CURRENT DRUG THERAPY



The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: insights and highlights from the chairman

RAY W. GIFFORD, JR, MD

The fifth Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V) has recommended a new algorithm for treating hypertension that emphasizes the use of drugs shown in randomized clinical trials to reduce cardiovascular morbidity and mortality---namely, diuretics and beta blockers. The report contains several new sections, including new data from the National Health and Nutrition Examination Survey (NHANES III) on prevalence, awareness, treatment, and control of hypertension, a new classification schema that includes systolic and diastolic criteria, and sections on the effects of cocaine, lithotripsy, cyclosporine, and erythropoietin to induce or aggravate hypertension. Other topics have been greatly expanded, including special populations and situations, primary prevention of hypertension, and life-style modifications. The INC V report has also added alpha-1 adrenergic blocking agents and the alpha-beta blocker labetalol to the list of drugs suitable for initial monotherapy in managing hypertension.

■ INDEX TERMS: HYPERTENSION; PRIMARY PREVENTION; PRACTICE GUIDELINES ■ CLEVE CLIN J MED 1993; 60:273–277

From the Department of Nephrology and Hypertension, The Cleveland Clinic Foundation.

Address reprint requests to R.W.G., Department of Nephrology and Hypertension, A101, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195. INCE ITS INCEPTION IN 1972, the National High Blood Pressure Education Program (NHBPEP) of the National Heart, Lung, and Blood Institute (NHLBI) has published state-of-the-art guidelines for physicians and other health professionals on detection, evaluation, and treatment of patients with high blood pressure. The fifth report has recently been published.¹

These reports are based on scientific evidence when it exists, and on consensus when it doesn't. The committees, known as Joint National Committees (JNC), are appointed by the Coordinating Committee of the NHBPEP and include authorities on hypertension from a variety of health care disciplines including physicians, nurses, pharmacists, epidemiologists, biostatisticians, public health officials, nutritionists, and health educators.

In the past few years, a great deal of new information has been published in the field of hypertension, and debate has ensued on many is-

TABLE CLASSIFICATION OF BLOOD PRESSURE FOR ADULTS AGE 18 AND OLDER*

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal†	< 130	< 85
High normal	130 - 139	85 - 89
Hypertension‡ Stage 1 (mild)	140 - 159	90 - 99
Stage 2 (moderate)	160 - 179	100 - 109
Stage 3 (severe)	180 - 209	110 - 119
Stage 4 (very severe)	≥ 210	≥120

*Not taking antihypertensive drugs and not acutely ill. When systolic and diastolic pressure fall into different categories, the higher category should be selected to classify the individual's blood pressure status. For instance, 160/92 should be classified as stage 2, and 180/120 should be classified as stage 4. Isolated systolic hypertension is defined as systolic blood pressure ≥ 140 mm Hg and diastolic blood pressure < 90 mm Hg and staged appropriately (eg, 170/85 mm Hg is defined as stage 2 isolated systolic hypertension). (From the fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, reference 1.)

[†]Optimal blood pressure with respect to cardiovascular risk is a systolic blood pressure < 120 mm Hg and a diastolic blood pressure < 80 mm Hg. However, unusually low readings should be evaluated for clinical significance.

*Based on the average of two or more readings taken at each of two or more visits following an initial screening.

Note: In addition to classifying stages of hypertension based on average blood pressure levels, the clinician should specify the presence or absence of target-organ disease and additional risk factors. For example, a patient with diabetes and a blood pressure of 142/92 mm Hg plus left ventricular hypertrophy should be classified as "stage 1 hypertension with target-organ disease (left ventricular hypertrophy) and with another major risk factor (diabetes)." This specificity is important for risk classification and management.

sues. As chairman of the fifth JNC, my duty was to help the committee synthesize volumes of data and find the common ground among the occasionally divergent views of the experts. Since it would take too long to review all of the many features of the JNC V report here, I have chosen to comment on four major areas of the report.

DATA FROM NHANES III

We are indebted to the National Center for Health Statistics of the Centers for Disease Control for permitting us to publish, for the first time, data from the 1988-1991 National Health and Nutrition Examination Survey (NHANES III) concerning the prevalence, awareness, treatment, and control rates of hypertension in the United States.

