Distribution and Correlates of Serum High-Density Lipoprotein Subclasses (LpA-I and LpA-I:A-II) in Children From a Biracial Community. The Bogalusa Heart Study

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High-density lipoprotein (HDL) subclasses are considered to differ in terms of antiatherogenic potential. Therefore, the distribution and correlates of serum lipoprotein A-I (LpA-I) and LpA-I:A-II were examined in a random community-based subsample of black (n = 1,021) and white (n = 1,087) children aged 5 to 17 years. Black children had significantly higher LpA-I levels than white children. With respect to LpA-I:A-II, prepubertal (age 5 to 10 years) black males and pubertal (age 11 to 17 years) white children showed significantly higher values than their counterparts. With the exception of the LpA-I:A-II difference among prepubertal males, the observed black-white difference was independent of the racial differential in serum triglycerides, a metabolic correlate of HDL. A significant sex differential (males > females) was noted among blacks and whites for both HDL subclasses, with the exception of LpA-I levels at the pubertal age. Among the pubertal age group, a male-female crossover trend (females > males) in LpA-I levels was apparent after age 14. Sexual maturation and age were the major factors (negative) contributing to the variability in the levels of HDL subclasses among race-sex groups; adiposity (negative), insulin (negative), alcohol intake (positive), and oral contraceptive use (positive) emerged as minor but significant predictor variables. In terms of a relation to other lipoprotein variables, LpA-I compared with LpA-I:A-II correlated much more strongly with HDL cholesterol. Unlike LpA-I, LpA-I:A-II was associated significantly (positively) with low-density lipoprotein (LDL) cholesterol. These findings are indicative of intrinsic metabolic differences among the race-sex groups early in life, resulting in variability in the HDL subclass pattern and attendant antiatherogenic potential.

SERUM LEVELS OF HIGH-DENSITY lipoprotein (HDL) cholesterol are independently and inversely related to coronary artery disease (CAD).[1,2] Apolipoprotein A-I (apoA-I), the principal protein moiety of HDL, is considered directly protective against atherosclerosis.[3] In the United States, the incidence of premature CAD is relatively lower in blacks, especially black males, than in whites, although blacks have a greater prevalence of hypertension and other cardiovascular disease risk factors than whites.[4,5] It has been suggested that increased levels of HDL in blacks may account for their reduced CAD risk.[6]

Since HDL particles are heterogeneous in terms of size, hydrated density, lipid and apolipoprotein composition, physiological properties, and metabolism,[7-9] their antiatherogenic potential may vary accordingly. Based on immunological methods, two types of HDL particles have been identified: particles that contain apoA-I without apoA-II (LpA-I) and particles that contain both apoA-I and apoA-II (LpA-I:A-II).[7,10] Both lecithin:cholesterol acyltransferase and cholesteryl ester transfer protein (CETP), mediators of reverse cholesterol transport, are mainly found in LpA-I,[11] while LpA-I:A-II is a preferred substrate for hepatic lipase.[12] Metabolically, LpA-I particles are cleared more rapidly than LpA-I:A-II.[13] Some but not all studies have shown that LpA-I levels have a stronger inverse relation to CAD risk than do LpA-I:A-II levels.[14-16] Therefore, measurement of these HDL subclasses could provide additional information concerning CAD risk assessment.

The pathologic precursors of cardiovascular disease begin in childhood.[17] Further, the initial stages of atherosclerosis relate strongly to adverse levels of lipoproteins in youth.[18,19] Consequently, there has been a great deal of interest in studying the evolution of serum lipoprotein profiles in pediatric populations.[20] However, with respect to LpA-I and LpA-I:A-II, studies have been confined mainly to a small number of white children.[21-23] As part of the Bogalusa Heart Study, a community-based investigation of cardiovascular disease risk factors in early life,[17] this report describes the distribution and correlates of serum LpA-I and LpA-I:A-II in 5- to 17-year-old black and white children of both sexes.

