R219K Polymorphism of the ABCA1 Gene and Its Modulation of the Variations in Serum High-Density Lipoprotein Cholesterol and Triglycerides Related to Age and Adiposity in White Versus Black Young Adults. The Bogalusa Heart Study

Sathanur R. Srinivasan, Shengxu Li, Wei Chen, Eric Boerwinkle, and Gerald S. Berenson

Mutations in adenosine triphosphate (ATP)-binding cassette transporter 1 (ABCA1) gene have been established as the molecular defect in Tangier disease and familial hypoalphalipoproteinemia, uncommon genetic disorders characterized by deficient or depressed high-density lipoprotein (HDL) cholesterol and increased triglycerides. However, information regarding the frequency of common variants, including Arg219Lys (R219K) within the coding region of the ABCA1 gene and their effect on these phenotypes in the general population is limited. This study examined the frequency and phenotypic effect of R219K variant in a community-based sample of 887 white and 390 black young adults aged 20 to 38 years. The frequency of the variant allele (K219) was higher in blacks than in whites (0.595 *v* 0.262, $P < .001$), with carriers (KK+RK) representing 83.8% of blacks versus 44.2% of whites. After adjusting for age, body mass index (BMI), and sex, the genotype effect on HDL cholesterol and natural logarithm of triglycerides was not apparent in whites or blacks. However, significant interaction effects of genotype and age on HDL cholesterol ($P < .001$) and genotype and BMI on triglycerides ($P = .029$) were found in whites. Carriers (KK+RK), unlike noncarriers (RR) showed a positive relationship between age and HDL cholesterol (regression coefficient $\beta = 0.28$, $P = .029$ for carriers *v* $\beta = -0.18$, $P = .112$ for noncarriers). In addition, the variant allele attenuated the adverse positive relationship between BMI and triglycerides ($\beta = 0.032$, $P < .001$ for carriers v $\beta = 0.046$, $P < .001$ for noncarriers). These results indicate that the K219 allele frequency differs markedly between blacks and whites, and that the variant-allele modulates the association between age and HDL cholesterol, as well as body fatness and triglycerides in a beneficial manner only in whites.

SERUM HIGH-DENSITY lipoprotein (HDL) cholesterol is inversely related to coronary artery disease (CAD).[1] This has been attributed, in part, to the key role HDL plays in the transport of cholesterol from peripheral tissues including the arterial wall to the liver, an antiatherogenic process known as reverse cholesterol transport.[2] In addition, HDL is metabolically inversely related to triglyceride-rich lipoproteins,[3,4] another strong risk factor for CAD.[5] In the general population, factors such as age, race, sex, body fatness, variability in lipoprotein lipase, hepatic triglyceride lipase, and cholesteryl ester transfer protein activities and apolipoprotein (apo) A-I production rate influence HDL cholesterol levels.[6-10]

It has been known that familial disorders of HDL metabolism contribute to very low levels of HDL cholesterol.[11] Mutations in the gene encoding adenosine triphosphate (ATP)-binding cassette transporter 1 (ABCA1) have been identified as the molecular basis of 2 familial HDL disorders, Tangier disease and familial hypoalphalipoproteinemia.[12-14] As a cholesterol efflux regulatory protein, ABCA1 participates in the biogenesis of HDL by facilitating both translocation of cholesterol and phospholipid to the plasma membrane and efflux on to lipid poor apo A-I particles.[15,16] Because mutations associated with severe functional impairment of ABCA1 are not common among individuals with low HDL cholesterol, research has been focused recently on common single nucleotide polymorphisms in the coding and promotor regions of ABCA1.[17-20]

The ABCA1 gene, localized on chromosome 9q31, contains 49 exons that range in size from 33 to 249 bp and is over 70 kb in length.[21] A G to A transversion at nucleotide position 1051 in exon 7 results in the substitutions of a lysine for arginine at amino acid residue 219 (R219K). It has been reported that homozygous carriers of this variant had reduced severity of CAD, decreased triglyceride levels, and a trend toward increased HDL cholesterol levels.[17] However, whether the above phenotypic effect observed in an European cohort with proven CAD is applicable to the general population is not clear. As part of the Bogalusa Heart Study, a biracial (black-white) community-based investigation of early natural history of cardiovascular disease, the present study examines the 219K allele frequency and the effect of R219K polymorphism on serum HDL cholesterol and triglycerides in young adults.

