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The Clinical Spectrum of Essential Hypertension

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The majority of hypertensive patients fall into the borderline and mild groups. A smaller percentage of the hypertensive population falls into the groups with persistent elevations in diastolic blood pressure of 105 mm Hg or higher. However, they are a most important group because treatment has been effective in reducing their high risk of developing major complications. In mild hypertension, the physician will treat those who are at increased risk as judged by age, race, sex, target organ damage, family history, hyperglycemia, and hypercholesteremia. Even though most mild and borderline hypertensive patients are not treated, they should be followed up since some of these patients may progress to a more severe stage of hypertension and should then be treated.

The decision to treat a patient with hypertension rests primarily on the estimated risk of hypertensive complications developing in the patient. Risk varies with the degree of severity of the hypertension. Severity in hypertension is a continuum, beginning with the most mild or borderline hypertensive patients at one end of the scale and continuing to the most severe. The purpose of this report is to describe the characteristics of this continuum or clinical spectrum and to offer a guide on the indications for treatment.

The level of blood pressure is the most important single criterion for correctly diagnosing the degree of hypertension. Consequently, it is of great importance to obtain blood pressure data from the patient that will be truly representative of his average blood pressure.

A major difficulty in evaluating and classifying hypertensive conditions, particularly in office practice, is the great variability in the level of blood pressure. Actual continuous recordings of blood pressure during a 24-hour period have indicated a variation as great as from 150/74 to 244/105 mm Hg in one patient and 110/90 to 220/165 mm Hg in another.[1] Even normal persons have been found to have occasional periods of hypertension.[1] Such marked variations in blood pressure appear to be emotionally influenced, apparently acting via the sympathetic nervous system. Any sort of emotionally alarming stimulus has been found to markedly raise the blood pressure, while sleep is associated with the lowest levels of blood pressure during a 24-hour period.

Patients generally visit doctor's offices because they do not feel well or they are in pain. During such episodes, they are quite likely to experience considerable apprehension. Therefore, it is not unusual to obtain an unrepresentatively high blood pressure, particularly on the initial visit. Only through repeated visits will enough blood pressure readings be obtained to permit one to derive an approximation of the average blood pressure for that patient.

A series of blood pressure readings is required in order to categorize and classify patients. Let us assume, for example, there are two patients with a diastolic blood pressure of 110 mm Hg on the initial visit. In one of these patients, the diastolic readings fall to 90 and 80 mm Hg on subsequent visits, whereas in the other patient the diastolic pressures remain in the 110 mm Hg range. Obviously, these two patients are at different points in the clinical spectrum of hypertension and will require different management.

Borderline Hypertension.—The subject of borderline hypertension has been extensively reviewed by Julius and Schork,[2] and much of the material presented in this section has been drawn from their review. The term "borderline" hypertension is used because the more traditional "labile" hypertension is not easily defined since it depends on the number of blood pressure determinations and the conditions under which they were taken. Also the term "labile hypertension" is meaningless because almost everyone exhibits considerable fluctuations in blood pressure from time to time.[1] Borderline hypertension is defined by Julius and Schork as blood pressure readings averaging between 150/90 and 160/100 mm Hg with occasional normal readings and no evidence of target organ damage.

The prevalence of borderline hypertension is very high, including 10% to 15% of the adult population of the United States. The prevalence is higher in older than in younger age groups, approaching 30% to 40% in the groups older than the age of 60 years. Among women younger than 50 years, there is a lower prevalence than among men of the same age. After the age of 50, borderline hypertension becomes more common in women than in men.[3,4]

There is no question that patients with borderline hypertension later develop established hypertension with a higher frequency than the normal population. Oberman et al[5] carried out a 24-year follow-up of naval aviators, some of whom developed hy-

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pertension in middle age. In the majority of the latter, blood pressures at the time of admission to service had been in the upper range of the normal zone of blood pressure. With the passage of time, these graduated from high normal to overtly hypertensive blood pressures. Since blood pressure normally rises with age and since the borderline hypertensive patient begins from a higher average level than normal, it is not surprising that he is more likely than the normal to go on and develop a definite hypertension. While the follow-up results vary greatly from one study to another, the consensus indicates that established hypertension develops about three times more commonly in the borderline than in the normotensive group with 10 to 20 years or more of follow-up.[6-8]

Borderline or mild hypertension carries a higher-than-normal risk of morbidity and mortality. The most extensive data are those supplied by the life insurance studies.[9] According to these data, the group at highest risk are men between the ages of 30 and 39 years. At a blood pressure 90 mm Hg, the 20-year mortality is 1.4 times that of the normal population; with a blood pressure of 152 systolic or 95 mm Hg diastolic, it is 2.7 times that of the normal. In women and in men in older age groups, the risk is not as high. For example, in men between the ages of 50 and 59, a blood pressure of 152/95 mm Hg is associated with an increased 20-year mortality of 1.7 times the standard risk.

