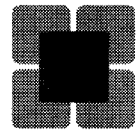

1988 Joint National Committee guidelines for managing hypertension: how are they different?

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■ The new Joint National Committee guidelines on managing hypertension retain the stepped care concept but add flexibility. The 1988 report recommends that, in addition to diuretics and beta blockers, calcium-channel blockers and ACE inhibitors be considered for initial monotherapy. Compared to previous JNC reports, lower starting doses of most antihypertensive drugs, especially diuretics, are recommended. For the first time, the guidelines discuss the cost of antihypertensive therapy. Specific nonpharmacologic therapy and its role in relation to drug therapy are discussed in greater detail than previous reports.

□ INDEX TERM: HYPERTENSION □ CLEVE CLIN J MED 1989; 56:41–47

SINCE its inception in 1973, the National High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute, through its Coordinating Committee, has published state-of-the-art guidelines on detection, evaluation, and treatment of high blood pressure. These consensus documents are written by a committee of authorities appointed by the director of the National Heart, Lung, and Blood Institute. The first report, which was titled the Data Base for Effective Antihypertensive Therapy, was published only as a document of the Department of Health, Education and Welfare.[1] Subsequent communications have been issued as reports of the Joint National Committee (JNC) on Detection, Evaluation, and Treatment of High Blood Pressure (*Table 1*).[2–5] Composition of these committees varies from report to report. The members of JNC IV are listed in *Table 2*.

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The 1988 report (JNC IV),[5] which was published in May (Hypertension Month), introduced some new issues and updated some others. Key differences between this and the previous report are outlined here.

STEPPED CARE

The stepped care approach to managing hypertension was introduced in the Data Base for Effective Antihypertensive Therapy,[1] in 1973, when the only available choices among antihypertensive drugs were ganglion blocking agents, guanethidine, hydralazine, methyldopa, reserpine, and thiazide diuretics. Given the limited choices, it is not difficult to understand that a diuretic was selected as Step 1 because it was more effective and/or better tolerated as monotherapy than the alternatives. Hydralazine was recommended for Step 3 because without an adrenergic inhibitor the regimen frequently caused reflexive tachycardia. Guanethidine was relegated to Step 4 because of its high side-effect profile, leaving reserpine or methyldopa for Step 2.

Despite the advent of new drugs—mostly adrenergic inhibitors—subsequent reports (JNC I in 1977 and JNC II in 1980) continued to recommend a diuretic as Step 1,

TABLE 1
JNC REPORTS

Report	Year	Chairperson
Data Base	1973	H. Mitchell Perry, MD
JNC I	1977	Marvin Moser, MD
JNC II	1980	Iqbal Krishan, MD
JNC III	1984	Harriet Dustan, MD
JNC IV	1988	Aram Chobanian, MD

with the newer agents (beta blockers, clonidine, prazosin) added to the menu for Step 2.

As a result, many interpreted stepped care to mean that a diuretic always had to be Step 1. This approach was criticized as being inflexible, empiric, and unresponsive to recognized hemodynamic and neurohumoral differences in hypertensive patients. This view prevailed, even though stepped care was defined originally by the Data Base Task Force as follows: "It calls for beginning therapy with a small dose of an antihypertensive drug, increasing the dose of that drug, and then adding, one after another, additional drugs as needed."[1] This is a generic concept of building a regimen, the ingredients of which change as new agents are introduced and older ones are discarded.

The criticism of stepped care persisted even after JNC III,[4] in 1984, recommended beta blockers as an alternative to diuretics for Step 1. JNC III explained the stepped care approach as follows:

"This approach leaves room for individualization and flexibility in management, and it has been used effectively in major clinical trials demonstrating reduction of morbidity and mortality. . . . The Stepped Care program suggests initiating therapy with a small dosage of an antihypertensive drug, increasing the dose of that drug, and then adding or substituting one drug after another in gradually increasing doses as needed until goal blood pressure is achieved, side effects become intolerable, or the maximum dose of each drug has been reached."

Between the 1980 and 1984 reports, it became evident from numerous controlled trials that beta blockers and diuretics were nearly equally effective as monotherapy in controlling hypertension.

