Treating hypertension to prevent coronary disease

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■ Because most patients with mild to moderate hypertension will not suffer a cardiovascular event due to elevated blood pressure, the presence of other risk factors must be assessed. Many of these are alterable with nondrug therapies, which cost little and carry no risks if applied sensibly. Drug therapies have costs, discomforts, and risks and should be used only for those at high risk or those who fail to respond adequately to nondrug therapies. When drug therapy is necessary, start with low doses and aim for a slow reduction of blood pressure, avoiding hypoperfusion and reducing as many risk factors as possible. Alpha blockers, angiotensin-converting enzyme inhibitors, and calcium-channel blockers may avoid metabolic risks associated with high-dose diuretic and beta-blocker therapy. The establishment of therapeutic goals, individualized assessment of status, and a conservative approach to treatment are the basis for optimal management of patients with hypertension.

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SINCE THE MAJOR GOAL in the treatment of hypertension is protection against coronary heart disease (CHD), it is appropriate to review current practices in hypertension management to determine if that goal is being met. An examination of past successes and failures in therapy suggests that changes in the current approach to treatment can be made to provide better overall therapy and to reduce the incidence of coronary disease among patients with hypertension.

The results of many clinical trials showing long-term effects of drug therapy are now available. In patients with mild to moderate hypertension, we see uniform and impressive protection against stroke, but disappointingly insignificant and spotty protection against CHD. This apparent failure is all the more disturbing because beta blockers have been shown to offer considerable protection against second heart attacks.[1] In an effort to explain why clinical trials do not show that the treatment of hypertension has resulted in a reduction of CHD, several reasonable possibilities have been suggested. McMahon[2] proposes that the causative role of hypertension in CHD is less significant than its role in other cardiovascular diseases, particularly stroke. Thus, relief of hypertension will not necessarily lower the incidence of CHD to the same extent as stroke. The results of the MRFIT study[3] suggest that the duration of therapy in clinical trials may have been too short (and too unidirectional) to achieve regression of coronary atherosclerosis. It also seems reasonable to assume that, because patients who were at high risk were usually excluded from the clinical trials, the power of the trials to detect treatment effects was markedly reduced. It is also possible that therapy may not have been aggressive enough to reduce the risk of CHD. Havlik et al[4] compared normotensive patients with hypertensive patients whose diastolic blood pressures had been reduced with treatment to below 90 mm Hg and found that CHD

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mortality rates remained higher in the hypertensive group. On the other hand, there is concern that if therapy is too aggressive, coronary hypoperfusion could be induced and, as is reflected in the J-curve of CHD, when diastolic pressure is reduced below 90 mm Hg, mortality rates increase.[5-10] Simply stated, inadvertent overtreatment, particularly but not exclusively among patients with preexisting coronary disease, likely contributes to the failure to demonstrate a reduction in heart attacks among patients being treated for mild to moderate hypertension[5] (*Figure 1*).

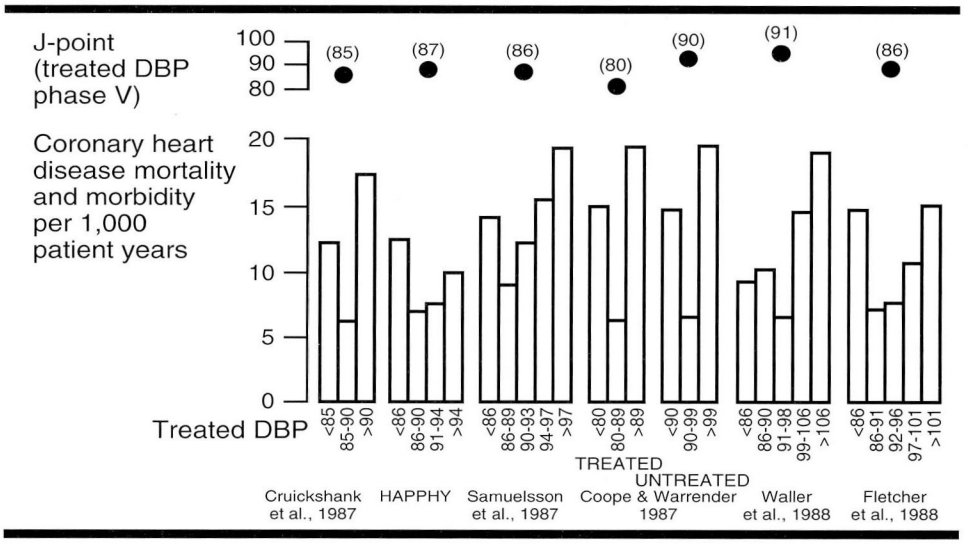

FIGURE 1. Relation of diastolic blood pressure during treatment to mortality or morbidity from coronary heart disease in six studies which included 14,536 patients. The numbers above the histograms indicate diastolic blood pressure (mm Hg) at which J point (lowest incidence of myocardial infarction) occurred. (From Cruickshank, reference 107, with permission)

