VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF HYPERTENSION

Guideline Summary

Update 2004 *Revision July 2005*

RECOMMENDATIONS WITH THE HIGHEST EVIDENCE: The highest evidence for recommendations is A, defined as "a strong recommendation based on randomized controlled trials that the intervention is always indicated and acceptable."

The following practices are strongly recommended based on evidence reviews:

1. Blood pressure should be measured with a technique using a properly calibrated and validated instrument **[R=A]**
2. Blood pressure measurement can identify adults at increased risk for cardiovascular (CV) disease due to high blood pressure **[R=A]**
3. The treatment of high blood pressure substantially decreases the incidence of cardiovascular disease and causes few major harms **[R=A]**

Drug Therapy:

4. **Thiazide-type diuretics** are recommended as first line therapy for drug treatment of hypertension either as monotherapy or in combination with other agents. **[R=A]**
5. The following may be used as alternative or supplementary therapy:
   a. Angiotensin-Converting Enzyme Inhibitors (ACEIs) **[R=A]**
   b. Angiotensin II Receptor Blockers (ARBs) **[R=A]**
   c. Beta-blockers (BBs) **[R=A]**
   d. Long-acting calcium channel blockers (CCBs)**[R=A]**

Other Supplemental Agents:

6. **Reserpine** can be used as supplemental therapy when other agents are not providing clinical adequate response **[R=A]**
7. **Adjust Therapy**
   a. If a thiazide-type diuretic is not chosen as the initial drug, it should be used as the second agent, unless contraindicated or not tolerated, because it frequently enhances the effects of the initial agent and has the best cardiovascular outcome data. **[R=A]**
   b. When using combination therapy, select those agents that have been shown to reduce morbidity and mortality. **[R=A]**

VA access to full guideline: http://www.oqp.med.va.gov/cpg/cpg.htm
DoD access to full guideline: http://www.qmo.amedd.army.mil/pguide.htm

September 2004

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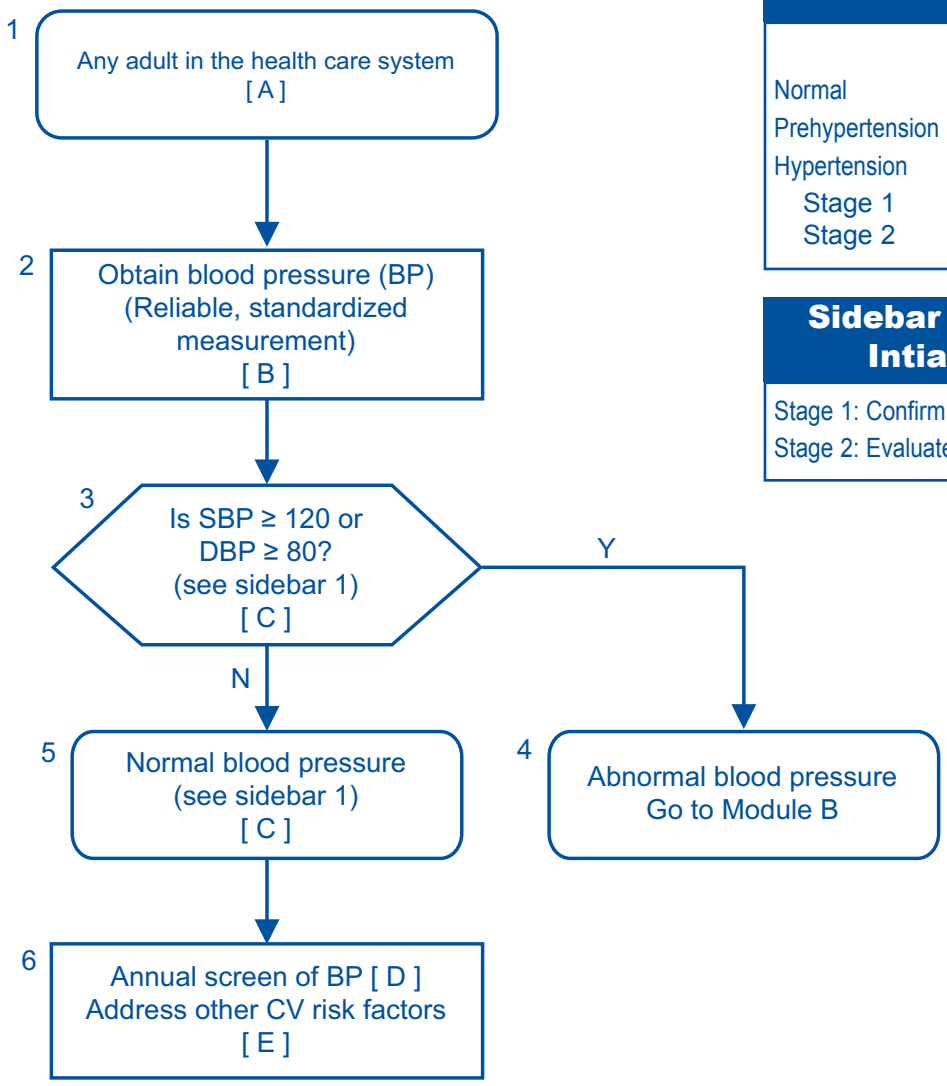
Key Elements

1. Screen blood pressure (BP) in adults annually since BP rises with increasing age
2. Encourage patients with prehypertension to engage in lifestyle changes to reduce risk of proceeding to hypertension
3. Explain to patients that blood pressure control reduces cardiovascular risks over a lifetime
4. Once hypertension is diagnosed, take aggressive action to reduce blood pressure
5. Include lifestyle modifications for all patients, as appropriate
6. Use thiazide-type diuretics, alone or in combination with other agents, as first line therapy
7. Choose other agents based on evidence for reduction of mortality and morbidity. These agents include (in alphabetical order): angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), beta-blockers, and long-acting calcium channel blockers
8. Strongly consider starting therapy with a combination of 2 drugs for patients with Stage 2 hypertension
9. Target blood pressure goals appropriately for each patient and titrate therapy to achieve that goal through:
   a. Informing patients about their blood pressure (BP) goal
   b. Following-up closely until goal achieved
   c. Adjusting medication as necessary at each visit
   d. Keeping the medication regimen as simple as possible
   e. Educating and involving patients in their care plan
   f. Using ancillary staff and available programs to support and help in reaching target goal

