The Effect of Nutrition on Blood Pressure

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Abstract

The incidence and severity of hypertension are affected by nutritional status and intake of many nutrients. Excessive energy intake and obesity are major causes of hypertension. Obesity is associated with increased activity of the renin-angiotensin-aldosterone and sympathetic nervous systems, possibly other mineralcorticoid activity, insulin resistance, salt-sensitive hypertension and excess salt intake, and reduced kidney function. High sodium chloride intake strongly predisposes to hypertension. Increased alcohol consumption may acutely elevate blood pressure. High intakes of potassium, polyunsaturated fatty acids, and protein, along with exercise and possibly vitamin D, may reduce blood pressure. Less-conclusive studies suggest that amino acids, tea, green coffee bean extract, dark chocolate, and foods high in nitrates may reduce blood pressure. Short-term studies indicate that specialized diets may prevent or ameliorate mild hypertension; most notable are the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruits, vegetables, and low-fat dairy products, and the DASH low-sodium diet. Long-term compliance to these diets remains a major concern.

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INTRODUCTION

Hypertension is a highly prevalent disorder, occurring in approximately 50 million people in the United States and in about one billion people worldwide (40, 116). The severity of elevated blood pressure and hypertension has been classified by the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (see **Table 1**) (40). The widespread concern over the high prevalence of hypertension is due to compelling evidence that it is a major cause of morbidity and mortality (124, 142, 209). Moreover, lifestyle clearly plays a major role in the pathogenesis and current high prevalence of hypertension. Overweight and obesity (particularly visceral obesity), low birth weight, and increased or reduced intake of a number of nutrients have been associated with high blood pressure (BP) (13, 66, 77, 161). Overweight and obesity have increased to epidemic proportions in industrialized countries, and the prevalence

of these conditions is increasing rapidly in the developing world (66, 68). Indeed, it is estimated that roughly 1.4 billion adults worldwide are overweight or obese (118), and this number appears to be increasing. These considerations have made the relationship between blood pressure and obesity, energy intake, and excessive or deficient intake of nutrients a subject of great importance. **Table 2** lists nutritional factors that may affect BP. Interactions between BP and both obesity and nutrient intake are discussed in turn below.

Table 1 Classification of blood pressure (BP) for adults*

BP classification	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Normal	<120	<80
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥160	≥100

*This classification is based on the average of two or more properly measured, seated, BP readings performed on each of two or more office visits. Reprinted from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. 2003. *JAMA* 289:2560–72. U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute, National High Blood Pressure Education Program, NIH Publication No. 04–5230, August 2004.

ENERGY INTAKE AND OBESITY

Body Mass and Obesity

Adult obesity can be defined as a body mass index (BMI) ranging above 30 kg/m^2; morbid obesity as a BMI more than 35 kg/m^2; and overweight as a BMI between 25 and 30 kg/m^2 (68). Overweight and obesity are considered to occur at a lower BMI in Asian peoples because the direct association of these variables with cardiovascular risk factors, including hypertension, occurs at lower weights-for-height in Asian peoples than in Caucasians (105, 163). Much evidence directly links obesity with elevated BP. Obesity, per se, appears to directly increase BP, and obese individuals are more likely than nonobese subjects to have elevated BP (56, 66, 163). Even in older adults, a higher BMI is associated with an increased risk for hypertension. In a study of adult family medicine patients, the prevalence of prehypertension [systolic BP (SBP) 120–139 mm Hg; diastolic BP (DBP) 80–89 mm Hg] increased significantly as the BMI rose from overweight to obese to morbidly obese (187). In obese people, a low dietary energy intake that induces weight loss reduces BP (183, 195). BP has been correlated with both fat cell size and number (56). Obese individuals may have larger adipocytes with altered metabolic activity that may produce bioactive molecules that predispose to hypertension (e.g., leptin, angiotensinogen, free fatty acids, reactive oxygen species) as discussed in the following paragraphs (74, 173, 220). Obese individuals may also exhibit enhanced infiltration of macrophages into adipose tissue, which promotes an inflammatory state (173).

The distribution of fat also influences BP. The ratio of the circumference of the waist to the hip correlates directly with both SBP and DBP (i.e., the male fat distribution is correlated with the blood pressure level) (56, 161). Moreover, the combination of abdominal obesity (waist circumference of 102 cm or greater in men and 88 cm or greater in women) and truncal obesity (ratio of the subscapular to triceps skinfold thicknesses of 2.24 or greater in men and 1.32 or greater in women) is associated with an increased risk of hypertension. The risk of hypertension associated with this altered fat distribution varies according to race and ethnicity (33, 103). These racial/ethnic

BMI: body mass index

SBP: systolic blood pressure

DBP: diastolic blood pressure

Table 2 Nutritional factors that may affect blood pressure

1. Obesity
2. Energy intake
3. Fat intake
4. Sodium intake
5. Potassium intake
6. Magnesium intake
7. Dietary fiber
8. Nutrient/gene interactions
9. Nutrient/medicine interactions

differences concerning the quantity and location of body fat and hypertension are consistent with the findings of several studies that there is a gene-obesity interaction in the pathogenesis of hypertension in some people (48, 174).

RAAS: renin-angiotensin-aldosterone system

Mechanisms by Which Increased Body Fat Causes High Blood Pressure

Overweightness and obesity are associated with many physiological and metabolic changes that promote hypertension as indicated in **Table 3** and in recent reviews (71, 133, 173, 193). These alterations include the elevated activity of the renin-angiotensin-aldosterone system (RAAS) (56, 203). Obesity is associated with increased plasma angiotensinogen, renin, aldosterone, and angiotensin-converting enzyme (ACE) levels and urinary aldosterone (42, 188). Plasma renin activity (PRA), relative to the sodium chloride intake, may be disproportionately high (56, 195). Obese individuals who undergo weight reduction display a decrease in PRA and plasma aldosterone levels, which occurs independently of changes in the sodium intake (56). In experimental models, adipocytes release factors that stimulate the release of aldosterone and other compounds that may activate the mineralcorticoid receptor and promote sodium retention (70). Obese people without heart failure or chronic kidney disease (CKD) and people with higher BMI may have lower levels of serum or plasma probrain natriuretic peptide as well as the saliuretic compound, brain natriuretic peptide (54, 170, 193, 206, 223). The subcutaneous adipose tissue in obese hypertensive individuals displays a reduced ratio of mRNA levels for the natriuretic peptide

Table 3 Mechanisms of hypertension in obesity

1. Activation of the renin-angiotensin-aldosterone system (RAAS).
a. Increased serum angiotensinogen, renin, aldosterone, and angiotensin-converting enzyme levels are found in obesity.
b. Plasma renin activity, relative to sodium chloride intake, is increased in obese subjects.
c. Adipose tissue releases factors that stimulate the release of aldosterone and other mineralcorticoid compounds.
2. Obese individuals often have increased sodium intake.
3. Activation of the sympathetic nervous system (SNS).
a. Glucose ingestion increases plasma norepinephrine.
b. Obese subjects have higher supine plasma epinephrine, norepinephrine, and plasma renin activity and greater norepinephrine response to upright posture and handgrip exercise.
c. Weight loss leads to more normal plasma hormone levels.
4. Thyroid hormone. Overeating increases triiodothyronine production. T3 increases beta-adrenaline receptors.
5. Insulin resistance (causes increased renal NaCl reabsorption, SNS overactivity, and proliferation of vascular smooth muscle cells).
6. Obesity-associated chronic kidney disease (e.g., from focal segmental glomerulosclerosis or diabetic nephropathy).
7. Release from adipose tissue of leptin, resistin (antagonizes insulin), proinflammatory cytokines (C-reactive protein, tumor necrosis factor-alpha, interleuken-6, nonesterified fatty acids), and reactive oxygen species. Rat studies indicate that these compounds may activate the mineralcorticoid receptor.
8. Endothelin-1 (causes vasoconstriction; may impair nitric oxide synthesis capacity).
9. Nonesterified fatty acids. Excessive nutrient intake may increase portal venous delivery of unsaturated nonesterified fatty acids, which are associated with increased blood pressure.
10. Increased leptin levels, which may promote SNS activity.
11. Low adiponectin levels in obesity. Low adiponectin is associated with hypertension, low nitric oxide production, and endothelial dysfunction.
12. Obstructive sleep apnea (may increase SNS activity, cause endothelial dysfunction, and enhance RAAS activity, and may be associated with low adiponectin levels).

membrane receptor, guanylyl cyclase type-A, which is activated by natriuretic peptides, as compared to the natriuretic peptide clearance receptor, which clears these peptides (54, 193, 223). These data suggest either that there is reduced synthesis of the natriuretic peptide membrane receptor or increased synthesis of the receptor that clears the natriuretic peptide from plasma. The natriuretic and diuretic response to atrial natriuretic peptide may be reduced in obesity (52).

Sympathetic nervous system (SNS) activity may be increased in both the metabolic syndrome and obesity (56, 112, 195). Insulin resistance with hyperinsulinemia and increased plasma leptin, which may be present in obesity, increase SNS activity (22, 112, 134, 154, 195). Obese subjects have higher supine plasma epinephrine, norepinephrine, and PRA, increased urinary norepinephrine, and a greater norepinephrine response to upright posture and isometric hand-grip exercise (195). Weight reduction in these individuals leads to more normal plasma levels of these hormones (195). Glucose ingestion increases plasma norepinephrine, and thyroid hormone may be increased. Overeating may enhance triiodothyronine production from thyroxine, and triiodothyronine may increase beta-adrenaline receptors (112, 115).

Obesity predisposes to obstructive sleep apnea (80, 112, 201). Persons with increased episodes of apnea or hypopnea during sleep are at increased risk for developing hypertension (175). Obstructive sleep apnea is associated with insulin resistance, increased SNS activity, endothelial dysfunction, enhanced RAAS activity, increased plasma leptin, and low serum adiponectin (80, 104, 112, 178). Possibly for these reasons, obstructive sleep apnea–associated hypertension may be resistant to pharmacological therapy. Effective treatment of obstructive sleep apnea is associated with a reduction in SNS activity and a decrease in both daytime and nocturnal BP and in refractory hypertension (19, 162).

