# The Treatment of Adults with Essential Hypertension

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Hypertension is arbitrarily defined as diastolic blood pressure (DBP) of 90 mm Hg or higher, systolic blood pressure (SBP) of 140 mm Hg or higher, or both, on 3 separate occasions. Essential hypertension is hypertension without an identifiable cause. Essential hypertension, also known as primary or idiopathic hypertension, accounts for at least 95% of all cases of hypertension.

According to the third National Health and Nutrition Examination Survey (NHANES III), approximately 60% of the 50 million Americans with hypertension are at increased risk for cardiovascular disease resulting from uncontrolled hypertension. This is because only 53% of hypertensive patients are being treated and only 24% have their hypertension under control.[1] Physicians must play an active role in identifying and treating hypertension.

In an earlier Applied Evidence article[2] an approach to the diagnosis of hypertension was presented. This article reviews the treatment of essential hypertension in adults and the prognosis of untreated hypertension. Risk stratification, alternative therapies, lifestyle modification, drug therapy, and prognosis will each be reviewed sequentially.

■ KEY WORDS Blood pressure; hypertension; prognosis; therapy; acupuncture; alternative therapy; biofeedback; herbal medicine; transcendental meditation; yoga.*(J Fam Pract 2002; 51:74-79)*

## RISK STRATIFICATION

The decision to treat hypertension and the choice of treatment is affected by the patient's risk of morbidity and mortality if the blood pressure remains untreated or under-treated. According to the recommendations of the sixth report of the Joint National Committee on the Prevention, Diagnosis, Evaluation, and Treatment of High Blood Pressure (JNC-VI), the first step in planning treatment of a patient with essential hypertension is to categorize the patient's risk status.[3] The patient is placed in 1 of 9 treatment categories according to his or her blood pressure

### KEY POINTS FOR CLINICIANS

- Only 53% of hypertensive patients are being treated, and only 24% have their hypertension under control.
- The first step in planning the treatment of a patient with essential hypertension is to categorize the patient's risk status.
- The target blood pressure of patients who have diabetes or renal failure should be less than 130/85.
- Diuretics are safe, well tolerated, effective, relatively inexpensive, and convenient for initial drug treatment of hypertension in patients who do not have concomitant illness.
- Alpha-adrenergic blockers should be used with caution in the treatment of hypertension.
- Ambulatory blood pressure measurements predict cardiovascular events more closely than clinic blood pressure measurements.

category, cardiovascular risk factors, and evidence of end-organ damage found during the initial evaluation (Table 1). Once the treatment category is identified, initial treatment should begin (Figure 1). Subsequent treatment depends on the patient's response to initial treatment (Figure 2).

Patients should be monitored regularly to be sure they do not develop signs and symptoms that would place them in a different category and mandate more aggressive treatment. After a patient's blood pressure has been controlled for 1 year, it may be possible to decrease the dose or the number of antihypertensive drugs—especially among patients who make significant lifestyle changes.[4]

The effectiveness of therapy varies depending on the patient's cardiovascular risk. The New Zealand

Guidelines Group has developed a helpful risk calculator based on the Framingham Heart Study for estimating a patient's cardiovascular risk. This calculator incorporates sex, age, systolic blood pressure, smoking status, total cholesterol, high-density lipoprotein cholesterol, presence or absence of diabetes, and presence or absence of electrocardiogram evidence of left ventricular hypertrophy. This helpful risk calculator may be downloaded from the Web site of the New Zealand Guidelines Group at http://www.nzgg.org.nz/library/gl_complete/blood-pressure/appendix.cfm#app3. Alternatively, the University of Sheffield Medical School has developed tables to estimate an individual's risk of heart disease based on cardiovascular risk factors including age, sex, cholesterol level, and presence or absence of smoking, hypertension, and diabetes—Sheffield tables.[5] Software for handheld computers (Palm and PocketPC) that helps you estimate risk is available at www.jfponline.com.

