The Conjoint Trait of Low High-Density Lipoprotein Cholesterol and High Triglycerides in Adolescent Black and White Males

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To evaluate the interrelationships among body composition, blood pressure, and lipid phenotypes in adolescent black and white boys, we assessed racial distributions of lipids, blood pressure, and obesity and their joint occurrence in black and white boys aged 10 to 15 years. Subjects were recruited from Cincinnati (OH) schools. Because the differences in high-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs) are the most profound coronary heart disease (CHD) risk factor differences between black and white males, we assigned subjects to one of four low-HDL-C and high-TG categories (normal and increased risk) using the age/race-specific 25th (HDL-C) and 75th (TG) percentiles. We then assessed racial distributions of lipids, blood pressure, and obesity by these phenotypes. Age differences between the black and white participants were significant, with the former about 3 months younger ($P = .03$), but black boys were more mature and were significantly taller and heavier and had a greater body mass index ([BMI] weight in kilograms divided by height in centimeters squared). Differences in the sum of the triceps, subscapular, and suprailiac skinfolds were not significant. Blacks had significantly higher HDL-C, lower TG, and higher diastolic blood pressure (DBP), but differences in systolic blood pressure (SBP) were not significant. In both racial groups, the body composition measures were significantly correlated with HDL-C, TG, and blood pressure levels; the correlations between HDL-C and both weight and BMI were significantly stronger in white boys. The proportion of boys of each race with low HDL-C and high TG was similar by design. In both racial groups, subjects with the conjoint trait had a significantly greater BMI, triceps skinfold, and sum of skinfolds than subjects in the other phenotypic groups. For white boys, participants with the conjoint trait had the highest SBP and DBP; differences in SBP were significant for comparisons to the normal- and high-TG group alone, and differences in DBP were significant for the comparison between normal and low HDL-C alone. For black boys, subjects with both normal HDL-C and TG had significantly lower SBP than boys with either the conjoint trait or high TG alone; none of the group differences in DBP were significant. Black had significantly less dense LDL (more LDL-C per apolipoprotein [apo] B). In each racial group, boys with the conjoint trait had the most dense LDL, significantly more dense than in any of the other phenotypes in black boys and significantly more dense than in boys with low HDL-C alone and normal boys in the white group. In both racial groups, the occurrence of no risk factors (>75th percentile TG, BMI, SBP, and DBP or <25th percentile HDL-C) and three or more risk factors was greater than expected by chance alone, and the occurrence of exactly one risk factor and two factors was less. When examined by phenotypic groups within race, boys in each racial group with the normal phenotype had a greater than expected percentage with no risk factors, and white boys with the conjoint trait were more likely to have a marked increase in multiple risk factors. Possible mechanisms for this clustering of risk factors and for the racial differences in the patterns are discussed.

RACIAL DIFFERENCES IN high-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs) are the most profound and unambiguous coronary heart disease (CHD) risk factor differences between black and white males: black boys have significantly higher HDL-C and lower TG than white boys,[1-4] and these differences persist into adulthood.[5,6] By contrast, data on racial differences in blood pressure during youth are less clear, with some investigators reporting no significant blood pressure differences between the races, some reporting higher blood pressure in blacks, and some reporting higher blood pressure in whites.[7-9] To some extent, the various findings are influenced by geography and neighborhood,[10,11] socioeconomic differences between subjects of different races,[12] the measuring devices used,[8] and the portion of the distribution examined.[8] In adulthood, racial differences in blood pressure become unequivocally different, statistically significant, and clinically important.[7]

The risk of CHD associated with low HDL-C is increased when elevated TGs are also present,[13,14] even though elevated TG levels have not been shown to be an independent risk factor for CHD in multivariate statistical analyses.[15] The combination of low HDL-C plus high TG (the conjoint trait) is more common in white versus black males.[16] HDL-C and TG levels and blood pressure are all significantly correlated with obesity, the correlations being direct for TG and blood pressure and inverse for HDL-C.[7,17,18] During ages 6 to 11 years, white boys have slightly but consistently larger mean values for the sum of triceps and subscapular skinfolds, while differences in the body mass index ([BMI] weight in kilograms divided by height in centimeters squared) are not consistent.[19]

Puberty is a period of marked growth in boys, with significant increases in the BMI and the sum of triceps and subscapular skinfolds[17,18]; during this period, there are concomitant changes in blood pressure and TG and HDL-C levels.[1-4,7] These changes in risk factor levels occur in both black and white males, but black boys have smaller decreases in HDL-C and smaller increases in TG.[1-4] Consequently, adolescent black males continue to have higher HDL-C and lower TG.[1-4] In adulthood, black men have higher blood pressure, without changes in the racial differences in HDL-C and TG.[7,16] The absolute and relative changes in these two lipid parameters and blood

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pressure levels from childhood to adulthood in black and white males are not fully understood, and the physiological basis for the interrelationships among obesity and HDL-C, TG, and blood pressure in each race remains unclear. Data on adults from the Atherosclerosis Risk in Communities (ARIC) study[20] suggest that black men have larger incremental changes (decrements) in HDL-C levels per unit increase in BMI than white men, despite having higher HDL-C. The racial contrasts in lipid profiles thus may be partially the result of differences in lipoprotein metabolism between blacks and whites.