Module A: Screening for Elevated Blood Pressure

A



Sidebar 1: Classification

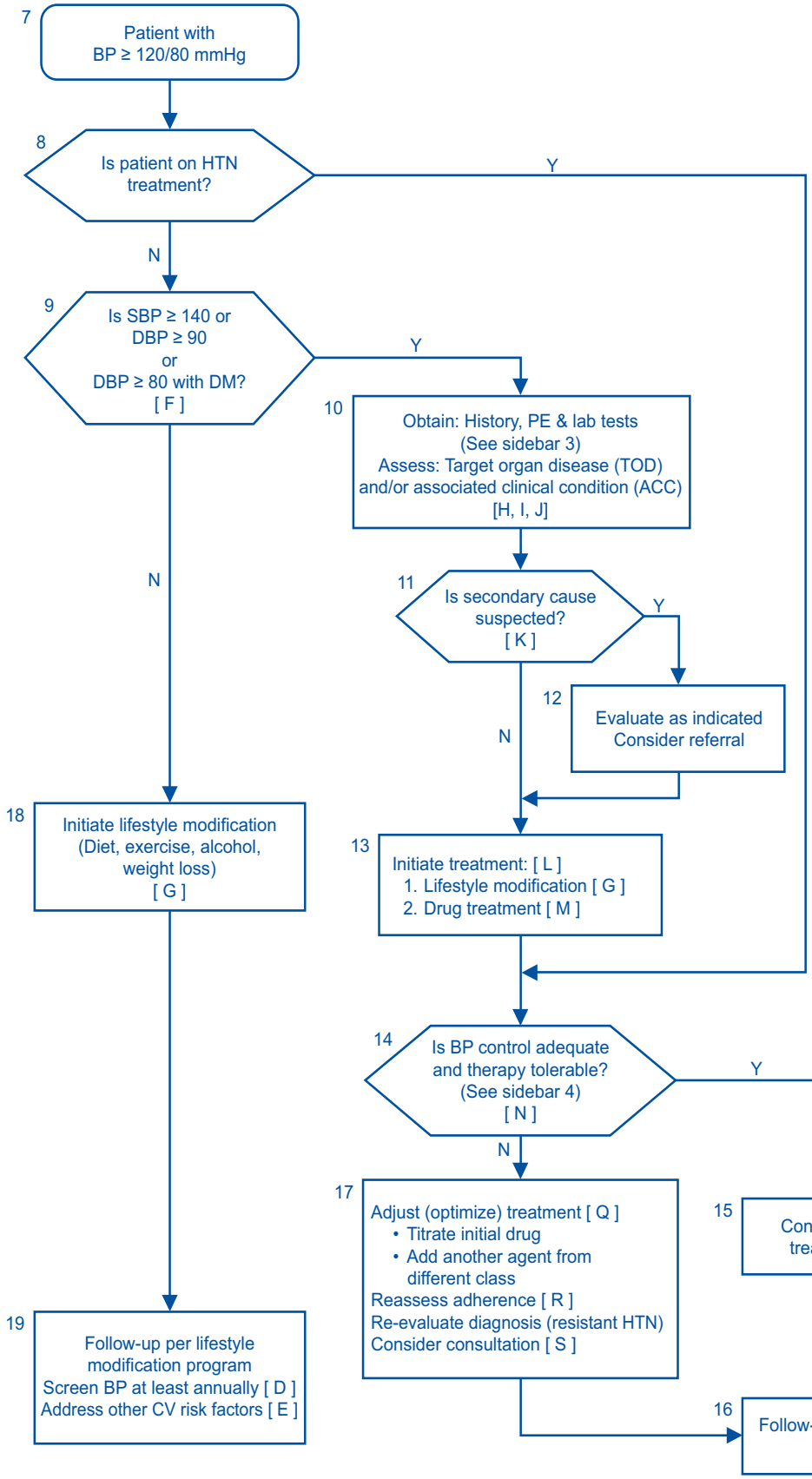
	SBP		DBP
Normal	<120	and	<80
Prehypertension	120-139		80-89
Hypertension			
Stage 1	140-159	or	90-99
Stage 2	≥160	or	≥100

Sidebar 2: Confirmation of Intial Measurement

Stage 1: Confirm within 2 months
Stage 2: Evaluate or refer within 1 month

Module B: Management of Elevated Blood Pressure

B



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Sidebar 3: Recommended Lab Tests

- Urinalysis (UA)
- Hematocrit (Optional)
- Blood chemistry (K, na, BUN, Cr, FBS)
- Fasting lipid profile
- 12-lead ECG
- Blood calcium (Optional)

Sidebar 4: Target Values for BP

Condition	Target
Uncomplicated HTN	<140[B]/90[A]
Diabetes	<140/80[A]
Renal disease	<140/90[A]

A = Based on RCTs
B = Based on epidemiological data

Abbreviations

BUN: Blood urea nitrogen
Cr: Creatinine
DBP: Diastolic blood pressure
FBS: Fasting blood glucose
K: Potassium
na: Sodium
PE: Physical examination
RCTs: Randomized control trials
SBP: Systolic blood pressure

ANNOTATIONS

A. Any Adult in the Health Care System

DEFINITION

In this document, an adult is defined as anyone 17 years of age or older.

This guideline is directed at screening for high blood pressure in adults, and management of chronic hypertension. It is not directed to the treatment of pregnant women who should be managed in consultation with appropriate specialists. This guideline is also not intended for patients presenting with acute illnesses and/or other urgent conditions involving high blood pressure as these patients should be managed according to their relevant diagnoses.

RECOMMENDATIONS

– Screen adults for elevated blood pressure (BP)

B. Obtain Blood Pressure

RECOMMENDATION

1. Blood pressure should be measured with a technique using a properly calibrated and validated instrument:
   - Patient should be seated quietly for 5 minutes with back supported, feet on the floor, and arm bared, unrestricted by clothing, and supported at heart level. Measurement of BP in the standing position may be indicated for patients at risk for postural hypotension or at the discretion of the clinician.
   - Smoking, exercise, or caffeine ingestion should not have occurred within 30 minutes prior to the BP measurement.
   - The appropriate blood pressure cuff size should be chosen for the patient. The cuff should be wrapped snugly around the arm with the bladder centered over the brachial artery. The bladder should encircle at least 80% of the arm.

   For Auscultatory Measurements Only:
   - Palpated radial pulse obliteration pressure should be used to estimate the systolic BP (SBP). The cuff should then be inflated 20-30 mm Hg above this level for the auscultatory determinations.
   - Position the stethoscope over the brachial artery and rapidly inflate the cuff. Deflate the cuff at a rate of 2 to 3 mm Hg per second, listening for Phase 1 and Phase 5 Korotkoff sounds. The first appearance of sound (Phase 1) is used to record the SBP. Phase 5, at the disappearance of sound, is the diastolic BP (DBP) in adults. Listen 10 to 20 mm Hg below Phase 5 for any further sound then deflate the cuff completely.
   - The BP should be recorded in even numbers with the patient's position, arm used, and cuff size documented.
   - BP readings should be repeated in the same arm and averaged, if different. Two minutes should elapse before repeating the BP measurement. If the readings differ by more than 5 mm Hg, additional measurements should be obtained.
2. Measurements can be taken with a mercury sphygmomanometer, but a recently calibrated aneroid manometer or a validated electronic device is an acceptable alternative.

C. Is SBP ≥ 120 or DBP ≥ 80 mm Hg?

RECOMMENDATION

1. Screen adults for elevated blood pressure, defined as a systolic blood pressure 120 mm Hg and above or a diastolic blood pressure 80 mm Hg and above.

D. Annually Screen For Blood Pressure

RECOMMENDATION

1. Blood pressure screening should occur periodically.
2. Blood pressure screening is recommended annually for adults 50 years of age and older and/or for those who have prehypertension and/or other cardiovascular risk factors.
3. Blood pressure screening is recommended at indeterminate intervals, preferably annually. This may occur at the time of routine preventive care or routine health assessments.

E. Address other cardiovascular risk factors

RECOMMENDATION

1. Screening lipid profile should be done per the VA/DoD Guideline [VA/DoD Guideline for Management of Dyslipidemia]

2. Screening for diabetes mellitus (DM) should be done per the VA/DoD Guideline [VA/DoD Guideline for Management of Diabetes Mellitus]
3. Reduction/cessation of the use of tobacco and cigarettes should be addressed per the VA/DoD Guideline [VA/DoD Guideline for Management of Tobacco Use]
4. A heart-healthy lifestyle including optimum weight maintenance (and/or weight loss, when needed), diet rich in fruits, vegetables and low fat dairy products and an exercise program emphasizing daily or near daily aerobic activity, should be recommended.
5. Aspirin should be recommended to patients who have hypertension and diabetes mellitus (see the VA/DoD Guideline for Diabetes) or IHD (see the VA/DoD Guideline for IHD) and should be recommended to patients who already have vascular disease (e.g., cerebrovascular disease or cardiovascular disease).

F. SBP ≥ 140 or DBP ≥ 90 or DBP ≥ 80 with DM?

RECOMMENDATION

1. The diagnosis of hypertension should be determined by BP readings on two separate patient visits. A minimum of two BP measurements should be performed during a patient visit:
   - Patients with SBP ≥ 140 or DBP ≥ 90 (Stage 1 hypertension) or with DBP ≥ 80 mm Hg and concomitant diabetes mellitus or chronic kidney disease should have their blood pressure confirmed generally within 1 to 2 months.
   - Patients with SBP ≥ 160 or DBP ≥ 100 (Stage 2 hypertension) should be appropriately evaluated by a healthcare provider, typically within 1 month – or sooner if the clinical situation warrants.

