Hypertension and diabetes mellitus are interrelated diseases that, if untreated, strongly predispose to atherosclerotic cardiovascular disease and renal disease. More than 3 million Americans have both hypertension and diabetes, which are particularly prevalent in the socioeconomically disadvantaged. Hypertension contributes substantially to morbidity and mortality in people with diabetes. This report is an update of the 1987 working group report on hypertension and diabetes and includes important new information on the management of hypertension in people with diabetes. Although treatment of hypertension in most people with diabetes does not differ from that in people who do not have diabetes, this report outlines some special considerations relevant to the presence of both diseases. Lifestyle modification is considered as an initial treatment modality or as an adjunct to pharmacologic measures. This report also includes a discussion of the treatment of hypertension and diabetes in children, an expanded review of sexual dysfunction, and an increased emphasis on the effect of hypertension and diabetes on target organs. A treatment algorithm represents a practical guideline for the physician. Since the previous report, there has been an increased awareness, through clinical trials and pharmacologic research, of the importance of flexibility in the use of antihypertensive drugs as well as a refinement of nonpharmacologic approaches in treating people with both hypertension and diabetes.

**Key Words** • diabetes mellitus • hypertension, renovascular • antihypertensive agents
published since the last consensus report, this current consensus report and other recent consensus reports serve as an update on this important topic.12-14

This report serves the following purposes: to increase awareness of the importance and implications of the problem of hypertension in people with diabetes in community control programs and to guide clinicians in their care of people with the concomitant problems of hypertension and diabetes.

Definitions and Diagnostic Criteria

Diabetes Mellitus

Diabetes mellitus comprises a genetically and clinically heterogeneous group of chronic metabolic disorders characterized by glucose intolerance. Type I diabetes (absolutely insulin-dependent) accounts for 5% to 10% of diagnosed cases; type II (usually with insulin resistance) comprises 90% to 95% of cases in the United States.3 Diagnosis of diabetes in nonpregnant adults should be restricted to those who have one of the following criteria: (1) random plasma glucose level of 11 mmol/L (200 mg/dL) or greater plus classic signs and symptoms of diabetes (eg, polydipsia, polyuria, weight loss), (2) fasting plasma glucose level of 7.8 mmol/L (140 mg/dL) or greater on at least two occasions, or (3) fasting plasma glucose level below 7.8 mmol/L (140 mg/dL) plus sustained elevated plasma glucose levels during at least two oral glucose tolerance tests. The 2-hour sample and at least one other sample between 0 and 2 hours after a 75-g glucose load should be 200 mg/dL or greater. Oral glucose tolerance testing is not necessary if patients have a fasting plasma glucose level of 7.8 mmol/L (140 mg/dL) or greater.

Diagnosis of Hypertension

Hypertension should not be diagnosed on the basis of a single measurement. Initial elevated readings should be confirmed on at least two subsequent visits over 1 week or more with an average diastolic blood pressure (DBP) of 90 mm Hg or greater or systolic blood pressure (SBP) of 140 mm Hg or greater required for a diagnosis of hypertension.16 Special care is warranted in diagnosing hypertension in people with diabetes because of greater blood pressure variability and a much greater likelihood of isolated systolic hypertension.3 Because of the greater blood pressure variability, more blood pressure measurements may be particularly useful in many of these patients.

Epidemiology

Epidemiology of Associations Among Diabetes, Hypertension, and Cardiovascular Disease

An association between overt diabetes mellitus and CVD has been observed in multiple studies conducted in a number of ethnic and racial groups. This excess of CVD in people with diabetes includes increases in both incidence and case fatality rates from acute myocardial infarction, in mortality in the months following discharge after an acute myocardial infarction, in unexplained chronic congestive heart failure, in cerebrovascular disease, in peripheral vascular disease, and in renal disease. Among people with type II diabetes in the United States, approximately 60% of death certificates mentioned ischemic heart disease and 20% mentioned other heart and vascular diseases as a contributing cause of death.17-18 The presence of diabetes may increase the risk of CVD more in women than in men.19

Obesity is a risk factor for the development of type II diabetes as well as hypertension. In addition, obesity (abdominal obesity) is associated with adverse changes in other cardiovascular risk factors. Recent studies have suggested that hyperglycemia may be part of a syndrome involving abnormalities in blood pressure and lipid levels linked to central distribution of body fat and elevations of insulin or insulin resistance.20-21 It has been suggested that the increased risk of CVD associated with diabetes may develop in the prediabetic period when glucose levels are normal or minimally elevated. Impaired glucose tolerance is associated with a normal fasting blood glucose level but an elevated postprandial blood sugar level between 7.8 and 11 mmol/L (140 and 199 mg/dL). Some patients with impaired glucose tolerance are hyperinsulinemic, and 30% progress to NIDDM. These observations suggest that elevations in insulin or insulin resistance may contribute to an increased risk of CVD in the general normoglycemic population.22 This syndrome may affect a substantially greater proportion of the US population than the estimated 22 to 30 million with detectable abnormalities in glucose tolerance. (For more information on obesity, see “Special Considerations in Diabetic Patients With Hypertension” below.) Most macrovascular complications of diabetes occur in people with concomitant hypertension.2 Compared with people with normal glucose tolerance, blood pressure is increased in both those with impaired glucose tolerance and those with diabetes.

Pathogenesis Factors: Type I and Type II

There are substantial differences in the causes of hypertension in type I and type II diabetes mellitus. Diabetic nephropathy appears to be the most common cause of hypertension in patients with type I diabetes. A strong family history of essential hypertension and diabetes mellitus appears to identify those people with type I diabetes who are most likely to develop renal disease and hypertension.23 Probably an equal number of people with type II diabetes mellitus develop renal disease, but hypertension often occurs with normal renal function associated with obesity or older age.