The Sex Hormones and Lipoproteins in Adolescent Males Study, a cohort study of adolescent growth and its effects on CHD risk factors in black and white boys, provides an opportunity to examine the interrelationships among body composition, blood pressure, and lipid phenotypes in black and white boys in the prepubertal and early, middle, and late pubertal stages of development. In this analysis, because of the profound racial differences in HDL-C and TG, we examined potential mechanistic differences by first assigning subjects to one of four HDL-C and TG categories (normal and increased risk) and then assessing racial distributions of lipids, blood pressure, and obesity by these phenotypes.

SUBJECTS AND METHODS

Study Population

Male students in grades 5 to 9 in selected Cincinnati (OH) elementary and high schools were enrolled for the study, targeting ages 10 to 15 years. In recruiting the students, a letter citing the endorsement of the program by the school principals was sent to the parents of all eligible students, explaining the purposes and methods of the study. A few days later, trained field workers contacted the students' parents by telephone and home visits to explain the study, answer any questions, and obtain signed informed consent. Demographic data were collected by interview with the subject's parents, including the subject's date of birth and race. A boy was eligible for the study if he and his parents declared him to be "black" or "white." The protocol was approved by the University of Cincinnati College of Medicine Institutional Review Board.

Clinical Assessments

Height was measured to the nearest 0.25 in with the subject's shoes off, feet together, and head in the Frankfort horizontal plane. Weight was measured to the nearest 0.1 kg using a calibrated hospital scale with the subject's shoes, sweaters, coats and jackets removed. Two methods for assessing body habitus were used for this analysis: (1) BMI (a measure of ponderosity, weight in kilograms divided by height in meters squared) and (2) skinfold thickness (adiposity). Skinfold measurements were made at the triceps, subscapular, and suprailiac sites by trained technicians (measurer and recorder) using Lange skinfold calipers according to the method of Behnke and Wilmore.[21] Skinfolds were measured to the nearest 0.5 mm on the subject's right side with the subject in a standing position. Two measurements were taken at each site, with a third measurement taken if the first two differed by greater than 1.0 mm. The mean of all readings was used in these analyses. Blood pressure was measured using a standard sphygmomanometer after the subject had been sitting quietly for 5 minutes. Measurements were taken on the right arm with the arm resting on a hard flat surface at heart level with an appropriate-size cuff as recommended by the National Heart, Lung, and Blood Institute (NHLBI) Task Force on Blood Pressure in Children.[22] The onset of the fifth Korotkoff phase was used to define diastolic blood pressure (DBP). One blood pressure measurement was taken.

The stages of puberty were scored by visual assessment of pubic hair according to Marshall and Tanner[23] and measurement of testicular size by comparison to an orchidometer, a series of ovoid beads calibrated to represent testicular volume from prepubertal through adult age. Pubertal maturation stages were then scored again using the modification of the Tanner method by Biro et al[24]: stage 1, no pubic hair and testicular volume less than 3 cc; stage 2a, no pubic hair and testicular volume at least 3 cc; and stages 2b, 3, 4, and 5, pubic hair at Tanner stages 2, 3, 4, and 5, respectively. Stage 1 represents prepuberty, stages 2a and 2b represent early puberty, stages 3 and 4 represent midpuberty, and stage 5 represents late puberty. The assessments were made by a specialist in adolescent medicine and by male physician assistants trained by the adolescent specialist. Ten milliliters of blood was drawn into tubes containing EDTA for lipid, lipoprotein cholesterol, and apolipoprotein analyses. Immediately following blood aspiration, the phlebotomist placed the tubes in a styrofoam rack in a cooler containing chemical coolant. All samples were separated in the laboratory within 2 hours.

Laboratory Measurements

Lipid profiles were measured in the Lipid Laboratory of the Department of Internal Medicine at the University of Cincinnati College of Medicine. The laboratory was NHLBI-Centers for Disease Control–standardized and in phase III of standardization. Analyses were performed on a Hitachi 705 analyzer (Boehringer Mannheim, Indianapolis, IN) using enzymatic procedures for cholesterol and TG measurement, as well as TG blanking, and the modified Lipid Research Clinics procedure (heparin–2-mol/L $MnCl_2$) for HDL-C.[25-27] Total apolipoprotein B (apo B) was assayed by electroimmunoassay.[28]

Statistical Analyses

All analyses were performed using SAS Version 5.18.[29] Age- and race-specific percentiles derived from the current cohort were used to classify participants into risk groups. For this analysis, HDL-C at or below the 25th percentile was defined as low, and HDL-C above the 25th percentile was defined as normal; similarly, TG at or above the 75th percentile was defined as high and TG below the 75th percentile as normal. The age/race-specific cutoff points for HDL-C ranged from 51 mg/dL (age 11 years) to 42 mg/dL (age 15 years) in white boys and from 54 mg/dL (age 12 years) to 46 mg/dL (age 14 years) in black boys. For TG, the cutoff points for white boys ranged from 63 mg/dL to 93 mg/dL, and for black boys, from 64 to 79 mg/dL. Four analysis groups were defined using these percentiles as follows: (1) low HDL-C/high TG, (2) low HDL-C, (3) high TG, and (4) normal. In similar fashion, the age/race-specific 75th percentile levels of selected risk factors were used to categorize black and white subjects into normal and high-risk subgroups: BMI, low-density lipoprotein cholesterol (LDL-C), and SBP. The number of subjects with zero, one, two, three, four, and five risk factors was determined, and the observed clustering was compared with that expected under an assumption of independence using a likelihood ratio chi-square test.

