

VHA/DOD CLINICAL PRACTICE GUIDELINE FOR
DIAGNOSIS AND MANAGEMENT OF
HYPERTENSION
IN THE PRIMARY CARE SETTING

Veterans Health Administration
Department of Defense

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INTRODUCTION

VHA/DOD CLINICAL PRACTICE GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING

Introduction

This clinical practice guideline (CPG) on the management of hypertension in the primary care setting is intended to promote evidence-based management of hypertension and thereby improve patient's clinical outcomes. It can assist primary care providers or specialists in the early detection of symptoms, assessment of the clinical situation, determination of appropriate treatment, and delivery of individualized interventions. Although it was developed for a broad range of clinical settings, it should be applied with enough flexibility to accommodate local practice and individual situations.

The guideline was developed under the auspices of the Veterans Health Administration (VHA) and the Department of Defense (DoD) pursuant to directives from the Department of Veterans Affairs Under Secretary for Health and the DoD Assistant Secretary of Defense, Health Affairs and by consultants of the contractor (West Virginia Medical Institute, Inc.) and the subcontractor (Birch & Davis Associates, Inc.). Topic selection was based on information about the prevalence of hypertension in the VHA and DoD populations and the risks that are associated with this condition. It is known that lowering blood pressure decreases deaths from stroke and coronary events, prevents progression to more severe hypertension, and reduces mortality (1).

VHA and DoD define clinical practice guidelines as:

“Recommendations for the performance or exclusion of specific procedures or services derived through a rigorous methodological approach that includes the following:

1. Determination of appropriate criteria, such as effectiveness, efficacy, population benefit, or patient satisfaction; and
2. Literature review to determine the strength of the evidence in relation to these criteria.”
(2)

This guideline is divided into three sections: Algorithm, Annotations, and Bibliography. An algorithm is a set of rules for solving a problem in a finite number of steps. A letter within the box of an algorithm refers the reader to the corresponding annotation. A clinical algorithm allows the practitioner to follow a linear approach to the recognition and treatment of hypertension. Clinical practice, however, often requires a nonlinear approach. For example, hypertension may be the initial presenting complaint, but a coexisting condition may require attention first.

The annotations elaborate on the recommendations and statements that are noted in each box of the algorithm. These annotations include a reference, when required, and evidence grading for each of these recommendations—the strength of recommendation (SR) and level of evidence (LE). The bibliography includes all the sources used directly or indirectly in the substantiation of this guideline.

The algorithm and annotations were based on an exhaustive review of the literature. The goal of the literature review was to provide a systematic basis for the development of an evidence-based guideline. The inclusion criteria for the literature search were related to the population being studied (adult) and the treatment setting (primary care).

The Medical Subject Headings (MeSH) terms used for the search were: key therapies in hypertension, study characteristics, and study design. In this search, “study characteristics” were those of analytic studies, case-control studies, retrospective studies, cohort studies, longitudinal studies, follow-up studies, prospective studies, cross-sectional studies, clinical protocols, controlled clinical trials, RCTs, intervention studies, and sampling studies. Study design included crossover studies, double-blind studies, matched pair analysis, meta-analysis, random allocation, reproducibility of results, and sample size.

The literature search was followed by critical analysis of the literature, primarily by the clinical experts. To promote the evidence-based approach, the quality of evidence was rated using a hierarchical rating scheme. The value of a hierarchical rating scheme is that it provides a systematic means for evaluating the scientific basis for health care services (3). The rating scheme used for this guideline is based on a system used by the Agency for Health Care Policy and Research. Decision points in the algorithm are annotated, and the primary source documents for the annotation are graded.

The grading scheme used for this guideline is:

STRENGTH OF RECOMMENDATION (SR) GRADING (4)

Grade	Strength of Recommendation
I	Usually indicated, always acceptable, and considered useful and effective
IIa	Acceptable, of uncertain effectiveness, and may be controversial. Weight of evidence in favor of usefulness/effectiveness
IIb	Acceptable, of uncertain effectiveness, and may be controversial. Not well established by evidence, can be helpful and probably not harmful

LEVEL OF EVIDENCE (LE) GRADING (5)

Level of Evidence Grade = A	Level of Evidence Grade = B	Level of Evidence Grade = C
Randomized clinical trials	Well-designed clinical studies	Panel consensus

The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) proved to be a very important source of information for this guideline. The literature search did not identify contrasting evidence to the findings of this document. The clinical experts who reviewed the literature were aware of the limitations of JNC-VI, but agreed with the fundamental assessments at most decision points.

This guideline is the product of many months of consensus building among knowledgeable individuals, including private sector experts provided by the contractor. Many of the experts involved in developing this guideline participated in the development of other guidelines. The process included contributions from internists, specialists, primary care providers, program specialists, administrators, external peer review physicians, and expert consultants in the field of guideline and algorithm development.

The clinical experts subjected all decision points in the algorithm to simulation exercises. A variety of hypothetical "patients" were "run through" the algorithm to test whether it was likely to work in a real clinical situation. Whenever an irregularity was encountered, changes were made. The clinical experts are thus reasonably confident that the algorithm will prove to be useful in real clinical encounters.

Although this guideline represents the best evidence-based practice on the date of its publication, it is certain that medical practice is evolving and that this evolution will require continuous updating of published information. In addition, the reader is reminded that this document is intended as a guideline and should not supersede the clinical judgment of the health care provider. This initial version will be updated as further research results become available.

