ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #181

1. Title:
Diabetes, Hemostasis and Carotid Atherosclerosis

2. Writing Group:
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3. Timeline:
As soon as the manuscript is approved, data analysis can be started. A first draft is expected by June, 1993.

4. Rationale:
Cardiovascular disease is a major cause of morbidity and mortality in diabetic patients. The risk for stroke, myocardial infarction, peripheral vascular disease, and vascular death is increased two- to fourfold in diabetic subjects. Abnormalities of coagulation, fibrinolysis and platelet function associated with diabetes mellitus have been implicated in the development of atherosclerotic heart disease, such as, increased von Willebrand factor, factor VIII, fibrinogen, antithrombin III, plasminogen, PAI-1, ß-thromboglobulin, and platelet factor 4. The pathogenesis of vascular lesions in patients with diabetes mellitus is thought to depend at least partly on defects in the hemostatic system as many alterations of the coagulation and the fibrinolytic system as well as of the reaction of platelets have been found in diabetics. While previous ARIC manuscripts have reported increased levels of fibrinogen, Factor VII, Factor VIII, von Willebrand factor, antithrombin III and Protein C, and increased carotid artery wall thickness in diabetic people, after controlling for other major cardiovascular risk factors, these studies have not examined the multivariate relationship between carotid arterial wall thickness and hemostatic variables to determine whether diabetes is a modifying factor for increased carotid wall thickness (in the sense that it interacts with one or more hemostatic variables). This approach is warranted because of the complex and multi-faceted interactions between the elements of the hemostatic systems and may suggest a possible mechanism for the accelerated rate of atherosclerosis in diabetics. It is also proposed to determine whether the multivariate relationship between hemostatic variables and diabetes is related to the presence of shadowing and plaque in the carotid in people without evidence of symptomatic cardiovascular disease.

5. Main Hypotheses:
1) In people with and without increased carotid wall thickness, people with diabetes mellitus have a more adverse pattern of some hemostatic variables then nondiabetic people. 2) The multivariate relationship between carotid arterial wall thickness and hemostatic variables indicates that diabetes is a modifying factor for some hemostatic variables. 3) The multivariate relationship between hemostatic variables and diabetes is also related to the presence of shadowing and plaque in the carotid.

6. Data:
ARIC Visit 1 data - Diabetes status, carotid arterial wall thickness, shadowing and plaque indicator variables, Factor VII, Factor VIII, von Willebrand Factor, fibrinogen, Protein C and antithrombin III, and

potential confounders, such as body mass index, age, race, lipids, blood pressure, sex, physical activity, cigarette smoking, alcohol intake, educational level, white cell count.
Case-control component - visit 1 data as above and Fibrinopeptide A, ß-thromboglobulin, Platelet Factor 4, Thromboxane B2 and Tissue Plasminogen Activator Inhibitor I.
Inclusions/exclusions: Inclusions: black or white participant, nonmissing gender, aged 44-66, nonmissing diabetes status, not on anticoagulant therapy and not missing at least one hemostatic variable at visit 1.