MATERIALS AND METHODS

Study Population

Young adults (n = 2,571) aged 18 to 38 years residing in the biracial (65% white, 35% black) community of Bogalusa, LA were examined in 1988 to 1991 and 1995 to 1996 cross-sectional surveys. Of these, 1,277 individuals (887 whites and 390 blacks) aged 20 to 38 years who had ABCA1 R219K genotype data formed the study sample for this report. This study was approved by the Institutional Review Board of the Tulane University Health Sciences Center. All participants gave their informed consent.

From the Department of Epidemiology, Tulane Center for Cardiovascular Health, Tulane University Health Sciences Center, New Orleans, LA; and the Human Genetic Center and Institute of Molecular Medicine, University of Texas-Houston Health Science Center, Houston, TX.

Submitted October 12, 2002; accepted January 6, 2003.

Supported by Grants No. HL-38844 from the National Heart, Lung and Blood Institute and AG16592 from the National Institute on Aging.

Address reprint requests to Gerald S. Berenson, MD, Tulane Center for Cardiovascular Health, Tulane University Health Sciences Center, 1440 Canal St, Suite 1829, New Orleans, LA 70112.

0026-0495/03/5207-0061$30.00/0

doi:10.1016/S0026-0495(03)00076-3

Table 1. Genotype and Allele Frequencies for the R219K Polymorphism of ABCA1 Gene by Race: The Bogalusa Heart Study

	White (n = 887) Count (%)	Black (n = 390) Count (%)
Genotype*		
RR	495 (55.8)	63 (16.2)
RK	320 (36.1)	190 (48.7)
KK	72 (8.1)	137 (35.1)
Allele*		
R	1,310 (73.8)	316 (40.5)
K	464 (26.2)	464 (59.5)

*Race difference, $P < .001$.

Examinations

Identical protocols were used by trained examiners in all surveys.[22] Subjects were instructed to fast for 12 hours before venipuncture, and compliance was determined by interview on the morning of the examination.

Height and weight were measured (average of 2 readings) to the nearest 0.1 cm and 0.1 kg, respectively. As a measure of overall adiposity, the body mass index (BMI = weight in kilograms divided by the square of the height in meters) was used. Subscapular skinfold was measured (average of 3 readings) to the nearest 1.0 mm and used as a measure of truncal body fatness. The reproducibility (intraclass correlation coefficients) was assessed in a 10% random sample, and the values ranged from 0.98 to 0.99 for height, weight, and skinfold measurements.

Triglycerides and HDL Cholesterol

Cholesterol and triglyceride levels were measured by enzymatic procedures in an Abbott VP analyzer (Abbott Laboratories, North Chicago, IL). HDL cholesterol was measured by a heparin-calcium precipitation procedure.[23] Measurements of these variables were monitored for accuracy by a surveillance program of the Centers for Disease Control and Prevention, Atlanta, GA. Intraclass correlation coefficients (a measure of reproducibility of the entire process from blood collection to data processing) between blind duplicate values were 0.99 for triglycerides and 0.96 to 0.98 for HDL cholesterol.