Three important additional reasons for the possible failure of clinical trials to demonstrate reductions in CHD mortality are proposed, and they have particular relevance to the improvement of overall treatment strategies. First, a considerable proportion of patients in these trials have "office" or transient hypertension and would be unlikely to benefit from further reductions in blood pressure levels. Second, it is currently not feasible to accurately ascertain the CHD risk status of individual patients and thus, the study cells are probably not comparable at baseline in terms of CHD mortality risk. Finally, the drugs used in the trials were effective in lowering blood pressure but may have adversely affected other CHD risk factors. An examination of these three issues should clarify the status of current therapeutic approaches. Further, it is suggested that changes in current clinical practice can be made, particularly in encouraging the use of nondrug therapies, that will improve the management of the majority of hypertensive patients and reduce their propensity for coronary disease.

DIAGNOSIS OF HYPERTENSION

The correct diagnosis of hypertension (diastolic blood pressure over 90 mm Hg) and of overall cardiovascular risk is crucial to achieving the goal of improved cardioprotection. It seems reasonable to institute therapy if the average ascertained blood pressure reading is accurately and consistently determined to be 140/90 mm Hg or higher. However, before drug therapy is initiated, the diagnosis of hypertension should be confirmed beyond question. Diagnosis cannot be based solely on a few blood pressure readings taken over a relatively short time in the office or clinic. Because the current practice is to initiate treatment at blood pressure levels lower than those previously thought to require treatment, the need for more measurements, carefully taken, is of even greater importance. The chance for misdiagnosis is fairly small when a diastolic pressure is above 100 mm Hg; however, when a diastolic pressure between 90 and 100 mm Hg, or even below 90 mm Hg, is considered high enough to treat, the chance of overdiagnosis is much greater. During an initial screening process in the large clinical trials, as many as half of the people with a diastolic pressure of 95 mm Hg or higher were normotensive (below 90 mm Hg) on second measurements. Moreover, in the Australian trial, 48% of those who were still above 95 mm Hg on the second screen remained below 95 mm Hg while on placebo for the subsequent 4 years.[11]

It is important to note that the basis for all of the current information on the long-term risks of hypertension are initial office readings. The Framingham study utilized two sets of office readings; insurance actuarial data are based on one set; the MRFIT data

