Acute-phase proteins have been recently found associated with the incidence of myocardial infarction among patients with angina (Liuzzo, NEJM 1994;331:417; Thompson, NEJM 1995;332:635) as well as among previously asymptomatic participants in the MRFIT study (Kuller, AJE 1995;141:S57). It has been speculated that these proteins could be markers of endothelial damage induced by a variety of stimuli, including ischemia, oxidized low-density lipoprotein, immune complexes, and viral and chlamydia infections (Liuzzo, 1994). Moreover, in vitro studies suggest that CMV and other herpes virus have procoagulant properties (Bruggeman, Thromb Haemost 1988;59:264; Vercelloti, Blood Cells 1990;16:209) and that these phenomenon seems to be dependent on plasma coagulation factors (van Dam-Mieras, Thromb Haemost 1992;68:364).

In the ARIC-Clue study, we found CMV antibody titers in 1974 sera to be associated with 1987-89 plasma levels of factors VIII, von Willebrand factor, and protein C. In addition, there was a significant inverse association with the activated partial thromboplastin time. These associations remain significant after adjusting for potential confounders, including serum cholesterol and triglycerides. No association with other acute-phase or hematologic parameters (e.g., fibrinogen, albumin, leukocyte count) was found.

The linkage between the data from the case-control studies on sialic acid hemostasis and infections (herpes and chlamydia) provide a unique opportunity to explore the association between serum antibody titers and a variety of hemostatic factors possibly related to atherosclerosis. The availability of these data linked to atherosclerosis case-control status will allow us to explore the possibility that the association of infections and atherosclerosis previously reported in the ARIC study (Sorlie, Melnick) is at least partially mediated by these hemostatic parameters.

As compared with the ARIC-Clue study, this study will be cross-sectional, will have larger sample size, will have available data on other hemostatic factors measured in ARIC cases and controls as well as sialic acid.

4. Hypotheses:

(1) Antibody titers for virus (HSV1, HSV2, and CMV) and chlamydia TWAR are associated with plasma levels of hemostatic and acute-phase reaction parameters.
(2) These associations partially explained the cross-sectional association between serum antibodies and atherosclerosis.

5. Data and Analysis Plan:

Data on chlamydia and herpes virus antibodies in cases and controls (visit 1).
Data on hemostatic factors from the full cohort, as well as from the case-control analyses (visit 1).
Data on sialic acid in cases and controls (visit 2).
Data on other major risk factors (age, gender, serum cholesterol, triglycerides, blood pressure, diabetes, smoking) (visit 1).

(1) The association between antibodies and hemostatic factors will be explored separately in cases and controls.
(2) If the associations are found to be homogeneous, pooled analysis will be conducted, with adjustment for case-control status if necessary.
(3) The association between antibodies and atherosclerosis will be re-examined after adjustment for the hemostatic factors found to be related to antibody status in the above analyses.