PRIMARY CARE REPORTS

The Practical CME Journal for Primary Care and Family Physicians

November 2021 VOL. 27, NO. 11

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Hypertension in Adults: An Update

Definition

Most major international guidelines define hypertension in adults as systolic blood pressure (SBP) in the office or clinic as ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg.[1-4] In 2017, the American College of Cardiology/American Heart Association (ACC/AHA) released guidelines defining stage 1 hypertension in adults as a systolic blood pressure of 130 mmHg to 139 mmHG or a diastolic reading of 80 mmHg to 89 mmHg. Stage 2 hypertension is defined as a blood pressure ≥ 140/90 mmHg.[2] These guidelines are based largely on the results of the SPRINT trial, which found improved overall and cardiovascular mortality with targeting a systolic blood pressure of < 120 mmHg compared to < 140 mmHg. However, these recommendations are not without controversy. For example, blood pressure measurements were based on the average of three automated readings after the patient had been seated for five minutes, which is in contrast to how most measurements actually are obtained in routine clinical practice.[5]

Other organizations have derived their own definitions based on review and interpretation of other data sources. For example, the European Society of Cardiology and European Society of Hypertension (ESC/ESH) and the International Society of Hypertension (ISH) define hypertension as a SBP of ≥ 140 mmHg or DBP ≥ 90 mmHg when office-based measurement is used.[1,3] The ISH further recommends a threshold of > 160/100 mmHg as grade 2 hypertension.

The American Academy of Family Physicians continues to endorse the findings of the Eighth Joint National Committee (JNC 8), which defines hypertension as > 140/90 mmHg in the general population and > 150/90 mmHg in adults older than 60 years of age.[4]

More recently, there has been an attempt to use different definitions based on setting, time of day, and age. To illustrate: Although the ACC/AHA uses a threshold of 130/80 mmHg in the office setting, when 24-hour ambulatory monitoring is used, the proposed cutoff is slightly less, at 125/75 mmHg.[2] Similarly, when 24-hour ambulatory monitoring is used, the ESC/ESH guidelines define hypertension as a blood pressure > 130/80 mmHg.[3] (*See Table 1.*)

Out-of-office blood pressure measurements are performed by patients at home using automated blood pressure monitors or ambulatory blood pressure monitoring (ABPM). According to the United States Preventive Services Task Force (USPSTF), blood pressure measurements obtained in this way are more reproducible and accurate predictors of hypertension-induced organ damage and cardiovascular events than office-based measurements.[6] Although ambulatory monitoring of blood pressures is preferred for diagnosis and confirmation of office readings, this remains impractical for many practicing primary care physicians, and office-based measurements remain the most common means of diagnosis. Whenever possible, alternative measurements,

EXECUTIVE SUMMARY

Hypertension remains the leading cause of death and disability-adjusted life years globally, accounting for 10.4 million deaths per year. In the United States, hypertension accounts for more cardiovascular disease deaths than any other modifiable risk factor and is second only to cigarette smoking as a preventable cause of death for any reason.

- Most major international guidelines define hypertension in adults as systolic blood pressure in the office or clinic as ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg.
- Although ambulatory monitoring of blood pressures is preferred for diagnosis and confirmation of office readings, this remains impractical for many practicing primary care physicians, and office-based measurements remain the most common means of diagnosis.
- Among secondary causes, renal disease, sleep apnea, medications, and hyperaldosteronism are among the more common causes. Consider these diagnoses in patients with severe hypertension, age of onset younger than 30 years (especially in the absence of clear risk factors), or an acute rise in blood pressure after a period of good control.
- Ideally, blood pressure should be obtained using an automated oscillometric device. Multiple measurements should be obtained and averaged. Some of the newer oscillometric devices can inflate automatically, allowing the patient to be alone when the blood pressure is measured.
- Measurements obtained by averaging multiple automated measurements while the patient remains alone in the room are aligned more closely with ambulatory measurements and offer more standardized and reproducible evaluation.
- Resistant hypertension is diagnosed when a patient takes three antihypertensive agents with complementary mechanisms of action (including a diuretic) without achieving blood pressure control, or when blood pressure control is achieved but requires four or more medications.
- Although lifestyle modifications are important and a cornerstone of management, most patients diagnosed with hypertension will go on to require pharmacotherapy. Thiazide diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and calcium channel blockers are first-line options either alone or in combination. Monitor monthly and escalate therapy until blood pressure is controlled to < 140/90 mmHg or < 130/80 mmHg if certain comorbidities, such as coronary artery disease, congestive heart failure, diabetes, or chronic kidney disease, exist.

including those using home-based readings, should be used in routine clinical practice for both diagnosis and monitoring of response to therapy. The different definitions are summarized in Table 1.

