Correlation of Factor VIIa Values With Factor VII Gene Polymorphism, Fasting and Postprandial Triglyceride Levels, and Subclinical Carotid Atherosclerosis

Habib M. Ghaddar, MD; Aaron R. Folsom, MD; Nena Aleksic, PhD; Leonard B. Hearne, PhD; Lloyd E. Chambless, PhD; James H. Morrissey, PhD; Kenneth K. Wu, MD, PhD; for the Atherosclerosis Risk in Communities Study Investigators

Background—Factor VII plays a pivotal role in coagulation. Factor VIIc levels were reported to be a risk factor for fatal coronary heart disease (CHD). Factor VIIc and VIIag levels were noted to be positively associated with plasma triglyceride (TG) levels and influenced by a VII gene polymorphism. The purpose of this study is to determine whether these associations are related to activated factor VII (factor VIIa).

Methods and Results—Fasting and 3.5-hour postprandial samples from 216 cases with subclinical atherosclerosis and 341 matched controls selected from the ARIC cohort were assayed for levels of factors VIIa, VIIc, and VIIag and TG, and factor VII codon 353 gene polymorphism. The level of factor VIIa was higher in Arg/Arg than in Arg/Gln or Gln/Gln genotypes, and the difference was in accord with that of factors VIIag and VIIc. However, the factor VIIa difference was statistically insignificant. Factor VIIa values were not correlated with fasting or 3.5-hour postprandial TG levels, nor were they associated with subclinical atherosclerosis.

Conclusions—Factor VIIa levels, like factor VIIag and VIIc levels, are influenced by factor VII gene codon 353 polymorphism. However, unlike factor VIIag or VIIc, factor VIIa is not influenced by TG levels; none of these is associated with subclinical atherosclerosis. (Circulation. 1998;98:2815-2821.)

Key Words: factor VIIa ■ genes ■ coronary disease ■ atherosclerosis

Factor VII plays a central role in initiation of coagulation reaction.1 The single-chain factor VII is inactive but becomes catalytically active after conversion to a 2-chain polypeptide. Recently, there has been a substantial interest in investigating factor VII coagulant activity in human arterial atherothrombotic diseases. Meade et al reported a statistically significant association of factor VII coagulant activity (factor VIIc) with fatal coronary heart disease (CHD) in the Northwick Park Heart (NWPH) study. Other population-based studies, including the Atherosclerosis Risk in Communities (ARIC) study, failed to show a significant association of factor VIIc with incident CHD.3,4 This has been attributed in part to different factor VIIc assays used.5 The factor VIIc assay used by the NWPH study appears to be more sensitive in detecting activated factor VII (factor VIIa). However, an association of CHD with factor VIIa has not been established in population studies. The role of factor VII activation in atherosclerosis is less clear. It is, however, theoretically possible that through generation of thrombin and fibrin formation, factor VIIa activation may contribute to atherosclerosis.

Plasma factor VII levels are influenced by genetic and environmental factors. A common polymorphism in factor VII gene codon 353, in which a single base difference results in coding for factor VII Arg353 versus Gln353, has been noted to affect plasma factor VII levels. The frequency of Arg353 and Gln353 alleles is estimated to be 0.9 and 0.1, respectively in white European populations.7,8 Carriers of the Gln353 allele have a lower factor VII level than carriers of the Arg353 allele.7,8 Plasma factor VII levels are reported to be associated with plasma triglyceride (TG) levels and a postprandial increase in TG levels is associated with a higher level of factor VIIa.9 Humphries et al further reported that the association of TG with factor VII was confined to the subjects with the Arg353 allele. These results imply that factor VII levels may be determined by an interaction between genetic and environmental factors. Because the number of subjects included in this study was small, these results require further confirmation.

To understand the correlation of factor VIIa levels with factor VII gene polymorphism, plasma TG levels, and sub-
clinical atherosclerosis, we analyzed fasting and 3.5-hour postprandial TG and factors VIIag, VIIc, and VIIa values in 216 subjects with carotid arterial atherosclerosis and 341 matched controls selected from the ARIC study.