References

- (1) The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 1997.
- (2) VHA Directive 96-053 and VA HSR&D MDRC 1998.
- (3) Woolf et al., 1996.
- (4) Modified by Birch & Davis Associates, Inc., from ACC/AHA Task Force Report. Guidelines for the early management of patients with acute myocardial infarction. *Journal of the American College of Cardiology*, August 1990;16:251.
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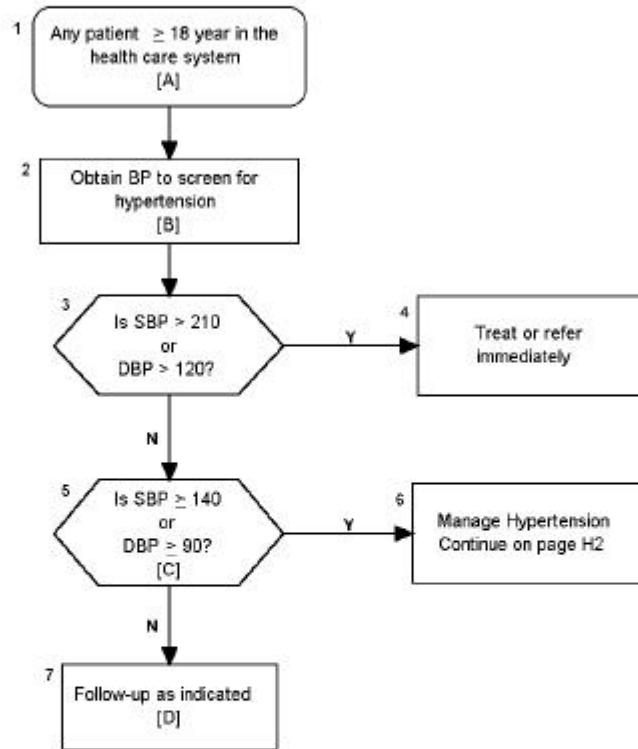
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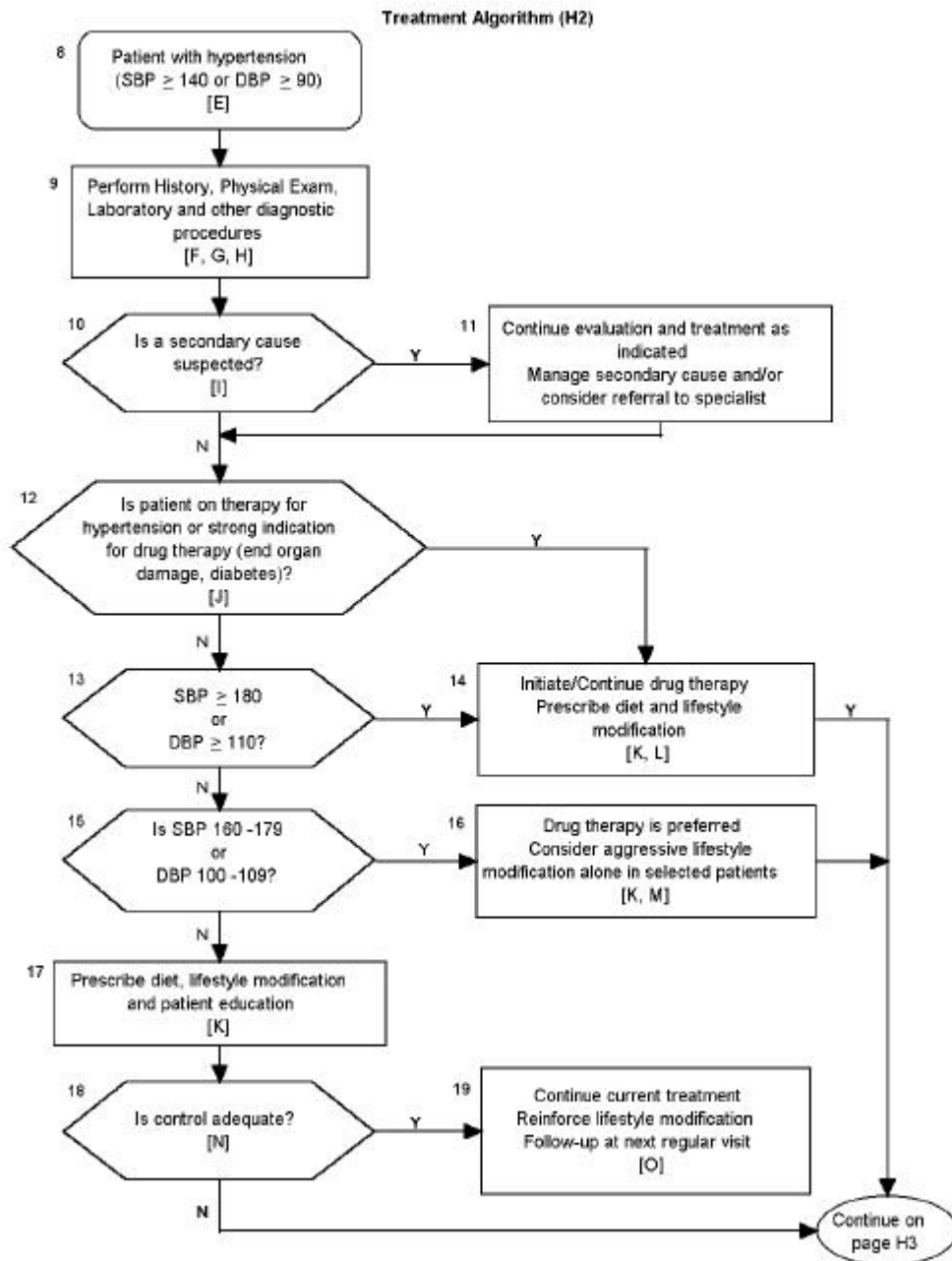
ALGORITHM

DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING

Screening Algorithm (H1)