SUBJECTS AND METHODS

Study Population

During the 1992 to 1994 school years, a cross-sectional survey of 3,135 children aged 5 to 17 years was conducted in the biracial (65% white and 35% black) community of Bogalusa, LA. For the present study, all fasting black children of both sexes and a random subsample of white children matched by age and sex were selected to provide equal race-sex distribution. After subjects with missing data for study variables were excluded, the remaining 2,108 subjects (51.6% white and 53.3% female) formed the study sample.

The Tulane University Medical Center Institutional Review Board approved the study. Informed written consent was obtained from a parent or guardian of each child.

General Examination

Children were instructed to fast for 12 to 14 hours, and compliance was determined by interview on the morning of examination. Sexual maturation was determined by visual assessment of secondary sex characteristics by the same physician as part of a physical examination. Ratings of sexual maturation ranged from 1 (no development) to 5 (complete development) according to the stages of female breast or male genitalia development described by Tanner.[24] Height was measured to ±0.1 cm, and weight to ±0.1 kg. The body mass index ([BMI]

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kilograms per square meter) and subscapular skinfold thickness measured to ±0.1 mm were used as measures of body fatness.

Information on life-style characteristics was obtained by questionnaires concerning smoking (grades 3 to 12), alcohol intake (grades 7 to 12), and oral contraceptive use (girls in grades 7 to 12).[25]

Laboratory Analyses

Serum/plasma (EDTA) samples were obtained from antecubital venous blood and sent in a cold-packed box to the New Orleans laboratory. A second blood sample (blind duplicate) was drawn on each screening day from an approximately 10% random subsample of children to estimate the measurement error. Aliquots of samples for LpA-I and LpA-I:A-II measurement were kept frozen at −70°C until analyses were performed. It has been previously found that freezing at −70°C does not influence LpA-I and LpA-I:A-II levels.[26]

LpA-I and LpA-I:A-II. Serum levels of LpA-I and LpA-I:A-II were measured in terms of apoA-I contained in these subclasses. Total apoA-I serum levels were measured by electroimmunoassay (EIA) using a modified Laurell method.[27] The electrophoresis gel consisted of 0.45% polyclonal anti-human apoA-I sera (Boehringer-Mannheim, Indianapolis, IN), 2% (wt/vol) agarose, 2% (wt/vol) dextran (molecular weight, 70,000), and 0.025 mol/L Tris-Tricine buffer (pH 8.6). A serum calibrator (Boehringer-Mannheim) was used as the standard for apoA-I.

Serum levels of LpA-I were measured by immunoprecipitating the particles containing apoA-II with polyclonal anti-human apoA-II sera (Boehringer-Mannheim)[10,27]; apoA-I in the supernatant was assayed by EIA. Levels of LpA-I:A-II were estimated as the difference between total apoA-I in the serum and apoA-I in the supernatant. In EIA, samples treated with and without anti–apoA-II sera were processed under identical conditions and applied next to each other in the gel.

The amount of anti-human apoA-II sera required to quantitatively precipitate LpA-I:A-II particles was determined by incubating serum aliquots (10 μL) containing about 60 mg/dL HDL cholesterol with varying amounts of antibodies (1.3% wt/vol solution) at 4°C for 48 hours and testing the supernatant following centrifugation for immunoreactivity with apoA-II by EIA. The supernatants of samples incubated with 30 and 40 μL anti–apoA-II sera were repeatedly negative for apoA-II by EIA, suggesting that the separation of particles containing apoA-II was complete. Accordingly, 40 μL anti–apoA-II sera was used to precipitate LpA-I:A-II particles from 10 μL serum. In cases where serum levels of HDL cholesterol exceeded 60 mg/dL, a reduced amount (5 μL) of serum was used in the incubation mixture.

Intraassay and interassay coefficients of variation (CVs) of directly measured variables were estimated by repeated measurements of apoA-I in serum and supernatant, using aliquots of frozen pooled serum samples. The respective CV for apoA-I in serum and supernatant was 1.5% to 2.2% and 2.8% to 3.2%. Measurement errors for apoA-I in serum and supernatant based on blind duplicate determinations were 7.5% and 10.3%, respectively. It should be noted that the measurement error from the blind duplicate samples represents the distribution of concentrations of measured variables in the study population and includes errors associated with collection, processing, and analysis of sample, as well as with data processing.

