Report of the NHLBI Working Group on Research in Coronary Heart Disease in Blacks

Claude Lenfant, MD

Despite impressive progress over the past several decades, diseases of the heart remain the leading cause of death for US men and women, and coronary heart disease (CHD) accounts for the largest share of deaths within that category. CHD is particularly important in blacks due to the higher prevalence of major CHD risk factors, such as hypertension, diabetes, obesity, and left ventricular hypertrophy.

Recent technological advances in the basic sciences provided unprecedented opportunities for new research to elucidate the pathogenesis of CHD in blacks, to improve management and treatment, and, ultimately, to develop effective preventive strategies.

To identify these new opportunities and chart a course for future research efforts, the National Heart, Lung, and Blood Institute (NHLBI) convened the Working Group on Coronary Heart Disease in Blacks in 1992. Comprising national experts in basic, clinical, population-based, behavior, and prevention research, the Working Group was charged to review the state of knowledge over the past 5 years; explore the pathophysiological mechanisms that underlie CHD in blacks; identify opportunities for development and assessment of new and improved approaches for clinical interventions and preventive and educational measures; and develop a specific plan, including scientific priorities, for NHLBI support of research on CHD in blacks during the next several years.

The summary that follows was prepared by the Working Group to highlight its overall findings. Research accomplishments and opportunities in each major area addressed by the Working Group are described more fully in the main report. It is available on the NHLBI Gopher (accessible through one's Internet Gopher client—Server: gopher.nhlbi.nih.gov, Port: 70). A printed copy can be obtained from Ms Charlene French, NHLBI, Bldg 31, Rm 5A03, National Institutes of Health, Bethesda, Md 20892.

We are very pleased to have this document to guide research activities with respect to CHD in blacks. We are grateful to the Working Group chair, Dr Charles K. Francis; cochair, Dr Augustus O. Grant; and the members for this valuable contribution to the institute's efforts.

Report of the NHLBI Working Group on CHD in Blacks

Introduction

Research on CHD has contributed to the decline in cardiovascular disease morbidity and mortality that has occurred during the past three decades in the United States. However, life expectancy and rates of illness and death from CHD have not improved as much for blacks as for whites. Blacks have not experienced the full benefit of research advancements for a variety of reasons, including insufficient scientific data, lack of research focused on minority populations, and limited access to health care resources and technology. Consistent and universally accepted racial and ethnic categories have not been established, and definitions may vary according to the social and scientific context. The limited data base currently available leaves a number of paradoxes unresolved. Controversy remains regarding, in particular, both chest pain and sudden death. Available data indicate that the probability of dying from CHD is greater in black Americans than in white Americans and that there is a higher prevalence of smoking, hypertension, diabetes, obesity, and left ventricular hypertrophy (LVH) in blacks. Blacks are also less likely to receive coronary angiography or coronary revascularization.

The NHLBI Working Group on Research in CHD in Blacks assessed the state of the science and identified research opportunities in four main areas of CHD in blacks: pathogenesis and pathophysiological mechanisms; clinical expression, diagnosis, and treatment; disease patterns and risk factors; and behavioral variables and strategies for education and prevention. In its deliberations, the Working Group identified 10 priority research areas, which are, in order of research priority, treatment, epidemiology (data collection and analysis), evaluation of chest pain and diagnosis of CHD, prevention and behavior, risk factors, genetics, vascular biology, LVH, coronary microvasculature, and sudden cardiac death.

These research priorities are considered in four chapters of the full report: basic research, clinical research, population-based research, and behavior and prevention research. Each chapter reviews the state of the science and identifies opportunities and recommendations for future research directions.

Although most studies show that there is little difference in the nature of the atherosclerotic process leading to CHD in blacks, it has become evident that there are important differences in the social and economic con-
text in which CHD develops in blacks. It is difficult to
determine whether phenotypic characteristics common
in blacks, such as high blood pressure and LVH, play a
primary role in the pathogenesis of CHD in blacks or
are merely markers for more fundamental differences in
mechanisms of disease. It is not clear whether differ-
ences in the biology of CHD or in the clinical expression
of common pathogenetic processes account for reported
racial differences. Differences in access to cardiovase-
cular care, the impact of risk factors, or variations in
clinical therapeutic responsiveness may be as responsi-
ble for the well-documented disparities in health out-
comes and resource utilization as any genetic or biolog-
ical mechanisms.

Research Accomplishments and Opportunities

Treatment
Although major advances in therapy for CHD have
occurred in recent years, few data are available on the
clinical value, effectiveness, and efficacy of newer ther-
apeutic modalities in blacks. Innovative therapeutic
approaches to CHD have been based on data obtained
primarily in white male populations. Blacks, especially
women, are at greater CHD risk. Therapeutic algo-
rithms focused primarily on the relief of chest pain have
been refined in majority populations, but other algo-
rithms may be more efficacious in populations with a
higher prevalence of hypertension or diabetes and with
differing clinical presentations. Although information
regarding the interactions of LVH, hypertension, and
CHD has increased, there are few data for blacks.