During this same interval, however, the labeling for captopril, the only available angiotensin-converting enzyme (ACE) inhibitor, carried a warning that it should be used only when other regimens had failed. Calcium-channel blockers had recently been introduced in the U.S. as antianginal and antiarrhythmic drugs, and

TABLE 2
MEMBERS OF THE 1988 JNC

Chairman
Aram V. Chobanian, MD (Boston University School of Medicine)

Committee
Michael H. Alderman, MD (Albert Einstein College of Medicine, Bronx, NY)
Vincent DeQuattro, MD (USC School of Medicine and Los Angeles County-USC Medical Center)
Edward D. Frohlich, MD (Alton Ochsner Medical Foundation, New Orleans)
Ray W. Gifford, Jr., MD (Cleveland Clinic)
Martha N. Hill, PhD, RN (University of Pennsylvania School of Nursing, Philadelphia)
Norman M. Kaplan, MD (The University of Texas Southwestern Medical Center at Dallas)
Herbert G. Langford, MD (University of Mississippi Medical Center, Jackson)
Michael A. Moore, MD (Bowman Gray School of Medicine, Winston-Salem, NC, and Danville Urologic Clinic, Danville, VA)
William A. Nickey, DO (Osteopathic Medical Center at Philadelphia)
Jerome G. Porush, MD (Brookdale Hospital Medical Center and State University of New York, Health Science Center, Brooklyn)
Gerald E. Thomson, MD (Columbia-Presbyterian Medical Center, New York)
Mary C. Winston, RD, EdD (American Heart Institution, Dallas)

Ad Hoc Members (Past Chairpersons)
Harriet P. Dustan, MD (University of Alabama School of Medicine, Birmingham)
Iqbal Krishan, MD (Mayo Clinic, Rochester, MN)
Marvin Moser, MD (Yale University School of Medicine, New Haven, CT)

Ex-Officio Members
Jeffrey A. Cutler, MD, MPH
Michael J. Horan, MD, ScM
Gerald H. Payne, MD
Edward J. Roccella, PhD, MPH
Stephen M. Weiss, PhD
(all from National Heart, Lung, and Blood Institute, Bethesda, MD)

TABLE 3
QUALITIES OF THE IDEAL STEP 1 DRUG

- Safe
- Effective as monotherapy in at least 50% of patients with mild hypertension (diastolic blood pressure, 90-104 mmHg)
- Should not produce occult salt and water retention that counteracts its antihypertensive effect (pseudotolerance)
- Duration of action long enough so that it can be given once daily to enhance compliance
- Flat dose-response curse so that titration can be accomplished in two or three office visits
- Few symptomatic side effects that might necessitate cessation of therapy
- Minimal drug-drug interactions and contraindications
- Relatively inexpensive
- Should be compatible with and augment the effect of other antihypertensive agents that might be added subsequently
- Should be effective in decreasing cardiovascular morbidity and mortality in long-term clinical trials
- Should reduce total peripheral vascular resistance with little or no change in cardiac output, which specifically addresses the hemodynamic abnormality in the vast majority of hypertensive patients
- Should reduce cardiac output with little or no effect on total peripheral resistance for the few patients who have hyperkinetic circulation

their antihypertensive properties were just being explored. None were approved for hypertension, and even today verapamil SR is the only calcium-channel blocker approved by the FDA for treating hypertension.

Opinion of the JNC IV participants was divided regarding the viability of the stepped care concept. There was general agreement that at least four classes of drugs (diuretics, beta blockers, ACE inhibitors, and calcium-channel blockers) could be used for initial monotherapy (Step 1) because, in varying degrees, they all exhibit the qualities of the ideal Step 1 drug (*Table 3*).

Some committee members wanted to open Step 1 to all drugs, abandoning any attempt to offer to practicing physicians guidelines about the construction of a therapeutic regimen.

To achieve consensus and retain some semblance of a structured but flexible approach, the concept of "individualized step-care" was adopted, with this caveat: "However, the large numbers of effective antihypertensive drugs provide many excellent therapeutic options for lowering blood pressure effectively and minimizing side effects." (In all previous documents, this approach to therapy was called "stepped care." Why JNC IV shortened it to "step-care" is not clear and was probably unintentional.)

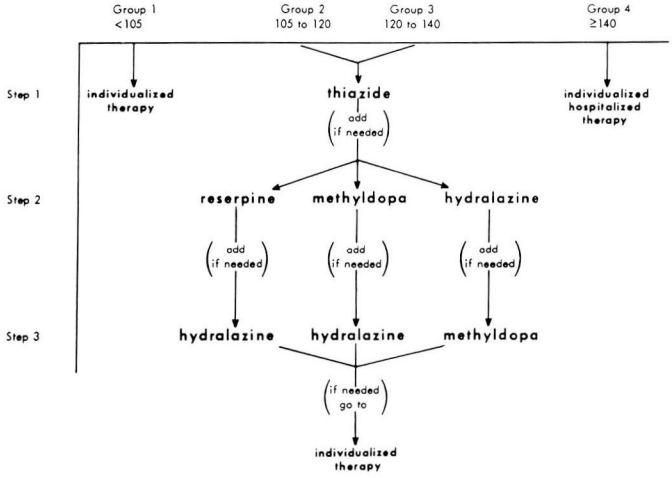
Figure 1 depicts the evolution of the stepped care approach since the National High Blood Pressure Education Program began issuing guidelines. Because this approach has been so successful and is familiar to most physicians, it was my position that it should be retained as a frame of reference, while broadening the options at each step.