Lipids and lipoprotein cholesterols. Serum total cholesterol and triglyceride levels were measured by enzymatic procedures in an Abbott VP Analyzer (Abbott Laboratories, North Chicago, IL). Lipoprotein cholesterol levels were measured by a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis.[28] Measurements of total cholesterol, triglycerides, and HDL cholesterol are being monitored by a surveillance program of the Centers for Disease Control and Prevention, Atlanta, GA. Measurement errors of blind duplicate determinations were 2.0% for total cholesterol, 3.2% for triglycerides, 3.5% for HDL cholesterol, 4.3% for low-density lipoprotein (LDL) cholesterol, and 10.0% for very–low-density lipoprotein (VLDL) cholesterol.

Glucose and insulin. The plasma glucose level was measured as part of a multiple chemistry profile (SMA20) by a glucose oxidase method. Plasma insulin determinations were performed with a commercial radioimmunoassay kit (Phadebas; Pharmacia Diagnostics, Piscataway, NJ). Measurement errors (blind duplicates) for glucose and insulin were 2.9% and 12.0%, respectively.

Statistical Analyses

Race and sex differences in the levels of LpA-I and LpA-I:A-II were examined by an ANOVA model that included race and sex main effects and race-by-sex interactions. For this purpose, data were grouped into prepubertal (5 to 10 years) and pubertal (11 to 17 years) age groups. The associations of these HDL subclasses with other lipoprotein variables, age, sexual maturation (Tanner stage), BMI, subscapular skinfold thickness, insulin, and glucose were examined by Spearman correlation coefficients. Within each race-sex group, polynomial regression models (including age, age^2, and age^3 terms as predictor variables) were used to estimate the changes in LpA-I and LpA-I:A-II with age.[29] Since these variables did not show a strictly linear relation to age, a nonlinear model was considered appropriate. Analysis of covariance was used to determine if black-white differences in the mean levels of LpA-I and LpA-I:A-II persisted among age and sex groups after adjusting for Tanner stage, subscapular skinfold thickness, BMI, cigarette smoking (cigarettes per week), alcohol consumption (milliliters per week), oral contraceptive use, and triglycerides. Significant predictors of LpA-I and LpA-I:A-II were identified using a stepwise regression procedure. The above-listed covariates (excluding BMI) along with insulin and glucose were included as independent variables.

RESULTS

Mean Levels and Percentile Distributions

Race- and sex-specific mean levels and percentile distributions of serum LpA-I and LpA-I:A-II by age group are shown in Tables 1 and 2, respectively. Black children in the prepubertal (5

Table 1. Serum Levels (mean ± SD) of LpA-I and LpA-I:A-II in Children by Race, Sex, and Age Group

Variable (mg/dL)	Age (yr)	Males		Females		Race Difference (*P*)	Sex Difference (*P*)
		Black	White	Black	White		
LpA-I	5-10	82 ± 14 (n = 217)	75 ± 14 (n = 223)	80 ± 15 (n = 251)	73 ± 13 (n = 268)	<.0001	<.01
	11-17	70 ± 16 (n = 259)	65 ± 13 (n = 286)	70 ± 16 (n = 294)	63 ± 14 (n = 310)	<.0001	NS
LpA-I:A-II	5-10	83 ± 14 (n = 217)	80 ± 12 (n = 223)	77 ± 14 (n = 251)	77 ± 12 (n = 268)	<.03*	<.0001
	11-17	69 ± 15 (n = 259)	71 ± 12 (n = 286)	64 ± 13 (n = 294)	68 ± 12 (n = 310)	<.0001	<.0001

*Males only.