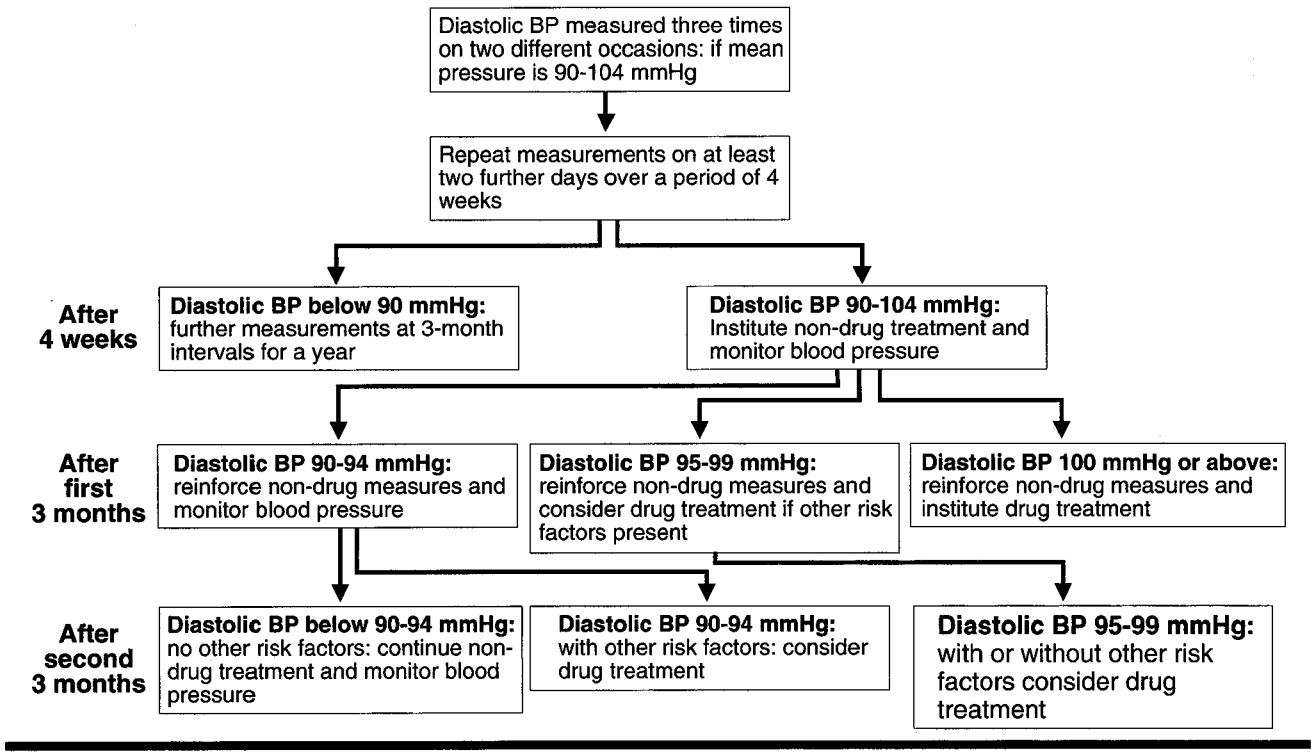

FIGURE 2. Recommendations for evaluation and management of mild hypertension by the World Health Organization and the International Society of Hypertension. (Adapted from reference 13, with permission)

were based on the average blood pressure obtained over two visits. Although it seems prudent not to disregard elevated initial office/clinic readings even if all subsequent ones are normal, this author does not believe that patients with blood pressure elevations at only the first or second office visit should be labeled as hypertensive or started on antihypertensive therapy. Rather, such elevations should be an indication to monitor the blood pressure more thoroughly and a motivation to encourage appropriate life-style changes that could prevent the development of persistent hypertension. The same caution is advised in those patients who are normotensive at rest but who have an exaggerated response to exercise—ie, systolic blood pressure above 200 mm Hg; they have a greater likelihood, but by no means a certainty, of developing persistent hypertension in the future.

BP reading variability

Variability in blood pressure readings has many causes. Those related to measurement can be controlled by proper technique. Those related to factors working within the patient can be reduced by obtaining multiple readings in the office or clinic over a period of at least 1 month,[12] or by using out-of-office measurements. The algorithm in *Figure 2* provides guidelines for appropriate evaluation and management of mild hypertension.[13]

Out-of-office measurements

For many patients, there is a need to obtain out-of-office measurements. Even after the tendency for initially higher readings has been modulated, many patients have a persistent pressor response in the clinic[14] or when seeing the doctor.[15] In the study by Pickering et al,[15] 292 clinic patients were evaluated for an average of 6 years; 21% had always been hypertensive at the clinic, but were normotensive when measured by ambulatory recording. As these authors and others[16] have noted, the "white-coat hypertensives" show neither a generalized increase in blood pressure lability, nor an exaggerated pressor response to exercise, mental stress, or work. Unless these patients are identified by out-of-office recordings, it could mean

that as many as one fifth of hypertensive patients will be misdiagnosed and unnecessarily treated.

Indications for home blood pressure monitoring are listed in *Table 1*. Home readings are stable over time[17] and, on average, are lower than office readings by about 10 mm Hg (systolic) and 5 mm Hg (diastolic)[18]; they are quite close to daytime readings obtained by automatic ambulatory recorders.[19,20]

Home readings may be particularly valuable in elderly patients susceptible to postprandial, postmedication, and postural falls in blood pressure[21] and in patients who appear to be resistant to increased doses of medication.[22,23] In the Waeber et al study,[22] half of the "resistant" hypertensive patients were actually normotensive by out-of-office recordings. Significant hypotension occurred in some patients after therapy had been increased on the basis of elevated office readings. There is, then, need for home recordings both to establish the presence of persistent hypertension and to monitor the course of therapy once the diagnosis is made. Readings should be taken at various times at home and at work. Those taken as soon as the patient awakens can assess whether once-a-day medications, taken early in the morning, provide sustained 24-hour antihypertensive action.

Almost all patients can obtain satisfactory and accurate readings by home devices. Inexpensive, reliable, and sturdy models are available[24]; however, some that are available are not reliable,[25] so caution is advised.

