD (men age <55, women age <65)
Hypertension
Cigarette smoking
Obesity (BMI >30 kg/m2)
Physical Inactivity
Dyslipidemia
Diabetes mellitus
Microalbuminuria or eGFR <60 mL/min

JAMA 2003; 289:2560.

24

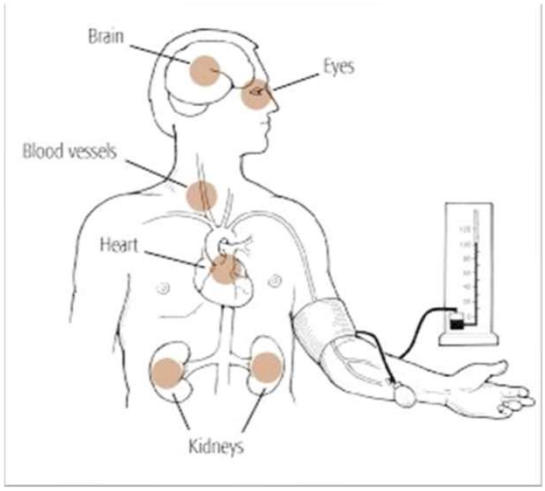
Signs and Symptoms

Most patients are asymptomatic

>50% of adults in U.S. unaware they have hypertension
- Hypertension aka "Silent Killer"

Persistently elevated blood pressure → Target organ damage

25



Target Organ Damage

Brain
- Stroke
- Transient ischemic attack
- Dementia

Retinopathy

Heart
- Left ventricular hypertrophy
- Heart failure
- Angina
- Myocardial infarction

Chronic kidney disease

Peripheral arterial disease

26

CLINICAL CONDITION(S)	BP THRESHOLD, MM HG	BP GOAL, MM HG
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130	<130
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention (lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

Goals of Therapy

- Reduce morbidity & mortality
- Select drug therapy based on evidence demonstrating risk reduction

Hypertension. 2018;71(19):e13–115.

27

SPRINT TRIAL

- The Systolic Blood Pressure Intervention Trial - 2015
- Randomized 9361 patients with HTN & elevated CV risk to either an intensive systolic blood pressure (SBP) target (<120 mm Hg) or a standard SBP target (<140 mm Hg)
- Results:
  - At 3.3 years, lower SBP target had a significantly lower rate of MI, ACS, stroke, acute decompensated heart failure, CV death
    - 1.8% per year vs. 2.4% per year; hazard ratio [HR] 0.73; 95% confidence interval [CI], 0.63 to 0.86
  - Lowered all-cause mortality with intensive targets
    - 1.1% per year vs. 1.4% per year; HR 0.75; 95% CI 0.61 to 0.92
- **Intensive blood pressure control improves cardiovascular outcomes and survival**

N Engl J Med. 2015;373:2103-16

28

Benefits of Lowering Blood Pressure

The blood pressure relationship to risk of cardiovascular disease (CVD) is continuous, consistent, and independent of other risk factors.

Each increment of 20/10 mmHg doubles the risk of CVD across the entire BP range starting from 115/75 mmHg.

Elevated BP or (pre-hypertension) signals the need for increased education to reduce BP in order to prevent hypertension.

JAMA 2003; 289:2560.

29

Patient Case

JP is a 67-year-old white woman who smokes ½ pack per day and has chronic obstructive pulmonary disease.

VS: BP 144/68 BP (last visit): 138/70 P: 76 RR: 18 T: 98°F
Ht: 71" Wt: 165 lbs

Fasting Labs:

Na-140 mEq/L	K – 4.3 mEq/L	Cl - 98mEq/L
CO2 – 28 mEq/L	BUN – 18 mg/dL	SCr – 1.4 mg/dL
Glu – 108 mg/dL	Ca – 9.3 mg/dL	

TC: 178 LDL: 112 HDL: 38 TG: 140

Medications:
- Albuterol (Ventolin®) inhaler 2 puffs Q6 H PRN SOB
- Ipratropium (Atrovent®) inhaler 2 puffs Q6H

30

Patient Case Questions

JP's blood pressure is classified as:

A. Normal
B. Elevated or prehypertension
C. Stage 1 hypertension
D. Stage 2 hypertension

31

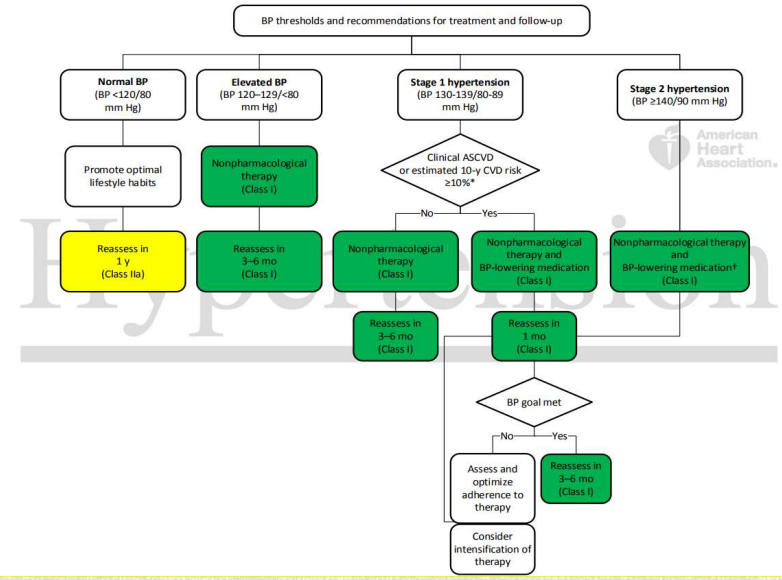
Patient Case Questions

What is JPs blood pressure goal?

A. <120/80
B. <130/80
C. <140/80
D. <140/90
E. <150/90

32

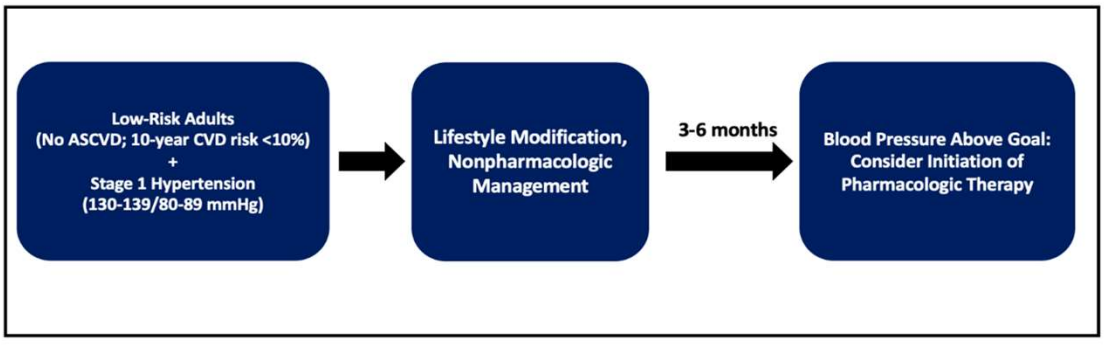
Figure 4. Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up



Hypertension. 2018;71(19):e13–115.