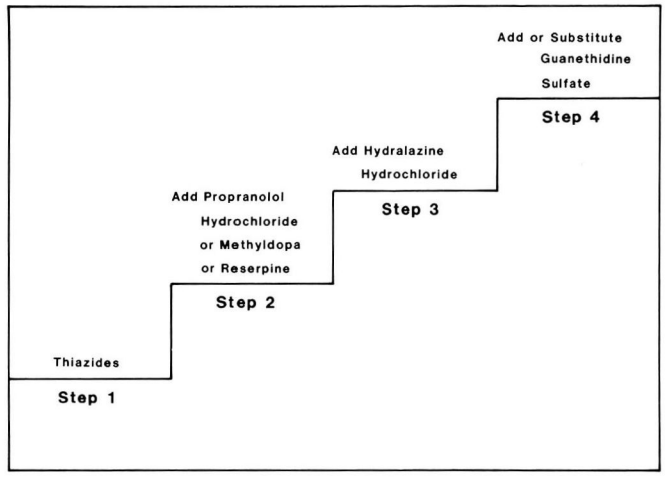
The individualized step-care approach of the 1988 report offers several options if the drug selected for Step 1 is not effective or produces unacceptable side effects (*Figure 1E*). If the drug initially selected for Step 1 is only partially effective, one might want to increase the dose or add a second agent from a different class. If the first drug selected is ineffective or produces side effects that detract from quality of life, another Step 1 agent may be substituted ("sidestep"). To minimize side effects, a second (or third) drug may be added to the regimen before the maximal dose of the original drug or drugs is reached.

There seems to be little if any advantage to including two drugs from the same class in a single regimen, although it is sometimes possible to reduce side effects by substituting one drug for another within the same class. The classes of drugs are shown in *Table 4*.

The 1988 report offers some guidance to physicians on selection of the appropriate Step 1 drug. These decisions should be influenced by certain demographic factors (race and age), concomitant diseases and therapies, the patient's lifestyle, physiologic and biochemical measurements, and economic considerations.

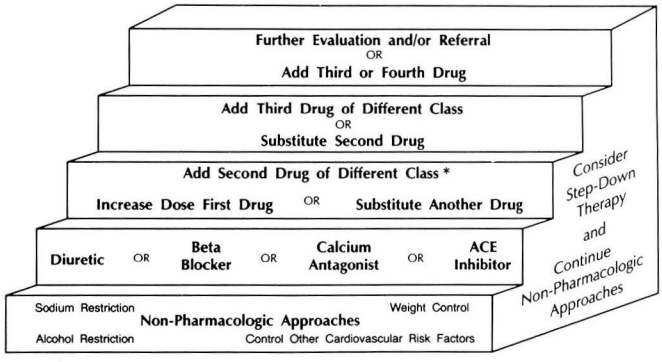
In general, blacks and older patients respond better to





Stepped-Care Regimens	
Step	**Drugs**
1	**Diuretic***
2	**Adrenergic Inhibiting Agents†** Clonidine hydrochloride Methyldopa Metoprolol tartrate Nadolol Prazosin hydrochloride‡ Propranolol hydrochloride *Rauwolfia* alkaloids
3	**Vasodilator§** Hydralazine hydrochloride
4	**Additional Adrenergic Inhibiting Agent** Guanethidine sulfate

Stepped-Care Approach to Drug Therapy	
Step	**Drug Regimens**
1	Begin with less than a full dose of either a thiazide-type diuretic or a β-blocker†; proceed to full dose if necessary and desirable
2	If BP control is not achieved, either add a small dose of an adrenergic-inhibiting agent‡ or a small dose of thiazide-type diuretic; proceed to full dose if necessary and desirable§; additional substitutions may be made at this point
3	If BP control is not achieved add a vasodilator, hydralazine hydrochloride, or minoxidil for resistant cases
4	If BP control is not achieved, add guanethidine monosulfate