Obesity may predispose to hypertension by promoting renal sodium retention through insulin resistance. Insulin stimulation of sodium reabsorption in the proximal tubules appears to be mediated primarily by stimulating insulin receptor substrate 2 (IRS-2) (71, 240). In isolated renal proximal tubules from knock-out mice for IRS-1, insulin still induces sodium reabsorption, presumably by activating IRS-2 (240). On the other hand, insulin stimulation of sodium reabsorption is significantly reduced in knock-out mice for IRS-2 (240). Thus the high circulating levels of insulin in obesity, in part due to insulin resistance, may on the one hand lead to alterations in carbohydrate metabolism and on the other hand enhance renal tubular sodium reabsorption, sodium retention, salt-sensitive hypertension, and edema. Weight loss reduces resistance to insulin (179).

Obesity increases the risk of CKD, which is due primarily to focal segmental glomerulosclerosis and diabetes mellitus and hypertension, which may lead to diabetic nephropathy and/or hypertensive nephrosclerosis (133). CKD, in turn, may promote sodium retention. Obesity may be associated with increased plasma leptin levels and resistance to leptin (22, 112), abnormal plasma levels of coagulation factors, increased reactive oxygen species, inflammation, and endothelial dysfunction, which may also contribute to hypertension (14, 26, 74, 112, 202). Weight loss in overweight and obese adults improves conduit and resistance artery endothelial function and reduces plasma leptin (179). Evidence, somewhat conflicting, suggests that increased leptin may contribute to SNS activation, sodium retention, and vascular resistance (22, 87, 133, 172). Adipose tissue releases leptin, resistin (which antagonizes the actions of insulin), such proinflammatory cytokines as tumor necrosis factor α (TNFα) and nonesterified fatty acids (NEFAs), and reactive oxygen species (71). Rat studies suggest that these latter compounds may activate the mineralcorticoid receptor (71). Endothelin-1 released from adipose tissue causes vasoconstriction and may impair the capacity for nitric oxide synthesis. Excessive nutrient intake may also increase portal venous delivery of NEFAs that may increase blood

SNS: sympathetic nervous system

IRS: insulin receptor substrate

NEFAs: nonesterified fatty acids

pressure (see above). Serum adiponectin levels are reduced in obesity, and low adiponectin is associated with low nitric oxide production, endothelial dysfunction, and hypertension.

As is evident, many of the foregoing processes may work additively to promote hypertension and particularly salt-sensitive hypertension in overweight and obese people. For example, the combination of hyperreninemia, hyperaldosteronism, increased levels of other compounds with mineralcorticoid-like actions, hyperinsulinemia, increased SNS activity, CKD, a propensity to retain sodium, and polyphagia with excessive sodium intake may cause sodium chloride–sensitive hypertension (133, 186, 233, 240). Insulin resistance also may predispose to both increased activity of the renin-angiotensin system (203) and inflammation (63). Increased SNS activity in association with increased endothelin-1 and other factors may promote endothelial and vascular dysfunction (133). The metabolic actions of adipocytes appear to contribute importantly to many of these processes.

Obese individuals are at increased risk for the metabolic syndrome. The Adult Treatment Panel III of the National Cholesterol Education Program defines the metabolic syndrome as the presence of at least three of the following constellation of findings (6, 84): an increased abdominal waist circumference (greater than 40 inches in men; greater than 35 inches in women), elevated BP (130/85 mm Hg or greater), hypertriglyceridemia (150 mg/dl or greater), low serum high-density lipoprotein cholesterol (less than 40 mg/dl in men and less than 50 mg/dl in women), and a fasting blood glucose of 110 mg/dl or greater. Other expert groups have defined the metabolic syndrome somewhat differently (84). People with the metabolic syndrome are likely to have hypertension (which can be considered a part of the metabolic syndrome) and are prone to develop diabetes mellitus, particularly of the type 2 variety. They are also at high risk for cardiovascular, cerebral-vascular, and peripheral vascular disease. In line with this association with vascular disease, some investigators have expanded the concept of the metabolic syndrome to include other cardiovascular risk factors, and particularly those risk factors associated with inflammation, chronic kidney disease, or cardiovascular disease (77). The usefulness of the concept of the metabolic syndrome has recently been challenged because, it is argued, the hazard ratios for morbidity and mortality associated with the metabolic syndrome may be no greater than the sum of the hazard ratios of the individual components of the syndrome (114).

A number of observers have described a direct relationship between BMI, obesity, diabetes mellitus, weight gain or increased waist circumference, nephrolithiasis, and hypertension (45, 61, 85, 168, 218, 219). Calcium oxalate and uric acid stones as well as elevated serum urate and altered urate metabolism have been associated with increased prevalence of obesity, diabetes mellitus, and hypertension (45, 61, 85, 168, 219). Several causes for these interrelationships have been proposed (61, 168, 218), but the exact mechanisms have not been clearly established. People who are psychologically depressed are at greater risk for hypertension. This relationship may be due, in part, to the greater likelihood that they are obese. Depression predisposes to obesity and hypertension (10, 23, 113). Obesity also increases the risk of developing depression (10). Thus the greater prevalence of hypertension in depressed individuals appears to be at least partly mediated by obesity (113).

Excess Fat in Neonates and Children

Overweight children are at increased risk for hypertension as they become older. On the other hand, children with low birth weights are also at greater risk for developing hypertension. This phenomenon was observed in the Helsinki study (59). These children often gain excessive weight by the end of the first 10 or 15 years of life, and presumably their increased body mass may contribute to their risk of developing hypertension (59). It has also been postulated that low-birth-weight children often have a smaller number of nephrons in their

kidneys, and this may predispose them to sodium chloride retention and hypertension (59). Other metabolic derangements in low-birth-weight or high-birth-weight babies may predispose to the metabolic syndrome, obesity, and hypertension (20, 44, 182).

Energy Intake: Weight-Reduction (Low-Energy) Diets

Weight loss due to dietary and behavioral intervention or bariatric surgery in obese, hypertensive persons is generally associated with a decrease in BP (100, 205). The effect on hypertension of medicine-induced weight loss is more nuanced (see below) (80, 81, 100, 145). High energy intake independent of obesity also seems to engender hypertension in obese individuals. Dornfeld and coworkers studied the BP of obese patients before and after they commenced treatment with a protein-sparing modified fast (55, 56). During this treatment, BP fell quickly and profoundly, even before much weight was lost. When their formula diets were discontinued and regular foods were reintroduced into their diet, many of these individuals began to ingest excessive quantities of energy and regained weight. The patients' BP continued to be measured even as their body weight rose back toward their pre-weight-loss levels. Interestingly, for a given body weight, their SBPs and DBPs were significantly greater when these same patients were ingesting excessive energy intakes and gaining weight as compared to when they were at the same body weight but eating a calorie-deficient diet and losing weight. Although there are several possible causes for the greater BPs for a given body weight during weight gain, the increased BPs most likely are related to the patients' excessive energy intake. The possible contribution to this elevated BP of metabolic processes associated with new fat deposition or the excessive intake of other nutrients, such as sodium, cannot be excluded. Among obese, normotensive individuals as compared to those with a stable weight, short-term weight gain, weight loss, or weight gain followed by weight loss was associated with an increased risk of developing hypertension within two years (196).

The reduction in BP that occurs with weight reduction does not appear to be due exclusively to reduction in energy intake and fat mass. Obese individuals often have increased dietary sodium intake (217), which may also promotes hypertension (see below). As indicated above, hyperinsulinemia, which is often present in obesity, tends to increase renal tubular sodium reabsorption. However, Reisin et al. (183) provided evidence that in obese, hypertensive individuals, ingestion of low-calorie diets and weight loss, independent of a reduction in dietary sodium intake, can lower BP. These investigators placed obese patients on an energy-restricted, weight-reduction diet (183). Each day each individual was fed an amount of sodium equal to the sodium content in his previous 24-hour urinary output. Even though the total body sodium content fell little if at all in these patients, they experienced a substantial fall in mean BP as they lost weight.

The foregoing considerations indicate that there are multifactorial causes for hypertension in overweight and obese people. Reduced dietary energy intake and weight loss in obese people probably reduces hypertension by a number of mechanisms. It is important to keep in mind that very obese individuals may have a falsely elevated BP when it is measured with a normal sized blood pressure cuff. For accurate BP measurements, the cuff size should be increased for individuals with large arm circumferences and reduced for people with small arm circumferences.

Fetal Undernutrition

The Dutch Famine, which led to undernutrition of mothers and newborn infants in the Netherlands near the end of World War II, is an example of the long-term effects of fetal undernutrition on the propensity for obesity and hypertension (211). Fetuses whose mothers were subjected to prenatal famine while the fetuses were in the second and, to a lesser extent, the third trimester of pregnancy, in the

Netherlands between November 1944 and May 1945, tended to be born with low birth weights. They also were more likely to become overweight in childhood and to have a high prevalence of obesity, hypertension, and diabetes mellitus, among other disorders, when they aged into their fifties and sixties (211).

INDIVIDUAL NUTRIENTS, OTHER SUBSTANCES, AND BLOOD PRESSURE

Sodium Chloride

There is abundant evidence for an association between high sodium chloride intake and elevated BP (14, 26, 112, 186, 202). Sodium chloride intake correlates directly with BP across population groups. The association of sodium chloride intake and BP increases with age, BP level, renal insufficiency, and among individuals with a family history of hypertension. The International Study of Salt and Blood Pressure (INTERSALT) indicated that in about 10,000 adults, aged 20–59 years old, who were evaluated at 52 centers in 32 countries, 24-hour urine sodium excretion was significantly and positively associated with the median SBP and DBP, the upward slope of SBP and DBP that occurs with age, and the prevalence of elevated BP (1, 207). Even in normal adults, salt intake affects extracellular volume, which in turn can affect the risk of hypertension; a reduction of dietary salt intake from 160 to 80 mEq/day reduces their body weight and extracellular volume by 1–1.5 liters (12). The chloride salt of sodium appears to have a substantially greater effect on raising BP than does sodium bicarbonate (50).

However, among individuals of similar age and BP level, the pressor response to high sodium intakes varies greatly. The BP of some individuals rises with high sodium chloride intakes, whereas in other individuals, the BP does not appear to be affected by the sodium chloride intake (127). Sodium chloride sensitivity can be diagnosed by a reduction in BP associated with low sodium chloride intake and/or an increase in BP with sodium chloride loading. It has been estimated that approximately 30% to 50% of hypertensive persons and a smaller percentage of nonhypertensive persons are sodium chloride sensitive. A limitation of these studies is that the testing for sodium chloride sensitivity with salt loading is generally carried out for only a few weeks or less. It is possible that a person in whom BP does not increase during several weeks of sodium chloride loading, and therefore is classified as sodium chloride resistant, might be predisposed to hypertension if he chronically ingested large quantities of sodium chloride for many months or years. This is of concern because the dietary sodium intakes in many societies are quite high and also because there is a high prevalence of hypertension among adults worldwide, particularly as people age.

