Change in LDL Particle Size Is Associated With Change in Plasma Triglyceride Concentration

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Low density lipoprotein (LDL) particle size is inversely associated with plasma triglyceride concentration in cross-sectional analyses. In the present study, changes in the LDL particle size of 227 participants of the Framingham Offspring Study were analyzed longitudinally by nondenaturing gradient gel electrophoresis at two examinations that were separated by 3–4 years. All subjects had triglyceride concentrations <400 mg/dl at both exams. Using laser scanning densitometry to assess mean LDL particle size, 56% of samples displayed a change in size: 41% had a one-band size change, 13% had a two-band change, and 2% had a three-band change. These changes in size corresponded to a 15% change in pattern type, based on pattern A and B terminology. There was a significant inverse association between change in LDL size and change in triglyceride (p < 0.001) and glucose (p < 0.004) concentrations, body weight (p < 0.02), and age (p < 0.03). There was also a significant positive association with change in high density lipoprotein (HDL) cholesterol concentration (p < 0.001). Change in LDL cholesterol concentration, as calculated by use of the Friedewald formula, however, showed no significant association with change in LDL size (p < 0.9). There was also no significant association with change in smoking or blood pressure, but there was a nonsignificant inverse trend associated with alcohol intake (p < 0.08). Women had more significant changes than men, but the relation between change in LDL size and change in lipids was the same for women and men. In stepwise regression analyses of biochemical indices, change in triglyceride concentration produced the best single-variable model (r = 0.460). When change in HDL cholesterol concentration was added to the model, the r value increased slightly to 0.481 for the two-variable model. No other variables entered the model. We conclude that the amount of circulating triglyceride appears to be the single most important factor affecting LDL particle size and that LDL size can be modulated by changes in plasma triglyceride concentration. (Arteriosclerosis and Thrombosis 1992;12:1284–1290)

KEY WORDS • low density lipoproteins • low density lipoprotein subspecies • triglycerides • high density lipoprotein cholesterol • gradient gel electrophoresis

Since low density lipoproteins (LDL) have been implicated in the development of coronary artery disease (CAD), they have been closely studied by a number of research groups.1-7 LDL have been shown to be a heterogeneous population of particles with respect to size, density, and composition and have been studied through the use of density gradient and analytical ultracentrifugation, as well as with nondenaturing polyacrylamide gradient gel electrophoresis.8-15 Through the use of GGE, the existence of seven different sizes of LDL has been reported.12,15 We previously reported that size was inversely associated with plasma triglyceride concentration and positively with high density lipoprotein (HDL) cholesterol concentration, but was not different in the fed versus the fasted state.15 In our studies, men generally had smaller LDL particles than women,15 and individuals with documented CAD generally had smaller LDL particles than age- and sex-matched individuals without CAD.18 In individuals with CAD, particle size was also found to be affected by the use of β-blockers.16 After controlling for the effects of β-blockers and other CAD risk factors, such as HDL and LDL cholesterol concentrations, size was no longer an independent risk factor for CAD.

Other investigators have reported genetic regulation of LDL size after dichotomizing the band patterns into large (pattern A) and small (pattern B) LDL.17,18 Although there may be some genetic regulation, we have noticed distinct changes occurring in LDL size when certain changes in diet, drug therapy, hormonal status, and/or exercise have been instituted (References 19–23 and authors’ unpublished data). To better understand the prevalence of LDL size fluctuations, our present study was designed to assess changes in LDL size as...
seen in a random set of free-living, normal adults after an interval of 3–4 years.

