Influence of HDL Subfractions on Erythrocyte Aggregation in Hypercholesterolemic Men

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Abstract Recent studies have suggested that rheological mechanisms may be involved in the pathogenesis of ischemic syndromes in hyperlipidemias. We investigated the association between erythrocyte aggregation and components of lipoproteins in the blood and asymptomatic, hypercholesterolemic men aged 45±8 years. The rheological parameters assessed were aggregation index (AI) and disaggregation shear rate threshold (yt) as determined by laser reflectometry, plasma fibrinogen, total serum protein, and hematocrit. The lipoprotein variables included total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol and its subfractions HDL1 cholesterol and HDL2 cholesterol, apolipoprotein (apo) B, apoA-I, HDL particles containing apoA-I without apoA-II (LpA-I), and HDL particles containing both apoA-I and apoA-II (LpA-I/A-II). Covariates considered for possible confounding effects were age, body mass index, and smoking behavior. Fibrinogen, total serum protein, and both aggregation parameters (AI and yt) were elevated in this hypercholesterolemic population. Univariate analysis showed that both AI and yt correlated positively with fibrinogen (P<.001) and total serum protein (P<.01) and negatively with HDL2 cholesterol (P<.01) and LpA-I (P<.01); yt also provided a positive correlation with LpA-I/A-II (P<.05). A multivariate model analysis demonstrated that HDL2, cholesterol, LpA-I, and LpA-I/A-II also emerged as significant factors influencing erythrocyte aggregation; 60% to 68% of the variance of AI and 47% to 64% of the variance of yt could be explained by these factors. The negative relation with HDL cholesterol, containing mainly LpA-I, suggested a possible role of one or both of these HDL subfractions in modifying erythrocyte aggregation induced by fibrinogen or other macromolecules. However, since LpA-I/A-II is positively related to yt, the possible influence of HDL particles on erythrocyte interactions might result from a balance between the respective effects of heterogeneous particles. (Arterioscler Thromb. 1994;14:361-366.)

Key Words • shear rate • shear stress • blood viscosity • HDL2 cholesterol • LpA-I • LpA-I/A-II

The fluidity of blood plays an important role in the physiological behavior of the circulation, and its alteration might promote cardiovascular complications in situations associated with low-flow states.1 In this condition red blood cells (RBCs) aggregate due to the increase in the bridging force of high-molecular-weight plasma proteins.12 Among these proteins, some are considered to be cardiovascular risk markers (eg, lipoproteins, fibrinogen) and are associated with increased plasma and whole-blood viscosity.3-13 Associations between rheology and components of lipoproteins in human blood are reported. Studies in patients with various forms of hyperlipoproteinemia show a concentration-dependent increase in plasma viscosity for low-density lipoprotein cholesterol (LDL-C) and chylomicrons and hence, for total triglycerides.9,10 These earlier studies are in line with the positive linear correlation of plasma viscosity with total cholesterol and apolipoprotein (apo) A-II and apoB observed in a recent study.11 Moreover, both blood viscosity11 and erythrocyte aggregation12 are negatively related to high-density lipoprotein cholesterol (HDL-C) concentration, which is known to be inversely correlated with coronary heart disease risk.4,5 However, high-density lipoprotein (HDL) is a heterogeneous population of lipoproteins separated by density into two main subfractions, HDL2 and HDL3.4,6 Furthermore, HDL may also be separated according to apolipoprotein composition, leading to at least two species of particles: LpA-I, which contains apoA-I without apoA-II, and LpA-I/A-II, which contains both apoA-I and apoA-II.15 These heterogenous HDL subfractions seem to have distinct metabolic roles, but the specific effect of one or another particle on the atherosclerotic process remains unclear.6-21 In the present study we investigated the relation of lipoprotein components, and especially HDL subfractions, to the aggregation and disaggregation of RBCs in a population of asymptomatic, hypercholesterolemic, normotriglyceridemic, normotensive subjects.

