The Ochsner Journal 14:532–537, 2014

Editorial

Coronary Heart Disease Risk Factors: Public Impact of Initial and Later-Announced Risks

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INTRODUCTION

The concept of risk factors is straightforward; however, the term has been frequently misinterpreted by the general public and media. The purpose of this communication is to help clarify some of the controversy and concerns that arise during discussions of risk factors with patients.

The definition of the term risk factors is important. We define risk factors as specific pathophysiological mechanisms or clinical entities underlying diseases that promote increased morbidity and mortality. With respect to coronary heart disease (CHD), risk factors do not relate exclusively to occlusive coronary artery disease produced by atherosclerosis; CHD risk factors also concern hypertensive cardiovascular disease (HCVD). Moreover, even though CHD is frequently considered synonymous with atherosclerotic heart disease, its diagnosis and management are more complex. Pathophysiologically, HCVD is promoted by coronary arteriolar constriction, oxidative stress of these vessels, increased ventricular oxygen demand responsible for increased coronary blood flow and flow reserve, ventricular fibrosis, myocardial apoptosis, and ventricular remodeling.[1-3]

The term risk factors was first introduced by the team of investigators of the Framingham Heart Study (sidebar) who identified specific ''factors of risk'' that predispose otherwise healthy individuals to the increased risk of premature morbidity and mortality from CHD.[4] In that 1961 publication, the first 3 risk factors identified to promote CHD were hypertension, hypercholesterolemia, and left ventricular hypertrophy (LVH). Throughout the following half-century, the Framingham investigators and other workers in the field identified a number of additional major risk factors that augment the risk demonstrated by the 3 initial CHD risk factors (Table).

This report aims to provide physicians, house staff members, and medical students with information intended to enhance communication in their doctor/patient relationships. It is necessary to comprehend why public confusion and controversy exist regarding the diagnostic and therapeutic management of the first 3 risk factors and the 3 more recently identified CHD risk factors (ie, smoking, obesity, and increased dietary sodium intake).

RECENT CONTROVERSIES

After acceptance of the first 3 risk factors more than 50 years ago, immediate excitement and promise were felt by healthcare providers, patients, the general public, and the increasingly sophisticated lay media. Not only was reduction of risks from hypertension, hypercholesterolemia, and LVH promising and convincing, but demonstration of their reversal was possible within a relatively short time. These first 3 risk factors were rapidly inculcated into medical practice because they were easy to identify by prescribing specific drugs. They were also easier to demonstrate than the very different and unique lifestyle factors that also promote CHD risk.

These lifestyle risk factors are more intensely personal and require the patient's total understanding and acceptance to achieve adherence and commitment and to prevent adverse consequences. A longer time is necessary to establish risk reversal in these patients. Periods of doubt and frustration are frequently complicated by patient recidivism. Consequently, enthusiasm over the lifestyle risk factors was not as evident, and management and prevention were far more complex than for the first 3 factors. Furthermore, the enthusiasm by the media was much less tangible. These difficulties were abetted by inadequate public education.

Examples of Controversy

Misinterpretation. Because of the great interest in health-related issues, much misinterpretation among healthcare professionals, patients, and the media resulted from anticipated gains concerning the severe lifestyle risks related to smoking, obesity, and increased dietary sodium intake (alone or in combi-

Table. Major Risk Factors Currently Known to Apply to Coronary Heart Disease

Risk Factor
Hypercholesterolemia
Hypertension
Left ventricular hypertrophy
Diabetes mellitus
Aging
Black race
Male sex
Smoking
Obesity
Excess dietary sodium (salt) intake

nation). This misinterpretation is understandable when one considers newer concepts concerning CHD and the significance of the more easily understood risks from hypertension, hypercholesterolemia, and LVH.

