RACIAL (BLACK-WHITE) CONTRASTS OF RISK FOR HYPERTENSIVE DISEASE IN YOUTH HAVE IMPLICATIONS FOR PREVENTIVE CARE: THE BOGALUSA HEART STUDY

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Cardiovascular (CV) diseases remain the major cause of illness and death in the United States. Adverse CV outcomes are influenced by race/ethnicity and sex. Race and sex contrasts of CV risk factors become evident early in life and have implications for prevention and medical care. Changes in the CV system in hypertensive disease are mediated by interplay among body fatness, insulin sensitivity, and other factors such as renin-angiotensin system and electrolyte homeostasis. Observations from the Bogalusa Heart Study found higher blood pressure levels in Black children even without obesity, renin as a component of the metabolic/insulin resistance syndrome mainly in Whites, and Black-White differences in electrolyte handling, eg, lower urinary excretion of potassium in Blacks. Understanding divergences in hemodynamic and metabolic parameters for developing hypertensive disease can help improve approaches to beginning prevention at an early age. The use of low doses of antihypertensive medications along with prudent diet and physical activity may be considered for children with elevated blood pressure. (*Ethn Dis*. 2006;16[suppl 4]: S4-2–S4-9)

Key Words: Black-White Contrasts, CV Risk Factors, Hypertension, Preventive Care

INTRODUCTION

That cardiovascular (CV) risk factors occur in childhood and are predictive of future risk for adult heart disease is now well established by long-term epidemiologic studies like the Bogalusa Heart Study.[1–4] Further, the presence of "silent," asymptomatic CV diseases, including hypertensive end-stage renal disease and coronary atherosclerosis, appear to begin in early life. Although the precise initiating factors of adult CV diseases are still being investigated, identifying the earliest determinants of CV risk offers hope for prevention of future clinical heart disease. Hypertensive CV diseases are complex traits governed by multiple genes, environmental factors, and their interactions.

Major advances in understanding CV risk for the development of adult heart diseases have been made during the past three decades by following children into adulthood.[5–9] For example, most observations concerning hypertension have been made by studying adults, with limited information concerning the pathophysiology of essential hypertension in early life. Most experience in treating primary hypertension has been in adults, but anatomic evidence of early target organ damage consistent with the onset of hypertensive target organ disease has been seen beginning in childhood.[10] Similarly, coronary atherosclerosis is found in

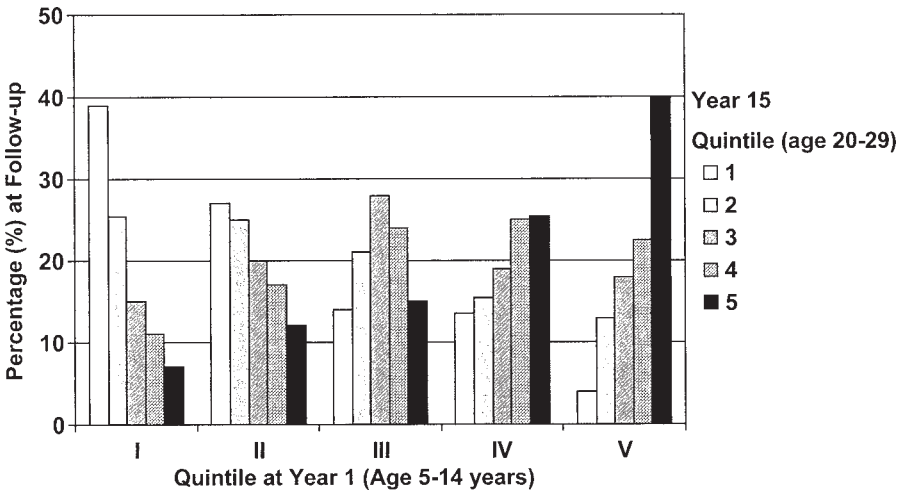

Fig 1. Systolic blood pressure of children is shown to persist from the top quintile in childhood to remain in the top quintile after a 15-year period. Baseline and follow-up blood pressures are stratified by quintiles. Of those individuals who had systolic blood pressure levels above the 80th percentile at baseline, 40% had levels above this percentile 15 years later. Another 23% had levels between 60th and 80th percentile. A similar persistence for low ranks was seen at the lower quintiles. As for the diastolic pressure, weaker but similar persistence was observed. Among individuals whose diastolic blood pressure levels were above the 80th percentile at baseline, 37% remained in the top quintile 15 years later. 9% had levels below the 20th percentile[13]