Methods

Study Subjects

The subjects were drawn from examinees of the ARIC study, a cohort selected as a probability sample of 15 800 men and women between the ages of 45 and 64 from 4 US communities. In 3 of these communities (Forsyth County, NC; Minneapolis suburbs, Minn; and Washington County, Md), all age-eligible residents were included in the sampling process. In the fourth community (Jackson, Miss) only black residents were sampled. Details of the sampling procedure have been reported.12 Participants in the Postprandial Lipids and Hemostasis (PPLH) study, an ancillary study of ARIC,13 were selected as case subjects with carotid atherosclerosis (cases) or control subjects (controls) on the basis of carotid artery intima-media far-wall thickness measured by ultrasound, according to the technique developed by Pignoli et al.14 The reproducibility of the scanning and reading procedures has been reported.15,16 Cases had 2 measurements of maximum carotid artery far-wall thickness >2.5 mm or bilateral thickening corresponding to a maximum thickness of >1.7 mm at the internal carotid, 1.8 mm at the carotid bifurcation, or 1.6 mm at the common carotid segments. These cut points exceed the 90th percentile for the respective carotid artery segments in the ARIC cohort. Controls had maximum far-wall thickness values <75th percentile in all carotid segments. After selection of all candidate cases and controls, individuals with any of the following self-reported manifestations of cardiovascular disease were excluded from the analyses: history of angina on effort, physician-diagnosed heart attack, transient ischemic attack or stroke, intermittent claudication, or use of oral anticoagulants. Case-matched controls were selected by criteria previously established.13 The PPLH cohort was identified by the ARIC coordinating center. Investigators were blinded to the case/control status of each subject. A screening interview was conducted during recruitment to exclude pregnant women and individuals with the following medical conditions: pancreatitis, hypertriglyceridemia (triglyceride >400 mg/dL), gall bladder disease, intestinal malabsorption, chronic liver or kidney disease, users of insulin or hypoglycemic or lipid-lowering medications, thyroid preparations, β-blocking agents, contraceptive hormones, and those reporting intolerance to dairy products or other constituents of the test meal.

Fat Tolerance Test

The fat tolerance test was performed as previously described.15 In brief, the liquid test meal11 was given between 7:00 and 8:00 AM to the PPLH participants after fasting and abstaining from heavy physical work for 12 hours. The test meal had to be consumed within 15 minutes. Participants were then instructed to take nothing by mouth except water, unsweetened black coffee, tea, or sugarless soft drinks until all postprandial blood samples had been collected. Blood specimens were collected at 3.5 hours for hemostatic studies and at 3.5 and 8 hours for lipid studies.

Laboratory Measurements

Blood samples were collected and processed at each field center according to standardized procedures and organizational plans described previously.17,18 Hemostasis tests were performed at the Central Hemostasis Laboratory at the University of Texas-Houston; lipid tests were done at Baylor College of Medicine, Houston, Tex. Factor VIIc was measured by determining the ability of the testing sample to correct the clotting time of human factor VII-deficient plasma as previously described.17 Presence of factor VIIag was determined by ELISA kits (American Bioproducts). Levels of factor VIIa were measured using the method described by Morrissey et al.19 This assay utilizes a soluble recombinant truncated tissue factor that is selectively deficient in promoting factor VII activation but retains factor VIIa cofactor function, thus allowing direct quantification of factor VIIa in plasma. Total plasma cholesterol and TG were measured enzymatically on a Cobas-Fara centrifugal analyzer (Roche Diagnostics) using enzymatic kits (Boehringer Mannheim Diagnostics). HDL-C was determined by measuring cholesterol in supernatant liquid after precipitation of the plasma with MgCl2 and dextran sulfate.20 The accuracy and reproducibility of laboratory measurements were reported previously.21 DNA was prepared from blood using standard techniques22 and amplified by polymerase chain reaction. The oligonucleotide primers and the cycle times, temperatures, and conditions for factor VII genotype determination have been described elsewhere.21 MspI digestion of the polymerase chain reaction product yielded 40-, 67-, and 205-bp fragments in Arg-353 allele, and 40- and 272-bp fragments in Gln-353 allele.

