Associations of Dyslipidemias From Childhood to Adulthood
With Carotid Intima-Media Thickness, Elasticity, and
Brachial Flow-Mediated Dilatation in Adulthood
The Cardiovascular Risk in Young Finns Study

Markus Juonala, Jorma S.A. Viikari, Tapani Rönnefmaa, Jukka Marniemi, Antti Jula, Britt-Marie Loo, Olli T. Raitakari

Background—Dyslipidemias are the major cause for atherosclerosis. They may act synergistically with nonlipid risk factors to increase atherogenesis. In the present study, we examined the effects of dyslipidemias from childhood to adulthood and their interaction with nonlipid risk factors on markers of subclinical atherosclerosis.

Methods and Results—Study subjects were participants of the longitudinal Cardiovascular Risk in Young Finns Study started in 1980 (n=2265, age 3 to 18 years). To phenotype type IIa, IIb, and IV dyslipidemias and hypoHDL-cholesterolemia, we calculated age and sex-specific z scores for lipid values for each subject in 1980, 1983, 1986, and 2001. Subjects with mean z score over 90th percentile for LDL-cholesterol or triglycerides were considered having type IIa or IV dyslipidemia. Subjects with mean z score over 90th percentile for LDL-cholesterol and triglycerides had type IIb dyslipidemia, and those with mean z score below 10th percentile for HDL-cholesterol had hypoHDL-cholesterolemia. Compared to controls, subjects with type IIb dyslipidemia had increased carotid IMT (P<0.01). This difference remained significant when adjusted with other risk factors (P<0.05). Carotid IMT also increased significantly more with increasing number of nonlipid risk factors (P<0.001) or presence of the metabolic syndrome (P<0.05) in subjects with type IIb than in controls. Subjects with type IIb or type IV dyslipidemia had decreased carotid elasticity (P<0.05), but these differences became nonsignificant (P>0.3) when adjusted with blood pressure.

Conclusions—Our findings suggest that type IIb dyslipidemia has deleterious effects on vasculature already since childhood. Subjects with type IIb dyslipidemia are more vulnerable to the effects of cardiovascular risk factors and metabolic syndrome. (Arterioscler Thromb Vasc Biol 2008;28:1012-1017)

Key Words: dyslipidemia ■ subclinical atherosclerosis

Dyslipidemias are the major cause for atherosclerotic diseases.1 Especially, the combination of increased concentrations of LDL-cholesterol and triglycerides, known as type IIb dyslipidemia according to Fredrickson classification,2 and its familial form familial combined hyperlipidemia (FCH), have been shown to increase the risk of cardiovascular disease. FCH affects 0.5% to 2% of the population and up to 20% of survivors of premature myocardial infarction.3,4 The mechanisms how increased cardiovascular risk associated with FCH/type IIb dyslipidemia is mediated are not completely understood. Evidence exists suggesting that part of the atherosclerotic risk associated with type IIb dyslipidemia is mediated by synergism with nonlipid risk factors and the components of the metabolic syndrome. Hopkins et al5 recently showed that the metabolic syndrome was more common in FCH families, and this increased prevalence of the metabolic syndrome alone could account for the increased coronary heart disease (CHD) risk among the family members.

Atherosclerosis begins in early life, and exposure to elevated LDL-cholesterol concentration in childhood and adolescence induce changes in arteries that contribute to the development of atherosclerosis.6–9 At present, however, there are no direct data linking childhood/early adulthood dyslipidemias to cardiovascular disease end points. As an alternative, the ultrasound measures of structural and functional changes in carotid and brachial arteries have been used as surrogate markers of cardiovascular health.9,10 Therefore, the aim of the present analysis was to examine in detail the effects of dyslipidemia phenotypes, including combined dyslipidemia, on risk of subclinical atherosclerosis in young adults, as there has been interest in early screening for lipid
disorders in an attempt to identify those at high-risk for cardiovascular disease later in life. To this end, we have examined the associations of different dyslipidemia phenotypes with carotid intima-media thickness (IMT), elasticity, and brachial flow-mediated dilatation (FMD) in the Cardiovascular Risk in Young Finns Study among 2265 men and women aged 3 to 18 years at baseline (in 1980). The phenotyping was performed using longitudinal data on serum lipids during several follow-up studies between 1980 and 2001. In addition, we examined whether dyslipidemic subjects are more vulnerable to the effects of metabolic syndrome and major nonlipid cardiovascular risk factors.