TABLE 1
INDICATIONS FOR HOME BLOOD PRESSURE MONITORING

For diagnosis
Recognize initial, short-term elevations in blood pressure
Identify persistent "white-coat" hypertension
Determine usual blood pressure levels in borderline hypertension
For therapy
Monitor response to therapy
Ensure adequate blood pressure control during awake hours
Evaluate effects of increasing or decreasing amounts of therapy
Ascertain whether poor office blood pressure response to increasing treatment represents overtreatment or true resistance
Identify periods of poor control when office readings are normal but target organ damage progresses
Identify relations of blood pressure levels to presumed side effects of therapy
Involve patient to improve adherence

From Kaplan NM. Clinical Hypertension, 5th edition, Williams and Wilkins, Baltimore, 1990

TABLE 2
INDICATIONS FOR AMBULATORY BLOOD PRESSURE MONITORING

For diagnosis
Same as for home blood pressure measurements
Patients unable to obtain self-measurements (home)
Need for immediate ascertainment
Need to measure sleep blood pressure levels
For prognosis
Provide better correlation with target organ damage
Identify role of sleep blood pressure
For therapy
Same as for home measurements
Identify effects during sleep
Establish duration and degree of effect of new agents

From Kaplan NM. Clinical Hypertension, 5th edition, Williams and Wilkins, Baltimore, 1990

Ambulatory monitoring

In certain hypertensive patients, ambulatory monitoring with automatic devices may be useful (*Table 2*).

The blood pressure in normotensive patients and in most hypertensive patients is considerably lowered during sleep. This is largely related to the absence of physical activity; there is no important endogenous circadian rhythm of blood pressure.[26,27] If the nocturnal pressure does not fall more than about 10%, there is evidence for more target organ damage—eg, left ventricular hypertrophy.[28] In both normotensive and hypertensive blacks, the fall in nocturnal blood pressure is less than in nonblacks who have comparable daytime or casual readings. This fact may help explain the greater cardiovascular disease (CVD) morbidity and mortality seen in blacks.[29] A lesser nocturnal fall in pressure has also been described in patients with malignant hypertension, pheochromocytoma, Cushing's syndrome, diabetes, congestive heart failure, cardiac transplantation, orthostatic hypotension, and sleep apnea.[30] Greater attention should be given to blood pressure during sleep because it has been claimed that as many as 80% of patients with sleep apnea are hypertensive and as many as 30% of hypertensive patients have sleep apnea.[31]

Another potential need for automatic recordings is to identify the rise in blood pressure which occurs soon after awakening in the morning[32,33] and which may contribute to the markedly higher incidence of stroke[34,35] (*Figure 3*), myocardial ischemia, infarction, and sudden death that occur on awakening[36,37] (*Figure 4*). The abrupt rise could serve as one of the major triggers for plaque fracture in the coronary and cerebral vessels or for vascular rupture in the brain.

Two critical problems must be addressed in connection with the early morning rise in pressure. Unfortunately, there are no data to clarify whether blood

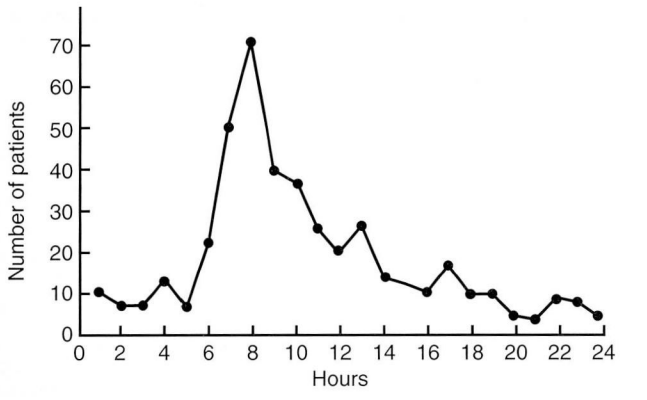

FIGURE 3. Graph of circadian variation of observed ischemic stroke onset in 426 consecutive patients seen within 12 hours after onset of their first hemispheric stroke. Not included are 91 patients who had onset of stroke while asleep between 11:01 pm and 8 am. (From Argentino et al, reference 35, with permission)

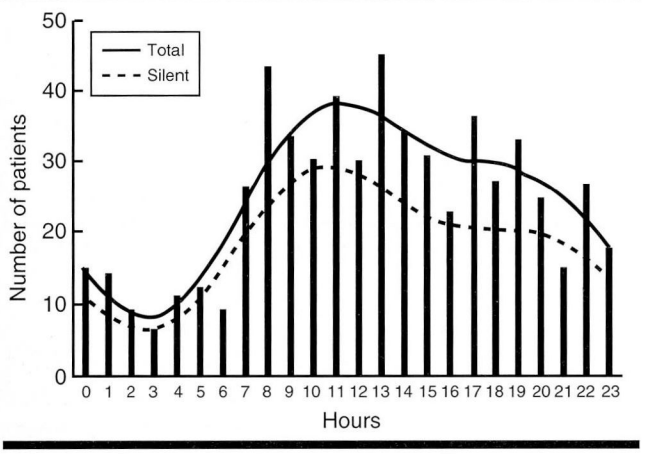

FIGURE 4. Circadian distribution of total and silent ischemic episodes identified by ambulatory ST-segment monitoring in 150 unselected patients with known coronary disease who were not on any drug therapy. (From Mulcahy et al, reference 36, with permission)

pressure rises on awakening or upon arising from bed. If it is the former, medications that have a significant action during the hours before awakening need to be given at bedtime; if the latter, patients could take a rapidly acting medication on awakening and remain in bed until it has had a chance to work. Data from the Beta-blocker Heart Attack Trial[38] showed that propranolol provides protection against sudden cardiac deaths in the morning. This, and the probable role of sympathetic nervous system activation as a trigger, are among the strongest reasons for using beta blockers to treat hypertensives at high risk for CHD.