Confusion. The confusion about the coexistence of hypertension, hypercholesterolemia, and myocardial infarction relates to the more recent risk factor control program experienced by primary care practitioners, cardiologists, and epidemiologists with respect to atherosclerotic CHD. Even in the initial Framingham Heart Study report, 2 of the first 3 risk factors attributed to HCVD (ie, hypertension and LVH) were confused by some healthcare professionals and their expanding knowledge.[1] Thus, while elevated arterial pressure may be a factor that precipitates cardiac endpoints, myocardial infarction is not the most common cardiac endpoint that occurred in the multicenter clinical trials of antihypertensive therapy. Heart failure (even without atherosclerotic coronary artery disease) is the most common cardiac endpoint and cause of hospitalization among Medicare-aged patients (whether or not hypertension exists). Unfortunately, this issue has been discussed in less detail in the literature than this fact demands. It is true that both diseases (ie, hypertension and atherosclerotic heart disease) frequently coexist, although each may occur independently. In this regard, elevated serum cholesterol levels frequently occur in hypertensive patients, although occlusive coronary artery disease may not always be demonstrated. This confusion about the coexistence of hypertension, hypercholesterolemia, and myocardial infarction frequently has been wrongly attributed to certain antihypertensive drugs (eg, diuretics). Publication of this possible coexistent example has generated much concern and controversy among the public, as well as some physicians, in associating CHD reversal when thiazide treatment may be related to hypercholesterolemia. Thus, slightly elevated serum cholesterol levels may erroneously be attributed to a complicating myocardial infarction.

Changing Risk Factor Definitions

Changed definitions of disease are important examples of confusion between the increased prevalence (numbers of event occurrences in a given population at risk) and the actual risks of a disease. This issue relates to the prevalence or frequency of a risk factor without actually relating its impact on overall morbidity and mortality. This is best exemplified by 4 important CHD risk factors (ie, hypertension, hypercholesterolemia, diabetes mellitus, and obesity) creating much ongoing concern. The prevalence of these factors has increased significantly without an increase in their intrinsic risk. In other words, whereas the manifestations and severity of CHD, per se, have not really changed, their prevalence in a given population has substantially increased. The change in definition has only permitted identification of more potential individuals who would benefit from control of that risk factor. While there is little wrong with this concept, the changed definitions may be interpreted erroneously to indicate an increase in actual potential morbidity and mortality. Thus, this overinterpretation relates primarily to the numbers in that population identified as at risk because of the redefined levels. This concept relates to each of the diseases discussed below.

Hypertension. Not long ago, clinicians termed the most common type of hypertension *essential hypertension*. Originally, clinicians used the word *essential* to indicate that the elevated blood pressure measured in their patients was an essential condition necessary to promote enhanced tissue perfusion of blood. With greater understanding and emphasis on hypertensive disease and the introduction of effective antihypertensive therapy through large multicenter drug trials (initially by the US Veterans Administration and many confirmatory studies), pharmacologic reduction of pressure actually reduced the risk of morbidity and mortality in patients whose diastolic pressure was $>$90 mmHg and whose essential hypertension required effective treatment.[5] Risk of hypertension was reduced following a number of confirmatory trials involving large numbers of patients having still higher diastolic pressures. Later, similar significant improvements were shown in people at risk whose systolic pressures were $>$160 mmHg and, still later, $>$140 mmHg. Consequently, the increased number of individuals at risk with elevated blood pressure demonstrated indications for antihypertensive treatment, and the number of at-risk patients with hypertension substantially increased from 23 million

to >65 million in the United States and as high as 2 billion people worldwide. It is necessary to understand that this changed definition only increased the number of patients who were at risk and accounted, at least in part, for the media-generated generality of the *hypertension epidemic*.

Redefinitions of Hypercholesterolemia, Diabetes Mellitus, and Obesity. Similar normal limits of serum cholesterol and glucose concentrations emerged, thereby advancing knowledge of the inherent risk in a greater number (or prevalence) of patients in that population earlier in their disease. This increased prevalence also occurred at earlier ages and provided evidence of disease with improved diagnostic techniques, resulting in a greater number of patients with elevated serum cholesterol, low-density lipoprotein, or serum glucose concentrations.

One event followed the recent release of guidelines by a joint committee of authoritative members of the American Heart Association and the American College of Cardiology for prescribing statins to patients with increased serum levels of total cholesterol and low-density lipoprotein. This controversy was stimulated by publicly shared opinions to the contrary generated by knowledgeable individuals who did not benefit from the joint committee's discussion and evaluation. The fact is that the risks of elevated serum cholesterol and low-density lipoprotein levels remained valid, although the potential number of at-risk individuals increased. Thus, disease prevalence relating to serum cholesterol, glucose levels, and body weight (or body surface area) was defined by their updated indices. A specific example is the recommended serum glucose levels that decreased progressively from >160 mg/dL in the 1950s to >120 mg/dL at present, accounting for the *diabetes epidemic*. This concern has also been attributed to a remarkable increase in the number of individuals with obesity (also related to revised definitions in the general population). These changed definitions, popularized by media-engendered controversies, remained until that discussion finally diminished. No doubt, these concerns generated by public and political discussions have prompted countless telephone calls and emails to healthcare providers from many concerned patients.