Other studies report somewhat similar findings. With respect to morbidity, Stamler et al[6] found that, during a 20- to 30-year period of follow-up on male gas company employees, the development of hypertensive heart disease was three to four times as common in those who initially had borderline hypertension as in normal individuals. Similarly, the Framingham study[10] disclosed that, in both sexes, coronary heart disease was about 1.6 times more common in patients with borderline hypertension. While these increased risks in the patients with borderline hypertension are important, they are not excessively high and are in no way comparable to the risk in established hypertension.

Although patients with borderline hypertension are thought to have a more labile blood pressure than normal persons, the available evidence does not support this view. Blood pressure readings taken once or twice daily for one to three weeks in college students failed to show any correlation between the mean systolic blood pressure and the extent of the pressure fluctuation.[11,12] Nevertheless, I have observed individuals in the older age groups, particularly women, who can and often do display quite elevated blood pressures in the physicians' offices and whose blood pressures recorded at home are in the normal range.

Unlike the cardiac output in established essential hypertension, the output in borderline hypertension frequently is elevated. The elevation is seen more often in young than in middle-aged or old patients.[13-15] The increase in cardiac output persists despite periods of rest for as long as one hour. However, the difference between output in patients with borderline hypertension and normal subjects disappears during exercise.[15-17] Total blood volume has been measured and has been found to be normal[18] or low.[19,20]

The mechanism of the increased cardiac output has not been clarified. It would appear that it is not due to increased venous tone.[16,21] After administration of propranolol hydrochloride (Inderal), the difference in cardiac output between the borderline hypertensive and normal subjects becomes minor, suggesting that β-adrenergic stimulation of the heart may be important in maintaining the increased cardiac output.[22] Although the peripheral resistance may be normal or low in borderline hypertension with high cardiac output, it is still higher than would occur in a normal individual with a high cardiac output.[20,23] In the latter, the peripheral resistance would adjust so that the blood pressure could remain in the normotensive range.

How should patients with borderline hypertension be managed? Should they be treated or should they not? Patients with borderline hypertension have approximately three times the risk of developing established hypertension as does the normal individual. Cardiovascular morbidity and mortality are significantly but not markedly greater than normal. There is, however, no evidence at the present time that treatment will prevent the subsequent development of hypertension or the excess cardiovascular morbidity and mortality. Furthermore, some individuals with borderline hypertension revert to normal levels of blood pressure. Probably no more than 25% of patients with borderline hypertension later develop established hypertension.

In view of this, it seems questionable that treatment with antihypertensive agents is justified in such patients. The exposure of the patient to side effects and the expense of lifelong treatment are disadvantages that should be weighed against the undemonstrated advantages of controlling an occasionally slightly elevated blood pressure.

Other therapeutic approaches that carry potentially less risk than drug treatment have been suggested for treating patients with borderline hypertension. One such approach is the use of a low-sodium diet. There is no convincing evidence, however, that a diet moderately restricted in sodium will have a beneficial effect on blood pressure. To reduce blood pressure by dietary means alone, the sodium intake must be reduced to 200 mg or less per day. A diet so low in sodium requires such diligent care and is so unpalatable that very few patients will adhere to it.

Another therapeutic approach has been to advise the patient to avoid stressful situations on the theory that

this would avoid the stimulus that would lead eventually to established hypertension. In borderline hypertension in particular, it seems possible that there may be a large emotional component to the elevation of blood pressure. However, it is doubtful that the stresses of life can truly be reduced. The long-term use of sedatives or tranquilizers would not appear to be justified in treating this condition, and there is no evidence to indicate that such treatment would be effective in preventing progression to an established form of hypertension.

Probably the best way to manage the patient with borderline hypertension is to follow up on him or her for six months or a year without undertaking any form of therapeutic intervention. During part of this time, it would seem highly desirable to obtain home recordings of the blood pressure. The patient or, preferably, a member of the family could be taught to take the blood pressure. The patient either purchases a blood pressure apparatus or, if he is not able to afford this, the physician may loan one to him for a two-week period. Recordings should be made in the home twice daily in the morning and at night.