Methods

Selection of Subjects

The study group was from a cholesterol-screening program conducted at a worksite by a group of occupational health physicians (PCVMETRA: prévention cardiovasculaire en médecine du travail; see "Appendix"). This group referred employees whose total cholesterol concentration at the worksite was above 6.2 mmol/L.22,23 Among them, the subjects selected for the present study were normotensive (diastolic pressure less than 95 mm Hg) men without any symptomatic cardiovascular disease and in whom cholesterol and triglycerides at repeated measurements in the hospital were above 5.2 mmol/L and below 2 mmol/L, respectively. Thus, 60 hypercholesterolemic men who were 45±8 (mean±SD) years old and had a body mass index (weight/height2) of 24±2 kg/m2 and a mean blood pressure (one third of the sum of systolic pressure and
twice the diastolic pressure) of 94±9 mm Hg entered the study. A control group of 16 normocholesterolemic men who were 43±10 years old and had a body mass index of 24±3 kg/m² and a mean blood pressure of 90±3 mm Hg participated in the study. Thirty percent of normocholesterolemic and 41% of hypercholesterolemic subjects were smokers (P<.05). Subjects with disease or factors causing secondary hypercholesterolemia were excluded from the study. No subject had ever been treated with any lipid-lowering drug.

**Lipids, Apolipoproteins, and HDL Subfractions**

Serum total cholesterol and triglycerides were measured by using enzymatic methods. 24 HDL-C was measured by an enzymatic method after the precipitation of low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) by a phosphotungstic acid-MgCl₂ reagent. 25,26 LDL-C was calculated according to the Friedewald formula, 27 which is accurate for triglyceride levels below 4.5 mmol/L: LDL-C=total cholesterol–HDL-C–(triglycerides/2.2).

Total serum apoA-I and apoB were determined by immunonephelometry using a BNA analyzer and monospecific antibodies. Calibration was obtained by using ready-to-use plates (Sebia) with hydrated agarose gels containing monospecific antibodies. Calibration was obtained by using a lyophilized normolipidemic plasma as a secondary standard that had been assayed for LpA-I concentration with reference to the apoA-I concentration of an immunofinity- and chromatography-isolated LpA-I. The concentration of LpA-I/A-II was calculated as the difference of total apoA-I determined by electroimmunoassay (Sebia) with LpA-I. 30 HDL₂ and HDL₃ cholesterol (HDL₂-C and HDL₃-C) concentrations were evaluated by a direct electrophoretic method in discontinuous gradient gels. 31 Briefly, serum (40 μL) pre-stained with Sudan Black was electrophoresed in cylindrical tubes over successive layers of 3.5%, 6%, 13%, and 17.5% acrylamide gels in a tris(hydroxymethyl)aminomethane-glycine buffer for 4 hours at 300 V. VLDL and LDL were retained by the 3.5% and the 6% gels, respectively. HDL₁ was concentrated at the interface between the 13% and 17.5% gels, and HDL₂ migrated into the 17.5% gel. The cholesterol distribution in HDL subfractions was quantified by scanning the gels in a Preference densitometer (Sebia). The percentage of cholesterol distribution between HDL subfractions determined by densitometry was applied to total HDL-C measured after precipitation and was expressed in absolute values as millimoles per liter.

**Rheological Variables**

Plasma fibrinogen levels were determined by a thrombin clotting method. 32 Plasma protein concentrations were measured with a spectrophotometer. Microhematocrit was determined in duplicate by use of a Hawksley centrifuge (12 000g for 3 minutes). All tests were performed at 37°C±0.5°C. Blood

| Table 1. Comparison of Lipids, Apolipoproteins, and Lipoproteins |
|-----------------|-----------------|-----------------|
| Variable        | Normocholesterolemic Men | Hypercholesterolemic Men |
| TC, mmol/L      | 4.64±0.46 (n=16) | 6.62±0.73 <.0001 |
| LDL-C, mmol/L   | 2.87±0.53 (n=16) | 4.65±0.74 <.0001 |
| HDL-C, mmol/L   | 1.35±0.34 (n=16) | 1.37±0.32 NS     |
| TG, mmol/L      | 0.97±0.43 (n=16) | 1.33±0.38 <.01   |
| ApoA-I, g/L     | 1.49±0.21 (n=12) | 1.55±0.24 NS     |
| ApoB, g/L       | 0.98±0.16 (n=12) | 1.42±0.23 <.0001 |
| LpA-I, g/L      | 0.44±0.09 (n=8)  | 0.49±0.16 NS     |
| LpA-I/A-II, g/L | 0.92±0.15 (n=8)  | 0.97±0.14 NS     |
| HDL₂-C, mmol/L  | 0.39±0.27 (n=8)  | 0.44±0.25 NS     |
| HDL₃-C, mmol/L  | 0.84±0.09 (n=8)  | 0.93±0.15 NS     |