The important message for the public was that the newly defined potential patients were at risk by virtue of these newly identified risk definitions. Potential patients were identified so the related risks could be brought under control. This message is related to the need to periodically obtain blood pressure, body weight, and serum glucose and cholesterol measurements. Consequently, if any abnormality is confirmed, the risk factor should be controlled by the patient's managing healthcare practitioner. This sound approach may only require appropriate lifestyle management or may necessitate pharmacologic therapy. Indeed, this wise intervention has been known for many years and should also be of value to members of the patient's family. Although public discourse and concern are, of course, exceedingly important, unnecessary and unsupported media-generated concerns should be discouraged.

RESPONSIBLE PUBLIC EDUCATION

Cigarette Smoking

After the publication of the relationship between tobacco smoking and carcinoma of the lung in 1937 by Alton Ochsner, the founder of Ochsner Clinic,[6] the morbidity and lethality associated with tobacco were shockingly ignored for years. The importance of this major risk was enhanced further by the dramatic establishment of tobacco's significant association with CHD, stroke, peripheral vascular disease, and other pulmonary diseases (including obstructive lung disease and emphysema). Our increasing knowledge relating to the risk of lung cancer and emphysema was dwarfed by the increase in knowledge relating smoking to the risks of CHD and other cardiovascular diseases. Fortunately, public education by organized medicine and the media has not been entirely ignored. The prevalence of cigarette smoking has been remarkably reduced in the adult male population; however, tobacco indulgence has been dramatically increasing among children, teenagers, and women. This major risk continues to increase in numbers, disabilities, and deaths despite the efforts of hospitals and governmental buildings (including clinics, physicians' offices, restaurants, stores, and other public areas) to prohibit smoking. Local, state, and federal taxation techniques have been relatively successful in reducing tobacco purchases. The bottom line to this dismal abuse is the progressive increase in the overall burden of healthcare for all who continue to smoke and their families, friends, and coworkers who suffer the added risk of side-stream smoke.[7]

Obesity

As mentioned above, obesity is another major risk factor for CHD and other diseases. Reversing the risk of obesity requires that the patient follow the recommendations of the healthcare provider and the guidance of nutritional specialists. As with each lifestyle risk factor, the patient's compliance, of course, is critical. The patient must follow the prescribed diet and weight reduction program. Often, with the time constraints of a busy medical practice, the healthcare provider does not have adequate time

to become familiar enough with the patient's well-being, complaints, and compliance with the prescribed dietary intake. A diet is only successful when the time, techniques, and experience of the dietician are workable and understood by all concerned. Even then, recidivism is all too frequent. We must also recognize that our knowledge about the pathophysiology of obesity, related habits, behaviors, and food addiction is sorely incomplete and unsatisfactory. Thus, the management of inculcated lifestyles and corrective behaviors continues to be unsuccessful.

In addition, the patient's awareness and understanding of a corrective diet may be incomplete. For example, the healthcare provider may suggest that the patient become aware of the nutritional facts about foods. Despite many efforts by the Food and Drug Administration to require meaningful food product labeling, many people are unaware of currently available information. The hypertensive patient may be thwarted by the labeling of frozen, canned, or other processed foods. Taste satisfaction may be reduced when the food product's preparation is changed. For example, a particular food may have once included a certain fat content, but when the preparation was changed to reduce fat content (to reduce calories), its new formulation and preparation may have resulted in the addition of more salt to satisfy taste. Thus, consumption of that prepared food by the patient with hypertension or cardiac or renal disease can aggravate the preexisting condition.