Regardless of the method used, the benefit of treatment increases steadily as the patient's current cardiovascular risk increases. With a 5-year cardiovascular risk of less than 2.5%, more than 120 patients have to be treated for 5 years to prevent 1 cardiovascular event; this number decreases to 25 patients with a risk of between 5% and 10%, and only 13 with a risk of between 20% and 24%.[6] It is tempting to assume that the benefit of hypertension treatment is related to reduction in blood pressure whether achieved by drug therapy, lifestyle modification, or alternative therapy. However, this has not been established and it is important to consider the evidence supporting the benefit of each of these therapeutic options (Table 2).

## TREATMENT
### Drug Therapy

Patients who require drug treatment for hypertension should begin with a low dose of the initial medication, and that dose should be slowly titrated upward every 1 to 2 months (Figure 2). The JNC-VI recommends a diuretic or a ß-blocker with once daily dosing and 24-hour efficacy as the initial treatment for most hypertensive patients. However, the choice of initial medication will be affected by concomitant illnesses: (1) ß-blockers are recommended for the initial treatment of patients with hypertension and a history of coronary artery disease; (2) diuretics are suggested for the initial treatment of isolated systolic hypertension; (3) and angiotensin-converting enzyme (ACE) inhibitors are recommended for hypertensive patients who have systolic dysfunction after myocardial infarction, diabetic nephropathy, or congestive heart failure. Angiotensin II receptor blockers may be used in patients who cannot tolerate ACE inhibitors because of cough or rash. Alpha-adrenergic blockers should be used with caution in light of evidence that they may increase the risk of cardiovascular events (especially congestive heart failure).[7]

Among patients who do not have concomitant illness, the choice of drug therapy is controversial. A case-control study and a meta-analysis suggested that short-acting calcium channel blockers (CCBs) increase cardiovascular mortality.[8,9] Unfortunately, these studies were not designed to establish a causal relationship. A recent nonsystematic review suggested that short-acting CCBs should be avoided and that conventional therapies were more effective than long-acting CCBs.[10] An earlier non-systematic review suggested that short- and intermediate-acting CCBs were associated with increased cardiovascular mortality and morbidity. However, a well-designed cohort study of patients with coronary artery disease failed to reveal an increase in adverse effects among patients taking short-acting CCBs.[11] Furthermore, randomized controlled trials suggest that diuretics, ß-blockers, and long-acting CCBs are equally effective in preventing cardiovascular mortality and morbidity.[12,13] Physicians who treat hypertension must choose the best initial treat-

**TABLE 1**

### HYPERTENSION RISK STRATIFICATION AND TREATMENT CATEGORIES

| Blood Pressure Category | Risk Group A* | Risk Group B* | Risk Group C* |
|---|---|---|---|
| High-normal (130 – 139/85 – 89) | Lifestyle modification† | Lifestyle modification | Lifestyle modification and drug therapy |
| Stage 1 (140 – 159/0 – 99) | Lifestyle modification (12-month trial) | Lifestyle modification (6-month trial) | Lifestyle modification and drug therapy |
| Stage 2 or 3 ( ≥160 / ≥100) | Lifestyle modification and drug therapy | Lifestyle modification and drug therapy | Lifestyle modification and drug therapy |

*Risk groups: A = no risk factors, end-organ damage, or clinical cardiovascular disease; B = ≥ 1 risk factor other than diabetes, no end-organ damage, and no clinical cardiovascular disease; C = Diabetes, end-organ damage, or clinic cardiovascular disease.
† Lifestyle modification should be included in the treatment plan of all patients receiving drug therapy.

