1. Full Title: Low toenail chromium as a risk factor for incident diabetes: results from the CLUE II study and the ARIC study

b. Abbreviated Title (Length 26 characters): Chromium and diabetes

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

   Lead: Megan Jehn
   Address: Welch Center for Prevention, Epidemiology and Clinical Research
             The Johns Hopkins Medical Institutions
             2024 E. Monument Street, Suite 2-604
             Baltimore, MD 21205-2223
   Phone: 410-614-6461       Fax: 410-955-0476
   E-mail: mjehn@jhsph.edu

   Writing group members: Eliseo Guallar, Fred Brancati, Joe Coresh, Peter Bode, Kathy Helzlsouer, others welcome

3. Timeline: This project will be submitted for NIH funding June 1, 2001. If funding is secured, it is anticipated that the analysis of toenail clippings from CLUE II for chromium content, using neutron activation analysis, will take approximately 12 months after approval. An additional 6 months is anticipated for data analyses and manuscript preparation.

4. Rationale:

   The results from the most recent National Health and Nutrition Examination Survey (NHANES III) have shown that the prevalence of diagnosed diabetes has increased dramatically in the U.S. and that a substantial proportion of the population has undiagnosed diabetes, impaired fasting glucose, and impaired glucose tolerance.[1] Although improving diet and exercise can substantially decrease the risk of diabetes and improve insulin resistance [2-4], many individuals at risk for diabetes do not accomplish these substantial lifestyle modifications. Additionally, many diabetics fail to achieve tight glucose control with current therapy. Over the years, micronutrient supplements have been investigated to help overcome the onset of insulin resistance. Chromium may be a potential useful adjuvant therapy in the treatment of diabetes and may have a role in diabetes prevention.[5]

   Chromium is an essential nutrient in human and animal nutrition.[6, 7] Chromium is a cofactor for insulin at the receptor level and may improve insulin binding to cells.[8] Chromium deficiency has been associated with impaired glucose metabolism, insulin resistance and altered lipid profiles and may contribute to the onset of type II diabetes.[5] The actual prevalence of chromium deficiency in the population has been difficult to determine because currently there are no reliable indicators of underlying chromium status. Estimates of dietary chromium intake are unreliable as measures of exposure because the chromium content of food is modified during
processing and secondly, because chromium is poorly absorbed.[9] However, chromium concentrations measured in toenails may be a useful biomarker of chromium nutritional status.

The aim of the proposed study is to determine the influence of baseline levels of toenail chromium on the development of type 2 diabetes during six years of follow in the ARIC study. To address these specific aims we propose to conduct a nested case-cohort study within subcohort of 1,745 residents of Washington County, MD participating in both the CLUE II and ARIC studies. Cases will be defined as incident type II diabetes identified during 6 years of follow-up in the Washington County site of the ARIC study (N=135). Controls (N=270) will be randomly selected from the 1,745 participants in both CLUE II and ARIC.

For the present study, we propose to use toenail clippings collected in 1989 in CLUE II, to assess chromium status. Nail samples will be analyzed using instrumental neutron activation analysis. This technique is capable of detecting small concentrations of chromium (below the mg/kg range) in biological specimens with virtually no risk of contamination.[10]

Examining chromium levels may enhance our understanding of the underlying relationship between type II diabetes, insulin resistance and cardiovascular disease. It is unclear whether chromium deficiency precedes diabetes onset, or whether the onset of diabetes contributes to increased chromium losses. Data from the CLUE II study and the ARIC study will provide a unique opportunity to test this hypothesis prospectively using appropriate biomarkers of exposure and the most accurate analytical methods available today. Identification of a nutritional deficiency as an underlying factor in the development of type II diabetes has various implications for establishing adjuvant therapies for prevention and treatment of this disease.

5. Main Hypothesis/Study Questions:
Chromium deficiency precedes the development of type II diabetes

6. Data (variables, time window, source, inclusions/exclusions):
All necessary ARIC data has previously been collected. Data analysis will be performed by Megan Jehn and Eliseo Guallar at Johns Hopkins. Variables of interest in the proposed study include: fasting glucose (visit 1-4), fasting insulin (visit1-2), lipids (visit 1-4), anthropometric data, age, center, race, diabetes, blood pressure, physical activity, medication, FFQ data. This analysis will be restricted to ARIC participants in Washington County. Participants with diabetes at baseline be excluded.

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/csc/aric/study/studymem.html

___X___ Yes _______ No

REFERENCES: