

in the clinic

Hypertension

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Hypertension affects more than 65 million people in the United States, with about 2 million new cases diagnosed annually (1, 2). Most patients have primary or essential hypertension and are likely to remain hypertensive for life. Risk factors for hypertension include a family history of hypertension, African-American ethnicity, obesity, a high sodium or alcohol intake, and a sedentary lifestyle. Treatment to control blood pressure level reduces the risk for cardiovascular, cerebrovascular, and renal outcomes of hypertension. Unfortunately, many people with hypertension do not receive optimal therapy.

Screening and Prevention

What long-term health risks are associated with hypertension?

The relationship between blood pressure level and cardiovascular disease is linear, continuous, and independent of and additive to other risk factors. For persons age 40 to 70 years, each increment of either 20 mm Hg in systolic blood pressure level or 10 mm Hg in diastolic blood pressure level doubles the risk for cardiovascular disease (CVD) across the range of blood pressure levels from 115/75 mm Hg to 185/115 mm Hg (2). When other cardiovascular risk factors, such as diabetes or chronic kidney disease, are present, the CVD risk associated with hypertension is even higher. Complications of hypertension include retinopathy, cerebrovascular disease, ischemic heart disease, atrial fibrillation, heart failure, chronic kidney disease, and peripheral vascular disease.

Should clinicians screen for hypertension?

The U.S. Preventive Services Task Force recommends screening the adult general population for hypertension. It does not recommend a specific screening interval because of lack of evidence to support one (3). The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends screening every 2 years if blood pressure level is less than 120/80 mm Hg and annually if blood

pressure level is 120/80 to 139/89 mm Hg (2).

What is prehypertension and what is its proper management?

Prehypertension is a category that first appeared in the seventh JNC report. Prehypertension is defined as a blood pressure level of 120/80 to 139/89 mm Hg (2). Patients with prehypertension are at increased risk for developing overt hypertension and CVD. These patients should restrict dietary sodium, lose weight, reduce alcohol intake, and increase aerobic exercise. Several trials have evaluated drug treatment for prehypertension. At present, drug therapy is not recommended for prehypertension.

The Trial of Preventing Hypertension randomly assigned participants with prehypertension to active treatment with candesartan (an angiotensin-receptor blocker [ARB]) or placebo for 2 years and followed them for 4 years. Active treatment delayed onset of hypertension but did not prevent it (4).

Trials of Hypertension Prevention (TOHP) 1 and 2 examined the benefits of reductions in weight, sodium intake, and stress and supplementation with potassium, magnesium, fish oil, and calcium in persons with diastolic blood pressure levels of 80 to 90 mm Hg. TOHP 1 suggested that weight loss (3/2-mm Hg reduction) and sodium restriction (2/1-mm Hg reduction) were effective. TOHP 2 confirmed that weight loss and sodium restriction delay hypertension (5, 6).

1. Ong KL, Cheung BM, Man YB, et al. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension*. 2007;49:69-75. [PMID: 17159087]
2. Chobanian AV, Bakris GL, Black HR, et al. National Heart, Lung, and Blood Institute. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206-52. [PMID: 14656957]
3. U.S. Preventive Services Task Force. Screening for high blood pressure: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med*. 2007;147:783-6. [PMID: 18056662]
4. Julius S, Nesbitt SD, Egan BM, et al. Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med*. 2006;354:1685-97. [PMID: 16537662]
5. Cook NR, Cutler JA, Obarzanek E, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ*. 2007;334(7599):885.

Screening and Prevention... Cardiovascular risk increases as blood pressure increases, starting at a blood pressure level of 115/75 mm Hg. Guidelines recommend screening all adults for hypertension. Although evidence supporting a specific screening interval is thin, consensus advocates intervals of 1 to 2 years. Prehypertension (a blood pressure level of 120/80 to 139/89 mm Hg) increases the risk for sustained hypertension and CVD. Lifestyle modification can delay onset of hypertension and CVD.

CLINICAL BOTTOM LINE

Diagnosis

How should clinicians diagnose and stage hypertension?

The steps in diagnosing hypertension are simple but often not followed. The most common errors (failure to have the patient sit quietly for 5 minutes before a reading is taken, failure to support the limb used to measure blood pressure, use of a too-small cuff, and too-rapid cuff deflation) lead to falsely increased readings. The best position for patients is sitting, because the studies that established the value of treating hypertension used this position to measure the blood pressures that diagnosed hypertension and guided dose adjustment (7). See Table 1 and the Box for instructions on blood pressure measurement.

A person's blood pressure can vary widely. A single accurate measurement is a good start but not enough: Measure blood pressure twice and take the average. The running average is more important than individual readings. Hypertension is diagnosed if the average of at least 2 readings per visit obtained at 3 separate visits each 2

to 4 weeks apart is 140 mm Hg or greater systolic and 90 mm Hg or greater diastolic. According to the JNC 7, a normal blood pressure level is 120/80 mm Hg or less (2). Prehypertension is a blood pressure level of 120/80 to 139/89 mm Hg. Stage 1 hypertension is a systolic blood pressure level of 140 to 159 mm Hg or a diastolic blood pressure level of 90 to 99 mm Hg. Stage 2 hypertension is a systolic blood pressure level greater than or equal to 160 mm Hg or a diastolic blood pressure level greater than or equal to 100 mm Hg. The JNC 7 classification combines the stage 2 and 3 categories of older classifications (2). In persons older than 50 years, systolic blood pressure levels greater than 140 mm Hg are a more important CVD risk factor than diastolic hypertension.

Pseudohypertension can occur in patients with stiff, incompressible arteries. To detect it, inflate the blood pressure cuff to at least 30 mm Hg above the palpable systolic pressure and then try to "roll" the brachial or radial artery underneath your fingertips ("Osler's

Instructions for Taking Blood Pressure

- Have patient relax, sitting (feet on floor, back supported) for ≥ 5 min before taking the blood pressure.
- Support patient's arm (for example, resting on a desk) for the measurement.
- Use the stethoscope bell, not the diaphragm, for auscultation.
- Check blood pressure first in both arms with the patient sitting. Note which arm gives the higher reading and use this arm for all other (standing, lying down) and future readings.
- Measure blood pressure in sitting, standing, and lying positions. All measurements should be separated by 2 min.
- Use the correct cuff size and note if a larger- or smaller-than-normal cuff size is needed (Table 1).
- Record systolic (onset of first sound) and diastolic (disappearance of sound) pressures.
- Record exact results to nearest even number.

Table 1. Blood Pressure Cuff Size Criteria

Arm Circumference	Weight		Cuff Size to Use
	Female	Male	
24–32 cm	<150	<200	Regular
33–42 cm*	>150	>200	Large
38–50 cm*	–	–	Thigh

* Either cuff is acceptable for the overlap circumferences.

