

ARIC MANUSCRIPT PROPOSAL #648

PC Reviewed: 02/19/99 **Status: Approved** **Priority: 1**
SC Reviewed: **Status: _____** **Priority: _____**

- 1.a. Full Title:** Fibrinolytic factors & CVD

 - b. Abbreviated title** (Length 26): Fibrinolytic factors & CVD
- 2. Writing Group (list individual with lead responsibility first):**

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3. Timeline:

Start spring 1999, analysis by Dr. Ahn.

4. Rationale:

Fibrinolysis is believed to play an important role in resolution of thrombi precipitating acute atherothrombotic events. A few prospective epidemiologic studies have suggested that elevated plasminogen activator inhibitor-1 (PAI-1) or tissue plasminogen activator (tPA) antigen levels may indicate increased CVD risk.

ARIC has measured PAI-1 and tPA in the case-cohort "simultaneous batch". It also measured, on CHD cases and a cohort sample, a polymorphism of the PAI-1 gene that appears to affect PAI-1 levels.

This paper will first focus on CHD in relation to PAI-1, tPA, and PAI-1 genotype. It also will eventually explore PAI-1 and tPA for the other case-groups: IMT, African American, and PAD. An existing manuscript proposal (544 - Salomaa) proposed to examine plasminogen level, which ARIC measured in the simultaneous batch. We may analyze it at the same time and consider whether to lump the two manuscripts vs. keep them separate.

5. Main Hypothesis:

- (1) tPA and PAI-1 are associated positively with CHD incidence.
- (2) PAI-1 genotype will be correlated with PAI-1 level but will not be associated with CHD.

6. Data:

Case-cohort sample, focussing first on CHD status in relation to PAI-1, tPA, and PAI-1 genotype.

Covariates: age, race, sex, smoking status and cigarette years, LDL, HDL, fibrinogen, CRP, WBC, SBP and antihypertensive meds, WHR, diabetes, and education. Special consideration of plasminogen and, in the analysis of PAI-1 genotype, of PAI level.

Possible effect-modifiers to be studied, if sufficient power: PAI-1 genotype by glycoprotein IIIa polymorphism (as in Pastinen T, et al. Human Molecular Genetics 1998;7:1453-1462) and ACE genotype; plasminogen by Lp(a).