An increased total body sodium and enhanced vascular reactivity are found in both type I and type II diabetes. These abnormalities are found in people with diabetes, both with and without hypertension or microvascular disease, suggesting that factors secondary to diabetes can lead to hypertension. Insulin levels are high in many patients with type II diabetes and can be high during treatment of either type I or type II diabetes. Hyperinsulinemia and insulin resistance may contribute to hypertension in diabetes mellitus through effects on sodium retention or direct effects on blood vessels.22,24

Clinical Trials

In the treatment of patients with both diabetes mellitus and hypertension, clinical trials relating different treatment strategies and regimens to at least the following four outcome measures are of interest: glycemic control, blood pressure control, microvascular disease (nephropathy,
neuropathy, and retinopathy), and macrovascular disease. In type II diabetes, macrovascular disease is undoubtedly the most significant chronic complication from both clinical and public health perspectives.

Only a few large-scale clinical trials enrolled people with diabetes in appreciable numbers, and many details on the experience of these subjects have not been reported. Ten percent of the participants in the Hypertension Detection and Follow-up Program (HDFP) had a fasting blood glucose level of 7.8 mmol/L (140 mg/dL) or greater at baseline or reported taking medication for diabetes. The effect of diuretic-based stepped care (SC) on total mortality in this subset did not differ significantly from the benefit in the overall cohort. For the subgroup of people with diabetes, compared with the group receiving referred care (RC), the trends were favorable for the SC group, both overall (adjusted 5-year mortality rates of 10.9 and 12.0 per 100 for SC and RC, respectively) and especially in the group with mild hypertension (9.2 per 100 for SC and 11.0 per 100 for RC). However, these differences were not statistically significant. Results for cardiovascular end points have not been reported separately for people with diabetes.

In the Systolic Hypertension in the Elderly Program (SHEP), 10% of participants had diabetes. This trial used chlorthalidone as the primary first-step drug; however, the doses used were lower than in HDFP. Relative risk reductions in the subgroup with diabetes for all major end points—fatal or nonfatal stroke, CHD death or nonfatal myocardial infarction, all major cardiovascular events, and total mortality—were very similar to results for the total cohort. As in the HDFP, the effect of treatment on the primary end point (which was fatal and nonfatal stroke in SHEP) was not statistically different in the subgroup with diabetes, neither trial having been designed specifically to test the questions in this subgroup. However, in the SHEP there was a significant benefit for people with diabetes and CHD, when the most inclusive definition of this end point was used. This beneficial effect occurred despite a rise of 0.3 mmol/L (5.6 mg/dL) in fasting plasma glucose levels with active treatment compared with placebo.

Diuretics and β-blockers are the only classes of drugs that have been studied and found to be effective in reducing cardiovascular morbidity and mortality in people with hypertension. The results of planned and ongoing trials are needed to compare different classes of antihypertensive drugs for effects on cardiovascular and renal end points in people both with and without diabetes.

Guide to Clinical Evaluation

Evaluation of patients with both hypertension and diabetes mellitus should take into consideration the following questions: Is the patient taking any drug known to alter blood pressure or blood glucose? Does the patient have a surgically curable form of hypertension? Are target organs involved (eg, heart, kidney, brain, eyes)? Are cardiovascular risk factors other than hypertension and diabetes present (eg, dyslipidemia, family history, smoking)? Are the diabetes and hypertension well controlled?

A careful history of all prescribed and over-the-counter medications should be obtained from all patients. Several medications may raise blood pressure and thus interfere with the effectiveness of antihypertensive drugs. These include oral contraceptives, steroidal compounds, nonsteroidal anti-inflammatory agents, nasal decongestants, appetite suppressants, and tricyclic antidepressants. Although relatively rare, coarctation of the aorta, primary hyperaldosteronism, Cushing’s syndrome, and pheochromocytoma also should be considered in patients with both diabetes and hypertension, as in essential hypertension.

A medical history should include (1) family history of hypertension, diabetes, renal disease, and CVD; (2) patient history of CVD, cerebrovascular disease, renal disease, and retinopathy; (3) known duration and levels of elevated blood pressure and blood glucose; (4) results and side effects of previous antihypertensive and hypoglycemic therapy; (5) use of drugs that may influence blood pressure or diabetes; (6) history of weight gain or loss, proteinuria, sodium intake, other dietary factors, exercise habits, and alcohol use; (7) symptoms suggesting secondary hypertension; (8) psychosocial and environmental factors (eg, emotional stress, cultural food practices, economic status) that may influence blood pressure or blood glucose control; (9) other cardiovascular risk factors, including obesity, smoking, and hyperlipidemia; and (10) date of last eye examination.

With regard to diabetes, information should be sought about the history of polyuria, polydipsia, polyphagia, fatigue, blurred vision, hypoglycemic reactions, sexual dysfunction, paresthesia or other signs of peripheral neuropathy in the extremities, and leg and foot ulcers.

Physical Examination

Because blood pressure may rise in response to physical exertion or emotional stress and because some patients with diabetes have blood pressures that fall when they are in the standing position, it is recommended that blood pressure be measured with patients in the supine, seated, and standing positions after patients have had time to relax (see "Definitions and Diagnostic Criteria" above).

Physical examination should include (1) two or more blood pressure determinations in all three positions (a wide arm cuff should be used to measure the pressure of patients with obese arms); (2) measurement of height and weight; (3) funduscopic examination for signs of hypertensive and diabetic retinopathy; (4) examination of the neck for carotid bruits, distended veins, and enlarged thyroid; (5) careful examination of the heart for a sustained point of maximal impulse (evidence of left ventricular hypertrophy), precordial heave, murmurs, arrhythmias, and S3 and S4 heart sounds; (6) examination of the abdomen for bruits and bladder enlargement; (7) examination of the extremities for diminished or absent peripheral arterial pulsations and edema; and (8) neurological assessment, especially sensory and vibratory. A periodic eye examination by an ophthalmologist is recommended, even in asymptomatic patients, to enable recognition of treatable retinal disease.