Table 2. Percentile Distribution of Serum LpA-I and LpA-I:A-II in Children by Race, Sex, and Age Group

Variable (mg/dL)	Age (yr)	Race/Sex*	Percentile 5	10	50	90	95
LpA-I	5-10	White male	53	60	75	92	98
		White female	51	57	72	90	94
		Black male	58	63	82	100	109
		Black female	53	61	80	98	103
	11-17	White male	45	50	65	82	87
		White female	41	48	63	82	87
		Black male	45	50	68	92	100
		Black female	42	50	68	90	95
LpA-I:A-II	5-10	White male	62	65	79	97	102
		White female	56	62	76	92	98
		Black male	60	64	82	100	107
		Black female	54	58	75	97	102
	11-17	White male	52	57	70	86	91
		White female	48	53	67	85	90
		Black male	45	53	68	89	97
		Black female	44	48	63	79	88

*Sample size is the same as in Table 1.

to 10 years) and pubertal (11 to 17 years) age groups alike had significantly higher levels of LpA-I than their white counterparts. With respect to the black-white difference in LpA-I:A-II, prepubertal black males showed higher levels than white males; in contrast, pubertal white children of both sexes had higher values than their black counterparts. A significant male-female difference in LpA-I and LpA-I:A-II levels, with males showing higher values than females, was noted among all race and age groups, with the exception of LpA-I levels among the pubertal age group.

In terms of percent distribution of apoA-I between HDL subclasses, 48% to 52% of apoA-I was associated with LpA-I in the study population, consistent with values (30% to 51%) previously reported for normolipidemic subjects.[21-23,27,30-32]

Evaluation of Black-White Differences

Serum triglycerides (VLDL) are inversely related to HDL,[33] and black-white differences in serum triglycerides and VLDL cholesterol are known.[34,35] Therefore, black-white differences in LpA-I and LpA-I:A-II were examined separately for each sex and age group, controlling for triglyceride levels (Table 3). In addition, sexual maturation, age, adiposity, cigarette smoking, alcohol use, and oral contraceptive use were also included as possible confounding covariates. In all age and sex groups, the observed significant black-white differences in HDL subclasses were independent of triglycerides and other covariates, with the exception of the LpA-I:A-II difference among the prepubertal males. In prepubertal males, the black-white difference in LpA-I:A-II disappeared only after controlling for triglycerides.

Relation to Selected Lipoprotein Variables

Both LpA-I and LpA-I:A-II showed a strong positive relation to apoA-I in all race-sex groups (Table 4). Although both HDL subclasses correlated positively with HDL cholesterol in all race-sex groups, the association was much stronger with LpA-I compared with LpA-I:A-II. Unlike serum total cholesterol, which showed a significant positive correlation with both HDL subfractions in all race-sex groups (data not shown), LDL cholesterol showed such an association with LpA-I:A-II but not with LpA-I. Triglycerides showed no association with both HDL subclasses in all race-sex groups, except for a significant inverse relation to LpA-I in white males.

Relation to Age and Sexual Maturation

In terms of sexual maturation, black children progressed through pubertal development at an earlier age than white children (black v white mean $\pm$ SD. Tanner stage for males: 1.2 ± 0.5 v 1.1 ± 0.3 at age 8 to 9, $P < .01$; 4.7 ± 0.5 v 4.4 ± 0.7 at age 16 to 17, $P < .01$; for females: 1.5 ± 0.7 v 1.3 ± 0.5 at age 8 to 9, $P < .01$; 4.5 ± 0.6 v 4.1 ± 0.6 at age 16 to 17, $P < .0001$).

Both age and sexual maturation were inversely associated with LpA-I and LpA-I:A-II in all race-sex groups (Table 5). Race- and sex-specific levels of LpA-I (Fig 1) and LpA-I:A-II (Fig 2) by age were estimated using a polynomial regression model to further evaluate the age-related trends. In general, LpA-I levels tended to increase between ages 5 and 7 years and to decrease between the ages 7 and 14 years in all race-sex groups. Black children showed a male-female crossover trend in LpA-I levels at age 14, with males having higher values before this age and females showing higher values after this age. However, for white children, there was a suggestion of a male-female crossover trend in LpA-I levels occurring at age 17. Although the age-related changes in LpA-I:A-II were similar to those of LpA-I, there was no evidence of a male-female crossover trend up to the age of 17.

