CME CREDIT

Coronary heart disease in African Americans: primary and secondary prevention

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SUMMARY Coronary heart disease develops sooner in African Americans than in whites and causes a higher rate of mortality. Because multiple risk factors and risk factor clustering are common, efforts at primary and secondary prevention in this population need to address the total risk-factor profile.

KEY POINTS Cigarette smoking, hypertension, diabetes mellitus, obesity, left ventricular hypertrophy, and physical inactivity are all more prevalent in blacks than in whites. Further, according to the National Health and Nutrition Examination Survey, blacks are 1.5 times more likely to have multiple risk factors than their white counterparts. Diet, weight reduction and control, increased physical activity, smoking cessation, and other nonpharmacologic measures are the cornerstones of therapy and should receive special emphasis.

When pharmacologic therapy is required, selection of the drug to use requires consideration of benefits, concomitant diseases, costs, and effects of treatment on quality of life.

INDEX TERMS: CORONARY DISEASE; RISK FACTORS; AFRICAN AMERICANS
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AMERICANS OF WEST African ancestry are at increased risk for cardiovascular disease mortality. Much of the higher risk is due to higher prevalences in African Americans of factors that can be modified.

Treating multiple, concomitant risk factors can be challenging, and formal practice guidelines have yet to be developed. But to be effective, primary and secondary prevention strategies will have to address the total risk-factor profile. This paper reviews how physicians and other health care providers can improve the cardiovascular health of their black patients.

BACKGROUND

Coronary heart disease (CHD) is the leading cause of death for African Americans.[1,2] CHD prevalence rates are similar in black men and white men, but higher in black women than in white women.[3–5] On average, CHD develops about 5 years earlier and has a higher associated mortality rate among blacks than among whites of the same age, at least through age 64 for men and age 74 for women.[4,5] In addition, although the age-adjusted CHD death rate

in the United States has been declining, it is declining less for African Americans than for whites.[6]

The reasons for the racial disparities in CHD morbidity and mortality have not been elucidated. Blacks have a higher prevalence of risk factors than whites, and this may contribute to differences in disease manifestation and natural history. The predictive value of conventional risk factors for the presence and severity of CHD appears to be similar in blacks and whites.[7] However, the prevalence of CHD is similar in black and white men, even though black men have a greater risk-factor burden; higher levels of high-density lipoprotein (HDL) in black men may account for this paradox.[8–10]

DYSLIPIDEMIA IN AFRICAN AMERICANS

Studies have generally found African Americans to have similar or lower total cholesterol, low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) levels compared with whites, but higher HDL levels, especially in men.[8,9,11] The National Health and Nutrition Examination Survey III (NHANES III) found the age-adjusted mean total cholesterol level to be 201 mg/dL in black men and 205 mg/dL in white men, black women, and white women.[12]

There are limited data on the importance of cholesterol as a risk factor in African Americans. However, among those screened for the Multiple Risk Factor Intervention Trial, the relationship between serum cholesterol level and CHD mortality was virtually identical in African American and white men over an average follow-up of about 12 years.[12]

Lipoprotein (a)

Lipoprotein (a), or Lp(a), consists of an LDL molecule covalently linked by disulfide bonds with apoprotein (a).[13] Apoprotein (a) resembles the fibrinolytic enzyme plasminogen, with a 94% amino acid homology. It has been postulated that Lp(a) may have a prothrombotic effect by competitively binding to plasminogen receptors and inhibiting the thrombolytic activity of tissue plasminogen activator.

Several investigators have reported correlations between elevated levels of Lp(a) and CHD,[14–16] and higher Lp(a) levels in blacks than in whites.[17–19] In a longitudinal study, 50% of black physicians had elevated Lp(a) levels, compared with only 17% of white physicians.[20]

NONLIPID CHD RISK FACTORS IN AFRICAN AMERICANS

Hypertension and left ventricular hypertrophy

Both systolic and diastolic hypertension are associated with increased rates of cardiovascular disease. Hypertension is more prevalent in blacks than in whites, develops at a younger age, and is associated with rates of morbidity and mortality three to five times higher. The principal structural alteration of the heart in patients with hypertension is left ventricular hypertrophy (LVH)—a relatively uniform increase in left ventricular thickness with little change in ventricular volume.[21] The prevalence of LVH by echocardiography in patients with mild to moderate hypertension is 43% to 48%.[21] Although much of the mortality and morbidity of hypertension appears to be related to LVH, the predictive value of LVH for morbidity and mortality is independent of hypertension and other atherosclerotic cardiovascular risk factors.[22] Arrhythmias are more frequent and severe in LVH, and when myocardial infarction occurs in patients with LVH, it is apt to be more extensive.[22] Hypertension and hypertensive heart disease appear to provide a substrate upon which CHD develops in blacks that is different compared with whites, and this may contribute to the increased morbidity and mortality in those patients who do develop CHD.