Methods

Study Population
A randomly selected subset of participants of the Framingham Offspring Study (n = 263), who had previously been assessed for LDL size during exam 3, were reassessed for LDL size at exam 4 under a previously approved protocol. Exclusions included two individuals because of technical problems with their exam 3 gels; five individuals with triglyceride levels >400 mg/dl at either exam, since ultracentrifugation was not performed at exam 4, making estimation of LDL cholesterol by use of the Friedewald formula necessary; and 29 individuals taking lipid-lowering medication. The final study population consisted of 227 subjects (109 men and 118 women) on whom data was collected at both exams for plasma lipid and glucose concentrations, blood pressure, body height and weight, smoking, alcohol intake, and menopausal status of the women. The age range was 28–74 years at exam 3 (48.4 ± 9.5 years, mean ± SD), and the interval between exam 3 and exam 4 ranged from 1.9 to 5.5 years (3.3 ± 0.4 years). There were no significant differences seen in age or examination interval between men and women.

Lipoprotein Analysis
Blood was drawn into tubes containing EDTA (0.15% final concentration) for lipid and glucose determinations after a 12-hour overnight fast under an existing, approved protocol. Plasma was separated after centrifugation (2,500 rpm [1,000g], 4°C, 20 minutes). Plasma cholesterol, triglyceride, HDL cholesterol, and glucose concentrations were measured on an ABA-200 bichromatic analyzer (Abbott Diagnostics, Dallas, Tex.) with enzymatic reagents (Abbott A-Gent) and dextran-Mg precipitation as previously described. Very low density lipoprotein (VLDL) cholesterol and LDL cholesterol were estimated by use of the method of Friedewald et al.

LDL Subfraction Analysis
LDL subfractions were separated by GGE using 2–16% nondenaturing polyacrylamide gels (Pharmacia Inc., Piscataway, N.J.). Plasma, which was combined 3:1 (vol/vol) with sucrose and bromophenol blue tracking dye, was loaded onto the gels and subjected to 2,700 volt hours of electrophoresis using the GE 2/4 electrophoresis apparatus (Pharmacia), as previously described. After Sudan black B staining and ethylene glycol monoethyl ether destaining, the gels were scanned on an LKB Ultrascan XL laser densitometer (LKB Instruments, Paramus, N.J.) and integrated with GSXL software (LKB).

Statistical Analysis
Data were collected and stored in a VAX 780 computer (Digital Equipment Co., Maynard, Mass.), using the RS/1 software package (BBN Research Systems). Statistical analyses were performed within RS/1 and with procedures available in the Statistical Analysis System (SAS) software (SAS Institute, Inc. Cary, N.C.). The parameters of interest were examined separately for men and women, but the data were pooled for most analyses related to size change, since the same changes occurred in both groups. Pearson correlation coefficients were computed to identify parameters that were significantly associated with change in LDL size. Stepwise multiple linear regression analysis was performed to examine significant contributions of these parameters to the prediction of change in LDL size.

Results
The Framingham Heart Study offspring, the offspring and spouses of the original Framingham cohort, represent a well-characterized segment of a normal, free-living American population. Exam visits are scheduled at 3-year intervals. Comprehensive questionnaires completed at each visit detail a number of clinical, medication, exercise, and dietary variables. In addition, fasting blood is drawn at each visit for plasma lipids and other testing. Plasma from a random subset of this population was previously used by us to examine the distribution of LDL bands in the general population, followed more recently by the LDL size characterization of the entire offspring cohort (approximately 3,000 subjects).

This population, therefore, was well suited to the longitudinal study presented here.

Lipid and glucose concentrations, body weight, blood pressure, and LDL scores for exam 3 and exam 4, along with percentage changes, are shown in Table 1 for premenopausal and postmenopausal women and in Table 2 for men ≤ 50 and > 50 years. During the 3.3-year mean interval between exam 3 and exam 4, HDL cholesterol concentrations were significantly decreased in all four groups (p < 0.04, 0.03, 0.0003, and 0.03, respectively). There were small but significant decreases in total (p < 0.03) and LDL (p < 0.04) cholesterol concentrations for men > 50 years. Body mass index rose significantly in the premenopausal women and men ≤ 50 years (p < 0.01 and 0.03), whereas systolic blood pressure rose in the postmenopausal women and men > 50 years (p < 0.0006 and 0.07). Diastolic blood pressure increased in postmenopausal women (p < 0.05) and men > 50 years (p < 0.03). LDL size decreased significantly in postmenopausal women (p < 0.00005) and showed a trend in premenopausal women (p < 0.09), but did not change significantly in men.