33

New 2021 Guidance on Stage 1 Hypertension Management in Low-Risk Adults.



Hypertension. 2021;77:e58–67.

34

NONPHARMACOLOGICAL INTERVENTION			APPROXIMATE IMPACT ON SBP	
			Hypertension	Normotension
Physical activity	Aerobic	• 90–150 min/week • 65%–75% heart rate reserve - Decrease time in sedentary activities -Increase physical activity (walking, biking, aerobic dancing, basketball, tennis)	-5/8 mm Hg	-2/4 mm Hg
	Dynamic resistance	• 90–150 min/week • 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/week • 8–10 week	-5 mm Hg	-4 mm Hg

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

35

Aerobic, Dynamic and Isometric

Aerobic	Dynamic	Isometric
• Swimming • Cycling • Walking • Rowing	• Jumping Jacks • Arm circles • Lunges • Squats	• Planks • Wall sit • Static lunge • Leg extensions

36

Nonpharmacological Intervention			Approx. Impact on SBP	
			Hypertension	Normotension
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. - Read food labels & OTC meds for sodium content -Use herbs and spices instead to flavor foods -Avoid processed foods (canned, frozen foods, cheeses & luncheon meats)	-5/6 mm Hg	-2/3 mm Hg

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

37

Dietary Sodium Reduction

Tips to limit sodium:

- Learn to read food labels to determine sodium content.
- Read over-the-counter medication labels for sodium content.
- Use herbs and spices instead to flavor foods.
- Avoid processed foods (canned and frozen foods, cheeses and luncheon meats)
- **Goal <1,500 milligrams daily**

Hypertension. 2018;71(19):e13–115.

38

The Salt Substitute and Stroke Study (SSaSS)

- 21,000 people with a history of stroke or high blood pressure in rural China
- Half using a lower-sodium salt substitute instead of regular salt
- Results after 5 years for those using salt substitute
  - **14% reduction in stroke**
  - **13% reduction in major cardiovascular events**
  - **12% reduction in death**
  - Benefits were achieved with little to no ADRs
- One of the largest dietary intervention trials ever conducted
- Simple and low-cost intervention
- Results from 2 meta-analyses support these findings

Am Heart J 2017;188:109-117.

39

Sodium Contents

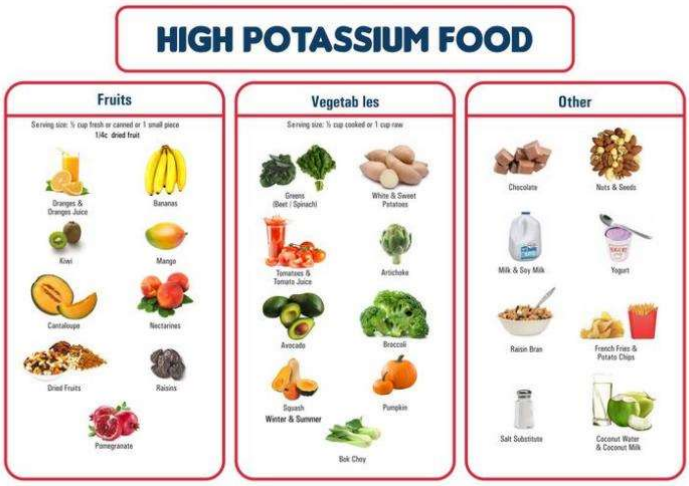
40

Nonpharmacological Intervention			Approx. Impact on SBP	
			Hypertension	Normotension
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

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

41



Potassium

- Regulates fluid balance, muscle contractions and nerve signals
- High-potassium diet may reduce BP and water retention
- May protect against stroke, osteoporosis and kidney stones
- Foods high in potassium:
  - Bananas, oranges, cantaloupe, honeydew, apricots, grapefruit
  - Cooked spinach and broccoli

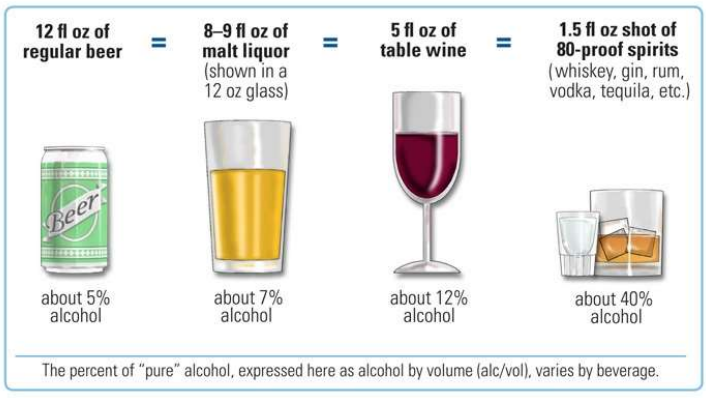
42

Nonpharmacological Intervention			Approx. Impact on SBP	
			Hypertension	Normotension
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

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

43



Alcohol Equivalents

One drink equals=

- 12 ounces of beer or wine cooler
- 5 ounces of wine
- 1.5 ounces of 80-proof liquor

Hypertension. 2018;71(19):e13–115.

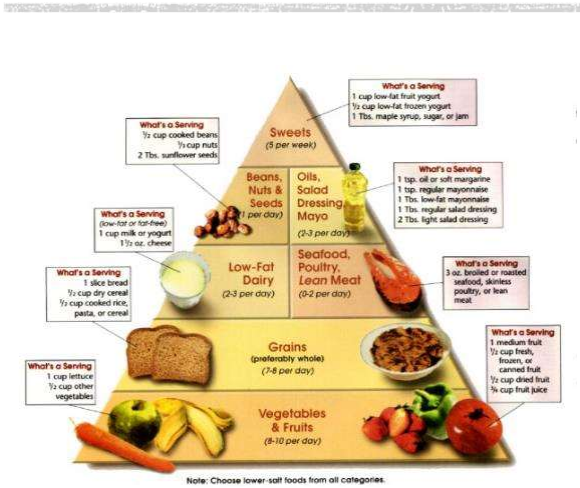
44

	Nonpharmacological Intervention		Approx. 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. • Decrease portion sizes for meals and snacks.	-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

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

45



DASH Diet

46

SUGAR CONSUMPTION

47

How many teaspoons of sugar does the average American eat and drink every day?

A. 9
B. 13
C. 17
D. 22

48

Twenty-two teaspoons of sugar a day…

22!