A number of ambulatory blood pressure monitors are currently available, and most seem reliable. If their use has been limited because it is not reimbursable by Medicare and many other third-party payers, it is unfortunate. Krakoff et al[39] have shown that their use in diagnosis could be cost-effective by rapidly excluding from therapy up to 40% of "suspected" hypertensives. However, their greatest cost benefit probably would be to monitor therapy and to recognize risk by identifying blood pressure abnormalities during sleep and the early morning hours.

ASSESSING OVERALL CARDIOVASCULAR RISK

Even though risk of CVD for the overall population rises directly with every increment in blood pressure, the risk is not shared equally by each individual patient. The majority of patients with mild to moderate hypertension—ie, diastolic pressure 90 to 114 mm Hg—will not suffer a cardiovascular event as a consequence of elevated blood pressure.

Considering risk factors

The risk for CVD as a consequence of hypertension is based on the average level of blood pressure over 24 hours, the degree of target organ damage, and the presence of other risk factors (*Table 3*). The "big three" risk factors are elevated systolic blood pressure (more important than diastolic), hypercholesterolemia, and cigarette smoking. Diabetes is less common but more deadly.[40] Alterable risk factors can be easily determined by the history, physical examination, and basic screening, and should be assessed in every hypertensive.

Lipids and blood pressure

Hypercholesterolemia and hypertriglyceridemia occur more often in hypertensive people than would be expected by chance alone. The combination may be part of the "deadly quartet" associated with upper body obesity and hyperinsulinemia.[41]

There is increasing evidence that hyperlipidemia and hypertension may be even more closely connected, each giving rise to or aggravating the other, and the two in concert markedly accelerating atherosclerosis. The interactions go beyond the obvious,

wherein hypertension is known to accelerate atherosclerosis in the presence of hyperlipidemia.[42] Diet-induced hypercholesterolemia in various animals causes impairment of endothelium-dependent vasodilation of arteries in vitro,[43] and vasodilation of forearm resistance vessels is impaired in hypercholesterolemic humans.[44] Hypercholesterolemia, even in the absence of obvious vascular damage, appears to interfere with the ability of vessels to dilate in response to the normally active endothelium-derived relaxing factor. Moreover, patients with essential hypertension who were not hypercholesterolemic (mean plasma cholesterol, 191 mg/dL) had impaired endothelium-dependent vascular relaxation when compared with normotensive individuals with an average cholesterol of 180 mg/dL.[45]

The role of this impaired relaxation is a subject of current interest in the pathophysiology of coronary artery disease. Even in angiographically smooth coronary arteries, endothelium-mediated vasodilation, as assessed by the response to acetylcholine, is abnormal in the presence of CHD risk factors including hypercholesterolemia, male gender, positive family history for CHD, and increasing age.[46] Moreover, a number of other effects of hyperlipidemia on the vasculature have been identified, including an increase in intracellular calcium and enhanced DNA synthesis;[47] increased contraction in response to norepinephrine by alteration of calcium channels in the smooth muscle cell membrane;[48] increased renal glomerular capillary pressure;[49] the correction of impairment of endothelium-dependent relaxation by dietary treatment in hypercholesterolemic monkeys;[50] and prevention by treatment with a calcium-entry blocker.[51]

The recognition that hypercholesterolemia causes multiple arterial dysfunctions even in the absence of overt atherosclerosis will be likely to further increase the movement toward drug treatment of hyperlipidemia. Although all authorities recommend diet modification first and drugs only if that is inadequate, the reality is a tremendous increase in the use of cholesterol-lowering drugs over the past 5 years.[52] In reporting the 10.1-year follow-up of 2,541 white men in the United States, Pekkanen et al[53] have shown that "high-normal" levels (serum cholesterol between 200 and 240 mg/dL) do not significantly increase CHD mortality in people who have no evidence of CHD. It is hoped that, in recognition of this, the rush toward cholesterol-lowering drugs will be tempered.

