Manuscript #160

1. Title (length 26):
Lp[a] and Incident CHD
Full title: Lipoprotein[a] as a risk factor for incident coronary heart disease

2. Writing Group:
(lead) P. Schreiner J. Morrisett G. Heiss
W. Patsch L. Wijnberg A. Folsom
R. Watson

3. Timeline:
Analyses will be initiated when incident cohort events are validated and released to investigators.

4. Rationale:
Lipoprotein[a] has been shown to be associated with coronary heart disease (CHD) in a wide variety of ethnic and age groups. Studies relating Lp[a] levels with prevalence of myocardial infarction (MI) are the most numerous and historically the oldest associations found for Lp[a] as a risk factor. While individuals who have either a history of MI or who are asymptomatic with a family history of MI have higher mean Lp[a] levels than comparison groups, the majority of studies have considered cross-sectional data, and therefore could not directly assess the role of Lp[a] as a risk factor for incident disease. To date, two prospective investigations of the effect of elevated Lp[a] concentrations on CHD (via a nested case-control design) have been reported in the literature with conflicting results. Jauhiainen et al. (1991), as a part of the Helsinki Heart Study, concluded that Lp[a] is not a predictor of future CHD; Rosengren et al. (1990), however, found that Lp[a] is an independent risk factor for nonfatal MI or CHD death.

The ARIC Study permits incident fatal or nonfatal CHD to be assessed in the context of an annual telephone interview, record abstraction of hospitalized and fatal cardiovascular events, and a re-examination every 3 years. By choosing participants without a history of prevalent CHD at baseline from an ambulatory population sample, acute phase changes in plasma lipoproteins immediately following a coronary event are avoided; in addition, increased tendency toward reinfarction in MI patients is eliminated as a potential bias. New infarction rates from these data are more likely to be the result of risk factor variability between individuals.

5. Main Hypothesis:
1) Elevated levels of Lp[a] are associated with increased incidence of CHD

6. Data:
Black and white participants in the cohort component of the ARIC Study who were free of prevalent CHD (MI diagnosed either by ECG or by physician, angina, coronary artery bypass surgery or angioplasty) at the baseline visit will be included in this study. CHD incidence will be determined via the standardized ARIC algorithm based on pain, enzymes, and ECG; an interview of physician or family members, and a review
At the time of analysis, at least 3 years of reasonably complete followup data are available for the visit 1 cohort (year 4 or potentially year 5 of the study). Lp[a] measured as its total protein component (apo[a] plus apoB) will be the main exposure (independent) variable. Other covariates that will be considered as potential confounders or effect modifiers include age, fibrinogen, LDL- and HDL-cholesterol, hypertension status, amount of cigarette smoking, diabetic status, and menopausal status in female participants—all collected at baseline. The association of Lp[a] and these risk factors with incident CHD will be assessed in race-specific (and gender-specific, sample size permitting) models using Cox proportional hazards modeling.

REFERENCES
