

## Management of hypertension: update and review

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Hypertension is one of the commonest diseases affecting humans throughout the world. The level of blood pressure has long been recognized as a determinant of risks for several common cardiovascular diseases including coronary heart disease and cerebrovascular disease. Cardiovascular disease presents a public health crisis, affecting over sixty million Americans with fifty million hypertensives, twelve million with coronary disease, seven million with myocardial infarction and over four million with stroke. Many of these categories are still growing with prevalence of hypertension increasing as population ages. High risk populations like the blacks have a higher frequency of end organ damage. They are also disproportionately affected by a variety of cardiovascular diseases and predisposing conditions like diabetes and obesity. The most recent classification of blood pressure designates a new category of prehypertension and patients in this category are at increased risk of hypertension. Adequate control

remains an essential therapeutic approach to prevent complications and premature death. It is also an effective way to retard progression of diabetic and non-diabetic renal diseases. It is evident that treatment, regardless of approach has decreased mortality and morbidity. However, reports show that patients with well-controlled blood pressure represent only a small percentage of the hypertensive population. Thus there is clearly need to develop effective strategies to improve management. To this effect, National and International guidelines for management of hypertension have been issued. Recommendations as to forms of treatment regimens to be adopted including non pharmacological, monotherapy and appropriate combination therapy are discussed.

*Key words:* Hypertension, classification, risk factors, goals, therapy

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### Clinical Background

Hypertension is one of the most common diseases affecting humans throughout the world. As a result of the associated morbidity and mortality and the cost to society, hypertension is an important public health challenge. It is present in one in four adults in the United States and the prevalence is higher among blacks and

older persons.<sup>1</sup> Over the past several decades, extensive research, widespread patient education have lead to decreased mortality and morbidity rates from the multiple organ damage emanating from years of untreated hypertension.

Hypertension is the most important modifiable risk factor for coronary heart disease (CHD), stroke, congestive heart failure, end-stage renal disease, and peripheral vascular disease. Therefore, healthcare professionals must identify and treat patients with hypertension but also promote a healthy lifestyle and preventive strategies to decrease the prevalence of hypertension in the general population. Treatment of hypertension reduces the risk of stroke, coronary artery disease and congestive heart failure, as well as overall cardiovascular morbidity and mortality from cardiovascular causes. However, only 54 percent of patients with hypertension receive treatment and only 28 percent have adequately controlled blood pressure.<sup>1</sup>

The sixth report of the Joint National Committee on the prevention, detection, evalu-

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ation and treatment of high blood pressure (JNC VI) released in 1997<sup>1</sup> is followed by the JNC VII.<sup>1</sup> The reason for this decision was based on a number of factors: publication of many new hypertension observational studies and clinical trials; need for a new, clear and concise guideline useful for clinicians; need to simplify the classification of blood pressure (BP); and a recognition that JNC reports were not being used to their maximum benefit.

## Definition

The definition of abnormally high blood pressure is extremely difficult and arbitrary. A level for high BP must be agreed upon in clinical practice for screening patients and for instituting diagnostic evaluation and initiating therapy. Because the risk to an individual patient may correlate with the severity of hypertension, a classification system is essential for making decisions about aggressiveness of treatment. Based on the JNC VI recommendations, classification of blood pressure (expressed in mmHg) for adults aged 18 years or older was as follows:

- Optimal\* – Systolic lower than 120, diastolic lower than 80
- Normal – Systolic lower than 130, diastolic lower than 85
- High normal – Systolic 130-139 or diastolic 85-89

Hypertension was classified as follows:\*\*

- Stage 1 – Systolic 140-159 or diastolic 90-99
- Stage 2 – Systolic 160-179 or diastolic 100-109

- Stage 3 – Systolic 180-209 or diastolic 110-119
- Stage 4 – Systolic greater than or equal to 210 or diastolic greater than or equal to 120
  - \* Optimal blood pressure with respect to cardiovascular risk is below 120/80 mmHg.
  - \*\* Based on the average of 2 or more readings taken at each of 2 or more visits after initial readings.

In contrast with above classification, the JNC VII provides a more recent classification (Table 1) with an additional new category designated prehypertension with stages 2, 3, and 4 merged.