49

AHA Scientific Statement

Dietary Sugars Intake and Cardiovascular Health

A Scientific Statement From the American Heart Association

Rachel K. Johnson, PhD, MPH, RD, Chair; Lawrence J. Appel, MD, MPH, FAHA; Michael Brands, PhD, FAHA; Barbara V. Howard, PhD, FAHA; Michael Lefevre, PhD, FAHA; Robert H. Lustig, MD; Frank Sacks, MD, FAHA; Lyn M. Steffen, PhD, MPH, RD, FAHA; Judith Wylie-Rosett, EdD, RD; on behalf of the American Heart Association Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism and the Council on Epidemiology and Prevention

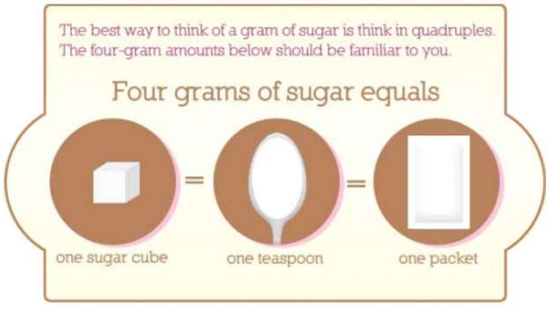
Abstract*—**High intakes of dietary sugars in the setting of a worldwide pandemic of obesity and cardiovascular disease have heightened concerns about the adverse effects of excessive consumption of sugars. In 2001 to 2004, the usual intake of added sugars for Americans was 22.2 teaspoons per day (355 calories per day). Between 1970 and 2005, average annual availability of sugars/added sugars increased by 19%, which added 76 calories to Americans' average daily energy intake. Soft drinks and other sugar-sweetened beverages are the primary source of added sugars in Americans' diets. Excessive consumption of sugars has been linked with several metabolic abnormalities and adverse health conditions, as well as shortfalls of essential nutrients. Although trial data are limited, evidence from observational studies indicates that a higher intake of soft drinks is associated with greater energy intake, higher body weight, and lower intake of essential nutrients. National survey data also indicate that excessive consumption of added sugars is contributing to overconsumption of discretionary calories by Americans. On the basis of the 2005 US Dietary Guidelines, intake of added sugars greatly exceeds discretionary calorie allowances, regardless of energy needs. In view of these considerations, the American Heart Association recommends reductions in the intake of added sugars. A prudent upper limit of intake is half of the discretionary calorie allowance, which for most American women is no more than 100 calories per day and for most American men is no more than 150 calories per day from added sugars. (Circulation*. 2009; 120:1011-1020.**)

Key Words: AHA Scientific Statements ■ cardiovascular diseases ■ carbohydrates, dietary ■ diet ■ beverages ■ carbonated beverages ■ lipids

50

American Heart Association

51



Sugar Conversions

52


11
Coca-Cola
classic
9
pepsi
9
Fanta
FRUIT TWIST
8

53


NEW
Minute Maid
Pure Squeezed
NO PULP
Is orange Juice healthy?

54

Orange Juice

100% JUICE

Nutrition Facts
Serving Size 8 fl. oz. (240 mL)
Servings Per Container 7

Amount Per Serving	
Calories 110	Calories from Fat 0
	% Daily Value*
Total Fat 0g	0%
Sodium 0mg	0%
Potassium 450mg	13%
Total Carbohydrate 26g	9%
Sugars 22g	
Protein 2g	

Calcium 2% • Iron 0% • Vitamin C 120%
Niacin 4% • Thiamine 10%
Vitamin B6 6% • Folate 15%

Not a significant source of calories from fat, trans fat, saturated fat, cholesterol, dietary fiber, vitamin A and iron. Percent Daily Values are based on a 2,000 calorie diet.

Ingredients: Organic orange juice and organic orange pulp

55

Is yogurt healthy?

56

Yogurt

57

Hidden Sugars

58

Weight reduction	
DASH eating plan	Fiber consumption (20-30 grams/day)
Dietary sodium reduction	Less than 1.5 grams
Increase intake of dietary potassium	Goal 3,500-5,000 mg/d
Aerobic physical activity	90-150 minutes/week
Moderation of alcohol consumption	
Smoking cessation	

Lifestyle Modifications

Hypertension. 2018;71(19):e13–115.

59

Patient Case

NL is a 44 YOW who comes into your community pharmacy with a prescription hydrochlorthiazide12.5 mg once daily for a new diagnosis of hypertension. She has no other medical conditions and is not taking any other medications. Her average blood pressure during her previous two physician visits was 146/96 mm Hg.

NL reports that she has a sedentary lifestyle, works 60 hours a week, has a body mass index of 31 kg/m^2 (obese), eats fast food frequently, and drinks 3 glasses of wine daily.

60

Patient Case Question

List lifestyle modifications that should be recommended:

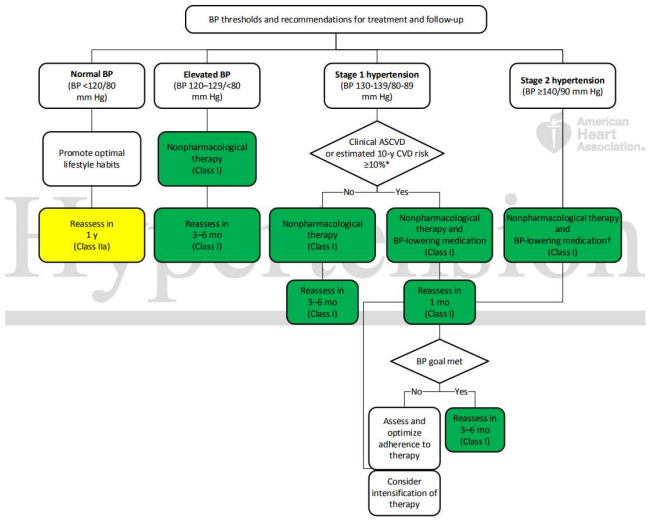
A. Educate her to balance her diet according to the food pyramid.
B. Instruct her to eliminate alcohol from her diet.
C. Counsel her to achieve and maintain optimal weight.
D. Suggest that she reduce her sodium intake to no more than 2.8 g/day.

61

2017 Hypertension Guideline Recommendations

62

Figure 4. Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up

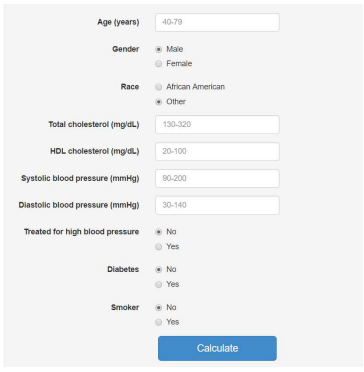


Hypertension. 2018; 71(19):e13–115.

63

ASCVD Risk Calculator

http://www.cvriskcalculator.com/



64

Patient Population	When to Initiate Pharmacotherapy
Clinical CVD (stroke, heart failure, CAD) or 10-year ASCVD risk ≥10%	≥ 130/80 mmHg
No clinical CVD and 10-year ASCVD risk <10%	≥ 140/90 mmHg
Secondary stroke prevention	≥ 140/90 mmHg

Pharmacotherapy Recommendations

Hypertension. 2018;71(19):e13–115.