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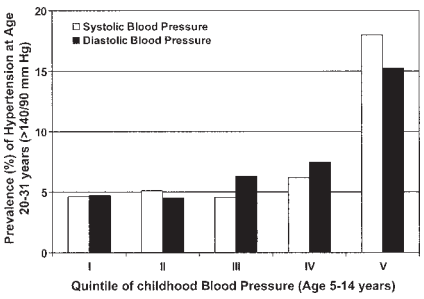

Fig 2. Approximately 15% of children at the top quintile developed adult hypertension levels (≥140/90 mm Hg) by 20–31 years of age, beginning at levels much lower than JNC VII. The prevalence of hypertension is given by age-, race-, and sex-specific quintiles of baseline childhood blood pressure level. Subjects who were in the highest quintile were likely to develop hypertension: 3.6 times (18% vs 5%) in systolic blood pressure and 2.6 times (15% vs 5.8%) in diastolic blood pressure. All other individuals had similar low prevalence around 5%, indicating that the hypertensive children were likely to develop adult hypertension[13]

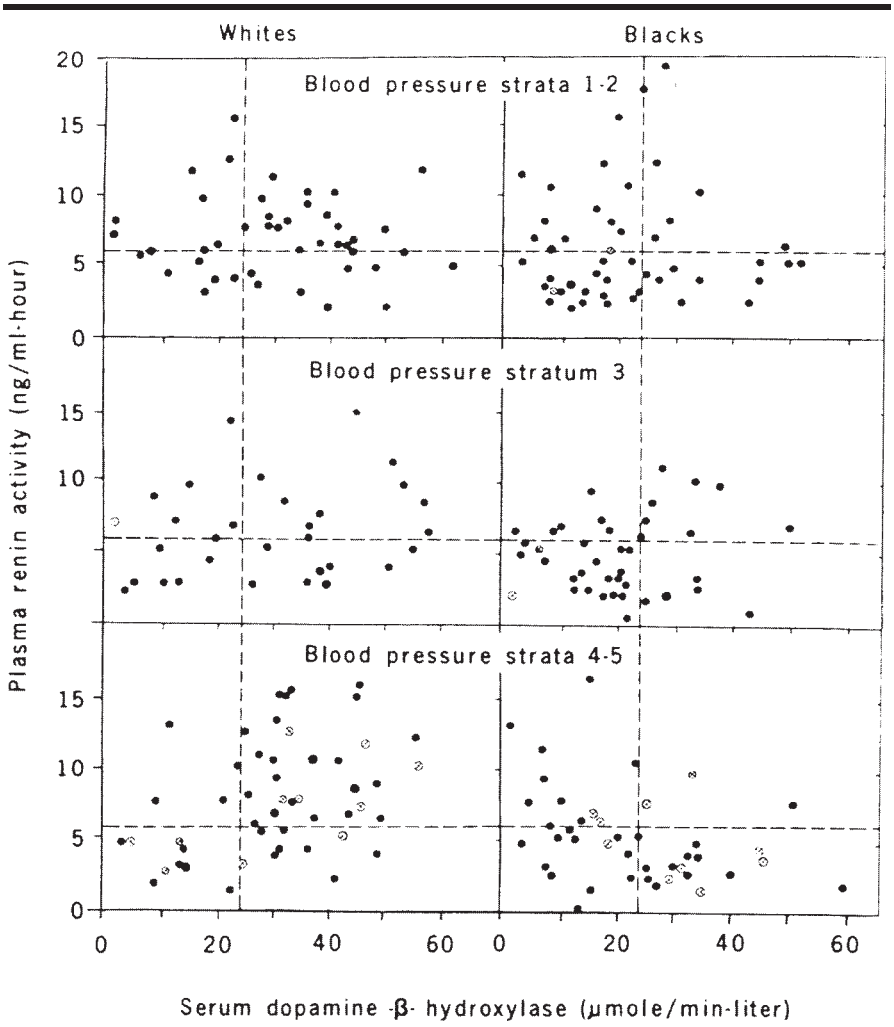

Fig 3. Renin and dopamine β hydroxylase levels by race and blood pressure strata. Note the low levels in Blacks at the high blood pressure strata. Figure 3 shows scattergrams of plasma renin activity compared to serum dopamine B-hydroxylase for the different blood pressure strata in White and Black young individuals (5 to 14 years). Strata 1 and 2 were the low quintiles and 4 and 5 were the high quintiles. Note the preponderance of children with combined high renin and high DßH, occurring in white children with low renin levels among the Blacks[28]

young individuals, and the prevalence of coronary atherosclerosis occurs broadly in the general population, even at a young age.[11,12] Understanding the early natural histories of hypertension and atherosclerosis becomes a prerequisite for early prevention to avoid the clinical ravages associated with heart disease in adulthood.

The Bogalusa Heart Study is a comprehensive epidemiologic study of early natural history of CV diseases in a population of children and young adults in a biracial (Black-White), rural, low socioeconomic community of Bogalusa, Louisiana. The cohort has been followed since 1973 to provide a database from birth to 45 years of age.

TRACKING OF CV RISK FACTORS

The tracking of risk factors over time is a good measure that adult CV risk factors and potential CV disease can be predicted from observations in early life. Risk factors track with varying degrees, and as might be expected, the greatest tracking occurs for anthropometric measurements, such as height and weight. Excess weight for height and obesity as measured by body mass index (BMI, kg/m^2) begins at an early age. Total serum cholesterol and low-density lipoprotein (LDL) cholesterol track almost as well; however, lower levels of tracking occur for triglycerides, high-density lipoprotein (HDL) cholesterol, and blood pressure. Systolic blood pressure (SBP) tracks better than diastolic blood pressure (DBP), which may in part be due to limitations in measurements. Because of the low order of tracking of single measurements of blood pressure, repeated and serial measurements are needed in childhood to predict future abnormally high levels. Figure 1 shows the persistence of SBP levels over a 15-year period.[13] Some 60% of subjects remain in the top two quintiles. Similar observations occur