Patients with prehypertension are at increased risk for progression to hypertension; those in the 130/80 to 139/89 mmHg BP range are at twice the risk to develop hypertension as those with lower values.<sup>2</sup>

## Strategies and Evidence

Prevalence of hypertension increases as population ages unless effective preventive measures are implemented. Data from the Framingham Heart Study indicates that normotensive individuals at 55 years have a 90% lifetime risk for developing hypertension.<sup>2</sup> Relationship between BP and risk of cardiovascular disease (CVD) events is continuous, consistent and independent of other risk factors. The classification of prehypertension recently introduced in the latest (JNC VII) report (Table 1) does recognize this relationship and pinpoints the need for increased education of health care professionals and the general public to lower BP levels thereby preventing development of hypertension in the general population.<sup>3</sup>

**Table 1. Classification and management of blood pressure for adults\***

BP Classification	SBP* mmHg	DBP* mmHg	Lifestyle Modification	Initial Drug Therapy	
				Without Compelling Indication	With Compelling Indications
Normal	<120	and <80	Encourage	No antihypertensive drug indicated	Drug(s) for compelling indications <sup>†</sup>
Prehypertension	120-139	or 80-89	Yes		
Stage 1 Hypertension	140-159	or 90-99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB or combination	Drug(s) for the compelling indications. <sup>‡</sup> Other antihypertensive drugs (diuretics ACEI, ARB, BB, CCB) as needed
Stage 2 Hypertension	≥160	or ≥100	Yes	Two-drug combination for most <sup>†</sup> (usually thiazide-type diuretic and ACEI or ARB or BB or CCB)	

DBP, diastolic blood pressure; SBP, systolic blood pressure

Drug abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; CCB, calcium channel blocker

\* Treatment determined by highest BP category

<sup>†</sup> Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

<sup>‡</sup> Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.

## Benefits of BP Lowering

Antihypertensive therapy has been associated with 35% to 40% mean reductions in the incidence of stroke; 20%-25% in myocardial infarction; and over 50% in heart failure.<sup>4</sup> Estimation is that in patients with Stage 1 hypertension with additional cardiovascular risk factors, achievement of a sustained 11 mm decrease in systolic BP for 10 years will prevent one death for every 11 patients treated.<sup>4</sup>

## Blood Pressure Control Rates

The most common primary diagnosis in the United States is hypertension.<sup>5</sup> Current control rates (SBP<140 mmHg and DBP < 90 mmHg), even though improved are still far below the Healthy People 2010 goal of 50%; with 30% unaware they have hypertension. Recent trials, have confirmed that effective BP control is achievable in most hypertensives but majority will require 2 or more antihypertensive drugs.<sup>6</sup> If there is failure to prescribe lifestyle modifications; adequate antihypertensive drug doses; or appropriate drug combinations, inadequate BP control does result.

## Proper Office BP Measurement

A properly calibrated and validated auscultatory BP instrument should be used.<sup>7</sup> Patients should be seated for at least 5 minutes in a chair and arm supported at heart level. BP measurement in the standing position is periodically indicated especially in those at risk of postural hypotension. An appropriate-sized cuff (cuff bladder encircling at least 80% of the arm) should be used to ensure accuracy and at least two measurements should be made. Systolic BP is the point at which the first 2 or more sounds is heard (phase 1) and diastolic BP the point before disappearance of sounds (phase 2).

## Ambulatory BP Monitoring (ABPM)

The purpose of ambulatory BP monitoring<sup>13</sup> is to provide information about BP during daily activities and sleep. It is warranted for evaluation of 'white-coat hypertension' (blood pressure elevated when measured during an office visit but otherwise normal) and prevent unnecessary treatment. White coat hypertension, present in 20% of patients with elevated BP is associated with lower cardiovascular

risk, than sustained hypertension, but may be a precursor of sustained hypertension and therefore warrants monitoring. Ambulatory monitoring may also be helpful in assessing patients with apparent drug resistance, hypertension and autonomic dysfunction. ABPM values are usually lower than clinic readings. The level of BP using ABPM correlates better than clinic measurements with target organ injury.<sup>8</sup> It also provides a measure of the percentage of BP readings that are elevated, and extent of BP reduction during sleep. In most individuals, BP decreases by 10% to 20% during the night; those in whom such decreases are not present are at increased risk of cardiovascular events.

## Self-Measurement of BP

BP self-measurements could benefit patients, providing information on response to anti-hypertensive medication, improving adherence with therapy<sup>8</sup> and in evaluating white coat hypertension. Individuals with a mean BP of more than 135/85 mmHg measured at home are generally considered to be hypertensive.

