

EDITORIAL COMMENT

The Ethnic-Specific Nature of Mechanisms for Coronary Heart Disease*

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Cardiovascular disease extracts an enormous toll from the life and health of America's black population. The increased differential effect of cardiovascular disease on African Americans is particularly marked in women (1). Figure 1 shows the annual rate of first heart attack by age in the U.S. for black and white men and women between 1987 and 1994 (2).

Recent reductions in cardiovascular morbidity and mortality in the U.S. have been less impressive in black individuals. Gillum (3) reported that the age-adjusted death rates for white men fell faster than the same statistic for black men between 1980 and 1990. Cooper (4) reported that, while a similar deceleration in coronary heart disease incidence existed for blacks and whites before 1979, incidence curves have been diverging since that year so that the ethnic gap in coronary heart disease incidence is widening.

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Evidently, we have been achieving less progress in reducing risk in black individuals. Some have attributed this differential to reduced deliverance of health care and health information to black individuals and have called for a targeted response, which would increase the quantity of preventive therapy to the African-American community (4-7). Few have considered the possibility that fundamental ethnic differences in disease mechanism might be present and that such differences might require a different preventive approach in different ethnic groups. The potentially enormous public health implications of examining such ethnic differences in disease mechanism behoove that they be addressed.

Pathologic substrates are an obvious, though imperfect, source to search for potential difference in disease mechanism. Strong and McGill (8) found a higher prevalence of fatty streaks but fewer fibrous plaques in the arteries of adult African Americans compared with adult Caucasians. In the tables displayed in another publication (9), they reported the ethnic-specific prevalence of calcific deposits in the diseased

aortas of these subjects. They found that fibrous plaques were calcified 60% more frequently in the aortas of blacks compared with whites. They also found a much lower relative prevalence of calcified versus noncalcified plaques in the coronary arteries of black individuals. Some recent reviews of pathologic material from adults whose death certificates attributed death to atherosclerotic disease have shown that instead many black individuals are misclassified and actually died from severe cardiomyopathy (10).

Modern technology allows assessment of preclinical cardiovascular disease of arteries and of the heart. Such pathologic markers such as increases in left ventricular mass and carotid intimal thickness and coronary calcific deposits can be related to disease risk factors in cross-sectional studies and to outcomes in longitudinal studies. The increased prevalence and severity of cardiac left ventricular hypertrophy in black individuals is well known. Liao et al. (11) found left ventricular hypertrophy to be a more powerful predictor of mortality in black individuals symptomatic of heart disease, and they found extent of arterial disease a more powerful predictor in a similar group of whites. This finding raises the possibility that myocardial disease may be a more important target for prevention in black individuals.

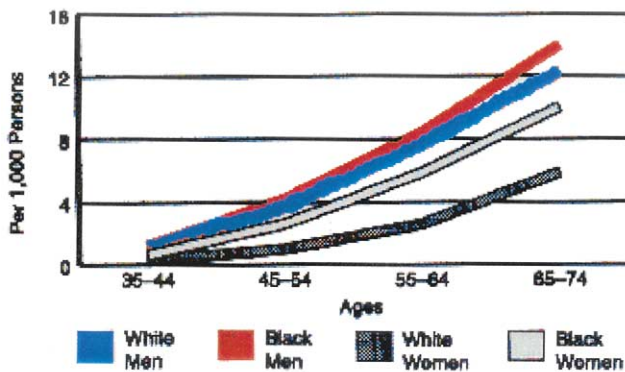
Carotid ultrasonic measurements of arterial intimal thickness were studied in the Atherosclerotic Risk In Communities (ARIC) and Cardiovascular Health Studies (CHS). In the former, Arnett et al. (12) found a lesser severity of carotid intimal thickness in black individuals and a stronger relationship between blood pressure and carotid intimal thickness in white men compared with black men. In a cohort of older men and women in the CHS study, Manolio et al. (13) found that black individuals had more pronounced carotid intimal thickness than whites. The ethnic-specific data on coronary calcification has been more consistent. The article by Lee et al. (14) in this issue of the *Journal* adds to the accumulating evidence (15-18) that computed tomographically measured atherosclerotic calcification is less prevalent and severe in blacks than it is in whites.

There are two intriguing hypotheses that might explain why clinical disease expression (higher incidence of myocardial infarction and coronary death) is not reflected by greater extent of coronary calcium in black individuals. The most obvious explanation is that symptoms in black individuals are more frequently related to intrinsic myocardial disease than to arterial occlusive disease. By this hypothesized mechanism, black individuals have lesser degrees of atherosclerosis but greater degrees of myocardial disease. Oxygen demand, electrical instability, and hemodynamic myocyte stress may be more important in black individuals while reduced oxygen supply and sudden occlusions with abrupt cessation of coronary flow may be more important in

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Annual Rate of First Heart Attacks by Age, Sex and Race
United States: 1987-94



Source: Rates in the NHLBI's ARIC surveillance study, 1987-94.

Figure 1. Annual rate of first heart attack by age, gender, and race, U.S.: 1987 to 1994.

whites. Much of the evidence presented above is consistent with this mechanistic difference.