6. Batey DM, Kaufmann PG, Raczyński JM, et al. Stress management intervention for primary prevention of hypertension: detailed results from Phase I of Trials of Hypertension Prevention (TOHP-I). *Ann Epidemiol*. 2000;10(1):45-58.

maneuver”) (8). Healthy arteries should not be palpable when empty. If you feel a stiff, tube-like structure, the patient may have pseudohypertension.

What is white coat hypertension?

White coat hypertension is defined as an elevated office blood pressure with lower blood pressure readings measured at home or with a 24-hour ambulatory blood pressure monitor (9). The prevalence of white coat hypertension is 10% to 20% (10). These patients are at elevated risk for overt hypertension and CVD (11). Current guidelines do not recommend pharmacologic treatment for these patients but do recommend lifestyle modifications and regular follow-up.

When is ambulatory blood pressure monitoring indicated?

The ambulatory blood pressure monitor is a 24-hour portable device that the patient wears during their regular activities. It measures blood pressure every 15 to 20 minutes during the day and every 30 to 60 minutes at night. Ambulatory blood pressure monitoring provides the most accurate assessment of blood pressure (10). Most patients with hypertension do not need it, and the Center for Medicare & Medicaid Services pays for only 1

indication: diagnosing white coat hypertension. The Box lists the other potential situations in which ambulatory monitoring may be helpful.

Ambulatory blood pressure monitoring may also be useful in identifying high-risk blood pressure patterns that are associated with increased cardiovascular events in patients with hypertension. One is loss of “dipping status,” which is associated with worse cardiovascular outcomes of hypertension. Blood pressure of patients with loss of dipping status falls less than 10% at night relative to daytime blood pressure, in contrast to the blood pressure of patients with dipper status, which falls at least 10% at night (12). The other high-risk pattern is blood pressure surges in the early morning hours (13), which is associated with increased cerebrovascular disease risk. A surge is generally defined as a greater than 55-mm Hg difference in systolic pressure level between sleeping and early hour waking. In these patients, physicians may wish to target treatment at the high morning systolic values.

What are the key elements of the history for patients with hypertension?

Assess the duration, rapidity of onset, and severity of the hypertension. Ask about cardiovascular risk factors, concomitant medical conditions, symptoms of target organ damage, past treatment and its effects, and lifestyle (dietary habits, alcohol consumption, tobacco use, and level of physical activity). Note any family history of hypertension, renal disease, cardiovascular problems, stroke, and diabetes mellitus. Ask about increased stress, physical inactivity, and dietary salt intake.

Sudden onset of severe hypertension with previously normal blood pressure levels suggests a secondary form of hypertension. Ask about symptoms that suggest secondary hypertension. Palpitations, tachycardia, paroxysmal

Potential Indications for Use of Ambulatory Blood Pressure Monitoring

- Unusual variability of blood pressure level
- Possible white coat hypertension
- Evaluation of nocturnal hypertension
- Evaluation of drug-resistant hypertension
- Determining the efficacy of drug treatment over 24 hours
- Diagnosis and treatment of hypertension in pregnancy
- Evaluation of symptomatic hypotension on various medications, suggesting that the patient may be normotensive
- Evaluation of episodic hypertension or autonomic dysfunction

- Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1. *Circulation*. 2005;111:697-716. [PMID: 15699287]
- Messerli FH. Osler's maneuver, pseudohypertension, and true hypertension in the elderly. *Am J Med*. 1986;80:906-10. [PMID: 2939716]
- Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. *N Engl J Med*. 2006;354:2368-74. [PMID: 16738273]
- Angeli F, Verdecchia P, Gattobigio R, et al. White-coat hypertension in adults. *Blood Press Monit*. 2005;10:301-5. [PMID: 16496443]
- Eguchi K, Hoshida S, Ishikawa J, et al. Cardiovascular prognosis of sustained and white-coat hypertension in patients with type 2 diabetes mellitus. *Blood Press Monit*. 2008;13:15-20. [PMID: 18199919]

headache, and sweating suggest pheochromocytoma. Muscle weakness and polyuria suggest hypokalemia from excess aldosterone. Snoring and daytime sleepiness can indicate sleep apnea, and heat intolerance and weight loss suggest hyperthyroidism.

Review current medications, including over-the-counter drugs. Ask about oral contraceptives, corticosteroids, licorice, sympathomimetics, which can increase blood pressure level, and anti-migraine drugs. Nonaspirin non-steroidal anti-inflammatory drugs can decrease the efficacy of anti-hypertensive drugs (14).

What are the essential elements of the physical examination of patients with hypertension?

The physical examination should look for signs of secondary causes of hypertension and end organ damage related to hypertension. Table 2 outlines key components of the examination of the patient with hypertension.

Which laboratory tests should clinicians perform in patients with newly diagnosed hypertension?

Newly diagnosed patients should have measurement of hemoglobin or

hematocrit, serum electrolytes, serum creatinine, serum glucose, and fasting lipid levels and a urinalysis with microscopic examination and a 12-lead electrocardiogram (ECG). Additional testing may be indicated by clinical factors, suspicion of secondary causes of hypertension, and anticipated treatment.

Table 3 summarizes tests that may be useful in evaluation of possible secondary hypertension. Echocardiography is more sensitive than ECG for left-ventricular hypertrophy, which would tip the scales towards drug treatment rather than just a trial of lifestyle changes or towards true hypertension rather than white coat hypertension. If a patient has gout, check serum uric acid levels before prescribing diuretics. The presence of microalbuminuria may help to guide selection of therapy in patients with diabetes.

Which patients should be evaluated for secondary hypertension and how should they be evaluated?

The Box lists symptoms and signs that suggest secondary hypertension. Table 3 outlines suggested tests for secondary hypertension.

Symptoms and Signs that Suggest Secondary Hypertension

- New-onset hypertension at age <25 or >55 years
- Drug-resistant hypertension (requires 3 or more drugs at maximal doses)
- Spontaneous hypokalemia
- Palpitations, headaches, and sweating
- Severe vascular disease, including coronary artery disease (CAD), carotid disease, and peripheral vascular disease
- Epigastric bruit
- Radial-femoral pulse delay, especially with an inter-scapular murmur.

Table 2. Physical Examination and Key Findings in the Patient with Hypertension

Item	Routine Evaluation
General appearance, height, weight, BMI, waist circumference, skin lesions	Look for signs of metabolic syndrome (overweight, abdominal obesity), skin changes can indicate rare causes of secondary hypertension (striae in Cushing syndrome, mucosal fibromas can indicate MEN II)
Funduscopy	Retinal changes reflect severity of hypertension: arteriolar narrowing (grade 1), arteriovenous compression (grade 2), hemorrhages or exudates (grade 3), and papilledema (grade 4)
Examination of neck	Assess for thyroid enlargement, carotid bruits
Cardiopulmonary examination	Rales and gallops may indicate heart failure, interscapular murmur during auscultation of the back can indicate renal arterial disease
Abdominal examination	Palpable kidneys suggest polycystic kidney disease; midepigastic bruits can indicate renal arterial disease
Neurologic examination	Look for evidence of previous stroke, evaluate cognition (hypertension is a risk factor for loss of cognition).
Peripheral pulses	Reduced leg pulses can indicate coarctation of the aorta or systemic atherosclerosis

MEN = multiple endocrine neoplasia.