Epidemiology

Following the ACC/AHA definition, the prevalence of hypertension among U.S. adults would be more than 45%, with medication recommended for 36.2% of U.S. adults.[7,8] The prevalence is higher in men than in women, 51% vs. 39.7%, respectively, and with increasing age. A National Center for Health Statistics (NCHS) report published by the Centers for Disease Control and Prevention (CDC) found that the prevalence was 22.4% among adults ages 18 to 39 years but rose to 74.5% among those older than 60 years of age. The age-adjusted prevalence was highest among non-Hispanic Black adults (57.1%) compared to non-Hispanic white (43.6%) and Hispanic (43.7%) adults.[8] The burden of hypertension is high and becoming higher, particularly in low- and middle-income countries where access to antihypertensive medication is limited.[8,9]

Even when the 140/90 mmHg cutoff is used, for adults 45 years of age without current hypertension, the risk of developing it over the subsequent 40 years is 93% for African American, 92% for Hispanic, 86% for white, and 84% for Chinese adults.[2]

Hypertension remains the leading cause of death and disability-adjusted life years (DALYs) globally, accounting for 10.4 million deaths per year.[9] In the United States, hypertension accounts for more cardiovascular disease (CVD) deaths than any other modifiable risk factor and is second only to cigarette smoking as a preventable cause of death for any reason.[2] Additionally, the risk of CVD increases in a log-linear fashion from SBP < 115 mmHg to > 180 mmHg, with each 20 mmHg increase in SBP corresponding to a doubling of the risk of death from stroke, heart disease, or other vascular disease. Furthermore, the increased risk of CVD is reported across a broad age spectrum, from 30 to 80 years of age and older.[2]

Etiology

There is no one unifying etiology of hypertension, but it can be divided roughly into primary and secondary types, with primary being the most prevalent, accounting for 90% to 95% of cases.[1,10]

Among cases of primary hypertension, a number of risk factors have been identified, including age, race, obesity, and family history. Lifestyle factors, including high sodium diet, physical inactivity, stress, and tobacco and alcohol use, also are important risk factors.[1]

Among secondary causes, renal disease, sleep apnea, medications, and hyperaldosteronism are among the more common causes. Consider these diagnoses in patients with severe hypertension, age of onset younger than 30 years (especially in the absence of clear risk factors), or an acute rise in blood pressure after a period of good control. Table 2 summarizes potential etiologies or contributors of secondary hypertension along with diagnostic clues in the history and physical examination that would prompt additional workup.[2,10]

Pathophysiology

The exact mechanism by which hypertension develops is not entirely clear, but, in most cases, hypertension in adults involves multiple causes, including genetic, environmental, neural, hormonal, and anatomic factors interacting together in what has been termed the "mosaic model."[11] Increasingly, the role of lifestyle, emotional stress, and other social determinants of health, such as suboptimal health insurance coverage, also have been

Table 1. Definitions of Hypertension

	International Society of Hypertension Practice Guidelines	European Society of Cardiology/ European Society of Hypertension	American College of Cardiology/American Heart Association	Eighth Joint National Committee (JNC 8)
Year of Publication	2020	2018	2018	2013
Definition				
1. Clinic BP	SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg	SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg	SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg	Age 18 to 59 years: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg Age 60 years and older: SBP ≥ 150 mmHg and/or DBP ≥ 90 mmHg
2. Self-Measured Home BP	SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg	SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg	SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg	N/A
3. Average 24-Hour ABP	SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg	SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg	SBP ≥ 125 mmHg or DBP ≥ 75 mmHg	N/A
4. Average Daytime ABP	SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg	SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg	SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg	N/A
5. Average Nighttime ABP	SBP ≥ 120 mmHg and/or DBP ≥ 70 mmHg	SBP ≥ 120 mmHg and/or DBP ≥ 70 mmHg	SBP ≥ 110 mmHg and/or DBP ≥ 75 mmHg	N/A

BP: blood pressure; ABP: ambulatory blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure

Adapted from: Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension* 2020;75:1334-1357.

implicated.[12-14] Genetic predisposition to form pro-oxidant enzymes may interact with environmental factors, such as pollution and psychological stress, to produce even more reactive oxygen species, which then can trigger vascular remodeling and increase vascular resistance.[11]

In addition, a typical Western diet, high in red meat, fat, and processed foods, has been known to promote inflammation and atherosclerosis, resulting in hypertension. Alternatively, a diet rich in fruits, vegetables, and reduced saturated fat and cholesterol has been shown to reduce systolic blood pressure.[15,16] Body mass index (BMI) and waist circumference also share a nearly linear relationship with hypertension.[2]

Clinical Features

Except for clinical features of secondary hypertension and signs and symptoms of end-organ damage from hypertensive emergency, hypertension typically is asymptomatic. It usually is brought to clinical attention when the blood pressure is assessed during a routine clinical interaction or referred to the primary care physician from outside sources when it is noted to be elevated unexpectedly.

On history and physical examination, note any risk factors, such as obesity, and assess for signs of hypertensive complications and secondary etiologies. Common complications of hypertension include congestive heart failure, chronic kidney disease, sexual dysfunction, peripheral artery disease, and blindness, in addition to heart attack and stroke.[1,2,14]

Hypertensive emergency may present with headache, visual changes, chest pain, dizziness, and shortness of breath among other symptoms.[17] When evaluating a patient with significantly elevated blood pressure (> 180/110 mmHg), take a careful history, specifically asking for signs of end-organ damage and refer to the emergency room if hypertensive emergency is suspected. Severe asymptomatic hypertension, which does not involve end-organ damage, generally can be managed in the outpatient setting with oral medications and close follow-up.[17]

Diagnostic Studies

The most important next step in the diagnosis of hypertension is to ensure the blood pressure is measured accurately. (*See Figure 1 and Table 3*.)

Office measurement of blood pressure is the most common basis for diagnosis and follow-up of hypertension. It is recommended that elevated blood pressure be confirmed during two to three visits at one- to four-week intervals rather than at a single office visit unless the blood pressure is > 180/110 mmHg and/or there is evidence of cardiovascular disease.[2] Whenever possible, confirm the diagnosis with out-of-office measurements, namely home blood pressure or 24-hour ambulatory blood pressure monitoring.

