ARIC MANUSCRIPT PROPOSAL #740

PC Reviewed: 08/29/00	**Status: A**	**Priority: 1**
SC Reviewed: 10/03/00	**Status: A**	**Priority: 1**

1.a. Full Title:

Venous thromboembolism, Factor V Leiden, and related factors

a. **Abbreviated Title (Length 26):** Factor V Leiden and VTE

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

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3. Timeline:

Fall 2000: analysis and first draft

4. Rationale:

The LITE Study is examining venous thromboembolism (VTE) in the combined ARIC and CHS cohorts. This nested case-control analysis will examine VTE incidence in relation to factor V Leiden, factor V HR2 haplotype, activated protein C resistance, and factor V antigen level.

Factor V Leiden is a factor V mutation shown to increase risk of VTE 4 fold (1), but it has been studied in few prospective studies. Carriers of factor V Leiden are resistant to the protein C-protein S system, a natural anticoagulant. Recently a factor V haplotype (HR2) has been described and scanty evidence (2, 3) thus far does not clarify whether it is associated with VTE. Factor V level has not been studied as a VTE risk factor prospectively. Interactions of other

VTE risk factors with these factor V related factors may be important.

5. Main Hypothesis/Study Questions:

a. VTE is positively associated with factor V Leiden, aPC resistance, and higher factor V levels. It is not associated with HR2 haplotype.

b. Factor V Leiden interacts with age, BMI, smoking, vWF, and factor VIII.

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

Sample: LITE nested case-control sample of 235 incident VTE cases and 688 frequency matched controls.

Data: baseline risk factors measured in ARIC and CHS, including factor V related factors measured only on this sample.

Analysis: (1) examine inter-relations among factors using cross-tabs and correlations
(2) logistic regression to test study hypotheses

7. a. Will the data be used for non-CVD analysis in this manuscript?
____ Yes __X__ No

c. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used?
____ Yes ____ No
(This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8. a. Will the DNA data be used in this manuscript? ___X_ Yes ____ No

b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = "No use/storage DNA"?
__X__ Yes ____ No

References

1. Rosendaal FR: Venous thrombosis: a multicausal disease. *Lancet* 1999;353:1167-73.
2. de Visser MC, Guasch JF, Kamphuisen PW, et al: The HR2 haplotype of factor V: effects on factor V levels, normalized activated protein C sensitivity ratios and the risk of venous thrombosis. *Thromb Haemost* 2000;83:577-82.
3. Faioni EM, Franchi F, Bucciarelli P, et al: Coinheritance of the HR2 haplotype in the factor V gene confers an increased risk of venous thromboembolism to carriers of factor V R506Q (factor V Leiden). *Blood* 1999;94:3062-6.