Table 3. Mean Black-White Differences in Serum LpA-I and LpA-I:A-II Levels by Sex and Age Group After Controlling for Selected Covariates

Group	Black-White Difference (mg/dL) Males LpA-I	Males LpA-I:A-II	Females LpA-I	Females LpA-I:A-II
Age 5 to 10 years				
Unadjusted	6.6 ($P < .0001$)	2.7 ($P < .03$)	7.1 ($P < .0001$)	0.4 (NS)
Adjusted*	7.3 ($P < .0001$)	2.4 (NS)	7.5 ($P < .0001$)	1.0 (NS)
Age 11 to 17 years				
Unadjusted	4.7 ($P < .0001$)	−1.8 (NS)	6.5 ($P < .0001$)	−3.8 ($P < .0001$)
Adjusted*	6.2 ($P < .0001$)	−0.8 (NS)	8.2 ($P < .0001$)	−4.8 ($P < .0001$)

*Covariates: triglycerides, age, Tanner stage, subscapular skinfold thickness, BMI, oral contraceptive use, cigarette smoking (no./wk), and alcohol use (mL/wk).

Table 4. Relation of LpA-I and LpA-I:A-II to Serum ApoA-I, HDL Cholesterol, and Triglycerides in Children by Race and Sex

	Spearman Correlation§			
Parameter	ApoA-I	HDL Cholesterol	LDL Cholesterol	Triglycerides
LpA-I				
White male	.74‡	.61‡	.07	−.11*
White female	.73‡	.57‡	.10	.00
Black male	.78‡	.64‡	.07	−.07
Black female	.75‡	.58‡	.07	.06
LpA-I:A-II				
White male	.68‡	.26‡	.14†	−.03
White female	.67‡	.16‡	.23‡	−.02
Black male	.77‡	.34‡	.25‡	−.05
Black female	.68‡	.11†	.28‡	.06

*$P < .05$.
†$P < .01$.
‡$P < .0001$.
§Sample size is the same as in Table 1.

Predictor Variables

Predictor variables that were related independently to LpA-I and LpA-I:A-II are presented in Table 6 by race and sex. In general, the effects of identified independent variables, which explained 12% to 25% of the variance, on these HDL subclasses were in the expected direction. Sexual maturation and/or age were the major factors contributing to the explained variance of these HDL subclasses in all race-sex groups. Adiposity, insulin, oral contraceptive use (females), and alcohol use influenced LpA-I and LpA-I:A-II levels to a lesser degree in certain race-sex groups. Of interest, an independent inverse association of insulin was seen with LpA-I but not with LpA-I:A-II among females of both races.

DISCUSSION

The present community-based study provides the race-, sex-, and age-related patterns of serum LpA-I and LpA-I:A-II in black and white children aged 5 to 17 years. The data presented here indicate for the first time significant black-white differences in the distribution of LpA-I, with blacks showing higher values than whites, and LpA-I:A-II, with prepubertal black males and pubertal white males and females showing higher values than their counterparts. Prior studies in children from the same community suggested the possibility of race-related differences in LpA-I based on the finding that apoA-I and HDL_2 subfractions were higher in blacks than in whites.[36,37] Further, a black-white difference in the apoA-I to apoA-II ratio

Table 5. Relation of Serum LpA-I and LpA-I:A-II to Age and Tanner Stage in Children by Race and Sex

	Spearman Correlation*†	
Parameter	LpA-I	LpA-I:A-II
Age		
White male	−.37	−.35
White female	−.31	−.36
Black male	−.41	−.46
Black female	−.28	−.44
Tanner stage		
White male	−.37	−.36
White female	−.35	−.36
Black male	−.43	−.44
Black female	−.30	−.41

*$P < .0001$.
†Sample size is the same as in Table 1.