Physical findings that suggest secondary hypertension include abdominal or flank masses (polycystic kidneys); abdominal bruits, particularly those that lateralize or have a diastolic component ( renovascular disease); delayed or absent femoral arterial pulses (aortic coarcta-
Diabetes mellitus is an independent risk factor for CHD, and the risk is doubled when hypertension is present. Recent awareness of a link between diabetes, hypertension, dyslipidemia, and coagulation abnormalities, all of which are risk factors for CVD, has added another dimension to our understanding. Among people with diabetes, hypertension appears to be the major risk factor for CHD, in addition to its contribution to left ventricular hypertrophy and congestive heart failure, both of which are increased with diabetes. A variety of factors may contribute to the interactions between these disorders in people with diabetes. The risk of peripheral vascular disease in individuals with diabetes is increased by the presence of hypertension as well as dyslipidemia and hypercoagulation.

Cerebrovascular Disease

Both men and women with diabetes mellitus have a 2.5- to 3.5-fold increase in atherothrombotic brain infarction. The Framingham Heart Study showed at the 30-year follow-up of men and women aged 35 to 64 that women with diabetes had 3.6 times the incidence of atherothrombotic brain infarction as did women without diabetes and that men with diabetes had 2.5 times the incidence of atherothrombotic brain infarction as did men without diabetes. The Honolulu Heart Program reported at 12-year follow-up that the incidence of thromboembolic stroke was two times higher in men with diabetes than in men without diabetes. In an epidemiologic study of subjects aged 50 to 79, multivariate analysis with adjustment for other risk factors demonstrated that the relative risk for stroke mortality and morbidity associated with diabetes was 1.8 in men and 2.2 in women. The relative importance of various risk factors has been estimated in a number of ways. The National Stroke Association has published a list of potentially modifiable risk factors for stroke. Hypertension increases the risk of stroke by six times the average risk and has a prevalence of 35%. Diabetes increases the risk of stroke by two to four times, with a prevalence of 4% to 6%. Addition of hypertension to diabetes substantially increases the risk and prevalence of stroke in people with diabetes.

Diabetic Retinopathy

Diabetic retinopathy is a highly specific vascular complication of both type 1 and type II diabetes mellitus. It is also the most frequent cause of new cases of blindness among American adults aged 20 to 74 years. The prevalence of retinopathy is strongly related to the duration of diabetes. Recently, the American College of Physicians, the American Diabetes Association, and the American Academy of Ophthalmology have published screening guidelines for diabetic retinopathy.

Among people with diabetes who are not treated with insulin, the 6-year incidence of retinal exudates was found to be more than doubled in patients with a mean SBP of 145 mm Hg compared with those whose SBP was less than 125 mm Hg. The Wisconsin Epidemiologic Study of Diabetic Retinopathy demonstrated that SBP was a predictor of the incidence of retinopathy. DBP was found to be a significant predictor of progression of retinopathy in younger-onset people with diabetes (almost always type 1). In older individuals with diabetes, neither SBP nor DBP was a significant predictor of retinopathy progression.

Special Considerations in Diabetic Patients With Hypertension

Kidney Disease

Diabetes mellitus is now the leading cause of end-stage renal disease in the United States. The risk of diabetic renal disease increases with age and duration of diabetes and is more prevalent in African Americans. The development of nephropathy after 15 years of diabetes has been observed in more than 30% of people with type 1 diabetes and in more than 20% of those with type II diabetes. In the former, microalbuminuria, mesangial cell hypertrophy, and blood pressure are correlated and herald the development of diabetic nephropathy. An exaggerated blood pressure response to exercise may unmask incipient nephropathy in people with diabetes. Hypertension accelerates the progression rate of diabetic renal disease, and control of blood pressure as well as glucose may retard this progression rate.

Secondary Forms of Hypertension

Both hypertension and diabetes mellitus are common in patients with Cushing's syndrome, pheochromocytoma, and primary aldosteronism. People with diabetes develop more atherosclerosis and do so at an earlier age than do those without diabetes. Atherosclerotic plaques can cause narrowing of one or both renal arteries, resulting in renovascular hypertension. A recent autopsy study found that 73% of patients with renal artery stenosis were hypertensive and 53% were diabetic.

Cardiovascular Disease

Diabetes mellitus is an independent risk factor for CHD, and the risk is doubled when hypertension is present. Recent awareness of a link between diabetes, hypertension, dyslipidemia, and coagulation abnormalities, all of which are risk factors for CVD, has added another dimension to our understanding. Among people with diabetes, hypertension appears to be the major risk factor for CHD, in addition to its contribution to left ventricular hypertrophy and congestive heart failure, both of which are increased with diabetes. A variety of factors may contribute to the interactions between these disorders in people with diabetes. The risk of peripheral vascular disease in individuals with diabetes is increased by the presence of hypertension as well as dyslipidemia and hypercoagulation.
DBP was found to be associated with incidence, progression, or progression to proliferative retinopathy.10

In a follow-up study of a large group of patients with long-duration, type I diabetes, Janka and colleagues38 identified some of the risk factors responsible for the development of severe forms of diabetic retinopathy. One definite finding was that the risk of retinopathy increased dramatically with an increase of DBP greater than 70 mm Hg. Controlling blood pressure reduces the progression of diabetic retinopathy.39

In addition, people with diabetes suffer a greater incidence of chronic open angle glaucoma than do people without diabetes.40 A possible explanation may be that diabetes-induced microangiopathy renders the optic nerve head more vulnerable to an elevation of the intraocular pressure that can produce optic nerve cupping, atrophy, and visual field defects, thereby increasing the risk of developing blindness. Hypertension is a known risk factor for ischemic optic neuropathy. Thus, people with both diabetes and hypertension are at higher risk for developing both glaucoma and ischemic optic neuropathy than are people with diabetes who do not have hypertension.41

**Hypertension With Orthostatic Hypotension**

Normal circulatory adjustment to upright posture includes activation of sympathetic reflexes that originate from cardiopulmonary and arterial baroreceptors. The reflex increase of vascular resistance and heart rate offsets gravitational pooling of blood in the lower part of the body and results in unchanged mean arterial pressure. A significant fall in standing blood pressure (ie, DBP drop of 10 mm Hg or greater) is observed in approximately 12% of patients with diabetes mellitus and is more frequent in the elderly and in those with long-standing and more severe forms of diabetes. Also, it may occur when individuals change from a supine to seated position and can be quite disabling. Orthostatic hypotension in people with both diabetes and autonomic dysfunction frequently is associated with supine hypertension.