## Patient Evaluation

There are 3 objectives in evaluating patients with proven hypertension: (a) to assess lifestyle and identify other cardiovascular risk factors (Fig. 1) (b) to reveal identifiable causes of high BP (Fig. 2) and (c) to assess the presence or absence of target organ damage (Fig. 3). Relevant data are acquired via medical history, physical examination, routine laboratory tests and other diagnostic procedures. Physical examination should include appropriate BP measurement and verification in the contralateral arm; examination of the optic fundi; body

**Figure 1. Major cardiovascular risk factors**

- Hypertension\*
- Cigarette smoking
- Obesity\* (body mass index >30 kg/m<sup>2</sup>)
- Physical inactivity
- Dyslipidemia\*
- Diabetes mellitus\*
- Microalbuminuria or estimated GFR <60mL/min
- Age (older than 55 for men, 65 for women)
- Family history of premature cardiovascular disease (men under age 55 and women under age 65)

GFR: glomerular filtration rate  
\* Components of the metabolic syndrome

**Figure 2. Identifiable causes of hypertension**

- Sleep apnea
- Drug-induced
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing's syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease

**Figure 3. Target organ damage**

- Heart
  - Left ventricular hypertrophy
  - Angina or prior myocardial infarction
  - Prior coronary revascularization
  - Heart failure
- Brain
  - Stroke or transient ischemic attack
- Chronic kidney disease
- Peripheral arterial disease
- Retinopathy

mass index (BMI) calculated as weight in kilograms divided by the square of height in meters; auscultation for carotid, abdominal and femoral bruits; palpation of the thyroid gland; thorough heart and lungs examination, abdominal examination for enlarged kidneys, masses and abnormal aortic pulsation; palpation of lower extremities for edema and pulses; and neurological assessments.

## Laboratory and Other Diagnostic Tests

The routine laboratory tests recommended before initiation of therapy include: electrocardiogram; urinalysis; blood glucose and hematocrit; serum potassium; creatinine (or corresponding estimated glomerular filtration rate) and calcium,<sup>9</sup> lipid profile (9-12 hours fasting) which includes high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides. Optional tests include measurement of urinary albumin excretion or albumin/creatinine ratio. More extensive investigation for identifiable causes is not generally indicated unless BP control is not achieved.

## Management

### TREATMENT GOALS FOR BLOOD PRESSURE

The risk of cardiovascular disease remains higher in treated patients with hypertension than in persons with normal blood pressure suggesting that treatment targets have not been low enough. Greater reductions in blood pressure have been shown to be safe and beneficial.<sup>10</sup> In the Hypertension Optimal Treatment (HOT) trial, the risk of major cardiovascular events was lowest amongst patients whose blood pressures had been reduced to 138.5/82.6 mmHg, additional reduction did not further reduce risk of events in nondiabetic patients, but was not harmful. In diabetic

patients, the lowest rates of major cardiovascular events and deaths from major cardiovascular causes were achieved with the lowest blood pressure. Most hypertensive patients, especially those over 50 years of age reach their diastolic blood pressure goal once the systolic BP is at goal. The primary aim therefore should be to achieve systolic BP goal (Fig. 4). In hypertensive patients with diabetes or renal disease, the BP goal is less than 130/80 mmHg.<sup>11</sup>