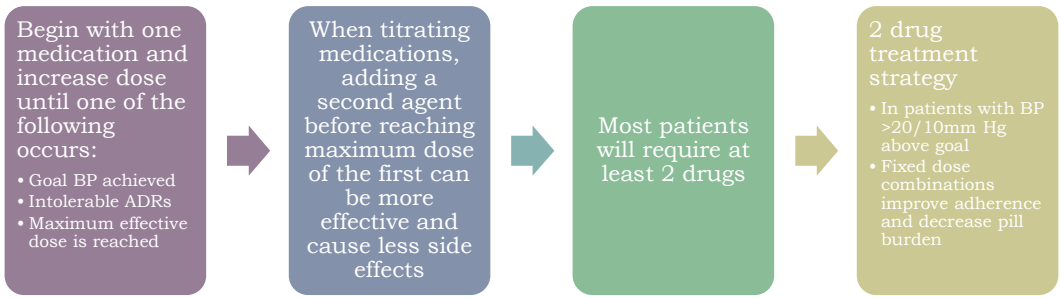
65

Patient Population	Pharmacotherapy Agents to Initiate
Nonblack	Thiazide, DHP-CCB, ACEI, or ARB
African American	Thiazide or DHP-CCB
Chronic kidney disease	ACEI or ARB
Diabetes with Albuminuria	ACEI or ARB

Pharmacotherapy Recommendations

Hypertension. 2018;71(19):e13–115.

66



Treatment Strategy

Hypertension. 2018;71(19):e13–115.

67

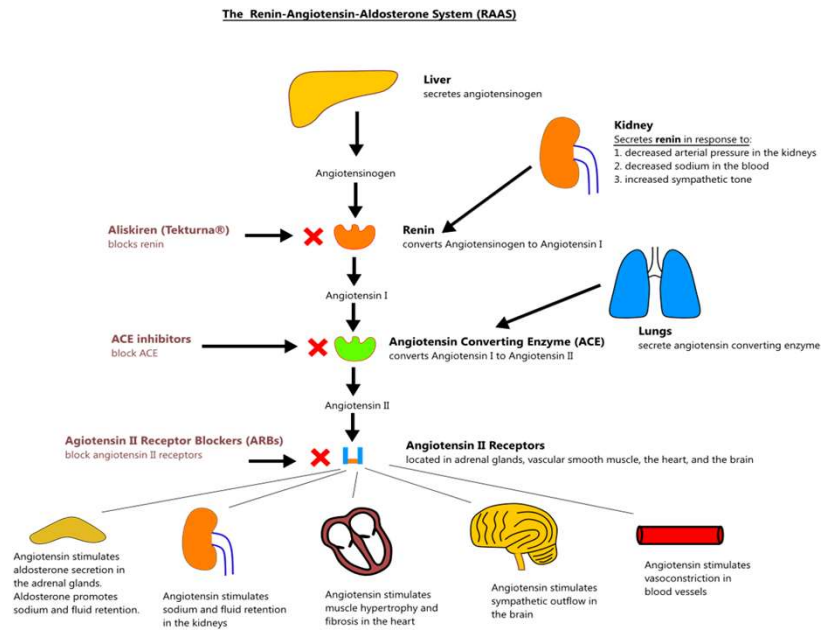
Medications

First-line agents
- Thiazide Diuretics
- Angiotensin Converting Enzyme Inhibitors (ACEI)
- Angiotensin II Receptor Blockers (ARBs)
- Calcium Channel Blockers (CCBs)

Second-line agents
- Beta Blockers
- Renin Inhibitors
- Combined alpha & beta-blockers
- Alpha-1 blockers
- Central alpha-2 agonists
- Peripheral Adrenergic Agonists
- Direct Vasodilators

Hypertension. 2018;71(19):e13–115.

68



The Renin-Angiotensin-Aldosterone System (RAAS)

69

FIRST-LINE AGENTS

70

THIAZIDE DIURETICS

Indications

- Hypertension, Heart failure (mild)
- Uncomplicated hypertension alone or in combination with other medications
- Increased efficacy in older patients and African Americans
- Beneficial if used in patients with: hypercalciuria & osteoporosis
- Less effective with decreased renal function (CrCL <30 mL/min)

Hypertension. 2018;71(19):e13–115.

71

Drug, Dose, & Frequency	• Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. • Use with caution in patients with history of acute gout unless patient is on uric acid– lowering therapy. • Chlorthalidone is preferred based on prolonged half-life and proven trial reduction of CVD. • Chlorthalidone & indapamide → longer T1/2, may have a greater effect in patients with resistant hypertension
Chlorthalidone 12.5-25 mg PO daily	
Hydrochlorothiazide12.5-50 mg PO daily	
Indapamide 1.25 - 5 mg PO daily	
Metolazone 2.5 - 5 mg PO daily	

Thiazide Diuretics

Hypertension. 2018;71(19):e13–115.

72

Hydrochlorothiazide	Chlorthalidone
• Doses >25 mg may cause greater ADRs without additional antihypertensive effect • Shorter half-life	• Preferred over HCTZ however not available in many combination formulations • 25 mg tablet – cut in half for 12.5 mg dose • 12.5 mg = 19-25 mg of HCTZ

Thiazide Diuretics

Hypertension. 2004;43:4–9

73

The Diuretic Comparison Project

Design: Multicenter, embedded, two-arm intervention, open-labeled trial

Aim → chlorthalidone vs. hydrochlorothiazide in reducing the risk of nonfatal major CVD outcomes and non-cancer-related deaths in older adults with hypertension

Inclusion: Veteran's Affairs (VA) patients, at least 65 years-of-age, hypertension with a systolic blood pressure (SBP) ≥ 120 mmHg at the most recent visit and receiving HCTZ 25-50 mg daily from a VA pharmacy

Exclusion: death expected within 6 months, potassium <3.1 mEq/L (3.5 mEq/L if on digoxin), sodium <130 mEq/L in the last 90 days, taking a fixed-dose HCTZ combination, unable to provide informed consent, or enrolled in Medicare Part C

Treatment: 13,523 patients randomized to continue HCTZ at their current dose (25 or 50 mg) or switch to chlorthalidone (12.5 or 25 mg).

N Engl J Med. 2022;387(26):2401-2410.

74

The Diuretic Comparison Project

Primary outcome:	First occurrence of a composite of non-cancer-related deaths and nonfatal CVD events (i.e., nonfatal MI, stroke, hospitalization for heart failure, or urgent revascularization for unstable angina).
Secondary outcomes:	Individual components of the primary composite and safety outcomes (i.e., electrolyte abnormalities, hospitalizations, and acute kidney injury).
Results (median follow-up of 2.4 years):	**No difference in event rate between the chlorthalidone (10.4%) and HCTZ (10.0%) groups (HR 1.04; 95% CI 0.94-1.16, p=0.45).**
	Higher rate of hospitalizations for hypokalemia (HR 1.35; 95% CI 1.00-1.82) and a greater incidence of potassium <3.1 mmol/L (HR 1.39; 95% CI 1.18-1.64) in the chlorthalidone group.
	Subgroup analyses → history of MI or stroke at baseline had significantly fewer events in the chlorthalidone group (HR 0.73; 95% CI 0.57-0.94).