Classification

Defining abnormally high blood pressure is somewhat arbitrary because the relationship between systemic arterial pressure and morbidity appears to be linear from around 120/80 mm Hg, and because there is insufficient evidence to determine which threshold goal(s) are optimal for reducing risk. Nonetheless, a classification system is essential for making decisions about aggressiveness of treatment or therapeutic interventions. Thus, based on recommendations of JNC 7, the classification of blood pressure (expressed in mm Hg) for adults aged 17 years or older is as follows:

Table 2. Follow-Up Based an Initial Classification of Blood Pressure for Adults

	SBP* mm Hg	DBP* mm Hg	Follow-up
Normal	< 120	< 80	Recheck in 1 year
Prehypertension	120-139	80-89	Recheck in 1 year **
Stage 1 Hypertension	140-159	90-99	Confirm within 1-2 months
Stage 2 Hypertension	≥160	≥100	Evaluate or refer to source of care immediately or within 1 month, or sooner, depending on clinical situation

* *If systolic and diastolic categories are different, follow recommendations for the higher measurement. (e.g. 160/86 mm Hg is considered Stage 2 hypertension and thus 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 comorbidities, or target organ disease.*

G. Initiate Lifestyle Modification (LSM)

OBJECTIVE

Provide dietary and lifestyle changes to help treat HTN and assist in reducing risk factors for cardiovascular disease.

RECOMMENDATIONS

1. Lifestyle modifications aimed at controlling hypertension should be recommended in all cases. These methods can be used by themselves or in combination with drugs. [B]
2. Individual LSM are effective however, addressing multiple modifications may have a greater effect on reducing blood pressure. [B]
3. Successful implementation will require multiple visits, and close follow-up. [B]
4. Education may take place in either individual or group settings involving allied health professionals. [B]
5. Clinician empathy increases patient trust, motivation, and adherence to therapy.
6. Physicians should consider their patients' cultural beliefs and individual attitudes in formulating therapy.

DISCUSSION

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

Table 3. Impact of Lifestyle Therapies on BP in Hypertensive Adults*

Intervention	Lifestyle Modification or Change	Systolic BP Reduction (range)
Daily sodium intake	Maximum of 100 meq/L day (2.4 g sodium or 6 gms sodium chloride)	2-8 mm Hg
Weight loss	Reduce to and/or maintain normal body weight (e.g., Body Mass Index, 18.5-24.9)	5-20 mm Hg/10-kg wt loss
Alcohol consumption	Limit to no more than 2 drinks per day for men, and no more than 1 drink per day in women and light weight persons	2-4 mm Hg
Exercise	Aerobic exercise for at least 30 minutes, most days of week	4-9 mm Hg
DASH Diet	Dietary Approaches to Stop Hypertension (DASH) diet rich in fruits, vegetables, and low-fat diary products, with overall reduced saturated and total fat content	8-14 mm Hg

** Modified from JNC 7*

H. Perform History

OBJECTIVE

Elicit historical features that may influence clinical decision-making.

RECOMMENDATIONS

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, DM, dyslipidemia, and gout.
3. Survey for baseline symptoms of sexual dysfunction, depression, cough, and angioedema.
4. Family history of hypertension, premature CHD, cerebrovascular accident (CVA), DM, dyslipidemia, or renal disease.
5. Other symptoms suggesting other causes of elevated BP.
6. Results and adverse effects of any previous antihypertensive therapy.

7. History of recent change in weight, physical activity, tobacco use.
8. Dietary assessment, including intake of sodium, saturated fat, and caffeine.
9. 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.
10. History of alcohol and illicit drug use (especially cocaine and other stimulants).
11. Psychosocial and environmental factors (e.g., family situation, employment status and working conditions, level of comprehension) that may influence HTN control.

The following major risk factors are the components of cardiovascular risk in patients with hypertension: (JNC 7)

1. Tobacco use
2. Dyslipidemia
3. Diabetes Mellitus
4. Obesity [body mass index (BMI) $\geq$ 30]
5. Physical inactivity
6. Microalbuminuria or estimated glomerular filtration rate (GFR) < 60 mL/min
7. Age (> 55 years for men, > 65 years for women)
8. Family history of cardiovascular disease for women younger than 65 or men younger than 55

Table 4: Categories of associated clinical conditions and target organ disease, as 'markers' for those at high or very high absolute risk of a primary or secondary cardiovascular event.

Associated Clinical Conditions (ACC)	Target Organ Disease (TOD)
Diabetes	• Left ventricular hypertrophy (LVH) (electrocardiogram, echocardiogram)
Cerebrovascular disease	• Microalbuminuria ≥30 mcg/min and/or proteinuria ≥200 mg/day and/or glomerular filtration rate (GFR) < 60 mls/min
• Ischemic stroke • Cerebral hemorrhage • Transient ischemic attack	• Ultrasound or radiological evidence of atherosclerotic plaque (aorta, carotid, coronary, femoral and iliac arteries)
Heart disease	• Hypertensive retinopathy (Grade II or more)
• Myocardial infarction • Angina • Coronary revascularization • Chronic heart failure	
Chronic kidney disease	
• Diabetic nephropathy • Glomerulonephritis • Hypertensive renovascular disease	
Aortic disease	
• Dissecting aneurysm • Fusiform aortic aneurysm	
Peripheral arterial disease	

Modified from: Guidelines Subcommittee of the WHO-ISH: 1999 WHO-ISH guidelines for the management of hypertension. J Hypertens 1999, 17:151-183.

I. Perform Physical Examination (PE)

OBJECTIVE

Elicit physical signs that may influence clinical decision-making.

RECOMMENDATION

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.

If the patient is at risk for postural hypotension 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 and pulses
   b. Jugular venous distention
   c. Thyromegaly
3. Heart
   a. Normal rate and regular rhythm
   b. Apical impulse
   c. Precordial heave
   d. Clicks, murmurs, third or fourth heart sounds
4. Lungs
   a. Crackles
   b. Wheezes or rhonchi
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
   b. Signs or symptoms of dementia

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. Chronic kidney disease (nephropathy)
4. Peripheral arterial disease
5. Retinopathy

J. Perform Laboratory and Other Diagnostic Procedures

OBJECTIVE

Determine the baseline data on patient's health status, the existence of secondary causes of HTN and the risk factors contributing to the disease process.

RECOMMENDATION

Routine laboratory tests for the investigation of all patients with hypertension

1. Urinalysis (UA)
2. Blood chemistry (potassium, sodium, blood urea nitrogen [BUN], creatinine, fasting glucose)
3. Fasting lipid profile (total cholesterol [TC], high density lipoproteins-cholesterol [HDL-C], low density lipoproteins-cholesterol [LDL-C], triglycerides [TG])
4. 12-lead electrocardiography

Optional laboratory tests*

1. Hematocrit, Complete Blood cell Count
2. GFR estimated by MDRD (Modification of Diet in Renal Disease Study Group) equation)**
3. Blood calcium
4. Urinary protein excretion (24-hour urine collection or spot urine for protein/creatinine ratio)
5. Uric acid
6. Glycosylated hemoglobin (HbA1c)

7. Thyroid-stimulating hormone (thyrotropin) (TSH)
8. Transthoracic echocardiography to determine the presence of left ventricular hypertrophy

* May have clinical utility in certain instances

**Calculators and modeling aids. Available at: http://www.nkdep.nih.gov/healthprofessionals/tools/gfr_adults.htm.

K. Is a Secondary Cause Suspected?

OBJECTIVE

Detect underlying disease(s) responsible for secondary HTN using additional laboratory tests.