- Ciconetti P, Morelli S, De Serra C, et al. Left ventricular mass in dippers and nondippers with newly diagnosed hypertension. *Angiology*. 2003;54:661-9. [PMID: 14666954]
- Kario K, Pickering TG, Umeda Y, et al. Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives: a prospective study. *Circulation*. 2003;107:1401-6. [PMID: 12642361]
- Fierro-Carrion GA, Ram CV. Nonsteroidal anti-inflammatory drugs (NSAIDs) and blood pressure [Editorial]. *Am J Cardiol*. 1997;80:775-6. [PMID: 9315588]

Table 3. Work-Up to Pursue Possible Secondary Hypertension

<i>Secondary cause</i>	<i>Evaluation (findings)</i>
Coarctation of aorta	Chest film (rib notching; reverse "3" sign), 2-dimensional echocardiogram, aortogram (coarctation directly seen), MRI
The Cushing syndrome	Dexamethasone suppression test (failure to suppress cortisol), 24-h urinary-free cortisol (elevated), CT (adrenomegaly)
Primary aldosteronism	Plasma aldosterone-renin ratio (increased), aldosterone excretion rate during salt loading (increased), adrenal CT (adenoma with low Hounsfield units)
Pheochromocytoma	Plasma catecholamines or metanephrines (increased), urine catecholamines or metanephrines (increased), clonidine suppression test (failure to suppress plasma norepinephrine after clonidine administration), adrenal CT, MRI (adrenal tumor; T2-weighted MRI has characteristic appearance), iodine ¹³¹ -metaiodobenzylguanidine scan (significant adrenal or extra-adrenal tumor uptake)
Renal vascular disease	Captopril renography (some limitations), renal duplex sonography (requires good operators; increased renal artery compared with aorta velocities suggests stenosis), MRA (renal vessel narrowing), CTA (renal vessel narrowing), angiography (gold standard; renal vessel narrowing), renal vein renin ratio (not commonly done)
Renal parenchymal disease	24-h urine protein and creatinine levels, renal ultrasound (small kidney size, unusual architecture), glomerular filtration rate (low), renal biopsy (usually done to determine type of glomerular disease)
Parathyroid disorders	Calcium and phosphorus levels (increased and decreased, respectively), serum parathyroid hormone level (increased), serum calcitonin level (when MEN is suspected)
Thyroid disease	Serum thyroid hormone level (increased in hyperthyroidism), thyrotropin level (suppressed in hyperthyroidism)

CT = computed tomography; CTA = computed tomographic angiography; MEN = multiple endocrine neoplasia; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging

Diagnosis... Diagnosis of hypertension requires careful measurement of blood pressure levels on several occasions. Systolic blood pressure levels 140 mm Hg or greater or diastolic blood pressure levels 90 mm Hg or greater, based on the average of 3 sets of 2 or more readings obtained 2 to 4 weeks apart establishes the diagnosis of hypertension. The goals of the diagnostic evaluation are to search for a secondary cause, to detect other CVD risk factors, and to detect damage to target organs. In addition, the history should focus on past treatment, current medications, and contributing lifestyle factors. The focal points of the physical examination are eyegrounds, cardiovascular system, and nervous system. Levels of hemoglobin, urinalysis, serum creatinine, glucose, lipids, electrolytes, and an ECG are routine laboratory tests for patients with newly diagnosed hypertension.

CLINICAL BOTTOM LINE

Treatment

What are treatment goals for patients with hypertension?

See Box for blood pressure goals from different guidelines. Goal blood pressure level is less than 140/90 mm Hg in a patient with hypertension without CVD-related comorbid conditions. In patients with comorbid illness or more than a 10% 10-year Framingham risk for cardiovascular events, goal blood

pressure is less than 130/80 mm Hg. Key diseases include diabetes; chronic kidney disease; established CVD or CAD equivalents, such as acute coronary syndrome, ST elevation myocardial infarction, stroke, and stable angina (2). In patients with more than 1 g proteinuria, the recommended goal blood pressure target is 125/75 mm Hg or less.

15. Cordain L, Eaton SB, Sebastian A, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr.* 2005;81:341-54. [PMID: 15699220]

Guidelines for Blood Pressure Level Goals

Joint National Commission (JNC): JNC 7 recommends treatment to a goal blood pressure of <140/90 mm Hg. The target for patients with chronic kidney disease and diabetes should be a blood pressure level of \leq 130/80 mm Hg. JNC 8 will publish new recommendations soon.

American Heart Association (AHA): AHA recommends a target blood pressure level of 140/90 mm Hg for most patients and 130/80 mm Hg for patients with chronic kidney disease, CAD or CAD equivalents, and a >10% Framingham cardiovascular risk. The target for patients with heart failure is \leq 120/80 mm Hg.

National Kidney Foundation (NKF): The target blood pressure level is 130/80 mm Hg for patients with chronic kidney disease and diabetes and <125/75 mm Hg for patients with >1 g of proteinuria.

What are the recommended lifestyle modifications for treating hypertension?

Practice guidelines recommend nonpharmacologic treatment of hypertension with lifestyle modification for all patients with hypertension and prehypertension. Although adherence to lifestyle changes can substantially lower blood pressure, these changes—and their benefits—can be difficult to maintain. Physicians must

encourage patients to maintain lifestyle changes when drug therapy becomes necessary. Table 4 shows the expected effects of lifestyle modification.

Salt restriction

The effect of salt intake on blood pressure is well-established. Dietary sodium restriction can reduce systolic blood pressure level by 1 to 4 mm Hg. Dietary sodium restriction to less than 2400 mg per day is often the first lifestyle change. The average Western diet contains 3800 mg of sodium per day (15), and patients are often unaware of the high sodium content of many foods (16). Patients should especially avoid processed foods, lunchmeats, soups, Chinese food, and canned processed food.

In TOHP I, adults with diastolic blood pressure levels of 80 to 89 mm Hg and systolic blood pressure levels <160 mm Hg were randomly assigned to 18-month interventions to lose weight or to reduce dietary sodium or to 2 control groups. After 7 years, the incidence of hypertension was 18.9% in the weight loss group and 40.5% in its control group and 22.4% in the sodium reduction group and 32.9% in its control group (6).