Several meta-analyses have examined the effects of salt reduction on BP (11, 46, 47, 82, 88, 136). Although most meta-analyses describe BP decreases in response to a lower sodium chloride intake, some do not (11, 82). This discrepancy may be due to the inclusion in these latter studies of acute salt loads or short-term periods of salt restriction, sometimes lasting for only five days. Large and abrupt changes in salt intake can increase sympathetic tone and plasma renin activity and angiotensin II levels (88, 153). When only studies of four or more weeks' duration were included in the meta-analysis, modest restriction of salt intake (i.e., a reduction to 78 mmol or 4.6 g of NaCl) was shown to be associated with lowering of BP (153). Simply following a "no added salt diet" may reduce SBP and DBP by a mean of 12.1 and 6.8 mm Hg during the day and 11.1 and 5.9 mm Hg at night (125). This "no added salt diet" is defined as no added salt to foods and no intake of salty foods; salt intake should be below 5 g/day with a urinary sodium excretion below 100 mEq/24 hours.

Obesity appears to increase the sensitivity of BP to sodium chloride intake in adolescents, possibly because of the hyperinsulinemia, hyperaldosteronism, and enhanced sympathetic nervous system activity that is commonly found

in obese individuals (186). Weight loss in these individuals appears to decrease their salt sensitivity. Patients with essential hypertension have higher urinary free cortisol excretion (37). Such hypertensive individuals who had higher urinary free cortisol excretion were found to have less decrease in SBP and mean arterial pressure in response to reduced sodium intake (37). Also, baseline plasma renin concentrations, obtained at the onset of an eight-week study, correlated inversely with salt sensitivity, whereas the baseline plasma N–terminal atrial natriuretic peptide levels correlated directly with this phenomenon (151).

There is direct evidence for a genetic link for the association between hypertension and sodium intake and possibly obesity. In people who were 60 years of age or older, there was a linear increase in SBP and DBP with sodium loading (109). This increase in BP with sodium loading was greatest in individuals with isolated systolic hypertension. The change in DBP in response to sodium loading varied in accordance to the type of gene polymorphism of the angiotensinogen gene, but not with regard to polymorphisms of the angiotensin converting enzyme gene (109). Obese hypertensives who were homozygous (TT genotype) or heterozygous (TC + CC genotype) for the T-786 endothelial nitric oxide synthase gene were studied (53). The product of this enzyme, endothelial-derived nitric oxide (NOx), is a vasodilator. The heterozygous obese hypertensive patients with the TC + CC genotype, as compared to the homozygous TT genotype patients, had a greater increase in diastolic and mean arterial BP and a significant decrease in renal plasma flow and glomerular filtration rate in response to sodium loading (53). Moreover, with sodium loading, the TT genotype has a significantly greater increase in plasma NOx, whereas the TC + CC genotype had a borderline significant increase ($p = 0.051$) in urinary NOx excretion.

BP in individuals with stage 4 (GFR 15–29 ml/min/1.73 m^2) or stage 5 (GFR <15 ml/min/1.73 m^2) CKD may be particularly sensitive to sodium or volume expansion (51, 192). Shaldon (199) reported that in a 23-year-old male with chronic renal failure who was fed a salt-restricted diet for eight weeks, BP fell from 230/145 mm Hg to 135/90 mm Hg, and there was a reduction in headache, nausea, vomiting, and papilledema and improvement in vision. The reduction in BP may continue for months after the removal of body NaCl by dietary restriction and dialysis ultrafiltration. The authors speculate that this delayed response may be due to the decrease in nonosmotically active sodium, which is possibly bound in proteoglycans and glycosoaminoglycans in the interstitial matrix that lines the intimal surfaces of blood vessels (200). A growing body of evidence suggests that high sodium intakes may promote more rapid progression of chronic kidney failure, possibly by an increase in oxidative stress, albuminuria, and BP and alterations in glomerular hemodynamics (111, 200). Some authorities postulate that salt-sensitive hypertension may be caused by subtle renal injury, which is associated with both renal microstructural and physiological abnormalities (110). These disorders may cause an impaired ability to excrete a sodium load and the development of volume expansion with attendant hypertension.

Potassium

Epidemiological and clinical studies concerning potassium intake support the thesis that potassium supplements (e.g., 60–120 mEq/day) lower BP, but results of randomized, prospective trials have yielded conflicting results. Nonetheless, in a meta-analysis of 19 clinical trials involving 586 hypertensives, Cappuccio & MacGregor (35) reported that oral potassium supplements significantly lowered both SBP and DBP by −5.9 mm Hg (95% CI, −6.6 to −5.2) and by −3.4 mm Hg (−4.0 to −2.8), respectively, in subjects with essential hypertension. In the meta-analysis of Whelton and coworkers (227), potassium supplementation was also associated with a significant reduction in mean SBP and DBP of −3.11 mm Hg (−1.91 to −4.31 mm Hg) and −1.97 mm Hg (−0.52 to −3.42 mm Hg), respectively.

Potassium deficiency, even of a mild nature, may induce renal sodium retention, increase BP, and engender salt sensitivity (75, 129, 157). Mu and associates (158) presented evidence that supplements of potassium and calcium could prevent hypertension in adolescents by promoting urinary sodium excretion. Pere and coworkers (176) fed a high-sodium diet and administered cyclosporine A to eight-week-old spontaneously hypertensive rats. The animals developed hypertension and renal injury, associated with renal dopaminergic deficiency (176). A combined dietary supplement of magnesium and potassium prevented hypertension in these rats. Potassium-deficient diets are particularly common in African Americans and have been associated with the high prevalence of hypertension and salt sensitivity in these individuals.

Potassium intake may lower elevated BP by a number of mechanisms (21). As indicated above, potassium intake may increase sodium excretion. Potassium may modulate baroreflex sensitivity, directly cause vasodilation, or reduce cardiovascular reactivity to norepinephrine or angiotensin II. A supplement of potassium, 217 mg/day, and magnesium, 71 mg/day, for four weeks increased small artery compliance and reduced BP in patients with essential hypertension (234). Thus, it has been recommended that a substantial potassium intake should be maintained to prevent or treat hypertension, particularly in subjects who are unable to reduce their sodium intake and in those who are salt sensitive or who have a family history of hypertension (21). Nowson and coworkers (164) reported that a reduction in Na+ intake to about 70 mmol/day and an increase of dietary potassium to 85 mmol/day could maintain a lower BP and reduce the burden of cardiovascular disease.

The Dietary Reference Intakes propose that an adequate potassium intake is 4.7 g (120 mmol) per day, which should lower BP and reduce the BP-raising effects of sodium chloride (7). In this regard, an increase in dietary potassium intake to 120 mmol/day abolished or suppressed the frequency or severity of salt sensitivity in normotensive African American men to the levels found in normotensive white men (157). Also, a randomized, double-blind, prospective controlled trial of potassium supplementation, 80 mmol/day, or placebo for 21 days in normotensive or mildly hypertensive African Americans ingesting a low-potassium (32–35 mmol/day) diet significantly reduced their SBP and DBP (25). A somewhat longer-term, six-week, randomized, double-blind placebo-controlled trial in mostly normotensive adults of European descent that provided only 24 mmol of KCl/day also showed that this modest potassium dose significantly lowered mean arterial BP, SBP, and DBP (159).

Calcium

Although it is possible that the higher calcium intake with the Dietary Approaches to Stop Hypertension (DASH) combination diet contributed to its greater BP-lowering effects (see below), there is substantial controversy in the literature concerning whether high calcium intakes lower BP. McCarron and coworkers (148) conducted a series of studies suggesting that calcium supplementation lowers BP. Indeed, they and others found an inverse correlation across populations and ethnic groups between the mean dietary calcium intake and BP (148–150). The Nurses' Health Study initially found an inverse relationship between dietary calcium and BP after the first four years of follow-up (232). With longer follow-up, no independent relationship between dietary calcium intake and BP could be demonstrated (17). Cappuccio and coworkers (34) carried out a meta-analysis of 23 observational studies and reported an inverse relationship between calcium intake (determined from dietary diaries and food frequency questionnaires) and BP. However, the effect was rather small, and there was evidence of publication bias and heterogeneity across the investigations.

Bucher and associates performed a meta-analysis of 33 randomized clinical trials

of dietary calcium supplementation involving 2,412 individuals with or without hypertension (27). They described for the entire group a small but significant reduction in SBP of −1.27 mm Hg (95% CI, −2.25 to −0.29 mm Hg; $p = 0.01$) but no change in DBP (−0.24 mm Hg; 95% CI, −0.92 to 0.44 mm Hg; $p = 0.49$). In six of these studies in which participants were classified according to whether they were hypertensive or not, there was a significant fall in SBP and DBP in the hypertensive individuals but not in the normotensives (27). Allender and coworkers (9) carried out a meta-analysis of 22 randomized clinical trials in 1,231 individuals. In this meta-analysis, calcium supplementation was associated with statistically significant pooled estimates for reduction in SBP of −1.68 mm Hg (95% CI, −3.18 to −0.18 mm Hg) in the hypertensive patients and −0.53 (95% CI, −1.56 to 0.49 mm Hg). The reduction in SBP, although small, was statistically significant for the hypertensive patients and the hypertensive and normotensive patients combined but not for the normotensive patients alone. DBP was not significantly affected by calcium supplements in either the hypertensive or normotensive patients (9). Griffith et al. (83), in a large meta-analysis on the effects of supplemental calcium on BP, reported a reduction in SBP of −1.44 mm Hg (95% CI, −2.20 to −0.68, $p < 0.001$) and in DBP of −0.84 mm Hg (95% CI, −1.44 to −0.24, $p < 0.001$).

Subjects in these studies were given calcium supplements of 400 to 2,000 mg/day (9, 17, 27, 34, 83). Calcium supplements that resulted in a median total daily calcium intake of about 1 g/day did not affect SBP or DBP in normotensive individuals (9, 83, 190, 239). In three small studies, the supplemental calcium intake diminished the rise in BP response to a high sodium intake (185, 190, 239).

It has been suggested that the discrepancies in the published results concerning the effects of calcium intake on BP may be related to the possibility that a low-calcium diet predisposes to hypertension (147, 149), whereas in individuals who are already eating adequate calcium, higher intakes of calcium have little or no BP-lowering effect (9, 27, 83). Further studies will be needed to resolve this question of a possible BP-lowering effect of calcium in individuals ingesting calcium-deficient diets.