Concerns have been raised about hazards associated with lower serum cholesterol levels. The most serious is the higher incidence of colon cancer, wherein the lower cholesterol levels do not appear to simply reflect preexisting cancer.[54,55] Also, in the MRFIT population, more hemorrhagic strokes were seen in those with lower cholesterol levels; however, the authors believe this problem "is overwhelmed by the positive association of higher serum cholesterol levels with death from nonhemorrhagic stroke and total CVD."[56]

TABLE 3
RISK FACTORS FOR CORONARY HEART DISEASE

Elevated systolic blood pressure
Hypercholesterolemia
Cigarette smoking
Decreased HDL cholesterol
Left ventricular hypertrophy
Upper-body obesity
Glucose intolerance
Hyperinsulinemia
Propensity to thrombosis
Low levels of physical activity

The role of hyperinsulinemia

Although a positive association has not been established, insulin resistance and hyperinsulinemia may play a role in the pathogenesis of hypertension. Their presence in obese hypertensive patients came as no surprise, but their presence in nonobese patients with hypertension has not been explained. Hyperinsulinemia has not been found in hypertensives in some ethnic groups, including Hindus, Muslim Indians, Chinese, or Mauritian Creoles[57]; Pima Indians[58]; or blacks.[59]

Risk assessment in ethnic groups

Almost all risk data have been obtained from middle-aged white males. The Framingham data base provides a reasonable estimate of risk in 50-year-old men (*Figure 5*). Plasma fibrinogen levels are an additional independent risk factor which interacts particularly with diabetes.[60] Risk factors identified in the Honolulu Heart Study[61] were higher body mass index, lower alcohol consumption, higher serum triglycerides, higher serum uric acid, lower forced expiratory volume in 1 second (FEV_1), higher blood hematocrit, and lower levels of physical activity.

In the 10-year follow-up of MRFIT, blacks with levels of blood pressure equal to those of nonblacks suffered fewer CHD deaths (2.26% vs 2.78%) but more

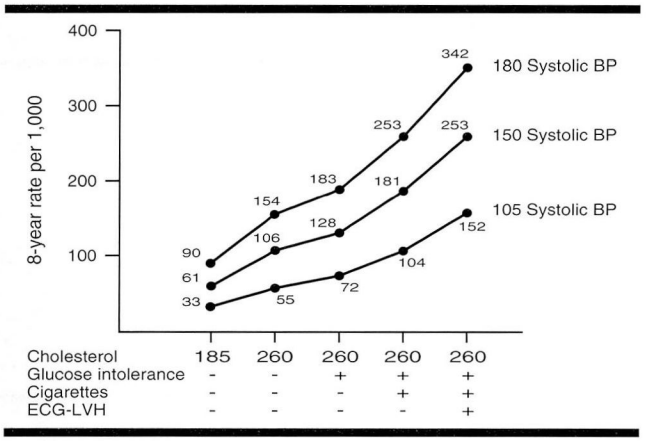

FIGURE 5. Risk of coronary heart disease by blood pressure level according to cardiovascular risk profile in 50-year-old men: Framingham study, 26-year follow-up. (From Kannel, reference 107.)

stroke deaths (0.63% vs 0.29%). Blacks have more hypertension, slightly lower serum cholesterol, but higher rates of cigarette smoking than nonblacks.[62,63] CHD mortality has not fallen as much for US black men and women as for US white men.[64]

Mexican-Americans in San Antonio have about 30% less hypertension[65] but worse overall CV risk status because of higher levels of serum triglycerides, body mass index, cigarette smoking, and diabetes, and lower levels of high-density lipoprotein (HDL) cholesterol.[66] Nevertheless, CVD mortality in Mexican-American men has been consistently found to be lower than in non-Hispanic men; no ethnic differences are observed in women. Mitchell et al[66] conclude "that some protective factors, either genetic or life-style, are present in Mexican-American males."

NONDRUG THERAPY

Nondrug therapy is the most underutilized strategy in the treatment of hypertension today. Most Americans need nondrug therapy and will comply if it is effectively presented. Nondrug therapies for hypertension are listed in *Table 4*.

Of all nondrug therapies, cessation of smoking is clearly the most important for all patients; it is even more important for those with hypertension who suffer additional insults. Smoking causes an immediate rise in blood pressure[67] and a fall in cerebral blood flow.[68] It is associated with more strokes,[69] more myocardial infarction,[70] more malignant hypertension,[71] higher serum cholesterol,[72] and more central, upper-body obesity.[73] It causes increased arterial wall stiffness,[74] vasoconstriction, and increased thromboxane production.[75] In addition, it interferes with the effectiveness of antihypertensive therapy, in particular with beta blockers.[76]

TABLE 4
NONDRUG THERAPIES FOR HYPERTENSION

Stop cigarette smoking
Lose weight, particularly for upper body obesity
Reduce sodium intake (2 g/d or 88 mmol/d)
Moderate alcohol intake (no more than three usual portions per day)
Do regular aerobic, isotonic exercise
Relaxation and relief of stress
Eat less saturated fat, more fish oil
Maintain adequate intake of potassium, calcium, and magnesium

Since the multiple hazards of smoking are so well known, the results of a survey of smokers in Michigan who had seen a physician within the previous year are rather surprising. Only 44% had been told to quit smoking.[77] Smokers who were hypertensive, obese, diabetic, or users of oral contraceptives were no more likely to have been told to quit than those without additional CVD risks. Physician face-to-face counseling and advice is the best intervention for patients.[78] Other interventions, including organized programs, are available and effective.