Table 2. Secondary Causes of Hypertension

Potential Cause of or Contributor to Secondary Hypertension	Prevalence	History, Physical, or Laboratory Findings	Diagnostic Workup
Obstructive sleep apnea	25% to 50%	• Snoring • Daytime sleepiness • Neck circumference ≥ 40 cm • Apneic episodes during sleep • Most common cause of secondary hypertension in adults	• Polysomnography • Epworth Sleepiness scale • Nighttime pulse oximetry
Primary hyperaldosteronism	8% to 20%	• Hypokalemia • Hypernatremia	• Renin and aldosterone levels to calculate aldosterone/renin ratio
Renal artery stenosis	5% to 34%	• Atherosclerotic disease in older patients or fibromuscular dysplasia in young women • Rise in creatinine ≥ 50% within one week of initiation of ACE-I or ARB • Renal bruit	• Imaging with Doppler ultrasound of renal arteries
Renal parenchymal disease	1% to 2%	• Family history of polycystic kidneys • Recurrent urinary tract infections • Palpable abdominal mass	• Creatinine • Urinalysis • Renal ultrasonography
Drugs/substances	2% to 4%	• NSAIDs, alcohol, OCPs, caffeine, amphetamines, decongestants, SSRIs, MAOIs, TCAs, corticosteroids, triptans, cocaine, bath salts, herbal supplements (such as ephedra, St. John's wort, yohimbe)	• Thorough review of medication list
Thyroid disorders	< 1%	• Cold/heat intolerance • Fatigue • Irregular menstrual periods • Constipation/diarrhea	• TSH with reflex T4
Pheochromocytoma	0.1% to 0.6%	• Flushing • Labile blood pressures • Sweating • Orthostatic hypotension	• Plasma-free metanephrins
Cushing syndrome	< 0.1%	• Central obesity • Abdominal striae • Moon facies	• Low-dose dexamethasone suppression test • Late-night salivary cortisol • 24-hour urinary free cortisol
Coarctation of the aorta	0.1%	• Discrepancy in arm to leg systolic blood pressure ≥ 20 mmHg • Murmur • Delayed femoral pulses	• Transthoracic echocardiogram • MR/CT angiography

ACE-I: angitotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; NSAID: nonsteroidal anti-inflammatory drugs; OCP: oral contraceptive pill; SSRI: selective serotonin reuptake inhibitor; MAOI: monoamine oxidase inhibitor; TCA: tricyclic antidepressant; TSH: thyroid-stimulating hormone; MR: magnetic resonance; CT: computed tomography

Adapted from: Whelton PK, Carey RM, Aronow WS, et al. 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: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71:1269-1324 and Charles L, Triscott J, Dobbs B. Secondary hypertension: Discovering the underlying cause. *Am Fam Physician* 2017;96:453-461.

Ideally, blood pressure should be obtained using an automated oscillometric device. Multiple measurements should be obtained and averaged.

Some of the newer oscillometric devices can inflate automatically, allowing the patient to be alone when the blood pressure is measured.[1]

Measurements obtained by averaging multiple automated measurements while the patient remains alone in the room are aligned more closely with ambulatory

measurements and offer more standardized and reproducible evaluation.[2] These readings also are often lower than those obtained through usual office practice. Furthermore, rechecking the blood pressure of a patient whose initial reading was elevated can result in a lower systolic reading of a median of 8 mmHg, resulting in an increased hypertension control rate from 61% to 73%, according to one study published in the *Journal of the American Medical Association* (*JAMA*) *Internal Medicine* involving 38,620 primary care patients diagnosed with hypertension.[18]

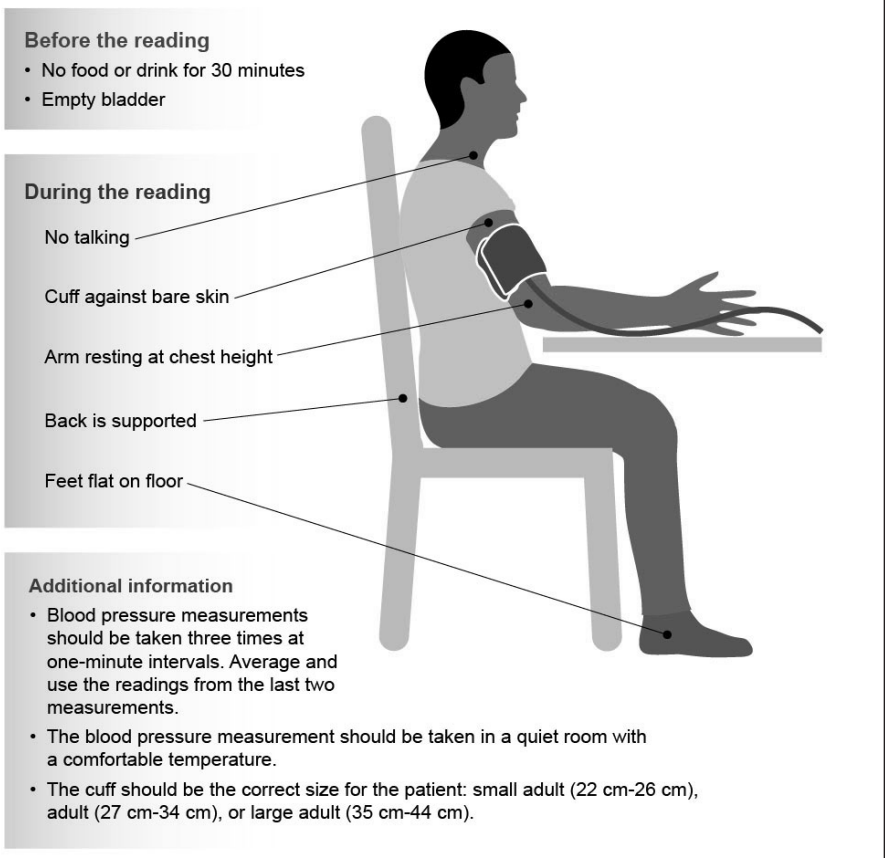
Measure the blood pressure in both arms and, if noted to be consistently different between arms by > 10 mmHg, use the higher of the two readings. If the difference is > 20 mmHg, consider further evaluation with CT/MR angiography to evaluate for coarctation.