The good news is that the prevalence of hypertension (diastolic blood pressure \geq 90 mm Hg or systolic blood pressure \geq 140 mm Hg) in the United States has fallen from 58 million in the 1976-1980 survey (NHANES II) to 50 million in the most recent survey. Some of this decrease may be due to methodologic differences between NHANES II and NHANES III in how data were obtained. Awareness rates (for hypertension defined as ≥160/95 mm Hg) have increased from 51% 1971-1972 in (NHANES I) to 84% now. and control rates for this level of hypertension have increased from 16% in 1971-1972 to 55% now. The bad news is that only 21% of all hypertensive patients have their blood pressure controlled to levels of less than 140/90 mm Hg.

The report also includes the most recent data from the National Center for Health Statistics; these data show that, since the inception of the NHBPEP in 1972, the mortality rate

from coronary heart disease has decreased by 50%, and the mortality rate from stroke has fallen by 57%. These declines in mortality rates have been shared by men and women, both black and white.

PREVENTION OF HYPERTENSION

Recent clinical trials^{2,3} have demonstrated the feasibility of preventing or delaying the onset of hypertension by life-style modifications, such as restricting sodium and alcohol intake, exercising regularly, and maintaining lean body weight. The evidence is so compelling that prevention has been given more attention in JNC V than in previous reports, and a companion report from the NHBPEP in the same issue of Archives of Internal Medicine is devoted to this topic.⁴

Some of the dramatic decline in the prevalence of hypertension reported by NHANES III suggests that people may already be changing their lifestyles.

NEW CLASSIFICATION OF HYPERTENSION

The JNC V presents a totally new classification system for hypertension, moving away from the traditional categories of mild, moderate, and severe, to the use of stages 1 through 4 (*Table*). For the first time, this classification incorporates systolic blood pressure criteria in addition to diastolic criteria. This is long overdue, because it has become increasingly apparent that systolic blood pressure is a better predictor of cardiovascular events and total mortality than is diastolic blood pressure.⁵

The terms "mild" and "moderate" hypertension frequently fostered a sense of complacency for both patients and physicians that was not conducive to effective treatment. We hope that "stage 1 hypertension" will be taken more seriously. To more accurately assess cardiovascular risk, the JNC V report also emphasizes the importance of qualifying the diagnosis by specifying the presence or absence of other risk factors and target-organ disease (*Table*). This has important implications for prognosis.^{6,7}

Toward the goal of reducing cardiovascular events overall, the JNC V report emphasizes the importance of identifying and treating all risk factors, in addition to hypertension.

A NEW ALGORITHM FOR TREATMENT

The JNC V report, like those before it, advocates life-style modifications as initial therapy for patients with stage 1 hypertension and as adjunctive therapy for all hypertensive patients.

Probably the most controversial aspect of this report, judging from the editorial comment that accompanied its publication,⁸ was the new algorithm for pharmacologic treatment (Figure), which recommends prescribing a diuretic or beta blocker first, unless there is a contraindication to their use or an indication for another class of agents. There is a compelling reason for this apparent "step backward" from the previous report,⁹ which recommended diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, or calcium antagonists for initial pharmacologic therapy. (JNC V has added selective alpha-1 adrenergic blockers and the alphabeta blocker labetalol to this list.) All of the numerous randomized clinical trials that have shown a reduction in stroke and cardiovascular events have used either a diuretic or a beta blocker as initial

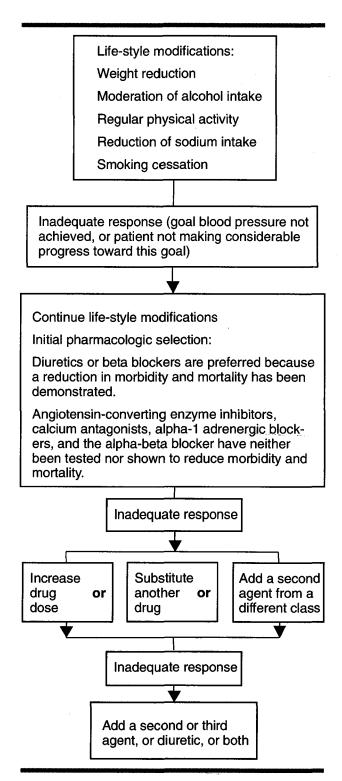


FIGURE. Algorithm for treating high blood pressure. (Adapted from the fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, reference 1.)

JNC V REPORT GIFFORD

therapy.¹⁰⁻¹³ Consequently, the recommendation to give preference to these agents is consistent with the goal of treatment as stated in JNC V, "to prevent morbidity and mortality associated with high blood pressure and to control high blood pressure by the least intrusive means possible."