- TC indicates total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; Apo, apolipoprotein; LpA-I, HDL containing apoA-I without apoA-II; LpA-I/A-II, HDL containing both apoA-I and apoA-II; HDL₁-C, HDL₂ cholesterol; HDL₃-C, HDL₃ cholesterol, and NS, not significant. Values are mean±SD.

| Table 2. Comparison of Rheologlcal Variables |
|-----------------|-----------------|-----------------|
| Variable        | Normocholesterolemic Men | Hypercholesterolemic Men |
| Hematocrit, %   | 45.1±2.5        | 45.2±2.6 NS     |
| TSP, g/L        | 66.2±2.7        | 69.8±4.3 <.01   |
| Fibrinogen, g/L | 2.79±0.32       | 3.50±0.90 <.01  |
| AI, units       | 16.0±2.1        | 19.8±3.5 <.0001 |
| yt, s⁻¹         | 46.7±4.0        | 58.2±12.5 <.001 |

- TSP indicates total serum protein; AI, aggregation index; yt, disaggregation shear rate threshold; and NS, not significant. Values are mean±SD.
was adjusted to 40%±0.5% hematocrit by removal or addition of autologous plasma.

**Determination of Erythrocyte Aggregation**

A previously validated laser technique (erythroaggregometer, SEFAM) was used to study the aggregation kinetics and disaggregation shear rate of blood samples. This technique measures the intensity of laser backscattered light (BSL) by a blood suspension situated in a narrow gap between two coaxial cylinders. The inner cylinder is fixed, and the outer cylinder is transparent and rotatable. The outer cylinder can be adjusted to provide shear rates from 7 to 600 s⁻¹. The intensity of BSL by blood suspension is recorded as a function of time and shear rate. The variation of intensity of BSL as a function of time and shear rate allows the determination of the aggregation index (AI), which is related to the aggregation kinetics, and the disaggregation shear rate threshold (yt), which is related to the shear rate needed to break up the aggregates.

**Statistical Analysis**

Data are expressed as mean±SD. Comparisons between normocholesterolemic and hypercholesterolemic subjects were performed by Student’s t test. Successive multivariate analyses were performed that included AI and yt as dependent variables. Age, smoking, fibrinogen, total serum proteins, and plasma fibrinogen were significantly higher in hypercholesterolemic men. In this group of subjects no differences were observed in triglycerides values. Table 4 gives the correlation coefficients of univariate analysis for the relation of the study variables to RBC aggregation parameters in hypercholesterolemic subjects. RBC AI correlated positively with plasma fibrinogen, total serum proteins, and apoB and inversely with HDL-C, LDL-C, and LpA-I. ApoB was negatively correlated with LpA-I/A-II (r=-.42; P<.01), and the correlation of apoB with AI disappeared at constant LpA-I/A-II values. yt correlated positively with plasma fibrinogen, total serum protein, and LpA-I/A-II and inversely with HDL-C and LpA-I. In control subjects fibrinogen

### Table 3. Comparison of Variables in Normocholesterolemic and Hypercholesterolemic Nonsmokers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normocholesterolemic (n=14)</th>
<th>Hypercholesterolemic (n=35)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>43±11</td>
<td>47±8</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.3±2.4</td>
<td>24.4±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>45.3±2.7</td>
<td>45.1±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>TSP, g/L</td>
<td>66.0±2.8</td>
<td>70.4±4.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td>2.78±0.32</td>
<td>3.50±0.82</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>4.67±0.43</td>
<td>6.46±0.65</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>1.03±0.34</td>
<td>1.23±0.38</td>
<td>NS</td>
</tr>
<tr>
<td>Al, units</td>
<td>15.9±2.2</td>
<td>19.7±3.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>yt, s⁻¹</td>
<td>46.3±4.1</td>
<td>59.7±11.9</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; TSP, total serum protein; TC, total cholesterol; TG, triglycerides; Al, aggregation index; yt, disaggregation shear rate threshold; and NS, not significant. Values are mean±SD.