TABLE 2

**NUMBER NEEDED TO TREAT (NNT) FOR SPECIFIC ANTIHYPERTENSIVE TREATMENTS**

| Medication | Level of Evidence | NNT (95% CI)* | Comment |
|---|---|---|---|
| Low-Dose Thiazide | 1a | 18 (14-23) | Adults with systolic blood pressure ≥160 or diastolic blood pressure ≥ 90 regardless of age or comorbidities. |
| High-Dose Thiazide | 1a | 67 (48-111) | |
| Beta-Blocker | 1a | 142 (71-1000) | Drug vs no treatment comparison.[14] |
| Calcium-Channel Blockers | 1b | 45 (30-102) | Isolated systolic hypertension in older patients, drug vs no treatment comparison.[22] |
| ACE inhibitors | 1b | NS | Captopril versus diuretic or ß-blocker. |
| Alpha-agonists | 1b | NS | Doxazosin versus chlorthalidone, increased congestive heart in doxazosin group.[7] |
| ARBs | NA | NA | Patient-oriented outcomes not available. |
| Sodium Restriction | 1a | NA | May reduce blood pressure but lacks evidence of reduced morbidity or mortality.[27-35] |
| Weight Loss | 1a | NA | |
| Exercise | 1a | NA | |
| Low-Fat Diet | 1b | NA | |
| Limited Alcohol | 5 | NA | |
| Potassium Supplement | 1a | NA | |
| Fish Oil Supplement | 1a | NA | |
| Acupuncture | NA | NA | No evidence of blood pressure reduction or reduced morbidity or mortality.[36-43] |
| Biofeedback | NA | NA | |
| Herbal Medicine | NA | NA | |
| Transcendental Meditation | NA | NA | |
| Yoga | NA | NA | |

*For total cardiovascular events over 5 years.
 NS denotes no significant difference from comparison drug; NA, not applicable; ACE, angiotensin-converting enzyme; ARBs, angiotensin-receptor blockers.

ment for patients who do not have concomitant illness. Fortunately, safety, tolerability, efficacy, price, and simplicity can guide the physician to an ideal drug for most hypertensive patients.

Low-dose thiazide diuretics (the equivalent of 25 to 50 mg of hydrochlorothiazide) appear better tolerated than ß-blockers or CCBs.[14] Treatment with ß-blockers, CCBs, and ACE inhibitors is also more expensive (75% to 85% more) than diuretic therapy.[15] The cost savings offered by diuretics complement the fact that diuretics are safe, effective, and may be dosed once daily. In short, in addition to being the drug of choice for isolated systolic hypertension, low-dose thiazide diuretics are the ideal initial drug treatment of patients without concomitant illness. It should be noted that higher doses of thiazide diuretics offer proportionately less blood pressure reduction and greater risk of hypokalemia.[16]