Diabetes mellitus

Both non-insulin-dependent diabetes mellitus (NIDDM) and insulin-dependent diabetes mellitus (IDDM) are serious health problems in the United States, affecting more than 13 million Americans. NIDDM is far more common, with prevalence rates disproportionately higher in African Americans than in whites.[22] Both NIDDM and IDDM increase the risk for CHD about threefold in men and even more in women. Although some of this increased risk appears to be related to alterations in serum lipoproteins, the diabetic state itself increases risk independently of its effects on the lipid profile.

The mechanisms responsible for the excess diabetes and cardiovascular risk in African Americans may be related in part to insulin resistance,[23] although a recent study by Banerji and colleagues[24] suggests distinct clusters of diabetic African Americans have clinical insulin resistance, whereas others are insulin-sensitive.

Cigarette smoking

Cigarette smoking is a strong risk factor for CHD, peripheral vascular disease, and other atherosclerotic diseases. The overall prevalence of cigarette smoking is higher among black men than white men, although black men smoke fewer cigarettes per day.[25] Data among women are conflicting, with some studies suggesting greater prevalence among black women than white women and other studies finding no differences.[26–28]

Obesity

Total body obesity. Obesity is associated with increased risk for CHD in men and women. The increased risk appears to be mediated chiefly through the metabolic consequences of obesity (glucose intolerance, diabetes mellitus, hypertension, decreased HDL, and increased LDL and VLDL); the contribution of obesity independent of these associated conditions is controversial.

Abdominal obesity. Although the relation of obesity per se to CHD risk is controversial, when obesity is predominantly abdominal (upper body, abdominal, central, visceral, android, apple-shaped) rather than gluteofemoral (lower body, gynecoid, pear-shaped), the risk for systemic hypertension, hyperinsulinemia, diabetes mellitus, lipid abnormalities, and CHD is increased.[29–33] These findings may be especially important in black women, in whom obesity occurs twice as frequently[34] and in whom abdominal obesity is more common[35] than in white women. Available data indicate that the risk is increased when the waist-to-hip ratio exceeds 0.90 for men and 0.80 for middle-aged and elderly women.[29–33,36]

Physical inactivity

Regular physical activity of moderate intensity provides an element of protection against CHD.[37] The protection appears to be partly related to a direct effect on the heart and arteries and partly a result of favorable effects on HDL, blood pressure, body weight, and insulin resistance. Blacks participate less often in regular physical activity than do whites, independent of income and education.[38]

RISK FACTOR CLUSTERING

CHD risk factors often occur in combination or clusters,[39,40] conferring a synergistic effect. In adults age 25 to 74 examined in NHANES II, 59% of black women, 53% of white women, 71% of black men, and 63% of white men had at least one cardiovascular risk factor.[41] In this same study, black subjects were 1.5 times more likely to have multiple risk factors than were their white counterparts.

Since cigarette smoking, hypertension, diabetes mellitus, obesity, LVH, and physical inactivity are all more prevalent in blacks than in whites, one would expect blacks to have multiple risk factors more often. Forty percent of Americans with hypertension have high blood cholesterol; 46% of those with hypercholesterolemia have hypertension; and hypertension, hypertriglyceridemia, and diabetes mellitus are two to three times more common in obese than in nonobese people. Dyslipidemia has proved to be a major component among clustered risk factors, especially in the presence of diabetes.

Some clusters of CHD risk factors have been defined as syndromes. Reaven[42] has termed the cluster of hypertension, hyperinsulinemia, glucose intolerance, hypertriglyceridemia, elevated levels of VLDL and intermediate-density lipoprotein (IDL), and low levels of HDL as "Syndrome X"; Williams[43] has termed a similar cluster "dyslipidemic hypertension." Kaplan[44] refers to the combination of abdominal obesity, hypertension, diabetes mellitus, and lipid abnormalities as the "deadly quartet."

