CME CREDIT

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JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE

New hypertension guidelines set aggressive goals based on risk factors

ABSTRACT

Physicians and public health officials need to intensify their efforts to detect and treat high blood pressure, because the incidence of hypertension-related morbidity and mortality has stopped declining, and fewer than 30% of hypertensive patients have their blood pressure under control. The JNC VI report outlines the current standard of care for treating hypertension.

KEY POINTS

Persons with the highest cardiovascular risk—those with diabetes, heart failure, or renal failure—should begin treatment with both lifestyle modifications and antihypertensive drugs, even if their blood pressure is in the high-normal range of 130–139/85–89 mm Hg. In these patients, the goal blood pressure is 130/85 mm Hg or lower, whereas the goal in persons without these risk factors is 140/90 mm Hg or lower.

The new guidelines still recommend diuretics and beta-blockers as initial drug choices for uncomplicated hypertension. However, other drug classes are also recommended when hypertensive patients have diabetes with proteinuria, heart failure, or isolated systolic hypertension.

THE UPPER LIMIT OF NORMAL blood pressure is not necessarily 140/90 mm Hg any more. Physicians need to treat hypertension more aggressively, intervene with lifestyle modifications and medication earlier, and, for some patients, pursue lower target blood pressures than in the past. These strategies are especially important for patients with risk factors for cardiovascular disease or who already have target organ damage.

Those are key messages in the report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[1] the sixth such report issued by the National High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute since its founding in 1972.

EDITOR'S NOTE

The sixth (and latest) report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure provides the most aggressive recommendations to date for reducing risk in hypertensive patients.[1]

The National High Blood Pressure Education Program has been issuing these reports since 1972, revising them periodically as new information has become available from clinical trials.

To obtain a copy, write to Ed Roccella, PhD, National Heart, Lung, and Blood Institute, 31 Center Drive-MSC2480, Bethesda, MD 20892-2480, or download the document from the NHLBI web site (www.nhlbi.nih.gov/nhlbi/nhlbi.htm).

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The report, dubbed "JNC VI," goes further than its predecessors in its scope and in basing its treatment recommendations on scientific evidence. Although many of its recommendations arose from extensive published findings, the new report is a consensus of the nation's experts in the treatment of hypertension, and will define the standard of care for hypertension for the next several years.

Among the key recommendations:

- A blood pressure of 140/90 mm Hg is no longer the target blood pressure for everyone. Patients with heart failure, diabetes mellitus, or renal insufficiency are candidates for immediate treatment with antihypertensive drugs and lifestyle modifications even if their blood pressures are as low as 130/85.
- For patients without serious risk factors but with blood pressure in the high-normal range of 130/85 to 139/89 mm Hg, physicians should be more aggressive in prescribing lifestyle modifications (weight loss, increased exercise, and reduced alcohol and salt intake) to lower the blood pressure to less than 130/85.

The new report still recommends diuretics and beta-blockers as initial drug choices for uncomplicated hypertension. However, it also recommends certain additional drug classes when hypertensive patients have diabetes, heart failure, or isolated systolic hypertension.

PHYSICIANS ARE UNDERTREATING HYPERTENSION

The new recommendations are more aggressive partly because there is disturbing evidence that we are undertreating hypertension. From 1972 until 1992, the rates of hypertension-related morbidity and mortality declined dramatically. However, since then, progress seems to be slowing or even regressing. For example:

- Age-adjusted stroke rates have risen slightly since 1993, while the age-adjusted rate of coronary heart disease has remained stable.[2]
- The incidence of end-stage renal disease is increasing. (Hypertension is the second most common cause of renal failure, after diabetes.)[3]
- The incidence of heart failure is increasing, especially in elderly patients. (The great majority of heart failure patients have antecedent hypertension.)[4]
- Today, fewer persons with hypertension are aware of it, receive treatment for it, and have it under control compared with 5 or 6 years ago. In 1991 through 1994, the National Health and Nutrition Examination Survey estimated that only 27.4% of persons with hypertension had their blood pressure controlled to the recommended level of less than 140/90 mm Hg. By comparison, the figure was 29% in 1988–1991 (an increase from 10% in 1976–1980).[5]

These trends indicate a need for intensified education for both health-care professionals and the public. In particular, the JNC VI report calls for Americans to pursue a healthier lifestyle that would lead to a lower prevalence of hypertension and cardiovascular disease, and says that preventing and treating hypertension will be a major public health challenge in the new millennium.[6]