The development of pharmacological agents that
stimulate regression of LVH, modulate insulin sensitiv-
ity, alter lipid metabolism, and control vascular tone
provide new avenues for research on the treatment of
CHD in blacks. Thrombolysis and coronary revascular-
ization procedures, such as coronary artery bypass
grafting (CABG) and percutaneous transluminal coro-
nary angioplasty (PTCA), have been significant therap-
etic innovations. Studies of CABG surgery indicate
better survival rates but less favorable functional out-
comes for blacks treated surgically than for those
treated medically. Relatively little is known about the
use of PTCA in blacks. Limited studies of thrombolytic
therapy in blacks show higher patency rates for infarct-
related arteries compared with whites and a higher risk
of bleeding complications, although survival to hospital
discharge and other clinical outcomes are similar. There
are minimal data on the value of coronary arteryectomy
in blacks.

Epidemiology (Data Collection and Analysis)
Since the late 1960s, CHD mortality for all four major
sex-race groups has declined; however, since 1980, CHD
rates have declined faster in whites than in blacks,
particularly for men. Attempts to explain the disparities
between blacks and whites in CHD morbidity and
mortality, as well as differences in the use of clinical,
diagnostic, and therapeutic resources, have been limited
by the scarcity of comprehensive data on CHD in
blacks. Relations between risk factors and CHD have
been clarified in recent years and appear to be univers-
sally applicable, although data from specific ethnic
subpopulations have not been consistent with findings in
whites. Prospective epidemiological studies indicate
that CHD rates are similar in black men and white men
but higher in black women than in white women. Local
and regional data suggest that blacks have higher out-
of-hospital deaths, fewer hospitalizations for acute myo-
cardial infarction (MI), and higher death rates from
cardiovascular disease and use cardiac diagnostic pro-
cedures and revascularization procedures less often
than whites. National surveys and clinical trial data
provide valuable information but have not been thor-
oughly analyzed for clinical comparisons of subpopula-
tions. Racial and ethnic identifiers are often variable or
absent in existing large data sets. Ongoing observational
studies may be informative in the future.

Data from many of these studies could be collected
and analyzed to provide a more comprehensive over-
view of CHD in blacks. Other than Medicare data,
which are confined to the population more than 65 years
old, there is no national data base that contains com-
prehensive clinical information on blacks. National data
on clinical characteristics, risk factor profiles, therapies
received, health-care providers, patient preferences,
and long-term health outcomes are not available in
blacks. An additional important issue in data analysis
relates to the interpretation of exposure (ie, outcome
relations in blacks compared with whites). In the com-
plex, causal pathway linking risk factors to disease
outcomes, available analysis procedures may not be
adequate to define differences between blacks and
whites.

Evaluation of Chest Pain and Diagnosis of CHD

Clinical evaluation of chest pain and establishment of
the diagnosis of CHD in blacks are often difficult. ECG
changes long accepted as common “normal variants” in
blacks may have greater clinical significance when the
increased prevalence of out-of-hospital death, LVH,
and hypertension in blacks is taken into account. Coro-
nary spasm and silent ischemia have become estab-
lished clinical entities. Preliminary findings suggest that
there may be racial or ethnic differences in the occur-
rence and manifestations of these clinical syndromes.
The advent of ambulatory ECG and blood pressure
monitoring has facilitated greater understanding of
these syndromes and circadian variation in coronary
syndromes in general.

Clinical studies suggest that the sensitivity and spec-
cificity of tests established in the white population may
der differ for blacks. Cardiac diagnostic accuracy and reli-
ability have not been validated in blacks to the same
extent as in whites with respect to risk assessment,
therapeutic responses, prognosis, natural history, and
long-term health outcomes. For example, echocardiog-
raphy has provided a link between structural and func-
tional measurements and epidemiological data, but its
value in assessing the risk and prognosis of CHD,
independent of LVH, has not been fully elucidated in
blacks.

Limited available data show higher rates of normal
coronary angiograms in blacks with chest pain than in
whites, raising the possibility of abnormalities in the
coronary microcirculation or in vascular tone. However,
existing angiographic data on blacks may not be repres-
entative because blacks are known to have reduced
access to cardiac diagnostic procedures. In addition,
newer imaging techniques, such as perfusion scintigraphy, intravascular ultrasound, nuclear magnetic resonance (NMR), and positron-emission tomography (PET), have not been adequately studied in blacks.

**Prevention and Behavior**

Prevention of CHD necessarily involves behavior change, since modification of risk factors for CHD is influenced primarily by individual choice and the decision to change one's lifestyle. Although behavior change is fundamental to the prevention of CHD by reducing risk factors, differences in health-care-seeking behavior between blacks and whites may also contribute to racial differences in CHD mortality and morbidity. For example, blacks delay longer than whites in seeking care for general medical problems as well as for acute CHD symptoms, including acute MI.