Why risk factors cluster in some patients is unknown. Both genetic and environmental factors have been implicated. Insulin resistance and hyperinsulinemia appear to be pivotal to clustering and to contribute to the pathogenesis of the coexistent hypertension, diabetes, dyslipidemia, and atherosclerosis. Most of the studies reporting a relationship between insulin concentrations, blood pressure, and risk factor clustering have been conducted in white populations. Investigations in blacks and Hispanics have produced conflicting results, with some studies supporting an association between hyperinsulinemia and blood pressure[45,46] and others not.[47,48] Relatively little information has been generated about the specific role of risk factor clustering and CHD risk in African Americans, and effective strategies and interventions that might reduce such clustering are lacking.

IMPLICATIONS FOR THERAPY

The high CHD morbidity and mortality rates in African Americans can, to a large degree, be accounted for by the high prevalence of CHD risk factors in this group. Many of these (cigarette smok-

TABLE 1
FACTORS THAT INFLUENCE THE DECISION TO INITIATE CHOLESTEROL-LOWERING THERAPY*

Risk factors	
Age	
Men	≥ 45 years
Women	≥ 55 years or premature menopause without estrogen replacement
Family history of premature coronary heart disease†	
Current cigarette smoking	
Hypertension	
Low high-density cholesterol (HDL) level (< 35 mg/dL)	
Diabetes mellitus	
Protective factor	
High HDL cholesterol level (≥ 60 mg/dL)	

*Adapted from the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, reference 49
†Myocardial infarction or sudden cardiac death before age 55 in father or other male first-degree relative, or before age 65 in mother or other female first-degree relative

ing, hypertension, physical inactivity, and obesity) are modifiable and thus present opportunities for primary and secondary prevention.

Diet and physical activity

All modifiable risk factors should be approached vigorously in patients with hypercholesterolemia. Patients who smoke cigarettes should be urged to stop. Dietary modification is the cornerstone of therapy for patients with hypercholesterolemia, hypertension, obesity, or diabetes mellitus. The principles of dietary modification for each of these disorders are similar and include reducing the intake of calories, saturated fat, total fat, cholesterol, and alcohol. Weight reduction and control and increased physical activity are also essential for effective management. Even limited weight loss is often helpful. It is important to remind patients that weight reduction and control are long-term rather than short-term therapies, and success will be achieved only through long-term lifestyle modifications that emphasize both nutritional balance and physical activity. Moderate exercise helps in losing weight, lowering cholesterol, reducing hyperinsulinemia (even without weight loss), lowering blood pressure, improving cardiovascular fitness, and decreasing overall cardiovascular risk.[37]

Treating hypercholesterolemia

The National Cholesterol Education Program's Adult Treatment Panel (ATP) recently released revised and updated recommendations for treating adults with hypercholesterolemia.[49] In specific reference to African Americans, the ATP noted that although LDL levels are similar in blacks and whites (and HDL levels are higher in blacks), efforts to reduce cholesterol and other CHD risk factors in African Americans are especially important because of their higher CHD mortality rates at younger ages and their higher prevalence and severity of hypertension, diabetes mellitus, cigarette smoking, and physical inactivity.

The ATP report addressed several new issues that have special significance for treating African Americans with high blood cholesterol. These included:

CHD risk status as a guide to intensity of therapy. The intensity of treatment of hypercholesterolemia should depend on the individual patient's risk status. Patients should be placed into one of three risk categories in order to determine the most appropriate cholesterol-lowering therapy: (1) those at highest risk because of previously diagnosed CHD or other atherosclerotic disease (peripheral arterial disease or symptomatic carotid artery disease); (2) patients without evident CHD but who have multiple other CHD risk factors and thus are at high risk; and (3) patients with hypercholesterolemia but who are otherwise at low risk.

Primary prevention. Primary prevention refers to the treatment of high blood cholesterol in patients without evident CHD. Patients with high-risk LDL levels (≥ 160 mg/dL) and those with borderline high-risk levels (130 to 159 mg/dL) who have two or more risk factors (*Tables 1* and *2*) should be evaluated clinically and receive active cholesterol-lowering dietary therapy. *Table 2* summarizes the cholesterol levels at which to initiate dietary therapy and consider drug treatment in patients with and without CHD.

Secondary prevention. Treatment of elevated LDL in patients known to have CHD or other atherosclerotic disease is referred to as "secondary prevention." These patients should begin dietary treatment if their LDL concentrations exceed 100 mg/dL. The goal of therapy is to reduce the LDL concentration to 100 mg/dL or less.