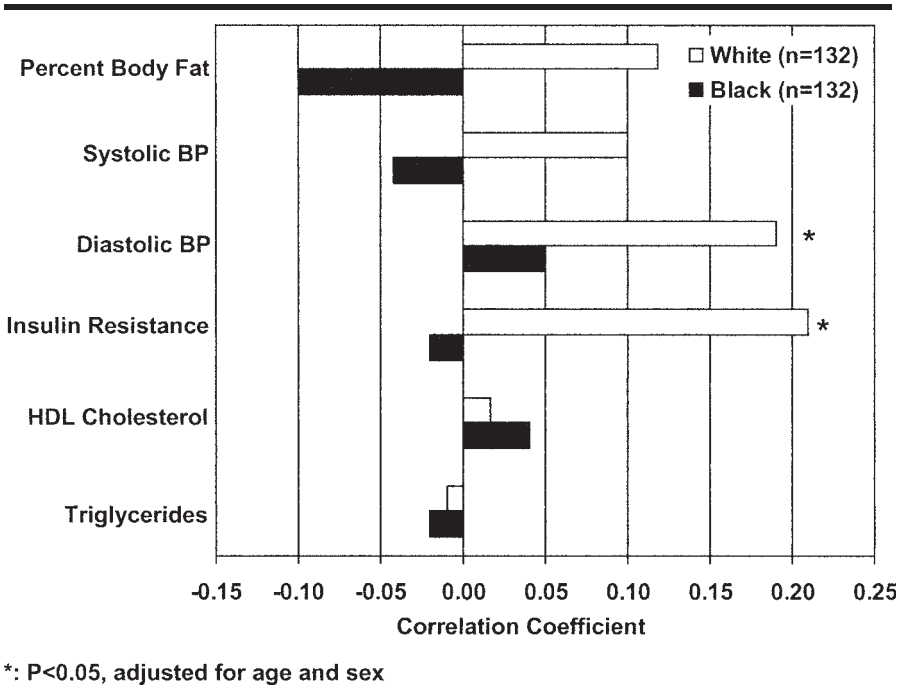

Fig 4. Correlations of various risk factors related to the metabolic syndrome with plasma renin activity by race. Figure 4 shows partial Pearson correlation coefficients, adjusted for sex and age, between renin activity and other risk variables by race. Renin activity was significantly correlated with diastolic blood pressure ($r = .21$, $P < .05$) and insulin resistance index ($r = .19$, $P < 0.05$), in White children but not with other variables. Note the direction of renin activity in Black children[32]

with diastolic levels. Long-term observations indicate childhood blood pressures are predictive of adult hypertension (Figure 2).[13] Identification of children tracking at the 90th percentile of blood pressure related to their height or body mass is consistent with target organ CV system change.[10,12,14]

Although less established than evidence of coronary atherosclerosis and hypertension, factors related to adult-onset type 2 diabetes mellitus and the metabolic syndrome can also be detected in childhood. For example, insulin resistance has been shown by careful insulin clamp studies to occur in young Blacks.[15] Racial contrasts of carbohydrate-insulin metabolism occur in offspring of parents with type 2 diabetes, noted by lower insulin secretion (C-peptide response to glucose load) in Black offspring than in White offspring.[16–18] In the overall studies of children, Blacks tend to have higher insulin levels but lower C-peptide levels.[17,18]

Long-term observations are still needed to show the predictability of diabetes from various childhood parameters and the evolution to overt type 2 diabetes. Of interest are the Black-White and sex differences in carbohydrate-insulin-C-peptide variables related to the metabolic syndrome and potential precursors of clinical diabetes.[17–20] As found in the metabolic syndrome, hypertension becomes one of the major components contributing to silent CV disease, and following the cluster of risk factors related to obesity and insulin resistance is of interest.[20,21]

SECULAR TRENDS

Of particular importance is the secular trend of markedly increasing obesity over the past 30 years. Obesity has increased in the general US population, including an increase of obesity in children. From the 1970s to 1980s, the average increase of body weight of Bogalusa children was 2.5 kg (≈5 pounds), and from the 1980s to 1990s it was 5.0 kg (≈12 pounds). These differences were significant ($P = .01$), without a significant increase in height.[22] Among the four race-sex groups, a greater secular increase in obesity occurs in young Black females and the overweight in all race-sex groups. Obesity along with insulin resistance is the driving force of the clustering of risk factors in metabolic syndrome.[20,21] Elevated blood pressure is part of the clustering even in childhood, especially in White children.[23–25] An increase in blood pressure levels is now being found in children by analysis of National Health and Nutrition Examination Survey data, likely related to this secular increase of obesity.[26]

Racial Contrasts in Blood Pressure

Although serum lipids and lipoproteins track and are associated with underlying anatomic disease, blood pressure with its racial contrasts will be discussed in more detail. The current options for prevention and medical management in childhood seem somewhat better based on a longer and broader experience using antihypertensive medication. Adult hypertension with its origin in childhood is the second most common CV disease in the United States and is closely related to the development of atherosclerosis and diabetes mellitus. Thus, we must understand its natural history and the various facets of the disease. Observations made in the biracial (Black-White) population of Bogalusa, Louisiana, have contributed to understanding the origin of hypertension and have noted some of the multiple mechanisms that appear to be involved in the disease. Studies have been conducted to show its complexity even in its early stages. To obtain such information, careful measurements must be made to identify abnormal