Genotyping of R219K Polymorphism

Genotyping of the ABCA1 R219K variant was performed using the TaqMan assay (Applied Biosystems, Foster City, CA). A 96-bp product was amplified utilizing 0.9 μmol/L of the forward primer TGATTCAACTTGGTGA CCAAGAAG and 0.3 μ mol/L of the reverse primer TGTCCATGTTGGAACGAAGTACTC, 30 ng DNA, 5.0 mmol/L $MgCl_2$, and 1X TaqMan Universal PCR Master Mix containing AmpliTaq Gold DNA Polymerase in a 22-μL reaction volume. After an initial step of 2 minutes at 50°C and 10 minutes at 95°C to activate the AmpliTaq Gold, the products were amplified using 40 cycles of 15 seconds at 92°C and 1 minute at 60°C. A total of 0.1 μmol/L of each of the sequence-specific probes 6FAM-CCAGTTTCTCCCTTGG-MGB and VIC-CCAGTTTCTCCTTTGGTA-MGB was used in the allele discrimination assay. Allele detection and genotype calling were performed using the ABI7700 and the Sequence Detection System software (Applied Biosystems). Based on the analysis of 67 pairs of blind duplicates, there was 98.5% concordance in R219K genotyping.

Statistical Analyses

Statistical analyses were performed using SAS software (version 8.0, SAS Institute, Cary, NC). Gene counting was used to estimate allele frequencies within each race. Race differences in the distribution of genotype and allele frequencies and estimates of Hardy-Weinberg equilibrium were tested using contingency and goodness-of-fit χ^2 test, respectively. Triglyceride levels were log-transformed in the analysis to improve normality. Subjects who were not fasting were excluded while examining genotype effect on triglyceride levels. Multiple regression model was used to examine the independent effects of R219K polymorphism and the interaction effect between genotype and age, sex, or BMI (or subscapular skinfold) on levels of HDL cholesterol and triglycerides.

RESULTS

The R219K genotype and allele frequencies by race are given in Table 1. Both genotype distribution and allele frequency showed significant race difference, with blacks having higher frequency of the variant allele than whites (0.595 *v* 0.262, $P < .001$). Carriers of the K219 allele (RK+ KK)

Table 2. Levels of Serum HDL Cholesterol and Triglycerides in Whites and Blacks by R219K Genotype of ABCA1: The Bogalusa Heart Study

	K219 Allele		
	Noncarrier	Carrier	*P*
Whites			
No.	495	392	
Age (yr)	29.7 ± 0.2	29.8 ± 0.2	.784
BMI (kg/m^2)	26.4 ± 0.3	26.4 ± 0.3	.830
Subscapular skinfold (mm)	21.8 ± 0.5	22.4 ± 0.6	.825
HDL cholesterol (mg/dL)	47.7 ± 0.6*	47.7 ± 0.6*	.988†
Triglycerides (mg/dL)	125.9 ± 5.0*	117.5 ± 5.0*	.307†
Blacks			
No.	63	327	
Age (yr)	27.8 ± 0.6	28.9 ± 0.3	.155
BMI (kg/m^2)	28.1 ± 0.9	29.2 ± 0.4	.241
Subscapular skinfold (mm)	25.7 ± 1.6	25.3 ± 0.8	.980
HDL cholesterol (mg/dL)	54.2 ± 1.7*	53.7 ± 0.9*	.835†
Triglycerides (mg/dL)	83.9 ± 6.3*	94.5 ± 4.2*	.695†

NOTE. Data are mean ± SE.

*Race difference (adjusted for age, sex, and BMI), $P < .001$.

†Adjusted for age, sex, and BMI.

Table 3. Effect of Interaction Between R219K Genotype of ABCA1 and Age, Sex or BMI on Levels of Serum HDL Cholesterol and Triglycerides by Race: The Bogalusa Heart Study

	White				Black			
	HDL Cholesterol		Triglycerides*		HDL Cholesterol		Triglycerides*	
Independent Variable	β†	*P*	β	*P*	β	*P*	β	*P*
Age	−0.122	.240	0.010	.045	0.385	.303	0.004	.736
Sex	7.056	<.001	−0.055	.265	−1.604	.692	−0.264	.052
BMI	−0.646	<.001	0.045	<.001	−0.899	<.001	0.016	.081
Genotype	−0.449	.697	−0.061	.276	−2.260	.531	0.015	.906
Age* genotype	0.524	<.001	−0.006	.391	−0.484	.233	0.014	.305
Sex* genotype	0.744	.624	0.041	.576	3.891	.375	0.029	.844
BMI* genotype	0.019	.883	−0.014	.029	0.293	.311	−0.003	.779

NOTE. Genotype: 0 = noncarriers of K allele, 1 = carriers of K allele; Sex: 0 = male, 1 = female.
*Log-transformed.
†Regression coefficient.

represented as much as 83.8% of blacks versus 44.2% of whites. The observed genotype distributions were in Hardy-Weinberg equilibrium in both whites ($P = .17$) and blacks ($P = .98$).