Methods

Subjects
The Cardiovascular Risk in Young Finns Study is an ongoing epidemiological study of atherosclerosis risk factors from childhood to adulthood. In 1980, altogether 4320 children and adolescents aged 3, 6, 9, 12, 15, and 18 years (born in 1977, 1974, 1971, 1968, 1965, and 1962) were invited to participate in the first cross-sectional study—a total of 3596 (83.2%) subjects participated. The study was carried out in all 5 Finnish university cities with medical schools (Helsinki, Kuopio, Oulu, Tampere, Turku) and their rural surroundings. Study subjects were randomly chosen from national population registers from these areas. Subjects gave written informed consent in 2001, and their parents gave it in 1980. The study was approved by local ethics committees. Details of the study design have been presented elsewhere.11

The follow-up-studies were performed for the whole study group in 1983 and 1986, when 2991 (83.2%) and 2799 (78.3%) subjects participated. The 21-year follow-up was conducted in all 5 centers between September 2001 and January 2002, when 2283 subjects from the original study cohort, ie, 63.5%, participated in the study.

Lipid Measurements

Venous blood samples were drawn after an overnight fast. All lipid and lipoprotein determinations were performed on serum using standard methods, as described previously.12,13 The concentration of LDL-cholesterol was calculated using the Friedewald-formula.14 In 2001, 35 subjects had triglyceride values ≥4 mmol/L, preventing reliable use of the Friedewald formula. Therefore, in these subjects, LDL-cholesterol was measured by a direct homogenous LDL-cholesterol assay (LDL-C plus 2nd generation reagent, Roche Diagnostics) on a clinical chemistry analyzer (AU400, Olympus Diagnostics) using latex turbidometric immunoassay. Details of the methods have been presented elsewhere.6,13

High-sensitive C-reactive protein (CRP) concentrations were analyzed by latex turbidometric immunoassay, glucose concentrations enzymatically, and homocysteine concentrations with microparticle enzyme immunoassay kit. Details of the methods have been presented elsewhere.6,13

The metabolic syndrome was identified by the updated NCEP definition when 3 or more of the following conditions were present: waist ≥102 cm in men and ≥88 cm in women, serum triglycerides ≥1.695 mmol/L, HDL cholesterol <1.036 mmol/L in men and <1.295 mmol/L in women, blood pressure ≥130 or ≥85 mm Hg for hypertension, and plasma glucose ≥5.6 mmol/L.16

Carotid IMT

The left carotid artery was scanned by ultrasound technicians following a similar standardized protocol in 5 study centers. The image was focused on the posterior (far) wall, and gain settings were used to optimize image quality. A resolution box function (zoom) was used to record an image of 25 mm in width and 15 mm height. A magnified image was recorded from the angle showing the greatest distance between the lumen-intima interface and the media-adventitia interface. A moving scan with a duration of 5 seconds which included the beginning of the carotid bifurcation and the common carotid artery was recorded and stored in digital format on optical discs for subsequent off-line analysis.

The digitally stored scans were manually analyzed by 1 experienced reader blinded to the subjects’ details. The analyses were performed using ultrasonic calipers. From the 5-second clip image, the best quality end-diastolic frame was selected (incident with the R-wave on a continuously recorded ECG). From this image, at least 5 measurements of the common carotid far wall were taken approximately 10 mm proximal to the bifurcation to derive mean carotid IMT. To assess intra-individual reproducibility of IMT measurements, 57 subjects were reexamined 3 months after the initial visit (2.5% random sample). These scans were measured twice by the same reader to assess intraobserver reproducibility. The between-visit coefficient of variation (CV) of IMT measurements was 6.4% and the intraobserver CV was 3.4%.

Carotid Elasticity

From the 5-second clip images, the best quality cardiac cycle was selected. The carotid diameter was measured at least twice in end-diastole and end-systole, respectively. Blood pressure was measured using ultrasonic calipers. From the 5-second clip image, the best quality frame was selected (incident with the R-wave on a continuously recorded ECG). From this image, at least 5 measurements of the common carotid far wall were taken approximately 10 mm proximal to the bifurcation to derive mean carotid IMT. To assess intra-individual reproducibility of IMT measurements, 57 subjects were reexamined 3 months after the initial visit (2.5% random sample). These scans were measured twice by the same reader to assess intraobserver reproducibility. The between-visit coefficient of variation (CV) of IMT measurements was 6.4% and the intraobserver CV was 3.4%.