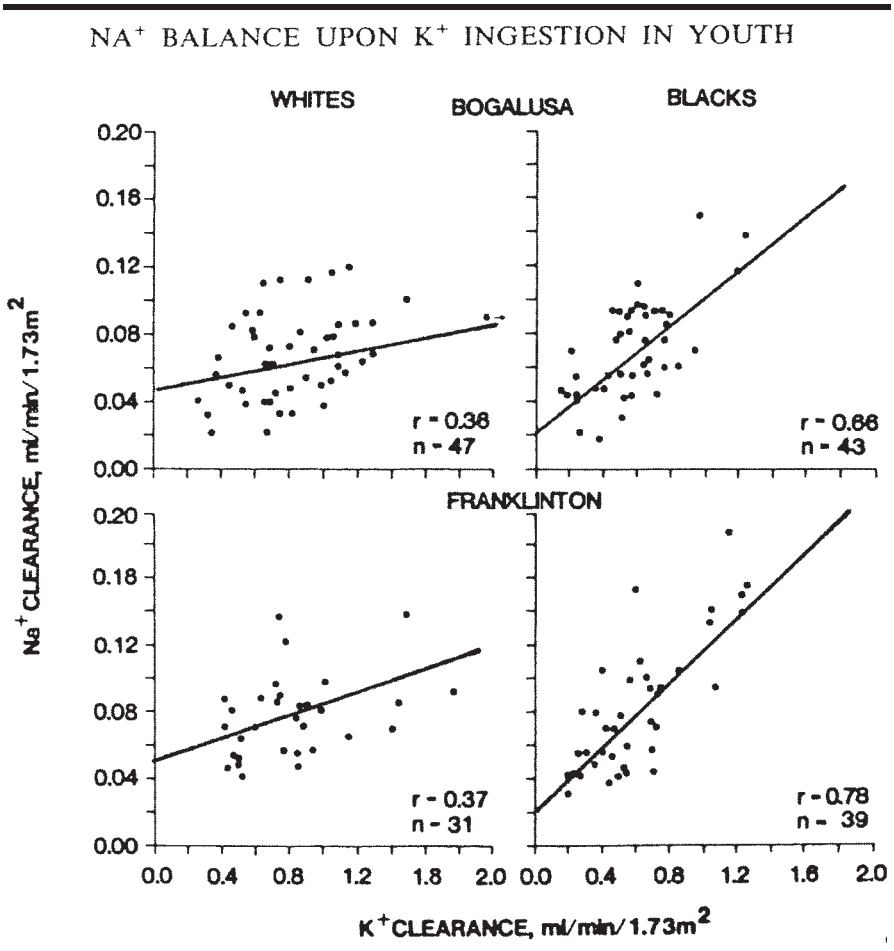

Fig 5. Slope of 24 hour urine Na+/K+ clearance ratios by race. Figure 5 shows relation of Na^+ vs K^+ clearance for children age 7 to 18 years in upper decile of blood pressure, by race and community. Blacks tended to have stronger correlation of Na^+ with K^+ clearance than Whites ($P < .01$)[33]

Table 1. Contrasts regarding correlates of blood pressure levels in Black and White children: The Bogalusa Heart Study

Whites>Blacks	Blacks>Whites
All blood pressure strata	
Percentage body fat	Blood pressure (BP)
Plasma renin activity	
Dopamine $^{\beta}$-hydroxylase ($D^{\beta}H$)	
Fasting plasma glucose	
24-hour urine K^+	
High blood pressure strata	
Resting heart rate	Peripheral resistance
Cardiac output	Correlation of 24-hour urine Na^+ with BP
Renin activity and DβH	Inverse correlation of plasma renin with BP (males only)
One-hour post glucose plasma glucose	

levels,[23,24] since levels are much lower than considered abnormal in adulthood. Further, blood pressure cannot be taken out of context with its interrelationship with other CV risk factors.[25,27]

