ARIC MANUSCRIPT PROPOSAL #677

PC Reviewed: 07/08/99 Status: Approved Priority: 1
SC Reviewed: 07/21/99 Status: Approved Priority: 1

1a. Full Title: ASSOCIATION OF CIRCULATING CELL ADHESION MOLECULES WITH CAROTID ATHEROSCLEROSIS IN AFRICAN AMERICANS

1b. Abbreviated Title (Length 26): ADHESION MOL, CAA, BLACKS

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

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3. Timeline:

   Measurement of levels of ICAM-1, VCAM-1, E-selectin, P-selectin, and L-selectin in the African American carotid atherosclerosis (CAA) cases and thin walled controls and the cohort representative sample are completed. This analysis should be finished within the next month. Within 3 months of completion of the data, preliminary statistical analysis should be completed and a report formatted as a draft manuscript will be presented to the steering committees.

4. Rationale:

   Leukocytes play a critical role in the initiation of atherosclerosis and are also postulated to play an important role in the transition from stable to unstable lesions. Adhesion of circulating leukocytes to the vascular endothelium is regulated by leukocyte–endothelial cell adhesion molecules. E-selectin, ICAM-1, VCAM-1, and P-selectin have all been shown to be increased in pathological studies of atherosclerosis. L-selectin is expressed on leukocytes and shed with activation. Circulating forms of cell adhesion molecules can be measured in plasma and are elevated during inflammatory conditions in which...
pathological studies have documented increased expression of cell adhesion molecules on endothelial cells and other cell types.

Plasma levels of ICAM-1 and E-selectin have been previously shown in ARIC to be increased in incident CHD and CAA cases compared with controls [, in race-adjusted analyses including only 44 African-American CAA cases. The odds of CHD and CAA were 5.5 and 2.6, respectively, for those with levels of ICAM-1 in the highest quartile compared with those in the lowest quartile. The odds of CAA were 2.03 for those with levels of E-selectin in the highest quartile compared with those in the lowest quartile. Odds of CHD events were also increased in the Physicians' Health Study for those individuals with levels of circulating ICAM-1 in the highest quartile.

5. **Main Hypotheses:**

   a) African-Americans with carotid atherosclerosis will have increased levels of circulating CAMs compared with [thin carotid wall and population-representative controls . The association is similar to that seen in other ARIC participants.
   b) Levels of circulating adhesion molecules will correlate with other CHD risk factors such as LDL, HDL, triglycerides and white blood cell count.
   c) Associations of circulating ICAM-1, E-selectin, and possibly other CAMs with carotid atherosclerosis will persist after adjustment for traditional risk factors.
   d) Individuals who have increased levels of ICAM-1, E-selectin, and WBC may be at greater risk for CAA than those having elevations of any single factor alone.

6. **Data (variables, time window, source, inclusions/exclusions):**

   The data will be analyzed locally by Eric Boerwinkle, then transferred to the CCSS for official analysis.

7. **References:**