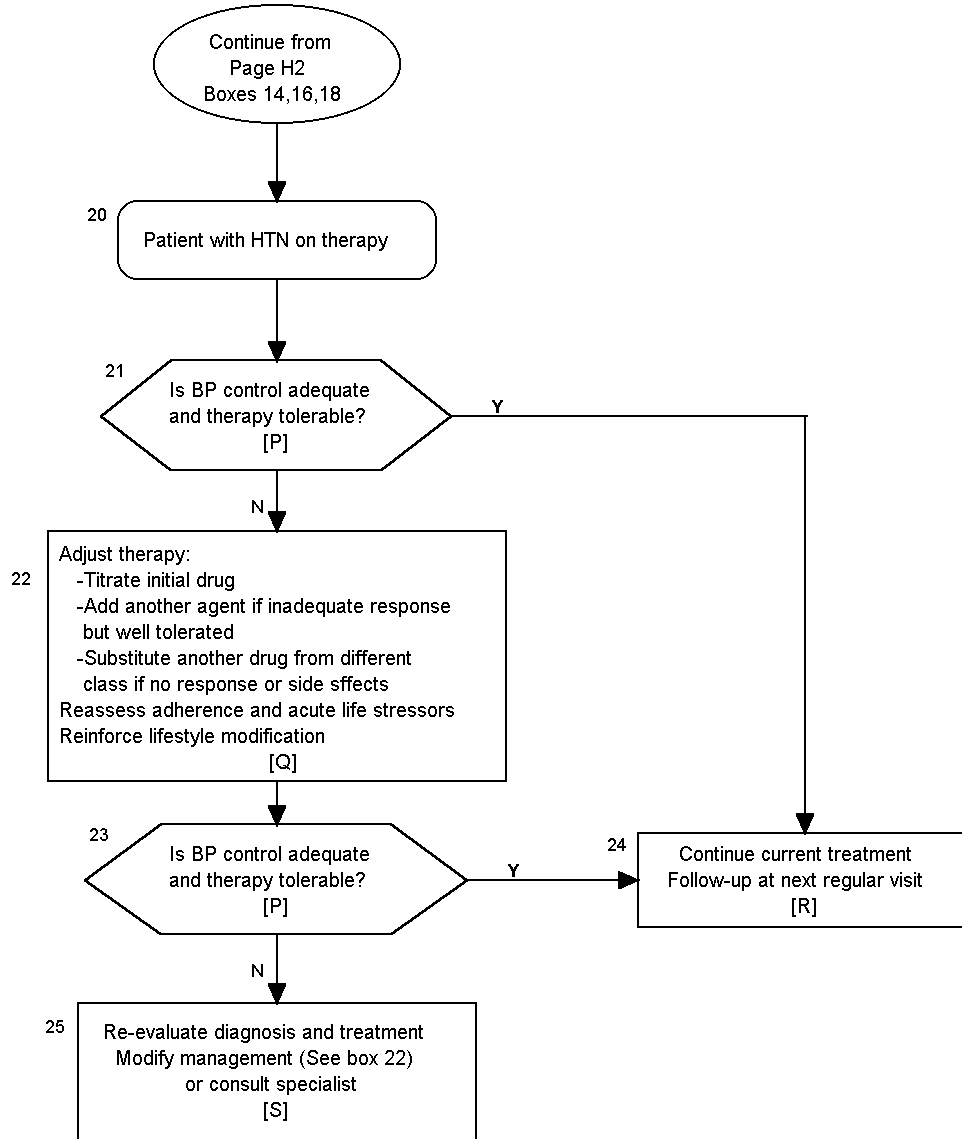


DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING



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Treatment Algorithm (H3)



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DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING

Annotations

A. Any Patient Greater than or Equal to 18 Years Old in the Health Care System

OBJECTIVE

To implement this guideline in adult patients.

ANNOTATION

In this document, an adult is defined as anyone older than 18 years. Older adults are considered to be 60 years old or older.

Note: This guideline is not directed to the treatment of pregnant patients. Pregnant patients with chronic or acute hypertension should be managed in consultation with appropriate specialists.

B. Obtain Blood Pressure to Screen for Hypertension

OBJECTIVE

To ensure that the blood pressure (BP) is checked properly and accurately.

ANNOTATION:

Any primary care manager/provider (PCM)/(PCP) can obtain the BP of a patient in any health care setting, e.g., clinic, doctor's office, emergency room, or hospital.

C. Is SBP > 140 or DBP > 90?

OBJECTIVE

To establish a diagnosis of hypertension.

ANNOTATION

The diagnosis of hypertension is usually not made on a first visit. In the absence of obvious hypertensive target organ damage, the provider should:

1. Perform a minimum of two BP determinations during a patient visit. The diagnosis of hypertension should be determined by two independent BP readings on two separate patient visits.
2. Demonstrate that systolic and diastolic BP are usually, but not necessarily always, higher than normal.
3. Obtain blood pressure readings with the patient in a seated position.

4. Verify BP reading on the contralateral arm; if values are different, the higher value should be used for diagnostic purposes.¹
5. Follow up at an appropriate interval, using Table 1 as a guide.

Table 1. Recommendations for Follow-up Based on Initial Blood Pressure Measurements for Adults²

Initial Blood Pressure, mm Hg*		Recommended Follow-up
Systolic	Diastolic	
< 130	< 85	Recheck in 2 years
130-139	85-89	Recheck in 1 year**
140-159	90-99	Confirm within 2 months***
160-179	100-109	Evaluate or refer to source of care within 1 month
> 180	> 110	Evaluate or refer to source of care immediately or within 1 week, depending on clinical situation

* If systolic and diastolic categories are different, follow recommendations for shorter follow-up (e.g. 160/86 mm Hg should be evaluated or referred to source of care within 1 month).

** Modify the scheduling of follow-up according to reliable information about past blood pressure measurements, other cardiovascular risk factors, or target organ disease.

*** Provide advice about lifestyle modifications (see annotation K, below).

D. Follow up as Indicated

OBJECTIVE

To provide clinicians with recommendations for follow-up intervals for normotensive patients.

ANNOTATION:

For patients with SBP < 130 and DBP < 85, BP should be rechecked in 2 years. For patients with SBP 130-139 or DBP 85-89, BP should be rechecked in 1 year.³

E. Patient with Hypertension—SBP ≥ 140 or DBP ≥ 90

OBJECTIVE

To define the parameters for blood pressure classification in adults; it is important to determine the level or stage once the diagnosis of hypertension is made.

¹ JNC-VI, 1997. SR=I LE=C

² Adapted from JNC-VI, 1997. See Table 3.

³ JNC-VI, 1997. SR=I LE=C

ANNOTATION

Table 2. Classification of BP for Adults Aged 18 Years And Older⁴

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Optimal ⁵	Less than or equal to 120 and	Less than or equal to 80
Normal	Less than or equal to 130 and	Less than or equal to 85
High Normal	130-139 or	85-89 ⁶
Hypertension Stage 1	140-159 or	90-99
Stage 2	160-179 or	100-109
Stage 3	Greater than or equal to 180 or	Greater than or equal to 110

1. When systolic and diastolic blood pressures fall into different categories, the higher category should be selected to classify the individual's blood pressure status. For example, 160/92 mm Hg should be classified as stage 2 hypertension; 174/120 mm Hg as stage 3 hypertension.
2. Isolated systolic hypertension is defined as systolic blood pressure greater than 140 mm Hg and diastolic blood pressure less than 90 mm Hg.