Antihypertensive treatment reduces morbidity and mortality for all stages of hypertension, but people with the greatest baseline cardiovascular risk (eg, older patients and patients with higher levels of blood pressure) have the most to gain from treatment.[17,18] There is no conclusive evidence to suggest that lowering blood pressure to below 140/80 reduces morbidity or mortality in most patients. However, patients who have diabetes or renal failure benefit from more aggressive management of blood pressure.[19,20] Therefore, the JNC-VI recommends a target blood pressure of less than 130/85 for these patients.
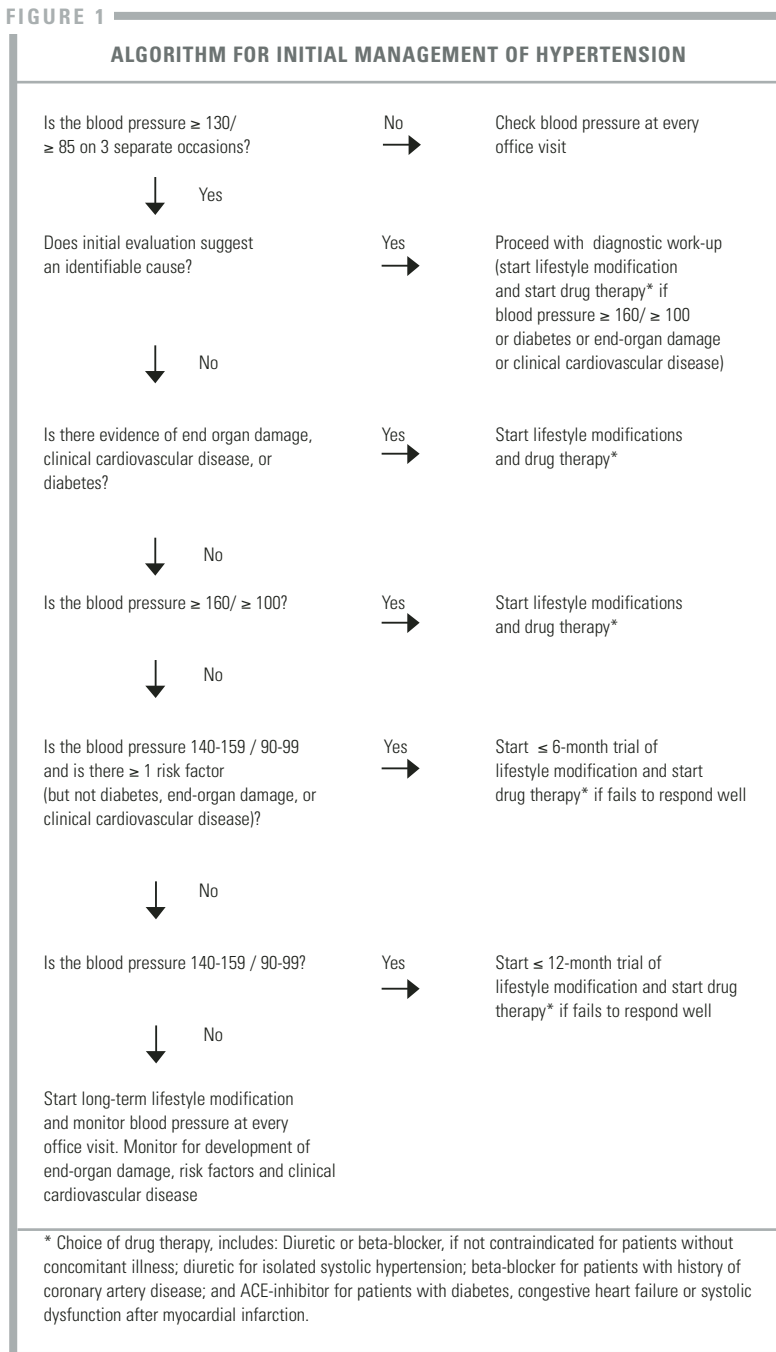
The JNC-VI recommendation to start with a low-dose diuretic is supported by the evidence across a spectrum of patient-oriented outcomes. The effectiveness of diuretics and ß-blockers as first-line agents has been confirmed by long-term clinical trials.[14,21] However, low-dose thiazides appear effective against a broader range of outcomes than high-dose thiazides and ß-blockers (Table 3). There is also evidence to suggest that CCBs and ACE inhibitors may be effective first-line agents, but fewer patients have been studied who take CCBs and ACE inhibitors than those who take diuretics and ß-blockers.[22,23]

Most patients with hypertension will respond to 1 (approximately 50%) or 2 (approximately 30%) antihypertensive medications.[19,24,25] As noted earlier, failure to respond to treatment suggests an identifiable cause of hypertension. Among patients who do not have a secondary cause of hypertension, inadequate drug treatment (often failure to start a diuretic) and noncompliance are among the most common causes of resistant hypertension.[26]

When patients who are receiving drug therapy fail to reach the target blood pressure goal or fail to

**ALGORITHM FOR INITIAL MANAGEMENT OF HYPERTENSION**

Is the blood pressure ≥ 130/ ≥ 85 on 3 separate occasions? —No→ Check blood pressure at every office visit

↓ Yes

Does initial evaluation suggest an identifiable cause? —Yes→ Proceed with diagnostic work-up (start lifestyle modification and start drug therapy* if blood pressure ≥ 160/ ≥ 100 or diabetes or end-organ damage or clinical cardiovascular disease)

↓ No

Is there evidence of end organ damage, clinical cardiovascular disease, or diabetes? —Yes→ Start lifestyle modifications and drug therapy*

↓ No

Is the blood pressure ≥ 160/ ≥ 100? —Yes→ Start lifestyle modifications and drug therapy*

↓ No

Is the blood pressure 140-159 / 90-99 and is there ≥ 1 risk factor (but not diabetes, end-organ damage, or clinical cardiovascular disease)? —Yes→ Start ≤ 6-month trial of lifestyle modification and start drug therapy* if fails to respond well