**Results**

Blood lipoprotein component data are given in Table 1. Compared with normocholesterolemic men, hypercholesterolemic men had by definition higher total cholesterol, LDL-C, and apoB but also higher triglycerides, although levels arbitrarily considered as pathological were not reached. No differences existed between the two groups in HDL-C, HDL₂-C, HDL₃-C, apoA-I, LpA-I, or LpA-I/A-II. A higher Al (P<.001) and yt (P<.001) were found in hypercholesterolemic patients than in normocholesterolemic subjects (Table 2). Furthermore, total serum proteins and plasma fibrinogen were increased in hypercholesterolemic men. Table 3 shows that when only nonsmokers were compared, Al, yt, total serum protein, and plasma fibrinogen were significantly higher in hypercholesterolemic men. In this group of subjects no differences were observed in triglycerides values. Table 4 gives the correlation coefficients of univariate analysis for the relation of the study variables to RBC aggregation parameters in hypercholesterolemic subjects. RBC AI correlated positively with plasma fibrinogen, total serum proteins, and apoB and inversely with HDL-C, LDL-C, and LpA-I. ApoB was negatively correlated with LpA-I/A-II (r=-.42; P<.01), and the correlation of apoB with AI disappeared at constant LpA-I/A-II values. yt correlated positively with plasma fibrinogen, total serum protein, and LpA-I/A-II and inversely with HDL-C and LpA-I. In control subjects fibrinogen

### Table 4. Correlations Between RBC Aggregation Parameters and Clinical and Biochemical Variables in Hypercholesterolemic Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>AI</th>
<th>yt</th>
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<tr>
<td>Age</td>
<td>.16</td>
<td>.05</td>
</tr>
<tr>
<td>BMI</td>
<td>.05</td>
<td>.13</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>.72*</td>
<td>.60*</td>
</tr>
<tr>
<td>TSP</td>
<td>.36†</td>
<td>.44*</td>
</tr>
<tr>
<td>TC</td>
<td>.05</td>
<td>-.09</td>
</tr>
<tr>
<td>TG</td>
<td>.12</td>
<td>.03</td>
</tr>
<tr>
<td>LDL-C</td>
<td>.15</td>
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<tr>
<td>HDL-C</td>
<td>-.31†</td>
<td>-.24</td>
</tr>
<tr>
<td>HDL₂-C</td>
<td>-.40†</td>
<td>-.34†</td>
</tr>
<tr>
<td>HDL₃-C</td>
<td>-.01</td>
<td>.06</td>
</tr>
<tr>
<td>ApoA-I</td>
<td>-.21</td>
<td>-.13</td>
</tr>
<tr>
<td>ApoB</td>
<td>.29‡</td>
<td>.14</td>
</tr>
<tr>
<td>LpA-I</td>
<td>-.34†</td>
<td>-.33†</td>
</tr>
<tr>
<td>LpA-I/A-II</td>
<td>.15</td>
<td>.30‡</td>
</tr>
</tbody>
</table>

AI indicates aggregation index; yt, disaggregation shear rate threshold; RBC, red blood cell; BMI, body mass index; TSP, total serum protein; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HDL₂-C, HDL₂ cholesterol; HDL₃-C, HDL₃ cholesterol; Apo, apolipoprotein; LpA-I, LDL containing apoA-I without apoA-II; and LpA-I/A-II, HDL containing both apoA-I and apoA-II. Values are based on univariate analysis.

*P<.001, †P<.01, ‡P<.05.
were elevated in this population compared with normo-
fibrinogen. Al independently of fibrinogen or in the absence of
variance of -yt could be explained by these factors.

Symptoms of cardiovascular disease. Both Al and -yt
olemic middle-aged male population without apparent

section with lipoprotein components in a hypercholester-

In addition, apoB levels were not
significantly. Ellipsis points indicate that the variable was not entered into the regression model.

