

ARIC STUDY MANUSCRIPT PROPOSAL

Manuscript #104

1. Title:

Apolipoprotein E Phenotyping: Case-Control Analysis of Atherosclerosis & Established Risk Factors

2. Writing Group:

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3. Timeline:

Ongoing determination and analysis of apolipoprotein E phenotypes in all case-control pairs.

4. Rationale:

Apolipoprotein E, as a ligand, mediates the uptake of lipoproteins via the LDL receptor-mediated pathway. In man, six apoE phenotypes can be distinguished, due to the presence of three alleles [E2, E3, E4] at one gene locus. There is an association of E2 homozygosity [E2/E2] with familial dyslipoproteinemia, although all E2/E2 individuals do not have familial dyslipoproteinemia. It has been shown that E2/E2 individuals without elevated plasma lipids do not have an increased risk of coronary heart disease. Also, individuals with a E2/E3 phenotype have reduced LDL chol levels. The pathophysiologic significance of E4 is less clear. Apolipoprotein phenotyping in case-control studies will serve to identify the association of apolipoprotein phenotype with atherosclerosis.

5. Main Hypothesis/Issues to be Addressed:

- 1). Individuals with the E2/E3 phenotype will have lower LDL chol levels.
- 2). Individuals with familial dyslipoproteinemia [E2/E2] will be identified.
- 3). Covariates, such as age, sex, medications, and race, will be examined by multivariate analysis to determine the effect and significance of these variables.

6. Data Requirements:

Data analysis will be performed by Dr. K. Dunn at Baylor College of Medicine, Department of Medicine. Apolipoprotein E phenotype data will be collected. Dependent variables: lipoproteins, apolipoproteins, hemostatic factors, medical history, body mass index, antihypercholesterolemic medication, diabetes, blood pressure, smoking status, alcohol consumption, physical activity, gender, race, age, field center. Independent variables: average and maximum far wall thickness at the common and internal carotid artery and its bifurcation.