The DASH trial randomly assigned 459 adults with systolic blood pressure levels of <160 mm Hg and diastolic blood pressure

Table 4. Lifestyle Modifications to Lower Blood Pressure Level

Lifestyle Modification	Recommendation	Potential Decrease in SBP
Dietary sodium restriction	Restrict dietary sodium to no more than 2400 mg/d or 100 meq/d	2–8 mm Hg
Weight loss	Maintain normal body weight; BMI = 18.5–24.9 kg/m ²	5–20 mm Hg per 10 kg weight loss
Aerobic exercise	Engage in regular aerobic exercise, aiming to do 30 min of aerobic exercise on most days of the week. It is suggested that patients walk about 1 mile per day above current activity level	4–9 mm Hg
DASH diet	Diet rich in fruits, vegetables, and low-fat dairy, with reduced content of saturated and total fat	4–14 mm Hg
Limit alcohol intake	No more than 2 mixed drinks, two 12-ounce cans of beer, or two 4-ounce glasses of wine daily for men and one half of this quantity for women	2–4 mm Hg

BMI = body mass index; DASH = Dietary Approaches to Stop Hypertension; SBP = systolic blood pressure

16. Mattes RD, Donnelly D. Relative contributions of dietary sodium sources. *J Am Coll Nutr.* 1991;10:383-93. [PMID: 1910064]

17. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med*. 1997;336:1117-24. [PMID: 9099655]
18. Bray GA, Vollmer WM, Sacks FM, et al. A further subgroup analysis of the effects of the DASH diet and three dietary sodium levels on blood pressure: results of the DASH-Sodium Trial. *Am J Cardiol*. 2004;94:222-7. [PMID: 15246908]
19. Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA*. 1998;279:839-46. [PMID: 9515998]
20. Xin X, He J, Frontini MG, et al. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2001;38:1112-7. [PMID: 11711507]
21. Fagrell B, De Faire U, Bondy S, et al. The effects of light to moderate drinking on cardiovascular diseases. *J Intern Med*. 1999;246:331-40. [PMID: 10583704]
22. McGuire HL, Svetkey LP, Harsha DW, et al. Comprehensive lifestyle modification and blood pressure control: a review of the PREMIER trial. *J Clin Hypertens (Greenwich)*. 2004;6:383-90.
23. Alexander CN, Schneider RH, Staggers F, et al. Trial of stress reduction for hypertension in older African Americans. II. Sex and risk subgroup analysis. *Hypertension*. 1996;28:228-37. [PMID: 8707387]
24. Taubert D, Roesen R, Schömig E. Effect of cocoa and tea intake on blood pressure: a meta-analysis. *Arch Intern Med*. 2007;167:626-34. [PMID: 17420419]

levels of 80-95 mm Hg to 8 weeks of a control diet, a diet rich in fruits and vegetables, or a "combination" diet rich in fruits, vegetables, and low-fat dairy products. The combination diet reduced systolic and diastolic blood pressure levels by 5.5 and 3.0 mm Hg more, respectively, than the control diet ($P < 0.001$); the fruits-and-vegetables diet reduced systolic blood pressure levels by 2.8 mm Hg more ($P < 0.001$) and diastolic blood pressure levels by 1.1 mm Hg more than the control diet ($P = 0.07$). Blood pressure reductions were larger in 133 patients with hypertension than in normotensive patients. A diet rich in fruits, vegetables, and low-fat dairy foods lowers blood pressure (17, 18).

Other lifestyle interventions

Encourage weight loss (to $<20\%$ above ideal body weight for height). Systolic blood pressure level falls approximately 1 mm Hg for every kilogram of weight loss. (19). Encourage at least 30 minutes of aerobic exercise on most days of the week. Strongly encourage smoking cessation (it does not directly lower blood pressure but does lower cardiovascular risk). Reduce alcohol intake to no more than 2 mixed drinks, two 12-ounce cans of beer, or two 4-ounce glasses of wine daily for men and one half of this quantity for women (20, 21).

The PREMIER trial randomly assigned 810 participants to behavioral intervention (weight loss, exercise, limited sodium and alcohol intake), the DASH diet plus behavioral intervention, or one-time advice only. Relative to advice-only, systolic blood pressure levels at 6 months declined by 3.7 mm Hg (behavioral change only) and 4.3 mm Hg (behavioral change plus DASH diet) (22).

Several lifestyle changes are of doubtful value. Fish oil, magnesium, and calcium supplementation do not reduce blood pressure. Although patients may consider relaxation therapies, such as meditation and yoga, their effect is short-term (23). Caffeine may transiently increase blood pressure, but caffeine has little sustained effect on blood pressure in patients with hypertension (24).

When is antihypertensive drug therapy indicated and which drugs should clinicians prescribe as initial therapy?

Many patients with stage 1 hypertension will require drug therapy to control blood pressure despite lifestyle modification. The JNC 7 recommends starting all patients on a diuretic unless they have a compelling reason to use another drug (2). Patients with stage 2 hypertension or those requiring a greater reduction than 20/10 mm Hg to reach goal blood pressure levels should start on 2 drugs, one of which should be a diuretic. Table 5 shows the doses, mechanisms, advantages, and disadvantages of a selection of commonly used antihypertensive drugs. The Figure provides an algorithm for treatment of hypertension, and Table 6 elaborates on compelling drug indications.

ALLHAT randomly assigned 44 000 patients age >55 years with hypertension and one additional cardiovascular risk factor to initial treatment with a diuretic (chlorthalidone), an α -blocker (doxazosin), an ACE inhibitor (lisinopril), or a calcium-channel blocker (amlodipine). Addition of a second drug was permitted as needed. The doxazosin group was discontinued when interim results showed that it could not be superior to diuretic and that heart failure was higher with doxazosin. The results with the remaining 3 drugs supported diuretics as first-choice therapy because of their efficacy in reducing cardiovascular death and nonfatal myocardial infarction, superiority in several secondary outcomes (heart failure and stroke), and low cost (25).

Clinicians should strongly consider treating hypertension in very elderly patients.

The HYVET trial randomly assigned 3845 patients older than 80 years with systolic blood pressure levels from 160 to 199 mm Hg to either placebo or diuretic (indapamide, 1.5 mg daily) with the addition of an ACE inhibitor (perindopril, 4-8 mg daily) as needed. The trial was stopped early because of the large benefit of active

