ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #501

1.a. Full Title: Longitudinal study of serum antioxidants and carotid atherosclerosis

b. Abbreviated Title (Length 25): Antioxidants & Atherosclerosis

2. Writing Group (list individual with lead responsibility first):

Lead: Javier Nieto
Address: Johns Hopkins
Phone: (410) 955 4380 Fax: (410) 955 8086
Electronic Mail Address: jnietophnet.sph.jhu.edu
Carlos Iribarren Myron Gross George Comstock
Richard Cutler

3. Timeline: Immediately

4. Rationale:

The hypothesis that antioxidants may prevent atherosclerosis ha3 been recently reviewed by Diaz et al (New Eng J Med 1997 337:408-16). In a case-control study within the ARIC Study, serum antioxidants were not consistently associated with carotid atherosclerosis (Iribarren et al, MS#194 , while among dietary antioxidants only dietary vitamin C and alpha-tocopherol seemed to be cross-sectionally related to carotid atherosclerosis in the entire AR1C cohort ; Kritchevskv et al, MS#69). Uric acid (another strong serum antioxidant) was cross-sectionally associated with carotid atherosclerosis only in unadjusted analysis; after adjusting for the main CVD risk factors, the association all but disappeared (Iribarren et al, Ann Epidemiol 1996; 6:331-40).

As part of the Washington .County Substudy outlined in the ARIC Study Renewal application, serum antioxidants (vitamins and uric acid), as well as total antioxidant capacity of the serum (ORAC) were measure in 1974 (CLUE) serum from 300 ARIC subjects selected on the basis of the average visit 1-2 carotid IMT. These samples offer an opportunity to examine the longitudinal association between serum antioxidants and atherosclerosis.

5. Main Hypothesis:

l) Serum antioxidant levels and total antioxidant capacity in serum collected in 1974 are associated with carotid atherosclerosis in the ARIC Study (1987-92).
2) These associations are independent of the main cardiovascular risk factors.

6. Data (variables, time window, sources, inclusions/exclusions):
? Cases are defined as the 150 individuals with the highest mean IMT over visit 1 and visit 2 among the 1,410 Washington County ARIC participants that participated in the 1974 survey.
? Controls are the 150-indnviduals with the lowest mean IMT over visit 1 and visit 2, frequency-matched to the case3 within age and gender strata.

The following data are available in these 150 Cases and controls-:
- 1974 serum levels of antioxidants (vitamins): zeaxnathin, cryptoxanthin, beta-carotene, lycopene, alpha-carotene, gamma--tocopherol, alpha-tocopherol, retinol.
- 1974 total serum antioxidant capacity (ORAC).
- 1974 and l 987-89 serum levels of uric acid, albumin, cholesterol.
- 1974 and 1987-89 blood pressure, smoking.

Analysis:
1) The mean 1574 levels of serum antioxidants and serum antioxidant capacity in cases and controls will be compared, before and after controlling for risk factors in both 1974 and 1987-89.
2) If an association between ORAC and case-control status is found, we will try to identify which antioxidants explain the association.