Studies suggest that less tangible social support may be associated with stroke mortality and hypertension. The effects of diminished social supports on CHD in blacks appear to be particularly strong. Since it is likely that stress related to racial prejudice, economic disadvantage, and social disintegration is more common in blacks, understanding their relation to CHD in blacks is likely to be helpful in elucidating strategies for lowering CHD rates. Studies also suggest that there may be differences between blacks and whites in symptom perception and symptom attribution. These factors may affect adherence to treatment recommendations and play a role in the use of cardiac procedures and ultimate health outcomes.

Until the roles of access to care, knowledge and beliefs concerning CHD, coping styles and the social environment, and biological variables, such as cardiovascular reactivity, are clarified, understanding racial differences will be difficult. Culturally and ethnically appropriate techniques for individual and community behavior modification and lifestyle change, which would affect primary and secondary prevention of CHD, have not been developed specifically for blacks.

**Risk Factors**

The decline in CHD mortality and morbidity that began several decades ago, and continues to the present, has been coincident with widespread acceptance of the effectiveness of risk factor reduction in preventing CHD. The significant change in lifestyle and secular trends in risk factors that has occurred in the majority population has been less dramatic in blacks. Because prevalence rates of modifiable CHD risk factors, such as hypertension, cigarette smoking, physical inactivity, and obesity, have been documented to be greater in blacks than in whites, the opportunities for prevention may be greater for blacks.

Smoking rates in persons 18 years of age or older have declined in the general population but remain higher in blacks than in whites. Studies of leisure time physical activity suggest that blacks are more sedentary and less fit than whites, independent of income and education. Obesity, which is associated with hypertension, hyperlipidemia, hyperinsulinemia, and glucose intolerance, may be more common in blacks. The prevalence of obesity appears to be higher in black women than in white women or black men, but racial differences are less apparent between black and white men. Dietary patterns may differ slightly between blacks and whites, but foods selected by blacks and whites do not differ substantially in nutritional composition. Data in blacks are conflicting about the relation of elevated levels of lipoprotein(a) [Lp(a)], a genetically determined lipoprotein associated with CHD, to CHD risk. Increased left ventricular (LV) wall thickness is more common in blacks, even in the absence of hypertension. The contribution of LVH to risk of sudden death and out-of-hospital death in blacks is not clear.

Both individual and community-based interventions have been successful in modifying CHD risk factors in blacks, although individual approaches may be less effective in blacks than in the general population. Local church and communitywide education programs have been particularly effective in the control of hypertension and smoking in some black communities.

**Genetics**

The recent, unprecedented progress over the past decade in genetics and molecular and vascular biology has enhanced understanding of the pathogenesis of human disease. Although initial progress was made in diseases resulting from mutations of a single gene, methods are now available that allow investigation of complex diseases, such as atherosclerosis, hypertension, and disorders of coagulation. One prerequisite for studying complex diseases is identification of aggregates of patients or families with relevant phenotypic characteristics.

Family history comparisons between blacks and whites demonstrate a higher prevalence of positive family history of hypertension, stroke, diabetes, or obesity in black families. However, family history of CHD is similar among black and other populations. Black families also appear to be similar to other populations in having strong correlations for major CHD risk factors between biological relatives but not with unrelated persons living in the same household.

Complex diseases, such as atherosclerosis, are typified by etiological heterogeneity, in which a variety of physiological systems interact to produce a clinical disease entity. Identification of a gene that occurs frequently in a population with a specific disease may not establish linkage to the disease. For example, although Lp(a) is found more commonly in blacks, it has only been established as a risk factor for whites. Similarly, polymorphisms of the angiotensinogen gene have been associated with increased risk of hypertension and preeclampsia in selected populations, and there are some interesting new findings at the angiotensinogen locus that deserve further attention.

Evidence suggests that pedigrees with a complex disease demonstrate genetic heterogeneity and that different individuals with a disease may be influenced by "nonoverlapping genetic components." As differences in the distributions of alleles are identified between affected and unaffected pedigrees, more precise phenotypic characterization becomes essential, regardless of whether the investigative strategy primarily involves linkage analysis, identification of candidate genes, or detection of mutations of candidate genes.
Vascular Biology

Significant advances in understanding the mechanisms active in the development of atherosclerotic lesions and pathogenesis of macrovascular and microvascular disease now offer greater opportunities for acquiring knowledge on the clinical presentation, natural history, and outcomes of CHD in blacks. Studies of the biology of the arterial wall have led to significant advances in understanding endothelial function and structure, cell–cell interaction, growth factors, connective tissue, and lipoprotein metabolism. There has been dramatic progress in understanding gene regulation of lipoprotein metabolism, biosynthesis, and mechanisms of action of lipoproteins. It is now possible to study the fibrous plaque and the fatty streak directly in the human artery using biopsy tissue, transplant tissue, and vascular rings or strips obtained during surgery or at autopsy. The growth in the clinical application of coronary atherectomy has provided an additional source of tissue for studying a wide array of pathogenetic mechanisms in atherosclerosis.

Greater understanding has been gained of the interaction of the vascular endothelium and the vessel wall with specific cellular elements in blood; the function and composition of specific lipoproteins, enzymes, hormones, and receptors; the contribution of genetic and immunological factors; the impact of alterations in the autonomic nervous system; and the role of coagulation and thrombosis in atherogenesis and the coronary syndromes. It is not known, however, whether there are significant racial differences in the cellular and molecular mechanisms of atherogenesis.