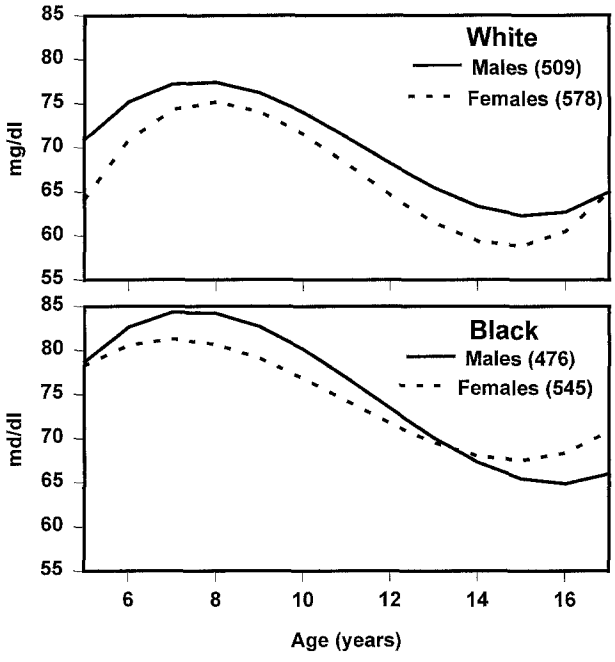

Fig 1. Relation of LpA-I to age in children by race and sex, estimated by a polynomial regression model. Sample size by race and sex is shown in parentheses.

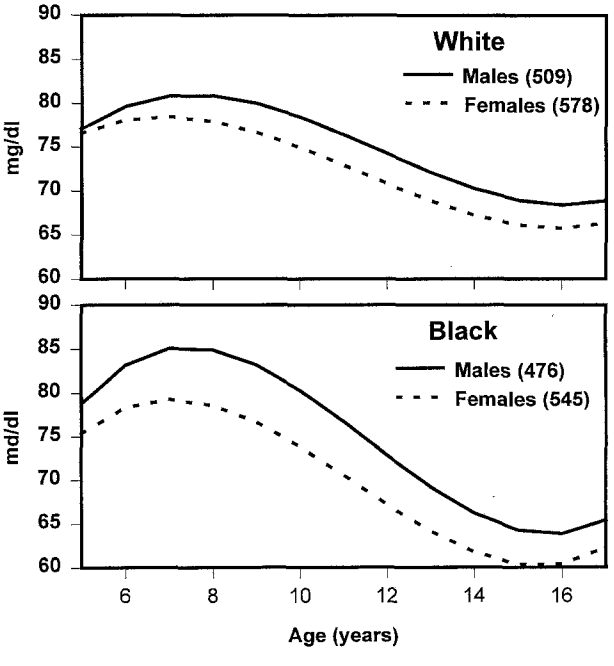

Fig 2. Relation of LpA-I:A-II to age in children by race and sex, estimated by a polynomial regression model. Sample size by race and sex is shown in parentheses.

Table 6. Predictor Variables for Serum LpA-I and LpA-I:A-II in Children by Race and Sex

	LpA-I		LpA-I:A-II	
Group	Independent Variable*	Partial R^2	Independent Variable*	Partial R^2
White male	Tanner†	.14	Tanner†	.12
	SSSF†	.03		
	Alcohol	.01		
White female	Tanner†	.12	Age†	.14
	OC	.03	SSSF†	.01
	Insulin†	.01		
Black male	Tanner†	.17	Age†	.18
			Tanner†	.01
Black female	Tanner†	.11	Tanner†	.21
	Insulin†	.01	SSSF†	.02
			OC	.01
			Age†	.01

Abbreviations: SSSF, subscapular skinfold thickness; OC, oral contraceptive.

*Retained in a stepwise regression model at $P < .05$.

†Negative relation.

(black > white) has been found in adults,[38] which may be related to LpA-I. Although children and adults alike show a black-white difference in the HDL_2 subfraction and apoA-I, it remains to be seen whether the divergent trend in the racial difference seen in pubertal children for LpA-I (blacks > whites) and LpA-I:A-II (whites > blacks) continues through adulthood.

The black-white difference in HDL subclasses persists after adjusting for the confounding covariates, including serum triglyceride (VLDL), which is lower in blacks[34,35] and metabolically inversely related to HDL.[33] Although dietary intake, a modifier of LpA-I concentration,[9] was not taken into account, previous dietary studies in Bogalusa children have shown no race-related difference.[39] Further, it has been suggested that dietary intake and physical activity could not account for the black-white divergence in HDL cholesterol.[6] Therefore, it is likely that metabolic responses to physiologic and environmental variables may be different between the two racial groups.