Table 5. Drug Treatments for Hypertension*

<i>Drug Class (daily dose, mg)</i>	<i>Advantages</i>	<i>Disadvantages</i>
Diuretics Hydrochlorothiazide (12.5–50) Chlorothiazide (250–500) Chlorothalidone (12.5–50)	Most effective in the elderly, those with isolated systolic hypertension, diabetics, and African Americans, who are likely to be salt-sensitive; inexpensive	May increase glucose, cholesterol, and uric acid levels; hypokalemia; photosensitivity
ACE inhibitors Enalapril (5–40) Fosinopril (10–40) Lisinopril (5–40) Perindopril (4–16) Quinapril (5–80) Ramipril (1.25–20)	Preferred for chronic kidney disease, heart failure, and diabetes. Work well with diuretics. Generic ACE inhibitors are inexpensive	Cough in 15% (switch to an ARB). Can accept up to 30% increase in serum creatinine with ACE inhibitors. Angioedema in 0.1%–0.7%. Contraindicated in pregnancy
Angiotensin-receptor blocker (ARB) Losartan (25–100) Candesartan (16–32) Irbesartan (150–300)	Usually well-tolerated. Angioedema uncommon. Work well with a diuretic; Do not cause cough	Dizziness. Relatively expensive. Contraindicated in pregnancy
Potassium-sparing diuretics Spironolactone (25–100) Triamterene (25–100)	Most useful when a thiazide causes hypokalemia	Hyperkalemia (rare with triamterene); gynecomastia (spironolactone); weak antihypertensives
β-blockers Atenolol (25–100) Metoprolol (50–300) Propranolol (40–480) Nebivolol (2.5–10) Carvedilol (12.5–50)	Carvedilol is an α- and β-blocker. Nebivolol is also a vasodilator. Note: Don't use β-blockers as initial therapy except in heart failure	Bronchospasm, bradycardia, heart failure; masks insulin-induced hypoglycemia; impairs peripheral circulation; insomnia; fatigue; decreased exercise tolerance; hypertriglyceridemia (unless ISA present); several trials show worse outcomes with atenolol than ACE inhibitors, ARBs, and CCBs
CCBs Amlodipine (2.5–10) Diltiazem (120–360) Verapamil (120–480) Nifedipine (30–120)	Well-tolerated and effective. Dihydropyridines, like amlodipine, are quite potent. Relatively inexpensive	Diuretic-resistant edema (lesser problem if ACE inhibitor or ARB added), headache, cardiac conduction defects, constipation, gingival hypertrophy
Reserpine (0.05–0.25)	Inexpensive	Nasal congestion, depression, peptic ulcer
Central β-agonists Methyldopa (500–3000) Clonidine (0.2–1.2)	Inexpensive	Sedation, dry mouth, bradycardia, withdrawal (rebound) hypertension
Guanethidine (10–50) α-blockers Prazosin (2–30) Doxazosin (1–16) Terazosin (1–20)	Very potent; inexpensive	Postural hypotension; diarrhea Postural hypotension; heart failure increased with doxazosin in ALLHAT
Hydralazine (50–300)	Inexpensive	Lupus reaction; headache; edema
Direct renin inhibitor Aliskiren (150–300)	Newly approved. Reduced plasma renin could be therapeutic per se; effective in combination	Diarrhea

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CCB = calcium-channel blocker; ISA = irregular spiking activity.

* For a full listing of drugs, see Oral Antihypertensive Drug Treatment table in PIER hypertension module.

treatment with an expected 30% reduction in fatal and nonfatal stroke and an unexpected 21% reduction in all-cause mortality. This study confirms the value of drug treatment for patients age ≥80 years who have systolic blood pressure levels ≥150 mm Hg (26).

How should clinicians modify choice of antihypertensive treatment based on patient characteristics and comorbid conditions?

Although diuretics are generally the recommended first-choice agent,

25. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone. ALLHAT Collaborative Research Group. JAMA 2000;283:1967-75. [PMID: 10789664]

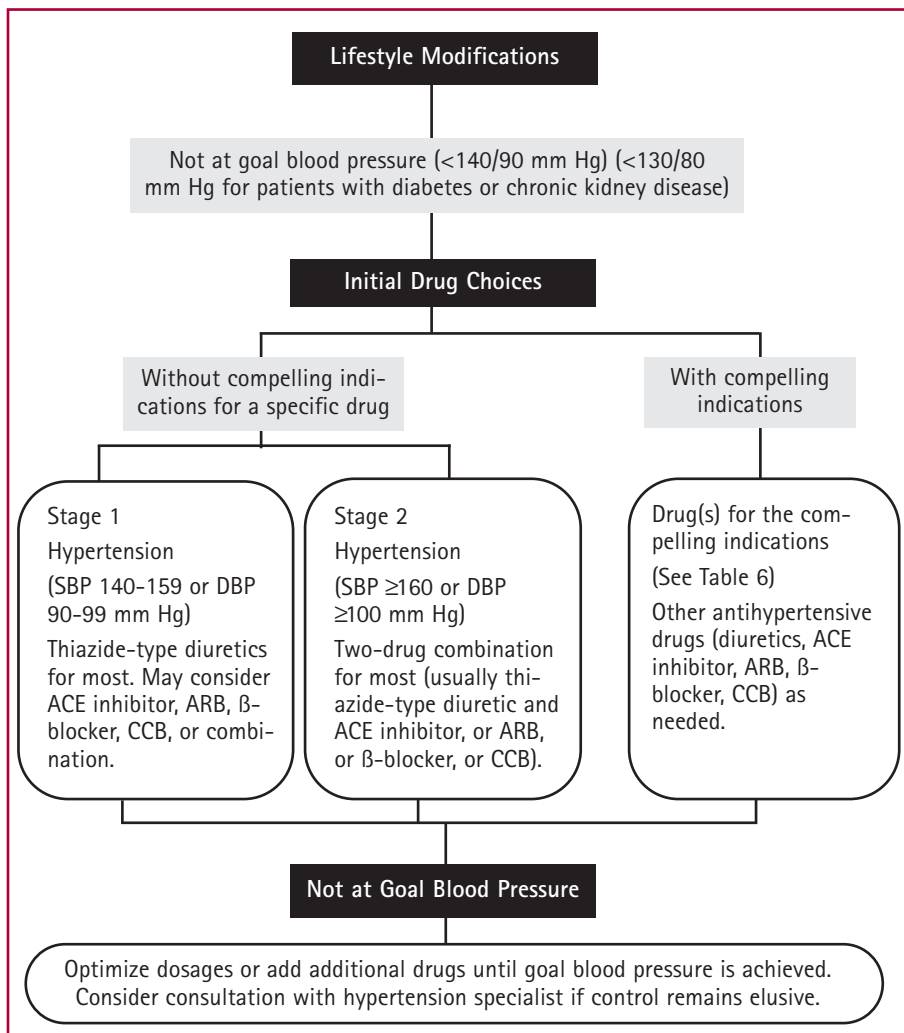


Figure. Algorithm for treatment of hypertension. Adapted from JNC 7 Hypertension Clinical Practice Guidelines (<http://www.nhlbi.nih.gov/guidelines/hypertension/express.pdf>). ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CCB = calcium-channel blocker; DBP = diastolic blood pressure; SBP= systolic blood pressure.

Table 6. Compelling Indications for Individual Drug Classes*

Compelling Indication [†]	Recommended Drugs
Heart Failure	Diuretic, β-blocker, ACE inhibitor, ARB, aldosterone antagonist
Postmyocardial infarction	β-blocker, ACE inhibitor, aldosterone antagonist
High coronary disease risk	Diuretic, β-blocker, ACE inhibitor, ARB + CCB
Diabetes	Diuretic, β-blocker, ACE inhibitor, ARB, CCB
Chronic kidney disease	ACE inhibitor, ARB
Recurrent stroke prevention	Diuretic, ACE inhibitor

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CCB = calcium-channel blocker.