↓ No

Is the blood pressure 140-159 / 90-99? —Yes→ Start ≤ 12-month trial of lifestyle modification and start drug therapy* if fails to respond well

↓ No

Start long-term lifestyle modification and monitor blood pressure at every office visit. Monitor for development of end-organ damage, risk factors and clinical cardiovascular disease

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* Choice of drug therapy, includes: Diuretic or beta-blocker, if not contraindicated for patients without concomitant illness; diuretic for isolated systolic hypertension; beta-blocker for patients with history of coronary artery disease; and ACE-inhibitor for patients with diabetes, congestive heart failure or systolic dysfunction after myocardial infarction.

maintain the blood pressure goal, they should have the initial drug dose increased until the goal is reached (Figure 2). Those who fail initial drug therapy at full doses should have a second drug added and increased until the blood pressure goal is reached. Those who fail initial and second drug therapy at full doses should have a third drug added and increased until the pressure goal is reached. Patients who fail to reach the goal on maximal doses of 3 drugs have, by definition, resistant hypertension and

will require evaluation by a physician with expertise in managing resistant hypertension. A cause should be sought each time a patient fails to respond to a drug or fails to maintain blood pressure control on a drug that had previously controlled the pressure (Table 3).

### LIFESTYLE MODIFICATIONS
Several lifestyle modifications are recommended in all treatment categories. Aerobic exercise (45 to 60 minutes at least 3 days per week), low-salt, low-fat, and high fruit and vegetable diet, limited alcohol consumption (less than 3 drinks per day), and modest weight loss (3% to 9% of total body weight) have been demonstrated to yield modest blood pressure reductions, but there is insufficient evidence to suggest that these measures alone reduce morbidity or mortality in hypertensive patients.[27-33] A systematic review of randomized controlled trials found an average 4.4/2.5 mm Hg reduction in blood pressure with no evidence of harm (among patients who were not at risk for hyperkalemia) when diet was supplemented with about 2000 mg of potassium daily.[34] A comparable reduction in blood pressure was seen with a daily supplement of more than 3 grams of fish oil.[35] Research concerning the value of calcium and magnesium supplementation is conflicting and insufficient for supplementation to be considered standard therapy at this time.

### ALTERNATIVE THERAPY
The number and the quality of studies evaluating acupuncture, biofeedback, herbal medicine, transcendental meditation, and yoga are, for the most part, limited. They have focused on reduction in blood pressure, not patient-oriented outcomes, such as a reduction in morbidity and mortality. Acupuncture does not appear to have a significant effect on blood pressure levels.[36,37] Biofeedback and

other behavioral techniques have not been demonstrated to reduce blood pressure.[38,39] The effect of garlic on blood pressure is unclear with mixed study results.[40,41] Transcendental meditation and yoga may reduce blood pressure, but studies of these modalities are small and the experimental designs have a limited capacity to detect an independent treatment effect or a placebo effect.[42,43]

Therefore, physicians who include any of these modalities in their hypertension treatment plan should carefully monitor each patient for adequacy of blood pressure control, development of risk factors, and evidence of end-organ damage. At this time, alternative therapies should be considered experimental adjuncts to lifestyle modification and medical therapy that have not been shown to improve patient-oriented outcomes.

## FOLLOW-UP OF PATIENTS WITH HYPERTENSION

Follow-up visits should be designed to identify new risk factors, evidence of end-organ damage, and adequacy of blood pressure control. Follow-up visits may include an interval history, limited physical examination, radiologic evaluation, and laboratory testing. The frequency and nature of follow-up hypertension evaluations will vary according to the presence or absence of preexisting risk factors, evidence of end-organ damage, the nature of the treatment the patient is receiving, and the stability of blood pressure control. Unfortunately, there is little evidence to support specific recommendations for the frequency and nature of follow-up hypertension evaluations.