It is interesting that the Canadian Hypertension Society Consensus Conference on Pharmacologic Treatment of Hypertension, meeting separately but concurrently with the JNC V, has come to similar conclusions regarding the recommendation of diuretics or beta blockers as preferred drugs for initial therapy—and for the same reasons.¹⁴

The metabolic side effects of the diuretics and beta blockers are well known and can readily be identified by monitoring serum levels of electrolytes, lipids, and glucose, which the report recommends. Many of these adverse metabolic events are minimized, if not eliminated, by prescribing low doses,¹⁵ which the report also recommends. In the placebocontrolled Treatment of Mild Hypertension Study,¹⁶ in which all participants were advised to adopt lifestyle changes with regard to diet, alcohol consumption, and exercise, the minimal adverse effect of chlorthalidone on serum cholesterol did not persist after the first year.¹⁷

If the response to initial therapy is inadequate after 1 to 3 months, the physician has three options to attain better control of the blood pressure as shown in the *Figure*. The dose of the first drug can be increased to or toward maximal levels, another agent may be substituted for the initial drug, or a second drug from another class may be added to the regimen.

The Committee discussed and rejected suggestions that ACE inhibitors, calcium antagonists, or alpha-1 adrenergic blockers should be recommended as preferred agents for diabetic hypertensive patients, and that diuretics and beta blockers should be contraindicated for these patients. In the Treatment of Mild Hypertension Study,¹⁶ none of the drugs had an adverse effect on fasting blood glucose, and in the Hypertension Detection and Follow-up Program, using chlorthalidone in doses of 50 to 100 mg daily, diabetic participants in stratum 1 (diastolic blood pressure 90 to 104 mm Hg) derived just as much benefit from stepped care as did nondiabetic participants with regard to reduction in total mortality.¹⁸

The Committee recognized the failure of some of the randomized trials using diuretics or beta-blockers to reduce coronary events as much as would be predicted from observational studies.¹⁰ However, most of the observational data were collected over periods of 6 to 25 years, whereas the average duration of randomized treatment trials was less than 5 years.¹⁹ Moreover, the 8.5-year follow-up data from the Hypertension Detection and Follow-up Program²⁰ and the 10.5-year follow-up data from the Multiple Risk Factor Intervention Trial²¹ showed greater decreases in coronary events than did the original, shorter trials. In controlled trials using lipid-lowering agents to reduce the incidence of coronary events, a beneficial effect is not usually realized until after 3 or 4 years.¹⁹

The JNC V report strongly recommends a randomized, controlled trial comparing a diuretic with an ACE inhibitor and a calcium antagonist to determine whether any of these drugs is superior to others in terms of reducing cardiovascular morbidity and mortality. Until such a trial is carried out, it is simply conjecture to conclude that newer agents with no metabolic side effects will be more effective than diuretics and beta blockers in reducing cardiovascular morbidity and mortality. The Committee was not as impressed by short-term studies using surrogate endpoints as it was by long-term randomized clinical trials.

The Committee labored diligently to craft the recommendation regarding the choice of the firststep agent in such a way that it would not deprive physicians of flexibility in selecting agents for treating hypertension. These are only guidelines, not rules. In the last 30 years, we have evolved from controversy regarding whether or not hypertension should be treated at all to controversy over which drug or drugs to use.

If, in the opinion of the treating physician, there are no special indications for other drugs, why not prescribe an agent that has been proved by clinical trials to reduce morbidity and mortality?

SPECIAL POPULATIONS AND SITUATIONS

The JNC V report goes on to describe hypertension in special populations and situations that require more attention from physicians and public health groups. For example, the frequency of hypertension in black Americans is among the highest in the world; blacks develop hypertension at an earlier age than whites; and, furthermore, at any decade of life, hypertension is more severe in blacks than in whites. Once again, diuretics are the drugs of first choice in this population because they have been shown to reduce morbidity and mortality.

The report discusses miscellaneous causes for increased blood pressure and describes management of hypertension in children, women, older patients, those with coexisting cardiovascular or other diseases, and patients undergoing surgery. The report also provides 117 selected references and a glossary of terms that deciphers the acronyms used for a number of important clinical studies.

This document is evidence of what can be accomplished when professionals with different views come together to address an important health issue.