Excess Dietary Sodium Intake

Our present knowledge about the systemic effects of sodium (or salt) excess is grossly incomplete. This point is best demonstrated by recent publications in the lay media and even in medical journals. Most of the information in medical journals deals primarily with the relationship of sodium intake and blood pressure. Recently, there has been some emphasis on the fact that increased dietary sodium intake may be related to renal disease or cardiac failure. We must appreciate that dietary sodium excess is responsible for unrecognized cardiac or renal structural or functional damage—both in normal individuals and in patients with hypertension and cardiovascular and renal diseases. This relationship has been clearly demonstrated in the laboratory, and we must take into account that a lifelong exposure to a sodium surfeit diet eventually results in impaired structure, function, and disability of the heart, the large arteries and arterioles, and the kidneys.[8] As we already know, these structural and functional endpoints of cardiovascular and renal disease outcomes are the most common causes of hospitalization in normotensive or hypertensive patients, particularly in those of Medicare age. Most notably, 2 reports by the American Heart Association have recommended that the daily dietary sodium intake be reduced to 1,500 mg,[9] and this recommendation was followed by a review presenting additional information and commentary on the issue. These phenomena have been attributed to the aging process.[10] But does this line of thinking also apply to a long-standing history of tobacco, alcohol, and caloric excess?

EFFECTIVE PUBLIC CHD EDUCATION

An outstanding example of the generation of excitement about the risks and treatment of CHD was the development and promotion of the Diagnosis, Evaluation, and Treatment of Hypertension reports. These reports were released—usually quadrennially—by the High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute (NHLBI) from the 1970s (Joint National Committee [JNC] 1) through 2007 (JNC 7).[11] Each of these reports has been extremely valuable as have been the frequent interim reports dealing with practical information on subjects such as nonpharmacologic treatment of hypertension and hypertension in the elderly, in minority populations, and in employees in the workplace environment. Each report was released to professional and public resources by the NHLBI and was supplemented for public education programs in the lay literature, radio, and television. Since then, public education programs have been far less effective. These programs have resulted in increased numbers of identified patients with elevated blood pressure and hypertension but in a decreased number of patients who were treated and fewer still who remained under adequate blood pressure control and treatment. In recent years, educational efforts have unfortunately diminished and are now considered old hat by the media.

However, in 2014 the current JNC 8 report appeared. JNC 8 was not released as an official report by the NHLBI and was published 10 years after the preceding JNC 7.[12] The publication also did not follow the protocol of the prior JNC reports, reflecting the diminished support by the NHLBI. Each of the former JNC reports was written by a drafting committee comprised of more than 50 JNC professional society representatives and upwards of 15 federal agencies (somewhat fewer in the earlier JNC years). All organizations that participated officially were identified in the earlier documents, indicating their organization's formal approval of these reports. In addition, members from the insurance and pharmaceutical industries were invited and participated (but without official approval by the attending representatives of the pharmaceutical industry to obviate concern over any conflict of interest). Each of these

organizations provided their formal endorsement of the report and voluntarily agreed to promulgate its vital message to their membership and the general public.

In contrast, the JNC 8 report committee included participants selected by the NHLBI without official nomination or approval by their respective organizations. The JNC 8 authors were comprised of members whose organizations apparently did not provide official endorsement or promulgation of the important message. The report was published in a peer-reviewed journal with accompanying editorial commentaries and widely available newspaper reviews reflecting comments by invited reviewers. This report was soon followed by a minority viewpoint.[13]

An outstanding concern related to JNC 8 (other than repetitive concerns voiced broadly) was its recommendation to initiate antihypertensive therapy in elderly hypertensive patients with a systolic pressure >150 mmHg (10 mmHg higher than that recommended in JNC 7). We add herein yet another major concern about JNC 8. Simply stated, the report found that there was no need to elaborate further concerning recommendations for lifestyle interventions that had been initially published in JNC 3 and updated regularly through JNC 7. This neglect diminishes the importance of valuable lifestyle improvement measures for treatment of hypertension and the value of nonpharmacologic therapeutic approaches in the large population of patients >60 years of age. These patients, clearly, are subject to increased risk from smoking, alcohol consumption, obesity, and excess dietary sodium intake (risk factors that are common in the elderly). Further, with respect to dietary sodium restriction, the report did not comment on the important recommendations of the American Heart Association to reduce the daily dietary sodium intake from 2,500 mg to 1,500 mg and the National Institute of Medicine recommendation to reduce daily sodium intake from 2,500 mg to 2,000 mg daily.[9] These important points from highly relevant organizations were ignored in the JNC 8 report.