PUFA: polyunsaturated fatty acids

Fish Oil

The higher percentage of polyunsaturated fatty acids in the DASH combination diet (see below) may have also contributed to the reduced BP. Two meta-analyses of controlled clinical trials of the use of omega-3 fatty acids have been published (15, 156). In the study of Appel and coworkers concerning 11 trials that enrolled 728 normotensive individuals (15), omega-3 polyunsaturated fatty acid (PUFA) supplements led to a significant reduction in SBP and in DBP in only two and one of these trials, respectively. In six studies involving 291 untreated mildly hypertensive individuals, reductions in SBP and DBP were observed in two and four of the trials, respectively (15). The weighted, pooled reductions in SBP and DBP in the normotensive individuals averaged −1.0 (95% CI, −2.0 to 0.0) and −0.5 (95% CI, −1.2 to +0.2) mm Hg. In the trials of untreated hypertensive persons, the weighted, pooled decreases in SBP and DBP averaged −5.5 (−8.1 to −2.9) and −3.5 (−5.0 to −2.1) mm Hg. The doses of omega-3 PUFA used in these studies tended to be rather high, usually 3 g/d or greater (15). Morris et al. (156) evaluated 31 placebo-controlled clinical trials involving 1,356 subjects and showed, with fish oil use, a mean reduction in SBP of −3.0 mm Hg (95% CI, −4.5, −1.5 mm Hg) and in DBP of −1.5 mm Hg (95% CI, −2.2, −0.8 mm Hg) with a statistically significant dose-response relationship. There was a dose-response relationship between fish oil dose and SBP and DBP reduction. The decrease in SBP and DBP was statistically significant in the hypertensive patients but not in the normotensive subjects, although the fish oil dose used was slightly higher in the hypertensives (5.6 g/d) as compared to the normotensives (4.2 g/d) (156). These meta-analyses indicate that in people who are assigned to a relatively high omega-3 fatty acid

intake, there is a statistically significant reduction in BP in hypertensive individuals and little or no effect in normotensive persons.

The mechanism by which fish oil lowers BP in hypertensive patients is not clear. It may be related to enhanced elaboration of prostaglandins, which in turn may increase sodium and water excretion, promote vasodilation, or inhibit the release of thromboxane (a vasoconstrictor). Also, it is possible that prostaglandins regulate renin release or decrease responsiveness to vasopressor hormones. The preponderance of studies with fish oil were of short duration (less than three months), and longer-term studies will be necessary to determine whether fish oil has a sustained antihypertensive effect in hypertensive persons. There are a number of side effects with fish oil intake, including most commonly eructation and a bad or fishy taste (15, 156).

Magnesium

The antihypertensive effects of magnesium supplements in hypertensive individuals are controversial. Some studies show that magnesium reduces BP (107), whereas other studies do not (36). The antihypertensive effects of magnesium supplementation are small in those studies that suggest such an effect. Jee et al. (107) performed a meta-analysis of 20 randomized clinical trials of magnesium supplementation in hypertensive persons (14 trials) and normotensive individuals (6 trials). The 20 trials evaluated a total of 1,220 persons. The dose of magnesium supplements ranged from 10 to 40 mmol/d, with a median intake of 15.4 mmol/d. The pooled net estimates of BP effects showed only a small reduction in SBP, −0.6 mm Hg (95% CI, −2.2 to 1.0, $p = 0.051$), and DBP, −0.8 (−2.1 to 0.5, $p = 0.142$), with magnesium supplements. There was no significant fall in SBP ($p = 0.06$) or DBP ($p = 0.17$) when analysis was restricted to the 14 hypertensive trials. There appeared to be a dose-dependent effect of magnesium, with an average reduction in SBP of −4.3 mm Hg (95% CI, −6.3 to −2.2, $p < 0.001$) and in DBP of −2.3 mm Hg (95% CI, −4.9 to 0.0, $p = 0.09$) for each 10 mmol/d increase in magnesium intake (107).

Protein and Amino Acids

Epidemiological studies indicate an inverse relationship between protein intake and BP (167). A small number of clinical trials indicate that supplements of soybean protein may decrease SBP or DBP (29, 90, 167). A larger-scale, randomized, double-blind, controlled trial was carried out in 302 adults in China in which subjects were assigned to receive either 40 g/day of supplemental soybean protein or 40 g/day of complex carbohydrates (90). All participants had prehypertension or stage 1 hypertension with an initial untreated SBP of 130–159 mm Hg and/or DBP of 80–99. During the 12 weeks of treatment, SBP and DBP fell in both groups but decreased significantly more in the soybean protein–treated group. The greater decrease in BP in the soybean protein–treated participants over the complex carbohydrate treated group was by −4.31 (95% CI, −2.11 to −6.51) mm Hg systolic and −2.76 (95% CI, −1.35 to −4.16) mm Hg diastolic at 12 weeks of intervention. In a subgroup analysis of the individuals with stage 1 hypertension, there were significantly greater decreases in SBP (−7.88 mm Hg) and DBP (−5.27 mm Hg) in the subjects treated with soybean protein versus those treated with carbohydrates (90). The prehypertensive individuals showed a trend, not significant, for a reduction in SBP and DBP. This study did not examine whether it was the protein or the isoflavones in the soybean that reduced the BP.

Several potential mechanisms have been suggested to explain how soybean protein may reduce BP (90). Soybean protein contains substantial amounts of arginine, which can be converted to nitric oxide, a potent vasodilator (160). Intravenous injection of arginine reduces peripheral vascular resistance and decreases BP in humans (94). Glutamic acid, which is high in vegetable proteins, may have special blood pressure–lowering effects (208). Digestion of proteins derived from foods

may release bioactive peptides that inhibit angiotensin-converting enzyme and that probably have other antihypertensive actions (191). Proteins derived from milk are particularly likely to yield these peptides (191). This may contribute to the antihypertensive effects of the DASH diet (see below). Protein may also increase urinary excretion of sodium, water, and free dopamine (130, 230). A dopamine-mediated natriuresis engendered by ingested protein may lower BP (130). Soybean protein may also increase insulin sensitivity and glucose tolerance (135); since insulin resistance and consequent hyperinsulinemia may predispose to hypertension (see above), this latter effect of soybean protein may decrease BP (228). Large protein supplements may not be indicated for individuals who have diseases that render them protein intolerant, such as chronic kidney disease, acute kidney injury, or liver failure.

Fiber

Dietary fiber is considered part of a healthy diet that may exert protective effects on the gastrointestinal tract and cardiovascular system. Streppel and coworkers reported in a meta-analysis that increasing dietary fiber intake in Western populations, where the usual fiber intake is well below recommended levels, may help to prevent hypertension (213). In another meta-analysis, Whelton and coworkers (228) reported that increased intake of dietary fiber may reduce BP in hypertensive patients; in normotensive individuals, there was a smaller, less conclusive reduction in BP. A randomized, controlled trial in hypertensive individuals indicated that dietary protein and fiber had significant, additive effects on the lowering of both 24-hour and awake SBP (29). It is possible that some of the antihypertensive effects of dietary sodium restriction may involve changes in the intake of such other nutrients as fiber. Sciarrone and associates (197) report that reduction in sodium intake may decrease the dietary content of both fats and fiber, which might independently affect BP and lipid metabolism.

Alcohol

Excessive alcohol intake often increases BP. However, these effects are generally transient, and BP usually falls rapidly when individuals stop drinking alcohol (141). A time-dependent association between alcohol consumption and BP levels was reported by Moreira in experimental studies of free-living individuals; on the other hand, the frequency of alcohol consumption and type of beverage ingested were not independently associated with BP levels (155). Subjects of African ancestry who consumed large amounts of alcohol showed a high risk of developing hypertension (210). In hypertensive individuals, heavy alcohol consumption leads to a significant increase in the risk of cerebral hemorrhage, suggesting a synergistic effect of alcohol and hypertension (122). On the contrary, light alcohol consumption significantly reduces the risk for stroke. In the North American free-living population, the consumption of alcohol in amounts greater than 210 g per week is an independent risk factor for hypertension, whereas consumption of low to moderate amounts appears to be associated with higher risk of hypertension in black men but not in white men or black or white women (69). In Chinese males, a higher intake of alcohol is associated with a higher risk for isolated systolic hypertension, both systolic and diastolic hypertension, and isolated diastolic hypertension (229).

The mechanisms involved in alcohol-generating hypertension appear to include the effects of vasoconstriction, modification of smooth muscles, and calcium movement (137). Zilkens and coworkers (242) studied 24 healthy men who underwent four regimens, in random order, for four weeks each: (*a*) abstinence from all alcohol and grape products or (*b*) a daily intake of 375 ml of red wine containing 39 gm alcohol, (*c*) a daily intake of 375 ml of dealcoholized red wine, or (*d*) a daily intake of 1125 ml of beer providing 41 gm alcohol. Daily consumption of about 40 grams of alcohol either as red wine or beer resulted in a similar mild increase in 24-hour SBP and awake SBP and

24-hour heart rate, whereas dealcoholized red wine did not lower BP. The red wine, beer, and dealcoholized red wine did not affected vascular function (flow-mediated dilatation). These observations suggest that in men it is the alcohol in red wine and beer that increases SBP and that nonalcoholic components of red wine do not mitigate the BP-elevating effects of alcohol (242). Notwithstanding evidence that alcohol intake, particularly in larger amounts, is associated with increased BP, there are abundant epidemiological data indicating that alcoholic drinks, and perhaps particularly red wine, may reduce the risk of death from cardiovascular disease. The mechanisms for this protective effect are not completely understood and may involve the actions of alcohol per se and possibly also the effects of the antioxidant and vasodilator phenolic compounds.