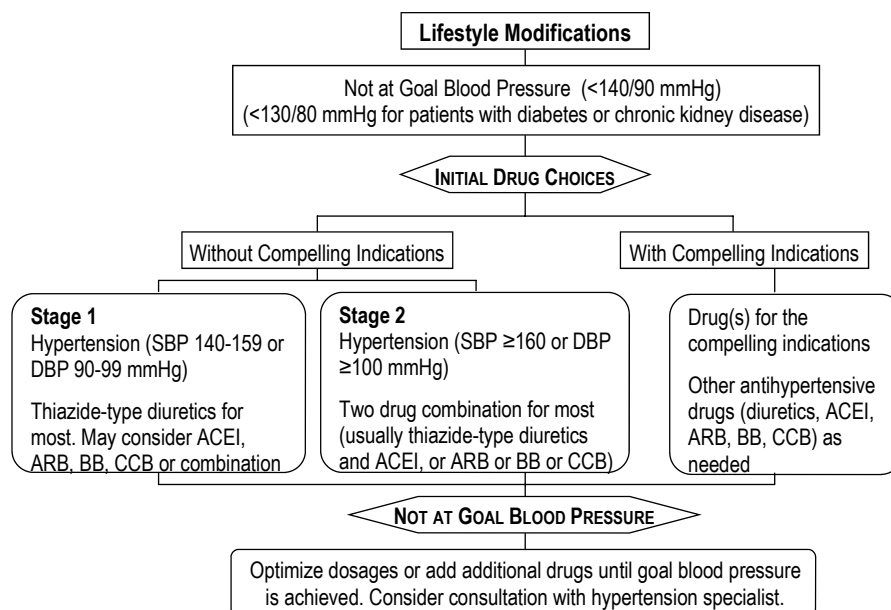
### LIFESTYLE MODIFICATIONS

Lifestyle modifications should be encouraged since they are safe and inexpensive and when combined with drug therapy may result in better blood pressure control and an improved quality of life.<sup>12</sup> The Dietary Approaches to Stop Hypertension (DASH) study showed that eight weeks of a diet of fruits, vegetables, low-fat dairy products, whole grain, poultry fish and nuts, with limited fats, red meat and sweets, reduced systolic pressure by 11.4 mmHg and diastolic pressure by 5.5 mmHg.<sup>13</sup> Major lifestyle modifications shown to lower BP include weight reduction in overweight or obese individuals<sup>14</sup> adoption of the DASH eating plan, dietary sodium reduction,<sup>15</sup> physical activity<sup>16</sup> and moderation of alcohol consumption.

### PHARMACOLOGIC THERAPY AND CHOICE OF ANTIHYPERTENSIVE DRUGS

Most antihypertensive drugs reduce blood pressure by 10-15%. Monotherapy is effective in about 15% of unselected patients and those with stage 2 hypertension often need more than one drug. Lowering BP with various classes of drugs, including angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs)  $\beta$ -blockers (BBs), calcium channel blockers (CCBs) and the thiazide-class diuretics, will all reduce com-

Figure 4. Algorithm for treatment of hypertension



DBP: Diastolic blood pressure, SBP: Systolic blood pressure  
 Drug abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker;  
 BB: beta-blocker; CCB: calcium channel blocker

plications of hypertension.<sup>4,17</sup> provides a list of classes of commonly used antihypertensive agents their contraindications and side effects. Most clinical trials confirm that thiazide-type diuretics form the basis of antihypertensive treatment.<sup>20</sup> They have been proven to prevent cardiovascular complications resulting from hypertension. In the Antihypertensive and Lipid-lowering Treatment to prevent Heart Attack (ALLHAT) trial, the largest randomized trial comparing several antihypertensive agents as initial therapy in patients older than 55 years, diuretic based therapy was more effective than treatment with CCBs in preventing heart failure; and more effective than ACE inhibitors in preventing stroke and heart failure.<sup>21</sup> Diuretics have an enhancing effect on multidrug regimens, thereby helping to achieve BP goal. Price-wise, they are cheaper than other hypertensive agents, but unfortunately still under used.<sup>21</sup>

The appropriate strategy for choosing initial antihypertensive therapy is still unresolved.<sup>22</sup> However, on the basis of available data, diuretics or BBs remain appropriate for the initial treatment of uncomplicated hypertension, in spite of the concern that these agents could be associated with adverse metabolic effects (e.g. hyperuricemia and impaired glucose tolerance). Alternative drugs are preferable for patients with certain coexisting medical conditions. In particular, ACE inhibitors and ARBs

are appropriate initial therapy in patients with diabetes mellitus, renal disease or congestive heart failure<sup>23</sup> (though  $\beta$ -blockers and diuretics are also useful in patients with heart failure). ACE inhibitors can also be used in patients with prior myocardial infarction or coronary artery disease. Short-acting CCBs cause a rapid, acute drop in blood pressure, which may precipitate coronary ischemia and long-acting CCBs are therefore preferred when this class of agents is chosen.<sup>24</sup>

#### TO ACHIEVE BP CONTROL

Most hypertensive patients will receive two or more antihypertensive drugs to achieve their BP goals.<sup>6</sup> Addition of a second drug from another class should be started when adequate doses of a single drug fail to achieve the BP goal. If BP is more than 20/10 mmHg above stated goal, consideration should be given to using two drugs singly or in fixed-dose combinations. The use of lower doses of two or more drugs with complementary mechanisms may lower blood pressure with fewer adverse effects than use of higher doses of a single agent.<sup>25</sup> Most combination therapies include small doses of a diuretic, which potentiate the effects of other drugs (ACEIs, ARBs or BBs). Combination therapy may improve compliance and achieve target BP more rapidly.<sup>25</sup> Use of lower cost generic drugs requiring less frequent doses can improve compliance.