The women were divided into three groups for further analysis: premenopausal at both exams (n = 53), premenopausal at exam 3 but postmenopausal at exam 4 (n = 5), and postmenopausal at both exams (n = 60). All of the women in the latter two groups were > 50 years at exam 4, and all but one of the premenopausal women were ≤ 50 years at exam 4. The premenopausal women as a group had a significantly less decrease in LDL size than the perimenopausal women or the postmenopausal women. The changes in the perimenopausal women were difficult to evaluate because of the small sample
TABLE 1. Values for Women at Exam 3 and Exam 4 of the Framingham Offspring Study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exam 3</th>
<th>Exam 4</th>
<th>Δ (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>53</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.6±5.4</td>
<td>42.9±5.4</td>
<td>−2.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>192±37</td>
<td>188±37</td>
<td>0.0</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>83±40</td>
<td>82±36</td>
<td>+7.6</td>
<td>&lt;0.07</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>121±34</td>
<td>119±37</td>
<td>+0.7</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>55±14</td>
<td>53±13</td>
<td>−3.6</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>88±9</td>
<td>88±8</td>
<td>+2.1</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Body mass index (wt/ht²)</td>
<td>24.5±5.9</td>
<td>25.6±6.5</td>
<td>+4.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>115±14</td>
<td>117±16</td>
<td>+1.7</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>75±10</td>
<td>76±9</td>
<td>+1.3</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>LDL score</td>
<td>2.4±1.0</td>
<td>2.6±0.8</td>
<td>−8.3</td>
<td>&lt;0.09</td>
</tr>
</tbody>
</table>

Postmenopausal women at exam 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exam 3</th>
<th>Exam 4</th>
<th>Δ (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>65</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.5±6.5</td>
<td>58.8±6.2</td>
<td>0.0</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>224±37</td>
<td>224±36</td>
<td>0.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>131±70</td>
<td>141±75</td>
<td>+7.6</td>
<td>&lt;0.007</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>141±37</td>
<td>142±37</td>
<td>+0.7</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>56±16</td>
<td>54±15</td>
<td>−3.6</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>96±26</td>
<td>98±27</td>
<td>+2.1</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Body mass index (wt/ht²)</td>
<td>26.4±5.1</td>
<td>27.0±5.9</td>
<td>+2.3</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>125±15</td>
<td>130±18</td>
<td>+4.0</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>77±7</td>
<td>79±9</td>
<td>+2.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LDL score</td>
<td>2.7±1.1</td>
<td>3.2±1.1</td>
<td>−18.5</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

LDL, low density lipoproteins; HDL, high density lipoproteins; BP, blood pressure.

LDL score was calculated by multiplying the relative percent area of each band by its band size; an increase in score equals a decrease in LDL particle size. Values are mean±SD.

For 44% of the subjects, there was no change in LDL size between exam 3 and exam 4 (Table 5). Moreover, these individuals had a mean change in triglyceride concentration of <5%. However, 41% of the subjects showed a one-band change, 13% showed a two-band change, and 2% showed a three-band change. Of the 41% with a single-band change, 15% represented an
increase in LDL size, which was associated with a 12% decrease in triglycerides, while 26% represented a decrease in size and a 20% increase in triglycerides. The two-band changes were composed of 4% with an increase in size and 9% with a decrease in size, accompanied by −34% and +42% mean changes in triglycerides, respectively. In addition, there were two individuals in whom LDL size increased by three band sizes and whose triglycerides decreased by 34%, and two individuals whose size decreased by three band sizes and in whom triglycerides increased by 74%. Table 5 shows the percent changes in triglyceride, HDL cholesterol, glucose, and body weight with change in LDL size.

