

COMMENTS AND RESPONSES

Cross-Sectional and Prospective Study of Lung Function in Adults With Type 2 Diabetes: The Atherosclerosis Risk in Communities (ARIC) Study

Response to Yeh et al.

The study of Yeh et al. (1) raises awareness of the pulmonary dysfunction associated with type 2 diabetes. Prospective 2-year controlled lung function data regarding subjects with type 2 diabetes from the inhaled insulin (Exubera) development program have recently been published (2,3) and extend the results reported by Yeh et al. The subjects enrolled in these studies were predominantly middle-aged, type 2 diabetic Caucasian men and women who had never smoked or who had stopped smoking and who had normal or near-normal lung function at study entry. Barnett et al. (2) observed mean annualized declines in forced expiratory volume in 1 s (FEV_1) and carbon monoxide diffusing capacity (DL_{CO}) of -0.066 l/year ($n = 145$) and -0.739 ml \cdot min $^{-1}$ \cdot mmHg $^{-1}$ ($n = 143$), respectively, in the comparator-treated group of type 2 diabetic patients failing single-oral agent therapy. Similarly, Rosenstock et al. (3) observed mean annualized declines in FEV_1 and DL_{CO} of -0.061 l/year ($n = 301$) and -0.385 ml \cdot min $^{-1}$ \cdot mmHg $^{-1}$ ($n = 301$), respectively, in a subcutaneously treated group of

insulin-requiring patients with type 2 diabetes.

The accelerated declines in FEV_1 observed by Barnett et al. and Rosenstock et al. are consistent with those reported by Yeh et al. In addition, the annualized declines in DL_{CO} are higher than those reported in healthy nonsmokers (4), suggesting that type 2 diabetes may deleteriously affect the gas-exchange function of the lung as well.

In the study by Rosenstock et al. (3) enrolling patients with type 2 diabetes requiring insulin therapy, the percent predicted FEV_1 and DL_{CO} at baseline were low compared with data in historical control subjects, which were similar to the results reported by Yeh et al. in their diabetic population. This contrasts with the study by Barnett et al. (2) in which the baseline FEV_1 and DL_{CO} were similar to those in historical control subjects. One possible explanation for this difference may be the stage of diabetes upon study entry, with patients requiring insulin in the study by Rosenstock et al. exhibiting more advanced diabetes compared with the patients receiving oral agents in the study by Barnett et al.

Yeh et al. speculate that pulmonary inflammation may be one mechanism mediating the pulmonary dysfunction associated with type 2 diabetes. However, a recently published study by Liu et al. (5) demonstrated an absence of inflammatory changes in an analysis of the soluble and cellular characteristics of the airway lining fluid of patients with type 1 and type 2 diabetes. A multifactorial pathophysiology that includes obesity-induced abnormalities of the chest wall, diabetic microangiopathy, and protein glycosylation may all contribute to the pulmonary end-organ effects of type 2 diabetes.

Given the results of Yeh et al. and others, the lungs are emerging as a body system that is significantly affected by type 2 diabetes. As with other end-organ disease, it is intriguing to speculate that im-

proved glycemic control could reduce the accelerated loss of lung function that is associated with type 2 diabetes.

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References

1. Yeh H-C, Pujabi NM, Wang N-Y, Pankow JS, Duncan BB, Christopher EC, Selvin E, Brancati FL: Cross-sectional and prospective study of lung function in adults with type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) Study. *Diabetes Care* 31:741–746, 2008
2. Barnett AH, Lange P, Dreyer M, Serdarevic-Pehar M, the Exubera® Phase 3 Study Group: Long-term tolerability of inhaled human insulin (Exubera®) in patients with poorly controlled type 2 diabetes. *Int J Clin Pract* 61:1614–1625, 2007
3. Rosenstock J, Cefalu WT, Hollander PA, Belanger A, Eliaschewitz FG, Gross JL, Klioze SS, St. Aubin LB, Foyt H, Ogawa M, Duggan WT: Two-year pulmonary safety and efficacy of inhaled human insulin (Exubera) in adult patients with type 2 diabetes. *Diabetes Care* 31:1723–1728, 2008
4. Sherrill DL, Enright PL, Kaltenborn WT, Lebowitz MD: Predictors of longitudinal change in diffusing capacity over 8 years. *Am J Respir Crit Care Med* 160:1883–1887, 1999
5. Liu MC, Riese RJ, Van Gundy K, Norwood P, Sullivan BE, Schwartz PF, Teeter JG: Effects of inhaled human insulin on airway lining fluid composition in adults with diabetes. *Eur Respir J* 32:180–188, 2008