**Autonomic Neuropathy in Diabetic Patients**

It is customary to classify patients with diabetes mellitus and orthostatic hypotension as those showing signs of neuropathy and blunt sympathetic responses and those who have exaggerated sympathetic function in the upright posture. Diabetic autonomic neuropathy typically is characterized by abnormal Valsalva and isometric handgrip responses, blunting of respiratory arrhythmia, and inability to increase heart rate in the upright posture.42 The less frequent hyperadrenergic type of neuropathy is characterized by excessive tachycardia and an excessive response of plasma norepinephrine to upright posture. A decreased blood volume and possibly decreased vascular responsiveness to reflexogenic elevations in norepinephrine are thought to be of pathophysiological importance in these patients. Postural hypotension may be present even in the absence of clinical peripheral neuropathy.43

**Sexual Dysfunction**

Both diabetes mellitus and hypertension are independently associated with an increased prevalence of sexual dysfunction in both men and women.44-52 Frequency of sexual dysfunction in men with diabetes ranges from 27.5% to 75% in various studies.44-47,52 Several investigations47-52 have reported an estimated 40% to 80% of adult men with both diabetes and hypertension to have sexual dysfunction. In addition, an increasing proportion of patients with diabetes and hypertension are elderly, and aging itself appears to have a negative effect on sexual function in both men and women.49,52 Hypertension, neuropathy, vascular insufficiency, and psychological problems all have been implicated in impotence, impaired ejaculation, and decreased libido in men and in decreased vaginal lubrication, orgasmic dysfunction, and decreased libido in women.

**Lipid Disorders**

Alterations in circulating lipids are different in type I versus type II diabetes mellitus. Hypertriglyceridemia occurs in type I diabetes because of a lack of insulin; in general, this can be corrected with proper insulin administration.54 People with type II diabetes and impaired glucose tolerance experience twice the incidence of hypertriglyceridemia and low HDL cholesterol than people who do not have diabetes.55 These changes are thought to be related to insulin resistance and hyperinsulinemia.55 Elevated cholesterol is not more common in people with diabetes; compared with nondiabetics, however, LDL cholesterol in diabetes is more prone to glycation and oxidation. These biochemical changes increase the atherogeneity and decrease the metabolism of LDL cholesterol.57
Other Metabolic Concerns

The insulin resistance that leads to type II diabetes mellitus and impaired glucose tolerance is due to a defect in insulin-mediated glucose uptake by skeletal muscle. This is associated with hyperinsulinemia, which also characterizes impaired glucose tolerance and early type II diabetes. Insulin resistance and hyperinsulinemia have been linked epidemiologically to hypertension, dyslipidemia (which includes increased circulating triglycerides and low HDL cholesterol), and elevated uric acid. These associations are more common among whites and possibly African Americans compared with American Indians and Mexican Americans; whether these associations are linked pathophysiologically is currently under intense investigation. Insulin resistance and hyperinsulinemia affect the mechanisms that (1) regulate blood pressure, including sodium handling, sympathetic nervous system, and vascular remodeling, and (2) regulate liver triglyceride production and HDL cholesterol metabolism.

Obesity

Approximately 34 million adults in the United States are obese. The health risks of obesity rise with its severity. Obesity is associated with an increased risk for hypertension, diabetes, hypertriglyceridemia, and low HDL cholesterol as well as increased levels of total cholesterol, LDL cholesterol, and very-low-density lipoprotein cholesterol. The deposition of excess fat in the upper body (abdominal obesity), with an increased waist-to-hip ratio above 0.85 in women and 0.95 in men, also has been correlated with hypertension, diabetes, dyslipidemia, and increased mortality from CHD. Insulin resistance has been proposed as a common link among these risk factors.

An excess of calories, a high-fat diet that promotes positive energy balance, and a sedentary lifestyle all contribute to overweight and obesity as well as to type II diabetes.

Pregnancy

Diabetes mellitus occurs in 2% to 5% of pregnant women and is more common in obese women, women of certain minority populations, and older women. Of these, only 10% will have been known to have had diabetes before pregnancy. Thus, most patients with diabetes during pregnancy or gestational diabetes are diagnosed while pregnant. Pregnant women should be screened for gestational diabetes at 24 to 28 weeks of gestation using a 50-g glucose challenge; a positive test occurs when the glucose level exceeds 150 mg/dL 1 hour after an oral load. It is currently unclear whether patients with gestational diabetes have a significantly increased prevalence of hypertension. Treatment of hypertension associated with gestational diabetes, in addition to dietary factors directed at the diabetic state, should include drug therapy when blood pressure is greater than 140/90 mm Hg.

In patients with diabetes before pregnancy and coexisting hypertension, blood pressure should be maintained at less than 140/90 mm Hg. In those patients with proteinuria at the onset or the development of significant proteinuria during the first two trimesters of pregnancy, a more aggressive therapeutic approach is in order—maintaining DBP at 80 to 90 mm Hg to prevent further renal glomerular damage. Angiotensin converting enzyme (ACE) inhibitors are contraindicated. There is substantial evidence that pregnant women with both diabetes and hypertension are more likely to develop superimposed preeclampsia; thus, these patients should be watched carefully for worsening hypertension and proteinuria as they approach term. Patients who have hypertension and diabetes during pregnancy are at very high risk and require special monitoring care or consultation from a perinatal specialist.

Children: Type I

Diabetes mellitus of childhood onset is usually type I, and hypertension occurs with greater frequency in such children. Hypertension in children or adolescents with type I diabetes often reflects incipient nephropathy but may represent essential hypertension as well. Patients, including children and adolescents, with type I diabetes who exhibit albuminuria frequently have a positive family history of hypertension. The Task Force on Blood Pressure Control in Children has established blood pressure criteria to define hypertension in children and adolescents. Children and adolescents with blood pressure levels repeatedly above the 95th percentile for age and sex meet the criteria for the diagnosis of hypertension, and these values also apply to children with diabetes. Fig 2 provides the blood pressure values for the 50th, 95th, and 99th percentiles in the childhood blood pressure distribution.