The effectiveness of weight loss has been documented in numerous well-controlled studies summarized by Staessen et al.[79] Moreover, Schotte and Stunkard[80] have shown that most of the weight loss and the concomitant fall in blood pressure occurs rather quickly. A small amount of weight loss has a significant effect on blood pressure.

Most authorities recommend moderate sodium restriction,[81] although objections to it have been raised. Data showing risks when severe stress was applied to rats on a sodium diet far below the level practical for humans do not constitute a valid objection to moderate sodium restriction. However, the objections of Swales[82] are valid. He warns against applying the "epidemiological associations to public advice without at least persuasive evidence from intervention trials and physiology." Nonetheless, his own portrayal of the antihypertensive effect of moderate sodium restriction support the recommendations.

Multiple studies have shown lower blood pressure, less coronary disease, and lower mortality rates among people who consume one or two drinks per day (up to

30 mL of ethanol).[83] Some of the higher mortality in abstainers may reflect the cessation of drinking when a patient becomes terminally ill, but I remain a firm believer in allowing patients to drink nonharmful and possibly helpful amounts of alcohol.

Exercise has been shown to be protective for hypertension and for coronary disease, and it is very difficult to achieve weight loss without exercise.[84] Carefully controlled studies such as that of Martin et al[85] show that exercise even without weight loss lowers blood pressure.

Fish oils have been endorsed as protection against coronary atherosclerosis,[86] and evidence of favorable influences of monounsaturated fatty acids on blood lipids has been provided.[87] Both monounstaurated and polyunsaturated supplements have been shown to favorably alter the composition and cation transport across cell membranes.[88,89]

Whether these changes translate into long-term antihypertensive effects remains uncertain; however, in fairly short-term studies, most results,[90] but not all,[91] show that fish oils do lower blood pressure.

Muscle relaxation, yoga, and stress management often make people feel better, but in a well-designed 1-year study,[92] they were found to have no effect on lowering blood pressure.

With regards to calcium supplements, most of the epidemiologic studies relating dietary calcium intake to blood pressure show an inverse association: the lower the calcium intake, the higher the blood pressure.[93] However, the majority of interventional studies fail to document an antihypertensive effect from calcium supplements. Pooled analyses of 19 randomized trials showed a small (1.8 mm Hg) reduction in systolic blood pressure, but no effect on the diastolic.[94]

The use of postmenopausal estrogen replacement therapy (ERT) continues to receive strong support as an effective way to prevent coronary disease and prolong survival.[95] Presumably, it works to prevent the unfavorable changes in lipid metabolism that develop after menopause.[96] ERT has also been shown to reduce levels of plasma insulin, both fasting and postglucose-challenge,[97] which may help to explain the generally lower pressure levels found in ERT users.[98]

There are a few long-term controlled studies of the antihypertensive efficacy of multiple nondrug therapies as they would be used in clinical practice. Recently, preliminary (and, as yet, unpublished) data from the Treatment of Mild Hypertension Study (TOMHS) have shown that after 18 months patients placed on a program of weight reduction, sodium and alcohol intake reduction, and increased exercise had an average fall in blood pressure from 140/90 to 131/82 mm Hg. For those patients who were given an antihypertensive drug in addition, the average pressure was reduced to 123/78 mm Hg.

In a similar multiple nondrug program, a 5-year follow-up showed that when patients followed the intervention program the number of "hypertension-prone" patients whose blood pressures advanced into the hypertensive range was reduced by half, even when compliance was only modest.[99]

The possibility of preventing or at least postponing the development of hypertension by such easily attained life-style changes should encourage us to use them more rigorously. Nondrug interventions, particularly weight loss and exercise, are also effective against other cardiovascular risk factors.

