ARIC Manuscript Proposal # 994

PC Reviewed: 02/25/04	**Status: A**	**Priority: 2**
SC Reviewed: 02/25/04	**Status: A**	**Priority: 2**

1.a. Full Title: Associations Between IgG Antibody to Oral Organisms and Carotid Intima-Medial Wall Thickness in Community-Dwelling Adults.

b. Abbreviated Title (Length 26 characters):
Antibody status and IMT

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

Lead: James Beck
Address: Dept Dental Ecology, CB 7450
University of North Carolina
Chapel Hill, NC 27516

Phone: (919) 966-2787 Fax: (919) 966-6761
E-mail:

Writing group members: Paul Eke, Dongming Lin, Kevin Moss, David Couper, Phoebus Madianos, Gerardo Heiss, Steven Offenbacher,.

3. Timeline:

MS Proposal #687 was very general, including many aspects of periodontal disease with CHD and IMT. The manuscript published under that number involved clinical periodontal disease and IMT. This proposed manuscript concentrates on antibodies to oral organisms and IMT. . Rather than splitting MS proposal #687 into multiple manuscripts we would like to request a different manuscript number for this paper. The manuscript has been written and distributed to the writing group. Thus, the manuscript can be submitted to the ARIC Publications Committee sometime during March, 2004.

4. Rationale:

Some studies have reported significant positive associations between periodontal disease and CHD, while others have not. Speculations regarding reasons for this variability have included the suggestion [1] that since the clinical signs of periodontal disease are a consequence of the interaction between the infectious microorganisms and the host immune and inflammatory response, it is likely that including measurement of this interaction would be a more direct measure of the systemic component of the periodontal exposure that is a consequence of periodontal disease. Evidence in support of this concept has been recently provided by Pussinen [2] who demonstrated that the presence of serum IgG-antibodies to *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* was associated with CHD adjusting for age and several CHD risk factors. A second major criticism of the data linking CVD to periodontitis focuses on the role of smoking. Smoking is accepted as a risk factor for both periodontal disease and heart disease and must be considered as a confounder of any periodontal disease – heart disease association. While most studies have controlled for smoking by means of multivariable analyses, Hujoel and his colleagues have focused on the possibility that smoking has such a strong influence on both diseases that statistical control cannot completely adjust for

its effects and stratification on smoking is needed [3-6]. In fact, these investigators hypothesize that both periodontal disease and heart disease are co-morbid conditions that result from smoking. Certainly, these points on confounding and stratification raise important considerations worthy of further study. The aim of this study is to describe the relationships between IgG antibodies to 17 oral organisms and atherosclerosis as indexed by carotid intima-medial wall thickness (IMT).

1. **Beck, J. and S. Offenbacher, *Relationships among clinical measures of periodontal disease and their associations with systemic markers.* Ann Periodontol, 2002. 7: p. 79-89.**
2. **Pussinen, P., et al., *Antibodies to periodontal pathogens are associated with coronary heart disease.* Arterioscler Throm Vasc Biol, 2003. 23(7): p. 1250-1254.**
3. **Hujoel, P., et al., *A hidden periodontitis epidemic during the 20th century?* Community Dent Oral Epidemiol, 2003. 31(1): p. 1-6.**
4. **Hujoel, P., et al., *An exploration of the periodontitis - cancer association.* Ann Epidemiol, 2003. 13(5): p. 312-316.**
5. **Hujoel, P., et al., *Periodontitis - systemic disease associations in the presence of smoking --causal or coincidental?* Periodontol 2000, 2002. 30: p. 51-60.**
6. **Hujoel, P., *Does chronic periodontitis cause coronary heart disease? A review of the literature.* J Am Dent Assoc, 2002. 133 Suppl: p. 31S-36S.**

5. Main Hypothesis/Study Questions:

Two hypotheses to be tested are:

High serum antibody IgG levels (above the Median) to oral organisms will be positively associated with the prevalence of IMT scores of 1mm or more, adjusting for relevant confounders.

The association between antibody levels and IMT will be restricted to current and former smokers when stratifying on ever (current and former) and never smokers.

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

The data needed for this manuscript are already available. We plan only to use data from ARIC visit 4 for IMT measures, supplementing from visit 3 when needed. Participants included in the study would have had periodontal examinations at visit 4, IMT status recorded primarily from visit 4, have serum samples available, and information on potential confounders.

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

b. If Yes, is the author aware that the file ICTDER02 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 ICTDER02 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? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. **The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.** ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

   ___X___ Yes _____ No

10. **What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?** See explanation under Timeline.