Brachial FMD

Brachial artery ultrasound studies were performed successfully for 2109 subjects.14 To assess brachial FMD, the left brachial artery diameter was measured both at rest and during reactive hyperemia. Increased flow was induced by inflation of a pneumatic tourniquet placed around the forearm to a pressure of 250 mm Hg for 4.5 minutes, followed by a release.19 Three measurements of arterial diameter were performed at end-diastole at a fixed distance from an anatomic marker at rest and 40, 60, and 80 seconds after cuff release. The vessel diameter in scans after reactive hyperemia was expressed as the percentage relative to resting scan. The average of 3 measurements at each time point was used to derive the maximum FMD. The between-visit CV for brachial diameter was 3.2% and for FMD 26.0%.18

Statistical Methods

To phenotype type Ia, Iib, and IV dyslipidemias and hypo-HDL-cholesterolemia, we first calculated age and sex-specific z scores for LDL-cholesterol, HDL-cholesterol, and triglyceride values in 1980,
1983, 1986, and 2001. Then, we assessed the mean z score value (using 2 to 4 z score values per subject for each variable). Subjects with mean z score over 90th percentile for LDL-cholesterol or triglycerides were considered having type IIA or IV dyslipidemia. Subjects with mean z score over 90th percentile for LDL-cholesterol and triglycerides had type IIB dyslipidemia, and those with mean z score below 10th percentile for HDL-cholesterol had hypolDL-cholesterolemia.

Group comparisons between nondyslipidemic subjects and those with certain dyslipidemia were performed using t tests for continuous variables and \( \chi^2 \)-tests for categorical variables with Bonferroni correction attributable to multiple testing. To study, whether nonlipid risk factors for CHD have different influence on markers of subclinical atherosclerosis in nondyslipidemic and dyslipidemic subjects, we first calculated a nonlipid risk score. Risk factors were defined as systolic blood pressure \( \geq 130 \) mm Hg or diastolic blood pressure \( \geq 85 \) mm Hg, diabetes, cigarette smoking, and positive family history of CHD. Thereafter, we examined with linear regression model, whether there are significant risk score \times \) dyslipidemia interactions in association with ultrasound variable between dyslipidemic and control subjects. Similarly, we studied the association between metabolic syndrome and ultrasound variables.

Values for triglycerides, insulin, and C-reactive protein were log-transformed before analyses because of skewed distributions. The statistical tests were performed with Statistical Analysis System version 8.1, and statistical significance was inferred at a 2-tailed probability value of 0.05.

**Results**

Clinical characteristics of study subjects according to dyslipidemia phenotypes are shown in the Table. In adulthood, subjects with type IIB or type IV dyslipidemia had higher blood pressure, BMI, insulin, and CRP levels, and increased prevalence of the metabolic syndrome compared to nondyslipidemic subjects. Type IV dyslipidemia was also characterized by higher glucose levels and higher prevalence of diabetes. In type IIA subjects, the prevalence of positive family history of CHD was increased. HypoHDL-cholesterolemia was associated with increased prevalence of the metabolic syndrome. In childhood, type IIB subjects had increased BMI, and type IV subjects had increased BMI and systolic blood pressure.

**Life-Time Dyslipidemias and Markers of Subclinical Atherosclerosis**

Carotid IMT was increased in type IIB dyslipidemia (Table). The difference between nondyslipidemic subjects and those with type IIB dyslipidemia in IMT remained significant in multivariable analysis adjusted for sex, age, carotid diameter, blood pressure, BMI, CRP, homocysteine, insulin, glucose, family history of CHD, and smoking (adjusted IMTs [mean \pm SEM] 0.579 \pm 0.002 versus 0.607 \pm 0.022 mm, \( P=0.03 \)).

Carotid compliance was decreased in type IIB and type IV dyslipidemia (Table). These differences between dyslipidemic and nondyslipidemic subjects became nonsignificant when adjusted for age, sex, and blood pressure levels. In brachial FMD, there were no differences between dyslipidemic and nondyslipidemic subjects (Table).