A, B
C, D
E

FIGURE 1. The different approaches to stepped care recommended in each of the reports are reproduced here by permission. FIGURE 1A. Task Force I.[1] FIGURE 1B. JNC I.[2] FIGURE 1C. JNC II.[3] FIGURE 1D. JNC III.[4] FIGURE 1E. JNC IV.[5]

TABLE 4
DOSES OF ANTIHYPERTENSIVE AGENTS RECOMMENDED IN JNC IV

Type of Drug	Dosage Range (mg/d)* Initial	Maximum†
Diuretics		
Thiazides and related sulfonamide diuretics		
Bendroflumethiazide	2.5	5.0
Benzthiazide	12.5–25	50.0
Chlorothiazide	125.0–250	500.0
Chlorthalidone	12.5–25	50.0
Cyclothiazide	1.0	2.0
Hydrochlorothiazide	12.5–25	50.0
Hydroflumethiazide	12.5–25	50.0
Indapamide	2.5	5.0
Methyclothiazide	2.5	5.0
Metolazone	1.25	10.0
Polythiazide	2.0	4.0
Quinethazone	25.0	100.0
Trichlormethiazide	1.0–2	4.0
Loop diuretics**		
Bumetanide‡	0.5	5.0
Ethacyrnic acid‡	25.0	100.0
Furosemide‡	20.0–40	320.0
Potassium-sparing agents		
Amiloride hydrochloride	5.0	10.0
Spironolactone	25.0	100.0
Triamterene	50.0	150.0
Adrenergic inhibitors		
Beta-adrenergic blockers§		
Acebutolol	200.0	1200.0
Atenolol	25.0	150.0
Metoprolol	50.0	200.0
Nadolol	40.0	320.0
Penbutolol sulfate	20.0	80.0
Pindolol‡	10.0	60.0
Propranolol hydrochloride‡	40.0	320.0
Propranolol, long-acting (LA)‡	60.0	320.0
Timolol‡	20.0	80.0
Central-acting adrenergic inhibitors		
Clonidine hydrochloride‡	0.1	1.2
Clonidine TTS (patch)	0.1	0.3
Guanabenz acetate‡	4.0	64.0
Guanfacine	1.0	3.0
Methyldopa‡	250.0	2000.0
Peripheral-acting adrenergic antagonists		
Guanadrel sulfate‡	10.0	100.0
Guanethidine monosulfate	10.0	150.0
Rauwolfia alkaloids		
Rauwolfia (whole root)	50.0	100.0
Reserpine	0.1	0.25
$Alpha_1$-adrenergic blockers		
Prazosin hydrochloride‡	1.0–2	20.0
Terazosin hydrochloride	1.0–2	20.0
Combined alpha- and beta-adrenergic blocker		
Labetalol‡	200.0	1800.0
Vasodilators		
Hydralazine‡	50.0	300.0
Minoxidil‡	2.5	80.0
Angiotensin-converting enzyme inhibitors		
Captopril‡	25.0–50	300.0
Enalapril maleate	2.5–5	40.0
Lisinopril	5.0	40.0
Calcium antagonists		
Diltiazem hydrochloride¶	60.0	360.0
Nifedipine¶	30.0	180.0
Nitrendipine	5.0	40.0
Verapamil¶	120.0	480.0
Verapamil SR (long-acting)	120.0	480.0

* The dosage range may differ slightly from the recommended dosage in *Physician's Desk Reference* or package insert.
** Larger doses of loop diuretics may be required in patients with renal disease.
† The maximum suggested dose may be exceeded in resistant cases.
‡ This drug is usually given in divided doses twice daily.
§ Atenolol, metoprolol, and acebutolol are cardioselective; pindolol and acebutolol have partial agonist activity.
¶ This drug is usually given in divided doses three or four times daily.
Adapted by permission.[5]

diuretics and calcium-channel blockers than to beta blockers and ACE inhibitors. Diuretics are particularly effective in obese patients and patients with chronic renal failure because fluid retention frequently plays a role in this type of hypertension. Beta blockers and calcium-channel blockers are effective antianginal agents (the "two-for-one" concept in hypertensive therapy). Beta blockers are the only agents that have been shown to have a cardioprotective effect after a myocardial infarction.

The reliability of measurements of hemodynamic parameters and plasma renin activity has not been great enough to justify their routine use in selecting the appropriate Step 1 drug.

The truth is that our desire to select prospectively the appropriate drug for a given patient exceeds our ability to do so. To a great extent we still play, by hunch and intuition, the trial-and-error game.