RECOMMENDATION

An early discussion or consultation with an appropriate specialist is encouraged when a patient is suspected of having secondary hypertension.

DISCUSSION

Although fewer than five percent of patients have secondary hypertension, clinicians should constantly be alert to secondary causes of HTN. Referral to appropriate experts as needed may lead to the most accurate and cost-effective workup if an underlying cause of HTN is diagnosed.

Table 5: Recommended Testing for Patients Suspected of Having Secondary Hypertension

Disease	Features	Recommended Test/Referral
Cushing's syndrome and other glucocorticoid excess states including chronic steroid therapy	Amenorrhea Increased dorsal fat Diabetes mellitus Edema Hirsutism Moon facies Purple striae Truncal obesity	History 24- hour urine for free cortisol Dexamethasone suppression test
Hyperparathyroidism	Hypercalcemia Polyuria/polydipsia Renal stones	Serum calcium and parathyroid hormone (PTH) level
Hyperthyroidism	Anxiety Brisk reflexes Hyperdefecation Heat intolerance Tachycardia Tremor Weight loss Wide pulse pressure	Thyroid Stimulating Hormone (TSH) Free T4
Pheochromocytoma	Labile BP Orthostatic hypotension Paroxysms (headaches, palpitations, sweating, pallor) Tachycardia	Plasma metanephrines or 24-hour urine for metanephrines and/or catecholamines Consider referral to specialist
Primary hyperaldosteronism	K+ ≤ 3.5 mEq/l in patients not on diuretic therapy; or K+ ≤ 3 mEq/l in patients on diuretic therapy Muscle cramps Polyuria Weakness	Plasma aldosterone and plasma renin activity 24 hour urinary aldosterone level on a high sodium diet
Kidney disease	Abnormal urine sediment Elevated serum creatinine Hematuria on two occasions or structural renal abnormality (e.g., abdominal or flank masses) Proteinuria	Urinalysis; estimation of urinary protein excretion and creatinine clearance by using a single random urine test; renal ultrasound may also be considered (See annotation H.) Consider referral to nephrology

Table 5: Recommended Testing for Patients Suspected of Having Secondary Hypertension *(continued)*

Disease	Features	Recommended Test/Referral
Renovascular disease	Abdominal bruits over the renal arteries Abrupt onset of severe HTN Diastolic BP ≥ 115 mm Hg Initial onset age ≥ 50 years old Worsening BP control when previously stable Evidence of atherosclerotic vascular disease	There are a variety of screening tests for renovascular HTN, depending on equipment and expertise in institutions. Magnetic Resonance Angiography renal artery Doppler, and post-captopril renograms are used. However, there is no single best test for renovascular HTN, and consultation with experts in your institution is recommended. Intravenous pyelogram is relatively contraindicated in diabetes and no longer recommended as screening test for renovascular disease.
Sleep apnea	Daytime somnolence Fatigue Obesity Snoring or observed apneic episodes	Referral for sleep study
Aortic Coarctation	Weak or delayed femoral pulses	Computerized tomography angiography
Drug or substance Induced	Non-steriodal anti-inflammatory drugs (NSAIDs), including cyclooxygenase-2 (COX-2) Inhibitors Sympathomimetics (e.g., decongestants, anorectics) Oral contraceptives Adrenal steroids Erythropoietin Cyclosporine, tacrolimus Cocaine, amphetamines Excessive alcohol use Licorice Selected dietary supplements (e.g., ma huang, ephedra, bitter orange)	History Urine toxicology as indicated.

L. Initiate Treatment for Hypertension

OBJECTIVE

Select the most effective therapy to control blood pressure.

RECOMMENDATIONS

PHARMACOTHERAPY (see also annotation M)

1. According to the baseline blood pressure and the presence or absence of complications, it appears reasonable to initiate therapy either with a starting dose of a single agent or with starting-doses of two agents. (See Appendix B Recommended Dosage for Selected Hypertension Drug Therapy).
2. To reach target blood pressure, it is likely that a large proportion of patients will require combination therapy with more than one agent.
3. Drug therapy should be initiated in conjunction with LSM.
4. Initial combination therapy of two drugs - particularly low-dose combinations is more effective in achieving target level BP. [B]
5. Initial combination therapy of two drugs maybe preferable for patients in STAGE 2 HTN.

NON-PHARMACOLOGIC THERAPY (see also annotation G)

1. Prescribe lifestyle modifications in all patients with prehypertension or 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.
2. If patients with stage 1 HTN do not adhere to LSM or are adherent to LSM and show no improvement in blood pressure level for 3-6 months – INITIATE DRUG THERAPY

3. In addition to lifestyle modifications, drug therapy should be considered in patients with prehypertension and DM.
4. Additional compelling indications should be considered in determining non-pharmacologic, as well as pharmacologic treatment.

Table 6. Management of Elevated Blood Pressure for Adults

BP Classification	SBP	DBP	LSM	Initial Drug Therapy
Prehypertension	120-139	80-89	Yes	Consider for those with DM when BP 140/80 or greater
Stage 1 Hypertension	140-159	90-99	Yes	Thiazide-type diuretic unless contraindicated or not tolerated (Consider ACEI, ARBs, BB, CCB). For compelling indication see Table 8.
Stage 2 Hypertension	≥ 160	≥ 100	Yes	Drug therapy with 2 drugs for most patients. This should include a thiazide-type diuretic unless contraindicated or not tolerated (Consider ACEIs, ARBs, BB, CCB). For compelling indication see Table 8.

M. Drug Treatment

OBJECTIVE

Determine the most appropriate drug therapy regimen based on available evidence and patient comorbidities.

BACKGROUND

The recommendations for most patients with hypertension also apply to patients with selected comorbid conditions for which—based on outcomes—there are only minor cautions or modifications to standard therapy. For more detail on dosages and contraindications please refer to Appendix B - Recommended Dosage for Selected Hypertension Drug Therapy.

RECOMMENDATIONS

1. **Thiazide-type diuretics** are recommended as first line therapy for drug treatment of hypertension either as monotherapy or in combination with other agents. [A]
2. The following may be used as alternative or supplementary therapy:
   a. **Angiotensin-Converting Enzyme Inhibitors (ACEIs) [A]**
   b. **Angiotensin II Receptor Blockers (ARBs) [A]**
   c. **Beta-blockers (BBs)[A]**
   d. **Long-acting calcium channel blockers (CCBs) [A]**

Other Supplemental Agents:

3. **Reserpine** can be used as supplemental therapy when other agents are not providing clinical adequate response [A]
4. Other agents may be used as additional therapy in refractory hypertension or as supplementary therapy when other drugs are contraindicated or limited by adverse effects. These include:
   a. **Centrally acting drugs** (e.g. clonidine, methyldopa) [B]
   b. **Vasodilators** (e.g. hydralazine, minoxidil) [B]
   c. **Aldosterone antagonists** (e.g., spironolactone, eplerenone) [B]
   d. **Combined alpha-beta blockers** [B]
   e. **Alpha blockers** [B]

Avoid use of:

5. **Alpha-blockers** should be avoided as monotherapy (I,D), may be used as supplemental therapy [B]
6. **Short-acting calcium channel blockers** should not be used as there is no evidence of benefit [D]. **Short-acting dihydropyridine (DHP) calcium channel blockers** may cause harm [D]

Table 7. Preferred Agents In Patients With Uncomplicated Hypertension				
Condition	**Preferred agents**	**Alternate agents**	**Other agents**	**Comments**
HTN - without compelling indications	Thiazide-type diuretic	ACEI ARB Beta-blocker CCB	Aldosterone antagonist Alpha-blocker Clonidine Reserpine Vasodilator	1. Immediate-release nifedipine should not be used. 2. An ARB may be considered in a patient who is intolerant to an ACEI. 3. Alpha-blockers are useful in treating symptomatic BPH, but are not recommended as monotherapy for treating HTN.