Statistical Methods

Distributions of TG and factors VIIa, VIIag, and VIIc at time zero and 3.5 hours postprandially were nearly normal after transformation by natural logarithms. A 66% CI was computed as the antilogarithm of transformed values ± 1 SD. Mean values and proportions were compared between cases and controls using a t test; however, because of matching, these mean values and proportions should be interpreted as data adjusted for the matching factors. Throughout this analysis, cases and controls were always held separately. Associations between varying measures of factor VII and TG were determined by Pearson’s correlation coefficient. The odds ratio of Gln carriers relative to Arg homozygotes in cases and controls was determined using conditional logistic regression models. Statistical computations were performed using the Statistical Analysis System.23

Results

Characteristics of Participants

Of the 15 211 ARIC subjects who had fasting hemostatic and lipid measurements, 557 subjects (216 cases and 341 controls) participated in the PPLH study. More cases than controls were excluded because of factors described in the Methods. Of these 557 subjects, 395 (158 cases and 237 controls) had a factor VII genotype determination. Because our PPLH population excludes subjects with carotid wall intima-media thickness between the 75th and 90th percentiles, all results are stratified by case-control status. Characteristics of participants in the PPLH study are presented in Table 1. As expected, cases were more likely than controls to have elevated risk factors for CHD, an observation in keeping with the notion that ultrasound measured carotid wall thickness is indicative of early atherosclerosis.25-27

### TABLE 1. Characteristics of Postprandial Lipid and Hemostasis Study Participants

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=216)</th>
<th>Controls (n=341)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years*</td>
<td>56.0 (50.5–61.5)</td>
<td>55.1 (49.6–60.6)</td>
<td>0.062</td>
</tr>
<tr>
<td>Body mass index, kg/m²†</td>
<td>27.4 (23.3–32.2)</td>
<td>26.2 (22.2–30.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Systolic BP, mm Hg†</td>
<td>125 (107–147)</td>
<td>117 (102–134)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg†</td>
<td>71.6 (62.3–82.3)</td>
<td>70.9 (62.0–81.0)</td>
<td>0.419</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL†</td>
<td>204 (172–241)</td>
<td>195 (160–238)</td>
<td>0.007</td>
</tr>
<tr>
<td>Triglyceride, mg/dL†</td>
<td>123 (80–190)</td>
<td>101 (62–163)</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL-C, mg/dL‡</td>
<td>41.1 (29.9–56.5)</td>
<td>45.7 (33.5–62.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>37</td>
<td>18</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Arithmetic mean (66%) CI. †Geometric mean (66%) CI.
Correlation of Factor VII Polymorphism With Factor VIIa, VIIc, and VIIag Levels

Of the 395 subjects who had factor VII polymorphism analysis, 308 (78%) were homozygous for Arg (AA), 83 (21%) were heterozygous for Arg/Gln (AG), and 4 (1%) were homozygous for Gln (GG). Given the small number of subjects with GG genotype, this group was added to the AG group in all analyses (AG+GG). The AG+GG group had 17% lower geometric mean fasting factor VIIc levels than the AA group (81% versus 98%, \( P<0.001 \)). Similarly, mean fasting factor VIIag values were 18% lower in the AG+GG group (85% versus 103%, \( P<0.001 \)). Mean factor VIIa values were lower in the AG+GG group, but the difference was not statistically significant (2.4 versus 2.9 ng/mL, \( P=0.98 \)). The AA and AG+GG groups had similar geometric mean fasting TG values (106 versus 104 mg/dL, \( P=0.59 \)). Mean values and proportions were compared by genotype within case and control groups (Table 2). The AG+GG group had 12% lower geometric mean fasting factor VIIc levels than the AA group (83% versus 95%) for controls, and 21% lower for cases (79% versus 100%). Similarly, mean fasting factor VIIag values were 22% lower in the AG+GG than in the AA case group (85% versus 107%) and 13% lower in controls (85% versus 98%). Mean fasting factor VIIa values of AG+GG were also lower than those of the AA in the cases (2.3 versus 3.0 ng/mL) and controls (2.5 versus 2.9 ng/mL).

Cross-Sectional Correlation Between Factor VII and TG

As reported previously,9 there was a statistically significant cross-sectional correlation between fasting factor VIIc and TG levels in the whole ARIC sample \( (r=0.31, \ P<0.001, \ n=15\ 211) \). There was also a statistically significant correlation between factor VIIc and TG levels in PPLH cases and controls \( (r=0.26 \) and 0.21, respectively; \( P<0.001 \)) (Table 3). Correlations between factor VIIag and TG paralleled those observed for factor VIIc and TG in both cases and controls (Table 3). There was no significant correlation, however, between fasting factor VIIa and TG in either cases or controls.