In the absence of evidence, several general principles may be suggested. Patients should be seen within 2 months of initiation of treatment. Follow-up history should focus on the cardiovascular and neurologic review of systems. The examination should include a focused cardiovascular work-up (eg, retinopathy, carotid bruits). Consideration should be given to periodic laboratory testing for diabetes, renal insufficiency, and hyperlipidemia.

FIGURE 2

### ALGORITHM FOR SUBSEQUENT MANAGEMENT OF HYPERTENSION



Has the patient reached or maintained target blood pressure level in 1 to 2 months? — Yes → Check blood pressure at every office visit, monitor for onset of new risk factors, cardiovascular disease, or end organ damage.

No ↓

Increase initial agent * (consider reasons for lack of response)

Has the patient reached target blood pressure level in 1 to 2 months? — Yes → Check blood pressure at every office visit, monitor for onset of new risk factors, cardiovascular disease, or end organ damage.

No ↓

Add a second agent † (consider reasons for lack of response)

Has the patient reached target blood pressure level in 1 to 2 months? — Yes → Check blood pressure at every office visit, monitor for onset of new risk factors, cardiovascular disease, or end organ damage.

No ↓

Add a third agent ‡ (consider reasons for lack of response)

No ↓

Has the patient reached target blood pressure level in 1 to 2 months? (consider reasons for lack of response) — Yes → Check blood pressure at every office visit, monitor for onset of new risk factors, cardiovascular disease, or end organ damage.

No ↓

Resistant hypertension; refer for subspecialty consultation

* This step can be repeated until the full dose is reached.
† An agent from a second class -- usually a diuretic if this was not used as first-line agent; repeat until full dose of second agent reached.
‡ This step can be repeated until the full dose is reached.

Periodic (but less frequent) chest x-rays and electrocardiograms may be helpful to detect cardiomegaly, but there is no evidence to support such testing in the absence of symptoms.

Follow-up visits should be more frequent among patients who have marginal blood pressure control, preexisting risk factors, or end-organ damage. Evaluations may be less frequent among those with
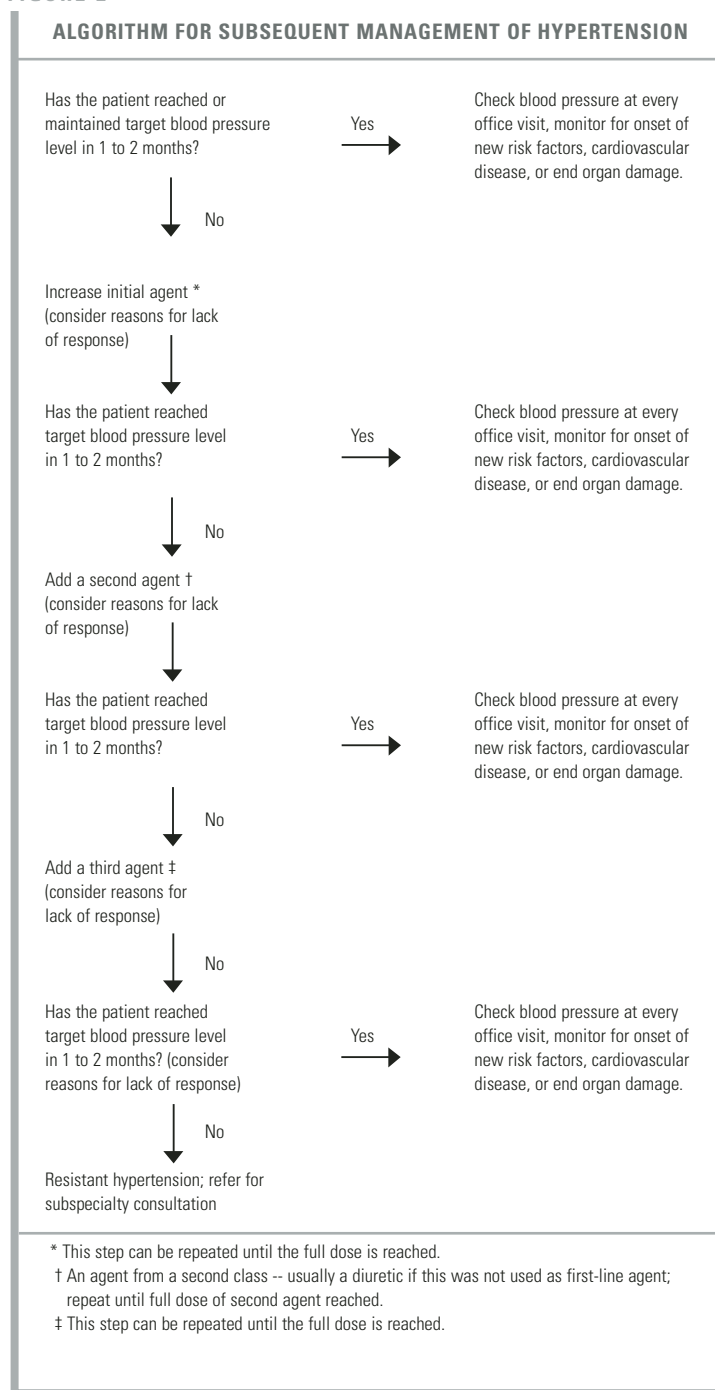
**TABLE 3**