With growth, children's blood pressure increases considerably, by systolic 1.7 mm Hg/year and diastolic .7 mm Hg/year until adult stature is reached at ≈15 years of age in girls and ≈18 years of age in boys.[24] Blood pressures were somewhat higher in Black children than in Whites, detected with an automatic instrument and later during the adolescent age with use of the mercury sphygmomanometer.[23] Children, ages 7 to 15 years, at low, middle, and high blood pressure levels, were studied to explore early determinants of blood pressure levels in Blacks versus Whites.[28–31] Obesity was clearly related to elevated blood pressure levels in White but not in Black children. Black males, especially, tend to be thin and have slower heart rates but higher peripheral resistance. One-hour post glucose load plasma glucose levels were greater in Whites than in Blacks. Further, insulin levels tend to be higher and glucose and C-peptide levels lower in Blacks.[19] In addition, at the high levels of blood pressure, renin and dopamine β-hydroxylase were much greater in White children; that is, renin levels were lower in Black children as have been noted in Black adults with hypertension (Figure 3).[28] The correlations of plasma renin levels showed significant racial contrasts; risk variables were related to the metabolic syndrome (Figure 4).[32] Although dietary intakes were comparable, Black children showed approximately 25% lower 24-hour urinary K^+ excretion than White children. Further, at high blood pressure levels a relationship of Na^+ excretion to blood pressure tended to be positive in Black children. The lower excretion of K^+ was also found by examining slopes of 24-hour urinary Na^+/K^+ clearance (Figure 5).[33] Correlation of Na^+ with K^+ clearance, shown in Table 1, further illustrates these electrolyte differences.

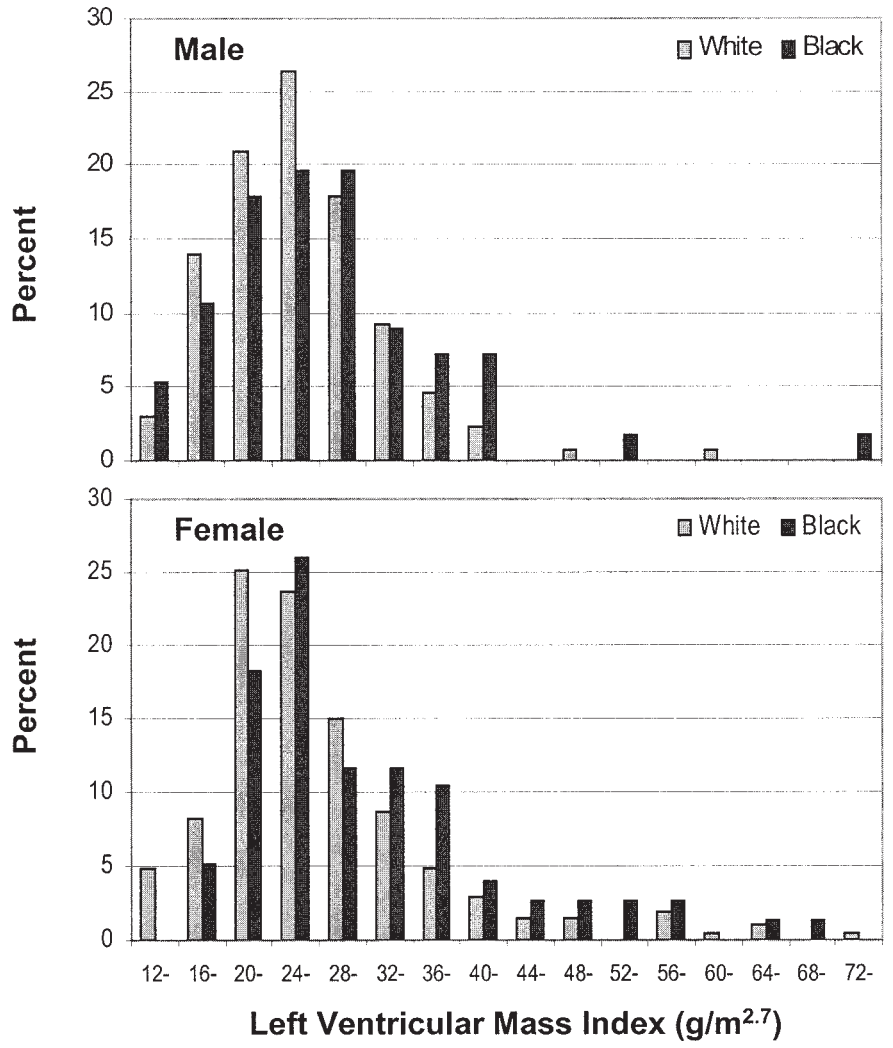

Fig 6. Distribution of left ventricular mass ($g/m^{2.7}$) in a biracial population of young adults (*N*=467) aged 20-38 years. Consistently greater left ventricular mass was found in Blacks

Supplementation of 80 mEq of K^+ to a regular diet over a period of four days in young Black and White adults showed that Blacks tended to retain more K^+ than Whites.[33] Further, potassium administration resulted in lowering of blood pressure, more so in Blacks than in Whites. The racial contrasts presented above provide clues to mechanisms contributing to the development of hypertension at an early age among Blacks vs Whites. Of note, dietary intake of children showed two- to three-fold higher sodium intake and lower levels of potassium in the diet than the recommended levels.

