Preterm Bronchopulmonary Consequences Endure

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

BY PATRICE WENDLING
Chicago Bureau

MONTREAL — The first long-term follow-up of infants 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.

The analysis included 60 adults, aged 20-22 years, from an original cohort of 300 babies with chronic lung disease of prematurity, and 50 new, age-matched term controls. The preterm group included 23 adults who were defined as small for gestational age (less than 1,500 g) and 37 defined as appropriate for gestational age (1,500-2,000 g). Evaluations included spirometry, exhaled nitric oxide testing, skin-prick tests, and exercise tests.

Forced expiratory volume in 1 second (FEV_1) z scores were not significantly different among the three groups. But when those scores were plotted by birth weight, birth weight was found to be a significant determinant of FEV_1 outcomes for preterm small-for-gestational-age (SGA) babies even after 20 years of environmental influences and self-abuse, said Dr. Bush, professor, National Heart and Lung Institute, Royal Brompton Hospital, London.

Birth weight also was a determinant of FEV_{25-75} scores in this group. No association between birth weight and lung function was found in preterm appropriate-for-size survivors or controls, he said.

Using respiratory mass spectrometry, the investigators, led by Indra Narang, also of Royal Brompton Hospital, measured cardiac output and carbon monoxide transfer (DL_{CO}). During exercise in healthy subjects, there can be a five-fold rise in cardiac output as a result of increases in both heart rate and stroke volume. DL_{CO} can increase by up to 50% because of recruitment and distention of the pulmonary capillaries, particularly in the upper airways.

Cardiac output was reduced at rest, but normalized on exercise in preterm SGA survivors.

DR. BUSH

Both cardiac output and DL_{CO} were reduced at rest, but normalized on exercise in preterm SGA survivors. Here, too, these findings were not present in the other groups.

Dr. Bush hypothesized that an adaptive mechanism may be at work.

"Is it 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 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 pulmonary 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 volumes, 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 (FEV_1) and residual forced vital capacity (FVC) declined significantly, whereas the fasting blood glucose levels of nondiabetic individuals increased. FEV_1 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 FEV_1 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 3,911 women aged 60-79 years reported that FEV_1 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 17,506 patients, 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 additional testing, both FEV_1 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 that 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 postmortem 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 diabetes, but some evidence is beginning to show that such an association might exist, 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 FEV_1/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 were 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 incident diabetes prospectively showed that over the course of a 9-year follow-up in 11,479 patients, both the absolute values of FEV_1 and FVC and the percentage of predicted FEV_1 and FVC were associated with incident diabetes. No relationship was found with the FEV_1/FVC ratio (Diabetes Care 2005;28:1472-9).

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 lead to diabetes, he 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 precursor of diabetes but just a marker of what's going to happen eventually anyway," Dr. Punjabi speculated. ■

Rhinoviruses Lurk Behind Upper Respiratory Illnesses

Rhinoviruses are the most common pathogens in the upper and lower respiratory tract of infants in their first year of life, according to findings from a study of 263 infants in an upper-class community who were followed up from birth until 1 year of age.

Although respiratory syncytial virus (RSV) accounts for many acute respiratory illnesses that are severe enough for hospitalization, other pathogens have been underrecognized because it is difficult to identify them, reported Dr. Merci Kusel of the University of Western Australia in West Perth and colleagues.

The expanded use of polymerase chain reaction detection gives physicians a look at the pathogens behind respiratory tract illnesses. Nasopharyngeal aspirates were collected from children during 984 episodes of acute respiratory illnesses and compared with 456 control samples taken when the children were healthy (Pediatr. Infect. Dis. J. 2006;25:680-6).

Rhinoviruses appeared in 52% of upper respiratory tract illnesses (URIs), 41% of lower respiratory tract illnesses (LRIs), and 45% of LRIs with wheezing. By comparison, RSV appeared in 9% of URIs, 15% of LRIs, and 17% of LRIs with wheezing. Additionally, parainfluenza viruses appeared in 5% of URIs and 7% of LRIs, and human metapneumoviruses appeared in 3% of LRIs.

Rhinoviruses were the viruses most often detected in both LRIs and URIs, but rhinoviruses were twice as likely to cause URIs as LRIs in the cases when these viruses were detected. The other pathogens (RSV, parainfluenza, and human metapneumovirus) were equally likely to cause either URIs or LRIs. Rhinoviruses may have a particular affinity for the upper respiratory tract in infants younger than 1 year of age, but additional research is needed in a diverse population, they noted.

—Heidi Splete