**FOLLOW UP CARE**

Regular patient follow up and adjustment of medications in the first instance at monthly intervals until target blood pressure is achieved is of utmost importance. Stage 2 patients and those with comorbid complications should be seen more frequently. Laboratory work-up like serum creatinine and potassium should be monitored about twice a year.<sup>26</sup> When target BP is achieved and stable, follow up visits could now be at 4-6 months intervals. Attention should be paid to comorbid conditions and diseases like heart failure and diabetes mellitus respectively in terms of laboratory investigations and regularity of visits. Smoking should be rigorously avoided. Low dose aspirin should only be prescribed if target BP is achieved in order to avoid the risk of hemorrhagic stroke.

**Hypertension in Special Situations****ISCHEMIC HEART DISEASE**

In hypertensives Ischaemic Heart Disease (IHD) is the most frequent form of target organ damage. If there is evidence of stable angina pectoris, then first drug of choice is commonly a BB; or long acting CCBs could be used in the alternative. In unstable angina or myocardial infarction, initial treatment should be with BBs & ACEI.<sup>27</sup> Other drugs could be added as needed for adequate control. With postmyocardial infarction ACEs, BBs and aldosterone antagonists are useful.<sup>28</sup> Aspirin and close lipid regulation are also indicated.

**HEART FAILURE**

Systolic and diastolic ventricular dysfunction usually result from systolic hypertension and CAD. For those at risk of heart failure, tight BP and cholesterol control are the main preventive measures. If patients are asymptomatic but with evidence of ventricular diastolic dysfunction, ACEI & BBs would be the drugs of choice. Symptomatic and end stage heart disease patients will benefit from treatment with ACEIs, BBs, aldosterone antagonists, with loop diuretics.<sup>29</sup>

**DIABETES**

To achieve target goal of blood pressure for diabetes (<130/80 mmHg), a combination of two or more drugs are usually needed.<sup>11</sup> Thiazides, BBs ACEIs, ARBs and CCBs reduce the incidence of CVD and stroke,<sup>30</sup> while ACEI or

ARBs reduce albuminuria and progression of diabetic nephropathy.<sup>31</sup>

**CHRONIC KIDNEY DISEASE**

Chronic kidney disease is defined by either (a) reduced excretory function with GFR below 60 ml/min/1.73m<sup>2</sup> (equivalent to a creatinine of > 1.5 mg/dl (men) or > 1.3 mg/dl in women<sup>9</sup> (b) presence of albuminuria (>300 mg/day or 200 mg alb/gm of creatinine). Therapeutic goals in this situation are to slow deterioration in renal function and to prevent CVD. Most of these patients are hypertensive and target BP values (<130/80 mmHg) should be achieved by aggressive management – usually with a combination of three or more drugs.<sup>32</sup> ACEIs and ARBs have shown proven efficacy in retarding the progress of both diabetic and nondiabetic renal disease.<sup>31</sup> In the absence of hyperkalemia, a limited rise of serum creatinine up to 35% above baseline while treating is not a contraindication for the use of ACEIs and ARBs.

**CEREBROVASCULAR DISEASE**

In acute stroke, control of BP at intermediate levels (about 160/100 mmHg) should be the present line of management since risks and benefits of acute lowering of BP are still controversial. A combination of an ACEI and a thiazide diuretic reduces the rates of recurrent strokes.<sup>19</sup>

**SPECIAL POPULATIONS****RACE**

Blacks have a higher prevalence of hypertension and a much higher frequency of end organ damage as occurs in end-stage kidney disease, strokes and heart failure. They also demonstrate reduced BP responses to monotherapy with ACEIs, ARBs, BBs compared to diuretics or CCBs. Socioeconomic factors and lifestyle could be important barriers to BP control in blacks and some other minority groups. The differential responses are largely diffused by drug combinations which include adequate doses of a diuretic. ACEI-induced angioedema occurs 2-4 times more frequently in black hypertensive patients than in other groups.<sup>18</sup>

**GENDER**

Prevalence of hypertension is similar between men and women but women are protected from coronary artery disease prior to menopause. Premenopausal women have a higher heart rate, cardiac index and a lower peripheral

resistance than men. These changes are not encountered in postmenopausal females. Therefore, in premenopausal situations a medication such as a BB may be effective. Postmenopausal hypertension however is treated similarly to that in men.