Mean levels of serum HDL cholesterol and triglycerides along with covariates in carriers (RK+KK) and noncarriers (RR) are provided by race in Table 2. In both races, age, BMI, and subscapular skinfold were similar between carriers and noncarriers. Levels of HDL cholesterol and triglycerides were not significantly different between carriers and noncarriers in whites or blacks, after adjusting for age, BMI, and sex. Similar results were obtained when homozygous carriers (KK) were compared with noncarriers (data not shown). Further, black carriers and noncarriers alike had significantly higher HDL cholesterol and lower triglyceride levels than whites, independent of age, sex, and BMI.

To test whether the apparent lack of genotypic effect on HDL cholesterol and triglycerides was due to any interaction with age, sex, or BMI, a multiple regression model including the interaction terms was used, and the results are presented in Table 3. Whites, unlike blacks, displayed significant interaction effects of genotype and age on HDL cholesterol ($P < .001$) and genotype and BMI on triglycerides ($P = .029$). As shown in Fig 1, HDL cholesterol was associated positively with age in white carriers (KK+RK) of the variant allele ($P = .029$); whereas no such age-related trend was noted in noncarriers (RR). In addition, although BMI was related positively with triglycerides in white carriers ($P < .001$) and noncarriers ($P < .001$) alike, the variant allele attenuated ($P = .029$) this adverse relationship (Fig 2). With respect to blacks, carriers and noncarriers alike showed no significant age-related trends in HDL cholesterol; also both carriers and noncarriers displayed significant positive association between triglycerides and BMI, but the slopes were not significantly different. Substitution of subscapular skinfold for BMI as a measure of truncal body fatness did not change the outcome (data not shown).

DISCUSSION

The present community-based study demonstrates that (1) the relative allele frequency of the R219K polymorphism of the ABCA1 gene differs markedly between blacks and whites and (2) the R219K variant significantly alters association of HDL cholesterol with age, and triglycerides with adiposity in whites, but not in blacks. These observations are noteworthy in that, to our knowledge, no such black-white comparative data are available on a population basis.

The observed frequency of the K219 allele among whites (0.262) in this study is similar to that found in Europeans (0.254).[17] Of note, in the current study, blacks compared with whites displayed markedly higher frequency of the variant allele (0.595 *v* 0.262), with the carriers representing as much as 83.8% of blacks. More comparative studies in other black-white populations are needed to confirm the present findings.

Heterozygotes for ABCA1 deficiency have decreased HDL cholesterol and increased triglycerides.[24,25] In contrast, the phenotypic effects of the common variants, such as R219K and I823M located in the coding region of the ABCA1 gene, are found to be just opposite, suggesting these common variants are associated with an enhanced ABCA1 function.[17,18] In the current study, no genotypic effects on HDL cholesterol and triglycerides were apparent in whites or blacks. However, when interaction terms of genotype with age, sex, or adiposity were included in the model, significant interaction effects of genotype and age on HDL cholesterol and genotype and adiposity on triglycerides were noted in whites, but not in blacks.

