

Reduced LDL particle size in children consuming a very-low-fat diet is related to parental LDL-subclass patterns¹⁻³

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See corresponding editorial on page 1390.

ABSTRACT

Background: A genetically influenced atherogenic lipoprotein phenotype characterized by a predominance of small, dense LDL particles (subclass pattern B) can be induced by low-fat diets in healthy subjects with large LDL particles (pattern A).

Objective: The aim of this study was to test whether genetic predisposition to subclass pattern B contributes to susceptibility to induction of this trait by a low-fat diet.

Design: The prevalence of pattern B in children is relatively low compared with that in older individuals, but genetic susceptibility to this trait in offspring can be inferred by its presence in their parents. Plasma lipoproteins were analyzed 10 d after a change from a usual diet to a very-low-fat (10% fat), high-carbohydrate diet in offspring (mean age: 14 y; range: 7–28 y) of 22 families according to parental LDL-subclass patterns when consuming a low-fat diet: A×A mating (9 families with 19 children), A×B mating (5 families with 10 children), and B×B mating (8 families with 21 children).

Results: The very-low-fat, high-carbohydrate diet produced significantly greater decreases in LDL particle size in offspring of B×B parents ($\bar{x} \pm \text{SE}$: -0.55 ± 0.16 nm) and A×B parents (-0.48 ± 0.19 nm) than in offspring of A×A parents (0.14 ± 0.20 nm). The number of children expressing pattern B with the 10%-fat diet and the proportion of children converting from pattern A to pattern B was significantly greater in offspring of B×B parents than in those with 1 or 2 pattern A parents.

Conclusion: A very-low-fat, high-carbohydrate diet can induce expression of LDL-subclass pattern B in genetically predisposed children with low expression of the trait while consuming their usual diets. *Am J Clin Nutr* 2000;71:1611–6.

KEY WORDS Lipoproteins, diet, children, low-density-lipoprotein subclasses, genetics, LDL, LDL peak particle diameter, very-low-fat, high-carbohydrate diet

INTRODUCTION

Evidence supports the existence of genetic and environmental influences on LDL peak particle size (1). Complex segregation analyses in family studies (2, 3) indicate that a phenotype characterized by a predominance of small, dense LDL particles (LDL-subclass pattern B) appears to be under the influence of one or more major genes with an overall allele frequency of ≈ 0.25 (1, 4). Maximal expression of

pattern B occurs in males aged >20 y; much lower expression occurs in younger males and in premenopausal females (1, 5). Although the specific gene or genes responsible for this trait remain unidentified, family studies have linked LDL particle size to regions near genetic loci on chromosomes 19, 11, 16, and 6 (6, 7). However, twin studies (8) have shown relatively weak overall heritability of LDL particle size. In these twins, nongenetic influences on plasma lipoprotein metabolism such as age, adiposity, diet, hormones, and drugs override the genetic influences on LDL particle size (9, 10).

Metabolic differences associated with pattern B compared with those of pattern A (predominance of large LDL) include higher concentrations of triacylglycerol-rich lipoproteins and apolipoprotein (apo) B, reduced HDL cholesterol and apo A-I (2, 11), and reduced glucose uptake in response to insulin (12). Case-control (13, 14) and prospective (15, 16) studies have associated smaller LDL particle size with increased risk of myocardial infarction and angiographically determined coronary artery disease.

We found previously that low-fat, high-carbohydrate diets cause a subset of men with pattern A to convert to pattern B (17). In premenopausal women, a group with low expression of pattern B, we showed a significant trend toward smaller, denser LDL particles when consuming a low-fat diet (20% of energy) with increasing number of pattern B parents (18). Although this result was consistent with a genetic influence on LDL particle profiles, the low prevalence of pattern B with the experimental diet precluded testing for heritability of the induction of pattern B by low-fat, high-carbohydrate diets. In the present study, we used a more extreme low-fat test diet (10% fat) in children of both sexes to determine whether expression of pattern B was predicted by parental LDL-subclass patterns.

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SUBJECTS AND METHODS

Experimental design

We studied 50 children who exchanged their usual diet for a 10-d, outpatient, very-low-fat (10% fat), high-carbohydrate diet. The 10-d diet was chosen on the basis of initial studies that showed that LDL-subclass patterns with the 10%-fat diet were not significantly different between 10 d and 3 wk. Because of low expression of pattern B in children (1), the presumed genetic predisposition for the trait was assessed in families by parental LDL-subclass pattern (ie, A×A mating, A×B mating, or B×B mating). Lipid and lipoprotein measurements were taken from children at baseline and at completion of the experimental diet. Body mass index [BMI; wt (kg)/ht (m)²] was calculated at baseline and after the experimental diet.