ACKNOWLEDGMENT

It was my privilege to be general chairman of the fifth Joint National Committee. In all, there were 55 members who

REFERENCES

- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). Arch Intern Med 1993; 153:154– 183.
- Stamler R, Stamler J, Gosch FC, et al. Primary prevention of hypertension by nutritional-hygienic means. Final report of a randomized, controlled trial. JAMA 1989; 262:1801–1807.
- 3. The Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. JAMA 1992; 267:1213-1220.
- National High Blood Pressure Education Program Working Group. National High Blood Pressure Education Program Working Group report on primary prevention of hypertension. Arch Intern Med 1993; 153:186–208.
- 5. Rutan GH, McDonald RH, Kuller LH. A historical perspective of elevated systolic vs diastolic blood pressure from an epidemiological and clinical trial viewpoint. J Clin Epidemiol 1989; 42:663-673.
- Hypertension Detection and Follow-up Program Cooperative Group. Results of the Hypertension Detection and Follow-up Program. The effect of treatment on mortality in "mild" hypertension. N Engl J Med 1982; 307:976–980.
- Gifford RW Jr. Role of multiple risk factors in cardiovascular morbidity and mortality. Cleve Clin J Med 1993; 60:211–218.
- Weber MA, Laragh JH. Hypertension: steps forward and steps backward. The Joint National Committee's fifth report (editorial). Arch Intern Med 1993; 153:149–152.
- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The 1988 report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1988; 148:1023–1038.
- Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease. Part 2, short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. Lancet 1990; 335:827–838.
- 11. SHEP Cooperative Research Group. Prevention of stroke by

worked in the following four subcommittees: Clinical Evaluation and Public Health Aspects—Chairman, Jeremiah Stamler, MD, Chicago, Ill; Pharmacologic Treatment—Chairman, Edward Frohlich, MD, New Orleans, La; Life-style Modifications—Chairman, Norman Kaplan, MD, Dallas, Tex; and Special Populations and Situations—Chairman, James Reed, MD, Atlanta, Ga.

Reports of these subcommittees were collated and reviewed by a parent committee consisting of 15 members including the chairpersons of the subcommittees. This group, acting as mediators, arbitrators, and editors, made the final decisions in consultation with the respective committees. The process began in June 1991, and the final manuscript was sent to the editor of the Archives of Internal Medicine in September 1992.

Brilliantly masterminding this monumental effort was Edward Roccella, PhD, MPH, who has been coordinator of the NHBPEP for 10 years. Assisting him was Gail Brito, RN, who attended and recorded the minutes of all 15 committee meetings and was responsible for transcribing the document and updating it through its many iterations.

antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). JAMA 1991; **265**:3255–3264

- Dahlöf B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). Lancet 1991; 338:1281–1284.
- MRC Working Party. Medical Research Council trial of treatment in older adults: principal results. Br Med J 1992; 304:405– 412.
- 14. Ogilvie RI, Burgess E, Cusson J, Feldman R, Leiter, Myers M. Recommendations for the pharmacological treatment of essential hypertension: Report of the Canadian Hypertension Society Conference Committee on Treatment. Can Med Assoc J (in press).
- Carlsen JE, Køber L, Torp-Pedersen C, Johansen P. Relation between dose of bendrofluazide, antihypertensive effect, and adverse biochemical effects. Br Med J 1990; 300:975–978.
- The Treatment of Mild Hypertension Research Group. The Treatment of Mild Hypertension Study. Arch Intern Med 1991; 151:1413–1423.
- Grimm RH, Elmer PJ, Grandits G, Prineas R, et al. Long-term lipid results of drug treatment and weight loss in the treatment of mild hypertension study (TOMHS). Circulation 1992; 86(Suppl I):1145.
- Langford HG, Stamler J, Wassertheil-Smoller S, Prineas RJ. All-cause mortality in the Hypertension Detection and Follow-up Program: findings for the whole cohort and for persons with less severe hypertension, with and without other traits related to risk of mortality. Prog Cardiovasc Dis 1986; 14:29–54.
- MacMahon S. Antihypertensive drug treatment: the potential, expected and observed effects on vascular disease. J Hypertens 1990; 9(Suppl 7):S239–S244.
- Hypertension Detection and Follow-up Program Cooperative Group. Persistence of reduction in blood pressure and mortality of participants in the Hypertension Detection and Follow-up Program. JAMA 1988; 259:2113-2122.
- The Multiple Risk Factor Intervention Trial Research Group. Mortality rates after 10.5 years for participants in the Multiple Risk Factor Intervention Trial. Findings related to a priori hypotheses of the trial. JAMA 1990; 263:1795–1801.