Compelling Indications for Individual Drug Classes

Recommendations for initial antihypertensive therapy in patients with HTN who also have certain compelling conditions may differ from other patients with HTN but in general, these patients should still be considered for thiazide-type diuretics – in addition to the compelling medication – based on the benefit seen in ALLHAT in patients on diuretics. More specifically, the recommendations in Table 8 include medications that have demonstrated improved outcomes or provided clinical improvement in the treatment of patients with certain conditions that may or may not be directly related to hypertension itself. These conditions addressed include: post-myocardial infarction, systolic heart failure (HF), kidney disease, diabetes, and stroke prevention.

Other specific recommendations are for choice of agent in treatment of pilots and patients whose work/duty require special consideration (pilots, and service person in extreme weather conditions.)

MOST COMPELLING INDICATIONS SHOULD INCLUDE A THIAZIDE-TYPE DIURETIC

Table 8. Preferred Agents in Patients with Comorbidities			
	Preferred agents	**Additional/Alternative**	**Other agents**
DM †	Thiazide-type diuretic and/or ACEI	ARB CCB Beta-blocker	
Systolic HF	ACEI Beta-blocker	ARB Hydralazine-Nitrate Aldosterone antagonist	Diuretic (for treatment of volume overload) LADHP
CKD ‡	ACEI ARB Diuretic (thiazide or loop, based on kidney function)	Beta-blocker NCCB LADHP	
Post Stroke	Thiazide-type diuretic and ACEI		
Post – MI	Beta-blocker ACEI	NCCB Thiazide-type diuretic	LADHP

ACEI = angiotensin- converting enzyme inhibitor; ARB = angiotensin receptor blocker; NCCB = nondihydropyridine calcium channel blocker; CKD = chronic kidney disease; LADHP = long-acting dihydropyridine calcium channel blocker

† *For patients with Diabetes Mellitus, please refer to the VA/DoD Clinical Practice Guideline, Management of Diabetes Mellitus in the Primary Care Setting, at www.oqp.med.va.gov/cpg/cpg.htm.*

‡ *For patients with Kidney Disease, refer to the VA/DoD Clinical Practice Guideline, Management of Pre-ESRD in the Primary Care Setting, at www.oqp.med.va.gov/cpg/cpg.htm*

Table 9. Preferred Agents for Patients in High Ambient Temperatures or in Other Extreme Conditions that Increase Dehydration Risk			
	Preferred agents	**Alternate agents**	**Comments**
High ambient temp and/or extreme conditions	LADHP ACEI ARB	CCB Low dose Thiazide-type diuretic	For patients already deployed to high ambient conditions consider LADHPs

Revision July 2005

Compelling Conditions;

DM
See Appendix C1: Compelling Indications - Diabetes

HF
See Appendix C2: Compelling Indications – Heart Failure

CKD
See Appendix C3: Compelling Indications – Chronic Kidney Disease

Stroke
See Appendix C4: Compelling Indications – Prevention of Stroke

In addition, special patient populations may require additional considerations in selecting the most appropriate antihypertensive drug therapy.

African Americans

The low-sodium DASH eating plan was associated with greater reductions in BP in African Americans than other demographic subgroups. In clinical trials, lowering BP prevents sequelae of hypertension in all racial or ethnic groups. Nonetheless, monotherapy with beta-blockers, ACEIs, or ARBs lowers BP to a somewhat lesser degree in African Americans than whites. In the ALLHAT trial with more than 15,000 blacks, the ACEI lisinopril was less effective in lowering blood pressure than either the thiazide-type diuretic chlorthalidone or the CCB amlodipine. There was a 40% greater risk of stroke, 32% greater risk of HF, and 19% greater risk of CVD in those randomized to the ACEI versus the diuretic. There were no differences in major CVD outcomes between the diuretic and the CCB in blacks, except for a 47% higher incidence of heart failure with the CCB. The interracial differences in BP-lowering observed with these drugs are abolished when they are combined with a diuretic. Racial differences in incidence of antihypertensive drug side effects may occur; African Americans and Asians have a 3- to 4-fold higher risk of angioedema and have more cough attributed to ACEIs than whites.

Aviators

Aviators (pilots, navigators, flight surgeons, or special duty personnel) are disqualified from aviation duty when diagnosed with hypertension or placed on hypertension medications. A waiver is required to be returned to flying duties. Certain drugs require a grounding trial only while others require more. Details are spelled out within the Air Force Instructions (AFI). This AFI applies to active duty, Air National Guard, and AF Reserve aviators.

Hypertension and the treating agent are both disqualifying. In general, only those medications listed in aircrew medication list are waiverable. The underlying medical condition must be adequately controlled prior to waiver submission.

The USA Aeromedical Policy Letter may be downloaded from http://usasam.amedd.army.mil/_aama/policyLetter.htm. The USN Aeromedical Waiver Guide may be found at http://www.nomi.med.navy.mil/NAMI/WaiverGuideTopics/index.htm#text

The medications are specifically addressed in AFI 48-123, Medical Examinations and Standards, Attachment 7.32.

High Ambient Temperature And/Or Extreme Conditions

BACKGROUND

Conditions and physiologic responses may be different if patients with hypertension are exposed to high ambient temperature and/or extreme conditions that increase risk of dehydration (e.g., desert deployment). In such conditions, the general recommendations for drug therapy need to be modified.

RECOMMENDATIONS

The following recommendations are based on consensus opinion that considers the available literature, experience in the field, and physiology.

1. Clinicians should discuss how deployment might affect blood pressure control and describe potential complications of treatment with their patients as part of pre-deployment processing.
2. For active duty Soldiers who might be going into high temperature zones (e.g., desert deployment) or who may be exposed to other extreme conditions that increase the risk of dehydration, long-acting dihydropyridine CCBs (LADHP) or ACEI/ARBs would be the preferred agents, rather than a diuretic.
3. If Thiazide diuretics are used, low doses are recommended. If possible, the patient should be monitored for signs and symptoms of dehydration and adequate blood pressure control for the first 7-10 days of deployment while they are becoming acclimatized.
4. For active duty Soldiers who are diagnosed with hypertension during a deployment and who are in areas with high temperatures or in extreme ambient conditions that increase the risk of dehydration, LADHPs are preferred. These agents are available in once a day formulations, do not limit heart rate, and do not require electrolytes to be checked after initiation.

For detailed considerations for treatment of hypertension in these environmental situations please see Appendix C-5: High ambient temperature and/or extreme conditions that increase dehydration risk.

N. Is BP Control Adequate and Therapy Tolerable?

OBJECTIVE

Assess adequacy of HTN control and adverse effects to treatment.

RECOMMENDATIONS

The primary objective in hypertension treatment is to decrease blood pressure to less than 140/90 mm Hg, or to lower goals in selected patient populations.