LVH

Research on CHD in blacks presents a unique challenge because of the increased prevalence of LVH and hypertension in the black population. In studying CHD in blacks, LVH and hypertension may be confounding factors, challenging investigators to identify the separate and common pathogenetic mechanisms of atherosclerosis, hypertension, and LVH and to explain their interaction. LVH has been shown to be an important risk factor for CHD, sudden death, and congestive heart failure, and it confers significant risk for future cardiovascular events, independent of atherosclerotic disease in the epicardial coronary vessels. Many of the pathogenetic features of LVH, such as endocrine, paracrine, and autocrine factors, can now be studied in humans.

Because hypertension is common in blacks, the increased prevalence of LVH in blacks is often attributed to concurrent hypertension, but young blacks tend to have increased LV wall thickness compared with whites, even in the absence of increased blood pressure. Cardiac myocytes constitute 75% of the heart mass, and the interstitium comprises 25%. Hypertension is the major stimulus to myocyte hypertrophy. Studies of the cellular response and remodeling of the interstitium in hypertension suggest that blacks have a tendency toward increased muscle cell mass.

It is not clear whether there are racial differences in systolic and diastolic function in the ventricle with LVH alone, with CHD and LVH, or with isolated CHD. Selected pharmacological agents have been widely shown to cause regression of LVH. The impact of LVH regression on the course of CHD, hypertension, congestive heart failure, and sudden death in blacks needs further exploration.

Coronary Microvasculature

Blacks demonstrate high rates of angiographically normal epicardial coronary arteries despite a higher prevalence of multiple CHD risk factors and disproportionate morbidity and mortality from CHD. This paradox has led investigators to seek explanations in the microvasculature of the heart. However, because of the small size of the vessels that compose the microvasculature, gross examination has been difficult and histological studies have been limited primarily to microscopic examination at autopsy.

Still, much has been learned from studies of microvascular functional responses to physiological and pharmacological interventions. The microvasculature may respond differently to pharmacological agents than do large muscular arteries and veins. Endothelial dysfunction may play a role in microcirculatory disease and may occur in atherosclerosis, diabetes, low-renin states, coronary vasospasm, and reperfusion injury. Increased sensitivity to the vasoconstrictive effects of catecholamines may also occur with endothelial dysfunction.

Clinical diagnosis of abnormal microcirculation has been based largely on the demonstration of reduced coronary reserve. Abnormal coronary reserve is implicated if coronary blood flow does not increase when coronary resistance is lowered, usually in response to the administration of a potent coronary vasodilator, such as dipyridamole or papaverine, or to exercise. Numerous reports note the frequent occurrence of the syndrome in hypertensive patients with and without LVH or with hypercholesterolemia.

Microvascular disease, or nonatherosclerotic CHD (the clinical syndrome of angina-like chest pain and angiographically normal coronary arteries), may occur in up to 20% of patients undergoing coronary angiography. In some studies of blacks, however, nearly half of those with angina-like chest pain have normal coronary angiograms. Black women in particular have a higher incidence of chest pain with normal coronary arteries. Abnormal coronary microvascular function may limit appropriate flow response to stress, possibly due to endothelial dysfunction.

Pharmacological probes and provocative testing with agents such as acetylcholine may be helpful in determining whether there are physiological differences between blacks and whites in the microvasculature. The relative role of microvascular disease versus macrovascular disease in the pathogenesis of myocardial ischemia and vascular disease of the heart has not been studied extensively in blacks.

Sudden Cardiac Death

Death certificates and autopsy data indicate that more blacks than whites die out of the hospital or experience out-of-hospital cardiac arrest. Studies have not confirmed a relation between race and access to emergency cardiac care or outcome of cardiac resuscitation. Out-of-hospital deaths may also be related to delay in the prehospital phase of acute MI care. LVH may be associated with increased atrial and ventricular arrhythmogenesis and, potentially, sudden death.
It is not clear whether there are racial differences in the electrophysiological substrate in blacks related to the increased prevalence of LVH and hypertension. Diminished coronary reserve may also be more common in blacks and predispose to life-threatening arrhythmias. The value of newer electrophysiological monitoring techniques in predicting risk of sudden death is also not clear, and the value of signal-averaged ECG in predicting arrhythmias has not been well studied in blacks.

Smoking may also increase the risk of sudden death in some individuals, most likely through enhanced platelet adhesion and attendant thrombogenicity, increased vasomotor reactivity, and reduced threshold for sustained ventricular arrhythmias. The contribution of smoking to differences in sudden death and out-of-hospital deaths in blacks has not been studied extensively.

Research Recommendations

For many years, evidence has been accumulating that blacks, compared with whites, in the United States suffer disproportionately from death and illness due to cardiovascular disease. Recently, the documentation of disparities in access to care, use of medical resources, and health outcomes has accelerated. Now is an opportune time for intensifying research efforts on coronary disease in blacks.