Because hypertension is a major cardiovascular risk factor, obtain a thorough history and physical examination and assess the hypertensive patient for overall cardiovascular risk and signs of organ dysfunction. Additional cardiovascular risk factors are found in more than half of all patients with hypertension.[2] These confer increased risk of coronary, cerebrovascular, and renal disease in hypertensive patients. The most common additional risk factors include obesity (49.5%), diabetes (27.2%), dyslipidemia (63.2%), and chronic kidney disease (15.8%).[2]

The ISH recommends obtaining a serum sodium, potassium, creatinine, fasting glucose, and lipid profile, in addition to a urinalysis and electrocardiogram, in all adults with a new diagnosis of hypertension.[1] The ACC/AHA recommends these in addition to a complete blood count, calcium, and thyroid-stimulating hormone.[2] These recommendations are summarized in Table 4.

The USPSTF recommends using the Pooled Cohort Equations from the American College of Cardiology to assess 10-year risk of a cardiovascular event. For asymptomatic adults with low risk, defined as 7.5% or less, it also recommends against screening with resting or exercise electrocardiography to prevent cardiovascular disease, citing lack of benefit and potential for harm.[19] Additional studies, such as echocardiography, renal artery imaging, carotid ultrasound, and sleep study, are not indicated routinely but may be reasonable, depending on the history and physical exam. For example, a 67-year-old with a smoking history and symptoms of claudication should be screened additionally for abdominal aortic aneurysm and vascular studies, such as ankle-brachial index.

Figure 1. Measuring Blood Pressure



Adapted from: Centers for Disease Control and Prevention. The correct way to measure blood pressure. https://www.cdc.gov/heartdisease/images/AHM2020_BP_Infographic.jpg and Centers for Disease Control and Prevention, Effective Diagnosis, Treatment, and Monitoring of Hypertension in Primary Care, Participant Guide 2, Measurement of Blood Pressure, https://www.cdc.gov/globalhealth/healthprotection/ncd/training/files/Session2_ParticipantGuide.pdf

Differential Diagnosis

White Coat Hypertension

This refers to individuals who have elevated blood pressure only in the office, with normal ambulatory or home blood pressure. When untreated, this category of patients has been associated with cardiovascular risk intermediate between those with normal blood pressure and those with hypertension.[1] If the overall cardiovascular risk, calculated using a validated tool, is low and there is no evidence of hypertension-mediated end organ damage, pharmacological treatment may be deferred. Lifestyle modifications should be recommended, and the patient should be followed closely for development of sustained hypertension requiring pharmacological treatment. The ACC/AHA 2017 guidelines recommend screening adults with untreated blood pressure > 130/80 mmHg but < 180/100 mmHg for white coat hypertension using ambulatory or home blood pressure monitoring before making the diagnosis of hypertension.[2]

Masked Hypertension

This refers to individuals whose blood pressure readings in the office are normal, but who have elevated ambulatory or home blood pressure. When untreated, these patients have a similar risk for cardiovascular events as those with overt, sustained hypertension and may be offered drug treatment with the goal of normalizing their out-of-office blood pressure.[1]

Resistant Hypertension

Resistant hypertension is diagnosed when a patient takes three

Table 3. Recommendations for Taking Blood Pressure Measurements in the Office

Conditions for the Measurement
- The room should be quiet.
- The temperature of the room should be comfortable.
- Smoking, caffeine, and exercise should be avoided for 30 minutes before measurement.
- The patient should empty their bladder before the measurement.
- The patient should be seated and relaxed for three to five minutes before the measurement.
- Before, during, or between measurements, there should be no talking (either the patient or the staff).

Positioning the Patient
- The patient should sit with their arm resting on a table.
- Their arm should be at mid-heart level, their back should be supported by the chair, their legs should not be crossed, and both their feet should be flat on the floor.

Measurement Device
- For the measurement, use a validated electronic (oscillometric) upper-arm cuff device.
- As an alternative, a calibrated auscultatory device (aneroid or hybrid; in most countries, mercury sphygmomanometers are banned) with first Korotkoff sound for systolic blood pressure and fifth Korotkoff sound for diastolic blood pressure with a low deflation rate.