DRUG THERAPY

Major developments in the use of antihypertensive drugs have occurred which should help to improve protection against coronary disease. The recognition of the significant abnormalities in blood lipids and plasma insulin that may accompany the use of high doses of diuretics and beta blockers—but which are not seen with alpha blockers, angiotensin-converting enzyme (ACE) inhibitors, or calcium-channel blockers—has encouraged changes in the approach to antihypertensive therapy. As previously noted, the often persistent and rather profound alterations in various coronary risk factors by diuretics and beta blockers could help to explain the failure to see protection against CHD in the multiple clinical trials. The increased use of the newer hypertensive agents, which is recommended by the majority of US authorities, seems rational and possibly even cost-effective.[100] The newer agents provide practitioners with the tools to more closely tailor therapy to the individual patient's needs, and surveys indicate a significant shift from a diuretic-first stepped-care approach.[101] The change is not universal; the Report of the British Hypertension Society[102] suggests that diuretics and beta blockers should still be the primary therapies, since they alone have been tested and found to favorably reduce stroke and overall mortality.

Practical treatment considerations

The need to "start low" has been amply documented, particularly with diuretics.[103] Clearly, larger doses increase the risk of progressive adverse metabolic

effects and provide little benefit for most patients.

It is also important to slowly titrate the pressure down over 3 to 6 months, providing "a gentle seduction rather than an aggressive assault."

With almost every antihypertensive agent, doses which are lower than those usually prescribed should be considered so that hypoperfusion of vital organs will be avoided. The heart is the most susceptible, but other vital organs, including the genitals, may suffer from too aggressive a reduction in blood pressure. The need to avoid hypoperfusion by too great or too fast a fall in blood pressure is particularly important in hypertensive patients with left ventricular hypertrophy and coronary atherosclerosis who need more perfusion but lack adequate vasodilation because of poor autoregulation (ie, reduced coronary reserve).

With the use of ACE inhibitors, alpha blockers, and calcium-channel blockers, it is possible to avoid the multiple aggravation of other CVD risks that may accompany diuretic and beta blocker therapy. More effective regression of left ventricular hypertrophy has been shown with ACE inhibitors[104] and calcium-channel blockers[105] than with diuretics, beta blockers, or direct-acting vasodilators. The changes in insulin sensitivity may or may not turn out to have a significant influence on CVD risk, but the overall effect of reducing them will be more positive than negative.

Therapeutic goals

An initial goal of 150/90 mm Hg seems reasonable for maximal coronary protection in most patients. Some may need greater reductions in blood pressure to protect vulnerable target organs. This seems particularly true for diabetic patients who have more microvascular complications (ie, retinopathy, albuminuria) at higher blood pressures, even those below the hypertensive range.[106] To protect eyes and kidneys, blood pressures may need to be lowered even below 120/80 mm Hg, although good prospective data on which to base this judgment are not available.

SUMMARY

An examination of current practices in the treatment of hypertension suggests that many changes can be made in the current management of the majority of hypertensive patients to reduce their risk for coronary disease. The basis for this conclusion rests in the disappointing results, as reported in recent literature, of the effects that hypertensive treatment has had on mortality rates from CHD. Although the reasons for the apparent failure of treatment are numerous, the most important seem to revolve around the need for the accurate diagnosis of hypertension, the evaluation of the individual patient's overall cardiovascular risk status, and the emergence of data confirming serious long-term risks associated with the drugs that have been the primary approach to therapy.

The correct diagnosis of hypertension requires more time and care than is usually given. Most of the problems in diagnosing can be overcome by taking more blood pressure readings more accurately. Both home and ambulatory blood pressure measurements will overcome the difficulty of obtaining accurate readings from patients who are victims of "white coat hypertension." Automatic blood pressure measuring devices provide the potential to recognize two major hazards in assessing patient cardiovascular risk status—a failure of pressure to fall during sleep, and a marked rise of pressure upon awakening.

Because the majority of patients with mild to moderate hypertension will not suffer a cardiovascular event as a consequence of elevated blood pressure, it is necessary to determine the presence of other risk factors in order to provide maximally beneficial therapy. Many of these factors are alterable with life-style changes, and nondrug therapy is strongly recommended both as an initial approach to therapy and as concomitant therapy with antihypertensive drugs. Nondrug therapies cost little and carry virtually no risks if applied sensibly.

Drug therapies, on the other hand, have costs, discomforts, and risks. Therefore, drugs should be prescribed only for those whose risks are so great or whose response to nondrug therapies is so inadequate as to far outweigh the risks of drug therapy. It is particularly true of patients with mild hypertension that many more are treated than are helped, so care must be taken to see that drug therapy is both needed and appropriate.

When drug therapy is necessary, start with low doses and aim for a slow reduction of blood pressure avoiding hypoperfusion and reducing as many risk factors as possible. The newer antihypertensives, alpha-blocking agents, ACE inhibitors, and calcium-channel blockers are being increasingly used as primary therapy to avoid the metabolic risks that have become associated with high-dose diuretic and beta-blocker therapy. The establishment of therapeutic goals, individualized assessment of status, and a conservative approach to treatment provide the rational basis for good management of patients with hypertension.

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