

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #173

1. Title:

Elevated Homocyst(e)ine and Vascular Endothelial Damage

2. Writing Group:

(lead) P. Schreiner	K. Wu	R. Malinow	V. Stinson
L. Chambless	M. Szklo	G. Heiss	

3. Timeline:

Data on plasma homocyst(e)ine and on various markers of fibrinolytic activity and platelet activation exist on the set of ultrasound cases and their controls. If approval is obtained, a consolidated data file can be assembled and analyses started after the November AHA meetings.

4. Rationale:

Plasma homocyst(e)ine levels are reported to be higher in patients of arterial occlusive disease compared to disease-free controls. Analyses of the ARIC data indicate that asymptomatic individuals with carotid artery wall thickening have higher levels of plasma homocyst(e)ine than controls, after statistical adjustment for other risk factors of atherosclerosis. The goal of the proposed writing group is to examine markers of fibrinolytic activity and of increased platelet activation, in support of a postulated link between elevated homocysteine levels and endothelial damage.

5. Hypotheses:

Elevated homocyst(e)ine levels are associated with increased tPA and PAI-1 levels, increased platelet activation (increased beta-thromboglobulin), and coagulation activities.

6. Data Requested:

Homocyst(e)ine, tPA, PAI-1, b-thromboglobulin, coagulation factors measured in the full cohort, demographic variables, and "established" cardiovascular risk factor for possible use as covariates. Because the study question examines the hypothesized associations between variables measured on the set of ultrasound cases and their controls, consideration will be given in the analyses to (a) effect modification by case/control status and (b) estimates weighted to reflect the sampling scheme (sample controls are a stratified random sample of potential controls, with sampling fractions determined by the number of cases in the corresponding case stratum).