The associations among study variables (the body composition measures of BMI, triceps skinfold thickness, and the sum of the three skinfold measures, HDL-C, LDL-C, TG, SBP, and DBP) were evaluated using Spearman's rank-order correlations. Racial differences in correlations were evaluated using Fisher's Z test. A regression model was used to test for differences in the BMI, triceps skinfold, sum of truncal skinfolds, SBP and K5 DBP, and the ratio of LDL-C to apo B across the four phenotypic groups and between races. Adjustments for age and maturation stage were made by entering age into the model as a linear term and maturation stage as a set of indicator variables. Racial differences in the distribution of maturation stages were tested using a chi-square analysis. All analyses were repeated using overall quartiles and race-specific deciles to define high and normal risk, and results similar to those obtained when race-specific quartiles were used to

Table 1. Study Variables in Black and White Males Aged 10 to 15 by Race: The Sex Hormones and Lipoproteins in Adolescent Males Study

Characteristic	White (n = 282)	Black (n = 249)	P
Age (yr)	12.7 ± 0.09	12.9 ± 0.09	.059
Height (cm)	155.2 ± 0.45	158.0 ± 0.48	<.001
Weight (kg)	46.7 ± 0.63	50.6 ± 0.68	<.001
BMI (kg/m²)	19.0 ± 0.20	20.0 ± 0.21	<.001
Maturation stage			<.001
Prepubertal	19%	9%	
Early puberty	46%	37%	
Middle puberty	31%	48%	
Late puberty	4%	6%	
HDL-C (mg/dL)	53.5 ± 0.69	60.8 ± 0.73	<.001
TG (mg/dL)	67.4 ± 2.00	54.9 ± 2.14	<.001
LDL-C/apo B ratio	1.07 ± 0.015	1.16 ± 0.016	<.001
Triceps skinfold (mm)	13.2 ± 0.38	13.1 ± 0.40	.944
Sum of skinfold (mm)	39.3 ± 1.32	40.6 ± 1.41	.507
SBP (mm Hg)	109.8 ± 0.70	110.8 ± 0.74	.295
DBP (mm Hg)	67.9 ± 0.51	70.2 ± 0.55	.002

NOTE. All means, with the exception of age, are presented as the least-squares mean ± SE adjusted for age. Mean age is unadjusted.

define risk levels were obtained, except that using quartiles provided larger numbers of participants in the subgroups and therefore more power. Thus, the analyses based on quartiles are presented.

RESULTS

Measurements were obtained on 285 white students and 251 black students, representing 74% and 68% of eligible white and black students, respectively. Of 536 subjects, three white and two black boys were missing HDL-C data and were excluded from further analyses. Population characteristics of the analysis sample of 282 white and 249 black boys are summarized by race in Table 1. On average, the black boys were younger than the white boys, but the age difference, albeit significant, was less than 0.3 years (4 months). Because more black boys had started puberty and black boys were more mature than white boys (Table 1, $P < .001$), least-square means are presented after adjusting for age and pubertal maturation stage. After adjusting for age and pubertal stage, the more mature black males were still taller and heavier and had a greater BMI than the white males. Differences in SBP between black and white boys were not significant, but black males had higher DBP. Racial differences in triceps skinfold thickness and the sum of truncal skinfolds were not significant. Black boys had higher HDL-C and lower TG than white boys. No subjects were diabetic.

Table 2 presents the correlations between the anthropometric measures (BMI, triceps skinfolds, and sum of skinfolds) and the lipid (HDL-C and TG) and blood pressure measures. In both black and white boys, all body composition measures were significantly and positively correlated with TG and blood pressure and significantly and negatively correlated with HDL-C. Testing for racial differences in the correlation coefficients indicated that correlations for HDL-C with weight ($-.26$ *v* $-.50$) and BMI ($-.20$ *v* $-.44$) were stronger in whites than in blacks. Adjusting the correlations for pubertal maturation had only a minimal effect on the correlations and did not alter the racial differences (data not shown).

Table 3 presents the mean ± SD values for the anthropometric variables (BMI, triceps skinfold thickness, and the sum of three truncal skinfold measures), SBP and DBP, and the ratio of LDL to apo B in each of the four HDL-C-TG groups. The means have been adjusted for age and pubertal maturation stage. There was no significant association between pubertal maturation and the HDL-C-TG phenotype (data not shown). The proportion of subjects in each race with low HDL-C or high TG was similar by design. When deciles were used to define the phenotypic groups, the proportion of participants with low HDL-C or high TG was also similar by design, but the percentage of white participants with the conjoint trait was 1.5-fold the percentage in black boys ($P < .05$; data not shown). In black boys, subjects with the conjoint trait had a significantly greater BMI, triceps skinfold, and sum of skinfold thicknesses than black boys with low HDL-C alone or with the normal phenotype; differences in these measures compared with boys with high TG alone were significant for both skinfold indices but not for BMI. Similarly, white boys with the conjoint trait had a significantly greater BMI, triceps skinfold, and sum of three skinfolds than boys in any of the other groups. White boys with high TG alone had the second highest means for the triceps skinfold and the sum of skinfolds; differences were significant for comparisons to normal boys for the sum of skinfolds. Interestingly, boys with low HDL-C alone had a lower triceps skinfold thickness than white boys with normal HDL-C and TG, although the differences did not reach statistical significance. By comparison, black boys with low HDL-C alone had a mean sum of skinfolds, mean triceps skinfold, and mean BMI that were significantly lower than in boys with high TG alone. The range of the mean BMI, triceps skinfold, and sum of skinfolds across the four