Detrimental renal effects of elevated blood pressure were studied in terms of microalbuminuria. Higher blood pressure levels beginning in childhood were associated with microalbuminuria in young Black adults but not in their White counterparts.[6] These observations are consistent with the long-term burden of blood pressure levels contributing to more rapidly advancing renal disease in Blacks.[6,34,35]

CV Structure-Function Studies Related to Blood Pressure Levels

Anatomic observations provide evidence of the effect of elevated blood pressure on target organ changes that begin in childhood. As an example, small arteries, 200–400 μm, show increasing thickening at autopsy related to blood pressure levels.[10] Nephrosclerosis related to hypertension occurs more often in Blacks than Whites.[35] Echocardiography showed increased posterior wall thickness at the top quintile of blood pressure levels, even when adjusted for body size.[14] Cardiac output was greater in White males and peripheral vascular resistance greater in Black males.[36] More detailed studies showed greater left ventricular mass in young Black adults compared to Whites (Figure 6). Additional anatomic studies of carotid vessel intima-media thickness (IMT), particularly at the bifurcation or the bulb region, showed a significant trend to be greater with an increasing Framingham risk factor score or multiple risk factors.[37,38] In general, IMT is greater in males and in Blacks. Heart rate variability studies suggest increased parasympathetic activity in young Blacks,[39] while a blunted nocturnal decline in blood pressure with generally high levels by 24-hour ambulatory measurements have been documented.[40,41] Further, less brachial artery distensibility occurs in Black subjects.[42] Although the racial contrasts are often related to socioeconomic factors, the above ethnic variations occur, especially in youth in a total population within a similar environment.

Approaches to Prevention

The importance of beginning primary prevention early has to be emphasized. A goal is to establish the effectiveness of primary prevention; however, this alone in a large population is almost impossible. Extrapolating treatment experiences from adult heart diseases to needs for prevention beginning in youth, without understanding clinical physiologic and metabolic characteristics occurring in early life, produces a disparate medical approach to prevention by age. We feel primary prevention begun in childhood

