Editorial

Hypertension: Our Major Challenges

As the tenure of our 8-year editorship of Hypertension nears its end, a number of scientific issues concerning this very complex multifactorial disease burn in my mind. At the outset of our editorial term, we indicated that a sea change was taking place in our scientific information and clinical thinking about the hypertensive diseases. A virtual upheaval was looming in our fundamental thinking about the genetic, molecular biological, biochemical, physiological, and pharmacological aspects dealing with arterial pressure control and the involvement of the various target organs and systems. Indeed, over these 8 years, massive changes have appeared in the explosion of knowledge concerning our field of investigation. Molecular-biological knowledge has burgeoned, and heretofore unenvisioned genetic information is published each month. Clinically oriented information dealing with the pathophysiology of hypertension and its treatment provides hope that not only can cardiac and renal failure be treated effectively but, when treated early enough, may even be prevented. Each of the fundamental areas of scientific endeavor will most assuredly have a tremendous impact on how clinicians will understand the disease mechanisms of their patients with hypertension and how they will employ new modes of treatment.

In reflecting about the progress already made in our understanding and treatment of hypertensive diseases, the quantity of new information amassed over the past several decades has been nothing less than monumental and mind-boggling. Much of the gains made in treatment have already been translated into the remarkable reduction of morbidity and mortality using our initially employed antihypertensive agents. Thus, we have witnessed dramatic downturns in the mortality from stroke, coronary heart disease, hypertensive emergencies, and cardiac failure related to the tremendous systolic function imposed on the functionally and structurally adapting left ventricle. These gains reflect the ability of the earlier antihypertensive agents to control arterial pressure and pressure-related events. However, the very real challenges that now confront the basic and clinical scientist as well as the clinician are other complications of hypertensive diseases that have not yet been affected by these earlier antihypertensive agents and demand constant revision of thought. The following highlight some necessary thinking concerning our challenges.

Challenge 1: Fulfillment of the Responsibility for Treatment

Clearly, none of newfound knowledge concerning the mechanisms and treatment of the disease can be appreciated if the fundamental information is not translated into everyday clinical practice. The most recent national data in the United States are no different from what is experienced elsewhere around the world: organized medicine is doing a very poor job in controlling the hypertensive diseases in our communities. Thus, in the early 1970s, only 12% of all hypertensive patients were treated and controlled (the old concept of “one-half of one-half of one-half”). Although this experience had improved by the 1980s to slightly >30%, the data published in the Sixth Joint National Committee Report, in 1997, demonstrated a reduction and reversal of that number. Consequently, the 31% of hypertensives who are effectively treated are not even remotely close to the ideal. Clearly, all of the new information concerning disease mechanisms and treatment is to no avail if it is not translated into daily practice. Thus, hypertension control not only must be approached more effectively in the teaching of preclinical sciences but also must be focused on more effectively in medical school clinical teaching and, most certainly, in our graduate medical education training programs.

Challenge 2: Cardiac Failure

As it was in the early years of the Framingham Heart Study, before any of the effects of antihypertensive therapy were achieved, hypertension still remains the most common cause of cardiac failure. Indeed, at the present time, the most common cause of hospitalization of Medicare-eligible patients in the United States is cardiac failure. Yet the main causes and a clearer understanding of the involved disease mechanisms and their treatment are incompletely understood. Most multicenter, controlled clinical trials studies presently concerned with cardiac failure restrict patient inflow to nonhypertensive individuals having had a recent myocardial infarction, and they make a deliberate effort to exclude patients who have an elevated arterial pressure. Yet we know from other reports that deal with the newer and more effective classes of antihypertensive therapy that we can definitely reduce hospital admission of patients with cardiac failure. What we are now beginning to appreciate is that the expression of ventricular failure no longer is primarily that of systolic ventricular dysfunction related to pressure overload. The problem now is cardiac failure in the presence of preserved systolic function (ie, diastolic dysfunction) that is related primarily to ischemia of the ventricular wall, fibrosis, and aging. Moreover, the myocardial ischemia is not exclusively a problem of occlusive atherosclerotic disease of the epicardial coronary arteries. It is also produced by hypertensive vascular disease of the coronary arterioles and by endothelial dysfunction associated with hypertension, atherosclerosis, cardiac failure, obesity, hyperlipidemia, smoking, aging, and many other co-morbid problems. Therefore, what is clearly necessary is a comprehensive inquiry into the fundamental mechanisms involved and the inclusion of patients with hypertension in large clinical trials.