#### OBESITY AND METABOLIC SYNDROME

Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) is a prevalent risk factor for the development of hypertension and CVD. Metabolic syndrome is defined as the presence of three or more of the following conditions: abdominal obesity (waist circumference  $> 40$  inches in men or  $< 35$  inches in women), glucose intolerance (fasting glucose  $\geq 110$  mg/dl), or low HDL ( $< 40$  mg/dl in men or  $< 50$ mg/dl in women).<sup>33</sup>

#### ELDERLY HYPERTENSIVES

More than two thirds of individuals of the age of 65 and over suffer from hypertension and also have the lowest rates of BP control. Treatment regimen for this group with hypertension, including those with isolated systolic hypertension should be along the same lines outlined for the general care of hypertension. Lower initial doses may be appropriate in many individuals to avoid symptoms. Standard doses and drug combinations may be necessary in a majority of these patients to achieve appropriate BP targets.

#### OTHER CONSIDERATIONS IN CHOICE OF THERAPY

As already indicated, hypertension is more severe and target organ damage, (especially

**Table 2. Indications for the use of antihypertensive drugs, contradictions and side effects**

Class of drug	Indications	Contradictions	Side Effects
<b>Diuretics</b>	Heart failure advanced age, systolic hypertension	Gout	Hypokalemia, hyperuricemia, glucose intolerance, glucose intolerance, hypercalcemia (thiazides), hyperlipidemia, hyponatremia, impotence (thiazides)
<b>Beta-blockers</b>	Angina, heart failure, previous myocardial infarction, tachyarrhythmias, migraine	Asthma, chronic obstructive pulmonary disease, heart block	Bronchospasm, bradycardia, heart failure, impaired peripheral circulation, insomnia, fatigue, decreased exercise tolerance, hypertriglyceridemia
<b>ACE inhibitors</b>	Heart failure, left ventricular dysfunction, previous myocardial infarction, diabetic or other nephropathy or proteinuria	Pregnancy, bilateral renal artery stenosis, hyperkalemia	Cough, angioedema, hyperkalemia, rash, loss of taste, leukopenia
<b>Calcium-channel antagonists</b>	Advanced age, systolic hypertension, cyclosporine-induced hypertension	Heart block (verapamil, diltiazem)	Headache, flushing, gingival hyperplasia, edema; short-acting calcium-channel antagonists may precipitate coronary ischemia
<b>Alpha-blockers</b>	Prostatic hypertrophy	Orthostatic hypotension	Headache, drowsiness, fatigue, weakness, postural hypotension
<b>Angiotensin-receptor antagonists</b>	ACE inhibitor-associated cough, diabetic or other nephropathy or proteinuria, congestive heart failure	Pregnancy, bilateral renal artery stenosis, hyperkalemia	Angioedema (rare), hyperkalemia

Strict lifestyle modification should be adopted by individuals with the metabolic syndrome and appropriate drug therapy should be instituted for each component as indicated.

#### LEFT VENTRICULAR HYPERTROPHY (LVH)

LVH is an independent risk factor which increases the risk of CVD. Regression results with aggressive BP management, including weight loss, sodium restriction, and treatment with all classes of antihypertensive agents except direct vasodilators hydralazine and minoxidil.<sup>1</sup>

end-stage kidney disease) more prominent among blacks. Salt sensitivity is common and sodium restriction should be encouraged. Although the magnitude of BP response to monotherapy with a diuretic or CCB may be greater than the response to monotherapy with another agent, significant reductions occur with ACEIs, ARBs and BBs when an adequate dose is given.