Since the seven bands in our nomenclature (LDL 1−7) correspond to the seven bands in the Krauss nomenclature (LDL I−IVB) and since Austin and

### Table 2. Values for Men at Exam 3 and Exam 4 of the Framingham Offspring Study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exam 3</th>
<th>Exam 4</th>
<th>Δ (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men ≤50 years of age at exam 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>50</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>40.2±4.7</td>
<td>43.5±4.6</td>
<td>−1.5</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>204±38</td>
<td>201±43</td>
<td>−3.4</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>60±11</td>
<td>55±10</td>
<td>−6.2</td>
<td>&lt;0.0003</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>92±8</td>
<td>91±12</td>
<td>−1.1</td>
<td>&lt;0.3</td>
</tr>
<tr>
<td>Body mass index (wt/ht²)</td>
<td>27.9±4.7</td>
<td>28.8±3.9</td>
<td>+3.2</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>121±12</td>
<td>124±14</td>
<td>+2.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>80±9</td>
<td>82±11</td>
<td>+2.5</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>LDL score</td>
<td>3.0±1.1</td>
<td>3.2±1.2</td>
<td>−6.7</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Men &gt;50 years at exam 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>59</td>
<td>59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.2±5.1</td>
<td>58.4±5.1</td>
<td>−3.7</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>215±40</td>
<td>207±43</td>
<td>−2.9</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>143±35</td>
<td>137±39</td>
<td>−4.2</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>101±19</td>
<td>105±38</td>
<td>+4.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Body mass index (wt/ht²)</td>
<td>27.9±3.2</td>
<td>28.1±3.0</td>
<td>+0.7</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>129±14</td>
<td>131±15</td>
<td>+1.6</td>
<td>&lt;0.07</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>84±9</td>
<td>83±9</td>
<td>−1.2</td>
<td>&lt;0.4</td>
</tr>
<tr>
<td>LDL score</td>
<td>3.5±1.1</td>
<td>3.4±1.2</td>
<td>+2.9</td>
<td>&lt;0.4</td>
</tr>
</tbody>
</table>

LDL, low density lipoprotein; HDL, high density lipoprotein; BP, blood pressure. LDL score was calculated by multiplying the relative percent area of each band by its band size; an increase in score equals a decrease in LDL particle size. Values are mean±SD.

FIGURE 1. Bar graphs show changes in low density lipoprotein (LDL) particle size associated with age. Panel A: Changes in LDL size (mean±SD) for women in 5-year intervals from 30 years to >70 years of age (n=118). Panel B shows the same distribution for men (n=109). Changes in LDL size in premenopausal women who were <40 years of age were significantly different from older premenopausal women (p<0.03) and from all other age categories (p<0.006). Changes in older premenopausal women (40−50 years) were not significantly different from postmenopausal women. Men <45 years of age had significantly greater decreases in size than men >45 years of age (p<0.03), but none of the individual 5-year age categories was significantly different from another.
Krauss assigned pattern A to sizes I–IIB and pattern B to sizes IIIA–IVB. We assigned an A or B designation to each of our subjects for each exam for comparison. Pattern A was assigned to those samples with a major band size of LDL-1, -2, or -3, or an LDL score of ≤3.50. Pattern B was assigned to samples with LDL-4 to LDL-7, or an LDL score >3.50. Changes from A to B and vice versa between exams were assessed by comparing them separately with changes in the major band and LDL score. Both methods produced a similar change rate between patterns of 15% in the 3.3-year interval (15.0% compared with a change in a major band; 15.4% when compared with a change in LDL score), as shown in Table 5.

When stepwise regression analysis was performed, change in triglycerides produced the best single-variable model (r=0.460); the addition of change in HDL cholesterol produced the best two-variable model (r=0.481), with both variables being significant. No other parameters entered the model.