N Engl J Med. 2022;387(26):2401-2410.

75

Question

Which thiazide (and dose) would you recommend for a patient with hypertension being switched from HCTZ 25 mg daily?

A. Chlorthalidone 12.5 mg
B. Chlorthalidone 25 mg
C. Indapamide 25 mg
D. Indapamide 5 mg

76

ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEI)

Indications

- Hypertension, heart failure, diabetic nephropathy, chronic kidney disease with proteinuria, myocardial infarction (MI), coronary artery disease (CAD)

Specific Patient Populations

- Lower complications of hypokalemia from diuretics when used concurrently
- Morbidity and mortality benefits in most compelling indications.
- ACEI slow rates of diabetic nephropathy
- Synergy with diuretics

Hypertension. 2018;71(19):e13–115.

77

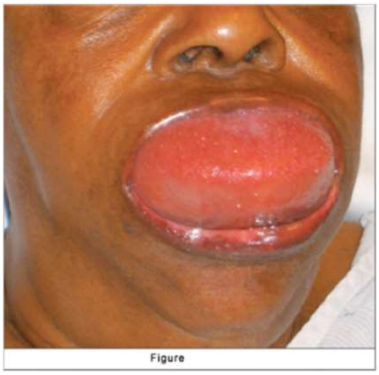
Drug, Dose, & Frequency
Benazepril 5-40 mg PO daily
Captopril 12.5-100 mg PO BID
Enalapril 5-40 mg PO div daily-BID
Fosinopril 10-40 mg PO daily
Lisinopril 10-40 mg PO daily
Moexipril 7.5-30 mg PO daily
Perindopril 4-8 mg PO daily
Quinapril 10-80 mg PO daily
Ramipril 2.5-10 mg PO daily or BID
Trandolapril 1-4 mg PO daily

- Do not use in combination with ARBs or direct renin inhibitor.
- Increased risk of hyperkalemia, especially in patients with CKD or in those on K+ supplements or K+-sparing drugs.
- Risk of acute renal failure in patients with severe bilateral renal artery stenosis.
- Do not use if patient has history of angioedema with ACE inhibitors.
- Contraindicated to use within 36 hours of a neprilysin inhibitor
- Do not use in pregnancy

Angiotensin Converting Enzyme Inhibitors (ACEI)

Hypertension. 2018;71(19):e13–115.

78



Figure

Angioedema

Icatibant (*Firazyr®)* – off label use for angioedema

79

ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS)

- **Indications**
  - Hypertension, Heart failure, Diabetic nephropathy, post MI
- **Place in Therapy/ Class Advantages**
  - Lower incidence of cough comparing to ACEI
  - Alternative for patients with ACEI-induced angioedema

Hypertension. 2018;71(19):e13–115.

80

Drug, Dose, & Frequency
Azilsartan 40-80 mg PO daily
Candesartan 8-32 mg PO daily
Eprosartan 600-800 mg PO daily or BID
Irbesartan 150-300 mg PO daily
Losartan 50-100 mg PO daily or div BID
Olmesartan 20-40 mg PO daily
Telmisartan 20-80 mg PO daily
Valsartan 80-320 mg daily

- Do not use in combination with ACE inhibitors or direct renin inhibitor.
- Increased risk of hyperkalemia in CKD or in those on K+ supplements or K+- sparing drugs.
- Risk of acute renal failure in patients with severe bilateral renal artery stenosis.
- Do not use if patient has history of angioedema with ARBs.
- Patients with a history of angioedema with an ACE inhibitor can receive an ARB **beginning 6 weeks** after ACE inhibitor is discontinued.
- Avoid in pregnancy.
- Sprue-like enteropathy (olmesartan) – severe chronic diarrhea months to years after initiation

Angiotensin II Receptor Blockers (ARBs)

Hypertension. 2018;71(19):e13–115.

81

Dihydropyridines: directly act on vascular smooth muscle to produce peripheral arterial vasodilation

Non-dihydropyridines: Greater depressive effect on cardiac conduction & contractility compared to dihydropyridines

Calcium Channel Blockers (CCBs)

Hypertension. 2018;71(19):e13–115.

82

Drug, Dose, & Frequency	
Amlodipine 2.5-10 mg PO daily	• Avoid use in patients with HF*r*EF; amlodipine or felodipine may be used if required. • Associated with dose-related pedal edema, which is more common in women than men. • No effect on asthma, COPD or PAD • May be used in combination with beta blockers for angina d/t CAD • Immediate release dihydropyridines should be avoided • Used in treatment of Raynaud's syndrome • Adalat® CC & Procardia® XL: counsel regarding possibility of **ghost tablet shell in stool.** • Reflex tachycardia
Felodipine 5-10 mg PO daily	
Isradipine 5 -10 mg PO BID	
Nicardipine SR 5-20 mg PO daily	
Nifedipine LA 60-120 mg PO daily	
Nisoldipine ER 30-90 mg PO daily	

CCBs - Dihydropyridines

Hypertension. 2018;71(19):e13–115.

83

SECOND-LINE AGENTS

84

Drug, Dose, & Frequency	
Diltiazem SR 180-360 mg PO daily	• *Not good first-line antihypertensive agents* • Useful for arrhythmias • Rate control in atrial fibrillation • Useful in CAD with angina in patients unable to take a beta blocker • Do not use in HFrEF. • Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. • Monitor CYP3A4 drug interactions • Delayed onset formulations are 4-5 hour delayed release, administer at bedtime → prevent morning surge of increased BP
Diltiazem ER 120-480 mg PO daily	
Verapamil IR 40-80 mg PO TID	
Verapamil SR 120-480 mg PO daily to BID	
Verapamil delayed onset 100-480 mg PO QHS	

CCBs - non-Dihydropyridines

Hypertension. 2018;71(19):e13–115.

85

Drug, Dose, & Frequency	
Bumetanide 0.5-4 mg PO div daily to BID	▪ Preferred diuretics in patients with symptomatic HF. ▪ Preferred over thiazides in patients with moderate-to-severe CKD (e.g., GFR <30 mL/min). ▪ May need higher doses for patients with severe chronic kidney disease or HF ▪ Dose in the morning to avoid nocturnal diuresis (2nd dose if BID should be at least 6 hrs before HS) ▪ Monitor for hypokalemia and hyponatremia.
Furosemide 20-80 mg PO divided BID	
Torsemide 5-10 mg PO daily	

Loop Diuretics

Hypertension. 2018;71(19):e13–115.