Vitamin D

Vitamin D deficiency—deficiency of 25-hydroxycholecalciferol (25[OH]D)—is reported to occur in almost 50% of the world's population (98). Vitamin D insufficiency is often defined as serum 25[OH]D 20–30 ng/ml (50–75 nmol/L), and vitamin D deficiency is defined as a serum 25[OH]D below 20 ng/ml (<50 nmol/L) (98). Approximately 80%–90% of the body's vitamin D levels are considered to come from the effects of sunlight on the skin (98), and the high risk of vitamin D deficiency is considered to be due to reduced outdoor activities, the desire to avoid sun exposure, air pollutants, living at high latitudes, dark skin, and frequent use of sunscreens. Knockout mice for the vitamin D receptor or the 1α-hydroxylase enzyme develop high renin hypertension and cardiac hypertrophy hypertension (235, 241). In hypertensive patients, there may be an inverse relationship between plasma renin activity and serum 1,25[OH]2D levels (184). Studies at the cellular and molecular level indicate that 1,25$[OH]_2$D is a negative regulator of renin gene expression by binding of the vitamin D receptor to the transcription factor cAMP-response element-binding protein (237). 1,25[OH]2D also suppresses vascular endothelial and smooth muscle cell tissue factor, thrombospondin and plasminogen activator inhibitor-1, and increases synthesis of vascular endothelial growth factor, prostaglandin, and hepatic thrombomodulin (24). These effects would appear to be cardioprotective, inhibitory of thrombosis, and promotive of fibrinolysis (24, 180). Epidemiological and other studies also suggest that, in addition to bone mineral and divalent ion metabolism, vitamin D may reduce insulin resistance and have vascular, renoprotective, and anti-inflammatory effects (86, 131, 181, 215). Hence, vitamin D may not only reduce blood pressure but may prevent or ameliorate a number of the vascular and renal complications of hypertension. On the other hand, excessive vitamin D intake leading to toxic levels (serum 25[OH]D >150 ng/ml, >374.4 nmol/L) may induce hypercalcemia, arterial stiffness, hypertension, and progressive renal failure (98).

Some, but not all, of the epidemiological cross-sectional studies describe an inverse relation between serum 1,25$[OH]_2$D and especially 25[OH]D levels and SBP or DBP (24, 180). Clinical trials of vitamin D supplementation on BP are less consistent. One double-blind trial of 1200 mg calcium/day alone or with 800 IU vitamin D/day in elderly vitamin D–deficient women showed significant reductions in SBP and DBP in both groups, but with a significantly greater reduction in SBP, by −7.4 mm Hg, in the vitamin D–treated group (177). Most, but not all, of the other trials of vitamin D supplements on SBP or DBP were negative (180). However, it has been argued that most of these studies were not primarily or adequately designed to assess the effects of vitamin D on BP, the subjects were not hypertensive or vitamin D deficient, the vitamin D dose might have been too low (e.g., 400 IU/day), or the BPs may not have been measured in a sophisticated fashion (180). An example is the Women's Health Initiative, which conducted the largest randomized clinical trial of vitamin D (144). This trial, which was carried out for a mean of seven years, randomized over 32,000 postmenopausal

women to receive 400 IU vitamin D plus 1,000 mg calcium per day or placebo. There were no significant differences in changes in SBP or DBP or in the incidence of hypertension during the study. Possibly the vitamin D dose was too small.

Supplementation with $1,25[OH]_2D$ or its analogs, paricalcitol or 1α-hydroxyvitamin D, have also given inconsistent results with regard to BP reduction (180). Some evidence suggests that BP-lowering effects of vitamin D supplements may be more effective in people who are vitamin D deficient. Clearly, well-designed, adequately powered randomized controlled clinical trials are needed to assess the possible effects of vitamin D on BP.

Miscellaneous Nutrients and Chemicals

Chocolate. A randomized, cross-over, short-term (seven-day) study was conducted to assess the effect of ingestion of chocolate on BP in 20 patients with grade I essential hypertension who had never received antihypertensive treatment (79). Eating dark chocolate, but not white chocolate, was associated with a significant lowering of SBP ($-11.9 \pm$ SD 9.7 mm Hg, $p < 0.0001$) and DBP (-8.1 ± 5.0 mm Hg, $p < 0.0001$). The authors suggest that dark chocolate may lower BP by its high flavonol content, which induces vasorelaxation. Dark chocolate has also been shown to decrease isolated systolic hypertension in geriatric patients (216), and in one (78), but not in all (58, 64), studies in healthy persons.

Coffee. Suzuki et al. showed hypotensive effects of green coffee bean extract and its metabolites in spontaneously hypertensive rats (214). Kozuma et al. reported a dose-responsive antihypertensive effect of green coffee bean extract given to mildly hypertensive individuals for 28 days (128). These findings were confirmed by Watanabe and coworkers, who studied essential hypertension in rats and humans (224). The BP-lowering effect of green coffee bean extract is attributed to the effects of chlorogenic acid and its metabolites on vascular reactivity (128, 169, 214, 224). Interestingly, roasted coffee extract may not have these antihypertensive effects (214). Caffeine induced fluctuations in BP by stimulating cardiovascular mechanisms that are not well specified (171). Corti et al. (43) studied the acute effects of coffee in volunteers who drank a triple espresso or a decaffeinated triple espresso or who were infused intravenously with 250 mg of caffeine. After receiving the coffee, the subjects showed an increase in sympathetic nerve activity and BP that was independent of whether caffeine was present (43). An epidemiological study showed an association between coffee intake, even as low as one cup per day, and a small increase in SBP and DBP; coffee drinking was also associated with a small increase in risk of hypertension (123). A meta-analysis of 11 interventional trials of coffee drinking, 10 of which were randomized, found that it was associated with a mild increase in SBP and DBP (106). The median coffee intake in the studies was five cups per day. It has been suggested that pregnant women should limit their ingestion of coffee to no more than three cups per day and ingest no more than 300 mg of caffeine per day to reduce the probability of spontaneous abortion or impaired fetal growth and to reduce such cardiovascular disease risk factors as elevated BP and hyperhomocysteinemia (93). On the other hand, prehypertensive or hypertensive men who were habitual alcohol drinkers demonstrated a reduction in SBP and DBP when they drank more than three cups of coffee per day over four weeks (72).

Tea. The relationship between BP and tea drinking is particularly relevant, because the volume of tea consumption is second only to water intake in the world (238). The effect of tea on BP may be less consistent than the effects of coffee, according to different reports (238). However, Yang and coworkers report that chronic, moderate consumers of green tea or oolong tea are less likely to develop hypertension (236). The effect may be due to flavonoids, which affect endothelial function (95). Green, oolong, and black tea contain a number of

flavonoids and other compounds that in animal or human studies engender vasodilatation, protect against endothelial dysfunction, and have antioxidant, anti-inflammatory, or hypolipidemic effects (97, 236, 238). Hodgson et al. (96) studied the acute effects of tea on fasting and postprandial vascular function and BP in humans and showed that consumption of foods altered the acute beneficial effects of tea on vascular function and blood pressure. Consumption of either diet or sugar-containing cola beverages was associated with increased risk for hypertension, possibly due to their caffeine content (231).

Urate. As indicated in the section on obesity (see above), elevated urate levels may predispose to hypertension. In a double-blind placebo-controlled cross-over trial in adolescents with newly diagnosed stage 1 essential hypertension and serum urate levels of 6.0 mg/dl or greater, short-term treatment with allopurinol, which decreased serum urate levels, lowered BP (62). Twenty-two of the 30 participants in this study were overweight or obese.

HEALTH-ENHANCING DIETS AND LIFESTYLES

In the past 20 years, there has been a growing focus on the use of complex diets to prevent or treat hypertension, usually of the mild to moderately severe variety. The composition of these diets is generally based on pre-existing evidence that the individual constituents of these diets have preventative or therapeutic effects on hypertension. Much of this pre-existing evidence is summarized in the first part of this review. Experience regarding the effectiveness of and compliance with these diets is discussed below.

The Hypertension Prevention Trial

The Hypertension Prevention Trial (HPT) was a multicenter trial in which 841 adults with diastolic blood pressures of 78–89 mm Hg were randomly assigned to a control treatment group (with no dietary counseling) or to one of four dietary counseling treatments (decreased energy intake, decreased sodium intake, decreased sodium and energy intake, or decreased sodium and increased potassium intake) or a control group that received no dietary counseling (2). Men and women with lower BMIs (n = 211) were not assigned to the two low-energy intake groups. Subjects assigned to one of the four treatments underwent group counseling weekly for the first 10 weeks, then every other week for the next four weeks, and finally bimonthly for the duration of study. Phone calls, newsletters, and other methods were employed to facilitate training and compliance. People were followed for three years. Attendance at counseling sessions declined significantly with time. At six months, overnight urine sodium excretion had fallen −13%, urine potassium increased by 8%, and body weight fell by −7% as compared to changes in the control group. At three years, the reductions in urine sodium and weight, compared to changes in controls, were −10% and −4%, respectively, whereas there was no change in urine potassium. The net reductions in weight in the low-energy groups at three years were due in large part to the increase in weight in the control group. BP decreased from baseline in all treatment groups, including the controls. The largest net reduction in SBP and DBP occurred in the low-energy group alone, −5.1 and −2.4 mm Hg and −2.8 and −1.8 mm Hg, at six months and three years, respectively ($p < 0.05$ for each BP at each time). The sodium reduction groups sustained a significantly lower composite of hypertensive events (i.e., SBP ≥140 mm Hg, DBP ≥90 mm Hg or intake of antihypertensive medicines); the other treatment groups experienced a nonsignificant trend in this same direction.

The Trials of Hypertension Prevention

PHASE I. The Trial of Hypertension Prevention (TOHP) was a multicenter trial involving two phases. TOHP Phase I was a short-term trial designed to test the effect of three different lifestyle interventions and four

nutritional supplements on BP control in individuals with high normal DBP. TOHP Phase II was a longer-term trial (36–48 months) designed to test those interventions that were demonstrated in TOHP Phase I to lower BP. In phase I, 2,182 men and women with average high normal DBP (80–89 mm Hg) and with SBP ≤160 mm Hg were randomized in a parallel-controlled fashion to receive weight loss intervention, dietary sodium reduction, stress management, or usual care for 18 months (3, 194). In addition, in Phase I, four nutritional supplements were fed in a double-blind, placebo-controlled design. The nutritional supplements were fed in two stages, each of six months duration. In stage 1, participants were fed a daily supplement providing 1.0 g calcium, 360 mg magnesium, or placebo. After a washout period, participants entered stage 2, where they were rerandomized to be fed a supplement providing, each day, 6 g fish oil (containing 3.0 g omega-3 fatty acids), 60 mmol potassium, or placebo. The weight loss, sodium reduction, and stress management groups underwent weekly group counseling sessions for 14, 10, and 8 weeks, respectively, and then at semimonthly or monthly intervals for the rest of the 18-month intervention.