Frequent measurement of blood pressure should be a routine part of the clinical management of children with diabetes. For children and adolescents with type I diabetes, lifestyle modification is beneficial for blood pressure as well as for metabolic control. These lifestyle parameters include physical exercise, appropriate diet, and avoidance of tobacco. Although optimal growth is an important clinical goal for children with diabetes, obesity should be avoided.

The development of proteinuria in children with diabetes should be considered evidence of nephropathy. With signs of nephropathy, dietary protein intake should be reduced to less than 15% of the total caloric intake to conserve renal function.

When children or adolescents with diabetes are discovered to have hypertension, it is likely that the hypertension is related to the diabetes. However, if the hypertension is severe, the possibility of other underlying causes should be considered. Severe hypertension (eg, DBP 10 mm Hg above the 95th percentile) in children with diabetes should be evaluated carefully in consultation with a specialist. Pharmacologic therapy is appropriate for children and adolescents with diabetes when DBP is fixed at or above the 95th percentile. When pharmacologic therapy is used to lower blood pressure in children with both diabetes and hypertension, a reasonable goal is to lower the blood pressure to the 90th percentile or less. Drug regimens that are recommended for adults with both diabetes and hypertension are effective and may be used in children and adolescents. There are some special considerations in determining antihypertensive drugs for children. In
general, β-blockers are avoided because these agents may mask hypoglycemia. Centrally acting drugs, such as methyldopa, clonidine, and centrally acting β-blockers, should be used with caution because the central action may cause excessive drowsiness or depression and may interfere with school performance. Despite the concern about long-term use of antihypertensive drugs in children, control of high blood pressure in children with diabetes is especially important because of the high risk of diabetic nephropathy.

**Treatment**

The goal of treating hypertension in patients with diabetes mellitus is to prevent associated morbidity and mortality. Clinicians must consider the severity of the levels of blood pressure and blood glucose as well as the presence of other complications or additional risk factors. The least intrusive means to managing the concomitant diseases should be sought. Lifestyle modifications—including weight management, diet (ie, salt reduction), moderation of alcohol intake, increased physical activity, and smoking cessation—are the cornerstones of therapy. Patients must be counseled about guidelines for safe exercise, including monitoring blood glucose and taking appropriate action, altering food or insulin if needed, carrying identification (eg, medical bracelet or tag) and easily absorbed carbohydrates (eg, candy), and monitoring exercise intensity to avoid risk of metabolic complications. Fig 3 summarizes the treatment algorithm for patients with diabetes.

**Lifestyle Modifications**

Lifestyle modifications have particular relevance for all patients with hypertension and diabetes. Lifestyle modifications can enable those individuals who are on drug therapy to reduce the number and dosage of medications needed to manage their hypertension and diabetes.81,82

**Weight Management**

Weight loss in overweight individuals can improve control of both hypertension and diabetes mellitus. Studies have shown that even modest reductions in body weight can improve blood pressure and glycemic control.83 Reductions in weight may be associated with blood pressure reductions because of reductions in insulin levels, sympathetic nervous system activity, correction of cellular cation metabolism, and vascular resistance.84,85 Even small amounts of weight loss in overweight individuals can help reduce LDL cholesterol levels and triglycerides as well as raise HDL cholesterol levels.86 Weight reduction in obese individuals also diminishes the insulin response to a glucose load, probably by enhancing tissue sensitivity.87 In fact, many patients normalize blood glucose and insulin levels simply by losing weight. Reducing caloric intake by 500 cal/d or expending this amount can lead to 1 lb of weight loss per week. The recommended diet for the treatment and management of type II diabetes provides less than 30% of calories from fat, approximately 15% of calories from protein, and 55% to 60% of calories from carbohydrates. The assistance of a registered dietitian in devising meal plans is strongly advised. Exercise also is recommended not only for weight control but also for other beneficial effects in the management of type II diabetes and hypertension.88,89

**Nutritional Considerations**

For patients receiving exogenous insulin, caloric intake and insulin administration should be adjusted temporally so that adequate calories are consumed to cover periods of peak insulin action. Within this framework, however, flexibility should be allowed so that patients are not locked into fixed times at which meals and snacks must be consumed on a daily basis. Thus, with proper education, patients can learn to adjust the time of insulin administration to coincide with the time of day a meal is desired.90

Recent evidence from the Diabetes Control and Complications Trial suggests that selected nutritional interventions—healthy food choices, exchange systems, carbohydrate counting, and total available glucose, eg, glucose available as simple sugars—can be coupled with intensive insulin therapy to obtain normoglycemia.91

**Carbohydrates.** Approximately 50% to 60% of total daily calories should be derived from carbohydrates, preferably complex carbohydrates.28 Complex carbohydrates from different vegetables, fruits, and whole grains are good sources of vitamins and fiber. A diet rich in soluble fibers including oat bran, legumes, barley, and most fruits and vegetables may be effective in reducing elevated plasma glucose and cholesterol. A high-fiber diet also may aid in weight management by promoting satiety at lower levels of calorie and fat intake. For optimal blood glucose control, up to 5% of total carbohydrates may be derived from simple carbohydrates in...
Treatment Goal <130/85 mm Hg

**Lifestyle Modifications**
- Weight reduction
- Control of hyperglycemia
- Moderation of alcohol intake
- Regular physical activity
- Reduction of sodium intake
- Smoking cessation

**Inadequate Response**

**Continue Lifestyle Modifications**

*Initial Pharmacologic Selection (in alphabetical order):*
- ACE inhibitors, alpha-receptor blockers, calcium antagonists, and diuretics in low doses are preferred because of fewer adverse effects on glucose homeostasis, lipid profiles, and renal function.