F. Perform History

OBJECTIVE

To elicit historical features that may influence clinical decision-making.

ANNOTATION

The patient's medical history pertinent to hypertension should include:

1. Duration, levels, and nature of BP elevation
2. History or symptoms to rule out coronary heart disease (CHD), heart failure, cerebrovascular disease, peripheral vascular disease, renal disease, diabetes mellitus (DM), dyslipidemia, gout, and sexual dysfunction
3. Family history of hypertension, premature CHD, cerebrovascular accident (CVA), DM, dyslipidemia, or renal disease
4. Other symptoms suggesting other causes of elevated BP
5. Results and adverse effects of any previous antihypertensive therapy
6. History of recent change in weight, physical activity, tobacco use
7. Dietary assessment, including intake of sodium, saturated fat, and caffeine

⁴ Adapted from JNC-VI, 1997. See Table 2.

⁵ Regarding cardiovascular risk, optimal BP determined from population studies is defined as less than 120/80 mm Hg.

⁶ Based on the average of two or more readings taken at each of two or more visits.

8. History of all prescribed and over-the-counter medications, herbal remedies, and dietary supplements, some of which may raise blood pressure or interfere with the effectiveness of antihypertensive medications
9. History of alcohol and illicit drug use (especially cocaine and other stimulants)
10. Psychosocial and environmental factors (e.g., family situation, employment status and working conditions, level of comprehension) that may influence HTN control.⁷

G. Perform Physical Examination

OBJECTIVE

To elicit physical signs that may influence clinical decision-making.

ANNOTATION

A physical exam should evaluate for signs of secondary HTN or hypertensive organ damage. At a minimum, vital signs should include height, weight, and two or more blood pressure readings with the patient seated. Verification should be carried out on the contralateral arm; if values are different, the higher value should be used for diagnostic purposes.⁸

If the patient has diabetes mellitus (DM), is elderly, or has symptoms of orthostasis, a standing blood pressure should also be measured in addition to seated or supine. The two blood pressure measurements should be separated by 2-minute intervals.

A focused examination should include the following:

1. Fundoscopy
 - a. Arteriovenous (AV) nicking or arterial narrowing
 - b. Hemorrhages
 - c. Exudates
 - d. Papilledema
2. Neck
 - a. Carotid bruits
 - b. Jugular venous distention
 - c. Thyromegaly
3. Heart
 - a. Regular rate or rhythm
 - b. Apical impulse
 - c. Precordial heave
 - d. Clicks, murmurs, third or fourth heart sounds
4. Lungs
 - a. Rales
 - b. Wheezes or rhonchi

⁷ JNC-VI, 1997. SR=I LE=C

⁸ JNC-VI, 1997. SR=I LE=C

5. Abdomen
 - a. Masses, e.g., aortic aneurysm, polycystic kidneys
 - b. Bruits
6. Extremities
 - a. Peripheral arterial pulses
 - b. Femoral bruits
 - c. Edema
7. Central and peripheral Nervous systems
 - a. Signs of prior CVA

H. Perform Laboratory and Other Diagnostic Procedures

OBJECTIVE

To determine:

1. Baseline data on patient's health status.
2. The existence of secondary causes of HTN.
3. Risk factors contributing to the disease process.

ANNOTATION

Routine laboratory tests help to determine the presence of target organ damage and some risk factors. Optional tests may be used, depending on findings obtained in the history and physical examination and previously known comorbidities. A greater, more inclusive assessment, e.g., cardiovascular anatomy and function, can be determined by ad hoc specialized testing.

Table 3. Laboratory and Other Diagnostic Procedures for Hypertension⁹

Recommended	Urinalysis (UA)
	Complete blood cell count (CBC)
	Blood chemistry (potassium, sodium, blood urea nitrogen (BUN), creatinine, fasting glucose)
	Lipid profile (total cholesterol and high-density lipoprotein cholesterol)
	12-lead electrocardiography
Optional	Creatinine clearance
	Microalbuminuria
	24-hour urine protein
	Blood calcium
	Uric acid

⁹ JNC-VI, 1997.

Table 3. Laboratory and Other Diagnostic Procedures for Hypertension (cont)

	Fasting triglycerides
	Glycosylated hemoglobin
	Low-density lipoprotein cholesterol
	Thyroid-stimulating hormone (thyrotropin) (TSH)
	Limited echocardiography to determine the presence of left ventricular hypertrophy
	Standard echocardiography

I. Is a Secondary Cause Suspected?

OBJECTIVE

To identify underlying disease(s) responsible for patient's HTN.

ANNOTATION

Although fewer than 5 percent of patients have secondary hypertension, clinicians should constantly be alert for secondary causes of HTN.

Table 4. Recommended Testing for Patients Suspected of Having Secondary Hypertension

Disease	Recommended Test/Referral
Renovascular disease	There are a variety of screening tests for renovascular HTN, depending on equipment and expertise in institutions. There is no single best test for renovascular HTN. Therefore, consult experts in your institution for current recommendations. Note: Intravenous pyelography (IVP) is <i>not commonly used</i> , and is relatively contraindicated in diabetics.
Thyroid disease	Thyroid-stimulating hormone (thyrotropin) (TSH)
Pheochromocytoma	24-hour urine for metanephrines or urinary catecholamines Consider specialty referral
Cushing's syndrome	24-hour urine for free cortisol
Hyperaldosteronism	Serum potassium
Hyperparathyroidism	Serum calcium and parathyroid hormone (PTH) level
Renal parenchymal disease	Urinalysis, urine sediment, serum creatinine, 24-hour urine for protein and creatinine clearance Consider referral to nephrology
Sleep apnea	Referral for sleep study

J. Is Patient on Therapy for Hypertension or Strong Indication for Drug Therapy (End Organ Damage, Diabetes)?

OBJECTIVE

To identify patients who require drug therapy instituted after diagnosis.

