Implications for Research and Policy in the Treatment of Hypertension

Medical Considerations

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Hypertension, or high blood pressure, is a disease and a risk factor. Cardiovascular risk is directly proportional to the level of blood pressure. Current therapeutic approaches include the classical medical model of detection, evaluation, and drug treatment of high-risk patients who have elevated blood pressure and also a less-well-studied population approach that seeks to manipulate environmental variables in large groups of subjects to reduce blood pressure and subsequent cardiovascular risk. Future research should center on more precise delineation of cardiovascular risk, evaluation of alternative environmental manipulations to reduce blood pressure, enhanced understanding of the pathophysiological mechanisms of hypertension, better matching of antihypertensive drug therapy to pathophysiology, development of new drugs that not only lower blood pressure but also provide additional benefits with minimal side effects, and finally, investigations to further our understanding of the behavioral aspects of the physician–patient encounter, as well as studies on compliance and other issues that influence therapeutic outcome. (Hypertension 1989;13(suppl I):I-164–I-166)

It has long been established by actuarial statistics1 and epidemiological data2 that cardiovascular risk is directly proportional to the level of blood pressure. This relation is graphically displayed in Figure 1, which depicts Framingham cohort data for men and women 55–64 years of age.3 Although the group experience with increasing blood pressure is one of increasing cardiovascular risk, this trend is not necessarily true for everyone within the cohort. There is, in fact, prognostic heterogeneity. High blood pressure alone is neither necessary nor sufficient for the full expression of cardiovascular morbidity and mortality. Other factors, some of which are known, like cigarette smoking and elevated serum cholesterol levels, and other factors that are unknown influence the final expression of whom among hypertensive subjects experience premature cardiovascular morbidity or mortality.

The prognostic heterogeneity among hypertensive subjects notwithstanding, the question remains: what can be done about this problem, which is not only a serious clinical disease for individuals, but, because of its high prevalence, is also a major public health problem? On a conceptual level, there are at least two broad solutions.4 The first involves the classical medical model, which focuses on the high-pressure–high-mortality group of patients. The objective of this model is to identify high-risk individuals, diagnose them correctly, and intervene in a manner that is efficacious and safe, that is, in a way that lowers blood pressure and subsequent cardiovascular risk with minimal or no side effects. Antihypertensive drug therapy is generally prescribed for these patients because there is considerable evidence from several clinical trials documenting the efficacy of this approach.5–13 An alternative to the classical medical model is the population approach, which seeks to manipulate the environment to shift the entire blood pressure distribution in Figure 1 to the left, thus reducing the absolute numbers of people exposed to various levels of cardiovascular risk. Nonpharmacological strategies for controlling blood pressure are useful in both models, as long as it can be demonstrated that implementation of such interventions is efficacious and safe.

As indicated in the preceding articles in this supplement, many well-designed and executed studies have been devoted to the epidemiological characterization of hypertension and to the evaluation of nonpharmacological and pharmacological thera-
The control of blood pressure has been the ultimate aim of therapeutic strategies. There is no doubt that blood pressure control leads to a reduction in cardiovascular morbidity and mortality. However, it is time for us to become more sophisticated in our approach to this problem by designing strategies that are more precise and efficient. Applying them only to those individuals who can truly benefit from them. Current research needs are as follows: 1) more precise delineation of risk. Because not everyone with hypertension experiences the same level of cardiovascular risk, it behooves us to reexamine available epidemiological data as well as new data (e.g., cation transport markers like sodium-proton antiport) to delineate more precisely the subsets of patients who are at increased risk and therefore who are most likely to benefit from intervention. Moreover, because mortality in hypertensive patients is usually mediated through stroke, heart disease, or renal failure, it is in our best interest to promote research that investigates the variables other than blood pressure that contribute to these disease processes as well as interactions among risk factors. 2) environmental manipulations to reduce blood pressure. As shown in Figure 1, the blood pressure distribution with its attendant cardiovascular risk does not appear biologically mandated. Examination of similar data in nonacculturated societies shows a blood pressure distribution that is substantially shifted to the left with correspondingly low cardiovascular morbidity. There is at least the theoretical possibility that certain environmental variables, like dietary sodium intake, dietary calcium intake, and level of physical activity, can be manipulated to reduce the blood pressure in large groups of people and thereby accomplish an overall reduction in cardiovascular morbidity and mortality. More research on this population-based environmental change strategy is needed. 3) pathophysiological mechanisms. In addition to prognostic heterogeneity, there seems to be, in accordance with the predictions of Irvine Page, a pathophysiological heterogeneity among hypertensive patients. People who have hypertension do not appear to have it for the same reasons. Therefore, in addition to defining subsets of patients by prognosis, it behooves us to define patient subsets by the pathophysiology characterizing their hypertension. Such an approach is likely to produce more systematic and precise interventions, with theoretically less opportunity for inappropriate treatment and unnecessary side effects. 4) better matching of drugs to pathophysiology. It is now possible to develop highly specific drugs that act not only as diagnostic probes but also as therapeutic agents because of the availability of sophisticated techniques that incorporate molecular biologic and cellular biologic technologies. An example is the development of the renin inhibitors. This approach to drug development deserves continued support. 5) development of drugs that not only lower blood pressure but also provide additional benefits with minimal side effects. We can redouble our investment by designing drugs that not only lower blood pressure but that also provide additional benefits relative to diseases to which the hypertensive patient may be prone. An example is the treatment of high blood pressure in a patient who already has signs of left ventricular hypertrophy with an agent that not only lowers blood pressure but also leads to the

**Figure 1.** Bar graph showing relation of mortality (annual death rate per thousand) to diastolic blood pressure (mm Hg) in men and women aged 55--64 years in the Framingham Heart Study.
regression of left ventricular hypertrophy. Although long-term studies on this particular strategy are unavailable, the principle is theoretically sound and is one that ought to be pursued more rigorously in the research setting. 6) holistic approach to prevention of vascular disease. In the final analysis, regardless of the level of sophistication of our pathophysiological insights into the disease processes and the excellence of our pharmacological understanding, the ultimate success of our therapeutic interventions depends on good physician–patient interaction. Thus, we should never lose sight of the importance of promoting the quality of this interaction as well as continuing to support research that furthers our understanding of the behavioral aspects of the physician–patient encounter, compliance, and other issues that impact on therapeutic outcome.

Basic, clinical, epidemiological, behavioral, and public health research investigations have contributed enormously to our understanding of hypertension as a disease and as a risk factor. With continued research, we can anticipate not only more fundamental insights into hypertension but also refinements in our understanding of the progress made to date.

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