Another hypothesis involves differences in deposition of hydroxyapatite in already diseased vessels. By this hypothesis, black individuals may have the same, lesser, or greater extent of atherosclerosis, but more of the unstable noncalcified variety (19). This could result from known ethnic differences in calcium metabolism (20). This would imply that the atherosclerotic process, itself, is ethnic-specific. The intriguing finding of ethnic-specific variation of the effect of hypertension on arterial intimal thickness (12) and the marked ethnic differences in coronary calcium severity noted in both pathological and clinical studies (9,14-18) support this hypothesis.

Establishment of a fundamental ethnic-specific mechanism of symptom expression, whether involving arteries, myocardium, blood rheology, or other aspects would be an important first step toward developing an ethnic-specific strategy for risk reduction. The Multi-Ethnic Study of Atherosclerosis (MESA) (21) will evaluate over 6,500 asymptomatic men and women in four ethnic groups with carotid ultrasound, coronary computed tomography, and cardiac magnetic resonance imaging. Study personnel will follow these subjects for seven years for cardiac end points. Analysis will be able to establish ethnic- and gender-specific relationships between subclinical markers and cardiac outcomes. If studies like MESA support ethnic differences in the relationships between these markers and future events, a firm basis for further research into such differences will have been established, and a more aggressive ethnic-specific approach toward national guidelines for risk reduction will be justified.

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REFERENCES

- Gillum RF, Mussolin ME, Madans JH. Coronary heart disease incidence and survival in African American women and men. *Ann Intern Med* 1997;127:111-8.
- American Heart Association. American Heart Association. 2002 Heart and Stroke Statistical Update. Dallas, TX: American Heart Association, 2001.
- Gillum RF. Trends in acute myocardial infarction and coronary heart disease deaths in the United States. *J Am Coll Cardiol* 1994;23:1273-7.
- Cooper R. A note on the biologic concept and its application in epidemiologic research. *Am Heart J* 1984;108:715-23.
- Rosenman R, Friedman M, Straus R, Jenkins CD, Zysanski S, Wurm M. Coronary heart disease in the Western Collaborative Group study. *J Chronic Dis* 1970;23:173-82.
- Marmot MG, McDowell ME. Mortality decline and widening social inequalities. *Lancet* 1986;2:274-6.
- Stamler J. Coronary heart disease: doing the "right things." *N Engl J Med* 1985;312:1053-5.
- Strong JP, McGill HC. The natural history of aortic atherosclerosis: relationship to race, sex, and coronary lesions in New Orleans. *Exp Mol Pathol* 1963;Suppl I:15-27.
- Tejada C, Strong JP, Montenegro MR, Restrepo C, Solberg LA. Distribution of coronary atherosclerosis by geographic location, race and sex. *Lab Invest* 1968;18:509-26.
- Crawford-Green C, Green W, Allen C. Is coronary artery disease the leading cause of death in black Americans (abstr)? *J Am Coll Cardiol* 1994;23:338A.
- Liao Y, Cooper RS, McGee DL, Mensah GA, Ghali JK. The relative effects of left ventricular hypertrophy, coronary artery disease and ventricular dysfunction on survival among black adults. *JAMA* 1995; 273:1592-6.
- Arnett DK, Tyroler HA, Hutchinson RG, Heissw HG. The paradoxical effect of hypertension and its association with sub-clinical atherosclerosis in African Americans (abstr). *Circulation* 1995;91:P17.
- Manolio TA, Burke GL, Psaty BH, et al. Black white differences in subclinical disease among older adults: the Cardiovascular Health Study (CHS) (abstr). *Circulation* 1993;88:1913.
- Lee TC, O'Malley PG, Feuerstein I, Taylor AJ. The prevalence and severity of coronary artery calcification on coronary artery computed tomography in black and white subjects. *J Am Coll Cardiol* 2003;41: 39-44.
- Newman AB, Naydeck BL, Sutton-Tyrell K, Feldman A, Edmondowicz D, Kuller LH. Coronary artery calcification in older adults to age 99: prevalence and risk factors. *Circulation* 2001;104:2679-84.
- Tang W, Detrano RC, Brezden OS, Puentes G, Reed J, Grim C. Racial differences in coronary calcium prevalence among high risk adults. *Am J Cardiol* 1995;75:1088-91.
- Khurana C, Rosenbaum C, Howard B, et al. Coronary artery calcification in African-American and white women. *Am Heart J*. In Press.
- Loria CM, Detrano R, Liu K, et al. Sex and race differences in prevalence and predictors of early coronary calcification: the CARDIA study (abstr). *Circulation* 2002;105:e86.
- Detrano R, Doherty T, Davies MJ, Stary HC. Predicting coronary events with coronary calcium: patho-physiologic and clinical problems. *Curr Probl Cardiol* 2000;25:374-402.
- Doherty TM, Tang W, Dascalos S, et al. Ethnic origin and serum levels of 1,25-dihydroxyvitamin D3 are independent predictors of coronary calcium mass measured by electron-beam computed tomography. *Circulation* 1997;96:147-8.
- Multi-Ethnic Study of Atherosclerosis (MESA), sponsored by the NHLBI. Available at: <http://140.142.220.3/mesa/>. Accessed on June 10, 2002.