Table 2. Partial Correlations (Spearman) Among Body Composition, Blood Pressure, HDL-C, and TG in the Study Cohort by Race Adjusting for Maturation Stage: The Sex Hormones and Lipoproteins in Adolescent Males Study

	White					Black				
Variable	HDL-C	TG	LDL-C	K1	K5	HDL-C	TG	LDL-C	K1	K5
Weight	−.39*	.26	.13	.36	.17	−.20	.20	.06†	.38	.26
BMI	−.36*	.30	.23	.38	.22	−.15	.22	.16	.27	.20
Triceps skinfolds	−.17	.32	.25	.29	.23	−.07†	.24	.24	.19	.15
Sum of truncal skinfolds	−.24	.34	.24	.38	.27	−.10†	.30	.24	.26	.18

Abbreviations: K1, systolic blood pressure; K5, diastolic blood pressure (disappearance of sound).

*$P < .05$ for comparison of correlations between black and white boys.

†Correlation not significantly different from zero.

Table 3. Body Composition Measures, Blood Pressure, and Lipid Levels by HDL-C/TG Group and Race: The Sex Hormone and Lipoproteins in Adolescent Males Study

Parameter	Low HDL-C/High TG (W: n = 25; B: n = 24)	Low HDL-C (W: n = 36; B: n = 31)	High TG (W: n = 42; B: n = 35)	Normal (W: n = 179; B: n = 156*)
BMI				
White	21.6 ± 0.55‡§‖	19.4 ± 0.47†‖	19.4 ± 0.42†‖	18.4 ± 0.20†‡§
Black	23.1 ± 0.71‡‖	19.8 ± 0.63†§	21.9 ± 0.60‡‖	19.2 ± 0.28†§
Triceps SF				
White	17.2 ± 1.09†‡‖	12.1 ± 0.91†	14.2 ± 0.85†	12.7 ± 0.40†
Black	19.7 ± 1.37†‡‖	12.3 ± 1.21†§	15.9 ± 1.15†‡‖	11.7 ± 0.53†§
Sum of SFs				
White	54.8 ± 3.84†‡‖	37.8 ± 3.19†	43.3 ± 2.99†‖	36.6 ± 1.40†§
Black	66.1 ± 4.70†‡‖	37.6 ± 4.13†§	52.0 ± 3.94†‡‖	35.0 ± 1.82†§
SBP				
White	115.8 ± 2.32§‖	111.9 ± 1.92	108.1 ± 1.78†	108.7 ± 0.85†
Black	116.3 ± 2.31‖	110.9 ± 2.03	116.4 ± 1.94‖	109.3 ± 0.90†§
DBP				
White	70.5 ± 1.72	69.1 ± 1.44‖	67.0 ± 1.33	67.5 ± 0.63‡
Black	72.2 ± 1.77	71.3 ± 1.55	72.0 ± 1.48	69.7 ± 0.69
LDL/apo B				
White	0.89 ± 0.05‡‖	1.08 ± 0.04†	1.00 ± 0.04‖	1.11 ± 0.02†§
Black	1.03 ± 0.05†‡‖	1.18 ± 0.05†	1.18 ± 0.04†	1.17 ± 0.02†

NOTE. Values are the least-squares mean ± SE adjusted for age and maturation.
*Three black males with normal HDL-C and TG had missing apo B measurements.
†$P < .05$ *v* low HDL-C/high TG group of same race.
‡$P < .05$ *v* low HDL-C group of same race.
§$P < .05$ *v* high TG group of same race.
‖$P < .05$ *v* normal group of same race.

phenotypic groups was greater in black boys than in white boys (Table 3).

Within the white group, boys with the conjoint trait had the highest SBP, significantly higher than in boys with either high TG alone or normal HDL-C and TG (Table 3). White boys with the conjoint trait had the highest DBP (70.5 mm Hg), but only the difference between boys with low HDL-C alone (69.1 mm Hg) and boys with the normal phenotype (67.5 mm Hg) was statistically significant. In black subjects, boys with the conjoint trait and boys with high TG alone had the highest mean SBP (116.3 and 116.4 mm Hg), both significantly higher than in boys with the normal phenotype. None of the differences in mean DBP were significant.

Black boys had significantly less dense LDL (more LDL-C per apo B) than white boys (1.16 ± 0.28 *v* 1.14 ± 0.25, $P = .01$), and there were racial differences in the pattern of LDL density across HDL-C-TG phenotypes. In both races, LDL was most dense in boys with the conjoint trait. In white boys, the differences between subjects with the conjoint trait and those with either the normal phenotype or low HDL-C alone were significant, as was the comparison between boys with high TG alone and boys with the normal phenotype. In black boys, subjects with the conjoint trait had significantly less LDL-C per apo B than any of the other three phenotypic groups, all of whom had similar levels of dense LDL (1.17 or 1.18).