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Challenge 3: End-Stage Renal Disease
Here, again, we also find that our current epidemiological data point to an increasing prevalence of this complication of hypertension in our society and most others. Effective presentation of the current demographic and epidemiological data point to 3 major factors underlying end-stage renal disease (ESRD): hypertension, diabetes mellitus, and those incompletely understood pathophysiological mechanisms that affect patients of the black race. However, even when we consider that hypertension is a major cardiovascular problem in patients with diabetes as well as in the black patient, it is clear that hypertension is truly the major underlying factor of ESRD. Moreover, when we focus our attention on this problem, most of the large clinical trials that have been conducted or that are ongoing today are primarily concerned with the problem of diabetes in patients with ESRD, with the hope that the scientist and clinician will extrapolate the experiences and findings derived from these costly observational efforts to the overall problem of hypertension, a disease that is far more prevalent. Hypertension and diabetes mellitus are not synonymous pathophysiologically, and in exploring the information concerning the fundamental mechanisms involved in both disease (the role of insulin, growth factors, and other fundamental mechanisms), these 2 situations may not be equivalent or interchangeable issues.

Challenge 4: Obesity
All of us, scientist, clinician, and layman, are well aware that the problem of obesity is of growing major worldwide concern. Yet, our knowledge about the fundamental and other clinical information has not explained why the pathophysiological mechanisms of obesity and hypertension are so inextricably intertwined with each other. Once again, our knowledge about this major cardiovascular risk factor, particularly as it relates to hypertension, is very rudimentary and unsophisticated. Moreover, very little effort and information is available concerning its effective treatment and control of this risk factor other than to appreciate that recidivism associated with diet therapy is high and that the most of the potential pharmacological interventions are usually not indicated because of side effects, including further elevation of the patient’s blood pressure. Development of effective techniques in behavioral modification are only one of the necessities; and pharmacological therapeutic agents without adverse effects on arterial pressure are long overdue.

Challenge 5: Atherosclerosis
We are all well aware that both hypertension and atherosclerosis are closely involved with one another, each disease feeding on and exacerbating the other. Fundamental and clinical studies have focused on the common targets of the disease, the heart, blood vessels, and the endothelium, and currently, we find exciting areas for newly focused investigation. This reflects very recent experiences with the relatively recent drug class of “statins,” which not only points to their initial raison d’être for therapeutics to lower the LDL cholesterol but to their novel actions on generating endothelial superoxides and free radicals. Thus, we now have some early insights that these agents may also involve other metabolic actions of these agents in oxidative metabolism and in control of vascular smooth muscle tone. There is no doubt that more intensive work in this area will provide much exciting new information that should be translated very rapidly into clinical practice. This will also require much effort and attention of the laboratory worker, clinician, and the pharmaceutical industry.

Finally, in an earlier editorial, we discussed the need and our challenge to develop a new cadre of clinical investigators; and I shall not discuss this point in any greater detail. The National Institutes of Health has appreciated this problem by initiating new granting mechanisms for potential clinical scientists. But this innovation will be of no avail if we cannot recruit young new clinical investigators earlier in their education (in college as well as in medical school). We must provide for their recruitment, stimulation, and education by a corps of exciting clinical mentors. Many of our potential mentors on active medical faculties are so preoccupied with other teaching, personal investigative work, and patient care in order to generate their personal salary and fiscal support that we are lacking sufficient necessary faculty to assume the much-needed mentoring responsibilities. In that earlier editorial, I suggested that this gap in our needs might be filled by retired or soon-to-be-retired clinical scientists. Hopefully, this major challenge will be resolved; if it can with the necessary dispatch that it deserves, then the other challenges that I have discussed above will also be resolved. There is little doubt that this will come to pass!

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