**Discussion**

Our present study was instituted to evaluate the extent to which LDL size could be expected to change in the normal population. We had previously looked at the short-term effects of feeding and found no change in size in the 12 hours after a high-fat meal, but had found changes in some individuals after a triathlon. Changes have also been associated with alterations in menstrual and menopausal status, exercise, and hormonal and pharmaceutical interventions. The population in the present study is followed at approximately 3-year intervals, and we had the availability of extensive data for further follow-up. By eliminating all individuals on any kind of hormonal or drug intervention that might affect lipid concentrations, we concentrated on a spectrum of relatively normal individuals throughout a wide range of adult age and with varying ethnic backgrounds and lifestyles.

One theory regarding LDL particle size hypothesizes that large or small particle size is inherited through a dominant mode of transmission encompassing a single locus, two-allele polymorphism. The phenotypic expression of small LDL is said to be modulated by an age effect that masks it in men <20 years old and in premenopausal women. Previous studies by us and other investigators, however, have clearly shown a strong inverse association between LDL size and plasma triglyceride concentration and a strong positive association with HDL cholesterol concentration, that in a study by us, when combined into a two-variable model, accounted for 69% of the variability in particle size. Triglyceride and HDL cholesterol levels are partially determined through genetic transmission, but environmental effects also play a substantial role. A recent study of twin congruity in the National Heart, Lung, and Blood Institute Twin Study indicated no statistically significant differences in LDL size between the monozygotic and dizygotic twins. The magnitude of change in LDL size in the present study was far greater than we had initially predicted. We saw a change of at least one band size in 56% of this population within a 3-year period. In all age categories from 30 to 70 years old, there were some individuals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
<th>Combined</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Δ Triglycerides</td>
<td>-0.471</td>
<td>&lt;0.0001</td>
<td>-0.442</td>
<td>&lt;0.0001</td>
<td>-0.459</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Δ HDL cholesterol</td>
<td>0.204</td>
<td>&lt;0.03</td>
<td>0.388</td>
<td>&lt;0.0001</td>
<td>0.277</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Δ Glucose</td>
<td>-0.185</td>
<td>&lt;0.05</td>
<td>-0.207</td>
<td>&lt;0.04</td>
<td>-0.193</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>Δ Weight</td>
<td>-0.145</td>
<td>&lt;0.2</td>
<td>-0.180</td>
<td>&lt;0.07</td>
<td>-0.162</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Δ Age</td>
<td>-0.224</td>
<td>&lt;0.02</td>
<td>-0.022</td>
<td>&lt;0.9</td>
<td>-0.150</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Δ Alcohol intake</td>
<td>-0.108</td>
<td>&lt;0.3</td>
<td>-0.112</td>
<td>&lt;0.3</td>
<td>-0.126</td>
<td>&lt;0.08</td>
</tr>
<tr>
<td>Δ LDL cholesterol</td>
<td>-0.019</td>
<td>&lt;0.9</td>
<td>0.009</td>
<td>&lt;0.9</td>
<td>-0.132</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>Δ Systolic BP</td>
<td>0.086</td>
<td>&lt;0.4</td>
<td>-0.041</td>
<td>&lt;0.7</td>
<td>0.038</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>Δ Diastolic BP</td>
<td>0.120</td>
<td>&lt;0.2</td>
<td>-0.058</td>
<td>&lt;0.6</td>
<td>0.021</td>
<td>&lt;0.8</td>
</tr>
</tbody>
</table>

HDL, high density lipoprotein; LDL, low density lipoprotein; BP, blood pressure.
whose LDL size increased and others whose size decreased. The amount and the direction of change were very closely associated with changes in plasma lipids.