There is no need to initiate treatment immediately in patients with borderline hypertension. It is possible and probably desirable to wait for a year or more before deciding whether treatment is required. If the blood pressure falls to normal during this period or if it remains in the borderline range, the patient should be rechecked in another year. However, if the blood pressure rises and remains in the hypertensive range, appropriate treatment may then be started. In either event, it is important to maintain contact with the patient. He should be followed up because of the increased risk of developing established hypertension in the future. By monitoring his blood pressure periodically, one can determine if he develops established hypertension; if he does, treatment can be instituted before major vascular damage has occurred.

Mild Hypertension.—By mild hypertension I mean that the diastolic blood pressure is persistently elevated to more than 90 mm Hg, in contrast to borderline hypertension where the readings are normal at some outpatient visits. In addition to a persistent elevation, the average of the diastolic readings at three or more visits is in the range of 90 to 104 mm Hg.

There is a wide divergence of opinion as to how such patients should be managed. Some physicians advocate bringing the blood pressure down to normal in every case. Others would not treat any patients in the mild group until or unless their hypertension becomes more severe. The reason for the divergence of opinion is that it is precisely in this group of patients that controlled trials have failed to supply a definitive result. The Veterans Administration trial included such mild cases.[24] Unfortunately, because of the higher levels of blood pressure (diastolic pressure, 105 to 114 mm Hg), the study was terminated after an average follow-up of only 3.3 years. At that time, there was evidence of a protective effect of treatment against the major hypertensive complications that included stroke, congestive heart failure, renal damage, and accelerated hypertension. When the results were further analyzed, however, it was apparent that the effectiveness of treatment, though favorable, was not important in the group of patients with initial diastolic pressures of 90 to 104 mm Hg.

Patients with mild hypertension develop complications less frequently than those with higher levels of blood pressure. When mildly hypertensive persons develop complications, they are often atherosclerotic in type. Myocardial infarction or sudden death can occur. While antihypertensive drug treatment has been shown to be effective in preventing hypertensive complications, there is little evidence to indicate that treatment is effective in preventing atherosclerotic complications such as myocardial infarction.

Since hypertension is known to aggravate and accelerate atherosclerosis, it was hoped that reduction of blood pressure might have a beneficial effect on atherosclerotic complications. However, in the Veterans Administration Study, the incidence of myocardial infarction was essentially the same in the control and treated groups. The benefits of treatment were related more to complications that are associated specifically with elevated blood pressure such as congestive heart failure, stroke, particularly hemorrhagic stroke, renal damage, accelerated hypertension, and dissecting aneurysm. It is possible that, if antihypertensive drug treatment had been instituted at a very early stage in the hypertension, a beneficial effect on prevention of myocardial infarction might have been observed. However, on the basis of currently available data, I have no evidence to support the concept that controlling blood pressure with antihypertensive drugs has a favorable effect on the atherosclerotic complications.

I take an intermediate position between those who will not treat any patient with mild hypertension and those who will treat all such patients. Blood pressure is not the only indicator of risk, and in the group of patients with diastolic pressure levels averaging in the range of 90 to 104 mm Hg there are some patients who are at much higher risk than others. The known determinants of risk other than blood pressure include age, race, sex, target organ damage, family history, hyperlipoidemia, and hyperglycemia.

At any given level of elevated blood pressure, the younger the age of the patient, the greater is the reduction of life expectancy. For example, the life insurance data[9] indicate that, for men between the ages of 50 and 59, a blood pressure level of 152 systolic or

95 diastolic mm Hg is associated with a 1.7 increase of the normal 20-year mortality rate. However, in the 30- to 39-year age group, the 20-year mortality for similar levels of blood pressure is 2.7 times the normal for that age. It is apparent that even a modest elevation of blood pressure is associated with an increased risk when the hypertension appears at a relatively early age.

Men have a poorer prognosis than do women. Various follow-up studies indicate that mortality is about 1½ times as high in men as in women.[25,26] The prognosis is not much different than normal in women age 60 or older who have mild elevations of blood pressure. According to the 20-year follow-up study of Bechgaard, the mortality in this sex and age group was the same as that of the normal.[25]

With respect to race, hypertension is not only more prevalent in blacks but it also tends to be more severe. Data from the National Health Survey found definite hypertension in 27% of black adults as compared to 14% of white adults.[3] However, the death rates for hypertension and hypertensive heart disease in blacks were increased out of proportion to their increased prevalence of hypertension. For example, the vital statistics for the year 1967 indicate a death rate of 66 per 100,000 from hypertension in black males as compared to 16 per 100,000 in white males.[27] This represents a difference in mortality of four to one in blacks as compared to whites.