Choosing the Correct Cuff
- Choose the cuff size according to the patient's arm circumference. A larger cuff will underestimate blood pressure and a smaller cuff will overestimate blood pressure.
- Use cuffs according to instructions for electronic devices.
- The inflatable bladder of manual auscultatory devices should cover 75% to 100% of the patient's arm circumference.

Measurement Protocol
- For each patient visit, three blood pressure measurements should be taken. Each measurement should be separated by one minute.
- For the last two measurements, calculate the average. No further measurements are needed if the first measurement is < 130/85 mmHg.

Interpreting the Results
- Hypertension is indicated if the blood pressure measurements taken in two to three office visits are ≥ 140/90 mmHg.

Adapted from: Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension* 2020;75:1334-1357.

antihypertensive agents with complementary mechanisms of action (including a diuretic) without achieving blood pressure control, or when blood pressure control is achieved but requires four or more medications. On the basis of a 140/90 mmHg cutoff, the prevalence of resistant hypertension in the adult population is 13%.[20] Risk factors for resistant hypertension include older age, obesity, chronic kidney disease, Black race, and diabetes.[20] The risk of stroke, myocardial infarction, and death with resistant hypertension was significantly higher than in hypertensive patients without resistant hypertension.[21] Do not confuse resistant hypertension with secondary hypertension. Secondary hypertension refers to hypertension caused by a specific separate etiology. Furthermore, neither term should be confused with uncontrolled hypertension, which is an umbrella term for hypertension that is not at goal and includes cases related to a suboptimal treatment regimen or medication nonadherence.[1]

Management

The approach to management should include both blood pressure control to normal range and the effective treatment of other known risk factors. Use a validated tool to calculate overall cardiovascular risk with the aim to simultaneously address modifiable risk factors, such as obesity, smoking, and diabetes. Statin medications, when indicated, should be prescribed. This strategy reduces the rate of cardiovascular disease beyond what can be achieved with blood pressure control alone.[1,2]

Lifestyle Modifications

Lifestyle modification is the first-line antihypertensive treatment and also can enhance the efficacy of other therapies for hypertension. Healthy lifestyle choices can reverse, delay, or prevent the onset of elevated blood pressure and, additionally, attenuate cardiovascular risk.[2] However, it is important to note that lifestyle modifications alone should not be used if a patient is determined to be at high risk for CVD, the blood pressure is ≥ 160/100 mmHg, or if appropriate reduction is not achieved within three to six months.[1] A summary of lifestyle modifications and their expected effect on SBP is presented in Table 5.

Pharmacologic Treatment

A difference in blood pressure of 20/10 mmHg is associated with more than a 50% reduction in cardiovascular risk in hypertensive patients 40 to 69 years of age.[22] As such, all patients who are candidates for pharmacologic treatment of hypertension should receive adequate and efficacious antihypertensive medications with a goal to reduce blood pressure to < 140/90 mmHg within three to six months in most cases. Additionally, if coronary artery disease, prior stroke, diabetes, chronic kidney disease, or congestive heart failure is noted, treat to a target of < 130/80 mmHg unless the patient is elderly, in which case a target of < 140/90 mmHg should be used.[1]

Recommendations for the initial antihypertensive agents of choice have differed over the years. The ACC/AHA guidelines

recommend initiation of therapy with any agent from the first-line classes of antihypertensive agents, namely thiazide diuretics, angiotensin converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), or calcium channel blockers (CCB). Dosage titration and sequential addition of other first-line agents to achieve the blood pressure target also are recommended.[2]

However, based on data finding that most patients will require combination therapy, the ESC/ESH and ISH guidelines both recommend starting with combination therapy of two first-line agents, preferably as an affordable, single, once-daily combination pill. If blood pressure is not at goal with the maximum dose of two first-line agents, a third first-line agent should be added and titrated as appropriate.[1,3] This largely is in line with the ACC/AHA recommendations, which recommend consideration of starting with two agents of different classes for patients with blood pressure ≥ 140/90 mmHg, which they define as stage 2 hypertension.[2] Patients with blood pressure unresponsive to three first-line agents are considered to have resistant hypertension, and another agent, such as spironolactone, may be added. These patients also should be evaluated for secondary hypertension or medication and/or lifestyle nonadherence.[1,2]

The ACC/AHA guidelines also state that in Black adults with hypertension but without heart failure or chronic kidney disease, including those with diabetes, initial antihypertensive therapy should include a thiazide diuretic or CCB unless there is a compelling reason to use an ACE-I or ARB, such as microalbuminuria or heart failure with reduced ejection fraction (HFrEF).[2] Beta-adrenergic blocking agents are not included among first-line agents for hypertension and should not be used for control of blood pressure unless there is another compelling reason for their use (e.g., thoracic aortic disease, recent myocardial infarction, or HFrEF). Medications used commonly for the treatment of hypertension are summarized in Table 6.

To enhance adherence to therapy, the following strategies are suggested:

1. Physicians should assess for adherence as appropriate at each visit and most importantly prior to escalation of antihypertensive therapy.