### PARTIAL LISTING OF CAUSES OF FAILURE TO REACH OR MAINTAIN TARGET BLOOD PRESSURE

Volume overload: failure to start a diuretic
Nonadherence to therapy: dementia, side effects, complex regimen
Drug-induced: prescription, over-the-counter, herbal, or illicit drugs
Diet/stimulant induced: caffeine, licorice, salt, alcohol, nicotine
Associated conditions: obesity, sleep apnea, anxiety, chronic pain
Identifiable causes: chronic renal disease, renovascular disease,
   hyperaldosteronism, Cushing's syndrome, pheochromocytoma
Pseudoresistance: wrong cuff size, white-coat hypertension

good control and no preexisting risk factors or end-organ damage. Office visits and testing should be more frequent whenever changes are made in treatment. The frequency and nature of follow-up testing will also depend on the nature of treatment. Patients taking diuretics should have their potassium levels checked periodically. Renal function and potassium should be monitored in patients who are taking ACE inhibitors, especially during the first few weeks of therapy.

Patients willing to regularly monitor their blood pressure at home may require less frequent follow-up than those who leave it to the physician to check. Patients who monitor their blood pressure at home should have their sphygmomanometers validated initially and periodically.[44] It is important to remember that home blood pressure measurements are consistently lower and more closely correlated with cardiovascular outcomes than are clinic blood pressure measurements.[45-47]

## PROGNOSIS

It is difficult to estimate the precise impact blood pressure control has on morbidity and mortality, but it is clear that high blood pressure, if unrecognized or untreated, substantially increases the morbidity and mortality associated with coronary disease, heart failure, renal failure, and stroke.[17] In an early study of untreated hypertension there was a close relationship between blood pressure level and cardiovascular morbidity over 14 years of observation. This study revealed that hypertensive patients (those with a blood pressure of ≥ 160/95) had cardiovascular morbidity rates (coronary artery disease, claudication, stroke, and congestive heart failure) 2 to 3 times higher than normotensive patients.[48] The impact of inadequately controlled blood pressure on morbidity and mortality among patients with diabetes is especially problematic.[49] Over 9 years, when compared with diabetic patients with less tight control (< 180/105 mm Hg), those with tight blood pressure control (< 150/85 mm Hg) had a 24% reduction in sudden

death, hyperglycemic or hypoglycemic death, fatal or nonfatal myocardial infarction, angina, heart failure, fatal or nonfatal stroke, renal failure, amputation, vitreous hemorrhage, and retinal hemorrhage.

Finally, renal function deteriorates more rapidly when blood pressure control is inadequate in patients with chronic renal disease of diverse causes.[20] Over 2 years, when compared with patients with renal failure who had less tight control (mean arterial pressure ≤ 107 mm Hg), renal failure patients with tight control (mean arterial blood pressure ≤ 92 mm Hg) had significantly less proteinuria and lower rates of decline in renal function. Whether this translates into a significant improvement in the risk of end-stage renal disease is unknown.

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