ANNOTATION

1. For patients without additional cardiovascular risk factors, the clinician may initially recommend aggressive lifestyle modification alone for up to 6 months if risk factors warrant and patient is highly motivated to alter lifestyle.
2. In hypertensive patients who have end organ damage, diabetes, or stage 2 or 3 hypertension, drug therapy is preferred.
3. For all other patients, risk stratification should determine therapy (see below and Table 5). Since the combination of diabetes mellitus and hypertension can accelerate renal failure, drug therapy is recommended.

The following major risk factors are the components of cardiovascular risk stratification in patients with hypertension:

1. Smoking.
2. Dyslipidemia.
3. DM.
4. Age greater than 60 years.
5. Sex (men and postmenopausal women).
6. Family history of cardiovascular disease for women younger than 65 or men younger than 55.

Target organ damage associated with clinical cardiovascular diseases includes:

1. Heart diseases
 - a. Left ventricular hypertrophy
 - b. Angina or prior myocardial infarction
 - c. Prior coronary revascularization
 - d. Heart failure.
2. Stroke or transient ischemic attack.
3. Nephropathy.
4. Peripheral arterial disease.
5. Retinopathy.

Table 5. Risk Stratification and Treatment¹⁰

	Risk Group A	Risk Group B	Risk Group C
	1. No risk factors 2. No TOD/CCD ¹¹	1. At least 1 risk factor not including DM 2. No TOD/CCD	1. TOD/CCD and/or DM 2. With or without other risk factors
BP stages SBP/DBP in mmHg			
High normal 130-139/85-89	Lifestyle modification	Lifestyle modification	Drug therapy ¹²
Stage 1 140-159/90-99	Lifestyle modification— Up to 12 months	Lifestyle modification— Up to 6 months ¹³	Drug therapy
Stages 2 and 3 ¹⁴ Greater than 160/ Greater than /100	Drug therapy	Drug therapy	Drug therapy

An example of risk stratification: A patient with BP of 142/94 mm Hg and left ventricular hypertrophy. Hypertension should be classified Stage 1, risk group C, with a target organ disease (left ventricular hypertrophy). Lifestyle modification should be adjunctive therapy for all patients in addition to the recommended pharmacotherapy.

K. Prescribe Diet and Lifestyle Counseling

OBJECTIVE

To provide guidance on beneficial dietary and lifestyle changes to help treat HTN and assist in reducing risk factors for cardiovascular disease.

ANNOTATION

Clinicians should begin by prescribing lifestyle modifications in all patients with HTN. Certain lifestyle modifications have been shown to decrease blood pressure in randomized clinical trials; other lifestyle modifications are also important in decreasing cardiovascular risk. These non-pharmacologic measures can be sufficient to control BP or to decrease the amount of required medication.^{15, 16, 17}

¹⁰ Modified from JNC-VI, 1997.

¹¹ TOD/CCD indicates target organ disease/clinical cardiovascular disease (See Table 4, JNC-VI, 1997).

¹² For those with heart failure, renal insufficiency, or diabetes.

¹³ For patients with multiple risk factors, clinicians should consider initial pharmacotherapy plus lifestyle modification.

¹⁴ Stage 2—Aggressive lifestyle modification for no more than 6 months may be an option if the patient has no cardiovascular risk factors and is highly motivated to alter lifestyle.

¹⁵ World Hypertension League, 1991. SR=I LE=C

¹⁶ The Multiple Risk Factor Intervention Group, 1990. SR=I LE=A

¹⁷ Hypertension Detection and Follow-up Program Cooperative Group, 1982.

Patients with HTN should receive counseling on the following lifestyle modifications:

1. WEIGHT REDUCTION

Overweight patients should reduce their weight to within 10 percent of their ideal body weight. However, reduction even of 5 to 10 pounds can be helpful in controlling HTN.^{18, 19, 20, 21, 22, 23}

2. ALCOHOL INTAKE

Alcohol intake should be limited to no more than one ounce (24 ounces of beer; or 10 ounces of wine; or 2 ounces of 100-proof whiskey) per day for men or 0.5 ounces of alcohol per day for women and for lighter weight men.^{24, 25, 26, 27}

3. SODIUM INTAKE

Sodium intake in the patient with HTN should be limited to no more than 100 mmol/day (2.4 g of sodium or 6 g of sodium chloride).^{28, 29, 30}

4. EXERCISE

The target for aerobic exercise should be 30 to 45 minutes per session, three to five times per week if possible.^{31, 32, 33}

5. DIET

An adequate dietary intake of potassium, calcium, and magnesium can be obtained from fresh fruits and vegetables. Other dietary advice should include a heart-healthy diet such as the DASH Diet. This is one means of satisfying the dietary steps above. See the DASH Diet table below.^{34, 35, 36}

6. TOBACCO USE CESSATION

¹⁸ Langford et al., 1991. SR=I LE=A

¹⁹ Schotte and Stunkard, 1990. SR=I LE=B

²⁰ Hypertension Prevention Trial Research Group, 1990. SR=I LE=A

²¹ World Hypertension League, 1991. SR=I LE=C

²² Hypertension Prevention Trial Research Group, 1990. SR=I LE=A

²³ Klatsky et al., 1977. SR=I LE=B

²⁴ Puddey et al., 1987. SR=I LE=B

²⁵ National High Blood Pressure Program Working Group, 1993. SR=I LE=C

²⁶ Law et al., 1991. SR=I LE=A

²⁷ JNC-VI, 1997. SR=I LE=C

²⁸ Trials of Hypertension Prevention, Collaboration Research Group, 1992. SR=I LE=A

²⁹ Blair et al., 1989. SR=I LE=B

³⁰ Morris et al., 1980. SR=I LE=B

³¹ Working Group on Management of Patients with Hypertension and High Blood Cholesterol, 1991. SR=I LE=C

³² Shepherd et al., 1995. SR=I LE=A

³³ Trials of Hypertension Prevention, 1992. SR=I LE=A

³⁴ Stamler et al., 1997. SR=I LE=B

³⁵ Cappuccio et al., 1995. SR=I LE=B

³⁶ Appel et al., 1997. SR=I LE=C

Counsel to stop tobacco use and offer smoking cessation classes or other aids to quit. (See VA/DoD Guideline on Tobacco Use Cessation).