Table 4. ISH and ACC/AHA Screening Recommendations

ISH	ACC/AHA
• Serum - Sodium, potassium, creatinine, lipid profile, fasting glucose • Urinalysis • Electrocardiogram	• Serum - Sodium, potassium, creatinine, lipid profile, fasting glucose, complete blood count, calcium, thyroid-stimulating hormone • Urinalysis • Electrocardiogram

ISH: International Society of Hypertension; ACC: American College of Cardiology; AHA: American Heart Association

Table 5. Lifestyle Modifications for Hypertension

Intervention	Notes	Approximate Effect in mmHg on SBP (Hypertensive Patients)
Healthy (DASH) diet	• http://www.dashforhealth.com	-11
Reduced dietary sodium	• < 1,500 mg/day to < 1,000 mg/day	-5 to -6
Moderation of alcohol intake	• Men: < 2 drinks/day • Women: < 1 drink/day	-4
Increased intake of dietary potassium	• 3,500 mg to 5,000 mg/day, ideally through potassium-rich diet	-4 to -5
Regular physical activity	• 90 to 150 minutes/week moderate aerobic activity • Weight-bearing exercise	- 5 to -8 -5
Weight reduction	• Maintain a healthy weight or lose excess weight	-5

SBP: systolic blood pressure

Adapted from: Whelton PK, Carey RM, Aronow WS, et al. 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: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71:1269-1324.

2. Reduce polypharmacy by using single pill combinations.
3. Use once-daily dosing.
4. Advise home BP monitoring.
5. Use a multidisciplinary team approach (including pharmacists).

Clinicians should employ effective behavioral and motivational approaches to help patients achieve a healthy lifestyle. Team-based care for hypertension has been shown to improve blood pressure control and medication adherence. Such teams include the patient, their family, the primary care provider, and other professionals, such as cardiologists, nurses, pharmacists, social workers, community health workers, and dietitians. Use of the electronic health record and patient registries to identify patients with undiagnosed or undertreated hypertension also is recommended.[1]

Special Populations and Considerations

Pregnancy

Women with hypertension who become pregnant, or who are planning to become pregnant, should be transitioned

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Table 6. Antihypertensive Medications

Class	Drugs and Usual Starting Dose/Day	Notes
Primary Agents		
Thiazide diuretics	Chlorthalidone 12.5 mg; indapamide 1.25 mg; hydrochlorothiazide 25 mg; metolazone 2.5 mg	Chlorthalidone preferred because of longer half-life and proven reduction of cardiovascular disease
Angiotensin converting enzyme inhibitors (ACE-I)	Lisinopril 5 mg to 10 mg; enalapril 5 mg; captopril 25 mg (12.5 mg 2-3 times daily); ramipril 2.5 mg; benazepril 5 mg to 10 mg; fosinopril 10 mg; quinapril 10 mg; trandolapril 1 mg	Should not be used in combination with ARB or direct renin inhibitor; avoid in pregnancy
Angiotensin receptor blockers (ARBs)	Candesartan 8 mg; irbesartan 150 mg; losartan 25 mg; olmesartan 20 mg; valsartan 80 mg	Should not be used in combination with ACE-I or direct renin inhibitor; avoid in pregnancy
Calcium channel blockers: dihydropyridines	Amlodipine 2.5 mg to 5 mg; felodipine 2.5 mg to 5 mg; isradipine 5 mg; nifedipine LA 30 mg to 60 mg	Caution in HFrEF; dose-related pedal edema is more common in women
Calcium channel blockers: nondihyrdropyridines	Diltiazem ER 120 mg; verapamil SR 120 mg	Caution in combination with beta blockers or in patients with HFrEF
Secondary Agents		
Diuretics: aldosterone antagonists	Eplerenone 50 mg, spironolactone 25 mg	Preferred agents in primary aldosteronism and resistant hypertension
Diuretics: loop	Bumetanide 0.5 mg, furosemide 20 mg, torsemide 5 mg	Preferred diuretics in patients with symptomatic heart failure; preferred over thiazides in patients with GFR < 30 mL/min
Diuretics: potassium-sparing	Amiloride 5 mg, triamterene 50 mg	Minimally effective for BP reduction
Beta blockers: cardioselective	Atenolol 25 mg, betaxolol 5 mg, bisoprolol 2.5 mg to 5 mg, metoprolol succinate 25 mg to 100 mg, nebivolol 5 mg	Not recommended for hypertension unless patient has heart failure or ischemic heart disease. Use this category if beta blocker needed in patient with reactive airway disease. Nebivolol is also vasodilatory. Caution with abrupt cessation of all beta blockers
Beta blockers: noncardioselective	Nadolol 40 mg, propranolol 80 mg	Caution in patients with reactive airway disease
Beta blockers: combined alpha and beta receptor action	Carvedilol IR 625 mg, carvedilol ER 20 mg, labetalol 200 mg	Carvedilol is preferred in patients with HFrEF. Avoid abrupt cessation of all beta blockers
Alpha-1 blockers	Doxazosin 1 mg, prazosin 2 mg, terazosin 1 mg	Orthostatic hypotension; may be considered second-line agents in patients with BPH
Central alpha-2 agonists and other centrally acting agents	Clonidine (oral and patch) 0.1 mg, methyldopa 250 mg, guanfacine 0.5 mg	Agents of last resort because of central nervous system side effects; abrupt discontinuation of clonidine may induce hypertensive crisis
Direct vasodilators	Hydralazine 40 mg, minoxidil 5 mg	Associated with water and sodium retention and reflex tachycardia; use with a diuretic and beta blocker; minoxidil associated with pericardial effusion and hirsutism and requires a loop diuretic

LA: long acting; HFrEF: heart failure with reduced ejection fraction; ER: extended release; SR: sustained release; BP: blood pressure; IR: immediate release; GFR: glomerular filtration rate; BPH: benign prostatic hyperplasia