Correlations between factor VII and TG were largely similar among the 2 genotypic groups (Table 3). Among controls, the correlation coefficients for factor VIIag or factor VIIc versus TG were similar among the AA and AG+GG subsets. The differences in the statistical significance of the similar \( r \) values are likely to be entirely due to the differences in the sample size. Among cases, the correlation coefficient between factor VIIc and TG was higher in the AG+GG subset \( (r=0.43, \ P<0.05) \) than in the AA subset \( (r=0.19, \ P<0.05) \), whereas the \( r \) value between factor VIIag and TG was higher in the AA subset \( (0.23, \ P<0.001) \) than in the AG+GG subset \( (0.14, \ P\geq0.05) \). Thus, the positive cross-sectional correlation of factor VIIc or factor VIIag with TG was not generally genotype specific, an observation that differs from what was previously reported by others.5,6 Again, the correlation between factor VIIa and TG was equally low in both genotypic groups.

Influence of Postprandial Transient Hypertriglyceridemia

With the fat load given, the 3.5-hour postprandial geometric mean TG level increased \( \approx2 \)-fold over the fasting level. This rise was seen in the whole group as well as in various subsets (Figure, A). Postprandial increase in TG levels were not

---

**TABLE 2. Geometric Mean Values With 95% CIs of Fasting TG, VIIa, VIIag, and VIIc**

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th></th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n=216)</td>
<td>AA (n=127)</td>
<td>AG+GG (n=31)</td>
<td>Total (n=318)</td>
</tr>
<tr>
<td>TG, mg/dL</td>
<td>123 (116–130)</td>
<td>125 (116–134)</td>
<td>113 (95–134)</td>
<td>101 (96–106)</td>
</tr>
<tr>
<td>VIIa, ng/mL</td>
<td>2.9 (2.6–3.2)</td>
<td>3.0 (2.7–3.4)</td>
<td>2.3 (1.6–3.2)</td>
<td>3.1 (2.8–3.4)</td>
</tr>
<tr>
<td>VIIag, %</td>
<td>102 (96–106)</td>
<td>107 (103–113)</td>
<td>85 (78–92)</td>
<td>96 (93–98)</td>
</tr>
<tr>
<td>VIIc, %</td>
<td>95 (92–98)</td>
<td>100 (96–103)</td>
<td>79 (74–85)</td>
<td>94 (91–97)</td>
</tr>
</tbody>
</table>

**TABLE 3. Cross-Sectional Correlation Between TG and VIIc, VIIag, or VIIa**

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th></th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA (n=127)</td>
<td>AG+GG (n=31)</td>
<td>Total (n=216)</td>
<td>AA (n=181)</td>
</tr>
<tr>
<td>VIIa</td>
<td>0.049</td>
<td>0.107</td>
<td>0.128</td>
<td>0.036</td>
</tr>
<tr>
<td>VIIag</td>
<td>0.225†</td>
<td>0.142</td>
<td>0.254‡</td>
<td>0.249†</td>
</tr>
<tr>
<td>VIIc</td>
<td>0.193‡</td>
<td>0.427‡</td>
<td>0.262‡</td>
<td>0.251†</td>
</tr>
</tbody>
</table>

*Total cases or controls including those without genotyping.
†\( P<0.001 \), ‡\( P<0.05 \).
AA indicates Arg-353 homozygote; AG, Arg-353/Gln-353 heterozygote; and GG, Gln-353 homozygote.
accompanied by an increase in factor VIIa, VIIag, or VIIc values in cases or controls (Figure B through D). As summarized in Table 4, there was no statistically significant correlation between the postprandial change in factor VIIa, VIIag, or VIIc values and the postprandial increase in TG levels in any subset of participants. Factor VIIc was correlated negatively with TG in AG+GG cases but not in AA cases or in either subset of controls (Table 4).
increase in factor VIIa. There are several possible reasons for day assay variability of factor VIIa reported previously,19 day-to-day variation, despite low within-day and between-
ever, it is possible that a low factor VIIa level and a high protein production and not with factor VII activation. How-
plasma TG level is associated primarily with factor VII productions by sustained high TG levels, which may require further investigation.