1. Patients should be seen within 1 month after the initiation of therapy to determine adequacy of HTN control, degree of patient adherence, and presence of adverse effects. (Allied health professional may be useful to conduct these follow-up visits).
2. Earlier follow-up may be necessary for patients:
   a. Requiring blood tests
   b. At increased risk for adverse outcomes from HTN due to very high BP or target organ damage
   c. At risk for postural hypotension
3. Assessment of blood pressure control should be based on measurement of BP in the clinic setting. Out of office measurements may provide useful clinical information [C]
4. Once the patient's BP is controlled, follow-up at 3 to 6 month intervals (depending on patient status) is generally appropriate.
5. Older persons, persons with diabetes, those with neurological disease and patients with postural

Table 10: Target Values For HTN control (ADOPTED FROM JNC7)

Condition	Target (SBP/DBP mm Hg)	Level of Evidence (QE,R)	Resource*
Hypertension	<140/90	<150/90 [A] <140/90 [B]	SBP: SHEP, Syst-Eur DPB: HDFP, HOT
Diabetes	<140/80	[A]	UKPDS, HOT
DM + Nephropathy	<140/80	[A]	IDNT RENAAL, MDRD
Chronic Kidney disease	<140/90	<140/90 [A] <130/80 [C]	AASK
Proteinuria >1g/day	<125/75	[C]	Post analyses MDRD

* *SHEP = Systolic Hypertension in the Elderly; Syst-Eur = Systolic Hypertension in Europe; HDFP = Hypertension Detection and Follow-up Program; HOT = Hypertension Optimal Treatment; UKPDS = United Kingdom Prospective Diabetes Study; IDNT = Irbesartan in Diabetic Nephropathy Trial; RENAAL = Reduction of Endpoints in NIDDM with the Angiotensin II Receptor Antagonist Losartan; MDRD = Modification of Diet in Renal Disease; AASK = African American Study Of Kidney Disease And Hypertension*

The VA/DOD Hypertension Guideline recommends a minimal target threshold that is based on level I evidence derived from randomized clinical trials. For persons with diabetes this is 140/80 mm Hg, and for persons without diabetes 140/90 mm Hg. The VA/DOD Hypertension Guideline also acknowledges that there are data from multiple observational studies, including pooled data from randomized clinical trials (level II evidence) demonstrating that lower blood pressure levels are associated with risk reduction for adverse outcomes; the relationship is linear without a threshold. Consequently, clinicians are encouraged to set target values for each patient based upon their individual circumstances, including tolerance of medications.

symptoms should be evaluated for postural hypotension.

6. Target level for blood pressure are included in the following table:

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

OBJECTIVE

Follow patients who attain the desired target BP.

BACKGROUND

Once an effective and well-tolerated regimen has been obtained periodic follow-up is important to the management of the hypertensive patient and should help to:

- Assess the long-term response and adherence to therapy
- Monitor the development of target organ damage
- Assess for adverse effect(s) of medication(s)
- Reinforce lifestyle modification.

RECOMMENDATION

1. Once the patient's BP is stabilized, follow-up at 3 to 6 month intervals (depending on patient status) is generally appropriate.
2. Decrease or cessation of antihypertensive drug therapy is possible in patients who are willing to do so, and whose BP is very well controlled. Cessation may be considered in patients well controlled on monotherapy. These patients should be closely followed-up. [B]

P. Self monitoring

RECOMMENDATIONS

1. Home blood pressures may be used as a supplement to, but should not wholly substitute for, obtaining clinic blood pressures to assess or promote blood pressure control.
2. If home blood pressure monitoring is used, a minimum of two measurements per day for at least two days should be obtained and then averaged in order to provide a reliable estimate of home blood pressure.*
3. In order to improve accuracy and interpretation of home blood pressure measurements, the use of a device with a memory function is recommended rather than relying on the patient's recall or diary.
4. Home blood pressure monitoring may assist in detecting a white coat effect or poorer control at home than in the office.

* *Note: Patients enrolled in a formal Care-Coordination /Telehealth (CC-TH) program should follow the instructions of the CC-TH program.*

Q. Adjust Therapy

OBJECTIVE

Modify drug therapy to help achieve BP control.

RECOMMENDATION

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.
   - Titrating the dose usually means doubling the dose. Be aware of the dose response that is not always linear although adverse effects may increase with higher doses.
2. Add another agent
   - If a thiazide-type diuretic is not chosen as the initial drug, it should be used as the second agent, unless contraindicated or not tolerated, especially because it frequently enhances the effects of the initial agent and has the best cardiovascular outcome data. [A]
   - When using combination therapy initially select agents that have been shown to reduce morbidity and mortality. [A]
   - When using combination therapy select agents from different classes and provide benefit for comorbid condition or compelling indications if they exist. [C]
   - Combination therapy includes a potential for drug-drug interactions, but these are uncommon.
3. Consider care management by pharmacist in the follow-up and adjustment of medication to improve blood pressure goal. [B]
4. Involving other allied health professionals in follow-up may as well improve blood pressure control. [C]

R. Reassess Adherence

OBJECTIVE

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

RECOMMENDATION

Adherence to an antihypertensive medication regimen can be improved by a multi pronged approach including:

a) Address barriers for obtaining the medications (administrative, economic, etc.)
b) Simplifying medication regimens incorporating patient's preference
c) Coordinate with other health care team members to improve monitoring of adherence with prescriptions of pharmacological and lifestyle modification
d) Educate patients and patients' families about their disease/treatment regimens
e) Encourage greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions.

Table 11. Causes of Inadequate Response to Therapy

Non-adherence to therapy	See Table 12, below.
Pseudo-resistance	"White Coat" hypertension or office elevation Pseudohypertension in older patients Use of regular cuff on large (>32 cm circumference) arm
Volume overload	Excess salt intake Progressive renal damage (nephrosclerosis) Fluid retention from reduction of blood pressure Inadequate diuretic therapy
Drug-related causes	NSAID(non steroidal anti-inflammatory drugs), COX-2 inhibitors 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 Cyclosporine, tacrolimus Erythropoietin Antidepressants
Associated conditions	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) Memory deficit
Identifiable secondary causes of HTN	See Table 5, Recommended Testing for Patients Suspected of Having Secondary Hypertension

The primary care provider should employ measures that assist in improving patient adherence to treatment. Many of these measures are designed to engage the patient in his or her wellness. Table 12 lists several suggestions to improve the patient's adherence to therapy.

Table 12. Strategies to Improve Patient Adherence to Antihypertensive Therapy
1. Be aware of signs of patient non-adherence to therapy (e.g., missed appointments, missed refills).
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.
5. Integrate pill taking into routine activities of daily living.
6. Prescribe medications that require no more than twice daily dosing if possible.
7. Ask about adverse effects and adjust therapy to prevent, minimize, or ameliorate side effects.
8. Enlist the support of pharmacist in adjusting medication with regular follow-up.
9. Consider group visits for education

S. Consider Consultation

OBJECTIVE

Determine appropriate point in time to consider consultation to improve hypertension management.

RECOMMENDATION

From a clinical perspective, referral to or consultation with hypertension specialists or those with particular expertise in the relevant clinical area should be considered if there is:

1. Failure to achieve target blood pressure goals when on appropriate doses of three medications, one of which should typically be a thiazide-type diuretic and assuming that other remedial causes of inadequate response have been identified and addressed.
2. Suspected secondary cause for hypertension.

APPENDIX B:
DRUG TABLES

Recommended Dosage for Selected Hypertension Drug Therapy		
Drug[a]	**Usual Oral Dose Range**[d]	**Comments**[g]
Thiazide Diuretics		
Chlorthalidone[b]	12.5-25 mg daily	May cause hyperuricemia/gout
Hydrochlorothiazide[b]	12.5-50 mg daily	Monitor K+ levels
HCTZ/Triamterene[b]	12.5/18.75-50/75 mg daily	May cause photosensitivity (rare)
Indapamide	1.25-2.5 mg daily	
Beta-blockers		
Noncardioselective		
Propranolol	IR: 80-160 mg/day (divided bid)	Discontinue with slow taper over 1 week
	SR: 80-160 mg daily	Avoid combination with NCCB
Cardioselective		As doses increase, cardioselectivity decreases
Atenolol[b]	25-100 mg daily (adjust dose in CRI[d])	Beta-blockers should be used cautiously in asthma
Metoprolol[b]	IR: 50-300 mg/day (daily or divided bid)	
CCBs		Use CCBs with caution in patients with liver or kidney dysfunction
NCCBs		
Verapamil SR[c]	120-480 mg/day (daily or divided bid)	Verapamil may cause constipation; verapamil is contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic HF and ↓ LV function
Diltiazem SR[b]	120-540 mg daily	Diltiazem may ↓ sinus rate and cause heart block
LADHPs		
Amlodipine[f]	2.5-10 mg daily	Monitor adverse effects (DHPs may cause
Felodipine	2.5-10 mg daily	ankle edema, dizziness, flushing, headache)
Nifedipine SR[b]	30-60 mg daily	
ACEIs		Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and
Captopril[b,e]	25-100[f] mg/day (divided bid)	neonatal morbidity and death
Enalapril	5-40 mg/day (daily or divided bid)	
Fosinopril	10-40 mg daily	Should not be used if history of angioedema
Lisinopril[b]	10-40 mg daily	Monitor K+ and kidney function; use caution if combined with ARB, K+ sparing diuretic, or K+ supplement
Ramipril[f]	2.5-20 mg/day (daily or divided bid) (10 mg daily for CV risk prevention)	
ARBs[g]		
Candesartan	8-32 mg daily	Contraindicated in 2nd and 3rd trimesters pregnancy due to potential for fetal and neonatal morbidity and death
Eprosartan	400-800 mg/day (daily or divided bid)	
Irbesartan	150-300 mg daily	Monitor K+ and kidney function; use caution if combined with ACEI, K+ sparing diuretic, or K+ supplement
Losartan	25-100 mg/day (daily or divided bid)	
Olmesartan	20-40 mg daily	
Telmisartan	20-80 mg daily	
Valsartan	80-320 mg daily	