**Early-Onset Dyslipidemias and Markers of Subclinical Atherosclerosis**

We also examined the relations between dyslipidemia phenotypes and ultrasound markers using only lipid data from childhood/adolescence (study years 1980 to 1986) in classifying dyslipidemias. In these analyses, IMT was increased in type IIB (0.624 versus 0.579 mm, \( P=0.006 \), after age, sex, and risk factor adjustment \( P=0.02 \)), whereas CAC was decreased only in univariate analysis (1.98%/mm Hg versus 2.20%/mm Hg, \( P=0.04 \), in multivariable model \( P=0.61 \)).

**Use of Quintile Cut Points in Dyslipidemia Definitions**

The data were also reanalyzed using 80th and 20th percentile points (lifetime data). In these analyses, type IIB subjects had increased IMT (0.602 versus 0.578 mm, \( P=0.01 \)) and decreased CAC (1.98 versus 2.22%/10 mm Hg, \( P=0.001 \)) compared to controls. In multivariable analyses adjusted with age, sex, and risk factors, the difference in IMT was significant (\( P=0.05 \)), whereas the difference in CAC became nonsignificant (\( P=0.09 \)). In addition, when using quintile cut points in childhood/adolescence data (study years 1980 to 1986), type IIB subjects had increased IMT (0.605 versus 0.578 mm, \( P<0.001 \), in multivariable analysis \( P=0.006 \)).

**Effects of Nonlipid Risk Factors and Metabolic Syndrome on Carotid IMT in Type IIB Dyslipidemic and Control Subjects**

To examine the possible mechanisms explaining increased IMT in type IIB dyslipidemia, we studied whether dyslipidemic subjects are more prone to the effects of other cardiovascular risk factors. The relations between IMT and the number of major nonlipid risk factors (smoking, elevated blood pressure, diabetes, and positive family history of CHD) in controls and subjects with type IIB dyslipidemia are shown in Figure 1. The association between IMT and the number of risk factors was stronger in those with type IIB dyslipidemia than in controls. Similarly, the association between IMT and the metabolic syndrome was stronger in subjects with type IIB dyslipidemia (Figure 2).

**Discussion**

We observed that type IIB dyslipidemia is related with increased carotid IMT in young healthy adults. In addition, subjects with type IIB dyslipidemia were more prone to the atherogenic effects of nonlipid cardiovascular risk factors and metabolic syndrome than nondyslipidemic subjects.

Our results concerning IMT are in line with previous studies, which have shown that subjects with type IIB dyslipidemia or FCH have increased carotid IMT.\(^{20–23}\) The present findings extend prior knowledge and suggest that the harmful atherogenic effects of type IIB dyslipidemia begin already in childhood/adolescence. The subjects with type IIB dyslipidemia had 0.043 mm thicker IMTs than controls. We have recently shown that in this cohort IMT increases by 0.0057 mm per year.\(^{24}\) Therefore, it can be estimated that there is about 7 years difference in the vascular age\(^{25}\) between subjects with type IIB dyslipidemia compared to normal controls.

The prior reports on association between dyslipidemias and endothelial function have been controversial. We have previously shown in a case-control study that abnormalities in coronary flow regulation exist in young FCH patients ex-
pressing phenotype IIb. In smaller studies, FCH has been associated with impaired brachial FMD, but in a recent report from a larger cohort (98 FCH patients, 230 unaffacted relatives, mean age approximately 50 years), there was no difference in FMD between patients and controls. Similarly, in the present study type IIb or other dyslipidemias were not associated with impaired brachial FMD. In another functional marker of subclinical atheroclerosis, carotid elasticity, we observed that subjects with type IIb or type IV dyslipidemia had impaired responses, but these were attributable to differences in blood pressure values between groups. The discrepancies in the associations between type IIb dyslipidemia and