Although this study was never intended to study the genetics of LDL size, the results would seem to indicate that there is a strong environmental component involved in the determination of LDL size. To make some comparisons between these data and the genetic findings of Austin and Krauss, we assigned patterns A and B to each of our subjects at each visit, based essentially on the criteria used by Austin and Krauss when establishing the pattern criteria. We found that 15% of our subjects changed pattern during the 3-year interval. A change of pattern was predicated on the combined factors of how close the initial size was to the cutoff value between patterns and how large a change in size occurred. A three-band change within the seven-band framework had a high likelihood of changing patterns, and in fact, all four individuals with a three-band change did have a pattern A→B shift. Change of pattern among those with one- and two-band changes, however, was more closely related to the proximity of the band size to the cutpoint between patterns. The fact that 15% of the population changed pattern in 3 years and the fact that the direction of those changes was fairly evenly distributed (44% from B to A and 56% from A to B) supports the existence of a strong environmental component.

One unfortunate deficiency in our study was the need to eliminate everyone with triglyceride levels >400 mg/dl at either exam. This was necessary, since the protocol under which this study was performed did not include ultracentrifugation analysis of lipoproteins at exam 4. Use of the formula of Friedewald et al has been shown to be unreliable when triglyceride levels are >400 mg/dl. The result of this restriction caused a blunting of the full range of potential variability and eliminated the potential for examining whether changes at very high triglyceride levels had the same effects on size as those at lower levels.

The changes in LDL size in the present study have reinforced our previous indications that particle size is a reflection of lipid status. The present study samples

| Table 5. Percentage Changes in Lipids and Glucose Associated With Changes in Particle Size |
|------------------------------------------|----------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Δ Size* | Δ Score† | n (%) | A→B | Δ % TG | Δ % HDLC | Δ % TC | Δ % Glucose | Δ Weight (lb) |
| +3 | -1.61 | 2 (0.9) | 2 | -33.9 | -12.1 | -18.4 | -15.6 | +1.5 |
| +2 | -1.42 | 9 (4.0) | 5 | -34.2 | +13.9 | 0.0 | -0.2 | +2.0 |
| +1 | -0.89 | 34 (15.0) | 8 | -12.0 | -1.9 | -4.5 | -4.2 | -2.1 |
| 0 | +0.01 | 101 (44.5) | 0 | +4.6 | -1.5 | -1.2 | +1.8 | +1.7 |
| -1 | +0.97 | 59 (26.0) | 9 | +19.6 | -7.2 | +0.5 | +4.6 | +5.2 |
| -2 | +1.41 | 20 (8.8) | 8 | +42.3 | -6.9 | -1.8 | +6.8 | +4.2 |
| -3 | +2.15 | 2 (0.9) | 2 | +74.0 | -18.6 | +13.1 | -1.9 | +11.0 |

Net % change to population during 3.3-year interval | +7.8 | -3.1 | -1.3 | +1.9 | +2.3 |

TG, triglycerides; HDLC, high density lipoprotein cholesterol; TC, total cholesterol.

*Change in size of major band, for example, +3 means that the band representing the major low density lipoprotein (LDL) subspecies at exam 4 was three sizes larger than at exam 3.

†Change in LDL score, where score was calculated by multiplying the relative percent area of each band by its band size; an increase in score equals a decrease in LDL size.

‡Change from pattern A to pattern B or from pattern B to pattern A, according to the nomenclature of Austin and Krauss: “A” was defined as LDL 1, 2, or 3; “B” was defined as LDL 4, 5, 6, or 7.
were randomly obtained from a set of free-living individuals enrolled in a prospective study who were of varying age, lifestyle, and ethnic background. When we subdivided the group into low, moderate, and high triglyceride levels, we found the same effects of change in all three subgroups: when triglyceride concentration increased, LDL size decreased; when triglycerides decreased, size increased. We also found the same relation when we subdivided the study group by age and gender.

Our interpretation of these data leads us to believe that these effects are outside the area of hereditary modulation and that in a given individual, LDL particles become larger or smaller as a response to lipid alterations. Lipid and lipoprotein concentrations are regulated by a combination of genetic, environmental, and hormonal factors. A change in LDL size for these individuals, regardless of genetic predisposition, appeared to be primarily associated with changes in lipid parameters where the amount and direction of the change was related to the amount and direction of the change in lipids, primarily triglycerides.

References


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