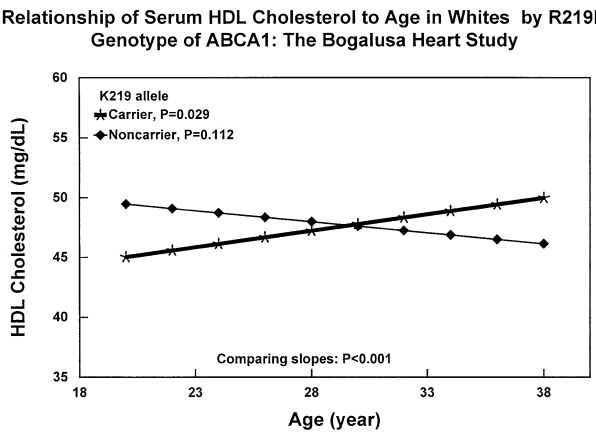

Fig 1. Relationship of serum HDL cholesterol to age in whites by R219K genotype of ABCA1. The Bogalusa Heart Study.

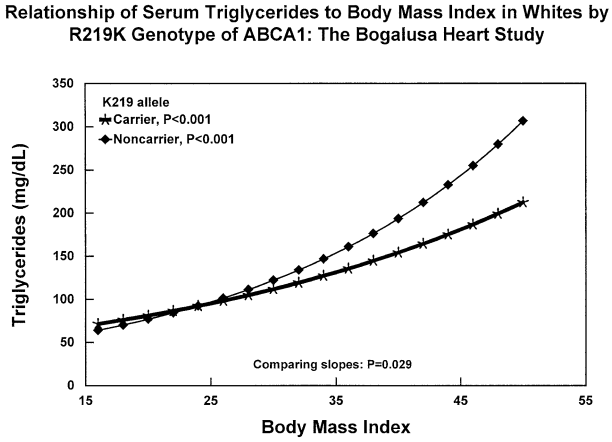

Fig 2. Relationship of serum triglycerides to BMI in whites by R219K genotype of ABCA1. The Bogalusa Heart Study.

White subjects homozygous for the wild-type allele showed no significant association between HDL cholesterol and age in this study, reflecting a trend generally seen in the young adult population at large.[7,8] In contrast, carriers of the K219 allele displayed a significant positive relationship between HDL cholesterol and age. The observed age-related trend in carriers of the common variant is opposite to that found in heterozygotes for ABCA1 deficiency.[24] A higher proportion of ABCA1 heterozygotes aged 30 to 70 years had HDL cholesterol levels below the fifth percentile compared with heterozygotes less than 30 years of age. Based on earlier findings that the expression and activity of P-glycoprotein, another ABC transporter, increases with age,[26] it has been suggested that ABCA1 activity may normally increase with age, but this was blunted in ABCA1 heterozygotes.[24] With respect to common R219K polymorphism, an earlier study found that the age-related increases in HDL cholesterol and cholesterol efflux in older age groups (median age, 56.7 years) were also blunted in carriers of the K219 allele, although homozygous carriers of this common variant displayed reduced severity of CAD, decreased progression of atherosclerosis, and a trend toward increased HDL cholesterol.[17] It is not clear whether differences in age and preexisting CAD among subjects between studies may account for the conflicting finding regarding R219K variant.

The current study also showed that, among whites, adiposity was significantly and positively associated with serum triglycerides in carriers (KK+RK), as well as noncarriers (RR), but the variant allele significantly attenuated this well-known relationship. In contrast, the effect of adiposity on triglycerides was found to be more severe in heterozygotes for ABCA1 deficiency than in controls.[24] Both overproduction and defective removal of very–low-density lipoprotein contribute to elevated serum triglycerides in obesity.[27] In a triglycerides-rich environment, cholesteryl ester transfer protein facilitates translocation of cholesteryl ester from HDL to triglyceride-rich lipoproteins in exchange for triglycerides.[28,29] A gain of ABCA1 function putatively associated with the K219 allele resulting in increased HDL cholesterol is thought to enhance this exchange process.[17] This may lead to increased catabolism of triglycerides in HDL by hepatic triglyceride lipase resulting in relatively lower serum triglyceride levels. Moreover, it has been theorized that increases in ABCA1 activity may divert free fatty acids from triglyceride synthesis to phospholipid synthesis in the liver.[17] Such diversion may attenuate the increases in serum triglycerides associated with obesity.