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to methyldopa, nifedipine, and/or labetalol during pregnancy. Because of the risk of fetal and neonatal morbidity and mortality, drugs that act directly on the renin-angiotensin system (ACE-I, ARBs, and direct renin inhibitors) should not be used in pregnancy and should not be prescribed to women of child-bearing age who may become pregnant.[2]

Seasonal Blood Pressure Variation

Blood pressure changes have been noted with lower levels at higher temperatures and higher levels at lower temperatures. This occurs seasonally, as well as in people traveling from areas with cold to hot temperatures or vice versa. Studies have demonstrated an average change of 5/3 mmHg, with more marked fluctuations in patients on treatment for hypertension. This should be considered when symptoms of hypotension occur with increased temperature, or when blood pressure is below goal during cold weather in a person who previously was well controlled.[1]

Special Treatment Considerations

Consider therapeutic strategies that are effective both for hypertension as well as any comorbidities or cardiovascular risk factors. For example, in patients with hyperuricemia, in addition to dietary changes, medications that influence serum urate levels, such as losartan and atorvastatin, should be added to urate-lowering therapy.[1] In addition, for patients with both diabetes and hypertension, first-line pharmacotherapy should include either an ACE-I or ARB if possible.[3] Because peripheral edema is a common side effect of CCBs, such as amlodipine, use caution when prescribing these agents for patients with additional risk factors for peripheral edema, such as those with a diagnosis of congestive heart failure. Furthermore, for patients with both HFrEF and hypertension, a preference for agents with a proven mortality benefit (certain beta blockers and ACE-I/ARB) should be considered.[2]

Disposition

Adults initiating or adjusting to a new drug regimen for hypertension should have a follow-up evaluation for adherence and response to treatment at monthly intervals until control is achieved. At each follow-up visit, also monitor for adverse effects of medications and address any additional pertinent cardiovascular risk enhancers. After blood pressure control is achieved, office visits may be spaced to every three to six months, depending on additional comorbidities. Systematic strategies to help improve blood pressure control, including home blood pressure monitoring, team-based care (especially including pharmacists), and telehealth, should be employed after initiation of therapy as appropriate.[1-3]

Summary

Hypertension, defined by most major societies as > 140/90 mmHg, is common and the prevalence is increasing. Although the office remains the most common setting for diagnosis, out of office and 24-hour ambulatory monitoring should be used increasingly if possible. Hypertension is a major modifiable risk factor for cardiovascular disease and, after diagnosis, it is important to screen for additional modifiable risk factors and calculate the overall cardiovascular risk. Screening for complications of hypertension through a careful history, physical examination, laboratory studies, and an electrocardiogram also is recommended. Suspect secondary causes if blood pressure is difficult to control or as otherwise guided by the clinical evaluation. Lifestyle modifications are important and are a cornerstone of management. However, most patients diagnosed with hypertension will go on to require pharmacotherapy. Thiazide diuretics, ACE-I, ARBs, and CCBs are first-line options either alone or in combination. Monitor monthly and escalate therapy until blood pressure is controlled to < 140/90 mmHg or < 130/80 mmHg if certain comorbidities, such as coronary artery disease, congestive heart failure, diabetes, or chronic kidney disease, exist. A multidisciplinary approach, including physicians, nurses, pharmacists, and the use of technology, such as telehealth and electronic health record registries, also can improve adherence and achievement of control.

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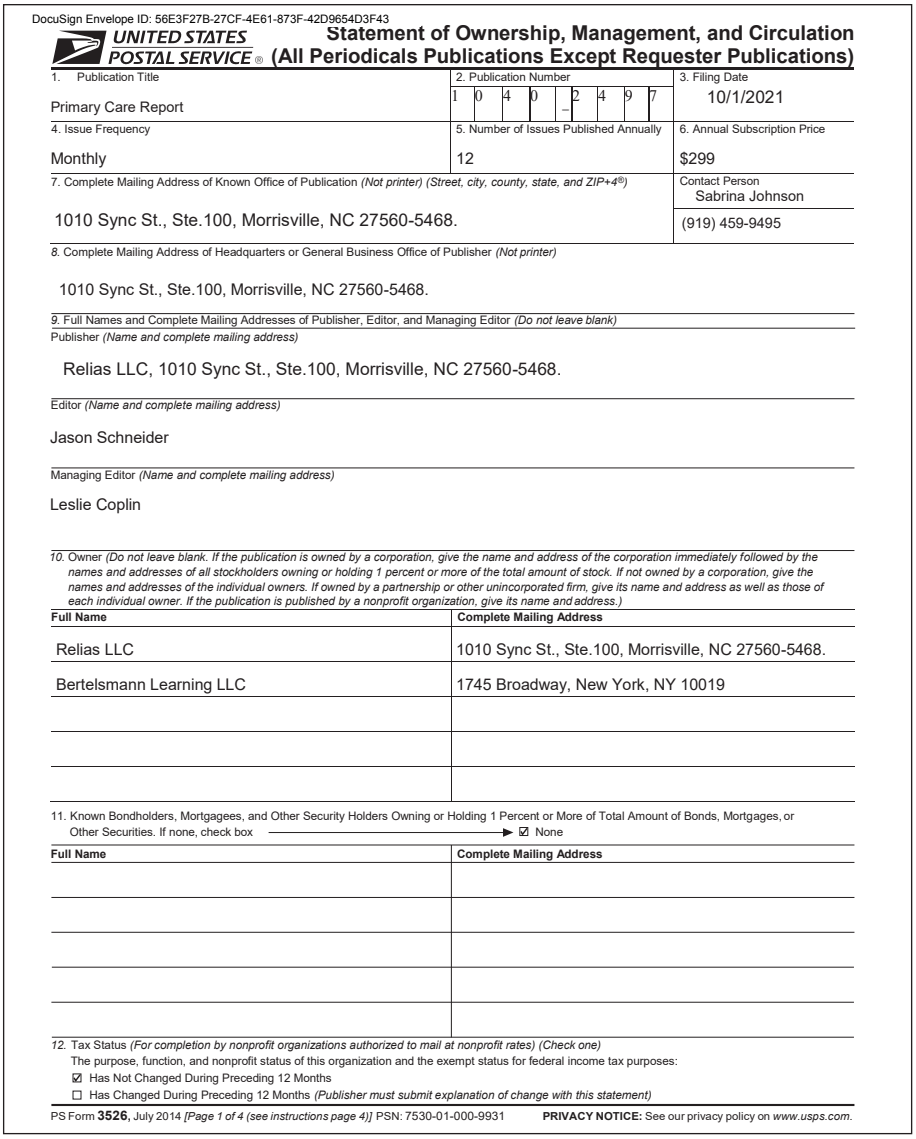
CME Questions