Clinical management of CHD has advanced dramatically with the advent of CABG surgery, thrombolysis, and PTCA. Despite extensive research on the efficacy of these therapeutic modalities, clinical data on their value and effectiveness in blacks are limited. More rapid progress in reducing the burden of CHD in blacks has been thwarted by lack of detailed information on the phenotypes of CHD in blacks. The increased availability of sophisticated diagnostic and therapeutic modalities offers an opportunity for studying the applicability of these techniques to blacks.

Development of new pharmacological therapies for CHD also affords greater possibilities for identifying and understanding racial differences in the pathogenesis of CHD and the therapeutic efficacy and effectiveness of these therapies and to relate any differences observed to short- and long-term clinical outcomes. The expanded application of computer technology and informatics to the collection and analysis of medical data will facilitate analysis of existing data sets as well as collection and analysis of prospective data on CHD in blacks.

Significant progress has been made in understanding the mechanisms of CHD and the control of atherosclerosis, as well as nonatherosclerotic coronary disease, blood pressure regulation, LVH, and arrhythmogenesis. Unprecedented advances in molecular genetics and vascular biology have enhanced opportunities for research, at the cellular and molecular level, on the mechanisms of CHD in blacks. When considering CHD in blacks, however, research on the interaction of environmental, biological, and genetic factors is especially important.

Basic research has contributed substantially to the progress already made in reducing death rates from cardiovascular disease in the white community. Population-based studies and behavioral research may provide crucial insights that will allow similar improvement in the rates of death and disease due to CHD in blacks living in the United States. In reviewing the state of science on CHD in blacks, it is clear that existing knowledge is incomplete and fragmentary. As clinical paradoxes in CHD in blacks are resolved and new questions at the cellular and molecular level are answered, opportunities for developing innovative and improved methods of preventing, halting, reversing, and treating CHD will be expanded, not just for blacks but for all Americans.

The research recommendations proposed by the Working Group are described in detail in the four main sections of its report. In developing these recommendations, the Working Group identified an overriding need in all areas of research on CHD in blacks for a comprehensive data base of information and a coordinated network of clinical researchers. Therefore, the Working Group strongly recommends the establishment of a centralized data base of existing data on CHD in blacks. Such a data base will be an important resource for planning and conducting future research studies of acute and chronic coronary syndromes in blacks. The Working Group also strongly recommends support for a comprehensive, multidisciplinary, national network of investigators in community-based clinical centers. Through this national network, clinical researchers will be able to collect and coordinate prospective data on environmental and behavioral determinants of CHD in blacks; clinical characteristics, disease course, and epidemiology of acute and chronic CHD syndromes in blacks; variations in cardiac care; and the extent and causes of differences between black and nonblack populations in the use of cardiac procedures.

Implementation of these two major recommendations of the Working Group will accelerate research on CHD in blacks and research findings that will be relevant to all US populations. The data base and clinical network are necessary steps to the future, integrating existing fragmentary and incomplete data and encouraging coordinated research in pursuit of well-planned hypotheses.

The Working Group’s recommendations for each of the 10 research areas, listed in priority order, are summarized below.

Treatment

Disparities in health outcomes of CHD in blacks, compared with whites, may result from differences in risk factor profiles, use of diagnostic tools, management of acute and chronic CHD syndromes, and access to revascularization procedures. Research should be expanded to identify the most effective means of increasing awareness about the value of reducing risk factors and treating symptoms and signs of CHD in black populations. The causes of differences in clinical characteristics and outcomes of CHD between blacks and whites also need to be determined.

Although reduction in the development of stroke attributable to control of hypertension has exceeded that predicted from epidemiological studies, reduction in CHD related to antihypertensive treatment has been much less striking. Given that hypertension is more common in blacks than in whites, studies should be conducted to define the possible contribution of antihypertensive therapy to mortality from CHD in blacks. Out-of-hospital CHD deaths also are more common in
blacks. Methodologies for identifying individuals at risk of acute coronary events, especially sudden death, should be evaluated further. Identification and evaluation of antiarrhythmic agents designed to reduce the risk of life-threatening arrhythmias have been difficult in the past; however, development of effective therapies for patients at high risk (eg, blacks and other patients with documented CHD, hypertension, LVH, normal coronary arteries with poor coronary reserve) should continue to be a goal of research.

Use of pharmacological therapy for ischemic heart disease has been influenced by recent major advances in coronary revascularization and thrombolysis. However, innovative research on the pathogenesis of atherosclerosis and greater understanding of the role of the endothelium, vascular smooth muscle, and vascular reactivity have led to renewed enthusiasm for established, as well as newer, therapeutic agents.

Clinical trials are needed, particularly related to CHD in blacks. These should address the efficacy of pharmacological agents (eg, antioxidants, anti-inflammatory substances, growth factor inhibitors) in modifying vascular and ventricular remodeling processes, as well as the impact of pharmaceuticals (eg, angiotensin-converting enzyme inhibitors, calcium channel blockers, estrogens) on the course of atherosclerotic and nonatherosclerotic CHD.