7. HYPERLIPIDEMIA

Counsel to reduce intake of dietary saturated fats and cholesterol. A diet rich in fresh fruits and vegetables as well as low in dietary saturated fats and cholesterol is also beneficial in lowering blood pressure.^{37, 38, 39}

Table 6. The DASH Diet⁴⁰

Food Group	Daily Servings	Serving Sizes	Examples and Notes	Significance
Grains and grain products	7 – 8	1 slice bread ½ C. dry cereal ½ C. cooked rice, pasta or cereal	Whole wheat bread English muffin Pita bread Bagel, cereal, grits	Major sources of energy and fiber
Vegetables	4 – 5	1 C. raw, leafy vegetables ½ C. cooked vege 6 oz. vege juice	Tomatoes, potato Carrots, peas Squash, broccoli Turnip greens Spinach, beans Sweet potatoes	Important sources of potassium, magnesium, and fiber
Fruits	4 – 5	6 oz fruit juice 1 medium fruit ¼ C. dried fruit ½ C. fresh, frozen, or canned fruit	Apricots, bananas, dates, grapes, oranges, orange juice, grapefruit, mangoes, melons, pineapples, prunes, raisins, etc.	Major sources of calcium and protein
Low- or nonfat dairy foods	2 – 3	8 oz milk 1 C. yogurt 1.5 oz cheese	Skim or 1% milk, nonfat or low-fat yogurt, part-skim mozzarella	Major sources of calcium and protein
Meats, poultry, and fish	Less than 2	3 oz cooked meats, poultry, fish	Select only lean meats; trim visible fat; broil, roast, or boil, instead of frying. Remove skin from poultry	Rich sources of protein and magnesium
Nuts, seeds, legumes	4 – 5/week	1.5 oz or 1/3 C nuts ½ C. cooked legumes	Almonds, filberts, mixed nuts, peanuts, kidney beans	Rich sources of energy, magnesium, potassium, fiber

³⁷ Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 1993. SR=I LE=C

³⁸ Stamler et al., 1997. SR=I LE=B

³⁹ Appel et al., 1997. SR=I LE=A

⁴⁰ JNC-VI, p. 2421, from the Dietary Approaches to Stop Hypertension (DASH) clinical study.

DASH's final results appear in the *New England Journal of Medicine*.⁴¹ The results show that the DASH "combination diet" lowered blood pressure and, therefore, may help prevent and control high blood pressure. The "combination diet" is rich in fruits, vegetables, and low-fat dairy foods and low in saturated and total fat. It also is low in cholesterol; high in dietary fiber, potassium, calcium, and magnesium; and moderately high in protein. The DASH eating plan shown above is based on 2,000 calories a day. Depending on energy needs, the number of daily servings in a food group may vary from those listed.

L. Initiate/Continue Drug Therapy

OBJECTIVE

To provide clinicians with recommendations for selecting drug therapy.

ANNOTATION

If not already done, clinicians should enlist patient participation in lifestyle modification. See annotation K. For uncomplicated HTN, diuretics and beta-blockers are the preferred medications. Comorbid conditions may be appropriate reasons to use other medication(s) when they can benefit both conditions.

Table 7. Special Populations, Comorbidities, and Preferred Agents^{42, 43}

Bold = compelling indication per outcome data (unless contraindicated)
 Italics = may have favorable effect on comorbid conditions

- | | |
|--|--|
| ACEI = angiotensin-converting enzyme inhibitor | DM = diabetes mellitus |
| BPH = benign prostatic hyperplasia | HDL = high-density lipoprotein cholesterol |
| CCB = calcium channel blocker | ISA = intrinsic sympathomimetic activity |
| CHF = chronic heart failure | LVD = left ventricular dysfunction |
| COPD = chronic obstructive pulmonary disease | MI = myocardial infarction |
| CRI = chronic renal insufficiency | TC = total cholesterol |
| DHP SR = long-acting dihydropyridine | TG = triglycerides |

	Preferred Agents	Alternate Agents	Other Agents	Comments
Uncomplicated	thiazide diuretic, β -blocker	ACEI, CCB	α -blocker clonidine reserpine	Short-acting nifedipine should not be used for the long-term management of HTN
African-American race	thiazide diuretic	CCB, β -blocker, ACEI	β -blocker clonidine, α -blocker	Differences in efficacy among patient populations are not as apparent when diuretics are added to ACEIs and β -blockers.

⁴¹ Appel et al., 1997. SR=I LE=A

⁴² Adapted from Medical Advisory Panel for the Pharmacy Benefits Management Strategic Health Group. The Pharmacologic Management of Hypertension, 1996 (Updated 1999).

