ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #473

1. Title: Carotid Artery Atherosclerosis and the Risk of Non-Insulin Dependent Diabetes Mellitus

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3. Timeline:
Begin February 1997, complete August 1997

4. Rationale:
NIDDM is associated with an excess risk of CVD; however, the explanation for this excess risk is uncertain. Previous studies have 1) confirmed the clustering of CVD risk factors with glucose intolerance and 2) documented that abnormalities in these CVD risk factors precede the onset of NIDDM. One possible explanation for excess CVD risk in NIDDM is that the early natural histories of NIDDM and atherosclerosis overlap greatly. These shared physiologic precursors, including obesity, high blood pressure, dyslipidemia, and hyperinsulinemia, might confer CVD risk long before NIDDM is clinically manifest. In this model, the association between hyperglycemia, which defines NIDDM, and CVD is merely an epiphenomenon and contributes little to subsequent CVD risk. To date, no study has been able to examine the development of atherosclerosis prior to NIDDM onset. Thus, we propose to conduct a nested case-control study to examine the association between subclinical atherosclerosis in the carotid artery prior to the onset of NIDDM and the subsequent development of NIDDM. The aforementioned model would predict that atherosclerosis advances more quickly in individuals who subsequently go on to develop NIDDM than in their counterparts who do not, and that differences in CVD risks factors would largely account for the disparity in atherosclerosis. ARIC's data on carotid wall thickness would provide a unique opportunity to test this hypothesis.

5. Hypothesis:
Higher carotid wall thickness at baseline exists in individuals who go on to develop NIDDM at visit 2 and visit 3, and this disparity is largely explained by the coexistence of the difference in their blood pressure, BMI, and fasting insulin and lipid levels.

6. Design:
Nested case-control study of ARIC participants who were non-diabetic at baseline and who were followed for at least 3 years. Three groups will be formed for comparison: 1) a control group, composed to those who remained non-diabetic at the end of the six-year follow up; 2) case group A, composed of those who became diabetic at visit 2; and 3) case group B, composed of those who became diabetic at visit 3.

7. Data:

**Case Definition**
Incident NIDDM after visit 1
1) Fasting blood glucose > 140 mg/dl or
2) Non-fasting blood glucose > 200 mg/dl or
3) Use of insulin or oral hypoglycemic agents or
4) Report of physician-diagnosed diabetes

**Exposure**
Carotid wall thickness at visit 1

**Covariates**
Age, race, gender, education, physical activity indices, dietary energy intake, parental history of diabetes, smoking, body mass index, waist to hip ratio, fasting insulin and glucose, blood pressure, use of cholesterol or blood pressure lowering medication at visit 1

8. Analysis:

1) Generalized linear regression of baseline carotid wall thickness on subsequent NIDDM status adjusting for baseline values of the covariates.