86

Drug, Dose, & Frequency	
Amiloride 5-10 mg PO daily to BID	▪ Minimally effective antihypertensive agents. ▪ Combination therapy with a thiazide can be considered in patients with hypokalemia ▪ Avoid in patients with significant CKD (eGFR <45 mL/min). ▪ Avoid in patients with serum K+ values >5.0 mEq/L ▪ Dose in the AM to prevent nocturnal diuresis
Triamterene 50-100 mg PO div daily to BID	

Potassium Sparing Diuretics

Hypertension. 2018;71(19):e13–115.

87

Drug, Dose, & Frequency	
Eplerenone 50-100 mg PO daily - BID	▪ Preferred agents in primary aldosteronism and resistant hypertension. ▪ Spironolactone is associated with greater risk of gynecomastia and impotence as compared with eplerenone. ▪ This is common add-on therapy in resistant hypertension. ▪ Avoid use with K+ supplements, other K+- sparing diuretics, or significant renal dysfunction. ▪ Combination with thiazide diuretics may provide less hypokalemia at an improved cost to the patient. ▪ Spironolactone: High affinity for androgen and progesterone receptors ▪ Eplerenone requires twice-daily dosing for adequate BP lowering. ▪ May take up to 6 weeks to see full antihypertensive effects.
Spironolactone 25-100 mg PO daily - BID	

Aldosterone Antagonists

Hypertension. 2018;71(19):e13–115.

88

BETA BLOCKERS

89

Indications

- CAD and Angina: reducing cardiac work & improve exercise tolerance and relieve symptoms
- Myocardial infarction: reducing rate of recurrence
- Arrhythmias
- Heart failure: survival benefits
- Hypertension
- Migraines and tremors

BETA BLOCKERS

Hypertension. 2018;71(19):e13–115.

90

Drug, Dose, & Frequency	
Nebivolol 5-40 mg PO daily	▪ Nebivolol; stimulation of nitric oxide release (may lead to less erectile dysfunction) ▪ Beta blockers are not recommended as first-line agents unless the patient has ischemic heart disease or heart failure. ▪ Bisoprolol and metoprolol succinate are preferred in patients with HFrEF. ▪ These are preferred in patients with bronchospastic airway disease requiring a beta-blocker. ▪ Useful in combination with vasodilators to decrease reflex tachycardia. ▪ Avoid abrupt cessation.
Atenolol 25-100 mg PO daily	
Betaxolol 5-20 mg PO daily	
Bisoprolol 2.5-10 mg PO daily	
Metoprolol tartrate 100-200 mg PO div BID	
Metoprolol succinate 50-200 mg PO daily	

Cardioselective Beta Blockers

Hypertension. 2018;71(19):e13–115.

91

Drug, Dose, & Frequency	
Nadolol 40-320 mg PO daily	▪ Avoid in patients with reactive airways disease. ▪ Propranolol: lipophilic→ crosses blood brain barrier (CNS side effects) – good for migraine prophylaxis and essential tremor ▪ Avoid abrupt cessation.
Propranolol IR 160 – 480 mg PO div BID	
Propranolol LA 80-320 mg PO daily	

Non Cardioselective Beta Blockers

Hypertension. 2018;71(19):e13–115.

92

Drug, Dose, & Frequency	
Carvedilol 12.5 – 50 mg PO div BID	▪ Carvedilol is preferred in patients with HF*r*EF. ▪ Carvedilol → Take with food to decrease orthostatic hypotension (food decreases rate but not extent of absorption. ▪ Labetalol → Taking with food increases BA and may decrease tolerability ▪ Avoid abrupt cessation.
Carvedilol phosphate 20 – 80 mg PO daily	
Labetalol 200-800 mg PO div BID	

Combined Alpha & Beta Blockers

Hypertension. 2018;71(19):e13–115.

93

Drug, Dose, & Frequency	
Acebutolol 200-800 mg PO div BID	▪ Generally, avoid, especially in patients with ischemic heart disease or heart failure. ▪ Avoid abrupt cessation.
Carteolol 2.5-10 mg PO daily	
Penbutolol 10-40 mg PO daily	
Pindolol 10-60 mg PO div BID	

Beta Blockers with intrinsic sympathomimetic activity (ISA)

Hypertension. 2018;71(19):e13–115.

94

Drug, Dose, & Frequency	
Aliskiren 150-300 mg PO daily	▪ Do you use in combination with ACEI or ARBs. ▪ Aliskiren is very long acting. ▪ Lowers blood pressure comparable to most other agents ▪ May cause acute renal failure in severe bilateral renal artery stenosis ▪ Decreased absorption with high fat meals ▪ Do not use in pregnancy or history of angioedema. ▪ Approved for use in children 6 and older.

Direct Renin Inhibitor

Hypertension. 2018;71(19):e13–115.

95

Drug, Dose, & Frequency	
Doxazosin 1-8 mg PO daily	▪ May consider as second-line agents in patients with BPH. ▪ Orthostatic hypotension especially in older adults. ▪ Caution with first dose syncope (Dose HS) ▪ Dizziness/ fatigue ▪ Intraoperative floppy iris syndrome in cataract surgery ▪ Cardura XL: ghost tablet and take with morning meal
Prazosin 2-20 mg PO div BID-TID	
Terazosin 1-20 mg PO div QHS-BID	

Alpha-1 Blockers

Hypertension. 2018;71(19):e13–115.

96

Drug, Dose, & Frequency	
Clonidine 0.1-0.3 mg PO BID (max 2.4 mg)	▪ Generally reserved for last-line because of significant CNS ADRs, especially in older adults. ▪ Clonidine is useful for resistant hypertension ▪ Abrupt discontinuation of clonidine may induce in hypertensive crisis. Taper to avoid rebound hypertension. ▪ Methyldopa is safe in pregnancy ▪ Methyldopa combined with HCTZ may decrease salt and water retention
Clonidine patch 0.1-0.3 mg weekly (max 0.6 mg)	
Methyldopa 250-1000 mg PO BID	
Guanfacine 0.5-2 mg PO QHS	

Central Alpha-2 Agonists

Hypertension. 2018;71(19):e13–115.

97

Central Alpha-2 Agonists

Clonidine

- Switching from PO → Patch
  - Continue PO for 1-2 days and decrease dose by 50% at day 2
  - Catapres-TTS-1: 0.1 mg/24 hr
  - Catapres-TTS-2: 0.2 mg/24 hr
  - Catapres-TTS-3: 0.3 mg/24 hr
- Clonidine patch needs to be replaced once every week
- Remove **clonidine patch before MRI**

98

Drug, Dose, & Frequency	
Hydralazine (Apresoline®) 10-50 PO QID	▪ Associated with sodium and water retention and reflex tachycardia. Use with a diuretic and a beta blocker. ▪ Hydralazine is associated with drug-induced lupus-like syndrome at higher doses. ▪ Minoxidil is associated with hirsutism and requires a loop diuretic. Minoxidil can induce pericardial effusion.
Minoxidil 5-40 mg PO daily	

Direct Vasodilators

Hypertension. 2018;71(19):e13–115.