The present study also shows a significant sex differential (males > females) for both HDL subclasses in blacks and whites, with the exception of LpA-I levels among the pubertal age group. A similar sex differential has been found among white children.[21] However, studies in adults demonstrated an opposite trend, with females having higher LpA-I levels than males.[21-23,31,32]

In the current study, the influence of age and sexual maturation (Tanner stage) on LpA-I and LpA-I:A-II is discernible in black and white children, with values showing significant inverse associations. Further, the male-female crossover trend seen among children after age 14 suggests that the sex-related difference in LpA-I among adults occurs after sexual maturation. The male-female crossover trend in LpA-I occurring at an earlier age in blacks than in whites may be due to the observed black-white difference in sexual maturation. Earlier studies, including our own, found that black children develop pubertal characteristics at an earlier age than white children.[40-43] The male-female crossover trend in LpA-I may also explain the lack of sex differential seen among the pubertal age group as a whole.

Since there was no sex differential reported in the levels of adult LpA-I:A-II, the well-documented increase in apoA-I levels in females after sexual maturation is attributed mainly to the elevation of LpA-I.[23] Endogenous sex hormones may, in part, influence the observed lipoprotein transition in adolescence.[44,45] It has been suggested that lower hepatic lipase activity in women versus men, a difference influenced by the makeup of gonadal hormones,[46] might be responsible for the increased levels of LpA-I in women.[32]

It is apparent from the present study that while sexual maturation and age remained as major factors contributing to the variability in LpA-I and LpA-I:A-II levels in children, adiposity, insulin, alcohol intake, and oral contraceptive use emerged as minor but significant predictor variables. The effects of adiposity, insulin, and life-style behaviors on apoA-I are now well established.[47-49] The observed relationships of adiposity and life-style behaviors to HDL subclasses have been noted previously, especially with respect to LpA-I.[9,21,50]

In the present study, LpA-I compared with LpA-I:A-II showed a much stronger correlation with HDL cholesterol. It has been reported that factors responsible for low HDL cholesterol levels preferentially reduce LpA-I compared with LpA-I:A-II.[27] If so, this would result in a stronger association of HDL cholesterol with LpA-I versus LpA-I:A-II.

Both HDL subclasses associated poorly with serum triglycerides despite the well-known inverse relationship between HDL and VLDL (triglycerides).[33] It should be noted that both HDL subclasses were measured in terms of apoA-I. Prior studies, including our own, have shown that serum triglycerides correlated strongly (inversely) with HDL cholesterol but poorly with apoA-I.[36,51] An exchange between HDL cholesteryl esters and triglycerides of apoB-containing lipoproteins, mediated by CETP,[52] could result in a reduction of HDL cholesterol without necessarily altering apoA-I levels in normolipidemic individuals.

It is of particular interest that, unlike LpA-I, LpA-I:A-II associated positively with LDL cholesterol. The reason for this association is not clear. As mentioned, CETP mediates the net transfer of HDL cholesteryl esters to VLDL remnants and LDL. It has been reported that although a minority of CETP is associated with LpA-I:A-II in normolipidemic subjects, this particle remains an efficient donor for cholesteryl ester transfer to apoB-containing lipoproteins, perhaps because its low affinityfor CETP enhances the transfer rate either by a shuttle mechanism or by formation of a ternary complex.[53] Whether such a transfer mechanism plays any role in the observed positive relationship between LpA-I:A-II and LDL cholesterol is not known. It is tempting to speculate that such a relationship might make LpA-I:A-II particles indirectly potentially proatherogenic.

In terms of CAD risk, it is of interest that the levels of LpA-I, considered the antiatherogenic subfraction of HDL,[9,14,15] are relatively higher among blacks early in life. Further, during sexual maturation, females begin to show a trend toward the adult pattern of female excess in LpA-I. On the other hand, LpA-I:A-II levels are relatively higher among pubertal white

children. Molecular genetic studies have shown that overexpression of human apoA-I in transgenic mice protects against the development of atherosclerosis,[54] whereas overexpression of murine apoA-II or both human apoA-I and apoA-II does not prevent atherosclerosis.[55,56] Further, LpA-I is considered more effective than LpA-I:A-II in promoting cell-derived cholesterol efflux.[3,14] Taken together, it appears that among the four race-sex groups, white males have an unfavorable HDL subclass pattern early in life that may account, in part, for their excess CAD.

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