GOAL OF THERAPY

The JNC IV report backed away from the JNC II and

III recommendation that "the initial goal of antihypertensive therapy is to achieve and maintain diastolic blood pressures at lower than 90 mmHg if feasible. A reasonable further goal is the lowest diastolic blood pressure consistent with safety and tolerance." The JNC IV report simply states that "the goal of antihypertensive therapy is achievement and long-term maintenance of goal blood pressure (< 140/90 mmHg) with minimal, if any, adverse effects."

CHANGES IN DOSES

The recommended dose range of diuretic agents has gradually been decreased from 50–100 mg of hydrochlorothiazide and chlorthalidone to 12.5–50 mg in JNC IV (*Table 4*).[5] Dose ranges of other diuretics have been comparably reduced. The recommended dose range for hydrochlorothiazide and chlorthalidone was 25–50 mg in JNC III.[4]

Compared to JNC III, the new report recommends lower initial doses for pindolol, propranolol LA, clonidine, guanabenz, methyldopa, minoxidil, captopril, enalapril, diltiazem, and verapamil. Higher initial doses are recommended for nadolol and reserpine. Lower maximal doses are recommended for propranolol and propranolol LA, guanadrel, guanethidine, and minoxidil. Higher maximal doses are recommended for atenolol, metoprolol, nadolol, timolol, labetalol, guanabenz, captopril, and diltiazem.

NEW DRUGS

The JNC IV report included the following new drugs that were not listed in JNC III: acebutolol, clonidine TTS, guanfacine, terazosin, lisinopril, nitrendipine, and verapamil SR.

NONPHARMACOLOGIC THERAPY

More attention is devoted to nonpharmacologic therapy in the JNC IV report than in any previous JNC reports. Weight reduction, with goal body weight within 15% of desirable weight, restriction of alcohol to the equivalent of no more than 30 mL (1 oz) of ethanol daily, and dietary sodium restriction to 70–100 mEq per day (approximately 1.5–2.5 g sodium or 4–7 g salt) are emphasized. There are reliable data to support each of these measures.[6]

Mentioned as possibly effective are potassium and calcium supplementation, biofeedback and relaxation, aerobic exercise, and modification of dietary fat to increase the polyunsaturated/saturated fat ratio. Modification of fat intake is undoubtedly more effective in reducing serum cholesterol than in reducing blood pressure. Similarly, prohibition of tobacco is mentioned in the JNC IV report, not because tobacco has an adverse effect on hypertension per se, but because it is a potent independent risk factor for stroke and coronary disease. The JNC IV report emphasizes the importance of detecting all risk factors and treating those that are amenable to therapy.

Although there is no evidence that ethanol raises blood pressure until daily consumption exceeds 60 mL (2 oz),[6] the committee considered other adverse effects of ethanol and elected to recommend that the upper limit be not more than 30 mL daily.

Because of the meager and sometimes conflicting evidence regarding the benefit of fish oils rich in polyunsaturated omega-3 fatty acids, the JNC IV report recommends increased consumption of fish rather than fish-oil capsules.

It is also recommended that a three- to six-month trial of nonpharmacologic measures be prescribed as initial treatment for patients with diastolic blood pressures 90–94 mmHg who have no other risk factors and no evidence of target-organ damage. For all others, appropriate nonpharmacologic modalities should be recommended as adjunctive measures to pharmacologic therapy in an effort to minimize dose requirements (*Figure 1*).

COST OF THERAPY

For the first time, the JNC addresses the issue of cost of antihypertensive therapy, cautioning health care providers that they "should be aware of the total cost of care to hypertensive patients (including indirect costs such as time lost from work and transportation costs) and should try to minimize these expenses."

In addition to the drugs, determinants of cost include the initial workup and follow-up visits, including laboratory examinations, needed to monitor therapy. Physicians are reminded that a high cost for medications may reduce compliance, but drugs that diminish quality of life, irrespective of cost, may also reduce compliance.

MISCELLANEOUS CHANGES AND ADDITIONS

Sections on managing hypertension in young and elderly patients, as well as diabetics, were revised to include some of the recommendations from the reports of the Second Task Force on Blood Pressure Control in Children,[7] the Working Group on Hypertension in the

Elderly,[8] and the Working Group on Hypertension in Diabetes.[9]

New sections on managing hypertension in patients with congestive heart failure, left ventricular hypertrophy, peripheral vascular disease, chronic obstructive pulmonary disease and asthma, hyperlipidemia, and gout were added.

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