⁴³ JNC-VI, 1997. LE=C

Asthma/COPD	thiazide diuretic	ACEI, CCB	clonidine, α -blocker	β -blockers are relatively contraindicated in patients with bronchospastic disease.
BPH-symptomatic	α -blocker	β -blocker, ACEI, CCB, thiazide diuretic (low dose)	clonidine	Diuretics may influence symptoms of polyuria and frequency.
CAD	β-blocker (Non ISA post-MI)	<i>verapamil, diltiazem</i>	DHP SR, ACEI, thiazide diuretic	Non-ISA β -blockers are the drugs of choice post-MI; ACEIs are also indicated post-MI.
LVD diastolic	β -blocker, diuretic	verapamil, diltiazem	ACEI, α -blocker	Diuretics are first-line agents if symptoms of volume overload exist.
LVD systolic	ACEI, diuretic	angiotensin II antagonists, hydralazine/nitrates	amlodipine, felodipine	ACEIs are preferred for their potential improvement in morbidity and mortality in this patient population; diuretics are first-line agents if symptoms of volume overload exist. angiotensin II antagonists may be used where an ACEI is not tolerated; other selected agents may be used in conjunction with an ACEI in stable CHF patients; β -blockers and CCBs should be used with caution.
CRI (Cr Cl < 25 ml/min or Scr > 2.5 mg/dL)	furosemide, ACEI	β -blocker, CCB, α -blocker, indapamide, metolazone	clonidine, minoxidil, hydralazine	Potassium (K ⁺)-sparing diuretics, K ⁺ supplements, and/or ACEI may cause increased K ⁺ ; use ACEI with caution in patients Scr > 3.0 mg/dL; metoprolol is the preferred β -blocker due to hepatic excretion.
Depression	thiazide diuretic	ACEI, CCB, α -blocker		Clonidine, reserpine, methyl dopa, β -blockers may exacerbate depression.
DM	ACEI* (types 1 and 2 DM with proteinuria)	<i>thiazide diuretic (low dose)</i> , CCB, β -blocker, α -blocker	angiotensin II antagonist	High-dose thiazide diuretics and β -blockers may worsen glucose control; β -blockers may mask hypoglycemia; use of DHP SR in patients with type 2 DM remains controversial.
Elderly (age > 65 years)	thiazide diuretic	β -blocker, CCB ACEI	α -blocker	Use caution with α -blockers in elderly due to risk of first-dose syncope or dizziness.
Gout	β -blocker	ACEI, CCB, thiazide diuretic (low dose)	α -blocker	Diuretic-induced hyperuricemia does not require treatment in the absence of gout or kidney stones.

Dyslipidemia	thiazide diuretic (low dose) β-blocker	ACEI, CCB, <i>α-blocker</i>		Thiazide diuretics may increase TC and increase TG; and non-ISA β-blockers may decrease HDL and increase TG, although these effects may be transient.
Isolated systolic HTN	thiazide diuretic	DHP SR, β-blocker, ACEI	α-blocker	The use of DHP SR as first-line therapy remains controversial, although studies are available to indicate benefit.
Left ventricular hypertrophy	ACEI, thiazide diuretic, β-blocker	CCB	α-blocker, clonidine	Direct-acting vasodilators do not reduce left ventricular hypertrophy.
Peripheral vascular disease	thiazide diuretic, ACEI	CCB, β-blocker	α-blocker	Non-selective β-blockers without ∇ blockade may worsen resting ischemia or severe claudication symptoms.
Pilots	thiazide diuretic, lisinopril			
Pregnancy (chronic HTN)	methyl dopa	labetalol	hydralazine (generally used for preeclampsia)	Except for ACEI and angiotensin II antagonists that are contraindicated during pregnancy, any antihypertensive drug may be continued if taken prior to pregnancy; β-blockers may cause growth retardation in 1 st trimester. Women with HTN of child-bearing age and women at risk for conception, not on contraceptives, should not use ACEI.

*Compelling indication in type 1 DM with proteinuria; preferred agent in types 1 and 2 DM with proteinuria

M. Drug Therapy is Preferred. Consider Aggressive Diet and Lifestyle Modification Alone in Selected Patients.

OBJECTIVE

To identify patients for whom drug therapy is preferred, but who may be suitable candidates for a trial of aggressive lifestyle modification without drug therapy.⁴⁴

ANNOTATION

Patients in this range of blood pressure have at least four times the relative risk for a cerebrovascular event and two to three times the relative risk for coronary heart disease.

Although JNC-VI recommends that these patients begin drug therapy upon diagnosis of hypertension,

⁴⁴ Hypertension Detection and Follow-Up Program Cooperative Group, 1982.

the recommendation is based on panel consensus rather than upon evidence from randomized clinical trials (RCTs). Some clinicians may wish to consider aggressive life style modification, without drug therapy, for selected patients at the lower end of this BP range who have no cardiovascular risk factors and who are highly motivated to reduce BP with diet and exercise. Otherwise, patients should begin drug therapy along with lifestyle modification, as described in annotation L.

If a trial of lifestyle modification alone is used as initial therapy, the trial should be relatively short, up to six months, with frequent monitoring. Drug therapy should be instituted if blood pressure goals are not attained. See also Table 5, Risk Stratification and Treatment.

N. Is Control Adequate?

OBJECTIVE

To decrease BP to less than 140/90.

ANNOTATION

The primary objective in hypertension treatment is to decrease blood pressure to less than or equal to 140/90. Results of the Hypertensive Optimal Therapy (HOT) trial suggested that BP of 135-140/85-90 may be an optimal level of control for most patients. For patients with diabetes mellitus, however, the HOT trial suggested that clinical outcome might be improved if the diastolic blood pressure is lowered to 80 to 85 mm Hg.⁴⁵ When renal disease is present and protein excretion is greater than or equal to 1 g/day, a target BP around 125/75 may slow the progression of renal disease.⁴⁶

O. Continue Current Treatment. Reinforce Lifestyle Modification. Follow up at Next Regular Visit

OBJECTIVE

To follow patients who attain the desired target BP.

ANNOTATION

Once an effective and well-tolerated regimen has been obtained, follow up can be scheduled at 3- to 6-month intervals. Periodic follow-up is important to the management of the hypertensive patient and should help to:

1. Assess the long-term response to therapy
2. Monitor the development of target organ damage
3. Reinforce lifestyle modification

P. Is BP Control Adequate and Therapy Tolerable?

OBJECTIVE

To assess adequacy of HTN control.⁴⁷

⁴⁵ Hansson, 1998. LE=A

⁴⁶ Lazarus et al., 1997. SR=II LE=B

⁴⁷ JNC-VI, 1997. SR=I LE=C

ANNOTATION

Patients should be seen within 1 or 2 months after the initiation of therapy to determine adequacy of HTN control, degree of patient adherence, and presence of adverse effects. Earlier follow-up may be necessary for patients:

1. Requiring blood tests
2. At increased risk for adverse outcomes from HTN
3. At risk for postural hypotension

Once the patient's BP is stabilized, follow-up at 3- to 6-month intervals (depending on patient status) is generally appropriate. Older persons, diabetics, and those at risk for postural hypotension (with orthostatic symptoms) may require BP measurement in the seated position and, to recognize postural hypotension, after standing quietly for 2 to 5 minutes.⁴⁸

Q. Adjust Therapy. Titrate Drug or Add Another Agent. Add Another Agent if Inadequate Response but Well Tolerated. Substitute Another Drug from Different Class if No Response or Side Effects. Reassess Adherence and Acute Life Stressors. Reinforce Lifestyle Modification.