The JNC Concept for Physician and Public Education

The concept of the original JNC was that of Theodore E. Cooper, MD, a former director of the National Heart Institute and member of the Department of Health, Education, and Welfare secretariat. The JNC reports were responsible for the official development and dissemination of information for the public by the National Institutes of Health (NIH). Further, these JNC reports successfully conveyed hypertension information for more than 40 years and later provided cholesterol education from the NHLBI's own guidelines.

William B. Kannel, MD

Dr William B. Kannel's home for many years was in Framingham, MA, a small city on the outskirts of Boston. In 1949, he and Dr Thomas A. Dawber were among the architects and the first 2 directors of the now-famous Framingham Heart Study. Dr Dawber retired as director in 1987; and Bill Kannel remained as the director until 2011 when he retired. In truth, he remained vitally active on behalf of the study until his death in 2011, a commitment of more than 60 years. Known internationally as the premier classic epidemiological cardiovascular research study, the Framington Heart study continues to be among the longest recipients of grant support from the National Institutes of Health.

It has been my personal privilege to know Bill as a friend, colleague, and *fan* since we first met in the late 1950s. When I was asked to assemble the initial selection team for the Alton Ochsner Award Relating Smoking and Disease, he was among my first choices to join that committee. Among his contributions to Ochsner during the 28 years of his service were his active participation in the selection committee and his 2008 lecture to our graduating house staff published in *The Ochsner Journal*.

Hence, this article is dedicated to Bill Kannel's memory. This warm and soft-spoken gentleman and well-versed clinician was one of the outstanding contributors to modern preventive medicine. Without doubt, he certainly will be included among the major epidemiologists, scientists, and clinicians in American medical history.

Recent Public Apathy

The preceding discussion has garnered less public understanding of the measures necessary for effective CHD control because of the media's misinformation. We strongly believe this discussion reflects a most important health issue that has received inadequate attention in recent years by the lay public. Our concern relates to the implementation, recommendations, and appropriate media education of the value of understanding, promoting,

and practicing effective control of CHD risk. This concern was initiated by the NIH but has now diminished markedly.

Public education efforts, beginning with effective control of the 3 major lifestyle risks, are most necessary. It is of great interest that there is relatively little new neurological research by the NIH aimed at understanding behavioral motivation and addiction relating to the clear-cut risks for CHD. The 3 major risk factors meriting public attention are tobacco smoking, obesity, and increased dietary consumption of excessive sodium; these risk factors are addressed far less often than risk factors unrelated to lifestyle. Decreases in the federal budget are not a sufficient excuse for the lack of attention these risk factors receive because 2 former national education programs dealing with hypertension and cholesterol were conducted on the proverbial shoestring budget with much voluntary extragovernmental support.

CONCLUSION

An understanding of the disease mechanisms and factors that contribute to the development and outcomes of CHD enhances our knowledge of the basic underlying factors responsible for cardiovascular and renal diseases. These events are still quantifiable in terms of the highest morbidity and mortality of disease in the United States. The identifiable mechanisms that can be attributed to these events are termed risk factors (ie, the "factors of risk" identified in healthy normal volunteers participating in the Framingham Heart Study concerning CHD). These risk factors have been established by the Framingham Heart Study and other similar large, long-term studies involving normal volunteer subjects. The knowledge derived from these valuable studies has clearly demonstrated mechanisms for effective control and reduction of the most common causes of morbidity and mortality of patients with CHD. Moreover, the cost of that study (supported by the NIH during the past 6 decades) is dwarfed by the dramatic increase in the value and benefits to society from the knowledge derived about CHD and other diseases. Unfortunately, the greatest underlying causes of CHD are major risk factors that require drastic changes in public behaviors, such as cigarette smoking, obesity, and excess dietary sodium intake. Effective control of these risks requires a renewed and revitalized joint program involving the active engagement of healthcare professionals and volunteer organizations, the pharmaceutical and insurance industries, media organizations, and the leadership of the NIH. These entities collaborated with great effect in public education relating to the CHD risks of hypertension, cholesterol, and LVH. The more recently identified lifestyle risk factors (cigarette smoking, obesity, and excess dietary sodium intake) have been less effectively controlled and demand renewed public efforts.

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