## American Heart Journal

Founded in 1925

JULY 1988 Volume 116, Number 1, Part 2

## MANAGING THE CARDIOVASCULAR RISKS IN HYPERTENSION

## Introduction

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The title of this conference, "Hypertension: A View Beyond the Numbers," is not just an intriguing phrase, it is a meaningful concept. Those of us in the field of hypertension today know by now that antihypertensive treatment prevents complications and decreases morbidity. The classic study pointing to this conclusion was the Veterans Administration (VA) study, which clearly showed that morbidity was much greater among hypertensive patients who were not treated than among those who were.

Two types of morbidity are associated with high blood pressure. One is the pressure-related set of complications, that is, those related to the level of the blood pressure at the time the complication occurs. These pressure-related complications are cerebral hemorrhage and congestive heart failure. Cerebral hemorrhage results when the pressure is so high in the blood vessels that the vessels burst; congestive heart failure develops when peripheral resistance is so high that it offers a major impediment to the function of the heart.

The other set of complications arising from hypertension is related to the premature development of atherosclerosis. This is the area in which recent epidemiologic studies have uncovered some problems.

Certainly, hypertension contributes to the premature development of atherosclerosis. However, treatment with antihypertensive medication has shown less influence on this complication of hypertension than on cerebral hemorrhage and congestive heart failure, the pressure-related events. This was one of the findings of the VA study. During a 4-year period, seven patients in the untreated group died of stroke and 14 had a nonfatal stroke; only one patient in the treated group died of stroke and only four had a

stroke without fatality. The use of antihypertensive treatment produced a major difference in this particular cause of morbidity. On the other hand, the study showed no improvement with antihypertensive treatment in the morbidity from coronary heart disease. These rates remained unchanged. In fact, when one reviews the results of all the major studies, it appears that if there is any effect of antihypertensive treatment on reducing the morbidity and mortality from coronary heart disease, it is very small.

This realization has been a source of disappointment to all of us, and it raises questions of more than a theoretical nature. In the United States, the morbidity and mortality curves have followed the trend demonstrated in the VA study, that is, a dramatic decrease in the incidence of stroke but a much smaller decline in the incidence of cardiovascular disease, particularly coronary heart disease. However, in comparison with the trends in other countries, the decrease in coronary morbidity in the United States has been greatest. Some countries have always had a low incidence and have retained this profile, whereas in others the rates are increasing. Why? Surely it is not because the people are intrinsically different or because cultural differences are that strong.

Two explanations have been proposed for the observation that lowering blood pressure can influence the stroke rate but not coronary morbidity. One relates to the fact that in all of the present studies, diuretics were the first step in therapy. Diuretics may, by virtue of their effects on lipids, potassium, and glucose, produce some deleterious effects in areas relevant to coronary disease.

However, this is probably not the whole explanation. More likely the explanation is that hypertension is only one of the risk factors in coronary heart disease. Several lines of evidence indicate the complexity of the risk factor situation. For example, a combination of high cholesterol levels with high

From the Division of Hypertension, University of Michigan. Reprint requests: Stevo Julius, MD, Division of Hypertension, University of Michigan, 3918 Taubman Center, Ann Arbor, MI 48109-0356. blood pressure levels increases the incidence of morbidity. For each increment in cholesterol and blood pressure levels, there is a corresponding increase in coronary morbidity. In the highest blood pressure and cholesterol groups, mortality is also very high. However, many of these people have additional risk factors, such as left ventricular hypertrophy, glucose intolerance, and cigarette smoking. The curves are much flatter, and therefore the relationship is much weaker, in nonsmokers and persons without the additional risk factors.

At one time there was some hope, which was partially justified, that  $\beta$ -blockers might improve the coronary risk factor picture. The study done in Great Britain with propranolol, a noncardioselective  $\beta$ -blocker, showed a decrease in the incidence of coronary events in nonsmokers with this treatment, although not in smokers. It is reasonable to expect that cardioselective  $\beta$ -blockers may offer better cardioprotection; the results of the MAPHY trial, which will be presented in this symposium, may support this theory.

Such studies underscore the need for a host of risk factors that have now been linked with cardiovascular disease to be considered in achieving truly effective treatment for the patient with elevated blood pressure. The contributors to coronary morbidity are more complex than previously thought. Behavioral characteristics, concomitant cardiovascular disease, demographic factors, and age are only some of the factors that need to be considered. The search should continue for specific antihypertensive drugs that may help prevent primary myocardial infarction as  $\beta$ -blockers have been shown to do for secondary, recurrent infarction. Thus, in addition to managing blood pressure levels, the practicing physician will also become involved in assessing risk factors and differentiating between various drugs with increasingly selective indications. The future treatment of hypertension will indeed become a view beyond the numbers.

## Cardiovascular risks: New insights from Framingham

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Although cardiovascular disease remains the leading cause of death in the United States, its incidence has decreased steadily during the past 20 years. This trend is largely attributable to improved detection and management of cardiovascular risk factors. The pioneering work of the Framingham Heart Study, which has followed subjects since the late 1940s, has helped shed light on the risks conferred by factors such as advancing age, hypertension, smoking, elevated serum cholesterol, diabetes, left ventricular hypertrophy, and obesity. As a result of this ongoing investigation, clinicians have gained a better understanding of the ways in which cardiovascular risks can be modified so that mortality rates will hopefully continue to decline.

(Am Heart J 1988;116:266.)

Cardiovascular disease is the leading cause of death in industralized nations. In the United States, the

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most common form of cardiovascular disease is coronary artery disease, which accounts for 550,000 deaths and 1,250,000 cardiac events each year.<sup>1</sup>

During the past 20 years, however, the incidence of mortality from cardiovascular disease has decreased by 33% in the United States, perhaps saving as many as 250,000 lives annually. At the same time, the incidence of death from stroke has