The data were analyzed in a multiple regression
model to determine the specific influence of lipopro-
teins on RBC aggregation parameters in hypercholester-
lemic subjects (Table 5). Three methods of analysis
were tested that systematically included age, smoking,
fibrinogen, total serum protein, and triglycerides as
covariates. The first model included the main protein
components of HDL (apoA-I) and LDL (apoB). The
second model included the cholesterol content in lip-
proteins, LDL-C, HDL2-C, and HDL3-C. Finally, the
third model included the apolipoprotein components of
HDL, LpA-I, and LpA-I/A-II. In these models, in addition to fibrinogen and total
serum protein, HDL2-C, LpA-I, and LpA-I/A-II emerged as significant factors influencing RBC AI and
-yt. These analyses showed that 60% to 68% of the
variance of RBC aggregation and 47% to 64% of the
variance of yt could be explained by these factors.

No correlations were observed between triglycerides and RBC aggregation parameters in either univariate or
multivariate analysis. In addition, apoB levels were not
shown in the multivariate analysis to be associated with
AI independently of fibrinogen or in the absence of
fibrinogen.

Discussion

We investigated erythrocyte aggregation and its rela-
tion with lipoprotein components in a hypercholester-
olemic middle-aged male population without apparent
symptoms of cardiovascular disease. Both AI and yt
were elevated in this population compared with normo-
cholesterolemic control subjects, and the aggregation parameters were strongly correlated with the concentra-
tion of fibrinogen. This result was expected, because fibrinogen is the major physiological mediator of RBC
aggregation. Mean fibrinogen concentrations were in-
deed significantly higher in the hypercholesterolemic
patients than in the normal group but were not corre-
lated with blood lipid parameters. The association of fibrinogen with the RBC aggregation parameters cannot
be explained by the differences in smoking habits bet-
ween control and hypercholesterolemic subjects. The
results of the analysis of the rheological data were not
affected by exclusion of smokers. Furthermore, smoking
did not enter as a significant categorical variable in any
multiple regression analysis models that evaluated fac-
tors independently related to aggregation, yt, and
fibrinogen.

In contrast to fibrinogen, little is known concerning
the association of erythrocyte aggregation and plasma
lipoproteins and especially HDL-C, which is reported to
be inversely related with coronary heart disease inci-
dence. The association of Al and apoB observed in
hypercholesterolemic patients disappeared after con-
trolling for age, smoking, fibrinogen, total serum pro-
teins, triglycerides, LpA-I, and LpA-I/A-II. In addition, the AI/apoB association also disappeared when fibrin-
ogen was not controlled, demonstrating that such an
association was not unmasked in the absence of fibrin-
gen. The inverse correlation of erythrocyte aggrega-
tion with HDL-C observed in our study is in good
agreement with those reported in both normal subjects
and patients with coronary heart disease. However,
HDL is a heterogeneous class of lipoproteins, and
although a specific association between HDL subclasses

TABLE 5. Multiple Regression Modelling of Aggregation Parameters and Age, Smoking, Fibrinogen, TSP, and Lipoprotein Components in Hypercholesterolemic Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th></th>
<th></th>
<th></th>
<th>Model 2</th>
<th></th>
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<th>Model 3</th>
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<tr>
<td>Age</td>
<td>β</td>
<td>P</td>
<td>β</td>
<td>P</td>
<td>β</td>
<td>P</td>
<td>β</td>
<td>P</td>
<td>β</td>
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<td>β</td>
</tr>
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<td>Smoking</td>
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<td>0.53</td>
<td>0.05</td>
<td>NS</td>
<td>-0.04</td>
<td>NS</td>
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<td>NS</td>
<td>-0.04</td>
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<td>Fibrinogen</td>
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<td>2.34</td>
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<td>0.001</td>
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<td>0.001</td>
<td>2.34</td>
<td>0.001</td>
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<td>TSP</td>
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<td>0.17</td>
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<td>0.72</td>
<td>1.31</td>
<td>NS</td>
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<td>NS</td>
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<td>NS</td>
<td>0.73</td>
<td>NS</td>
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<td>ApoA-I</td>
<td>-2.32</td>
<td>0.11</td>
<td>-6.01</td>
<td>NS</td>
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<td>NS</td>
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<td>NS</td>
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<td>0.01</td>
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<td>NS</td>
<td>-0.36</td>
<td>NS</td>
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<tr>
<td>LpA-I</td>
<td>6.07</td>
<td>0.01</td>
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<td>33.7</td>
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</table>