The prevalence of heart failure related to CHD is increasing as more patients survive acute coronary syndromes. Heart failure due to CHD or ischemic cardiomyopathy is now one of the most common diagnoses prompting hospital admission. Heart failure is more prevalent in blacks, perhaps because of coincident hypertension or diabetes mellitus. Research comparing ventricular dysfunction due to macrovascular versus microvascular disease and atherosclerotic versus nonatherosclerotic disease is needed, especially in blacks.

Ischemic cardiomyopathy is one of the major contributors to heart failure leading to cardiac transplantation. Studies are needed to determine more effective drug therapy for both systolic and diastolic dysfunction. The appropriateness and value of CABG surgery, PTCA, and thrombolysis, compared with conventional medical therapy, also need to be assessed. For this effort, existing data from multicenter interventional trials should be pooled as appropriate, and prospective clinical trials of various revascularization approaches should be conducted in blacks and compared with existing data in whites.

Epidemiology (Data Collection and Analysis)

The fundamental obstacle in studying CHD in blacks is the absence of sufficient data for resolving many of the questions related to racial comparisons. Because information is limited for specific racial and ethnic groups, determining whether differences and inconsistencies are due to chance findings, artifacts in reporting, or important genetic and biological factors is a difficult, but not insurmountable, problem.

Data collected previously from large clinical trials, national surveys, and vital statistics sources have not been analyzed collectively. When integrated, they may contain valuable information on CHD in blacks. By merging national and regional data on CHD in blacks, it will be possible to obtain a more complete picture of the effectiveness of therapeutic interventions, determinants in the use of cardiological care and resources, medical practice patterns, and outcomes of hospital and ambulatory services. Based on these data, research needs and information gaps can be further clarified, and plans for future analyses of prospectively collected data can be formulated.

In conducting research on CHD in blacks, it is important to distinguish health-related consequences of social and economic factors from biological or genetic processes that may be active in the pathogenesis, clinical expression, and outcomes of CHD in blacks. The appropriate use of racial categories in biomedical research should be defined and the limitations of these categories well understood. Studies of the magnitude of between-group genetic differences and within-group heterogeneity should be given high priority. Caution must be exercised in interpreting differences between population subgroups so that the contribution of genetic factors, such as race, is not overemphasized. The distinctive roles of environmental forces, such as socioeconomic status and stress related to minority status, and the genetics and biological aspects of race should be clarified.

Evaluation of Chest Pain and Diagnosis of CHD

The clinical evaluation of chest pain continues to challenge the diagnostic acumen of many clinicians. Accurate diagnosis of CHD in blacks may be more demanding because of the more common concurrence of hypertension, LVH, or both. How this information affects the diagnostic approaches of clinicians is not clear. It is known, however, that blacks receive cardiac procedures, both diagnostic coronary angiography and revascularization, less commonly than whites.

It is not clear whether this disparity between blacks and whites is a function of physician factors, limited access to health care, or individual health-care-seeking behavior. Providers may vary in their ability to convey educational messages to culturally diverse patient populations. Research on the roles of these factors is recommended.

Studies are also needed to compare the decision-making process by health care providers for ordering diagnostic procedures in blacks and whites and the role of patient preferences in choosing to accept recommended procedures. The relative roles of risk factors, disease severity, and other variables should be compared with the impact of race and socioeconomic status on the use of cardiac procedures in blacks.

Additional new and improved noninvasive techniques for monitoring the development, progression, and regression of CHD and LVH in blacks need to be developed. The implications of ECG findings considered to be normal in blacks should be reassessed, given the data indicating that out-of-hospital deaths and sudden death may be more common in blacks. Comparison of the relative value of imaging techniques for assessing CHD risk in blacks with signal-averaged ECG and other evolving noninvasive techniques should be undertaken. Also important is comparison of the relative value, reliability, accuracy, sensitivity, and specificity of noninvasive diagnostic techniques, such as ECG, echocardiography, stress testing (in conjunction with
ECG, echocardiographic, or radionuclide imaging), nuclear magnetic resonance, and positron emission tomography in blacks and whites. The applicability of these tests to individuals with atherosclerotic and nonatherosclerotic CHD, and with hypertension and/or LVH, should be compared in blacks and whites.

Research establishing the role of genetics in some forms of LVH suggests the need to determine the value of echocardiography and other imaging techniques, compared with genetic testing, in diagnosing individuals with genetically determined LVH or hypertrophic cardiomyopathy. Clinical trials will be important in evaluating the value of new and improved noninvasive diagnostic tools, such as intravascular ultrasound and three-dimensional echocardiography, in assessing ventricular structure and function and the physiology of the macrovasculature in blacks and whites.

The reasons for the paradoxically high rates of normal coronary angiographic findings in blacks with angina-like chest pain need to be elucidated. Also, given that individuals who enter angiographic trials may not be representative of the general black population, methods need to be developed to assess and control for selection bias in angiographic studies of blacks. Investigators are encouraged to assess the relation of coronary angiographic findings to the site of coronary occlusion, extent and severity of myocardial damage, and recurrence and outcomes of CHD events in blacks compared with whites.