Subjects

Families were recruited through public and private schools and by mass mailings to members of churches. The criteria for eligibility for parents and children were as follows: no medication use likely to interfere with lipid metabolism, body weight not >30% of ideal body weight (19, 20), no chronic disease, no smoking, a minimum family size of 2 children, and LDL-cholesterol values less than the 98th percentiles for age and sex (21). Each family member signed a consent form approved by the Committee for the Protection of Human Subjects at Lawrence Berkeley National Laboratory, University of California at Berkeley. Twenty-two families were willing to participate in the diet protocol: 17 families had 2 children, 4 families had 3 children, and 1 family had 4 children. Fifty children with a mean age of 14 y (range: 7–28 y) completed the study: 19 children from 9 families of A×A matings, 10 children from 5 families of A×B matings, and 21 children from 8 families of B×B matings. The 44 parents ranged in age from 34 to 60 y. Parental LDL-subclass patterns for most parents (16 fathers and 17 mothers) were determined from blood samples obtained after 10 d of the 10%-fat experimental diet (*see below*), whereas results for 6 fathers were those observed previously after 6 wk of a 24%-fat diet (17), and results for 5 mothers were those observed previously after 8 wk of a 20%-fat diet (18). Nineteen of the mothers were premenopausal, meaning that some may have had unexpressed pattern B.

Experimental diet

The nutrient composition of the experimental diet was based on a 10-d menu and was calculated by using the Minnesota Nutrition Data System (version 2.1) software developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis (22, 23). The very-low-fat, high-carbohydrate diet was designed to supply 10% of energy as fat (3% saturates, 4% monounsaturates, and 3% polyunsaturates), with 75% of energy as carbohydrate (half simple and half complex) and 15% of energy as protein. The cholesterol content was 150 mg/4.2 MJ (1000 kcal), the dietary fiber content was 7 g/4.2 MJ, and the ratio of polyunsaturated to saturated fat was 1:0. The diet was designed to meet age- and sex-specific recommended dietary allowances for energy, protein, and micronutrients. The subjects were allowed ad libitum consumption of non-energy-containing beverages and were instructed to maintain their customary level of physical activity.

Registered dietitians supplied the participants with personalized menus showing the number and size of servings for the experimental diet. The staff contacted the subjects during the study to encourage continued participation. Compliance was

assessed by analyzing a daily checklist of foods eaten from the menu. No subjects were eliminated for noncompliance (defined as daily diet deviations averaging >5% of total energy). The subjects measured their own body weights daily at home and the staff adjusted energy intake on the menu if necessary for body weight stability (± 1 kg).

Lipid and lipoprotein analyses

Subjects reported to our clinic in the morning, having abstained for 12–14 h from all food and vigorous activity. Plasma was prepared from venous blood collected in tubes containing 1.4 g Na₂EDTA/L at baseline (before dietary intervention) and at the conclusion of the experimental diet period. Plasma was kept at 4°C for no more than 2 wk before being processed.

We determined plasma total cholesterol and triacylglycerol concentrations by using enzymatic procedures on a Gilford Impact 400E analyzer (Ciba-Corning Diagnostics Corp, Oberlin, OH). These measurements were consistently monitored by the Centers for Disease Control and Prevention, National Heart, Lung, and Blood Institute standardization program. HDL-cholesterol concentrations were measured after heparin-manganese precipitation of plasma (24) and LDL-cholesterol concentrations were calculated with the formula of Friedewald et al (25).

