ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #256

1. Title:
Postprandial Factor VII Activation

2. Writing Group:
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3. Timeline:
Basal and 3 1/2 h postprandial factor VIIa, VIIc, and VIIag measurements are being performed and will be completed in 4 weeks. Data on triglycerides and other biochemical parameters were available. It is estimated that analysis data and manuscript preparation could take place in 2 months.

4. Rationale:
Previous studies reported a positive association between factor VIIc and plasma triglyceride levels (1). Further studies indicated that associations between factor VIIc and the plasma concentrations of triglycerides can be explained by strong and positive associations between VIIc and large lipoprotein particles, chylomicrons, VLDL and IDL (2).

Several in vitro laboratory studies suggested a role of triglyceride-rich lipoproteins in activation of factor VII (3). Techniques used in measuring activated factor VII (VIIa) in plasma in these studies were not specific and might measure other species of factor VII. A critical question remains unresolved: does hypertriglyceridemia activate factor VII? In this proposal, we postulate that factor VII activation is accelerated by postprandial hyperlipidemia.

The ARIC postprandial study (PPL) provides an excellent opportunity to test this hypothesis. The PPL study is a well-designed feeding study wherein each individual serves as his own control. All the lipid parameters have been measured with carefully standardized procedures. Furthermore, a new factor VIIa assay based on the use of a truncated form of tissue factor for factor VIIa-mediated coagulation (4) has been established in the ARIC Hemostasis laboratory. This assay works well as far as intralaboratory assay variability is concerned. This study will hence provide direct information regarding the activation of factor VII by postprandial hyperlipidemia.

Understanding of this association is important. It will enhance our understanding on how postprandial hyperlipidemia may cause increased risk of ischemic heart disease. Factor VII antigen (VIIag), VII coagulant activity (VIIc) and activated VII (VIIa) will be measured in basal and 3 1/2 h postprandial samples by standardized techniques. These samples have been stored at -70 degrees Celsius. The data will be analyzed by ARIC CC.

5. Main Hypothesis to be Addressed:
Factor VII activation is accelerated by postprandial hyperlipidemia.

6. Data Requirements:
Data will be sent to CC and will be analyzed by Woody Chambless and his staff at CC. In the analyzing of data, special attention will be paid to the case-control nature of the selection.
REFERENCE