A point not stated explicitly in the JNC VI report but which I believe is important: physicians should not accept less-than-optimal results when treating high blood pressure. If a patient begins with a blood pressure of approximately 180/110 mm Hg, and with treatment succeeds in lowering it to approximately 150/100 mm Hg, many physicians would be satisfied. But 150/100 is still too high. The JNC VI report says: "The goal of prevention and management of hypertension is to reduce morbidity and mortality by the least intrusive means possible. This may be accomplished by achieving and maintaining systolic blood pressure below 140 mm Hg and diastolic blood pressure below 90 mm Hg and lower if tolerated, while controlling other modifiable risk factors for cardiovascular disease. Treatment to lower levels may be useful, particularly to prevent stroke, to preserve renal function, and to prevent or slow heart failure progression."

Physicians should not accept less than optimal blood pressure control

URGENCY OF DRUG TREATMENT DEPENDS ON LEVEL OF RISK

Although it is well known that the risk of cardiovascular disease increases with blood pressure (recent evidence shows that systolic

TABLE 1

Using risk factors in deciding whether to give drug treatment for hypertension

BLOOD PRESSURE	RISK GROUP A No risk factors* No target organ damage† No clinical cardiovascular disease†	RISK GROUP B At least one risk factor, not including diabetes No target organ damage No clinical cardiovascular disease	RISK GROUP C Target organ damage, clinical cardiovascular disease, or diabetes, with or without other risk factors
High-normal 130/85–139/89 mm Hg	Lifestyle modification only	Lifestyle modification only	Drug therapy‡ (for those with heart failure, renal insufficiency, or diabetes)
Stage 1 140/90–159/99 mm Hg	Lifestyle modification trial (up to 12 months)	Lifestyle modification trial (up to 6 months) Or drug therapy (patients with multiple risk factors)‡	Drug therapy‡
Stages 2 and 3 ≥ 160/100 mm Hg	Drug therapy‡	Drug therapy‡	Drug therapy‡

*Smoking, dyslipidemia, diabetes mellitus, age > 60 years, gender (men and postmenopausal women), family history of cardiovascular disease in women younger than age 65 or men younger than age 55

†Heart diseases (left ventricular hypertrophy, angina, previous myocardial infarction, previous coronary revascularization, heart failure), nephropathy, peripheral arterial disease, retinopathy, stroke, transient ischemic attack

‡Lifestyle modification should be adjunctive therapy for all patients recommended for pharmacologic therapy

SOURCE: FROM THE JNC VI REPORT, REFERENCE 1

blood pressure is more important than diastolic pressure), high blood pressure is only one of many risk factors. Accordingly, the JNC VI devised a three-tiered risk classification system (TABLE 1). The urgency of starting antihypertensive drug treatment depends not on the patient's blood pressure alone, but also on his or her overall level of risk, as reflected by the patient's risk factor class.

As stated, everyone with a blood pressure of 130/85 mm Hg or higher should modify their lifestyle to lower their blood pressure: lose weight, exercise more, drink alcohol only in moderation, and decrease salt intake, while maintaining an adequate intake of potassium. (Avoiding tobacco and eating less fat do not affect blood pressure, but were recommended to decrease cardiovascular risk.)

Risk group A has the lowest risk: no risk factors other than hypertension, no target organ damage, and no clinical cardiovascular disease. Persons in this group with stage 1 hypertension (140/90–159/99 mm Hg) can undergo a trial of lifestyle modification alone for up to 12 months. Those with higher blood pressure should start lifestyle modification and drug therapy immediately.

Risk group B consists of persons with at least one additional risk factor (not including diabetes), but no target organ damage or clinical cardiovascular disease. Persons in this group with stage 1 hypertension can try lifestyle modification alone for up to 6 months if they have only one risk factor. Patients with higher blood pressure or with more than one risk factor should begin lifestyle modification and drug therapy immediately.

Risk group C has the highest risk: target organ damage, clinical cardiovascular disease, or diabetes, with or without other risk factors.

As stated above, persons with heart failure, diabetes, or kidney failure should begin lifestyle modification and drug therapy immediately, even if their blood pressure is in the high-normal range of 130/85 to 139/89 mm Hg.

