ARIC Manuscript Proposal # 1079

PC Reviewed: _05/13/05	**Status: __A__**	**Priority: _2__**
SC Reviewed: __05/13/05	**Status: __A__**	**Priority: _2__**

1.a. Full Title: Association of Antibodies to Periodontal Organisms with Renal Insufficiency

b. Abbreviated Title (Length 26 characters): Periodontal Antibodies and Renal Insufficiency

2. Writing Group:

Writing group members: Abhijit V. Kshirsagar, Kevin L. Moss, James Beck, Steve Offenbacher, Ronald Craig

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Corresponding/senior author (if different from first author correspondence will be sent to both the first author & the corresponding author): **N/A**

3. Timeline:

Obtain data set:	June 2005
Begin statistical analysis:	June 2005
Complete statistical analysis:	August 2005
Complete manuscript:	December 2005

4. Rationale:

Preliminary evidence has demonstrated a non-linear association of periodontal disease with renal insufficiency (1,2). These studies used a "local" definition of periodontitis—the extent of bone loss around the teeth as measured by pocket depth and attachment loss. The pathogens causing periodontal disease are known to elicit a local inflammatory response that can lead to measurable systemic changes.

Serum antibodies to periodontal pathogens are reflective of local and systemic exposure to the periodontal bacterial pathogens. We propose to examine the association of antibodies to periodontal organisms to renal insufficiency.

5. Main Hypothesis/Study Questions:

Our *a priori* hypothesis is that the presence of high levels of IgG antibodies to various periodontal disease organisms are positively associated with renal insufficiency after adjustment for relevant confounders.

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

All variables necessary for the analysis are available in the Dental ARIC cohort of the ARIC Study.

Outcome variable. The main outcome variable is calculated glomerular filtration rate (cGFR), (3).

$$cGFR = 186 * (\text{Serum creatinine})^{-1.154} * (age)^{-0.203} * 1.212(\text{if black}) * 0.742(\text{if female})$$

We will use calculated glomerular filtration rate as both a continuous variable, and as a categorical variable. All the demographic and medical variables needed for the calculation are available for the Dental ARIC cohort.

Main independent variable. The main independent variable is the presence of periodontal antibodies. This is determined using a whole bacterial immunocheckerboard, and is defined as high or low using the median value as the cut point. The method is semi-quantitative in nature.

Covariates. The covariables will be a composite of race and ARIC field center, 3 levels of education (to control for SES), hypertension, smoking (current heavy, current light, former heavy, former light, or never), diabetes mellitus, fibrinogen, white blood cell count, and plasma LDL, HDL, and triglyceride levels.

Planned Analysis.

1. Logistic regression with relative odds of impaired renal function (yes/no) with periodontal antibodies as the independent variable.
2. Linear regression with calculated glomerular filtration rate as a continuous outcome variable and periodontal antibodies as the independent organism.
3. Multivariable models will be adjusted for the *a priori* suspected confounders: race and ARIC field center, education, hypertension, smoking, diabetes mellitus, fibrinogen, white blood cell count, and LDL, HDL, and triglyceride levels.

Study Design. This will be a cross-sectional study of the data obtained from ARIC cohort members at Visit 4.

Inclusions/exclusions. This study will include all Dental ARIC cohort members for whom periodontal measures and serum creatinine were available, and exclude persons reporting being on dialysis. Approximately 6800 persons had periodontal examinations at Visit 4.

7.a. Will the data be used for non-CVD analysis in this manuscript? __x__ Yes ____ 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? __x__ 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://www.cscc.unc.edu/ARIC/search.php

_____ Yes ___**x**____ 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)? 775

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __x__ Yes ____ No

11.b. If yes, is the proposal
_x__ A. primarily the result of an ancillary study (list number* _15_____)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

References:

1. Kshirsagar AV, Moss KL, Elter JR, Beck JD, Offenbacher S, Falk RJ. Periodontal Disease is Associated with Renal Insufficiency in the Atheroclerosis Risk in Communities (ARIC) Study. *Am J Kidney Dis 45:650-657, 2005*
2. Kshirsagar AV, Elter JR, Offenbacher S, Craig R, Falk RJ. Periodontal disease is associated with renal insufficiency in NHANES III. Poster presentation at the National Kidney Foundation 2004 Clinical Meeting. *Am J Kidney Disease 43(4): A29, 2004*
3. Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Part 1. *Am J Kidney Dis 39 (Suppl1): S17-S31, 2002*