99

Quick Stop

100

Resistant Hypertension

Definition:

- Failure to reach goal BP despite adherence to full doses of a 3-drug regimen (including a diuretic) or
- Needing 4 or more medications to control BP

Hypertension. 2018;71(19):e13–115.

101

Resistant Hypertension

Causes:

- Non-adherence: ~50% of patients may not take medication appropriately
  - Due to miscommunication
  - Denial of illness b/c of lack of symptoms
  - Perception of taking drugs as bad health
  - Lack of patient involvement in therapy
  - Unanticipated adverse effects from medications
  - High cost
- Secondary hypertension
- Excess intake of Na+ (>1.5 grams/day)
- Volume retention due to decreased kidney function
  - Thiazide recommended for majority of patients
  - Loop diuretics for patients with CrCl < 30 mL/min/1.73 m2) or HF

Hypertension. 2018;71(19):e13–115.

102

Resistant Hypertension

Causes continued:

- Drug-induced
  - Cocaine, amphetamines, NSAIDs, etc.
- Excess alcohol intake
  - >2 drinks/day in men
  - >1 drink/day in women
- Poor medication selection
  - Select agents based on coexisting conditions
  - Risk of adverse effects
  - Previous therapies attempted
  - Ethnic/age characteristics

Hypertension. 2018;71(19):e13–115.

103

Resistant Hypertension

Causes continued:

- Treatment options
  - Maximize diuretic therapy
    - Chlorthalidone or indapamide
    - Consider loop in CrCl <30 mL/min and in patients on minoxidil
  - Spironolactone
  - Add medications with different mechanisms of action

Hypertension. 2018;71(19):e13–115.

104

Indication	Preferred Antihypertensive
Heart Failure with reduced Ejection Fraction	ARNI/ACEI/ARB, beta-blocker (carvedilol, metoprolol succinate, bisoprolol), MRA, SGLT inhibitors, loop diuretics
Post-myocardial Infarction	ACEI/ARB, beta-blocker, MRA
Chronic Kidney Disease with proteinuria	ACEI/ARB
Angina Pectoris	Beta-blocker, CCB
Atrial fibrillation/flutter	Beta-blocker, non-DHP CCB

Compelling Indications

Hypertension. 2018;71(19):e13–115.

105

Special Populations

Chronic Kidney Disease

- Importance of standardizing office BP measurements
- Use of ABPM or HBPM monitoring to complement office BP measurements
- Adults with high BP and CKD should have a target goal BP of <120 mmHg, when tolerated.
  - Specifically in patients >50 and <80 years old
  - High CVD risk
- Lifestyle interventions
  - Dietary sodium reduction to <2 g daily
  - DASH diet may not be appropriate as it may induce hyperkalemia
  - Moderate intensity physical activity ≥150 minutes weekly, as tolerated

Ann Intern Med. 2021; June 22.

106

Special Populations

Chronic Kidney Disease

- Patients with albuminuria +/- diabetes
  - ACEI or ARBs recommended
- Adult kidney transplant recipients
  - Target BP goal of <130/80 mmHg
  - DHP CCB and ARBs recommended

Ann Intern Med. 2021; June 22.

107

Special Populations

Pregnancy

- Acceptable therapy:
  - Methyldopa, hydralazine, nifedipine, labetalol
- Drugs NOT to use:
  - ACEIs, ARBs, direct renin inhibitors
- Preeclampsia
  - New-onset or worsening hypertension, albuminuria, and hyperuricemia and some coagulation abnormalities
  - Occurs after 20th week of pregnancy
  - Close monitoring required with activity restriction & bed rest
  - May develop into a hypertensive emergency and may result in hospitalization, early fetal delivery and/or IV antihypertensives

Hypertension. 2018;71(19):e13–115.

108

Drug/Class	Comments
Methyldopa	Long-term data supporting safety
β-Blockers	Generally safe, but intrauterine growth retardation reported
Labetalol	Increasingly preferred over methyldopa because of fewer side effects
Clonidine	Limited data but may be used in non-severe HTN. Patch can be useful in patients who can't take oral medications.
Calcium channel blockers	Limited data; no increase in major teratogenicity with exposure – **nifedipine most used from class with good data**
Hydralazine	IV hydralazine can be managing acute onset severe hypertension with preeclampsia or eclampsia in pregnant and postpartum women. Oral not recommended d/t reflex tachycardia.
Diuretics	Not first-line, probably safe in low doses
ACE Inhibitors, ARBs, Renin Inhibitors	Pregnancy category C in 1st trimester, category D in 2nd & 3rd trimester. Major teratogenicity has been reported with exposure (fetal toxicity, death)

HTN in Pregnancy

DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: Pharmacotherapy:A Pathophysiologic Approach, 9th Edition: http://www.accesspharmacy.com/

109

109

Monitoring

- After antihypertensive regimen initiation
  - Follow up and adjustments Q month until goal BP is reached
  - At goal BP → follow up every 3-6 months
  - Monitor serum K+ and SCr 1-2x/year

Hypertension. 2018;71(19):e13–115.

110

Monitoring

Class	Parameters
Diuretics	blood pressure BUN/serum creatinine serum electrolytes (K+, Mg2+, Na+) uric acid (for thiazides)
β-Blockers	blood pressure heart rate
Aldosterone antagonists ACE inhibitors Angiotensin II receptor blockers Direct Renin inhibitors	blood pressure BUN/serum creatinine serum potassium
Calcium channel blockers	blood pressure heart rate
Hydralazine	blood pressure Heart rate ANA titer (Hydralazine induced lupus syndrome (HILS))

DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: Pharmacotherapy: A Pathophysiologic Approach, 8th Edition: http://www.accesspharmacy.com/

111

Interventions to Achieve Control

If adherence to antihypertensive medication increased from 57 to 100%

- population hypertension control would improve by 11%.

If follow-up after alterations in antihypertensive therapy was 1 week rather than 14 weeks

- population hypertension control would improve by 22%.

If a new class of antihypertensive medication was prescribed for patients with uncontrolled blood pressure during 62% of clinician visits rather than 12% of visits

- population hypertension control would improve by 33%.

Circ Cardiovasc Qual Outcomes. 2019;12(6):e005624

112

- ***Does bedtime compared to usual upon awakening hypertension therapy exert better cardiovascular disease (CVD) risk reduction?***
- **Methods:**
  - Multicenter, controlled, prospective trial, 19,084 hypertensive patients
  - Ambulatory blood pressure (ABP) monitoring performed for 48 hours at inclusion and at every scheduled clinic visit (at least annually) throughout follow-up
- **Results:**
  - 1752 participants experienced the primary CVD outcome over 6.3 years
    - CVD death, myocardial infarction, coronary revascularization, heart failure, or stroke
  - Bedtime regimen → lower asleep systolic BP mean, sleep-time relative systolic BP decline, and decreased CVD outcomes [0.55 (95% CI 0.50-0.61), P < 0.001]
- **Conclusions:**
  - Taking ≥1 prescribed BP-lowering medications at bedtime, as opposed to upon waking, results in improved ABP control, decreased asleep BP and decrease in major CVD events.