**Prevention and Behavior**

Although a reduction in traditional risk factors has been shown to be an effective prevention strategy for the general population, data on the efficacy of prevention efforts in blacks are minimal. Collection of prevention data in blacks has been limited by the lack of culturally validated instruments for data collection and reliable methods for establishing risk factor profiles in minority communities. Still, even though existing data are not sufficient for making generalizations about the impact of behavioral risk factors on CHD in blacks, effective strategies can be developed based on these data.

New and improved tools for measuring risk factors in blacks, both in individuals and in populations, need to be developed and culturally validated. Data should be collected prospectively to allow assessment of the relative risk of factors that preferentially affect blacks compared with those that have been studied most in whites. Identification and treatment of behavioral risk factors of special significance to black populations should be a high priority.

Research on health-care–seeking behaviors is another priority area. These behaviors may be determined by a wide array of factors, most of which are functions of social and economic forces. Limited data are available on the impact of social supports, income, stress, acculturation, or personality on CHD risk in blacks. Studies are needed of the psychosocial predictors of CHD mortality and morbidity in blacks, interaction of psychosocial and biological factors and their effect on CHD outcomes, as well as the effectiveness of programs targeted to individuals and communities.

Adherence to medical recommendations, acceptance of diagnostic testing procedures, and interactions with the health-care system may be influenced by social and environmental forces. Educational strategies to improve adherence to prevention and treatment recommendations need to be developed, implemented, and evaluated. Innovative and effective research programs to increase long-term adherence to lifestyle modification programs are especially warranted.

**Risk Factors**

Prevention efforts in the general population have concentrated on identifying risk factors for CHD and treating specific risk factors in at-risk individuals. Differences in patterns of clinical CHD and short- and long-term outcomes of CHD may be related to differential effects of traditional risk factors in blacks and whites and/or the presence of factors in blacks that may not confer similar risk in whites. Increased prevalence of CHD risk factors, such as hypertension, diabetes, increased LV wall thickness, cigarette smoking, and obesity have been documented in blacks. However, other features, also common in blacks, such as enhanced thrombogenicity, increased vascular reactivity, and greater potential for ventricular arrhythmias, may also be significant in explaining racial differences in CHD.

If the mechanisms of CHD differ in blacks, the role of different risk factors may also vary. Smoking, for example, is more prevalent among blacks than whites. Yet, there are few data on the determinants of smoking habits in blacks. Valid and reliable instruments need to be developed for assessing the determinants of smoking topography and the contribution of smoking to the clinical manifestations and outcomes of CHD in blacks. Research also is needed to define the social, cultural, and environmental prerequisites for successful smoking cessation and to develop culturally relevant cessation programs. With regard to other risk factors, valid and culturally appropriate instruments need to be developed to assess nutrition, physical activity, and social supports.

**Genetics**

To demonstrate population-specific genetic susceptibility, it will be necessary to show that there are differential frequencies of genes that condition risk in similar ways in both black and white populations. Studies of possible gene–environment interactions are also recommended. A very large number of black sibships or families will have to be identified to study family-risk syndromes and to understand the interaction of cultural and genetic heritability. This research includes identification of major gene segregation and detection of linkage and susceptibility loci.

Trials of family prevention strategies will be important. Such trials should include identification of large numbers of high-risk families and longitudinal monitoring of the effect of risk factor reduction on CHD clinical expression and health outcomes. Detailed phenotypic data (eg, on blood pressure, diabetes, obesity, insulin levels, LVH, and other variables) need to be collected and correlated with genetic data obtained from stored white cells from sibships and families. Studies that correlate genotype and phenotype should be given high priority.

Studies of candidate genes and identification of specific genetic traits leading to pathophysiological pro-
cesses and CHD are encouraged. Also recommended is research on the frequencies of gene variants in black populations and assessment of possible associations with features of CHD in other populations with CHD.

**Vascular Biology**

Basic research has enhanced understanding of the mechanisms of atherosclerotic CHD. In recent years, there has been an increase in the rate of progress in research on the endothelium, cell–cell interaction, signal transduction, receptors, ion channels, growth factors, and vasoactive substances. Today, research on CHD in blacks should take advantage of modern techniques to study potential histopathological differences in coronary atheroma between blacks and whites. Investigations of necropsy, surgical, or explanted cardiac vascular tissue should be undertaken to define potential racial differences in lesion structure and the mechanism of transition from a stable lesion of chronic CHD to an active lesion of acute CHD. Studies of microvascular coronary artery function, using provocative pharmacological testing, are recommended for elucidating physiological differences between lesions in blacks and whites.

**LVH**

The increased prevalence of LVH in blacks makes knowledge of its pathogenetic role critical to understanding CHD in blacks. Research on LVH will be greatly advanced by development of techniques that will yield better understanding of the cellular and biochemical basis of abnormal myocardial contraction and relaxation and the role of the interstitium in myocardial hypertrophy. The differential effects of hemodynamic loading conditions and of hormonal, dietary, and other nonhemodynamic factors in development of myocardial hypertrophy need to be clarified in blacks and whites.