DRUG THERAPY RECOMMENDATIONS

Initiating drug therapy

Like the previous report, issued in 1993,[7] the JNC VI report recommends diuretics or beta-blockers as initial drug choices for hypertension that is not complicated by concomitant diseases. These are still the only classes of drugs proven in large-scale clinical trials to decrease morbidity and mortality (TABLE 2). This recommendation may change when the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial [ALLHAT] concludes,[8] which is expected in the year 2002.

In a departure from the previous report, the JNC VI report emphasizes four compelling indications for using other classes of drugs (TABLE 3):

Type 1 diabetes mellitus with proteinuria: Angiotensin-converting enzyme (ACE) inhibitors are indicated.

Heart failure due to systolic dysfunction: ACE inhibitors and diuretics are indicated.

Isolated systolic hypertension in older patients: Diuretics are preferred, but long-acting dihydropyridine calcium antagonists may also be indicated.

Postmyocardial infarction: Beta-blockers without intrinsic sympathomimetic activity (TABLE 3) are indicated; ACE inhibitors are indicated for patients with systolic dysfunction.

The report also identifies several less compelling indications, and some relative contraindications, for specific classes of drugs (TABLE 3).

Adjusting drug therapy

If the initial drug at a full dose has no effect on the blood pressure or causes troublesome side effects, JNC VI recommends *substituting* a drug from a different class. However, if the initial drug produces only a partial response but is tolerated well, JNC VI recommends *adding*

TABLE 2

Algorithm for treating hypertension

BEGIN OR CONTINUE LIFESTYLE MODIFICATIONS

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NOT AT GOAL BLOOD PRESSURE
< 140/90 mm Hg, or lower for patients with diabetes or renal disease

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Initial drug choices
Use unless contraindicated; start with a low dose of a long-acting once-daily drug, and titrate dose; low-dose combinations may be appropriate

- Uncomplicated hypertension
  - Diuretics
  - Beta-blockers
- Diabetes mellitus (type 1) with proteinuria
  - ACE inhibitors
- Heart failure
  - ACE inhibitors
  - Diuretics
- Isolated systolic hypertension (older persons)
  - Diuretics preferred
  - Long-acting dihydropyridine calcium antagonists
- Myocardial infarction
  - Beta-blockers without intrinsic sympathomimetic activity
  - ACE inhibitors (patients with systolic dysfunction)

↓

NOT AT GOAL BLOOD PRESSURE

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No response or troublesome side effects → **Substitute another drug from different class**

Inadequate response but well tolerated → **Add second agent from different class** (diuretic if not already used)

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NOT AT GOAL BLOOD PRESSURE

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Continue adding agents from other classes
Consider referral to a hypertension specialist

SOURCE: FROM THE JNC VI REPORT, REFERENCE 1

TABLE 3

Indications for using particular classes of drugs to individualize antihypertensive drug therapy

COMPELLING INDICATIONS*	LESS-COMPELLING INDICATIONS†	RELATIVE CONTRAINDICATIONS‡
Diabetes mellitus (type 1 with proteinuria) ACE inhibitors	**Angina** Beta-blockers Calcium antagonists	**Bronchospastic disease** Beta-blockers (contraindicated)
Heart failure due to systolic dysfunction ACE inhibitors Diuretics	**Atrial tachycardia and fibrillation** Beta-blockers Calcium antagonists (nondihydropyridine)	**Depression** Beta-blockers Centrally-acting alpha-agonists Reserpine (contraindicated)
Isolated systolic hypertension (older patients) Diuretics (preferred) Calcium antagonists (long-acting dihydropyridines)	**Cyclosporine-induced hypertension** Calcium antagonists (caution with the dose of cyclosporine)	**Diabetes (type 1 and 2)** Beta-blockers Diuretics (in high doses)
Myocardial infarction Beta-blockers without intrinsic sympathomimetic activity (ie, atenolol, betaxolol, bisoprolol, metoprolol, nadolol, propranolol, timolol) ACE inhibitors (patients with systolic dysfunction)	**Diabetes mellitus with proteinuria** ACE inhibitors (preferred) Calcium antagonists	**Dyslipidemia** Beta-blockers without intrinsic sympathomimetic activity Diuretics (high doses)
	Diabetes mellitus (type 2) Low-dose diuretics	**Gout** Diuretics
	Dyslipidemia Alpha-blockers	**Heart block (second- or third-degree)** Beta-blockers (contraindicated) Nondihydropyridine calcium antagonists (contraindicated)
	Essential tremor Beta-blockers (noncardioselective)	**Heart failure** Beta-blockers (except carvedilol) Calcium antagonists (except amlodipine, felodipine)
	Heart failure Carvedilol Losartan	**Liver disease** Labetalol Methyldopa (contraindicated)
	Hyperthyroidism Beta-blockers	**Peripheral vascular disease** Beta-blockers
	Migraine Beta-blockers (noncardioselective) Calcium antagonists (nondihydropyridine)	**Pregnancy** ACE inhibitors (contraindicated) Angiotensin II receptor blockers (contraindicated)
	Myocardial infarction Diltiazem Verapamil	**Renal insufficiency** Potassium-sparing agents
	Osteoporosis Thiazides	**Renovascular disease** ACE inhibitors Angiotensin II receptor blockers
	Preoperative hypertension Beta-blockers	
	Prostatic hypertrophy Alpha-blockers	
	Renal insufficiency ACE inhibitors (caution in renovascular hypertension and creatinine ≥ 3 mg/dL)	