For the children and their parents, nondenaturing polyacrylamide gradient gel electrophoresis was performed on whole plasma and on the plasma fraction with density < 1.063 kg/L (prepared by ultracentrifugation) by using Pharmacia PAA 2/16% gradient gels (Uppsala, Sweden) as described previously (26, 27). Stained gels were scanned with a Transidyne RFT Scanning Densitometer (Ann Arbor, MI) and peak particle diameters of the major LDL subclasses were calculated from calibration curves by using standards of known size (26). On the basis of the resulting scans, we identified LDL-subclass patterns using a modified version of the criteria described previously (4). Pattern B is characterized by a major peak of smaller, denser LDL particles (LDL-III or LDL-IV, diameter ≤ 25.7 nm), often with skewing to larger particle diameters. In pattern A, there is a predominance of larger, more buoyant LDL particles (LDL-I or LDL-II, diameter ≥ 26.4 nm), often with skewing to smaller particle diameters (26). Some individuals have an intermediate pattern with a single or double peak of LDL particles with diameters of 25.8–26.3 nm. For the analyses presented below, intermediate patterns were grouped with patterns A by using the narrow definition of pattern B (1, 2). Three readers, blind to the subjects' identities and diet treatment, assigned LDL-subclass patterns to the children and parents on the basis of the gradient gel results at baseline and at the end of the very-low-fat, high-carbohydrate diet intervention. If there was no initial agreement on subclass-pattern assignment, results were reviewed again by all readers to establish a consensus.

Statistical procedures

Comparisons between pattern type groups were made by univariate analysis of variance (ANOVA) and a post hoc analysis of significant results was done using Scheffe tests. Multivariate analysis was performed by multiple regression. Fisher's exact test was used to determine whether the number of children with pattern B differed according to the number of parents with pattern B. This test was also used to assess whether a greater proportion of conversions from pattern A to pattern B occurred in children with 2 parents with pattern B than in chil-



TABLE 1
Lipoprotein measurements¹

	Parental mating group			
	All (n = 50)	A×A (n = 19)	A×B (n = 10)	B×B (n = 21)
Triacylglycerol (mmol/L)				
Usual diet	0.98 ± 0.08	0.94 ± 0.11	1.03 ± 0.24	0.99 ± 0.11
Very-low-fat diet	1.37 ± 0.13	1.10 ± 0.13	1.49 ± 0.43	1.55 ± 0.18
Difference	0.39 ± 0.10	0.16 ± 0.14	0.46 ± 0.28	0.56 ± 0.16
Total cholesterol (mmol/L)				
Usual diet	4.08 ± 0.10	3.85 ± 0.16 ^{2,3}	3.77 ± 0.28 ^{2,3}	4.43 ± 0.11
Very-low-fat diet	3.78 ± 0.09	3.56 ± 0.16 ^{3,4}	3.63 ± 0.15 ⁴	4.05 ± 0.08 ⁴
Difference	-0.30 ± 0.05	-0.29 ± 0.10	-0.14 ± 0.12	-0.38 ± 0.08
LDL cholesterol (mmol/L)				
Usual diet	2.30 ± 0.09	2.05 ± 0.12 ^{5,6}	2.08 ± 0.21 ^{3,5}	2.64 ± 0.12 ⁵
Very-low-fat diet	2.05 ± 0.07	1.89 ± 0.15 ⁴	1.90 ± 0.15 ⁴	2.26 ± 0.07 ⁴
Difference	-0.25 ± 0.07	-0.16 ± 0.10	-0.18 ± 0.18	-0.38 ± 0.10
HDL cholesterol (mmol/L)				
Usual diet	1.33 ± 0.04	1.37 ± 0.09	1.22 ± 0.07	1.34 ± 0.06
Very-low-fat diet	1.11 ± 0.04	1.17 ± 0.06	1.06 ± 0.06	1.08 ± 0.06
Difference	-0.22 ± 0.03	-0.20 ± 0.05	-0.16 ± 0.04	-0.26 ± 0.04
LDL peak particle diameter (nm)				
Usual diet	26.48 ± 0.11	26.44 ± 0.16	26.88 ± 0.30	26.32 ± 0.17
Very-low-fat diet	26.21 ± 0.10	26.58 ± 0.11 ⁷	26.40 ± 0.25 ^{3,8}	25.77 ± 0.15
Difference	-0.27 ± 0.12	0.14 ± 0.20 ^{3,9}	-0.48 ± 0.19 ⁹	-0.55 ± 0.16 ⁹

¹ $\bar{x} \pm SE$.^{2,4,5,8,9}Significant effect of diet by mating type (ANOVA): ² $P = 0.01$, ⁴ $P = 0.04$, ⁵ $P = 0.004$, ⁸ $P = 0.0005$, ⁹ $P = 0.02$.^{3,6,7}Significantly different from B×B (post hoc Scheffe analysis): ³ $P < 0.05$, ⁶ $P < 0.01$, ⁷ $P < 0.001$.

dren with 1 or 2 parents with pattern A. All statistical procedures were performed by using STATVIEW software (Abacus Concepts, Berkeley, CA). Throughout the paper, group averages are reported as means ± SEMs.