LVH may also predispose to ventricular arrhythmias in blacks. The role of intracellular tonic and metabolic changes in initiating and maintaining a reduced threshold for ventricular fibrillation and complex ventricular tachyarrhythmias needs to be determined, and studies of the racial differences in these factors are recommended. Researchers are encouraged to use human biopsy specimens to delineate subcellular changes in the sarcolemma, sarcoplasmic reticulum, and contractile apparatus that may account for changes in intracellular calcium handling and excitation–contraction coupling that occur in LVH.

Valid and reliable noninvasive techniques should be developed for assessing the regression of LVH and its impact on the course of CHD in blacks. Experimental models are also needed for studying the role of hemodynamic, nonhemodynamic, and growth factors in development of LVH.

**Coronary Microvasculature**

Abnormalities of the coronary microvasculature have been proposed to explain the paradoxically high prevalence of normal-appearing epicardial vessels on angiography in patients with angina-like chest pain. However, the nature and pathogenesis of coronary microvascular disease have not been studied extensively in humans, and data in animals are relatively sparse compared with research data on the macrovasculature.

Investigations of the mechanisms that control microvascular function and structure, including endothelial function, intracellular ions, and vascular reactivity, are recommended. Interactions among endothelial, neural, and hormonal control of microvascular tone and coronary blood flow should be clarified using both animal and human vessels. The relative importance of the various control mechanisms in blacks and whites should be determined in in vitro microvascular reactivity profiles and how they are affected by CHD and hypertensive LVH. Studies of coronary vasodilator reserve in animal models (eg, the pig model) using positron emission tomography, nuclear magnetic resonance, or other imaging technologies may also be useful in assessing the determinants of microvascular function.

New and improved techniques are needed for human studies of the microvasculature and measurement of coronary reserve and microcirculatory flow in blacks with atherosclerotic and nonatherosclerotic CHD. The influence of inflammation, vasculitis, or immune complex disease on abnormal coronary reserve, microvascular function, and chest pain syndromes in blacks should be assessed. Also needed are investigations of the impact of controlling CHD risk factors, such as hyperlipidemia, LVH, diabetes, and smoking, on chest pain and the natural history of microvascular disease.

Further studies are recommended on the impact of microvascular disease on ventricular function and heart failure in blacks with angina-like chest pain and normal coronary arteries. Microvascular function should be compared in different vascular beds (ie, forearm versus heart), and studies are needed on the relation of abnormal microvasculature in different vascular beds to the signs and symptoms of CHD.

**Sudden Cardiac Death**

Although recent data suggest that out-of-hospital and sudden death rates are higher in blacks, much of these data are derived from local studies and have not been confirmed in broader populations. The incidence and prevalence of life-threatening arrhythmias need to be determined in blacks with chest pain syndromes related to nonatherosclerotic and atherosclerotic CHD. The relation of differences in cardiovascular reactivity to racial variations in sudden death and case-fatality rates in blacks and whites also should be explored.

Studies of diurnal variation in sudden death and other cardiac events are needed to identify the endocrine, paracrine, or autocrine factors that are most important in the pathogenesis of these events. Criteria for identifying individuals at high risk of arrhythmias and sudden death should be validated in blacks. Investigations are also needed on the relation of traditional risk factors (eg, LVH, hypertension, hyperlipidemia) and behavioral and environmental factors to the risk of sudden death and life-threatening ventricular arrhythmias.

**Working Group on Research in Coronary Heart Disease in Blacks**

Charles K. Francis, MD, Chair  
Professor of Clinical Medicine  
Columbia University  
College of Physicians and Surgeons  
at Harlem Hospital Center
Bibliography

The following references are provided as a guide for individuals interested in obtaining additional information on the research areas mentioned in this report. The list provided is not intended to be comprehensive or to reflect all of the important and wide-ranging studies in research on CHD in blacks. The references are listed alphabetically for each of the four main sections of the report.

Basic Research


**Clinical Research**


Maynard C, Fisher LD, Passamani ER. Survival of black persons compared with white persons in the Coronary Artery Surgery Study (CASS). Am J Cardiol. 1987;60:513-518.


Sane DC, Stump DC, Topol EJ, Sigmon KN, Clair WK, Kereiakis DJ, George BS, Stoddard MF, Bates ER, Stack RS, Calidd RM. Racial differences in responses to thrombolytic therapy with recombinant tissue-type plasminogen activator: increased fibrin(ogen) in blacks. Circulation. 1991;83:170-175.


**Population-Based Research**


Lee DK, Marantz PR, Cohen H, Devereux RB, Al-derman MH. Prevalence of left ventricular hypertrophy by electrocardiogram in blacks and whites: are racial differences overestimated? Circulation. 1991;83:8. Abstract.


**Behavior and Prevention Research**


**KEY WORDS**  •  Cardiovascular News  •  race  •  heart disease  •  risk factors
Report of the NHLBI Working Group on Research in Coronary Heart Disease in Blacks.
C Lenfant

_Circulation._ 1994;90:1613-1623
doi: 10.1161/01.CIR.90.4.1613

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1994 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/90/4/1613.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/