Recommended Dosage for Selected Hypertension Drug Therapy		
Drug[a]	**Usual Oral Dose Range**[d]	**Comments**
Alpha-blockers		
Doxazosin	1-16 mg daily	Initiate at low doses (1mg)
Prazosin[b]	2-20 mg/day (divided bid or tid)	Administer 1st dose at bedtime to avoid syncope
Terazosin[b]	1-20 mg daily	
Alpha-beta blockers		
Carvedilol[f]	12.5-50 mg/day (divided bid)	Precautions for beta-blockers apply
Labetalol	200-800 mg/day (divided bid)	
Centrally Acting		
Clonidine Tablet[b]	0.1-0.8 mg/day (divided bid)	Monitor for somnolence and dry mouth. Taper dose to discontinue
Clonidine Patch	0.1-0.3 mg patch weekly	Clonidine patches are costly but may be useful in selected patients
Methyldopa	500-2000 mg/day (divided bid)	
Peripherally Acting		Monitor for sedation, nasal congestion, activation of peptic ulcer
Reserpine	0.1-0.25 mg daily	
Vasodilators		Should be used with a diuretic and beta-blocker to reduce edema and reflex tachycardia
Minoxidil	2.5-80 mg/day (daily or divided bid)	Monitor for hypertrichosis, pericardial effusions with minoxidil
Hydralazine[b]	50-200 mg/day (divided bid)	Monitor for headache and SLE[d] (dose-related) with hydralazine
Aldosterone Antagonists		Monitor K+ and kidney function; use caution if combined with ACEI, ARB, K+ sparing diuretic, or K+ supplement
Eplerenone	50-100 mg/day (daily or divided bid)	
Spironolactone	25-50 mg daily	May cause gynecomastia
Fixed-Dose Combinations		
Chlorthalidone/Atenolol	Available as 25/50 mg, 25/100 mg (dose as above)	
HCTZ/Lisinopril	Available as 12.5/10 mg, 12.5/20 mg, 25/20 mg (dose as above)	Precautions apply as above

a Partial list; for medications not included on this list, refer to JNC 7; refer to www.vapbm.org for items available on VANF

b DoD BCF item; all BCF items are available through the DoD TMOP

c Calan® SR, Isoptin® SR, and generic equivalents are on the DoD BCF

d bid=twice a day; CRI=Chronic renal insufficiency; IR=immediate release; MAOI=monoamine oxidase inhibitor; SLE=systemic lupus erythematosus; SR=sustained release; tid=three times a day

e Patients should take 1 hour prior to food ingestion (empty stomach)

f VA criteria for use

g For complete drug information, review the manufacturer's prescribing information

APPENDIX C
HYPERTENSION AND COMORBID CONDITIONS

C1: DM – Hypertension

Management of Hypertension in Diabetes Mellitus

For complete management of hypertension see: VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting at http://www.oqp.med.va.gov/cpg/cpg.htm or http://www.qmo.amedd.army.mil .

Patients with Diabetes with SBP ≥140 or DBP ≥80 mm Hg

BACKGROUND

Early treatment of HTN in patients with diabetes, particularly type 2 DM, is important to delay the onset and/or retard the progression of cardiovascular disease and DM.

RECOMMENDATIONS

1. Patients with diabetes with hypertension (systolic BP ≥140 or diastolic BP ≥90 mm Hg) should:
   - Begin anti-hypertensive therapy with a diuretic or an angiotensin converting enzyme inhibitor (ACEI) [A]
   - If ACEI induced side-effects occur, consider switching to an angiotensin receptor blocker (ARB)
   - Use other preferred agents (beta blockers, long acting calcium channel blockers) as necessary, depending on other co-morbid conditions or compelling indications to achieve a blood pressure <140/80 mm Hg
2. Patients with diabetes with initial SBP <140 mm Hg and DBP 80 and 89 mm Hg (within the "pre-hypertensive" category identified by JNC 7) may benefit from lowering diastolic blood pressure to < 80 mm Hg [A].
3. Individuals with diabetes whose blood pressures is <140/80 mm Hg who have clinical cardiovascular disease may benefit from ACEI therapy even without a reduction in blood pressure [A].
4. In patients with diabetes with renal insufficiency (i.e., serum creatinine >1.5 mg/dL) and proteinuria (i.e., >1 g/24h) there are some data suggesting that further BP lowering (<125/75 mm Hg) may slow progression of renal disease. Lower BP should be achieved, if feasible and practical, depending on the tolerance of medications and side effects of BP lowering [B]. *See footnote of Table 10 on page 15 for target levels.*

C2: Kidney Disease

OBJECTIVE

To provide recommendations on pharmacologic therapy for renal preservation in patients kidney disease, regardless of blood pressure level.

RECOMMENDATION

1. ACEI may be preferred agent for patients with HTN and kidney disease (reduced kidney function with proteinuria). ARB may be substituted for patients with ACEI-induced cough.
2. In African Americans with hypertensive kidney disease, ACEI may be a first line therapy for treating HTN.
3. A diuretic should be used when a second blood pressure medication is needed, or if hyperkalemia occurs. Thiazide diuretic may be used if estimated GFR > 30 cc/min/1.73m^2 , but loop diuretics are usually needed for lower kidney function. Potassium-sparing diuretics should be avoided in patients with CKD.
4. A stable increase of serum creatinine as much as 35% above baseline after ACEI or ARB initiation may be tolerated, as long as hyperkalemia does not occur. ACEI or ARB should be discontinued, or other potentially reversible causes of kidney failure investigated if progressive and rapid rise of serum creatinine continues. Since CKD is associated with progressive rise in creatinine over years, ACEI or ARB should not be discontinued for this situation, since these medications are renoprotective.

5. When treating HTN in patients with non-diabetic kidney disease, use of combined therapy with ACEI and ARB may offer more renoprotection than with either class of medication alone.
6. Avoid potential nephrotoxic medications such as NSAIDs, COX2 inhibitor, aminoglicosides, IV contrast, and excessive diuretic use.
7. Monitor kidney function over time by estimating glomerular filtration rate (GFR) or creatinine clearance (Clcr). Consider consulting with a nephrologist if a non-diabetic patient has nephrotic range proteinuria, or kidney function is < 30 cc/min/1.73m^2.

Estimated Glomerular Filtration Rate (eGFR)

Serum creatinine level should be used to estimate the GFR to identify patients at risk and develop appropriate management plans.