*(Beta-blockers can have adverse effects on peripheral blood flow, prolongation of hypoglycemia, and masking of hypoglycemic symptoms.)*

**Inadequate Response**

- Increase drug dose
- Substitute another drug
- Add a second agent from a different class (e.g., a diuretic, if not selected initially)

**Inadequate Response**

- Add a second or third agent, one of which should be a diuretic, if not already prescribed

*Response means achieved goal blood pressure or considerable progress toward this goal.

Fig 3. Chart shows suggested approach to hypertension therapy in subjects with diabetes (see text for precautions with certain medications). Treatment goal for people with diabetes is to maintain blood pressure at less than 130/85 mm Hg. Diabetic renal disease, autonomic dysfunction, and adverse effects on glucose and lipid metabolism must be considered before the course of therapeutic intervention is chosen. ACE indicates angiotensin converting enzyme.

the form of sucrose. Simple carbohydrates generally should not be consumed alone but rather in concert with a mixed meal to slow their absorption rates. As with total calories, carbohydrates should be distributed evenly throughout the day.

**Fat, saturated fat, and cholesterol.** Because dyslipidemia often coexists in people with hypertension and diabetes, the fat content of the diet should be reduced to less than 30% of total calories, with less than 10% coming from saturated fat. Cholesterol intake should be less than 300 mg/d.

**Protein.** The protein recommendations for patients with both diabetes and hypertension do not differ from the recommendations for the general population. Approximately 10% to 15% of total calories (15% to 20% in children) should be derived from plant sources of
protein and lean sources of animal protein. Reduction of protein intake appears to delay the progress of diabetic nephropathy.92

**Cations (electrolytes).** A diet moderately restricting sodium chloride to a level of less than 100 mmol/d (approximately 2.3 g sodium or approximately 6 g sodium chloride) may reduce elevated blood pressure.16,98 Adequate dietary intake of potassium and magnesium may be particularly important in patients with diabetes. Hypomagnesemia may play a role in increasing carbohydrate intolerance, platelet aggregability, vascular resistance, and lipid abnormalities.94,95 These minerals should be consumed at the US Recommended Daily Allowances. It is premature to suggest supplementation of these minerals beyond the recommended levels.

**Alcohol**

Heavy alcohol consumption may raise blood pressure and cause resistance to antihypertensive therapy.96 In addition, alcohol provides unneeded calories, displaces more nutritious foods, and may interfere with the regular routine of diabetes self-management. Therefore, alcohol should be consumed in moderation in patients with diabetes and hypertension.16 Individuals should account for additional calories from alcohol in the meal plan by reducing the fat intake allowance. People with hypertriglyceridemia may need to refrain totally from drinking alcohol so that their serum triglyceride levels are not exacerbated.97

**Physical Activity**

Regular physical activity has many potential benefits for patients with diabetes and hypertension. In addition to improving insulin sensitivity and glucose tolerance in diabetes, it may help to lower blood pressure and reduce the need for and dosage of insulin or oral hypoglycemic drugs. Health professionals generally should advise patients with hypertension and diabetes who have been sedentary and are initiating an exercise program to do so gradually and after appropriate medical evaluation.98

**Smoking**

Cigarette smoking is a major risk factor for CHD and peripheral vascular disease and is the largest preventable cause of death and disease.99 For these reasons, people with diabetes and hypertension who smoke should be apprised of the risks associated with smoking and strongly advised to quit. For more information on smoking cessation programs, contact the National Heart, Lung, and Blood Institute (NHLBI) Information Center, PO Box 30105, Bethesda, MD 20824-0105.

**Pharmacologic Treatment of Hypertension**

The Joint National Committee16 recently conducted an extensive review of therapeutic approaches to treating patients with hypertension. Five classes of antihypertensive agents are generally available. However, the concomitant presence of diabetes mellitus in patients with hypertension carries a greater risk because of the independent effects of these two diseases on several common target organs (eg, heart, kidney, vascular system, eyes). Although the general approach to using pharmacologic agents in patients with diabetes and hypertension is similar to that used with only hypertension, there are several qualifications.

(1) Although the goal blood pressure is similar in patients with and those without diabetes, it is more important for physicians to work closely with patients with diabetes to achieve this goal. Therefore, patients with diabetes who have blood pressures at 140/90 mm Hg or greater specifically remain candidates for further therapeutic intervention, and a goal blood pressure of less than 130/85 mm Hg is recommended for these patients.

(2) Diabetic renal disease is an important complication that must be taken into consideration. Thus, therapeutic decisions need to consider effects of specific antihypertensive therapy on renal function and the progression of diabetic nephropathy.

(3) Therapeutic modalities can have adverse effects on glucose and lipid metabolism.

(4) Autonomic dysfunction, which can result in postural hypotension, is common in diabetes and must be considered in therapeutic decisions.

For those with stage 1 hypertension, a 3-month period of lifestyle modifications is indicated. If lifestyle modification does not lower blood pressure to the goal level (130/85 mm Hg), then drugs should be added. In patients with diabetes who have blood pressures greater than 140/90 mm Hg, pharmacologic intervention generally is indicated.

Of special concern is the proper determination of blood pressure to assess therapeutic response. A seated blood pressure is the most desirable because of its practicality and its ability to integrate both the beneficial and negative (hypotension) effects. In addition, it is highly desirable that postural blood pressure responses be assessed (ie, supine to standing, seated to standing). Home blood pressure monitoring should be performed in conjunction with home blood glucose monitoring, because good blood pressure control is critically important, and blood pressure is more likely to fluctuate over a 24-hour period in individuals with diabetes and hypertension.2

Renal disease contributes to hypertension in patients with diabetes through several pathogenic mechanisms: sodium and water retention (extracellular fluid volume expansion) and increased vascular resistance. Renal disease in patients with diabetes and hypertension may be associated with mesangial cell hypertrophy, increased glomerular capillary resistance, glomerular basement membrane thickening, and renal vascular disease. Microalbuminuria indicates the presence of diabetic nephropathy, and the progression of diabetic nephropathy appears to be correlated with a rise in blood pressure. Compounding these renal abnormalities is the contribution of hyperglycemia per se to the volume expansion and consequent hypertension. Thus, therapeutic approaches should include normalization of blood glucose in addition to the use of agents that will reduce both intravascular volume and intrarenal pressure.