Drug therapy. In secondary prevention, drug therapy is generally indicated if the LDL level equals or exceeds 130 mg/dL despite a trial of maximal dietary therapy. If the LDL level remains in the range of 100 to 129 mg/dL, the potential benefits of drug therapy

must be weighed against possible side effects and costs. For primary prevention, drug treatment can be considered for adults whose LDL levels equal or exceed 190 mg/dL with fewer than two other risk factors or 160 mg/dL with two or more other risk factors. In young men (35 years or younger) and premenopausal women who are otherwise at low risk, drug therapy should be reserved for those with LDL levels of 220 mg/dL or higher.

TABLE 2
TREATMENT DECISIONS BASED ON LOW-DENSITY LIPOPROTEIN LEVELS*

Risk group	Low-density lipoprotein level (mg/dL)		
	Threshold for diet therapy	Threshold for drug therapy	Goal of therapy
With coronary heart disease (CHD)	> 100	≥ 130	≤ 100
Without CHD and two or more risk factors	≥ 130	≥ 160	< 130
Without CHD and with fewer than two risk factors	≥ 160	≥ 190	< 160

*Adapted from the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, reference 49

The major drugs for cholesterol lowering are the bile-acid sequestrants (cholestyramine and colestipol), nicotinic acid, and the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors (ie, the "statins"—lovastatin, pravastatin, simvastatin, and fluvastatin). The fibric acid derivatives (gemfibrozil, clofibrate) and probucol are not listed as major drugs because they do not usually produce substantial reductions in LDL. The bile-acid sequestrants are useful in patients with moderately elevated LDL, especially young adult men and premenopausal women, because they do not cause systemic toxicity. Nicotinic acid lowers total cholesterol and triglyceride levels and raises HDL levels, but has several side effects that may limit its use. The statins appear relatively safe and are very useful for treating severe forms of hypercholesterolemia and for lowering the LDL level maximally in secondary prevention.

Estrogens may be useful as specific therapy for lipid modification in some postmenopausal women. Findings from observational[50] and prospective studies[51] suggest that estrogen replacement therapy has a beneficial effect on lipid levels and reduces CHD risk in postmenopausal women. Therefore, patients who require estrogens for other indications (ie, osteoporosis), may derive additional benefit in terms of lipid modification and overall cardiac risk reduction.

APPROACH TO MULTIPLE RISK FACTORS

The management of high blood cholesterol in African Americans is complicated by the frequent coexistence of other risk factors such as hypertension, diabetes, and obesity. When approaching a patient with high blood cholesterol, the potential impact of treatment for these other conditions must be kept in mind.

Hypercholesterolemia and concomitant hypertension

High blood cholesterol and hypertension frequently coexist in African Americans. Patients with high blood cholesterol have a higher-than-expected prevalence of hypertension, and patients with hypertension have a higher-than-expected prevalence of high blood cholesterol. Diet, exercise, and other nonpharmacologic therapies are the essential first step for both hypertension and hypercholesterolemia. Emphasis should be placed on weight reduction in overweight patients, as well as on decreasing the intake of saturated fat, total fat, cholesterol, and alcohol.

When drug therapy is required to lower the blood pressure, one should consider the treatment's expected benefits, its effects on quality of life, concomitant diseases, and the cost of treatment. Preference should be given to antihypertensive agents that do not adversely affect lipid levels. Calcium antagonists, angiotensin-converting enzyme inhibitors, hydralazine, minoxidil, potassium-sparing diuretics, and reserpine have minimal if any effects on lipid levels. Thiazide diuretics can cause modest and often transient increases (5 to 10 mg/dL) in the serum levels of total cholesterol, LDL, and triglycerides but have little or no adverse effects on HDL. The effects of loop diuretics are similar to those of thiazides, with increases in total and LDL cholesterol, whereas HDL levels are generally lower in patients receiving furosemide. Beta blockers without intrinsic sympathomimetic activity (ISA) or alpha-blocking properties tend to reduce HDL, increase triglycerides, and have variable effects on

total serum cholesterol. Beta blockers with ISA and the beta blocker labetalol (which has alpha-1-adrenergic blocking properties) produce no appreciable changes in lipid levels. Although the effects of antihypertensive drugs on the efficacy of lipid-lowering agents have not been carefully evaluated, among participants in the Coronary Primary Prevention Trial taking thiazide diuretics, LDL levels did not decrease as much as in those not using thiazide diuretics.[48]

Thiazide diuretics have proven particularly valuable for treating hypertension in African Americans. Therefore, even though thiazides may adversely affect lipids in some patients, their use should not be avoided if they are needed to achieve optimal blood pressure control. Their possible adverse effects on lipids should be balanced by considerations of efficacy, safety, and tolerability.