### Table. Characteristics of Study Subjects According to Dyslipidemia Phenotypes

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Type IIa</th>
<th>Type IIb</th>
<th>Type IV</th>
<th>HypoHDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>1709 (75.5)</td>
<td>182 (8.0)</td>
<td>45 (2.0)</td>
<td>182 (8.0)</td>
<td>147 (6.5)</td>
</tr>
<tr>
<td>Age in 2001, y</td>
<td>31.6±5.0</td>
<td>31.9±5.0</td>
<td>32.4±4.9</td>
<td>31.9±5.0</td>
<td>31.4±5.0</td>
</tr>
<tr>
<td>Risk factors in 2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>5.17±0.74</td>
<td>6.68±0.95</td>
<td>6.63±0.70</td>
<td>5.35±0.75</td>
<td>4.72±0.74</td>
</tr>
<tr>
<td>LDL-cholesterol, mmol/l</td>
<td>3.29±0.67</td>
<td>4.76±0.74</td>
<td>4.71±0.66</td>
<td>3.46±0.70</td>
<td>3.25±0.70</td>
</tr>
<tr>
<td>HDL-cholesterol, mmol/l</td>
<td>1.62±0.28</td>
<td>1.60±0.75</td>
<td>1.39±0.22</td>
<td>1.38±0.27</td>
<td>1.15±0.17</td>
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<tr>
<td>Triglycerides, mmol/l</td>
<td>0.60±0.24</td>
<td>0.69±0.24</td>
<td>1.16±0.44</td>
<td>1.13±0.44</td>
<td>0.70±0.28</td>
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<tr>
<td>Non-lipid risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>113±12</td>
<td>114±12</td>
<td>113±13</td>
<td>115±13*</td>
<td>111±12</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>69±9</td>
<td>69±9</td>
<td>72±10</td>
<td>69±10</td>
<td>68±9</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>17.7±3.0</td>
<td>17.9±3.0</td>
<td>19.3±3.2**</td>
<td>18.7±3.8***</td>
<td>18.3±3.3</td>
</tr>
<tr>
<td>Risk factors in 2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>4.99±0.83</td>
<td>6.41±0.94</td>
<td>7.11±1.12</td>
<td>5.45±0.96</td>
<td>4.66±0.79</td>
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<tr>
<td>LDL-cholesterol, mmol/l</td>
<td>3.13±0.72</td>
<td>4.49±0.83</td>
<td>4.72±0.88</td>
<td>3.14±0.74</td>
<td>3.15±0.72</td>
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<tr>
<td>HDL-cholesterol, mmol/l</td>
<td>1.34±0.30</td>
<td>1.34±0.33</td>
<td>1.19±0.35</td>
<td>1.15±0.35</td>
<td>0.93±0.18</td>
</tr>
<tr>
<td>Triglycerides, mmol/l</td>
<td>1.18±0.56</td>
<td>1.31±0.62</td>
<td>2.55±1.26</td>
<td>2.60±1.70</td>
<td>1.28±0.52</td>
</tr>
<tr>
<td>Apolipoprotein A-I, g/l</td>
<td>1.52±0.24</td>
<td>1.54±0.26</td>
<td>1.55±0.32</td>
<td>1.49±0.27</td>
<td>1.20±0.16</td>
</tr>
<tr>
<td>Apolipoprotein B, g/l</td>
<td>1.00±0.22</td>
<td>1.31±0.24</td>
<td>1.58±0.23</td>
<td>1.27±0.30</td>
<td>1.05±0.22</td>
</tr>
<tr>
<td>Non-HDL/ApoA-I-ratio</td>
<td>0.88±0.10</td>
<td>0.86±0.10</td>
<td>0.75±0.11</td>
<td>0.77±0.14</td>
<td>0.77±0.09</td>
</tr>
<tr>
<td>Non-HDL/Apo-B-ratio</td>
<td>3.67±0.30</td>
<td>3.88±0.27</td>
<td>3.75±0.44</td>
<td>3.42±0.33</td>
<td>3.56±0.30</td>
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<tr>
<td>Nonlipid risk factors†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>116±13</td>
<td>117±14</td>
<td>123±16**</td>
<td>121±16***</td>
<td>114±12</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>70±10</td>
<td>71±12</td>
<td>76±14**</td>
<td>74±13***</td>
<td>69±11</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.7±4.2</td>
<td>25.1±4.4</td>
<td>27.9±4.4***</td>
<td>27.0±4.9***</td>
<td>25.5±4.8</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>5.04±0.56</td>
<td>5.02±0.46</td>
<td>5.12±0.65</td>
<td>5.21±1.07*</td>
<td>5.03±0.56</td>
</tr>
<tr>
<td>Insulin</td>
<td>7.5±5.7</td>
<td>7.2±4.1</td>
<td>9.7±4.2**</td>
<td>10.9±8.2***</td>
<td>7.5±4.5</td>
</tr>
<tr>
<td>CRP, mikrog/l</td>
<td>1.9±4.1</td>
<td>1.7±2.7</td>
<td>2.7±4.3**</td>
<td>2.1±3.6*</td>
<td>1.8±3.6</td>
</tr>
<tr>
<td>Homocysteine, mikrog/l</td>
<td>9.8±3.8</td>
<td>9.9±4.1</td>
<td>10.2±4.8</td>
<td>10.1±4.2</td>
<td>9.9±2.9</td>
</tr>
<tr>
<td>Metabolic syndrome, NCEP, %</td>
<td>9.0</td>
<td>11.0</td>
<td>47.5***</td>
<td>40.4***</td>
<td>20.8***</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0.8</td>
<td>0.6</td>
<td>2.2</td>
<td>3.3**</td>
<td>0.7</td>
</tr>
<tr>
<td>Positive family history of premature CHD, %</td>
<td>12.2</td>
<td>18.7*</td>
<td>13.3</td>
<td>13.7</td>
<td>13.6</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>23</td>
<td>23.6</td>
<td>31.1</td>
<td>19.8</td>
<td>31.3*</td>
</tr>
</tbody>
</table>