**Antihypertensive Drugs**

ACE inhibitors are useful in patients with diabetes mellitus because they do not adversely affect the patient’s metabolic state and may reduce proteinuria associated with diabetic nephropathy.100 ACE inhibitors may be especially desirable in those patients who have evidence of renal parenchymal disease (ie, proteinuria,
microalbuminuria) because of their beneficial effects in reducing proteinuria in experimental studies and clinical studies.\textsuperscript{106-108} In a recently reported randomized multicenter clinical trial, during a median follow-up of 3 years, treatment with an ACE inhibitor significantly decreased the rate of increase in creatinine and the rate of decline of creatinine clearance. The combined end point of mortality, dialysis, and transplantation was reduced by 50% with ACE inhibitor therapy. These benefits appeared to occur independently of effects on blood pressure, suggesting that ACE inhibitors may have special salutary effects in people with type I diabetes and renal disease. It has not been determined whether similar beneficial effects have been observed in a similar study protocol with other antihypertensive drugs. It also has not been determined whether the results of Lewis and colleagues\textsuperscript{100} pertain to people with type II diabetes and renal disease.

A major risk of ACE inhibitors is an acceleration of renal insufficiency, particularly in patients with bilateral renal artery stenosis—a more common occurrence in people with diabetes. Close monitoring of renal function and serum potassium should be performed in the first few weeks after initiation of therapy if bilateral renal artery disease is suspected. ACE inhibitors may cause hyperkalemia, particularly in those individuals with renal failure or hyporeninemic hypoaldosteronism (type IV renal tubular acidosis). Care must be exercised in initiating ACE inhibitor therapy in patients receiving diuretics because there may be a profound drop in blood pressure and a decline in renal function.

\textit{\textbf{\textalpha-}} Receptor blocking agents, particularly those that have a 24-hour duration of action, are effective antihypertensive agents in patients with hypertension and diabetes. These agents may have beneficial lipid metabolism effects\textsuperscript{100}; however, they do need to be used with some caution because they may induce orthostatic hypotension.

Calcium antagonists also may be useful in treating hypertension in patients with diabetes. Calcium antagonists do not appear to have an adverse effect on glucose, lipid metabolism, or renal function. Caution does need to be exercised because of the potential of some calcium antagonists to induce orthostatic hypotension, which may be accentuated in patients with diabetes.

Thiazide diuretics are used frequently and successfully to treat hypertension in individuals with diabetes. If the dose is low (ie, 25 mg or less hydrochlorothiazide), adverse effects on carbohydrate metabolism, hypokalemia, and hypomagnesemia are uncommon. Furthermore, this class of agents is generally as effective as ACE inhibitors in lowering blood pressure in patients with diabetes.\textsuperscript{106} Indeed, long-term data (4 years) indicate that diuretics have the same effect as ACE inhibitors on reducing the progression of renal disease in patients with type II diabetes.\textsuperscript{106} It is likely that volume expansion contributes to the elevated arterial pressure in these individuals. On the other hand, as the dose of the diuretic increases, the diuretic-induced side effects are increased in patients with diabetes (ie, alterations in glucose and lipid metabolism, adverse effect on renal hemodynamics). The use of thiazide diuretics does not appear to increase the incidence of clinical diabetes to a greater extent than other antihypertensive drugs,\textsuperscript{107} nor do they adversely alter the beneficial mortality outcome in patients treated for diabetes and hypertension.\textsuperscript{106} Thus, thiazide diuretics are effective antihypertensive agents in these patients but should be used in low doses.

Several concerns limit the usefulness of \textit{\textbeta-} blockers in treating people with diabetes: (1) These agents have adverse effects on glucose and lipid metabolism,\textsuperscript{16} (2) they can reduce awareness of hypoglycemia in patients with diabetes and prolong recovery from hypoglycemia, and (3) they can reduce peripheral blood flow in patients who already have a compromised peripheral vascular system. Thus, except under special circumstances (eg, in the presence of angina pectoris and postmyocardial infarction), \textit{\textbeta-} blockers should be used with caution in patients with diabetes and hypertension. Potassium-sparing agents also should be used with caution in people with diabetes because of the increased susceptibility of these patients to developing hyperkalemia. ACE inhibitors may cause hyperkalemia in patients with renal impairment.

Patients with diabetes and isolated systolic hypertension, hypertensive crisis, or supine hypertension with orthostatic hypotension can be treated by algorithms similar to those used in people without diabetes. For the rest, beginning with an ACE inhibitor, a calcium antagonist, a peripheral \textit{\textalpha-} adrenergic blocker, or a small dose of a thiazide diuretic is appropriate initial therapy.

Much of the information concerning the potential benefit or risk of various therapeutic modalities in patients with diabetes and hypertension is based on limited results from clinical trials and experimental animal data. Thus, physicians still must rely heavily on clinical judgment in developing an effective treatment program for these patients. Furthermore, continued emphasis on lifestyle modification (eg, weight reduction, aerobic exercise) remains very important even though patients require pharmacologic treatment as well.

\textbf{Diabetes With Renal (Parenchymal) Hypertension}

A persistent increase in albumin excretion rates on at least three occasions and/or a progressive decline in renal function suggests a diagnosis of renal (parenchymal) disease. Hypertension in patients with diabetic nephropathy is manifested by sodium and water retention (extracellular fluid volume expansion), increased cardiac output, and increased peripheral vascular resistance. Although these mechanisms do not differ from those usually encountered in patients with hypertension who do not have diabetes, special consideration must be given in choosing antihypertensive agents for patients with diabetes and renal disease.\textsuperscript{104}

Several studies have been conducted or are in progress to determine the relative efficacy of differing antihypertensive agents on blood pressure and renal function in people with diabetes.\textsuperscript{106,108} The results of these studies are not yet sufficient to make definite recommendations. Some of the studies have been conducted in type I diabetes, representing 5% to 10% of Americans with diabetes. Others have included people with diabetes who do not have hypertension and have used microalbuminuria as a surrogate for alterations in renal function.\textsuperscript{106} Some, but not all, studies with calcium antagonists have suggested a reduction in albumin excretion, and at least one study has suggested an additive benefit when an ACE inhibitor and a calcium antagonist are combined.\textsuperscript{109} However, the longest accumulation of
data is from studies from Denmark, which indicate that lowering blood pressure (ie, with diuretics and β-blockers) reduces the progression rate of diabetic renal disease. When significant diabetic renal disease is present, the use of loop diuretics may be necessary for appropriate volume reduction.