THE HYGIA CHRONOTHERAPY TRIAL

Eur Heart J. 2019.

113

A patient with stage C HF also has HTN. Current medications include amlodipine 5 mg daily, digoxin 0.25 mg daily, and furosemide 40 mg daily. The patient's vital signs are currently: BP 145/90 mmHg and pulse 82 bpm. Which of the following changes should be recommended in this patient's drug therapy?

A. Increase amlodipine to 10 mg daily

B. Add metolazone

C. Discontinue amlodipine and initiate lisinopril and carvedilol therapy

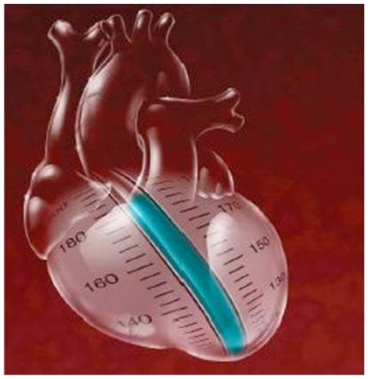
D. Add candesartan to the present therapy

114

Summary

- Lifestyle modifications are encouraged at elevated hypertensive
- Thiazide-type diuretics, ACEI, ARBs or DHP CCBs should be initial drug therapy for most, either alone or combined.
- Certain high-risk conditions are compelling indications for other drug classes.
- If BP is >20/10 mmHg above goal, initiate therapy with two agents, one usually should be a thiazide-type diuretic.
- Most patients will require two or more antihypertensive drugs to achieve goal BP.

115



ASYMPTOMATIC MARKEDLY ELEVATED BLOOD PRESSURE & HYPERTENSIVE EMERGENCIES

116

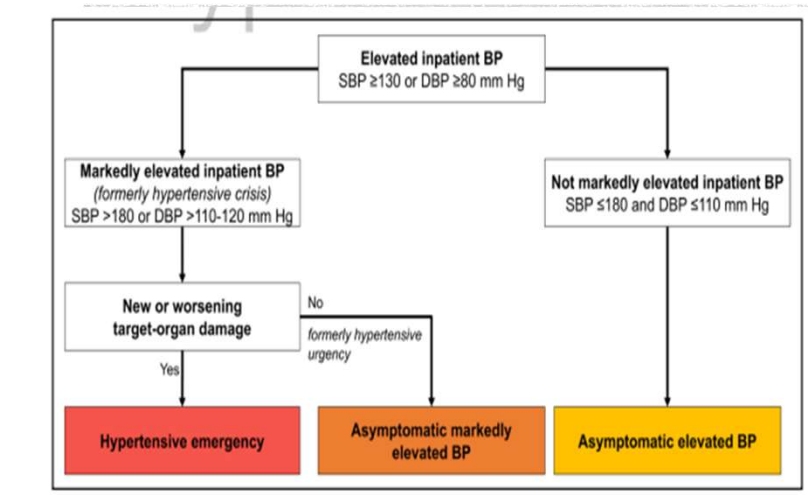


Figure 1. Terminology of elevated inpatient BP in the acute care setting.

Definitions

Hypertension. 2024;81:e01–e13.

117

Questions?

118

References

- Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999–2020. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2022. Accessed February 21, 2022.
- Centers for Disease Control and Prevention. Hypertension Cascade: Hypertension Prevalence, Treatment and Control Estimates Among U.S. Adults Aged 18 Years and Older Applying the Criteria from the American College of Cardiology and American Heart Association's 2017 Hypertension Guideline—NHANES 2015–2018. Atlanta, GA: U.S. Department of Health and Human Services; 2021. Accessed March 12, 2021.
- Kirkland EB, Heincelman M, Bishu KG, et. al. Trends in healthcare expenditures among US adults with hypertension: national estimates, 2003-2014. J Am Heart Assoc. 2018;7:e008731.
- Farley TA, Dalal MA, Mostashari F, Frieden TR. Deaths preventable in the U.S. by improvements in the use of clinical preventive services. Am J Prev Med. 2010;38(6):600–609.
- Charles R.V. Tomson, MA, BM, BCh, DM, Alfred K. Cheung, MD, Johannes F.E. Mann, MD, Management of Blood Pressure in Patients With Chronic Kidney Disease Not Receiving Dialysis: Synopsis of the 2021 KDIGO Clinical Practice Guideline. ANN Intern Med 2021;June22.
- *Heart J.* Published online October 22, 2019. doi:10.1093/eurhHermida RC, Crespo JJ, Domínguez-Sardiña M, et al; Hygia Project Investigators. Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial. *Eur* eartj/ehz754
- Whelton PK, Carey RM, Aronow WS, et al. 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: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2017: https://doi.org/10.1161/HYP.0000000000000065
- Chobanian, AV, Bakris, GL, Black, HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289:2560.

119

References

- Mancia G et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013 - See more at: http://www.jwatch.org/na31671/2013/07/23/2013-european-hypertension-guidelines#sthash.HhWMXlEu.dpuf
- Hapman, N, Dobson, J, Wilson, Sarah, et al. Effect of Spironolactone on Blood Pressure in Subjects With Resistant Hypertension. Hypertension 2007; 49:839.
- Davis, BR, Piller, LB, Cutler, JA, et al. Role of diuretics in the prevention of heart failure: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Circulation 2006; 113:2201.
- AUBellows BK, Ruiz-Negrón N, Bibbins-Domingo K, King JB, Pletcher MJ, Moran AE, Fontil V SO Circ Cardiovasc Qual Outcomes. 2019;12(6):e005624. Epub 2019 Jun 5.
- Grimm, R. Diuretics are preferred over angiotensin II-converting enzyme inhibitors for initial therapy of uncomplicated hypertension. Am J Kidney Dis 2007; 50:188.
- Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). ALLHAT Collaborative Research Group. JAMA 2000; 283:1967.
- Pool, JL, Schmieder, RE, Azizi, M, et al. Aliskiren, an orally effective renin inhibitor, provides antihypertensive efficacy alone and in combination with valsartan. Am J Hypertens 2007; 20:11.
- Prisant, LM. Nebivolol: Pharmacologic Profile of an Ultraselective, Vasodilatory {beta}1-Blocker. J Clin Pharmacol 2008; 48:225.
- Feldman RD, Zou GY, Vandervoort MK, Wong CJ, Nelson SA, Feagan BG. A simplified approach to the treatment of uncomplicated hypertension: a cluster randomized, controlled trial. Hypertension. 2009;53:646–653. doi:10.1161/HYPERTENSIONAHA.108.123455.
- Wang, JG, Staessen, JA. Antihypertensive drug therapy in older patients. Curr Opin Nephrol Hypertens 2001; 10:263.
- Rosendorff C, Black HR, Cannon CP, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: A scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. Circulation 2007;115(21):2761–2788.
- DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: Pharmacotherapy:A Pathophysiologic Approach, 9th Edition: http://www.accesspharmacy.com/

120