* Adapted from JNC 7 Hypertension Clinical Practice Guidelines (<http://www.nhlbi.nih.gov/guidelines/hypertension/express.pdf>).

[†] Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the blood pressure.

clinicians should modify drug selection on the basis of patient characteristics and comorbid conditions.

Elderly and African-American patients tend to be salt-sensitive and respond well to diuretics.

26. HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med*. 2008;358:1887-98. [PMID: 18378519]
 27. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med*. 2000;342:145-53. [PMID: 10639539]

Younger patients with hypertension often respond well to suppression of the renin-angiotensin system and an ACE inhibitor or ARB may be a good initial choice for these patients. ACE inhibitors are helpful in patients with diabetes, particularly if microalbuminuria is present. Patients with heart failure can benefit from ACE inhibitors, diuretics, cardioselective β -blockers, and ARBs. β -blockers and ACE inhibitors are good antihypertensive agents for patients who have had a myocardial infarction. Patients with renal insufficiency can benefit from ACE inhibitors, particularly if proteinuria is present.

The HOPE trial randomly assigned more than 9000 patients >55 years old with CVD to ramipril 10 mg at night or placebo and found that those on ramipril had less morbidity and mortality than those on placebo. Because one half of the patients also had hypertension, the authors concluded that an ACE inhibitor is reasonable initial hypertension therapy in patients with vascular disease (27).

In the ASCOT trial, more than 19000 adults with hypertension and 3 or more CVD risk factors were randomly assigned to either a β -blocker plus a thiazide-type diuretic (if needed) or to a combination of a calcium-channel blocker (amlodipine) and an ACE inhibitor (perindopril) if needed and, in a factorial design, to either a statin or placebo. After median follow-up of 5.5 years, the trial was stopped because cardiovascular events and total mortality were significantly lower in the group that received the amlodipine-based regimen. Although blood pressure level was well-controlled in

both groups, it was lower in the amlodipine group by an average difference of 2.7/1.9 mm Hg. The amlodipine and ACE inhibitor drug combination reduced the risk for stroke by about 25%, for coronary events and procedures by 15%, and for cardiovascular deaths by 25% (28).

What is the role of combination therapies for hypertension?

Combination therapies are gaining popularity. They have several advantages, including better medication adherence. Whether they ultimately cost less for patients than individual prescriptions for each of the drugs depends on the patients' insurance programs.

ACE inhibitors or ARBs combined with hydrochlorothiazide

Many different ACE inhibitors and ARBs are available in combination with a thiazide. This combination is well-tolerated and is often good initial therapy for stage 2 hypertension.

ACE inhibitors and ARBs combined with dihydropyridine calcium-channel blockers

An ACE inhibitor with amlodipine is available in various doses, including generics. ARBs are not available as generics. Adding an ACE inhibitor or ARB avoids the edema of amlodipine monotherapy.

ACE-ARB combination therapy

ACE-ARB combinations do not seem to have advantages. The recent ONTARGET (Ongoing Telmisartan Alone and in Combination with

Table 7. Drug Therapy for Specific Disease Mechanisms of Hypertension*

Disease Mechanism	Drug Class	Comment
Volume overload	Thiazide; loop diuretic; aldosterone antagonist	
Sympathetic overactivity	β -blocker	Use to counteract reflex tachycardia from vasodilators or in heart failure
Increased vascular resistance	Angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker	Use in heart failure
Smooth-muscle contraction	Dihydropyridine calcium-channel blockers; β -blockers; hydralazine	

* Adapted from reference 33.

28. ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*. 2005;366:895-906. [PMID: 16154016]

Ramipril Global Endpoint Trial) study confirms that ACE inhibitors and ARBs are not additive in combination therapy for hypertension and have more side effects, such as hyperkalemia and slight decline in glomerular filtration rate (29). ACE inhibitor, ARB, and ACE-ARB combination had the same effect on cardiovascular events.

When blood pressure is poorly controlled, how should clinicians decide between increasing dose, adding an additional agent, or switching to another drug class?

When blood pressure is poorly controlled, it is important to avoid clinical inertia (30). The following principles were formulated to deal with a particular form of poorly controlled blood pressure called “resistant hypertension,” but they are useful whenever the blood pressure is above the target level. Resistant hypertension is when the blood pressure is above the target level on a rational, full-dose, triple-drug regimen that includes a diuretic (31, 32). If the patient has no target organ damage, consider ambulatory blood pressure monitoring to see if the white coat effect is a contributing factor. Ask about co-medication with blood pressure-raising drugs and excessive alcohol or salt intake. Reconsider secondary causes of hypertension as they are much more common in resistant hypertension. Poor adherence is also common, so carefully evaluate adherence before changing treatment.

Because volume overload is common, start treating uncontrolled hypertension by adding or increasing diuretic therapy with a thiazide (with normal renal function) or a loop diuretic (with abnormal renal function). A key to success is using several different drugs, each of which attacks a different disease mechanism. Table 7 shows physiologic mechanisms and the drug class that counteracts each. If the patient

is taking 2 drugs that attack the same disease mechanism, replace 1 of them with a drug from a different class. If patient is taking 3 drugs and blood pressure remains uncontrolled, ensure that the patient is taking drugs from different classes. Consider adding a potassium-sparing diuretic, such as aldactone or amiloride, in patients taking 3 to 4 drugs if blood pressure is still uncontrolled. Consider a combined α - and β -blocker, a centrally acting agent, or reserpine (in low doses). If control remains elusive, consider consulting a specialist in hypertension management.

How often should patients with hypertension be seen?

Blood pressure levels and clinical judgment should guide decisions about the frequency of monitoring blood pressure. Suggested recheck intervals for blood pressure levels 140/90 to 159/99 mm Hg are 2 months, and within 1 month if levels are higher. If the systolic and diastolic blood pressure levels fall into different categories, follow recommendations for the shorter follow-up time. After adjusting medications, allow 2 to 4 weeks for the blood pressure level to stabilize before modifying therapy. Clinical opinion rather than evidence determines the interval for seeing patients with stable, well-controlled hypertension; 6- to 12-month intervals are typical practice.

What is the value of home blood pressure level monitoring?

Home blood pressure monitoring is a relatively inexpensive way to monitor blood pressure levels, especially before and after changing therapy. Measurements of home blood pressure levels are more accurate than office blood pressure levels (33). Some patients become obsessed with their blood pressure level, and the physician may have to set limits on how often they take home blood pressure readings, lest

29. ONTARGET Investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med*. 2008;358:1547-59. [PMID: 18378520]
30. Phillips LS, Branch WT, Cook CB, et al. Clinical inertia. *Ann Intern Med*. 2001;135:825-34. [PMID: 11694107]
31. Moser M, Setaro JF. Clinical practice. Resistant or difficult-to-control hypertension. *N Engl J Med*. 2006;355:385-92. [PMID: 16870917]
32. American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation*. 2008;117:e510-26. [PMID: 18574054]
33. Pickering T. Recommendations for the use of home (self) and ambulatory blood pressure monitoring. American Society of Hypertension Ad Hoc Panel. *Am J Hypertens*. 1996;9:1-11. [PMID: 8834700]
34. Wilson MD, Johnson KA. Hypertension management in managed care: the role of home blood pressure monitoring. *Blood Press Monit*. 1997;2:201-206. [PMID: 10234118]

their anxiety over the results raise their blood pressure level. Instruct patients on correct technique of taking blood pressure level and ask them to keep a journal in which they chart their blood pressure level once to twice daily.