*Proved to have beneficial effects on comorbid conditions in randomized clinical trials
†*May* have favorable effects on comorbid conditions
‡*May* have unfavorable effects on comorbid conditions; may be used with special monitoring unless contraindicated

SOURCE: FROM THE JNC VI REPORT, REFERENCE 1

another drug from a different class, preferably a diuretic if not already used (TABLE 2).

The point, in my experience, is to avoid substituting one drug after another ("sequential monotherapy") in a frustrating and futile search for a single, ideal drug to control the patient's blood pressure. Patients become dissatisfied with this approach and either drop out of therapy or consult another physician.

CHALLENGE TO MANAGED CARE: SAVE MONEY BY CONTROLLING HYPERTENSION

Treating high blood pressure is expensive, but in the long run it costs less than treating the consequences of hypertension: heart disease, stroke, and renal failure.[9–11] Herein lies an opportunity for managed care organizations, which have a vested interest in keeping their patients healthy. The JNC VI report suggests that managed care organizations could "...use a coordinated approach to care, using various health care professionals and featuring an appropriate frequency of office visits, short waiting times, supportive patient counseling, and controlled formularies." By so doing, they could avoid many hospitalizations, surgical procedures, and use of expensive technology.

The role of hypertension specialists, the report says, will be to provide cost-effective care by adapting national guidelines for local care, by providing guidance for using new drugs and diagnostic procedures, and by managing patients with resistant hypertension, secondary hypertension, and complex concomitant conditions.

EVIDENCE-BASED APPROACH TO HYPERTENSION MANAGEMENT

The new JNC report, more than earlier reports, references the published studies from which each prevention or treatment recommendation emanated. Codes next to the references in the section of the JNC VI report on prevention and treatment specify what kind of data is the basis for the recommendation (meta-analysis, randomized controlled trial, retrospective analysis, prospective follow-up study, cross-sectional population study, review or position statements, and nonrandomized clinical interventions).

Shortcomings of randomized controlled trials

Where possible, the committee tried to base its recommendations on randomized controlled trials. Nonetheless, as the report notes, this approach has its limitations.

For instance, randomized controlled trials are of short to moderate duration, whereas the benefit of hypertension treatment accrues over a lifetime. Most do not include a true placebo group, thus underestimating the benefit of the trial. Most do not truly represent clinical practice because some patients, typically those at higher risk, are excluded. The average reduction in blood pressure in clinical trials is modest and underestimates the additional benefits that accrue from larger decreases in blood pressure, which may be seen in individual patients.

Trials focus on predetermined endpoints and not necessarily on other benefits of therapy such as improved quality of life, reduced impact of comorbid conditions, fewer workdays missed due to illness, and prevention of progression to disease endpoints.

Thus, in making their recommendations, the JNC VI members stated that they "extrapolated the treatment effects beyond the duration of clinical trials, based on physiological and epidemiological data."[1]

This need to extrapolate beyond existing evidence underscores the evolving state of hypertension treatment and the interplay between the science and the art of medicine.

Treating high blood pressure costs less than treating its consequences

THE PRIMARY MESSAGE OF JNC VI

The most important message of JNC VI, however, is the simplest one, that despite our knowledge of the long-term beneficial effects of treating hypertension, much remains to be done until Americans are treated properly for this potentially devastating condition.

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