RESULTS

Characteristics of children at baseline

Plasma lipid concentrations in the 50 children (23 boys and 27 girls) at baseline (Table 1) were similar to the 50th percentiles reported for American children (21). Three of the 19 children from A×A matings had pattern B, 1 of the 10 children from A×B matings had pattern B, and 4 of the 21 children from B×B matings had pattern B. The average ages of the children were not significantly different for children of A×A matings (13.63 ± 1.11 y), A×B matings (12.60 ± 0.82 y), or B×B matings (14.71 ± 1.31 y). There was also no significant difference in the mean BMI for A×A (19.71 ± 0.95), A×B (18.57 ± 1.04), or B×B matings (21.82 ± 1.69). BMI did not change significantly during the 10-d diet period (-0.05 ± 0.05; $P = 0.39$).

Lipoprotein measurements

The offspring's lipoprotein variables at baseline and after the 10%-fat diet are shown in Table 1 by parental mating group. At baseline, the offspring of B×B matings had significantly higher ($P < 0.02$) total cholesterol and LDL-cholesterol concentrations than did offspring of either A×A or A×B matings. Other lipid and lipoprotein variables at baseline, including LDL peak particle diameter, were unrelated to the parental mating group. With the 10%-fat diet, offspring of B×B matings had higher concentrations of total cholesterol ($P < 0.04$) and LDL cholesterol

($P < 0.04$), and had smaller LDL particle sizes ($P < 0.001$) than did offspring of A×A matings, and smaller LDL particle sizes ($P < 0.04$) than offspring of A×B matings.

Also shown in Table 1 are the differences from baseline in the children's lipid and lipoprotein measurements after the 10%-fat diet by parental mating group. There were significantly greater reductions in LDL peak particle diameter in offspring of B×B matings than in offspring of A×A matings. The same results were obtained when we compared values by averaging all children in each family or by randomly choosing 1 child within each family to create 17 observations rather than treating the 50 children as independent observations. There were no significant differences between male and female offspring for any of the results in Table 1 except for higher HDL-cholesterol concentrations in the females at baseline ($P < 0.01$).

At baseline, LDL peak particle diameter in offspring was correlated inversely with triacylglycerol ($r = -0.55$, $P < 0.0001$), positively with HDL-cholesterol ($r = 0.45$, $P < 0.005$), and weakly positively with LDL-cholesterol ($r = 0.27$, $P = 0.06$) concentrations. Changes in LDL peak particle diameter, however, were not significantly correlated with baseline concentrations or changes in triacylglycerol, LDL-cholesterol, or HDL-cholesterol concentrations. There were significant inverse correlations of baseline peak LDL diameter in the offspring with both age and BMI ($r = -0.48$ and -0.44 , respectively, $P < 0.005$). Age and BMI were strongly correlated, however ($r = 0.64$, $P < 0.0001$), and the relation of age to baseline LDL peak particle diameter was not significant after adjustment for BMI. Greater age and BMI were also correlated with greater reductions in LDL peak particle diameter with the low-fat diet (data not shown). However, these reductions remained significantly greater ($P < 0.002$) in offspring of B×B parents than of A×B or A×A parents when

TABLE 2
LDL-subclass pattern of offspring after consuming a 10%-fat diet

Offspring's LDL pattern	Parental mating group		
	A×A (n = 19)	A×B (n = 10)	B×B (n = 21)
A	19	9	12
B	0	1	9 [†]

[†]Significantly different from A×A mating and from A×A and A×B matings combined, $P < 0.001$ (Fisher's exact test).

adjusted for age and baseline BMI.

LDL-subclass patterns

The children's LDL-subclass pattern after consuming the 10%-fat diet in each parental mating group is shown in **Table 2**. The number of children expressing pattern B was greatest for offspring of B×B matings. More than 40% of offspring of B×B parents expressed pattern B compared with 10% of children of A×B parents and none of the offspring of A×A parents (the 3 offspring of A×A parents with pattern B at baseline were found to have pattern A with the low-fat diet). The 9 pattern B offspring of B×B parents came from 6 families. One of the offspring of a B×B mating who had pattern B at baseline was found to have pattern A with the low-fat diet.