In TOHP Phase I, in a comparison of baseline data to the final measurements, weight reduction produced a weight loss of −3.9 kg ($p < 0.01$) and a decrease in SBP of −2.9 mm Hg ($p < 0.01$) and DBP of −2.3 mm Hg ($p < 0.01$) (3); the sodium reduction diet decreased urine sodium excretion by −44 mmol ($p < 0.01$), SBP by −1.7 mm Hg ($p < 0.01$), and DBP by −2.9 mm Hg ($p < 0.05$). There was no significant decrease in SBP or DBP between the baseline and final measurements with either stress management or the dietary supplements despite good compliance. Essentially similar results were observed for the lifestyle interventions at the six-month follow-up and for the nutritional supplements at the three-month follow-up, except that DBP fell significantly at three months with the potassium supplement (3). A post-trial follow-up seven years later of 181 of the subjects indicated that the weight loss group and dietary sodium-restriction group displayed a 77% and 35% decrease in the odds ratio of having hypertension, respectively (194).

Phase II. TOHP Phase II tested whether weight loss, reduced sodium intake, or a combination of weight loss and reduced sodium intake will decrease DBP, SBP, or the incidence of hypertension (defined as DBP of 90 mm Hg or greater, SBP 140 mm Hg or greater, and/or the use of antihypertensive medications) in overweight or moderately obese individuals with high normal DBP (83–89 mm Hg) and SBP below 140 mm Hg at entry into the study (4, 91, 132, 212). In a two-by-two factorial design, 2,382 men and women who were 110% to 165% above desirable body weight were randomly assigned to the following groups: (*a*) weight loss alone, (*b*) sodium reduction alone, (*c*) weight loss and sodium reduction, or (*d*) usual care. Subjects were followed for three to four years. During this time, patients participated in group meetings and received individual counseling, which initially was intensive and then became less frequent as the study progressed. Weight, urinary sodium, and BP were measured every six months, although at 18 and 36 months, Bp was measured over a series of three visits separated from each other by 7–10 days.

In the two weight reduction groups combined, mean body weight loss was −4.1 kg, −2.2 kg, and −0.3 kg at 6, 18 and 36 months, respectively (4, 212). The usual care group displayed a progressive weight gain that reached 1.8 kg at 36 months. The decrease in weight in the weight loss groups, calculated as the difference between the weight change in the two weight loss groups combined and the weight change in the usual care group, was significantly negative at each of these three time points. Mean SBP and DBP decreased by −6.0/−5.5, −3.6/−4.5, and −0.8/−3.2 mm Hg in the two weight loss groups combined at 6, 18, and 36 months, respectively. The reduction in SBP and DBP were each significantly greater in the two weight loss groups combined as compared to the usual care group at these three time points.

Urinary sodium excretion decreased by −64.3, −45.4, and −34.1 mmol/day with the two dietary sodium reduction groups combined at 6, 18, and 36 months, respectively. In the usual care group, urinary sodium excretion decreased by −27.6, −16.8, and −10.5 mmol/day at these three time points (4). The decrease in urinary sodium excretion in the two sodium reduction groups, calculated as the difference between the decrease in urinary sodium in the two sodium reduction groups combined as compared to the decrease in urinary sodium in the usual care group, was significantly greater at 6, 18, and 36 months. The decrease in mean SBP and DBP in the two sodium reduction groups combined was −5.1/−4.4, −3.8/−4.4, and −0.7/−3.0 mm Hg, respectively, at these three time points. In the two sodium reduction groups combined as compared to the usual care group, the reduction in SBP was significantly greater at all three time points, whereas the reduction in DBP was significantly greater only at 6 and 18 months. Throughout the 48 months of the clinical trial, the incidence of hypertension, defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg or the use of antihypertension medicines, was less, and usually statistically significantly less, in the two weight loss groups combined, the two sodium reduction groups combined and the weight loss and sodium reduction–intervention group as compared to the usual care group (average relative risks, 0.78–0.82). Those subjects who displayed greater and sustained weight loss had the greatest reduction in BP and the lowest risk ratio for hypertension. The effects of weight loss and decreased sodium chloride intake combined were not additive. After six months of treatment, the two interventions were less effective in maintaining both weight loss and low sodium intake, and, possibly for these reasons, the reduction in BP was also attenuated (4, 132, 212).

The Dietary Approaches to Stop Hypertension Diet

The DASH study provides much relevant information concerning appropriate dietary therapy to control BP (16). The DASH study was a multicenter study that compared a "control" typical American diet (low in fruits, vegetables, dairy products, essential minerals, and fiber and high in saturated and total fat) to a diet rich in fruits and vegetables and also to a combination diet rich in fruits, vegetables, and low-fat dairy products and with a reduced saturated and total fatty acid content. The study was carried out in 459 adults with a mean age of 44 years, SBPs less than 160 mm Hg and DBPs 80–95 mm Hg. About 65% of the study subjects were racial minorities, particularly African American.

The control diet was fed to all subjects for three weeks, and individuals were then randomly assigned to remain on this diet or to ingest the diet rich in fruits and vegetables or the combination diet for an additional eight weeks. All meals were prepared for the participants in a research kitchen, and five meals per week were ingested on the study site. The study used food rather than nonfood sources of calcium. As can be seen from **Table 4**, the control diet was low in calcium, potassium, and magnesium. The sodium content of all diets was similar. Baseline SBPs and DBPs averaged 131.3 ± SD 10.8 mm Hg and 84.7 ± 4.7 mm Hg, respectively. Hence, many individuals had only high-normal or normal BPs.

After the subjects commenced their experimental diets, there was a rapid, significant, and sustained fall in SBP and DBP with both the fruits and vegetables diet and the combination diet (16). SBP and DBP fell more with the fruits and vegetables diet than with the control diet, by −2.8 (97.5% CI, −4.7 to −0.9) mm Hg ($p < 0.001$) and −1.1 (97.5% CI, −2.4 to −0.3) mm Hg ($p = 0.07$), respectively. SBP and DBP also decreased more with the combination diet than the fruits and vegetables diet, by −2.7 (97.5% CI, −4.6 to −0.9) mm Hg ($p = 0.001$) and −1.9 (−3.3 to −0.6) mm Hg ($p = 0.002$). These declines in BP with both experimental diets occurred within two to three weeks and essentially persisted throughout the rest of the eight-week study period. Thus, this study indicates that a diet high in fruits and vegetables significantly

Table 4 Key prescribed nutrients in the control, DASH combination, and DASH-Sodium diets*,†

Item	Western control diet	DASH combination and DASH-Sodium diet
Nutrients		
Fat (% of total kcal)	37	27
Saturated	16	6
Monounsaturated	13	13
Polyunsaturated	8	8
Carbohydrate (% of total kcal)	48	55
Protein (% of total kcal)	15	18
Cholesterol (mg/day)	300	150
Fiber (g/day)	9	31
Potassium (mg/day)	1700	4700
Magnesium (mg/day)	165	500
Calcium (mg/day)	450	1240
Sodium (mg/day)**	3000 (130 mmol/day)	3000 (130 mmol/day)

*Adapted from (16).

†Values are for diets designed to provide an energy level of 2100 kcal/day.

**For the DASH-Sodium Trial, the prescribed daily sodium intakes were 150 mmol (high intake, 3.45 g), 100 mmol (intermediate intake, 2.30 g), and 50 mmol (low intake, 1.15 g) (178).

reduces BP, and the addition of about three daily servings of dairy products, predominantly low-fat milk, in association with a reduced saturated and total fat intake, approximately doubled the degree of BP reduction observed with the fruits and vegetables diet. It should be pointed out that these diets were provided for only eight weeks, and therefore the long-term effects of these diets were not investigated.

The DASH Low-Sodium Diet

The DASH-Sodium Trial was carried out to examine whether a restricted sodium intake would have an additional BP-lowering effect in people ingesting either the DASH combination diet or the control diet (189). The DASH-Sodium Trial was a multicenter study in which three different dietary sodium intakes were prescribed: a high-sodium diet, 3.45 g Na/day—roughly a typical American sodium intake; an intermediate-sodium diet, 2.3 g Na/day—a currently recommended intake; and a low-sodium intake, 1.15 g Na/day. A total of 412 individuals were studied in four clinical centers (189). Acceptance criteria included adults 22 years or older who had average SBPs of 120 to 159 mm Hg or who had DBPs of 80 to 95 mm Hg. Study subjects first underwent a two-week run-in period with a high-sodium Western diet. They were then randomly assigned to the DASH combination diet or to the Western diet. Both diet groups were fed each of the three levels of sodium intake for 30 days each in a randomized cross-over design (189). The primary and secondary end points of the study were the SBPs and DBPs with the three different sodium intakes. Statistical analyses were performed by intention-to-treat methods.

The results indicated that with the control Western diet, the intermediate sodium intake, as compared to the high intake, was associated with a reduction in SBP of −2.1 (95% confidence limits, −3.4 to −0.8) mm Hg ($p < 0.001$) and a reduction in DBP of −1.1 (−1.9 to −0.2) mm Hg. When those individuals fed the DASH diet were also fed the intermediate-sodium diet, as compared to the high-sodium

diet, there was also a reduction in SBP and DBP of −1.3 (−2.6 to 0.0) mm Hg ($p < 0.05$) and −0.6 (−1.5 to 0.2) (p = NS), respectively. A comparison of the intermediate- to the low-sodium intake with the control Western diet indicated an even greater reduction in SBP, by −4.6 (−5.9 to −3.2) mm Hg ($p < 0.01$) and −1.7 (−3.0 to −0.4) mm Hg ($p < 0.01$). The SBPs and DBPs with the DASH diet were also lower with the low as compared to the intermediate levels of sodium intake, by −1.7 (−3.0 to −0.4) mm Hg ($p < 0.01$) and −1.0 (−1.9 to −0.1) mm Hg ($p < 0.01$), respectively.

These BP reductions with the DASH low-sodium diets were in addition to the BP-lowering effects of the DASH diet itself. At each level of sodium intake, the SBPs and DBPs were usually substantially lower with the DASH diet as compared to the control Western diet. The BP-lowering effects of low-sodium intakes were greater in the subjects who were hypertensive than in those who were normotensive; this was observed in the individuals assigned to the control Western diet as well as in those assigned to the DASH diet. A greater reduction in BP was observed in black subjects at intermediate and low levels of sodium intake as compared with white participants. The low-sodium and the DASH diets were each associated with lowering of SBP and, to a rather lesser extent, DBP in many subgroups of individuals, including both the hypertensive and normotensive subjects. However, the DASH diet combined with reduced sodium intake tended to lower SBP and DBP more than either the DASH diet or the low-sodium diet alone (222), and lowered SBP and DBP in patients who were older than 45 years and those who were 45 years of age or younger (222).