Table 4 presents the number and percentage of subjects by race with zero, one, or more risk factors and the probability of such clustering by chance alone. In each race, the risk factors clustered at much higher rates than would be expected on the basis of chance alone: the percentages of subjects with no risk factors and with three or more were greater than predicted under the assumption of independence, and the percentage with only one risk factor was less than predicted. Racial differences in the extent of clustering were not significant. Table 5 presents the percentage of subjects by race and phenotypic group with zero, one, or more risk factors and the probability of such clustering by chance alone. In both races, boys with normal HDL-C and normal TG were more likely to have no other risk factors (overweight, top-quartile LDL-C, or top-quartile SBP) and less likely to have one or two risk factors than expected. In white boys, 4.5% of the participants with normal HDL-C and TG had an elevated BMI, LDL-C, and SBP, compared with an expected percentage of 1.5%. In this secondary analysis, results were

Table 4. Observed and Expected Percentages of Risk Factors by Race: The Sex Hormones and Lipoproteins in Adolescent Males Study

No. of Risk Factors	Expected Percent	Observed Percent	
		White (n = 285)	Black (n = 251)
0	23.7	36.1	38.7
1	39.6	31.9	28.7
2	26.4	18.6	17.9
3	8.8	7.7	9.2
4	1.5	3.5	5.6
5	0.1	2.1	0.0

NOTE. Risk factors included are HDL-C, TG, LDL-C, BMI, and SBP. Tests for significant difference between observed and expected frequencies: white boys, $\chi^2 = 22.1$, $df = 5$, $P < .001$; black boys, $\chi^2 = 23.1$, $df = 4$, $P < .001$. Test for significant difference in observed frequencies between black and white participants: $\chi^2 = 7.6$, $df = 5$, $P = .179$.

Table 5. Observed and Expected Percentages of Risk Factors by Race and HDL/TG Group: The Sex Hormones and Lipoproteins in Adolescent Males Study

No. of Risk Factors	% Expected	White				Black			
		Normal*	High TG	Low HDL	High TG/Low HDL*†	Normal*	High TG	Low HDL	High TG/Low HDL
0	42.2	57.0	35.7	63.9	32.0	61.0	40.0	38.7	25.0
1	42.2	28.5	47.6	19.4	16.0	28.3	22.9	45.2	37.5
2	14.1	10.1	11.9	13.9	28.0	10.1	25.7	12.9	37.5
3	1.5	4.5	4.8	2.8	24.0	0.6	11.4	3.2	0.0

NOTE. Risk factors included are LDL-C, BMI, and SBP.

*$P \leq .01$, frequencies observed *v* expected.

†$P \leq .05$, between races within risk groups.

affected by the small number of participants in the three subgroups with abnormal lipids. Nevertheless, white boys with the conjoint trait clustered significantly, with fewer boys having no other risk factors or only one other risk factor and more boys than predicted having two and three risk factors ($P < .05$). Black boys with the conjoint trait also exhibited a pattern of fewer boys with none and more boys with two risk factors, but the deviation of the pattern from expected did not reach significance. Similarly, the clustering in white boys with low HDL-C alone and with high TG alone deviated from the expected level, but did not reach significance (Table 5).

DISCUSSION

Using race-specific distributions of HDL-C and TG to classify subjects, similar percentages of white and black boys were identified with low HDL-C and/or high TG, as would be expected. When the more extreme portions of the distributions of HDL-C and TG (deciles) were used to classify participants, the magnitude of the differences in cutoff points for HDL-C and TG was greater but, by design, similar percentages of participants were identified. However, the occurrence of the conjoint trait was about 1.5 times more common in white than in black boys ($P = .05$). The range of body composition measures across HDL-C-TG quartile groups was greater in black boys, with a greater increment in mean levels compared with normal subjects in the group of black boys. However, there were similarities between the races in the relative pattern of body composition measures across groups: in both black and white boys, subjects with the conjoint trait had the highest mean BMI, triceps skinfold, and sum of skinfolds, and subjects with high TG alone had the second highest means.

In black boys, high TG with or without low HDL-C was associated with increased SBP, whereas in white boys, participants with the conjoint trait alone had markedly increased SBP.

White boys had more dense LDL than black boys (less LDL-C per apo B), consistent with the racial differences in TGs, which also have apo B as a major apolipoprotein. The pattern for the ratio of LDL-C-apo B across phenotypic groups also differed between blacks and whites. In both racial groups, subjects with the conjoint trait had a low ratio of LDL-C-apo B and normal boys had high ratios, but in blacks, boys with high TG alone and low HDL-C alone had a ratio similar to that in normal boys, and in whites, boys with high TG alone had a low ratio (ie, dense LDL) and boys with low HDL-C had a higher ratio, which did not differ from the ratio in normal boys. Apo B is the total apo B in a fasting sample, targeting apo B-100. Generally, in individuals with TG concentrations less than 200 mg/dL, the LDL-C to apo B ratio correlates highly with LDL particle size. In the two subgroups in each race with high TG (the conjoint trait and high TG alone), the correlation may weaken, and only four boys (all white) in this sample had fasting TG above 200 mg/dL (205, 210, 215, and 238). Thus, racial differences should be robust. Decreased ratios of LDL-C to apo B have been reported in offspring of parents with premature CHD.