The observed lack of phenotypic effects of R219K polymorphism and its interaction with age or adiposity in blacks suggests that other factors may play a dominant role in determining levels of HDL cholesterol and triglycerides in this group. Blacks compared with whites generally have higher HDL cholesterol and lower triglycerides, regardless of age, adiposity, and sex.[7,8] In the current study, the black-white differences in HDL cholesterol and triglycerides were seen among carriers and noncarriers alike. Further, obesity has relatively less impact on these variables in blacks.[9,10] Studies, including our own, have shown that blacks versus whites have markedly higher lipoprotein lipase activity and lower hepatic triglyceride lipase activity,[30-32] key parameters associated with metabolism and systemic levels of triglyceride-rich lipoproteins and HDL.[33] Because these metabolic parameters favor a relatively higher HDL cholesterol and lower triglyceride trait in blacks, the phenotypic effects of the R219K variant per se may not be evident in this group.

In conclusion, the K219 allele frequency differs markedly between blacks and whites, and the variant allele modulates the associations between age and HDL cholesterol, as well as body fatness and triglycerides in a beneficial manner only in whites. Mechanisms underlying these interaction effects cannot be identified by this observational study. Also, more population-based association studies are needed to generalize these findings.

ACKNOWLEDGMENT

The Bogalusa Heart Study is a joint effort of many investigators and staff members whose contribution is gratefully acknowledged. We are especially grateful to the study participants.

REFERENCES

1. Gordon DJ, Probstfield JL, Garrison RJ, et al: High-density lipoprotein cholesterol and cardiovascular disease: Four prospective American studies. Circulation 79:8-15, 1989

2. Fielding CJ, Fielding PE: Molecular physiology of reverse cholesterol transport. J Lipid Res 36:211-228, 1995

3. Eisenberg S: Plasma lipoprotein conversions: The origin of low-density and high-density lipoproteins. Ann N Y Acad Sci 348:30-47, 1980

4. Tall AR: Plasma high-density lipoproteins: Metabolism and relationship to metabolic and genetic control of HDL cholesterol levels. J Intern Med 231:661-668, 1992

5. Hokanson JE, Austin MA: Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: A meta-analysis of population-based prospective studies. J Cardiovasc Risk 3:213-219, 1996

6. Vega GL, Grundy SM: Hypoalphalipoproteinemia (low high density lipoprotein) as a risk factor for coronary heart disease. Curr Opin Lipidol 7:209-216, 1996

7. Srinivasan SR, Wattigney W, Webber LS, et al: Race and gender differences in serum lipoproteins of children, adolescents and young adults—Emergence of an adverse lipoprotein patterns in white males: The Bogalusa Heart Study. Prev Med 20:671-684, 1991

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

9. Wattigney WA, Harsha DW, Srinivasan SR, et al: Increasing impact of obesity on serum lipids and lipoproteins in young adults. Arch Intern Med 151:2017-2022, 1991

10. Folsom AR, Burke GL, Byers CL, et al: Implications of obesity for cardiovascular disease in blacks: The CARDIA and ARIC studies. Am J Clin Nutr 53:1604S-1611S, 1991

11. Breslow JL: Familial disorders of high density lipoprotein metabolism. In: Scriver CR, Beandet AL, Sly WS, et al (eds): The Metabolic and Molecular Basis of Inherited Disease. ed 7. New York, NY, McGraw-Hill, 1995, pp 2031-2052

12. Brooks-Wilson A, Marcil M, Clee SM, et al: Mutations in ABC1 in Tangier disease and familial high-density lipoprotein deficiency. Nat Genet 22:336-345, 1999

13. Bodzioch M, Orso E, Klucken J, et al: The gene encoding ATB-binding cassette transporter 1 is mutated in Tangier disease. Nat Genet 22:347-351, 1999

14. Rust S, Rosier M, Funke H, et al: Tangier disease is caused by mutations in the gene encoding ATP-binding cassette transporter 1. Nat Genet 22:352-355, 1999

15. Wang N, Silver DL, Thiele C, et al: ATP-binding cassette transporter A1 (ABCA1) functions as a cholesterol efflux regulatory protein. J Biol Chem 276:23742-23747, 2001