TSP indicates total serum protein; Al, aggregation index; yt, disaggregation shear rate threshold; TG, triglycerides; Apo, apolipoprotein; LDL-C, low-density lipoprotein cholesterol; HDL_2-C, high-density lipoprotein_2 cholesterol; HDL_3-C, high-density lipoprotein_3 cholesterol; LpA-I, HDL containing apoA-I without apoA-II; LpA-I/A-II, HDL containing both apoA-I and apoA-II; and NS, not significant. Ellipsis points indicate that the variable was not entered into the regression model.

Model 1: Al, R^2 = 0.61, P < 0.0001; yt, R^2 = 0.48, P < 0.0001.
Model 2: Al, R^2 = 0.67, P < 0.0001; yt, R^2 = 0.55, P < 0.0001.
Model 3: Al, R^2 = 0.68, P < 0.0001; yt, R^2 = 0.65, P < 0.0001. R^2 is the square of the multiple correlation coefficient.
and atherosclerosis is reported, the mechanisms by which those factors are linked to cardiovascular damage are not yet clarified. By determining the respective roles of the main subfractions of HDL we demonstrated that the negative correlation between HDL-C and aggregation parameters was due to HDL₂-C but not to HDL₃-C. As shown by multiple regression, this association is independent of fibrinogen, the major determinant of erythrocyte aggregation. According to the protein definition of HDL subfractions, LpA-I, which is HDL containing apoA-I without apoA-II, was also related to aggregation parameters in a negative manner. LpA-I constitutes the majority of the HDL particles in the HDL₂ subtraction. Both HDL₂-C and LpA-I concentrations are decreased in different events of coronary artery disease. The relation of HDL-C and HDL₂-C with aggregation parameters cannot be explained by the classic increase in correlation between HDL-C and triglycerides, since both univariate and multivariate analyses showed that RBC aggregation parameters were not related to the triglyceride concentrations.

The observation that HDL₂ and LpA-I are related to a decrease in RBC aggregation may be a relevant finding concerning the mechanisms for the protective effects of these components in ischemic heart disease. Under normal circulation conditions the shear forces in medium-sized arteries are such that RBC aggregation and blood viscosity are of minor importance. However, at sites of geometric alterations (e.g., bends, angulation, flow separation, stenosis), low-flow areas, i.e., low shear rates, may allow erythrocyte aggregation. Such conditions may exist in ischemic necrosis or infarction, which are well-known complications of hypercholesterolemia and atherosclerosis and might contribute to the induction or aggravation of the course of the disease. We have recently reported that the prevalence of arterial lesions in our population of hypercholesterolemic subjects reached values as high as 74% for coronary artery disease.

In conclusion, in the presence of high blood cholesterol the erythrocyte aggregation that occurs with macromolecules bridging the membranes of erythrocytes is strongly influenced by fibrinogen. The negative relation between erythrocyte aggregation and HDL₂, mainly containing LpA-I, suggests a possible role of this lipoprotein subfraction in reducing the RBC aggregation induced by fibrinogen or other macromolecules. On the other hand, HDL containing apoA-II, i.e., LpA-I/A-II, is positively related to erythrocyte aggregation. Thus, the possible influence of HDL particles on RBC interactions would result from a balance between the respective effects of heterogeneous particles. Such phenomena might help us to better understand the disparate influence of HDL particles on atherosclerosis risk and in particular its thrombotic components.

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Appendix

The PCVMETRA Group included the following individuals: P. Segond (chairman), D. Badet, C. Baylac-Lebot, P.
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Influence of HDL subfractions on erythrocyte aggregation in hypercholesterolemic men.

PCVMETRA Group.
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