Low HDL-C and high TG have each been associated with obesity in both children and adults.[18] Therefore, it is not surprising that the groups with high TG or low HDL-C would have higher mean levels of the obesity measures. Even though the three body measures used in this study were significantly correlated with both HDL-C and TG, the individual obesity measures may not operate in perfect concert for both HDL-C and TG. Low HDL-C and high TG have different metabolic bases, and the conjoint presence of both low HDL-C and high TG may represent a combination of two defects or, perhaps more likely, a unique, separate entity.[30] In each racial group, subjects with the combined phenotype had the highest BMI and skinfold measures, but there were racial differences in the pattern of skinfold measures in other phenotyptic groups. In white boys, increased adiposity was not associated with low HDL-C alone (increased BMI was), and the mean triceps and sum of truncal skinfolds were lower than the means observed in normal boys. In black boys, low HDL-C alone does appear to be associated with increased adiposity, and the mean triceps and sum of skinfolds were higher than in normal boys, although the difference was not significant. Thus, in white boys, elevated TG appears to be the primary factor associated with increased adiposity in childhood. However, the correlations of obesity measures with HDL-C and with TG in white boys were approximately twice those in black boys, the racial differences here being statistically significant. The correlations of obesity with blood pressure were significant in each race, and there were no racial differences in these correlations.

It is unknown whether the physiologic connection between HDL-C-TG phenotypes and obesity is based on a third (antecedent) factor or is derived from each factor. According to one school of thought, racial differences in the effects of lipoprotein lipase (LpL)[31,32] and insulin[33-35] could be operative in the HDL-C-TG phenotypes here. After matching black and white males for fat distribution, Ama et al[36] found that adult black males expressed higher LpL levels. Since HDL-C and TG levels grossly represent the LpL functional level,[37] this finding is

consistent with the higher HDL-C and lower TG values found in black boys. Ama et al[36] also found that body mass was inversely correlated with LpL levels in blacks, but not in whites. The higher fasting insulin levels reported in black males[38] may explain the upregulation of LpL, since insulin is known to enhance LpL expression posttranslationally. Thus, the relatively lower TG values in black boys could be determined by one or more of three mechanisms: (1) insulin's limiting effect on hepatic very–low-density lipoprotein (VLDL) synthesis, a lipoprotein particle that is TG-rich; (2) insulin's upregulation of LpL, enhancing the metabolic processing of TG-rich lipoprotein particles; or (3) the higher levels of free fatty acids, possibly related to mild insulin resistance and resulting in delayed glucose clearance in white boys. The last explanation is consistent with that of Radhakrishnamurthy et al,[39] who suggested that a higher production of insulin in blacks leads to a condition of relatively greater insulin sensitivity. In summary, the high TG value, then, would reflect an atypical situation of a particularly low output of insulin or some insulin resistance in obese black boys, thus leading to reduced LpL activity, markedly reduced HDL-C, and increased body mass. White subjects with high TG represent a more typical case of insulin resistance, with increased hepatic VLDL secretion. The lack of a primary influence on LpL protects HDL-C from any significant transference onto VLDL, thus preserving the HDL-C value within the usual range. The metabolic route that results in high TG and low HDL-C escapes the concomitant elevation in blood pressure in white boys. It is unknown whether the transfer proteins for HDL-C/VLDL lipid exchange, ie, cholesteryl ester transferase, are influenced by insulin differently between the races.

It is interesting to note the clustering of risk factors in these boys. In both racial groups, the percentage of boys having no risk factors and the percentage having three or more were greater than expected by chance alone, while the percentage of boys with only one risk factor was much less than expected. The percentage with two risk factors was slightly less than expected, but the difference between the observed and the expected value here did not contribute much to chi-square. This finding suggests the presence of an underlying syndrome that carries with it abnormal levels of HDL-C, TG, BMI, and SBP and DBP. This combination of risk factors closely resembles syndrome X. When the clustering of risk factors was further examined in the separate phenotypic groups, significant clustering was noted in normal boys of each race (more participants than expected with no risk factors) and in white boys with the conjoint trait.

Increases in SBP have been associated with defects in the LpL gene,[40] and the related region on chromosome 8 has been linked to SBP in siblings.[41] Thus, alterations in LpL function may partially explain the association of high TG levels and SBP. However, since the LpL gene defects have not been associated with body mass, it is difficult to argue for LpL gene defects as the basis for all aspects of the low-HDL–elevated blood pressure–obesity risk factor complex.

Sympathetic neural tone has been implicated in the development of elevated blood pressure through its effects on vasoregulation and on renin expression and concomitant salt retention. This common approach to elevated blood pressure can be reached through different pathways. First, abnormalities related to insulin receptors may trigger this cascade of risk factors. Insulin resistance and the resulting hyperinsulinemia produce an upregulation of glucose uptake in the ventral medial nucleus of the hypothalmus.[42] Glucose disinhibits an active link in this sympathetic regulatory center to the brain stem, which results in increased sympathetic activity.[43] Dietary excess and the resulting hyperinsulinemia lead to an increase in sympathetic activity and a concomitant increase in energy expenditure. Energy balance is achieved through such a thermogenic process. Thus, insulin resistance and the resulting obesity could result in hypertension as a secondary product of the hypersympathetic state.