The target organs that are involved by hypertension are the brain, the optic fundi, the heart, and the kidneys. Mortality risk is directly related to the amount of damage detectable on examination.[26,28] The control or untreated patients in the Veterans Administration Cooperative Study were divided into two groups depending on whether they did or did not show evidence of target organ damage at the time of entry into the study. During the follow-up period, the group with evidence of target organ damage developed 2½ times as many complications as the group that did not.[29]

With respect to symptoms, a history of occipital headache in the morning is characteristic of severe or malignant hypertension only. Headache is not a characteristic symptom of mild or moderate hypertension. Cerebral vascular atherosclerosis may be suggested by failing memory for recent events, unsteady gait, or transient ischemic attacks. In the optic fundi hemorrhages, exudates and papilledema are found only in malignant hypertension and never in mild hypertension. With respect to vascular sclerotic changes, the presence of arteriovenous nicking is a useful sign of arteriolar sclerosis, particularly if the nicking is seen at crossings that are more than two disc diameters peripheral to the optic disc. Tortuosity, irregularity, segmental spasm, and narrowing of retinal arterioles also are useful indicators. However, they are not definitive because such changes can be seen in some normal fundi.

In the cardiac evaluation, there may be some symptoms of early heart failure such as a decrease in exercise tolerance, dyspnea on mild exertion, or recent increase in nocturia. The presence of a third heart sound would be confirmatory of the presence of failure. Of equal importance is angina, since coronary artery disease is common in patients with mild hypertension. A fourth heart sound is frequently heard in hypertensive patients; it reflects decreased compliance of the left ventricular wall. A most important feature of the examination is the electrocardiogram, in which one looks especially for evidence of left ventricular hypertrophy and for evidence of coronary artery disease including conduction defects, ischemic changes, rhythm disturbances, and evidence of old infarction.

Renal damage is not a characteristic finding in mild hypertension. The type of renal damage resulting from hypertension is nephrosclerosis, which is generally a manifestation of severe hypertension. Atherosclerotic changes in the large renal arteries may occur in mild hypertension but only rarely lead to any clinically apparent renal damage. If there is evidence of renal disease, such as the presence of proteinuria, casts, cells, or elevated levels of blood urea nitrogen or serum creatinine, one should suspect an independent renal disorder such as chronic pyelonephritis, rather than renal damage secondary to the mild hypertension.

In addition to the factors already mentioned of sex, age, race, and target organ damage, it is also useful to consider the family history. There is a strong inherited tendency in hypertension that is strikingly demonstrated in studies on identical twins.[30] Even though such twins may have lived apart for many years, similar levels of blood pressure have been found in both. A family history of hypertension suggests that one is dealing with essential rather than secondary hypertension. The family history also has prognostic value. A history of severe or fatal hypertensive complication in a parent or sibling makes it more likely that the patient with mild hypertension may progress to a more severe stage. According to Platt,[30] the sibling of a patient with severe essential hypertension has an eight times greater chance of developing a diastolic blood pressure of 100 mm Hg or greater in middle age than does the average individual.

Knowledge of factors that affect prognosis is useful in making the decision about treatment. For example, a 28-year-old black man with a diastolic blood pressure averaging 100 mm Hg during three successive visits should be treated, in my opinion, because of the greater chance he has of developing a progressively more severe hypertension. On the other hand, a 65-year-old woman with no evidence of hypertensive complications and whose diastolic blood pressure averages 95 mm Hg probably would be observed rather than treated ac-

tively.

It should be emphasized that patients with mild hypertension are in no immediate danger of developing cardiovascular complications. It is possible, therefore, to delay the decision to treat the patient until one has had the opportunity to observe the course of the hypertension over a period of time. Whereas the tendency for the blood pressure is to progress slowly, it may remain stable or even regress. Repeated checks of the blood pressure at three- or six-month intervals will detect the individuals who revert spontaneously to normal levels of blood pressure and who therefore do not require treatment. Others who progress during this period can be treated. In many instances, hard and fast guidelines as to treatment cannot be made because there is a lack of definitive data on the results of treatment in mild hypertension. It is hoped that such data will become available in a few years' time so that therapeutic decisions can be made on the basis of fact rather than on opinion.

