

Physiological and Biochemical Measurements. Some clinicians have found certain physiological and biochemical measurements (e.g., body weight, heart rate, plasma renin activity, hemodynamic measurements) to be helpful in choosing specific therapy.

Economic Considerations. The cost of therapy may be a barrier to controlling high blood pressure and should be an important consideration in selecting antihypertensive medication. Generic formulations are acceptable. Nongeneric newer drugs are usually more expensive than diuretics or beta-blockers. If newer agents eventually prove to be equally effective, then cost should be considered in choosing them for initial therapy; if they prove to be more effective, then cost should be a secondary consideration. Treatment costs include not only the price of drugs but also the expense of routine or special laboratory tests, supplemental therapies, office visits, and time lost from work for visits to physicians' offices. The costs of medications may be reduced by using combination tablets and generic formulations. Patients should be advised to check prices at different sources. Some larger tablets can be divided, saving money when larger doses cost little more than smaller doses. Some sustained-release formulations should not be divided because cutting the tablet eliminates the sustained-release function.

Managed Care. Because high blood pressure is so common, its management requires a major commitment from clinicians and managed care organizations. This commitment will need to expand even further because the majority of patients with hypertension do not have adequately controlled blood pressure (see chapter 1) and additional demands will develop from the projected increase in numbers of persons with hypertension due to the aging of the population. However, the cost of managing hypertension is lower overall than the sum of direct and indirect costs that may be avoided by reducing hypertension-associated heart disease, stroke, and renal failure, especially because these

adverse events often lead to expensive hospitalizations, surgical procedures, and high-cost technologies.^{131Pr,132Pr,133Pr} Randomized controlled trials have demonstrated that these reductions occur in a relatively short time and are sustained for years.

Managed care programs offer the opportunity for 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. The outcomes of the management of hypertension will need to be monitored, in keeping with the requirements of organizations that monitor quality, such as the Health Plan Employer Data and Information Set (HEDIS). These outcomes may be divided into three categories: immediate (e.g., blood pressure levels, percentage of adherence to therapy), intermediate (e.g., cardiac or renal function, health resource utilization), and long-term (e.g., morbidity and mortality, cost-effectiveness).

Hypertension specialists may play an important role in providing more cost-effective management of high blood pressure by adapting national guidelines for local implementation, providing guidance for new drugs and diagnostic methods, and managing patients with identifiable causes of hypertension, resistance to therapy, or complex concomitant conditions.

Drug Interactions. As shown in table 11, some drug interactions may be helpful. For example, diuretics that act on different sites in the nephron, such as furosemide and thiazides, increase natriuresis and diuresis, and certain calcium antagonists reduce the required amount of cyclosporine. Other interactions are deleterious: nonsteroidal anti-inflammatory drugs (NSAIDs) may blunt the action of diuretics, beta-blockers, and ACE inhibitors.

Dosage and Followup

Therapy for most patients (uncomplicated hypertension, stages 1 and 2) should begin with the lowest dosage listed in table 7 to prevent

adverse effects of too great or too abrupt a reduction in blood pressure. If blood pressure remains uncontrolled after 1 to 2 months, the next dosage level should be prescribed. It may take months to control hypertension adequately while avoiding adverse effects of therapy. Most antihypertensive medications can be given once daily, and this should be the goal to improve patient adherence. Home or office blood pressure measurement in the early morning before patients have taken their daily dose is useful to ensure adequate modulation of the surge in blood pressure after arising. Measurements in the late afternoon or evening help monitor control across the day. Treatment goals based on out-of-office measurements should be lower than those based on office recordings^{45Pr} (see chapter 2).

Initial Drug Therapy

When the decision has been made to begin antihypertensive therapy (table 5) and if there are no indications for another type of drug, a diuretic or beta-blocker should be chosen because numerous randomized controlled trials have shown a reduction in morbidity and mortality with these agents (figures 6 and 7).

As shown in table 9 and figure 8, there are compelling indications for specific agents in certain clinical conditions, based on outcomes data from RCTs. In other situations where outcomes data are not yet available, there are indications for other agents and the choice should be individualized, using the agent that most closely fits the patient's needs.^{134Pr}

If the response to the initial drug choice is inadequate after reaching the full dose, two options for subsequent therapy should be considered (see figure 8 for treatment algorithm):

- If the patient is tolerating the first choice well, add a second drug from another class.
- If the patient is having significant adverse effects or no response, substitute an agent from another class.

If a diuretic is not chosen as the first drug, it is usually indicated as a second-step agent because its addition will enhance the effects of other agents. If addition of a second agent controls blood pressure satisfactorily, an attempt to withdraw the first agent may be considered.^{135F}

Before proceeding to each successive treatment step, clinicians should consider possible reasons for lack of responsiveness to therapy, including those listed in table 12.

High-Risk Patients

Although similar general approaches are advocated for all patients with hypertension, modifications may be needed for those with stage 3 hypertension, those in risk group C, or those at especially high risk for a coronary event or stroke (table 5). Drug therapy should begin with minimal delay. Although some patients may respond adequately to a single drug, it is often necessary to add a second or third agent after a short interval if control is not achieved. The intervals between changes in the regimen should be decreased, and the maximum dose of some drugs may be increased. In some patients, it may be necessary to start treatment with more than one agent. Patients with average SBP of 200 mm Hg or greater and average DBP of 120 mm Hg or greater require more immediate therapy and, if symptomatic target organ damage is present, may require hospitalization.

Step-Down Therapy

An effort to decrease the dosage and number of antihypertensive drugs should be considered after hypertension has been controlled effectively for at least 1 year. The reduction should be made in a deliberate, slow, and progressive manner. Step-down therapy is more often successful in patients who also are making lifestyle modifications.^{80Ra} Patients whose drugs have been discontinued should have scheduled followup visits because blood pressure usually rises again to hypertensive levels, sometimes months or years after discontinuance, especially in the absence of sustained improvements in lifestyle.