Side effects differ according to class of antihypertensives (Table 2). Adverse effects are reported by 10-20 percent of patients taking these drugs but quality of life improves when

hypertension is treated.<sup>12</sup> Treatment of Mild Hypertension Study and the Department of Veterans Affairs Cooperative Study both demonstrated that among the five main classes of antihypertensives, no one drug is more acceptable than the others, except that sexual dysfunction is more common among men treated with the thiazide diuretic chlorthalidone.<sup>12</sup>

## Resistant Hypertension

Resistant hypertension is failure to reach target BP in patients who are adhering to full dose of an appropriate three-drug regimen that include a diuretic. After excluding potential identifiable causes of hypertension (Fig. 2), reasons why the patient is not at target BP should be carefully explored (Fig. 5). Consultation with a hypertension specialist should be considered if target BP cannot be achieved.

**Figure 5. Causes of resistant hypertension**

### Improper BP measurement

#### Volume overload and pseudotolerance

- Excess sodium intake
- Volume retention from kidney disease
- Inadequate diuretic therapy

#### Drug induced or other causes

- Nonadherence
- Inadequate doses
- Inappropriate combinations
- Nonsteroidal anti-inflammatory drugs; cyclooxygenase 2 inhibitors
- Cocaine, amphetamines, other illicit drugs
- Sympathomimetics (decongestants, anorectics)
- Oral contraceptives
- Adrenal steroids
- Cyclosporine and tacrolimus
- Erythropoietin
- Licorice (including some chewing tobacco)
- Selected over-the-counter dietary supplements and medicines (e.g. ephedra, ma haung, bitter orange)

#### Associated conditions

- Obesity
- Excess alcohol intake

## Guidelines

National and International groups have issued guidelines for the treatment of hypertension. The main differences between these guidelines are the criteria for initiating drug therapy in low risk patients with stage 1 hypertension. The JNC (1) and the World Health Organization (WHO) – International Society of Hypertension recommended stratification of patients into risk categories on the basis of age, sex, smoking status, presence or absence of diabetes, cholesterol level, pre-existing CVD and

presence or absence of target-organ damage (Fig. 3). Drug treatment is recommended for stage 1 or higher hypertension if BP does not decrease after a certain period of lifestyle-modification counseling (6 to 12 months according JNC guidelines). When drugs are indicated, those that have been shown to improve cardiovascular outcomes, with co-existing conditions and demographic characteristics are taken into account.

## Conclusions and Recommendations

Hypertension affects 25 percent of adults in the United States and is adequately treated in less than 30 percent of them. Appropriate therapy does reduce BP and cardiovascular mortality. Persons with stage 1 hypertension and are at low risk for CVD should be treated with lifestyle modifications for up to one year. Those who have stage 1 hypertension with other cardiovascular risk factors or a higher stage of hypertension should be treated with drugs to reduce BP to a level below 140/90 mmHg or to reduce pressure to 130/80 mmHg or less if patient has diabetes, renal disease or both. Diuretics and BBs are appropriate as first line therapy for patients without coexisting conditions. ACEIs or ARBs are recommended for persons with type 2 diabetes, kidney disease or both and are useful in patients with heart failure. BBs and ACEIs are recommended in patients with heart failure. BBs and ACEIs are recommended in patients with prior myocardial infarction, and CCBs benefit elderly patients at risk of stroke. If BP is not controlled with an optimal dose of a single drug, then a single agent with a complementary mechanism of action should be added. Combination therapy provides more rapid control of BP than does monotherapy and is therefore an initial treatment option for patients with stage 2 hypertension.

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### CME Questions

After you have completed reading the above article, take the test given below. Circle T (True) or F (False) in the answer sheet on page 90 to show the correct answer to each question. Questions 11 to 20 are related to the content in this article.

11. The first line therapeutic agent for the treatment of a hypertensive with diabetic nephropathy is ACE Inhibitors.
12. Transient ischemic attack is a sign of target organ damage.
13. Use of thiazide-type diuretics has a favorable effect in the treatment of a patient with gout.
14. Ambulatory monitoring is NOT useful in the assessment of patients with apparent drug resistance.
15. Treatment of hypertension reduces the risk of cardiovascular morbidity and mortality.
16. Blacks have a lower prevalence of hypertension and lower frequency of end organ damage.
17. More than two thirds of individuals of the age of 65 years suffer from hypertension.
18. The risk of major cardiovascular events is lowest amongst patients whose blood pressure had been reduced to 138.5/82.6 mmHg.
19. Monotherapy is effective in about 70% of unselected patients with hypertension.
20. Most clinical trials confirm that thiazide-type diuretics form the basis of antihypertensive treatment.