†In nonlipid risk factors and ultrasound variables the differences between specific dyslipidemia group and controls tested with t test with Bonferroni correction attributable to multiple testing for continuous and chi-square test for categorical variables.

*P<0.05, **P<0.01, ***P<0.001.
structural (IMT) versus functional markers of atherosclerosis (FMD, elasticity) may be partly explained by higher intraindividual variabilities in the measurements of functional markers. It is also possible that different pathophysiological mechanisms are responsible for structural and functional changes in arteries.

In the present study cohort, the deleterious effects of nonlipid risk factors and metabolic syndrome on vasculature were more pronounced among subjects with type IIb dyslipidemia. Large population-based risk factor studies, such as the Multiple Risk Factor Intervention Trial and the Framingham study, have shown that CHD risk factors act synergistically. In addition, in a study by Hopkins et al it was shown that increased CAD risk associated with FCH could be explained by increased prevalence of the metabolic syndrome. Our findings suggest that the synergism of cardiovascular risk factors starts already in childhood/early adulthood. Therefore, identification of young subjects with increased levels of cardiovascular risk factors would be important. We and others have shown that LDL-cholesterol values in children and adolescents can be effectively and safely lowered by lifestyle intervention. The reduction in LDL-cholesterol levels achieved by lifestyle intervention has also been associated with improved endothelial function in healthy children. Thus, at present there is little doubt about the safety of lifestyle modification for young individuals to maintain recommended serum lipoprotein levels, avoid smoking, and maintain a normal body weight to reduce cardiovascular risk. In line, we have previously shown in the Young Finns cohort that body mass index measured in childhood/adolescence strongly predicts body mass index in adulthood (with a 21-year tracking correlation of $r=0.39$). Moreover, in the present study, type IIb subjects did not have an increased frequency of familial history of early-onset coronary disease. Instead, they had high prevalence of increased BMI and metabolic syndrome pointing to lifestyle rather than genetic influences as main determinants of the atherogenic IIb phenotype.

### Study Limitations

We do not have data on lipid values of study subjects’ family members. Therefore, we cannot study the associations between familial dyslipidemias and early atherosclerosis. As our study cohort is comprised of young adults without clinical atherosclerotic diseases, we are not able to study associations between risk factors and cardiovascular events. Instead, we have used vascular ultrasound measures as indicators of an atherogenic process. The number of subjects with type IIb dyslipidemia using the decile cut points was quite small. This might affect the statistical power of the present analyses, and especially the negative findings should be interpreted with caution. However, the relations to vascular markers remained essentially similar if less strict quintile cut points were used to define dyslipidemias. Finally, we have not genotyped the study subjects for LDL-receptor defects.

### Conclusions

Our findings suggest that type IIb dyslipidemia has deleterious effects on vasculature already since childhood/adolescence. In addition, subjects with type IIb dyslipidemia are more vulnerable to the effects of cardiovascular risk factors and metabolic syndrome.

### Sources of Funding

This study was financially supported by the Academy of Finland (grants no. 77841, 210283, 121584, and 34316), the Social Insurance Institution of Finland, the Turku University Foundation, the Juho Vainio Foundation, Research funds from the Turku University Hospital, the Research foundation of Orion Corporation, the Finnish Medical Foundation and the Finnish Cultural Foundation, the Yrjö Jahnsson Foundation, the Finnish Foundation for Cardiovascular Research.

### Disclosures

None.

### References


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Arterioscler Thromb Vasc Biol. 2008;28:1012-1017; originally published online February 28, 2008;
doi: 10.1161/ATVBAHA.108.163329

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