A greater proportion of conversions from pattern A to pattern B occurred in children of B×B parents than in children of A×B or A×A parents (**Table 3**). The 6 children who converted from pattern A to pattern B came from 4 families. The number of children with pattern B after consuming the 10%-fat diet (Table 2) and the proportion of conversions from pattern A to pattern B (Table 3) did not differ by the sex of the children.

DISCUSSION

LDL-subclass pattern B is a trait with both genetic and environmental determinants. Because consumption of low-fat, high-carbohydrate diets has been shown to induce expression of pattern B in a subset of individuals with pattern A (28), we sought here to test whether this response may be due to metabolic changes induced by the diet in genetically susceptible individuals. We challenged the subjects with used a short-term, very-low-fat (10% fat) diet to attempt to elicit expression pattern B in children, a group known to have a low prevalence of this trait. Increased likelihood of genetic predisposition to pattern B was inferred by its presence in one or both of the children's parents. At baseline, only 16% of the children expressed LDL pattern B and there were no significant differences in subclass pattern distribution or in mean LDL peak particle diameter among children of the 3 parental mating groups (A×A, A×B, and B×B). With the low-fat diet, however, the number of children with pattern B was greater in families with B×B parents than in those with A×B or A×A parents. This finding is consistent with the expectation that the number of pattern B parents a child has is related to the likelihood of that child carrying at least one allele that predisposes him or her to this trait, and with the hypothesis that a very-low-fat diet can elicit expression of this trait in offspring with a pattern B allele. These inferences are further supported by the observation that the only children who converted from pattern A to pattern B were offspring of B×B mat-

ings, and that reductions in LDL peak particle diameter were greatest in offspring of B×B matings.

The greater reductions in LDL peak particle diameter in offspring of B×B and A×B matings compared with those of A×A matings were independent of baseline lipid and lipoprotein concentrations or diet-induced changes in these measurements. There were, however, significant inverse correlations of both BMI and age with change in LDL peak particle diameter that were independent of the effects of parental LDL-subclass pattern. These observations suggest that dietary effects on LDL particle size are influenced by body weight, age, or both, as well as by factors related to parental LDL-subclass patterns.

In the current study, we used an extreme, short-term dietary change to test for the expression of pattern B. The intake of dietary fat was lower and intake of carbohydrate was higher than in our previous studies (7, 18). In a study of 105 men (17), we found that 36 of the 87 men with pattern A while consuming a high-fat diet (46% of energy) converted to pattern B while consuming a 24%-fat diet. Although we did not control fat intake at baseline in the current study, the finding that only 6 of 42 children (14%) converted from pattern A to pattern B with a 10%-fat diet suggests that children may be more resistant to the effects of a low-fat diet on LDL particle profiles than are adult men. Although it is possible that a longer dietary intervention may have yielded different results, we found that 8 wk of a 20%-fat diet in 72 premenopausal women, another group with a low prevalence of pattern B, also resulted in a very low rate of conversion from pattern A to B (16). In that study, however, only 4 women were offspring of B×B parents, making it difficult to assess the possibility of a genetic contribution to the effect of diet on LDL particle size.

The metabolic basis for the induction of LDL-subclass pattern B by a low-fat diet is not known. Pattern B is characterized by interrelated metabolic differences from pattern A, including higher triacylglycerol concentrations, lower HDL-cholesterol concentrations (2), and insulin resistance (12, 29). In addition, pattern B is associated with slower intravenous fat clearance (30) and higher postprandial lipemia (31), which raise the possibility that diet-induced changes in the LDL profile associated with pattern B may be connected with impaired clearance of triacylglycerol-rich lipoproteins and increased conversion of triacylglycerol-enriched remnants and larger LDL particles to small, dense LDL. In this regard, we found that there was a significant reduction in postheparin lipoprotein lipase activity in men in conjunction with conversion to pattern B while consuming a low-fat diet, although this change in lipoprotein lipase was not correlated with a change in LDL peak diameter (32). Because, in

TABLE 3
LDL-subclass pattern conversion when the offsprings' baseline diets were replaced by a 10%-fat diet[†]

Change in offspring's pattern	Parental mating group		
	A×A (n = 19)	A×B (n = 9)	B×B (n = 18)
A → A or B → A	19	9	12
A → B	0	0	6 ²

[†]Excludes 4 offspring with LDL pattern B while consuming both diets (1 from the A×B and 3 from the B×B group).