In selecting lipid-lowering therapy, several potential adverse effects on blood pressure control should be kept in mind. Bile-acid sequestrants may decrease the absorption of thiazide diuretics and propranolol, and these antihypertensive medications should therefore be given 1 hour before or 4 hours after the sequestrant. Nicotinic acid may enhance the decrease in blood pressure caused by vasodilators. Fibric acid derivatives are more likely to produce myopathy in patients with renal failure, and thus the dosage should be decreased in these patients, who should be carefully monitored.

Diabetes and dyslipidemia

In dyslipidemia secondary to untreated or poorly controlled diabetes, triglyceride levels are high, HDL levels are low, and LDL levels tend to be in the normal range or mildly elevated. In managing diabetic patients, attention must be given to reversible risk factors, especially cigarette smoking and weight control. Control of hyperglycemia will also help to lower cholesterol and triglyceride levels. The treatment of coexisting hypertension should be undertaken with lipid-neutral antihypertensive agents. Adherence to a diet low in saturated fat and cholesterol may further correct the dyslipidemia.

Some clinicians view diabetes as a special case and suggest that diabetic patients undergo aggressive lipid-lowering therapy, similar to that given patients with established CHD, especially patients who have other risk factors. This is true for women as well as men, since the protection against CHD enjoyed by women appears to be lost in the presence of diabetes. Diabetic patients who need to reduce their LDL levels markedly often require drug therapy. Bile acid sequestrants are effective but may raise triglyceride levels (which may already be high in diabetic patients). Nicotinic acid is relatively contraindicated in patients with NIDDM since it tends to worsen glucose tolerance. Fibric acid derivatives effectively lower triglyceride levels and may be preferred when hypertriglyceridemia predominates. The statins are generally the most practical agents to use in diabetic patients with hypercholesterolemia and have the advantage of producing a marked reduction of LDL levels with a moderate decrease in triglycerides, but they increase HDL levels only modestly.

COMPLIANCE CONSIDERATIONS

Although the benefits of lowering the cholesterol level and blood pressure, stopping smoking, and exercising are well documented, many patients do not adhere to recommended therapy and thus do not succeed in lowering their risk. Approximately 50% of patients with hypertension fail to keep follow-up appointments, and only 60% take medications as prescribed. From 15% to 46% of patients taking lipid-lowering drugs discontinue them within the first year, depending on the specific agent prescribed.[52] The reasons for poor adherence with recommended therapy are multiple and include poor doctor-patient communication, cost of therapy, and side effects of medications. Physicians and patients must be mutually committed to the goals of therapy and to achieving control of risk factors.

Physicians must select therapy that is convenient, affordable, and effective and that minimally detracts from quality of life. They must give clear instructions to their patients, spend time educating them about the importance of controlling risk factors, and communicate in a positive manner (giving reassurance, support, and encouragement) rather than a negative manner (showing anger or anxiety). Physicians must also regularly monitor patient adherence and drug side effects. Failure to monitor patients effectively long-term contributes to noncompliance, as shown by the numbers of hypertensive patients lost to medical follow-up or who continue in medical care but miss appointments and fail to follow physician advice.

Patients, on their part, must keep follow-up ap-

pointments, follow nonpharmacologic recommendations, and inform their physicians and nurses about other medications they may be taking and about problems with medications.

SUMMARY AND CONCLUSIONS

The myth that African Americans are immune to CHD has been largely dispelled. African Americans have a high level of CHD risk factors and are at increased risk of CHD mortality. Risk factor modification for both primary and secondary prevention is therefore especially important. Diet, weight reduction and control, increased physical activity, and other nonpharmacologic measures are the cornerstones of therapy and should receive special emphasis. When pharmacologic therapy is required, one should select the appropriate drug after considering the benefits, concomitant diseases, costs, and quality of life.

Effective strategies for modifying individual risk factors (hypertension, hypercholesterolemia, smoking) have been developed and promulgated. However, similar strategies for multiple risk factor reductions are lacking. Such strategies and interventions need to be developed, particularly for African American patients. Treatment for patients with multiple risk factors must be effective, safe, well tolerated, and affordable. The successful development and implementation of such programs is one of the major clinical practice challenges facing physicians and other health-care providers in the 1990s.

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