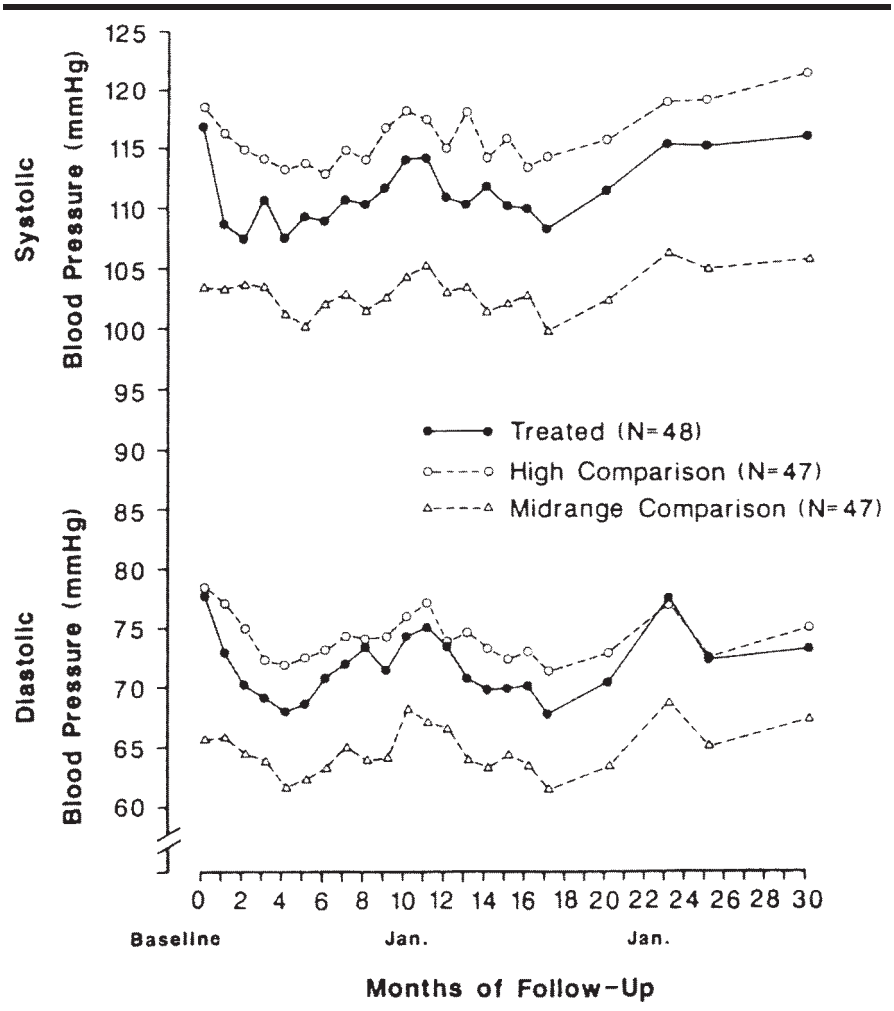

Fig 7. Blood pressure levels in children tracking at the 90th percentile treated with low dose medication, propranolol and chlorthalidone, diet, and exercise compared to controls at the 90th percentile and at mid-range levels. For all children (race/sex combined) in the treatment group, a significant decrease in BP occurred soon after onset of treatment. A drop of 10 mm Hg in systolic was noted during the first month. An overall decrease in systolic BP was noted when compared with the untreated high-comparison group. The decrease in BP in the treatment group persisted at 17 and 30 months of followup[44]

can have a tremendous effect over a lifetime. Improvement in lifestyles, such as increased physical activity, weight control, and improved nutrition, including dietary electrolytes, are basic. The observations showing racial differences, like with obesity more closely related to higher blood pressure in White children and low K^+ urinary excretion in Blacks, emphasize the importance of differential management beginning early in life. While the genetic influences are still being elucidated, weight control, exercise, and reduced Na^+ and increased K^+ are critical. Although the individual propensity for hypertension is related to an intrinsic genetic background, for example in salt-sensitive individuals, environmental factors can be altered that help control or prevent hypertension.[43]

A High-Risk Approach

Even in childhood, antihypertensive medication may be necessary to prevent progressive anatomic and organ changes that begin in early life, if abnormal blood pressure levels persist. We conducted a successful but short-term study that altered diet, increased exercise, and used low-dose medication for children tracking at the 90th percentile (Figure 7).[7,44] These children were selected after serial measurements of replicate blood pressure readings. We already had noted anatomic evidence of target organ changes by autopsy and by echocardiography.[10,14] Such an option for treatment has improved greatly with clinicians' experience using antihypertensive medication.

A Public Health or Population Approach

A more comprehensive prevention program and public health model is obviously needed because of the broad prevalence of risk factors in the general population. We have developed and conducted a comprehensive health education program at the elementary school age, since health education can reach a larger number of children who are destined to become adults with CV risk factors by adult criteria. The program is called "Health Ahead/Heart Smart."[45] It addresses the entire school environment, not only the classroom, with extensive teachers' guides, but includes, cafeteria, physical education with noncompetitive exercises, and programs to improve teachers' and parents' lifestyles. Health education in early life has the potential to produce tremendous benefits broadly and encompass health promotion for large numbers of children and parents at all socioeconomic levels.

COMMENT

Prevention should become a major role for physicians. Beginning prevention in early life to prevent or modulate CV risk factors, such as obesity and hypertension, has to be a goal of cardiologists, pediatricians, and primary care physicians.[46] Reduction of disparities in health care can be addressed by

health promotion beginning in childhood. Prevention of atherosclerosis, hypertension, and type 2 diabetes should be targets for preventive cardiology at a young age.

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