²Significantly different from the other groups and from A×A and A×B matings combined, $P < 0.02$ (Fisher's exact test).

the present study, changes in LDL peak particle diameter were not correlated with changes in plasma triacylglycerol induced by the very-low-fat diet, diet-induced metabolic changes other than those affecting triacylglycerol metabolism may be involved in the conversion from pattern A to pattern B.


This study was designed to test for possible genetic differences in lipoprotein response to a diet challenge and not to determine the effects on lipoproteins of replacing dietary fat with carbohydrates. Specifically, all of the children switched from their usual diet to a very-low-fat, high-carbohydrate diet (ie, there was no control group or crossover design) so that other variables concomitant with the reduction in fat could have contributed to the lipoprotein changes. Taken together with the extreme alterations in diet composition and the short duration of the diet challenge, the study design did not allow extrapolation to therapeutic dietary regimens.

Results of previous investigations, however, have indicated that LDL-subclass patterns influence the magnitude of LDL-cholesterol reduction during consumption of a low-fat diet. In 2 studies involving a total of 238 men, reductions in dietary fat (from 46% to 24% and from 40% to 20% of energy) resulted in significantly greater lowering of LDL cholesterol in men with pattern B than in those with pattern A during consumption of a high-fat diet (17, 33). In 72 premenopausal women, the prevalence of pattern B was too low to assess differential LDL-cholesterol responses to a reduction in dietary fat from 35% to 20% of energy (18). However, the magnitude of LDL-cholesterol reduction in the women increased as a function of the number of pattern B parents that they had (18), consistent with the hypothesis that genetic predisposition to pattern B leads to greater responsiveness of LDL cholesterol to dietary fat. In this regard, it is notable that in children consuming their usual diets in the present study, LDL-cholesterol concentration was significantly higher in offspring of B×B matings than in offspring of the other mating groups.

Information regarding baseline diet composition was not available in this study, and thus, it is not possible to rule out dietary differences (such as in saturated fat or cholesterol intake) that might have accounted for the higher LDL-cholesterol concentration in the offspring of the B×B group. Although the data in Table 1 indicate that the average LDL-cholesterol reduction in B×B offspring was 2-fold greater than that in the other groups, this difference was not significant. It is possible that a more substantial difference would have been achieved with a longer experimental diet period.

The limitations of the study design did not permit inferences to be drawn regarding longer-term differences in atherosclerosis risk that may result from variation in response to dietary fat reduction in children. The present studies may, however, have implications regarding the basis for interindividual variability in lipoprotein response to low-fat diets in children. Several studies have described the effects of reduced-fat diets [National Cholesterol Education Program (NCEP) Step I or II; 34] on plasma lipids in children with elevated LDL-cholesterol concentrations. As in adults, such diets reduce LDL-cholesterol and HDL-cholesterol and increase triacylglycerol concentrations, the magnitude of responsiveness being related to baseline lipoprotein concentrations (35, 36), the degree of dietary fat modification (37, 38), and demographic characteristics (39). However, as in adults, there is marked individual variability in the response of LDL cholesterol to dietary fat modification in children (38), with a mean reduction of ≈10% reported for children without primary hypercholesterolemia (36, 38, 40, 41). Children with hyperlipidemia or a

positive family history of heart disease appear to be even less responsive to dietary intervention. In one study, only 19% of children who adhered to an NCEP Step II diet reduced their LDL-cholesterol concentration by ≥15% (35). In another study, dietary modification did not appear to influence the change in blood lipids of children with family histories of heart disease (37). Few studies have addressed the possible influence of genetic factors on variation in diet-induced lipoprotein changes in children. One found that variations in the *APOA1* gene in children were not associated with diet-induced reductions in plasma lipids (42). In a cross-sectional study, higher concentrations of fat and cholesterol in the diet increased the significance of the association between apo E isoform phenotypes and LDL cholesterol (43).

In summary, after short-term consumption of a very-low-fat diet, offspring of B×B parents had smaller LDL peak particle diameters and a greater prevalence of pattern B than did offspring of A×B or A×A parents. Diet-induced reductions in LDL particle size and the proportion of subjects shifting from pattern A to pattern B were also greater in offspring of B×B parents. These findings suggest that parental LDL-subclass patterns are informative in determining which children may be genetically susceptible to expression of subclass pattern B if they consume a low-fat, high-carbohydrate diet. Whether parental LDL-subclass pattern predicts children's lipoprotein responses to longer-term consumption of less-extreme diets remains to be determined. 

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