Second, a primary increase in sympathetic tone may be the initiating factor. There is some suggestion that the increase in sympathetic activity causes a compromise in the insulin-mediated transport of glucose.[44]

Third, obesity itself may be the primary genetic cause of this risk factor cluster. Leptin, the result of the OB gene, binds to a hypothalamic receptor to reduce food consumption; it has been postulated to activate the sympathetic system. Alternatively, tumor necrosis factor-α increases in obesity and can lead to insulin resistance and downregulation of LpL.[45,46]

Racial differences in sympathetic activity have been reported. Using microneurographic probes to measure nerve activity in peripheral nerves revealed that blacks had greater impulse activity than whites, as well as higher blood pressure levels during cold pressure testing, even though "burst" rates were equivalent at rest.[3] Cold pressure tests, mental stress tests, and isometric handgrip tests all reveal greater increases in sympathetic activity and blood pressure in blacks than in whites.[47,48] The increased sympathetic activity and well-documented salt retention in blacks compared with whites could explain the enhanced blood pressure in blacks and the secondary metabolic changes that lead to lower TG and high HDL-C.

In summary, the conjoint trait of low HDL-C and high TG is associated with extreme body composition measures in boys as young as 10 years of age. Racial differences in HDL-C and TG values in a sample of adolescent boys suggest racial differences in LpL functional levels. The finding that low HDL-C alone in white boys is not linked to any increase in adiposity compared with normals suggests that the association of obesity is primarily with high TG with or without low HDL-C. In black boys, there was a small increase in adiposity in those with low HDL-C alone, which may be additive to that associated with high TG alone. Thus, in blacks, the conjoint trait appears additive. These differences probably reflect a racial difference in the interaction among adiposity, LpL, insulin, and hepatic lipoprotein metabolism.

REFERENCES

1. Morrison JA, deGroot I, Edwards BK, et al: Plasma cholesterol and triglyceride levels in 6,775 school children, ages 6-17. Metabolism 26:1199-1211, 1977

2. Morrison JA, deGroot I, Edwards BK, et al: Lipids and lipoproteins in 927 schoolchildren, ages 6-17 years. Pediatrics 62:990-995, 1978

3. Frerichs RR, Srinivasan SR, Webber LS, et al: Serum cholesterol and triglyceride levels in 3,446 children from a biracial community. Circulation 54:302-309, 1976

4. Srinivasan SR, Frerichs RR, Webber LS, et al: Serum lipoprotein profile in children from a biracial community. Circulation 54:309-318, 1976

5. Morrison JA, Khoury P, Mellies MJ, et al: Lipid and lipoprotein distributions in black adults: The Cincinnati Lipid Research Clinic's Princeton School Study. JAMA 245:939-942, 1981

6. Donahue RP, Jacobs DR, Sidney S, et al: Distribution of lipoproteins and apolipoproteins in young adults—The CARDIA Study. Arteriosclerosis 9:656-664, 1989

7. Morrison JA, Khoury P, Kelly K, et al: Studies of blood pressure in schoolchildren (ages 6-19) and their parents in an integrated suburban school district. Am J Epidemiol 111:156-165, 1979

8. Voors AW, Foster TA, Frerichs RR, et al: Studies of blood pressures in children, ages 5-14 years, in a total biracial community. Circulation 54:319-327, 1976

9. Alpert BS, Fox ME: Racial aspects of blood pressure in children and adolescents. Pediatr Clin North Am 40:13-22, 1993

10. Kotchen JM, Kotchen TA: Geographic effect on racial blood pressure differences in adolescents. J Chron Dis 31:581-586, 1978

11. Kotchen JM, Kotchen TA, Schwertman NC, et al: Blood pressure distributions of urban adolescents. Am J Epidemiol 99:315-323, 1974

12. Burns MD, Morrison JA, Khoury PR, et al: Blood pressure studies in black and white inner-city and suburban adolescents. Prev Med 9:41-50, 1980

13. Assman G, Schulte H: Role of triglycerides in coronary heart disease: Lessons from the Prospective Cardiovascular Munster Study. Am J Cardiol 70:10H-30H, 1992

14. Austin MA: Plasma triglycerides and coronary heart disease. Arterioscler Thromb 11:1-14, 1991

15. Castelli WP, Doyle JT, Gordon T, et al: HDL cholesterol and other lipids in coronary heart disease: The Cooperative Lipoprotein Phenotyping study. Circulation 55:767-772, 1977

16. Morrison JA, deGroot I, Kelly KA, et al: Black-white differences in plasma lipids and lipoproteins in adults: The Cincinnati Lipid Research Clinic Population Study. Prev Med 8:34-39, 1979

17. Laskarzewski P, Morrison JA, Mellies MJ, et al: Relationships of measurements of body mass to plasma lipoproteins in schoolchildren and adults. Am J Epidemiol 111:395-406, 1980

18. Gartside PS, Khoury P, Glueck CJ: Determinants of high density lipoprotein cholesterol in blacks and whites: The Second National Health and Nutrition Examination Survey. Am Heart J 108:641-653, 1984

19. Frisancho AR: Anthropometric Standards for the Assessment of Growth and Nutritional Status. Ann Arbor, MI, University of Michigan Press, 1993

20. Patsch W, Sharrett AR, Sorlie PD, et al: The relation of high density lipoprotein cholesterol and its subfractions to apolipoprotein A-I and fasting triglycerides: The role of environmental factors: The Atherosclerosis Risk in Communities (ARIC) Study. Am J Epidemiol 136:546-557, 1992

21. Behnke AR, Wilmore JL: Evaluation and regulation of body build and composition. International Research Monograph Series in Physical Education. Englewood Cliffs, NJ, Prentice-Hall, 1974

22. US National Heart, Lung, and Blood Institute: Recommendations of the task force on blood pressure control in children: Methodology and instrumentation for blood pressure measurements in infants and children. Pediatrics 59:800-802, 1977