Home blood pressure level monitoring can help to confirm a diagnosis of hypertension in an untreated patient (34, 35). Instruct the patient to check at least 2 readings on at least 3 (preferably 7) consecutive days in the morning between 6 and 10 a.m. and to repeat them in the evening between 6 and 10 p.m. If the average home blood pressure level is less than 125/76 mm Hg (after dropping the first day's values), hypertension is very unlikely in an untreated person (36). Average untreated home blood pressure levels of 135/85 mm Hg and higher suggest hypertension. In-between values are an indication for further evaluation by ambulatory blood pressure monitoring.

When should clinicians consider hospitalization or referral to a hypertension specialist?

The main indication for hospitalization because of elevated blood pressure is a hypertensive crisis (see Box). Indications to refer to a hypertension specialist include the following: drug-resistant

hypertension uncontrolled on 3 or more drugs; uncertainty about how to evaluate or manage suspected secondary hypertension—especially pheochromocytoma or primary hyperaldosteronism—or assistance needed to assess the extent of target organ damage.

When patients present with markedly elevated blood pressure levels, how should clinicians distinguish between a hypertensive emergency and a pseudocrisis?

A sudden rise in blood pressure level is classified as either hypertensive urgency or a hypertensive emergency (37). Hypertensive urgency is defined as an elevated blood pressure level greater than 180/110 mm Hg without target organ damage. Patients can usually be managed with oral medications as outpatients and sent home after a few hours of observation. A hypertensive emergency is defined as an elevated blood pressure level with impending or acute progressive target organ damage. These patients usually require admission to an intensive care unit and intravenous medication to lower blood pressure level (38). Several drugs lower blood pressure quickly. The choice depends on the physician's level of comfort and experience with the drugs. See the Box for situations in which severe hypertension constitutes a crisis.

Treatment... The goal blood pressure level should be less than 140/90 mm Hg unless the patient has other cardiovascular risk factors or diabetes, which lowers the target to less than 130/80 mm Hg. Lifestyle modifications can lower the blood pressure level, but most patients also need at least 1 drug to reach goal blood pressure. A diuretic is a good choice for initial therapy absent a compelling indication for another drug (for example, vascular disease is a strong indication to start with an ACE inhibitor). Failure to reach target blood pressure level on a near-maximal dose of one or more drugs is an indication to add a drug that attacks another mechanism for hypertension. Severe hypertension requires urgent treatment, often in the hospital, if acute cardiovascular or neurologic events are present, if the patient is pregnant, or if severe catecholamine excess is present.

CLINICAL BOTTOM LINE

Situations in which Severe Hypertension Constitutes a Crisis

Cardiovascular

- Left-ventricular failure
- Myocardial infarction
- Unstable angina
- Aortic dissection
- After vascular surgery or coronary artery bypass grafting

Neurologic

- Hypertensive encephalopathy
- Subarachnoid or intracranial hemorrhage
- Thrombotic stroke

Other

- Severe catecholamine excess, such as clonidine withdrawal, pheochromocytoma, tyramine-MAOI* interaction, or intoxication (cocaine, phenylcyclidine, phenylpropranolamine)
- Eclampsia in pregnancy

* MAOI = monoamine oxidase inhibitors.

35. Pickering TG, Miller NH, Oggedegbe G, et al. Call to action on use and reimbursement for home blood pressure monitoring: executive summary: a joint scientific statement from the American Heart Association, American Society Of Hypertension, and Preventive Cardiovascular Nurses Association. *Hypertension*. 2008;52:1-9. [PMID: 18497371]
36. Williams B, Poulter NR, Brown MJ, et al. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV. *J Hum Hypertens*. 2004;18:139-85. [PMID: 14973512]
37. Townsend R. Hypertensive crisis. In: Lanken PN, ed. *The Intensive Care Unit Manual*. Vol. 2000. Philadelphia: WB Saunders; 2000:602-14.
38. Lip GY, Beevers M, Beevers DG. Complications and survival of 315 patients with malignant-phase hypertension. *J Hypertens*. 1995;13:915-24. [PMID: 8557970]

Practice Improvement

How many patients with hypertension receive treatment, and how well is hypertension controlled in the United States?

Of the one third of U.S. adults that have hypertension, only two thirds are aware of their hypertension, and approximately 55% are on treatment. Hypertension control rates are improving: The blood pressure level control rate was $29.2\% \pm 2.3\%$ in 1999 to 2000 and $36.8\% \pm 2.3\%$ in 2003 to 2004 (1). The control rates increased substantially in both sexes, non-Hispanic blacks, and Mexican Americans. Among the group of patients age 60 years and older, awareness, treatment, and

control rates have all increased significantly (1). Among treated patients with hypertension, control rates approach 65%.

What do professional organizations recommend about the management of patients with hypertension?

The advice in this In The Clinic article generally represents the recommendations of the JNC 7 (2), the American Heart Association, the National Kidney Foundation, and the American College of Physicians. Links to the guidelines are listed in the Toolkit.

in the clinic Tool Kit Hypertension

PIER Modules

pier.acponline.org

Access the PIER module on hypertension, which provided the up-to-date evidence cited in this In the Clinic article. PIER modules provide evidence-based, current information on prevention, diagnosis, and treatment in an easy-to-use electronic format designed for rapid access at the point-of-care.

Patient Education Resources

www.annals.org/intheclinic

Access the Patient Information material that appears on the following page for duplication and distribution to patients.

Practice Measures

pier.acponline.org/qualitym/index.html

PIER has a list of practice measures, including those of the Physician Quality Reporting Initiative (PQRI). Hypertension quality measures appear under Endocrinology, Diabetes, and Metabolism and under Nephrology.

www.qualityforum.org/pdf/ambulatory/tbAMBALLMeasuresendorsed%2012-10-07.pdf

The National Quality Forum: This influential group's practice measures appear under Diabetes and Hypertension.

www.ama-assn.org/ama1/pub/upload/mm/370/hypertension-8-05.pdf

Practice measures from the Physicians' Consortium for Performance Improvement (PCPI). Among the tools is a good flow sheet for recording key data over time.

