

ARIC Manuscript Proposal # 829

PC Reviewed: 09/18/01
SC Reviewed: 09/18/01

Status: A
Status: A

Priority: 2
Priority: 2

1.a. Full Title: Pulmonary Function and Incidence of Type 2 Diabetes Mellitus

b. Abbreviated Title (Length 26 characters): Lung Function & Incident DM

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

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	Others welcome	

3. Timeline: Begin immediately

4. Rationale:

Diabetes Mellitus is a chronic condition that is characterized by a number of adverse microvascular and macrovascular complications. Well-established risk factors include obesity, African-American race, and a family history of diabetes. Recently, impaired lung function has also been associated with alterations in glucose tolerance and insulin resistance. Studies in normal subjects and in individuals with chronic respiratory disease demonstrate (Hjalmarsen et al., 1996, Larsen 1997) that hypoxia is associated with impaired glucose tolerance. Moreover, a number of studies over the last decade also indicate that patients with diabetes can have impaired lung function (Lange et al. 1989, Barrett-Connor et al. 1996, Davis et al. 2000). Although the available evidence suggests an association between impaired lung function and alterations in metabolic function, there are no data that support a causal link between decreased lung function and the occurrence of impaired glucose tolerance, insulin, resistance, and clinical diabetes.

The possibility of a causal link is based on some recent observations that hypoxemia may lead to alterations in glucose tolerance and insulin resistance. In a study of normal volunteers, Larsen et al. (1997) showed that hypoxia, induced by changes in altitude, in normal men can impair glucose homeostasis. In another study on patients with chronic respiratory lung disease, Hjalmarsen et al. (1996) observed that patients with hypoxemia were more likely to have an abnormal glucose tolerance test compared to patients without hypoxemia. Although a majority of individuals with abnormal lung function do not manifest daytime hypoxemia, it is well established that many such individuals can experience intermittent hypoxemia during sleep. Since onset of sleep is associated with a decrease in minute ventilation, individuals with borderline or abnormal lung function can have worsening of their ventilation-perfusion mismatch that can lead to decreases in the arterial oxygen levels during sleep. These physiologic derangements are often worsened during rapid eye movement sleep, a state that is characterized

by instability of the respiratory and cardiovascular systems. The occurrence of intermittent hypoxemia, a common finding in patients with sleep-disordered breathing, is associated with increase sympathetic neural traffic and can lead to the metabolic abnormalities including glucose tolerance and insulin resistance. In fact, in a recent study by Punjabi et al., the presence of disordered breathing during sleep in a relatively healthy cohort of men, a dose response relationship was observed between the degree of nocturnal hypoxemia and impairment in glucose tolerance and insulin resistance.

Although arterial oxygen saturation was not assessed in the ARIC Study, spirometry-related measures of lung function—particularly FVC and FEV1—are widely accepted markers for common lung diseases that are associated with hypoxemia. Therefore, in the context of the ARIC Study, we hypothesize that patients with abnormal lung function are at increased risk for the occurrence of metabolic abnormalities (elevated glucose and insulin levels) and are at risk for developing clinical diabetes independent of confounding risk factors such as body mass index.

5. Main Hypothesis:

Our main hypothesis is that diminished pulmonary function is an independent risk factor for the development of glucose intolerance, and type 2 diabetes. Diminished pulmonary function will be characterized based on a) baseline FVC and FEV1 and b) changes in FVC and FEV1 during the first 3 years of follow-up. The main outcome, incident diabetes will be characterized based on clinical and laboratory data collected in years 3, 6, and 9 of follow-up. In addition, glucose intolerance in persons without prior evidence of diabetes will be characterized based on results of the oral glucose tolerance test performed at year 9 of follow-up.

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

We propose to analyze data on all ARIC participants with complete data on diabetes status at baseline and during follow-up and pulmonary function at visits 1 and 2. Participants with pre-existing diabetes at baseline would be excluded. Key variables for the analyses would include: diabetes status, glucose levels, pulmonary function tests, height, weight, smoking history, and socio-demographic variables, cardiopulmonary diseases and other medical history at baseline.

7.a. Will the data be used for non-CVD analysis in this manuscript? ___ 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? N/A ___ 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 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”? N/A ___ 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/stdy/studymem.html>

Yes No

References:

Barrett-Connor E, Frette C: NIDDM, impaired glucose tolerance, and pulmonary function in older adults. The Rancho Bernardo Study. *Diabetes Care* 19:1441 – 1444. 1996.

Davis TME, Knuiiman M, Kendall P et al: Reduced pulmonary function and its association in type 2 diabetes: the Fremantle Diabetes Study. *Diabetes Research and Clinical Practice* 50:153-159. 2000.

Hjalmarsen A, Aasebo U, Birkeland K, et al: Impaired glucose tolerance in patients with chronic hypoxic pulmonary disease. *Diabetes Metab* 1996 Feb;22(1):37-42

Lange P, Groth S, Kastrup J, et al: Diabetes mellitus, plasma glucose and lung function in a cross-sectional population study. *Eur Respir J* 2:14-19, 1989.

Larsen JJ, Hansen JM, Olsen NV, et al: The effect of altitude hypoxia on glucose homeostasis in men. *J Physiol* 1997 Oct 1;504 (Pt 1):241-9