1. The International Society of Hypertension (ISH) and European Society of Cardiology/European Society of Hypertension (ESC/ESH) defines hypertension based on an office-based blood pressure reading of greater than:
   a. 140/90 mmHg.
   b. 135/85 mmHg.
   c. 130/80 mmHg.
   d. 120/70 mmHg.



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1. Publication Title	2. Publication Number	3. Filing Date
Primary Care Report	1 0 4 0 – 2 4 9 7	10/1/2021
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price
Monthly	12	$299

7. Complete Mailing Address of Known Office of Publication *(Not printer) (Street, city, county, state, and ZIP+4®)*: 1010 Sync St., Ste.100, Morrisville, NC 27560-5468. Contact Person: Sabrina Johnson; (919) 459-9495

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not printer)*: 1010 Sync St., Ste.100, Morrisville, NC 27560-5468.

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do not leave blank)*

Publisher *(Name and complete mailing address)*: Relias LLC, 1010 Sync St., Ste.100, Morrisville, NC 27560-5468.

Editor *(Name and complete mailing address)*: Jason Schneider

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2. Hypokalemia and hypernatremia are common laboratory findings in which of the following causes of secondary hypertension?
   a. Obstructive sleep apnea
   b. Hypothyroidism
   c. Primary hyperaldosteronism
   d. Renal artery stenosis
3. Which of the following features distinguishes severe asymptomatic hypertension (hypertensive urgency) from hypertensive emergency?
   a. Blood pressure reading
   b. The presence of signs and symptoms of acute end-organ damage
   c. The presence of a secondary cause of hypertension
   d. The need for medications to decrease the blood pressure
4. The U.S. Preventive Services Task Force recommends which of the following?
   a. Screening electrocardiogram for all adults regardless of overall cardiovascular risk or symptoms
   b. Screening electrocardiogram for all adults with a 10-year risk of cardiovascular event greater than 5%
   c. Against screening echocardiography for all adults unless blood pressure is > 160/100 mmHg
   d. Against screening electrocardiogram for asymptomatic adults at low cardiovascular risk

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5. The diagnosis of resistant hypertension is made when:
   a. blood pressure remains uncontrolled despite three different first-line medications from different classes and good adherence.
   b. there is a need for intravenous medication to lower the blood pressure acutely.
   c. a patient is noted to be intolerant of first-line antihypertensive medications.
   d. a patient is resistant to initiating pharmacotherapy for hypertension.

6. Which of the following patients is considered a good candidate for initial therapy with lifestyle modifications alone?
   a. A 62-year-old male with a history of diabetes and chronic kidney disease and an office blood pressure reading of 150/93 mmHg
   b. A 42-year-old female with no additional medical history and an ambulatory confirmed blood pressure of 160/100 mmHg
   c. A 50-year-old schoolteacher with a blood pressure of 145/76 mmHg but otherwise healthy
   d. A 72-year-old female with a blood pressure of 170/92 mmHg presenting to your office with chest pain and shortness of breath

7. According to the ISH and ESC/ESH, which of the following is considered appropriate initial pharmacotherapy for a patient diagnosed with hypertension but no other medical comorbidities?
   a. Chlorthalidone monotherapy, with follow-up in two months for titration
   b. Combination therapy with benazepril and hydrochlorothiazide, preferably as a single pill, to improve medication adherence and decrease risk of polypharmacy
   c. Maximizing dose of a single agent before proceeding with the addition of a second agent
   d. Initiation of spironolactone and furosemide because of differing effects on serum potassium and evidence of greater efficacy with two agents rather than one

8. How often should follow-up occur after initiating or adjusting pharmacotherapy for hypertension?
   a. Daily until blood pressure target is achieved, then weekly
   b. Biweekly until blood pressure target is achieved, then monthly
   c. Weekly until blood pressure target is achieved, then monthly
   d. Monthly until blood pressure target is achieved, then every three to six months

PRIMARY CARE REPORTS™ (ISSN 1040-2497) is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Primary Care Reports*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

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GST Registration No.: R128870672

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