**Preterm Bronchopulmonary Consequences Endure**

**Expert hypothesizes that low blood flow in adults is an adaptive mechanism learned in utero.**

BY PATRICE WENDLING

Montreal — The first long-term follow-up of a study with bronchopulmonary dysplasia suggests that the consequences of preterm birth lessen over time, but are enduring.

“The consequences of preterm birth clearly seem to lessen over time going from the newborn period into early adult life; but being small for gestational age and preterm, the effects are much more long-lasting, both in terms of airflow obstruction and cardiovascular reprogramming,” Dr. Andrew Bush said at the International Congress on Pediatric Pulmonology.

Dr. Bush also noted differences in a study comparing 23 adults with diabetes to 23 age-matched term babies with chronic lung disease of preterm birth. The term babies had lower lung function than would be predicted, Dr. Punjabi said. The diabetic patients had lower lung function than age-matched non-diabetic patients, compared with those who did not have diabetes (Diabetes. 2004;47:195-203).

“We find that diabetes is a marker of impaired lung function,” Dr. Punjabi said. “It is possible that being SGA in utero you’re programmed to protect your brain and kidneys at times of starvation, at times of low oxygen supply, and that this effect is persisting into adult life, so that at rest you have persistent low blood flow as an adaptive mechanism that’s been programmed into you from before birth,” he suggested. “I emphasize this is tentative and hypothesis-generating.”

Dr. Bush acknowledged that the follow-up numbers are small, but called the findings intriguing. “Questions for the future include how to monitor this aging preterm population; will their lung function deteriorate faster as they age, putting them at higher risk for chronic obstructive disease; and how to address new bronchopulmonary consequences that will arise as neonatologists become more skilled at salvaging even more immature babies.”

**Lung Function Is Compromised in Diabetes, But Trajectory With Aging Is Normal**

BY JEFF EVANS

Senior Writer

Washington — Diabetic patients have lower lung function than would otherwise be predicted, but the actual trajectory of their lung function parallels that of normal, healthy individuals as they age, Dr. Naresh M. Punjabi said at the annual scientific sessions of the American Diabetes Association.

Studies have shown that type 1 and 2 diabetic patients have reduced forced expiratory volume, total lung volumes, and diffusion capacities. But because most of these studies have been cross-sectional, it has been hard to “tease out” whether diabetes or reduced lung function came first, said Dr. Punjabi of the division of pulmonary and critical care medicine at Johns Hopkins University, Baltimore.

In one cross-sectional study of 3,254 individuals in the Framingham offspring cohort, both residual forced expiratory volume in 1 second (FEV1) and residual forced vital capacity (FVC) declined significantly, whereas the fasting blood glucose levels of nondiabetic individuals increased. FEV1 and FVC also were lower than predicted levels in diabetic participants. The pattern was even stronger in diabetic and nondiabetic former or current smokers, compared with those who never smoked. The ratio of FEV1 to FVC, which is a measure of expiratory airflow obstruction, was not related to fasting blood glucose levels in former smokers and in those who had never smoked (Am. J. Respir. Crit. Care Med. 2003;167:911-6).

Another cross-sectional study of 1,911 women aged 60-79 years reported that FEV1 and FVC were significantly and negatively correlated with insulin resistance and the prevalence of type 2 diabetes after adjustments were made for confounding variables (Diabetologia 2004;47:195-203).

“These are two large studies that show a cross-sectional relationship between spirometric measures and metabolic measures,” he said. “The question then becomes, can we prove causality?”

In a longitudinal study of 17,906 participants, 266 patients already had diabetes at the beginning of the study and another 451 developed diabetes during the study’s 15-year follow-up. In spirometric testing performed at baseline and during at least one round of annual testing, both FEV1 and FVC were 8% lower than their predicted values in patients with diabetes, compared with those who did not have diabetes (Eur. Respir. J. 2002;20:1406-12).

“This is a pretty substantial difference between those who have diabetes and those that don’t,” Dr. Punjabi said. But the longitudinal decline in lung function of diabetic patients was similar to that of nondiabetic patients for both men and women.

It is possible to speculate how diabetes could lead to impaired lung function, Dr. Punjabi said. There are data from post-mortem studies of diabetic individuals to suggest that the lung is a target organ for diabetic microangiopathy, as well as indirect data showing that diabetes may contribute to lower diffusion capacity.

There are fewer data to suggest that impaired lung function predicts future diabettes, but some evidence is beginning to show that this association persists, even though plausible biologic mechanisms are “shaky,” Dr. Punjabi said. Spirometric data on 4,830 men and women in the National Health and Nutrition Examination Survey showed that obstructive lung disease (represented by the FEV1/FVC ratio) was not significantly associated with the development of diabetes, but restrictive lung disease (signifying a lower FVC) was. The men and women were followed from their first interview and examination in 1971-1975 through 1992-1993. Only 68 patients had restrictive lung disease, but those who had the disease were 45% more likely to develop diabetes than those who did not have the lung condition. The associations did not differ according to smoking status (Diabetes Care 2004;27:2966-70).

Another study that addressed the effect of baseline pulmonary function on incidence diabetes prospectively showed that over the course of a 9-year follow-up in 11,479 patients, both the absolute values of FEV1 and FVC and the percentage of predicted FEV1 and FVC were associated with incident diabetes. No relationship was found with the FEV1/FVC ratio (Diabetes Care 2004;27:197-203).

Investigators in both studies adjusted the analyses for numerous confounding variables.

“The decrease in lung function that we’re talking about here is insufficient to cause any degree of hypoxemia,” thus eliminating it as a possible mechanism to explain how impaired lung function could affect diabetes, Dr. Punjabi said. But low lung function and diabetes risk may be determined by another underlying cause. It is possible that reduced lung function is a “not a marker” in the context of diabetes but just a marker of what’s going to happen eventually anyway,” he said. Dr. Punjabi speculated.