Abnormalities of urinalysis or reduced renal function identify patients with kidney disease (see Table C-2.1). Patients with chronic kidney disease are at risk for progressive loss of kidney function. Most clinicians first identify patients with abnormal kidney function when serum creatinine (Scr) is elevated on routine laboratory testing. However, as Exhibit R2 demonstrates, significant reduction in kidney function is required before the Scr rises significantly. Also, patients with baseline Scr in the lower range of normal may lose significant amounts of kidney function before the Scr increases above the normal range (typically >1.2 mg/dL in females and > 1.5 mg/dL in males). Therefore, Scr alone is not a good test.

Table C-2.1. Definition of Chronic Kidney Disease Criteria

Chronic Kidney Disease Criteria
1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*: • Pathological abnormalities; OR • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60ml/min/1.73m^2 for ≥3 months, with or without kidney damage

Measuring creatinine clearance (Clcr) or estimating Clcr or GFR by calculation formulas can be used to monitor abnormal kidney function. Measuring Clcr by 24-hour urine collection has been the traditional method for estimating GFR. However, collection inaccuracies and patient difficulties make this test unsatisfactory. Estimation of Clcr or GFR using routine clinical information is now recommended for estimating and monitoring kidney function. Cockroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) formulas are acceptable tools for estimating Clcr and GFR, respectively. CG is a simple formula that has been in use for over 2 decades. The MDRD formula is more precise, and online calculators are available.

Kidney Function Estimation Formula:

- MDRD formula (estimated GFR in ml/min/1.73 m^2): 186 x (Scr)$^{-1.154}$ x (Age)$^{-0.203}$ x (0.742 if female) x (1.210 if African - American)

http://www.nkdep.nih.gov/healthprofessionals/tools/gfr_adults.htm

The National Kidney Foundation's Kidney Disease Outcome Quality Initiative (K/DOQI Clinical Practice Guidelines for Kidney Diseases) has developed a staging system for grading kidney disease (see table below). These stages can be used to monitor and educate patients, assess impact of management, and assist the primary provider in coordinating care with specialists and making plans for ESRD care.

Table C2-2. Chronic Kidney Disease (CKD): A Clinical Action Plan			
Stage	**Description**	**GFR (mL/min/1.73m²)**	**Action***
No CKD	At increased risk	≥90 (with CKD risk factors)	Screening,CKD risk reduction
1	Kidney damage with Normal or ↑ GFR	≥90	Diagnosis and treatment, treatment of comorbid conditions, slowing progression, cardiovascular disease risk reduction
2	Kidney damage with Mild ↓ GFR	60 – 89	Estimating progression
3	Moderate	30 – 59	Evaluating and treating complications
4	Severe ↓ GFR	15 - 29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uremia present)

Shaded area identifies patients who have chronic kidney disease; unshaded area designates individuals who are at increased risk for developing chronic kidney disease. Chronic kidney disease is defined as either kidney damage or GFR, <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

*Includes actions from preceding stages

C3: Chronic Heart Failure (HF)

For complete management of HF, go to the clinical practice guideline for the pharmacologic management of chronic heart failure at http://www.oqp.med.va.gov/cpg/cpg.htm.

The following recommendations refer to patients with Stage C HF (e.g., patients with past or current HF symptoms and evidence of structural heart damage).

RECOMMENDATIONS

1) A diuretic should be used in the treatment of patients with signs of fluid overload [B].
2) All patients should be treated with an ACEI unless contraindicated or not tolerated [A]. These agents improve HF symptoms, functional status, and quality of life, while decreasing frequency of hospitalization and mortality.
3) A beta-adrenergic blocker should be used in conjunction with an ACEI in all patients who are considered stable (i.e., minimal or no signs of fluid overload or volume depletion and not in an intensive care unit), unless contraindicated or not tolerated. These agents have been shown to reduce mortality and decrease the symptoms of HF [A].
4) An ARB should be considered as an alternative to an ACEI in patients who are on a diuretic, beta-adrenergic blocker, and usually digoxin and are unable to tolerate an ACEI [A] due to cough or possibly, angioedema.
5) The combination of hydralazine and isosorbide dinitrate (HYD/ISDN) may be considered as an alternative to an ACEI in patients who are on a diuretic, beta-adrenergic blocker, and usually digoxin and are unable to tolerate an ACEI [B] due to hypotension, renal insufficiency, or possibly, angioedema.
6) Digoxin (although not effective for the treatment of HTN) should be used in patients whose symptoms persist despite treatment with an ACEI, a beta-adrenergic blocker, and a diuretic. Digoxin reduces symptoms associated with HF and decreases the risk for hospitalizations due to HF but does not improve mortality [A].
7) Low dose spironolactone (an aldosterone antagonist) should be considered in patients with recent New York Heart Association (NYHA) Class IV HF and current Class III or IV symptoms and left ventricular ejection fraction (LVEF) ≤ 35%, provided the patient has preserved renal function and normal potassium levels. This therapy improves symptoms (as assessed by change in NYHA functional class), decreases hospitalizations for worsening HF, and decreases mortality [A].

C4: Stroke Prevention

RECOMMENDATIONS

1. When an ACEI is used as principal therapy after stroke, a thiazide (or similar) diuretic should be used to assure maximal effect [A]

2. Diuretics remain a principal agent for risk reduction after stroke or TIA based on data on primary prevention studies and extrapolation from the PROGRESS trial on secondary prevention (Primary prevention of stroke: [A]; Secondary prevention [B])
3. Alternatives (in alphabetical order) include ACEI/ARB, beta-blockers, dihydropyridine (long-acting) or diltiazem calcium channel blockers (Primary prevention [A]; Secondary prevention [B]).
4. In post-stroke patients with pre-hypertension, the addition of an ACEI may be considered but should be with a diuretic, as noted above (level of evidence for secondary prevention [A]). An ACEI may provide additional benefit to existing antihypertensive therapies or for patients who are not hypertensive for primary stroke protection (Primary prevention: [A]).

C5: High Ambient Temperature and/or Extreme Conditions that Increase Dehydration Risk

BACKGROUND

There are special situations related to deployment and readiness when it comes to control of HTN and since conditions and physiologic responses may be quite different in extreme deployment conditions, the general recommendations for drug therapy need to be modified. Many drugs including diuretics and beta blockers might have negative effects on the heat acclimatization process.

It is critical for readiness that Soldiers are able to acclimate quickly and safely when they arrive in theater.

For example, treatment with an anti-hypertensive agent, especially a diuretic, may interfere with some changes such as increasing total body water and plasma volume. This might prolong the process of heat acclimatization. It may also make the increased sweating and altered electrolyte loss associated with heat acclimatization more dangerous. The physiologic changes induced by heat acclimatization may also make certain anti-hypertensive agents, such as diuretics, less effective since they work counter the effect(s) of the drug. Unfortunately, there is minimal high quality evidence available on the effects of anti-hypertensive (and other) medications on heat acclimatization.

RECOMMENDATIONS

The following recommendations are based on consensus opinion that considers the available literature, experience in the field, and physiology.

1. Clinicians should discuss how deployment might affect blood pressure control and describe potential complications of treatment with their patients as part of pre-deployment processing.
2. For active duty Soldiers who might be going into high temperature zones (e.g., desert deployment) or who may be exposed to other extreme conditions that increase the risk of dehydration, long-acting dihydropyridine CCBs (LADHP) or ACEI/ARBs would be the preferred agents, rather than a diuretic.
3. If Thiazide diuretics are used, low doses are recommended. If possible, the patient should be monitored for signs and symptoms of dehydration and adequate blood pressure control for the first 7-10 days of deployment while they are becoming acclimatized.
4. For active duty Soldiers who are diagnosed with hypertension during a deployment and who are in areas with high temperatures or in extreme ambient conditions that increase the risk of dehydration, LADHPs are preferred. These agents are available in once a day formulations, do not limit heart rate, and do not require electrolytes to be checked after initiation.

For detailed considerations for treatment of hypertension in these environmental situations please see Appendix C-5: High ambient temperature and/or extreme conditions that increase dehydration risk.