Possible role of nitrate in lowering blood pressure. Webb and coworkers described a possible role for nitrate in the BP-lowering effects of the DASH diet, which is high in vegetables (99, 225). Vegetables contain substantial amounts of nitrate. Ingested nitrate is absorbed from the stomach and small intestine into the circulation, where some nitrate is secreted into saliva and converted to nitrite by the action of bacteria on the tongue. This nitrite is then swallowed, and gastric acid converts the nitrite to the vasodilator nitric oxide. Healthy volunteers were randomized to drink beetroot juice, a source rich in inorganic nitrate, or water in a crossover design. After drinking beetroot juice, plasma nitrate and nitrite rose, and SBP and DBP fell by −10.4 and −8.0 mm Hg, respectively (225). The volunteers repeated this activity, but also spit out their saliva continuously for several hours so that the nitrite would not be swallowed and thereby exposed to gastric acid. During this time, plasma nitrate again rose, but there was no rise in plasma nitrite, and SBP was significantly higher as compared to when volunteers were allowed to swallow. Ingesting the beetroot juice and swallowing saliva also reduced endothelial dysfunction as indicated by protection against suppression of the flow-mediated dilation of the brachial artery following ischemia/reperfusion. Finally, swallowing beetroot juice also inhibited aggregation of platelets that were exposed to ADP or collagen.

The Mediterranean Diet

The Mediterranean diet, which is high in fruits, vegetables, and olive oil, has been associated epidemiologically with reduced cardiovascular disease and mortality (49, 89). Such diets also seem to improve vascular function, with a greater forearm blood flow in response to a vasodilator challenge (146). As indicated in the DASH study, a diet high in fruits and vegetables also may reduce blood pressure (16). This antihypertensive effect may be partly due to the associated higher intake of olive oil (165). The BP-lowering effects of nitrate (99, 220), glutamic acid, which is present in higher amounts in vegetable proteins (208), and PUFA, in olive oil, may contribute to the antihypertensive effects of diets high in fruits and vegetables.

The PREMIER Clinical Trial

Modifications have been made to the DASH low-sodium diet to add a weight loss

component and other interventions (222). In the PREMIER Clinical Trial, 810 individuals with above-optimal BP, including those with prehypertension or stage 1 hypertension (SBP 120–159 mm Hg; DBP 80–95 mm Hg), were studied for six months (14, 73). The PREMIER Clinical Trial tested the hypothesis that these individuals can make multiple lifestyle changes during this period that lower BP. Subjects, who were mostly overweight or obese, were randomly assigned to one of three treatment groups: (*a*) one 30-minute counseling session on diet and physical activity plus educational materials, but no counseling on behavioral changes (i.e., advice only); (*b*) an intensive behavioral intervention to achieve a set of established (EST) healthy lifestyle goals, including weight loss, dietary sodium reduction, increased physical activity, and limited alcohol intake; or (*c*) the EST intervention with the DASH combination diet (EST + DASH) (73, 138). Groups *b* and *c* were scheduled to have 18 counseling sessions over the six months of the trial.

The PREMIER Trial results indicated that both the EST and the EST + DASH interventions lowered SBP to a similar degree and significantly more than the advice only group. After subtracting the BP changes in the advice only group, the EST and the EST + DASH intervention groups showed significant reductions at six months in SBP and DBP of −3.7/−1.7 and −4.3/−2.6 mm Hg, respectively. The prevalence of hypertension at six months was similar in the two intervention groups and significantly lower than in the advice only group. However, in the subgroup of patients with the metabolic syndrome, the EST-lowering effect on SBP was not significantly greater than that of the advice only patients, whereas EST + DASH had a similar effect in those with and without this syndrome (138). Moreover, the EST + DASH regimen after six months lowered SBP equally effectively in prehypertension or stage 1 hypertension patients who did or did not have the metabolic syndrome, whereas the EST regimen alone did not lower SBP as effectively in individuals who had the metabolic syndrome (138).

Compliance to the treatment regimens was fairly good, and the EST and EST + DASH interventions also differed significantly from the advice only group with regard to greater weight loss, increased physical fitness, and reduced serum total cholesterol and insulin resistance (14, 138); a trend toward lower urine sodium was significant only in the EST group. The DASH diet also decreased the prevalence of the metabolic syndrome in other studies (18, 60). The benefits of these dietary and lifestyle interventions have been sufficiently impressive so that they have been incorporated into the recommendations for the prevention and treatment of hypertension by many national advisory groups and are included in the Therapeutic Lifestyle Changes of the JNC (40). These groups now commonly recommend a DASH low-sodium type of diet along with lifestyle changes similar to those of EST, as described above (8, 40, 120, 226).

Effect of Dietary Sources of Fuel on Blood Pressure

Since the DASH diet provides less fat and more protein, is it possible that these differences in fuel composition contribute to its BP-lowering effects? As indicated above, amino acids and peptides derived from ingested proteins may have BP-lowering effects (29, 46, 90, 94, 130, 135, 160, 167, 228, 230). The OmniHeart study examined the relative contribution of diets providing relatively high amounts of carbohydrates, proteins, or monounsaturated fatty acids to BP changes (13, 16). Adults with prehypertension or untreated stage 1 hypertension were randomly assigned to receive each of these three diets in a cross-over design. The high-protein diet increased protein intake to 25% of total energy intake, and the high-monounsaturated-fat diet increased fat to 37% of total energy intake. The carbohydrate content in these latter two diets was 48% of total calories, as compared to 58% of total

calories with the high-carbohydrate diet, which is similar to the composition of the DASH diet. Weight was kept stable by adjusting total energy intake. The higher-protein diet and the higher-monounsaturated-fat diet were each more effective at lowering BP as compared to the high-carbohydrate diet. Whether this was due to the lower carbohydrate intake or the higher protein or fat intake is not clear. However, these findings are consistent with observational studies indicating that higher protein or fat intakes are associated with a lower death rate from coronary heart disease and greater survival (102, 117). A meta-analysis of 10 studies comparing the effects of high-carbohydrate versus high-*cis*-monounsaturated-fat diets also indicated that the high-carbohydrate diets are associated with slightly but significantly higher SBPs (mean difference 2.6 mm Hg; 95% CI, 0.4 to 4.7) and DBP (mean difference 1.8 mm Hg; 95% CI, 0.01 to 3.6) (198). The same trends were noted when the analysis was restricted to crossover studies, but the results were no longer statistically significant.

It is pertinent that higher-protein diets have also been associated in the short term with improved serum glucose and possibly other metabolic benefits in patients with type 2 diabetes mellitus (119, 166). It is not yet clear whether these higher-protein diets are safe for long-term use, and they may be contraindicated in people with early chronic kidney disease, as they are in persons with more advanced stages of this condition. These questions merit further investigation.

LONG-TERM ADHERENCE AND BLOOD PRESSURE RESPONSES TO HEALTH-ENHANCING LIFESTYLES

Longer-Term Experience with the Previously Described Clinical Trials

Many studies have now examined the longer-term responses to healthy diet recommendations. As indicated above, the Hypertension Prevention Trial (HPT) and Trials of Hypertension Prevention (TOHP Phase II), in which patients were counseled on weight reduction and/or sodium reduction diets for up to four years, indicated that there was a progressive loss of adherence to these dietary intakes (2, 4, 132, 212). TOHP Phase I also indicated a reduced odds ratio of hypertension seven years after the onset of the trial, and the THP and TOHP Phase II also demonstrated that some antihypertensive effect remained three or four years after the onset of the trial (2, 4, 132, 212).

In the PREMIER Clinical Trial, participants were followed for an additional 12 months, during which the advice only group underwent one additional 30-minute counseling session and received educational materials; the EST and EST + DASH diet groups attended monthly group sessions and three individual counseling sessions, and they were asked to keep food diaries, monitor their dietary energy and sodium intake, and record the minutes of physical activity. At 18 months after the onset of the PREMIER Trial, the EST and EST + DASH diet groups, in comparison to the advice only group, each showed greater weight losses of −2.2 kg and −2.7 kg, respectively ($p < 0.01$ for each group), and significantly lower energy intakes (57). The target weight loss goal of −6.8 kg was attained by 25% of both groups. Urinary sodium excretion was also significantly lower in both intervention groups as compared to the advice only group, by −12.8 mmol Na and −18.9 mmol Na, respectively. Compared to the advice only group, the odds ratio for hypertension was 0.83 and 0.77 in the EST and EST + DASH groups at 18 months and was significantly lower only in the EST + DASH group. Among people who were hypertensive at baseline, the odds ratio for remaining hypertensive was significantly lower in both intervention groups as compared to the advice group. However, the change in blood pressure levels at 18 months was not different among the three groups.

A randomized, controlled trial conducted in Turkey involved 70 mildly hypertensive overweight or obese men and women, of whom 60 completed the trial (32). Subjects were counseled repetitively for three months to

follow lifestyle changes similar to those of the EST + DASH study. Six months after the onset of study, the interventional group showed improvements in body weight, BP, serum lipids, and lifestyle patterns.

Other Studies on Diet, Adherence, and Blood Pressure

Folsom et al. (65) employed a DASH diet index score to evaluate the long-term effects of complying with the DASH diet by nonhypertensive participants in the Iowa Women's Health Study. Adjusting for age and energy intake, they found that greater adherence to the DASH diet was associated with a lower incidence of hypertension and cardiovascular mortality, but these associations were not statistically significant after adjustment for other risk factors. However, these women were assessed while they ingested their usual intakes, and they did not undergo specific training and follow-up regarding adherence to the DASH diet. The Women's Health Initiative (WHI) Dietary Modification Trial evaluated the effect of intensive behavioral modification to ingest a diet of increased fruits, vegetables, and whole grains and reduced fat on BP and other clinical outcomes, including cardiovascular events (101). In this trial, 48,835 postmenopausal women were randomized to treatment or to receive dietary educational materials and followed for a mean of 8.1 years. The primary aim of this study was to assess reduction in the incidence of breast and colorectal cancer. The diet was not specifically designed to lower sodium or energy intake, although there was a small decrease in energy intake and body weight in the treatment versus the control group. Although intake of all dietary components changed in the prescribed direction, SBP did not change significantly, and there was a significant but very modest (−0.31 mm Hg) reduction in DBP. Moreover, there was no reduction in the incidence of coronary heart disease, stroke, or all cardiovascular events with this diet. In the DEW-IT study, a nine-week intensive healthy lifestyle modification intervention, which included a low-energy version of the DASH diet versus a nonactive intervention arm, were evaluated in 44 overweight and obese hypertensive patients (205). Although there was significantly greater weight loss with the lifestyle intervention at the end of the nine-week period, at one year of follow-up, the weight loss group had regained almost all of their lost weight, and their weight change was not different from the nonintervention group.

