ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #188

1. Title:
Apolipoprotein E Genotype and Relationships Among Glucose, Insulin, and Triglycerides

2. Writing Group:
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3. Timeline:
ApoE genotyping has been performed in case and control subjects. Data for glucose and insulin levels are available from Visit 1, and glycosylated hemoglobin levels are available from Visit II. Analyses can begin immediately.

4. Rationale:
Apolipoprotein E mediates the uptake of lipoproteins via the LDL receptor-pathway and the putative chylomicron-remnant receptor pathway. In man, six apoE phenotypes can be distinguished, due to the presence of three common alleles ([sigma]2, [sigma]3, [sigma]4) at one gene locus. Further studies have shown that the apoE polymorphism plays a significant role in the metabolism of plasma lipoproteins. VLDL and triglyceride levels are associated with hyperinsulinemia and insulin resistance. In addition, it was recently reported that the apoE polymorphism modifies the relationship between abdominal obesity and hypertriglyceridemia (Pouliet MC, et. al. J Lipid Res 1990;31:1023-9). Since abdominal obesity is correlated with insulin resistance, we would like to examine in ARIC subjects whether apoE alleles affect the relationships among indices of obesity, insulin, glucose, glycosylated hemoglobin, triglyceride and HDL levels.

5. Main Hypothesis/Issues to be Addressed:
1) In subjects carrying the [sigma]2 or [sigma]3 allele, BMI or other indices of obesity are correlated with glucose, glycosylated hemoglobin, and plasma triglyceride levels and insulin resistance. These relationships are altered or do not exist in subjects with the [sigma]4 allele.
2) The observed relationships are modified by case-control status.

6. Data Requirements:
Data analysis will be performed by Dr. Eric Boerwinkle. Variables: Apolipoprotein E, genotype, lipids, lipoproteins, apolipoproteins, hemostatic factors, medical history, body mass index, lipid lowering medication, hormones, insulin, glucose, glycosylated hemoglobin, diabetes history, blood pressure, smoking status, alcohol consumption, physical activity, gender, race, age, field center, case control status, average and maximum far wall thickness at the common and internal carotid artery and its bifurcation.