**Diabetes With Isolated Systolic Hypertension**

Several recent studies demonstrate that reducing an isolated elevation of systolic pressure (SBP >160 mm Hg and DBP <90 mm Hg) can reduce cardiovascular morbidity and mortality from stroke. Thiazide diuretics can be used in small doses as initial drug therapy. Initially, patients, especially older patients, should be seen frequently (at 2- to 4-week intervals) and observed for orthostatic hypotension associated with volume depletion. If a second drug is necessary, ACE inhibitors and calcium antagonists are generally efficacious and well tolerated. ACE inhibitors also provide additional therapeutic benefits in elderly patients with congestive heart failure. If SBP fails to respond to initial and second-choice drug therapy, hydralazine can be added as a third drug. Minoxidil also may be used in resistant cases if a vasodilator has not been used as a second-choice drug.

**Supine Hypertension With Orthostatic Hypotension**

Supine hypertension with orthostatic hypotension in patients with diabetes is associated with autonomic neuropathy and is the most difficult to treat. Occasionally, the upright blood pressure falls to such an extent that patients are unable to assume the upright posture, which may be aggravated by many antihypertensive medications that cause orthostatic hypotension. To reduce symptoms, the goal of therapy is to increase the upright pressure and lower the supine pressure. To increase the upright pressure, 9α-fluorohydrocortisone, which produces sodium retention and can increase volume, is prescribed in small doses of 0.05 to 0.20 mg daily. Elevation of supine blood pressure and precipitation of heart failure are potential complications of this mineralocorticoid agent. Good elastic hose personally fitted to cover the legs and thighs and perhaps to waist level (such as Jobst stockings) are sometimes beneficial.

Both drugs and mechanical maneuvers can help in lowering supine pressure. Short-acting vasodilators (ie, ACE inhibitors, calcium antagonists, hydralazine) can be taken shortly before bedtime to reduce nocturnal supine blood pressures. Initial doses should be small and slowly titrated upward to prevent orthostatic hypotension in the morning hours. Mechanically elevating the head of the bed 10 inches will allow gravity to decrease the supine blood pressure.

**Drugs for Managing Hypertensive Emergencies in Diabetic Patients**

The pharmacologic treatment of hypertensive emergencies in patients with diabetes is not different from that for people who do not have diabetes. Treatment usually is administered with parenteral agents, including sodium nitroprusside, and various adrenergic blocking agents. However, the potential detrimental effects of several agents in producing uncontrolled profound drops in blood pressure or increased cardiac output should be considered carefully in patients with diabetes who may have concomitant CVD and cerebrovascular disease. Diazoxide may exacerbate hyperglycemia and therefore is contraindicated.

**Considerations in Education, Control, and Maintenance**

Long-term maintenance of an effective treatment regimen requires continuing commitment by patients and health care providers. Physicians assume primary responsibility for establishing therapy and assisting patients in adhering to the regimen. Nurses, pharmacists, podiatrists, optometrists, dietitians, and other health professionals play an important role in the care, education, and support of patients. Patients should be urged to assume primary responsibility for mastering the self-care knowledge and skills necessary for following the treatment plan. Adherence to long-term antihypertensive therapy is improved when the regimens are simplified, clarified, reinforced, and coordinated with diabetes-related tasks. Patients benefit from specific and understandable written instructions regarding diet and exercise plans, medication, and common side effects.

Poor adherence to therapy, both lifestyle modifications and pharmacologic therapy, has been identified as the major reason for inadequate control of high blood pressure and blood glucose levels. Some of the common causes for the lack of poor adherence include cost of medication, unclear instructions and/or instructions that are not given to the patient in writing, inadequate or no patient education, lack of involvement of the patient in the treatment plan, and side effects of medication.

Patient education programs should be tailored for the individual and should use culturally sensitive communication strategies. Health professionals need to be knowledgeable about ethnic, regional, and religious issues. The learning styles of adults tend to be more self-directed than those of children, who are more dependent on the educator for direction. However, active learning experiences have proved successful in all age groups. Involving spouses and other family members in the educational process provides support in the learning experience.

Home monitoring (with family assistance) of blood glucose or blood pressure may be used to assist patients in attaining desired levels of blood glucose and blood pressure. They also provide an objective means of evaluating the effectiveness of interventions. Home monitoring is a potentially powerful tool for increasing patients’ understanding of the therapeutic regimen and encouraging their active participation in achieving the desired health outcomes. Adherence to home monitoring is improved by the availability of handy and easy-to-use materials for recording results, regular clinician feedback about the record of results, and patient awareness that the measurement procedure and results will be evaluated periodically for accuracy.

Physicians may find it helpful to coordinate their resources with health education programs operated in communities, worksites, and hospitals. Such programs can help emphasize the importance of long-term control and can help in long-term monitoring. Patient awareness of blood pressure or blood glucose levels also can...
be increased, thus reinforcing patients’ agreements with their providers on goal level.

The economic burden of chronic disease can be substantial. In many settings, hypertension and diabetes mellitus represent the most commonly encountered combination of diseases. Long-term adherence to a carefully prescribed and maintained therapeutic program oriented toward ambulatory care and self-care and the judicious use of home care can prevent the need for more expensive inpatient hospital services.116 Physicians and other health care professionals need to be aware of the economic issues in providing optimal long-term cost-effective care.16

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