The ADAPT study evaluated changes in lifestyle and clinical characteristics in 241 overweight or obese hypertensive adults after they were randomized to usual care or an intensive program of lifestyle counseling (28, 31). At four months and one year, a significantly greater weight loss was associated with a more healthy dietary intake in the group that received lifestyle counseling. Ambulatory BP was lower at four months after starting counseling but not at one year (28, 30). Three years after completion of the program, the changes in the lifestyles group, as compared to usual care, were limited to increased physical activity, some dietary intake improvements, and a minor decrease in serum cholesterol; no differences were reported in weight loss, BP, changes in antihypertensive medications, or other risk factors. Other programs also report that initial weight losses are not maintained long term (108). However, Viera et al. (221) evaluated adults who had participated in a survey and reported that they were told they were hypertensive. Those adults who also stated that they were advised on lifestyle changes were significantly more likely to describe healthy changes in lifestyle (e.g., changed eating habits including reduced salt and alcohol intake or increased exercise) than were those who did not recall being advised on lifestyle changes. It is emphasized that these data were obtained from participant reports.

A number of other researchers report rather mediocre adherence to this diet. Adherence to diet prescription and weight loss, although often statistically significant, was often small (57). Different ethnic groups may have difficulty adhering to some components of the DASH diet (76). Examination of the National Health and Nutrition Examination Survey (NHANES)

data for the years 1999–2004 indicates that in this cross-sectional analysis, only 19.4 ± 1.2 (SEM)% of 4,386 people with known hypertension were eating a diet consistent with the DASH diet (152). These values are substantially lower than the proportion of known hypertensives in the NHANES data for 1988–1994 who were ingesting a diet that provided the key nutrients found in the DASH dietary pattern (26.7 ± 1.1%) (152). Indeed, recent NHANES data indicate that adherence to healthy lifestyles appears to be diminishing in the United States (121). Although at least most of these patients probably had not actually been trained in the importance of or the preparation of the DASH diet, the principles of the DASH diet have been recommended by the JNC for many years (5, 39). Large numbers of Americans are now counseled in healthy lifestyle modifications, but some population groups are still not commonly counseled, particularly the young and people with low cardiovascular risk factors (140).

Thus, the results regarding compliance to the DASH or other dietary prescriptions to reduce BP or cardiovascular events are somewhat conflicting. As pointed out by Logan (139), there are several possible explanations for the differences in compliance to these diets. The DASH trial was short term, and all food was prepared in research kitchens and provided to the subjects at no cost. Moreover, on weekdays, either lunch or supper meals were eaten in a research unit (48, 84). In contrast, in other studies, the food had to be purchased and prepared by the participants. When food must be purchased and prepared for long or indefinite periods of time by the consumer who is not participating in an intensively controlled research protocol, compliance may fall.

The long-term, multiyear effects of strict compliance to the DASH or DASH-Sodium diets are not known (126). It also is not entirely clear that these diets are similarly effective for all racial and ethnic groups. In both DASH studies, the potassium content of the control diet was below the twenty-fifth percentile of the estimated usual potassium intake in the United States (139). Moreover, most of the DASH study patients were African American (16), a population whose BP is particularly potassium sensitive and who may require a high potassium intake in the range of the DASH diet to avoid sodium sensitivity induced by potassium deficiency (157). Thus, these results may not be as applicable to non-African Americans or to people who are already ingesting higher-potassium diets. On the other hand, the large-scale, observational, multiyear Nurses' Health Study II indicated that those individuals who followed a low-risk diet and low-risk lifestyle had a lower self-reported incidence of hypertension (67). It is relevant and encouraging that the demonstrated BP-lowering effects of healthy dietary regimens and lifestyles coupled with difficulty in adherence have provided a commercial incentive to develop functional foods and nutraceuticals that may supply recommended nutrients (38). Hopefully, these products will enhance the ability of people to follow the recommended guidelines.

Exercise

Some but not all studies of exercise and BP suggest that regular exercise training may reduce BP. Exercise, particularly when combined with a low fat intake, may lower serum cholesterol (41, 143). Exercise may also accelerate weight reduction in obese individuals who are ingesting a low-calorie diet (92). It is important to remember that the increase in BP that occurs when normal people exercise may be greatly exaggerated in hypertensive individuals. Thus, BP should be monitored carefully in hypertensive persons who are embarking on exercise training until it is ascertained that dangerous levels of hypertension do not occur (41). Aerobic exercise training and resistance training were reported to decrease BP in prehypertensive and stage 1 hypertensive individuals (41, 143). Two mechanisms by which regular physical exercise may lower BP include antagonism to oxidative stress and amelioration of insulin resistance and its consequent hyperinsulinemia (41). In the presence of

oxidative stress, 8-iso-PGF2α, a potent vasoconstrictor, is produced (41). Insulin resistance with hyperinsulinemia impairs nitric oxide synthesis, which will predispose to hypertension.

Bariatric Surgery and Weight-Reducing Medicines

Weight loss in obese, hypertensive persons that is due to dietary and behavioral intervention or bariatric surgery is generally associated with a decrease in BP (100, 205). Meta-analysis indicates that the drugs orlistat and sibutramine are more effective at inducing weight loss than placebo treatment, on average by roughly 4 kg (204). The effect of these drugs on BP is more nuanced. Selective CB_1 receptor blockade with higher doses of rimonabant in obese patients is reported to induce weight loss and modestly reduce BP (81). This reduction in blood pressure may be due solely to the effect of the weight loss (80). Orlistat also lowers BP (80, 81, 100, 145). In the meta-analysis, there was a statistically significant weighted SBP and DBP reduction with orlistat of −2.5 and −1.9 mm Hg, respectively (204). In contrast, sibutramine was associated with increased SBP (100) or DBP (204).

CONCLUSIONS AND RECOMMENDATIONS

Many studies indicate that nutritional intake and nutritional status have a major effect on the probability of developing hypertension and on the severity of hypertension in the general population. Appropriate dietary management may prevent the onset of hypertension, eradicate or improve mild hypertension, and can be a useful adjunct to pharmacological therapy for the treatment of more severe established hypertension. Key elements that prevent or ameliorate hypertension include prevention of obesity, the low-sodium DASH combination diet, adequate potassium intake, and possibly sufficient intake of fish oil and magnesium. Some evidence indicates that regular exercise may reduce resting BP; exercise, of course, has other health-enhancing advantages. A dietary approach to prevent or to treat hypertension is indicated in **Table 5**. For patients who have a major elevation in BP, it is very uncommon for their hypertension to respond adequately to dietary management alone. These individuals will almost certainly also require medicines to control their hypertension. Individuals who are obese or have other dietary habits that may predispose to hypertension (e.g., high sodium chloride intake) should be encouraged to inaugurate appropriate dietary therapy. If the BP is substantially elevated, a reasonable approach would be to start pharmacological antihypertensive therapy concomitantly with dietary management. Patients who are committed to dietary therapy of hypertension may do the following: Once the BP has stabilized at the target level, attempts may be made to gradually withdraw the

Table 5 A suggested dietary approach to prevent or treat hypertension[*,†]

1. Maintain desirable body weight. This may require use of calorie-restricted diets.
2. Use the DASH combination diet (a diet high in fruits, vegetables, and low-fat dairy products and low in saturated and total fat).
3. Limit daily NaCl consumption to 6 g/day or lower.
4. Maintain adequate potassium and magnesium intake.
5. Consume recommended amount of calcium (about 1,000 mg/day for persons aged 19–50 years and 1,200 mg/day for persons older than 50 years).
6. For individuals who drink alcohol, restrict to no more than two drinks (3–4 units) per day.
7. Consider a diet high in omega-3 fatty acid (i.e., about 3–6 g of fish oil per day).

*For any person with a chronic illness, each of these recommendations should be reviewed with a physician to ensure that it is compatible with medical management.

†Chronic exercise activity is also recommended.

antihypertensive medicines while maintaining strict dietary management. Exercise training should be encouraged, but only after careful medical evaluation of the cardiovascular and hemodynamic responses to exercise of persons who have hypertension, who are older, or who have major underlying illnesses, such as heart disease or kidney failure.

SUMMARY POINTS

1. Excessive energy intake and obesity is a major predisposing factor to hypertension.
2. The many mechanisms by which excessive energy intake and obesity predispose to hypertension include increased activity of the RAAS and possibly other mineralcorticoid activity, increased SNS activity, insulin resistance, salt-sensitive hypertension, excess salt intake, and reduced kidney function, which often occur in obese individuals.
3. High sodium chloride intake is another major predisposing factor to hypertension.
4. Higher intakes of potassium, PUFA, protein and possibly certain amino acids, vitamin D, green coffee bean extract, dark chocolate, and tea may lower blood pressure.
5. Excessive alcohol intake may acutely raise blood pressure.
6. Certain diets and lifestyle changes, including regular exercise, appear to lower blood pressure in people with prehypertension or mild hypertension or prevent the development of hypertension.
7. The DASH low-sodium diet, which is high in fruits and vegetables, low-fat dairy products, potassium, magnesium, calcium, and fiber, and is low in saturated fatty acids, total fat, and sodium, is such a diet.
8. Methods for obtaining long-term adherence to such diets and healthy lifestyles are still being investigated.

FUTURE ISSUES

1. Prevention of obesity and reduction in sodium chloride intake appear to be among the most effective ways to prevent hypertension. Thus, the increasing prevalence of obesity and the high salt intakes observed globally are among the most pressing matters in this field. Effective population strategies for preventing and treating obesity and reducing salt intake should be explored.
2. More effective techniques need to be developed to increase the use of other foods (e.g., fruits and vegetables, low-fat dairy products) that prevent or ameliorate hypertension.
3. There is a need for assessing the long-term effects of dietary management on the prevention and treatment of elevated blood pressure. Are dietary regimens that lower blood pressure over a period of many weeks also safe and effective over many years?
4. The need remains to continue to explore other effective nutritional approaches to lower the incidence and prevalence of increased blood pressure.
5. A current most critical issue is to develop effective and inexpensive methods to facilitate long-term adherence to the nutritional regimens that have already been demonstrated to prevent and treat hypertension.

DISCLOSURE STATEMENT

J.D. Kopple is a consultant for Novo Nordisk, Nephroceuticals, and Abbott Laboratories.

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Errata

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