The variation in the relationship between measures of factor VII and TG was also examined in subjects with different factor VII genotypes. The distribution of various genotypes in the population examined was similar to what has been reported for populations with similar ethnic backgrounds.7,8 Similarly, the lower factors VIIc and VIIag levels among Gln-353 carriers are similar to what has been reported.

TABLE 4. Correlation of Changes in TG Levels With Changes in VIIa, VIIag, and VIIc Values from Time Zero to 3.5 Hours After a Fatty Meal

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA (n=127)</td>
<td>AG+GG (n=31)</td>
</tr>
<tr>
<td>VIIa</td>
<td>−0.065</td>
<td>−0.037</td>
</tr>
<tr>
<td>VIIag</td>
<td>0.047</td>
<td>0.000</td>
</tr>
<tr>
<td>VIIc</td>
<td>−0.005</td>
<td>−0.549†</td>
</tr>
</tbody>
</table>

*Total cases or controls including those without genotyping.
†P=0.014.

Association of Factor VII Genotype With Carotid Atherosclerosis
The odds ratio of being a case with carotid atherosclerosis versus a control was 1.27 (95% CI, 0.23, 1.96) among the AG+GG subset compared with the AA group. This was not statistically significant ($P=0.35$). Likewise, there was no association of factor VIIa, VIIc, or VIIag with case versus control status (Table 2).

Discussion
A major finding of this study is that factor VIIa value is higher in factor VII AA than in AG+GG genotypes, and the magnitude of difference in factor VIIa values between these genotypes is in accord with that in factors VIIag and VIIc values. However, unlike differences in factors VIIag and VIIc values which are statistically significant, the difference in factor VIIa values between these 2 genotype groups does not reach statistical significance. We attributed this, in part, to a higher variability of factor VIIa measurements. Our results show no association of the factor VIIa values with fasting TG levels despite a positive association of factors VIIag and VIIc values. Furthermore, despite a marked increase in the 3.5-hour postprandial TG levels, the 3.5-hour postprandial factor VIIa value in either genotype group is not influenced by fat feeding. Our findings of a positive association of fasting factors VIIag and VIIc with TG levels and an absence of any correlation between factor VIIa and TG values are similar to those reported by Moor et al.28 These results imply that the plasma TG level is associated primarily with factor VII protein production and not with factor VII activation. However, it is possible that a low factor VIIa level and a high day-to-day variation, despite low within-day and between-day assay variability of factor VIIa reported previously, could have obscured any association between factor VIIa and TG.

Silveira et al29 and Kapur et al30 have recently reported an increased postprandial factor VIIa level without factor VIIag elevation in response to an oral fat load.6 factor VIIa elevation peaked at 6 hours and leveled off at 12 hours after a fat load.6 These results suggest factor VII activation by an acute and transient rise of TG. In our study, no change was observed in factor VIIa, VIIag, or VIIc levels despite a 2-fold increase in plasma TG concentrations at 3.5 hours after an oral fat load. Kapur et al30 found no correlation between postprandial factor VIIa and TG levels despite a significant 6-hour postprandial increase in factor VIIa. There are several possible reasons for the difference between the results from the present study and the reported results: (1) a different sample size (the sample size of the studies reported by Silveira and by Kapur was small), (2) a different postprandial time point (a single 3.5-hour sample was chosen in our study to coincide with the TG elevation at this time period). In the studies reported by Silveira et al29 and Kapur et al30 factor VIIa elevation was more evident at 6 hours. Other studies using nonspecific or different assays for factor VII activation also revealed a significant rise of factor VIIa at 6 hours after a fat load31–34; and (3) different subjects (postprandial elevation of factor VIIc/VIIa was limited to healthy controls and not postmyo-
cardial infarction patients, and factor VIIa elevation, varied markedly between these 2 groups and between normotriglyceridemic and hypertriglyceridemic subjects30,31). These observations suggest heterogeneity in response to a fat load among subjects and patients. Our results did not show a correlation of factor VII genotype with postprandial factor VII activation.