23. Marshall WA, Tanner JM: Variations in the pattern of pubertal changes in boys. Arch Dis Child 45:13-23, 1970

24. Biro FM, Lucky AW, Huster GA, et al: Hormonal studies and physical maturation in adolescent gynecomastia. J Pediatr 116:450-455, 1990

25. Lipid Research Clinics Program: Manual of Laboratory Operations, Lipid Research Clinics Program, vol 1. Lipid and Lipoprotein Analysis. Bethesda, MD, NHLBI, NIH, DHEW Publication No. (NIH) 75-628, 1974

26. Steiner PM, Freidel J, Bremner WF, et al: Standardization of micro-methods for plasma cholesterol, triglyceride, and HDL cholesterol with the Lipid Clinics methodology. J Clin Chem Clin Biochem 19:850, 1981 (abstr)

27. Gidez LI, Miller GJ, Bursten M, et al: Analyses of plasma high density lipoprotein subclasses by a precipitation procedure: Correlation with preparative and analytical ultracentrifugation, in Report of the High Density Lipoprotein Methodology Workshop. Washington, DC, US Government Printing Office, DHEW Publication No. 79-1661, 1979

28. Laurell CB: Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies. Anal Biochem 193:265, 1966

29. SAS Institute: SAS/STAT User's Guide, Version 6, vol 1 and 2 (ed 4). Cary, NC, SAS Institute, 1989

30. Sprecher DL, Feigelson HS, Laskarzewski PM: The low HDL cholesterol/high triglyceride trait. Arterioscler Thromb 13:495-504, 1993

31. Brunzell JD, Albers JJ, Chait A, et al: Plasma lipoproteins in familial combined hyperlipidemia and monogenic familial hypertriglyceridemia. J Lipid Res 24:147-155, 1983

32. Sprecher DL, Kobayashi J, Rymaszeewski M, et al: Trp^{64} nonsense mutation in the lipoprotein lipase gene. J Lipid Res 33:859-866, 1992

33. Zavaroni I, Bonara E, Pagliara M, et al: Risk factors for coronary artery disease in healthy persons with hyperinsulinemia and normal glucose tolerance. N Engl J Med 320:702-706, 1989

34. Mitchell BD, Haffner SM, Hazuda HP, et al: The relation between serum insulin levels and 8-year changes in lipid, lipoprotein, and blood pressure levels. Am J Epidemiol 136:12-22, 1992

35. Despres JP, Ferland M, Moojani S, et al: Role of hepatic-triglyceride lipase activity in the association between intra-abdominal fat and plasma HDL-cholesterol in obese women. Arteriosclerosis 9:485-492, 1989

36. Ama PF, Poehlman E, Simoneau J, et al: Fat distribution and adipose tissue metabolism in non-obese male black African and Caucasian subjects. Int J Obes 10:503-510, 1986

37. Kuusi T, Ehnholm C, Viikari J, et al: Postheparin plasma lipoprotein and hepatic lipase are determinants of hypo- and hyperalphalipoproteinemia. J Lipid Res 30:1117-1126, 1989

38. Burke GL, Webber LS, Srinivasan SR, et al: Fasting plasma glucose and insulin levels and their relationships to cardiovascular risk factors in children: The Bogalusa Heart Study. Metabolism 35:441-446, 1986

39. Radhakrishnamurthy B, Srinivasan SR, Webber LS, et al: Relationship of carbohydrate intolerance to serum lipoprotein profiles in childhood. The Bogalusa Heart Study. Metabolism 34:850-860, 1985

40. Sprecher D, Harris B, Stein E, et al: Higher triglycerides, lower high-density lipoprotein cholesterol, and higher systolic blood pressure in lipoprotein lipase–deficient heterozygotes. A preliminary report. Circulation 94:3239-3245, 1996

41. Wu D, Bu X, Warden C, et al: Quantitative trait locus mapping of human blood pressure to a genetic region at or near the lipoprotein lipase gene locus on chromosome 8p22. J Clin Invest 97:2111-2118, 1996

42. Young J, Lundsberg L: Impaired suppression of sympathetic activity during fasting in the gold thioglucose–treated mouse. J Clin Invest 65:1086-1094, 1980

43. Lerba C, Cepaldo B, Rendisa V, et al: Acute noradrenergic activation induces insulin resistance in human skeletal muscle. Am J Physiol 266:E242-E247, 1994

44. Calhoun DA, Zhu S, Wyss JM, et al: Diurnal blood pressure

variation and dietary salt in spontaneously hypertensive rats. Hypertension 24:1-7, 1994

45. Hotamamieligit GS, Budvari A, Murray D, et al: Reduced tyrosine kinase activity of the insulin receptor in obesity-diabetes. Central role of tumor necrosis factor alpha. J Clin Invest 94:1543-1549, 1994

46. Hauner H, Petruechke T, Rues M, et al: Effects of tumor necrosis factor alpha (TNFα) on glucose transport and lipid metabolism at newly-differentiated human fat cells in cell culture. Diabetologia 38:764-771, 1995

47. Harshfield GA, Alpert BS, Wiley ES, et al: Race and gender influence ambulatory blood pressure patterns of adolescents. Hypertension 14:598-603, 1989

48. Harshfield GA, Alpert BS, Pulliam DA, et al: Sodium excretion and racial differences in blood pressure patterns. Hypertension 18:873-878, 1991