Guidelines

hyper.abajournals.org/cgi/content/full/42/6/1206

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

circ.abajournals.org/cgi/reprint/CIRCULATIONAHA.107.183885

Guidelines from the American Heart Association for managing hypertension to prevent atherosclerotic cardiovascular disease.

www.kidney.org/professionals/KDOQI/guidelines.cfm

Guidelines from the National Kidney Foundation for managing hypertension in patients with renal disease.

diabetes.acponline.org/custom_resources/ACP_DiabetesCareGuide_Ch10.pdf?dbp

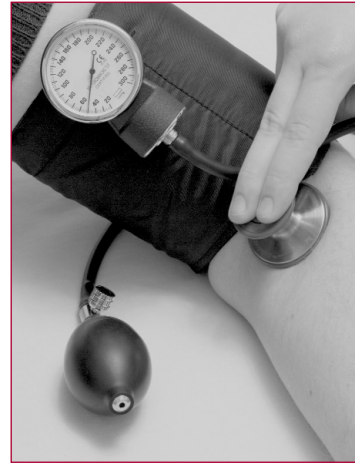
ACP Guidelines for the care of hypertension in patients with diabetes.

in the clinic

THINGS PEOPLE SHOULD KNOW ABOUT HYPERTENSION

In the Clinic
Annals of Internal Medicine
annals.org

- Hypertension, often called high blood pressure, is a common health problem.
- Most people do not know they have high blood pressure. Some people get headaches or swollen legs due to problems related to hypertension, such as heart failure.
- We don't know what causes hypertension. In a few people who have another disease that causes hypertension, it can be cured. But most people must take medicines to control their blood pressure.
- If you don't get treated for your hypertension, there is a better chance you could have a heart attack, stroke, or kidney failure.
- Just having healthy habits may lower your blood pressure. Follow these healthy habits even if you take blood



pressure medicine: Eat less salt, exercise more, eat more fruits and vegetables, lose weight, drink less alcohol, and stop smoking.

- Work with your doctor to have better health habits, measure your blood pressure at home, and take your medicine every day. Keep all of your doctor appointments.

For More Information

American College of Physicians: ACP Special Report: Living with Hypertension

www.doctorsforadults.com/images/healthpdfs/hypertension_report.pdf

American Heart Association: High Blood Pressure

www.americanheart.org/presenter.jhtml?identifier=2114

National Heart, Lung, and Blood Institute: Your Guide to Lowering Blood Pressure

www.nhlbi.nih.gov/health/public/heart/hbp/hbp_low/hbp_low.pdf

National Kidney Foundation: High Blood Pressure (Hypertension)

www.kidney.org/atoz/atozTopic.cfm?topic=1

ACP
AMERICAN COLLEGE OF PHYSICIANS
INTERNAL MEDICINE | Doctors for Adults®

1. A 58-year-old black man has had hypertension for 5 years. He has maintained a blood pressure of 135/85 mm Hg with use of hydrochlorothiazide, 25 mg/d. Laboratory assessment reveals a serum sodium level of 141 meq/L, serum potassium level of 4.1 meq/L, and fasting plasma glucose level of 132 mg/dL. These values are confirmed on remeasurement several days later.

What is most appropriate management of this patient's hypertension?

- Continue the current therapy, with a target blood pressure less than 140/90 mm Hg
- Discontinue hydrochlorothiazide therapy and begin ramipril therapy
- Add amlodipine to hydrochlorothiazide therapy
- Add ramipril to hydrochlorothiazide therapy
- Increase the hydrochlorothiazide dosage to 50 mg/d

2. A 31-year-old man is referred for management of multidrug-resistant hypertension. His hypertension was diagnosed 2 years ago, and treatment with multiple blood pressure medications, both alone and in combination, has been ineffective. His current medical regimen includes oral hydrochlorothiazide, 25 mg/d; oral amlodipine, 10 mg/d; and atenolol, 100 mg/d.

Blood pressure is 160/100 mm Hg, pulse rate is 80 per min and regular, and respiration rate is 18 per min. There is an S4 gallop and trace pretibial edema. The patient has been consistently hypokalemic in the past, with a serum potassium level of 2.5 to 3.4 meq/L even with potassium supplementation.

His serum creatinine level is 1.1 mg/dL, blood urea nitrogen is 12 mg/dL, serum sodium level is 136 meq/L, serum potassium level is 2.8 meq/L, serum chloride level is 108 meq/L, serum bicarbonate 30 meq/L. Electrocardiography shows left ventricular hypertrophy by voltage criteria.

What is the most likely diagnosis?

- Volume and potassium depletion secondary to chronic overdiuresis
 - Pheochromocytoma
 - Primary aldosteronism
 - Severe essential hypertension
 - The Bartter syndrome
3. A 68-year-old woman is hospitalized with palpitations and shortness of breath. She has a history of hypertension and chronic atrial fibrillation, and her medications include furosemide, candesartan, and warfarin. On physical examination, the heart rate is 120 bpm with an irregularly irregular rhythm, and blood pressure is 130/80 mm Hg; she has an elevated jugular venous pulse, crackles in both lungs, and marked lower extremity edema. Echocardiography shows left ventricular hypertrophy, an ejection fraction of 70%, and no significant valvular disease. She is treated with intravenous diuretics, with improvement in her symptoms and resolution of peripheral edema and of crackles on lung examination. Her heart rate is now 99 bpm and her blood pressure is 120/75 mm Hg.

Which of the following would be the most appropriate medication to add?

- Lisinopril
 - Spirolactone
 - Amlodipine
 - Metoprolol
 - Hydrochlorothiazide
4. A 58-year-old man who has longstanding diabetes mellitus and peripheral vascular disease involving the left leg comes to your office for a routine follow-up visit. He has intermittent claudication when he plays golf. He is obese, with a body mass index of 40 kg/m², and his blood pressure is 160/95 mm Hg.

Physical examination shows normal jugular venous pressure. Cardiac examination is normal. Examination of the extremities shows no edema and absent left pedal pulses. The left leg ankle-brachial index is 0.8. Electrocardiogram

obtained 1 year ago showed no significant findings. His last lipid profile showed a total serum cholesterol level of 260 mg/dL, high-density lipoprotein cholesterol level of 25 mg/dL, low-density lipoprotein cholesterol level of 165 mg/dL, and triglyceride level of 250 mg/dL. His hemoglobin A1c level was 8%. Heart failure has not been suspected or diagnosed. The patient smokes and is sedentary. However, he works and is apparently compliant with his medication regimen. He was taking simvastatin, 40 mg/d, last year, but discontinued this medication because of diffuse muscle and joint aches that have since resolved. He takes rosiglitazone, 4 mg/d; atenolol, 50 mg/d; hydrochlorothiazide, 50 mg/d; and aspirin, 80 mg/d. You suggest smoking cessation, weight loss, and physical conditioning.

Which of the following interventions would prevent the progression of complications of diabetes and atherosclerosis in this patient?

- Prescribe a nonstatin lipid-lowering agent
- Recommend vitamin E, 500 IU/d
- Substitute insulin for rosiglitazone
- Start treatment with amlodipine
- Start treatment with ramipril

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.