This is contrary to the reports of Silveira et al29,31,34 which showed a linkage between the Arg-353 genotype and a postprandial hypertriglyceridemia induced increase in factor VIIa levels. The reason for this discrepancy is unclear. In this study, we have shown a cross-sectional correlation between fasting TG and factor VIIag but a lack of correlation between 3.5-hour postprandial TG levels and factor VIIag. The reason for this is also unclear. However, it may be speculated that cross-sectional association may be related to increased factor VII productions by sustained high TG levels, which may reflect an environment-gene interaction, whereas elevation in postprandial TG levels is transient and does not exert a similar gene-environmental interaction. This postulate requires further investigation.
together, the data would indicate that the glutamine substitution predominantly results in lower factor VII production accompanied by a lower factor VII activation. Contrary to the report that association of factors VIIag and VIIc with TG levels is confined to AA genotype, the positive cross-sectional correlation of factor VIIag or VIIc with TG did not differ significantly by genotype in our study. It should be noted that the statistical power to detect differences may be too modest. However, the observation that such a correlation is limited to subjects with the AA genotype could not be duplicated by others. In fact, Saha et al reported that the correlation between factor VIIag and TG among healthy Dravidian Indian adults was stronger in Gln-353 carriers than in Arg-353 homozygotes and that that between factor VIIc and TG was limited to Gln-353 carriers. The variation in the relationship of factor VIIc or VIIag with TG among populations of the United Kingdom, Singapore, and the United States (the present report) suggests that other environmental or genetic factors affect the association of TG with factor VII.

A recent report from the ECTIM study investigators showed that factor VII Arg/Gln 353 genotype was not a major determinant of myocardial infarction risk; likewise, neither was factor VIIc. A similar conclusion was drawn from the results reported by Moor et al. Taken together, the reported data further support the notion that factor VII 353 Arg-Gln polymorphism influences primarily factor VII synthesis.

The odds ratio of Gln carriers relative to Arg homozygotes was similar in cases with carotid atherosclerosis and controls. Furthermore, there were no significant differences in factor VIIa, VIIc, or VIIag values between cases and controls. These results suggest that neither factor VII levels or activation nor factor VII codon 353 gene polymorphism is related to subclinical atherosclerosis. This finding is consistent with the viewpoint that factor VII activation is primarily involved in thrombogenesis.

Acknowledgments
This article was supported by grant number U01-HL45467 and contracts N01-HC-55015, -55016, -55018, -55019, -55020, and -55022 from the National Heart, Lung, and Blood Institute, NIH, Bethesda, Md.

Appendix
Field Centers: Johns Hopkins University, Baltimore, Md: Myoses Szklo, Carol Christman, Sonny Harrell, Joel Hill, Joan Nelling; University of North Carolina, Chapel Hill: Gerardo Heiss, Carol Smith, Catherine Burke, Deanna Horwitz, Carmen Woody; University of Minnesota, Minneapolis: Virginia Wynn, Margaret Skelton, Shirley Van Pilsum, Karen Birkholz; University of Mississippi, Jackson: Richard Hutchinson, MD, Cora Walls, Dorothy Washington, Mattye Wilson, Nancy Wilson.

Central Laboratories: Hemostasis - The University of Texas Medical School, Houston: Valerie Stinson, Pam Pfeile; Lipid - Methodist Hospital, Houston: Wolfgang Patsch, Maria Mecci, Val Creswell, Julitta Samora, Wanda Wright.

Coordinating Center: University of North Carolina, Chapel Hill: Doris Jones, Sharon Kerick, Mark Park, Debbie Rubin-Williams. Ultrasound Reading Center: Bowman-Gray School of Medicine, Winston-Salem, NC: Ralph Barnes, Regina de Lacy, Delilah Cook, Carolyn Bell, Teresa Crotts, Suzanne Pillsbury.

National Heart, Lung and Blood Institute Project Office: Richey Sharrett.

References


Correlation of Factor VIIa Values With Factor VII Gene Polymorphism, Fasting and Postprandial Triglyceride Levels, and Subclinical Carotid Atherosclerosis
for the Atherosclerosis Risk in Communities Study Investigators

Circulation. 1998;98:2815-2821
doi: 10.1161/01.CIR.98.25.2815
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1998 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/98/25/2815

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/