OBJECTIVE

To modify drug therapy to help achieve BP control.

ANNOTATION

Agents from all of the five major classes of antihypertensive medications are shown to decrease blood pressure. Diuretics and beta-blockers have consistently been shown to decrease morbidity and mortality in the treatment of HTN and should be considered first-line therapy. Diuretics should be used in low to moderate doses. Alternatively, clinicians may consider alpha-blockers, ACEIs, and calcium channel blockers (CCBs) as well as other medications as therapy for selected pre-existing conditions. Clinicians should consider cost where therapeutic effect is equal, and to maximize compliance, should choose medications that keep regimens simple.^{49, 50}

If the blood pressure continues to be elevated, clinicians may consider choosing one of the strategies that have proven effective in the treatment of HTN:

1. Increase the dose of the original medication

Approximately 50 percent of patients can be controlled with a single agent. Single-agent therapy is simpler and decreases the risk of interaction with other drugs. Note that cost may not be an issue: in many facilities within the VA and DoD, the higher doses are the same price as the lower doses.

2. Discontinue the first medication and start a new agent

Discontinuing the original medication and starting a new agent has also been studied in clinical trials, again with approximately 50 percent of patients controlled. This regimen offers similar advantages to the first, and may avoid side effects seen with higher-dose titration.

⁴⁸ JNC-VI, 1997. SR=I LE=C

⁴⁹ Klein, 1988.

⁵⁰ German, 1988.

If side effects occur, clinicians should consider discontinuing the agent and switching to a medication from a different class. Since side effects tend to be similar across classes, a medication from a different class is usually preferred.

3. Add another agent

Adding a second medication to the regimen, sometimes called step therapy, is also a well-studied procedure and was recommended by the Joint National Committee. The addition of a second agent has theoretical advantages in that the antihypertensive effects of different agents are often additive, resulting in better control of blood pressure. Disadvantages include a potential for drug-drug interactions; additive therapy may require a complicated regimen with which the patient must comply. Furthermore, adding another drug can increase cost. If a diuretic is not chosen as the initial drug, it is usually indicated as a second-step agent because its addition frequently enhances the effects of the initial agents. Monitor as previously stated.⁵¹

R. Continue Current Treatment. Follow Up at Next Regular Visit

OBJECTIVE

To follow up on patients who attain the desired target BP.

ANNOTATION

Once an effective and well-tolerated regimen has been obtained, follow-up can be scheduled at 3- to 6-month intervals. Periodic follow-up is important to the management of the hypertensive patient and should help to:

1. Assess the long-term response to therapy
2. Reassess for side effects that might complicate therapy or limit efficacy
3. Monitor the development of target organ damage
4. Reinforce lifestyle modification

S. Reassess Adherence and Acute Life Stressors. Reinforce Lifestyle Modification. Consider Referral or Consult

OBJECTIVE

To identify causes of inadequate response to therapy following dose or stepwise titration.

ANNOTATION

Poor adherence to antihypertensive therapy remains a major therapeutic challenge. Aside from simple inadequacy of the chosen agent, the clinician should consider alternate explanations for inadequate response to drug therapy. These include medical or psychosocial conditions that undermine blood pressure control.⁵² Poor patient response to the initial drug management strategy should always lead the primary care provider to explore important factors that may explain failure to achieve target blood pressure.

⁵¹ JNC-VI, 1997. SR=I LE=C

⁵² JNC-VI, 1997. See Table 13.

Table 8. Causes of Inadequate Response to Therapy

Non-adherence to therapy	See Table 9, below.
Pseudo-resistance	<ul style="list-style-type: none"> “White Coat” hypertension or office elevation Pseudohypertension in older patients Use of regular cuff on very obese arm
Volume overload	<ul style="list-style-type: none"> Excess salt intake Progressive renal damage (nephrosclerosis) Fluid retention from reduction of blood pressure Inadequate diuretic therapy
Drug-related causes	<ul style="list-style-type: none"> Nonsteroidal anti-inflammatory drugs Dose(s) too low Wrong type of diuretic Inappropriate combinations Rapid inactivation (e.g., hydralazine) Drug actions and interactions Sympathomimetics Nasal decongestants Appetite suppressants Cocaine and other illicit drugs Caffeine Oral contraceptives Adrenal steroids Licorice (as may be found in chewing tobacco) Cyclosporine, tacrolimus Erythropoietin Antidepressants
Associated conditions	<ul style="list-style-type: none"> Smoking Obesity Sleep apnea Hyperinsulinemia Ethanol intake more than 3 oz. (90 ml) per day Anxiety-induced hyperventilation or panic attacks Chronic pain Intense vasoconstriction (arteritis) Organic brain syndrome (e.g., memory deficit)
Identifiable secondary causes of HTN	See Table 4, Recommended Testing for Patients Suspected of Having Secondary Hypertension

The primary care provider should employ measures that assist in improving patient adherence to treatment.⁵³ Many of these measures are designed to engage the patient in his or her wellness. Table 9 lists several suggestions to improve the patient's adherence to therapy.

Table 9. General Guidelines to Improve Patient Adherence to Antihypertensive Therapy⁵⁴

1. Be aware of signs of patient nonadherence to therapy.
2. Establish the goal of therapy early: to reduce BP to non-hypertensive levels with minimal or no adverse effects.
3. Educate patients about the disease, and involve them and their families in its treatment. Have them measure blood pressure at home.
4. Maintain contact with patients; consider telecommunication.
5. Encourage lifestyle modifications.
6. Integrate pill taking into routine activities of daily living.
7. Prescribe medications according to pharmacologic principles, favoring long-acting formulations.
8. Be willing to stop unsuccessful therapy and try a different approach.
9. Anticipate adverse effects and adjust therapy to prevent, minimize, or ameliorate side effects.

⁵³ JNC-VI, 1997. SR=I LE=C

⁵⁴ Adapted from JNC-VI 1997.

CLINICAL PRACTICE GUIDELINES FOR DIAGNOSIS AND MANAGEMENT
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