Moderate Hypertension.—This is defined as diastolic blood pressure averaging between 105 to 114 mm Hg during a period of three or more office visits. Some patients may show readings within this range on the initial visit but on subsequent visits exhibit much lower or even normal readings. Therefore, it is always useful to see these patients several times in order to obtain an adequate estimate of the average blood pressure before proceeding directly to treatment. On the other hand, if the patient has definite evidence of target organ damage, such as arteriovenous nicking in the optic fundi or left ventricular hypertrophy on the ECG, treatment can be begun without delay. It is primarily when no signs of target organ damage are present that the average of a number of blood pressure readings taken at different visits is needed to judge the severity of the hypertension and the consequent need for treatment. If this average is 105 mm Hg diastolic blood pressure or higher, the patient should be treated.

The decision to treat all patients with average diastolic blood pressure levels of 105 mm Hg or higher is soundly based. The Veterans Administration Cooperative Study on Antihypertensive Agents showed that, in the group with diastolic blood pressures averaging 105 to 114 mm Hg at entry, there was a three-to-one difference in major complications between the treated and control patients during a 3.3-year follow-up.[24] Marked protection was demonstrated against stroke, congestive heart failure, accelerated hypertension, and progressive elevation of blood pressure but not against myocardial infarction.

The patients in the Veterans Administration Study tended to have more severe disease than the average patient with moderate hypertension. First, patients were excluded if their diastolic blood pressure averaged less than 90 mm Hg from the fourth through the sixth day of hospitalization. Thus, all the patients had fixed hypertension. Second, they were all male, and male hypertensives are at higher risk than females. Third, many patients exhibited target organ damage at the time of entry into the study. Nevertheless, it still seems justified to apply these results to the consideration of any patient with an average diastolic blood pressure of 105 mm Hg or more, regardless of sex, target organ damage, or other considerations. Epidemiologic studies indicate that patients with this degree of hypertension are at sufficiently high risk of developing hypertensive complications to justify treatment. This recommendation implies that the patient has a persistent diastolic blood pressure elevation of 105 mm Hg or higher as judged by repeated office visits.

Moderately Severe and Severe Hypertension.—A diastolic blood pressure in the range of 115 to 129 mm Hg is associated with a very high risk of developing major complications over a relatively short period of time. For example, of 70 untreated patients with this degree of hypertension followed up in the Veterans Administration Study, 21 developed complications during an average follow-up period of only 18 months.[31] These complications included the development of hemorrhages, exudates or papilledema in the optic fundi, congestive heart failure, azotemia, dissecting aneurysm, and stroke as well as other complications. The degree of risk, therefore, is unusually high in patients with diastolic blood pressures averaging 115 mm Hg or higher during several visits. With diastolic blood pressures of this degree, the physician probably should not wait for three or more visits. If a patient is seen with a diastolic blood pressure of 115 mm Hg or higher, an appointment should be made to return in several days for a second reading and for completion of laboratory studies such as chest x-ray films, ECG, urinalysis, complete blood cell count, and tests for levels of serum creatinine, fasting blood sugar, serum cholesterol, serum potassium, and uric acid. If the reading on the second visit is 115 mm Hg or higher, treatment should begin immediately and should be intensively pursued.

The effectiveness of treatment in patients with diastolic levels averaging between 115 and 129 mm Hg is indicated by the results of the Veterans Administration Study, where 21 of 70 control patients developed major complications during a brief period of only 18 months of follow-up. By contrast, during the same period of time, only one of 73 treated patients developed a complication. There were four deaths in the control group and none in the treated. Obviously, the higher the level of blood pressure, the more immediately apparent is the benefit of treatment.

If the diastolic blood pressure is 130 mm Hg or higher on the initial examination, the patient probably should be hospitalized as a medical emergency. If the blood pressure is persist-

ently elevated at this level, the patient may be close to entering or may already be in the accelerated or malignant phase of hypertension. Examination of the optic fundi is crucial in making this diagnosis. Papilledema is indicated by the presence of an elevated optic disc or blurred disc margins with hyperemia of the disc. The presence of accelerated hypertension is indicated by papilledema, soft, cotton-wool exudates, striate hemorrhages, or all three.

Patients with diastolic blood pressures of 130 mm Hg or higher generally need to be examined for a possible curable form of hypertension. This can be accomplished during the hospitalization and would include a rapid sequence intravenous pyelogram and a 24-hour urinalysis for catecholamines or their metabolites. Because of the high level of blood pressure, treatment should be instituted shortly after hospitalization without waiting for the various laboratory tests.

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