16. Oram JF, Vaughan AM: ABCA1-mediated transport of cellular cholesterol and phospholipids to HDL apolipoproteins. Curr Opin Lipidol 11:253-260, 2000

17. Clee SM, Zwinderman AH, Engert JC, et al: Common genetic variation in ABCA1 is associated with altered lipoprotein levels and a modified risk for coronary artery disease. Circulation 103:1198-1205, 2001

18. Wang J, Burnett JR, Near S, et al: Common and rare ABCA1 variants affecting plasma HDL cholesterol. Arterioscler Thromb Vasc Biol 20:1983-1989, 2000

19. Brousseau ME, Bodzioch M, Schaefer EJ, et al: Common variants in the gene encoding ATP-binding cassette transporter 1 in man with low HDL cholesterol levels and coronary heart disease. Atherosclerosis 154:607-611, 2001

20. Lutucuta S, Ballantyne CM, Elghannam H, et al: Novel polymorphisms in promoter region of ATP binding cassette transporter gene and plasma lipids, severity, progression, and regression of coronary atherosclerosis and response to therapy. Circ Res 88:969-973, 2001

21. Remaley AT, Rust S, Rosier M, et al: Human ATP-binding cassette transporter 1 (ABC1): Genomic organization and identification of the genetic defect in the original Tangier disease kindered. Proc Natl Acad Sci USA 96:12685-12690, 1999

22. Berenson GS, McMahan CA, Voors AW, et al: Cardiovascular Risk Factors in Children. The Early Natural History of Atherosclerosis and Essential Hypertension. New York, NY, Oxford, 1980, pp 1-450

23. Srinivasan SR, Berenson GS: Serum lipoprotein in children and methods for study, in Lewis LA (ed): CRC Handbook of Electrophoresis: Lipoprotein Methodology and Human Studies, vol 3. Boca Raton, FL, CRC, 1983, pp 185-204

24. Clee SM, Kastelein JJP, van Dam M, et al: Age and residual cholesterol efflux affect HDL cholesterol levels and coronary artery disease in ABCA1 heterozygotes. J Clin Invest 106:1263-1270, 2000

25. van Dam MJ, deGroot E, Clee SM, et al: Association between increased arterial-wall thickness and impairment in ABCA1-driven cholesterol efflux: An observational study. Lancet 359:37-42, 2002

26. Gupta S: P-glycoprotein expression and regulation: Age-related changes and potential effects on drug therapy. Drugs Aging 7:19-29, 1995

27. Grundy SM, Mok HY, Zech L, et al: Transport of very low density lipoprotein triglycerides in varying degrees of obesity and hypertriglyceridemia. J Clin Invest 63:1274-1283, 1979

28. Castro GR, Fielding CJ: Effects of postprandial lipemia on plasma cholesterol metabolism. J Clin Invest 75:874-882, 1985

29. Tall AR, Sammett D, Granot E: Mechanisms of enhanced cholesterol ester transfer from high density lipoproteins to apolipoprotein B-containing lipoproteins during alimentary lipemia. J Clin Invest 77:1163-1172, 1986

30. Vega GL, Clark LT, Tang A, et al: Hepatic lipase activity is lower in African American men than in white American men: Effects of 5' flanking polymorphism in the hepatic lipase gene (LIPC). J Lipid Res 39:228-232, 1998

31. Friday KE, Srinivasan SR, Elkasabany A, et al: Black-white differences in postprandial triglyceride response and postheparin lipoprotein lipase and hepatic triglyceride lipase among young men. Metabolism 48:749-754, 1999

32. Despres JP, Couillard C, Gagnon J, et al: Race, visceral adipose tissue, plasma lipids, and lipoprotein lipase activity in men and women. The Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study. Arterioscler Thromb Vasc Biol 20:1932-1938, 2000

33. Olivecrona T, Bengtsson-Olivecrona G: Lipoprotein lipase and hepatic lipase. Curr Opin Lipidol 1:222-230, 1990