Sheila G. Haworth, MD, Creator of the UK Network for the Care of Children with Pulmonary Hypertension, Reviews Milestones in Clinical Management


Sheila G. Haworth, MD

Professor Sheila Haworth has had a lifelong interest in pulmonary hypertension. In the early years she concentrated on pulmonary vascular disease in children with congenital heart disease, carrying out clinico-pathological studies to improve the accuracy of predicting the risk of surgical repair of a cardiac abnormality.

"As I became interested in the pathobiology of pulmonary vascular disease in the young, I began to look more closely at selecting children who could safely undergo surgery and those in whom pulmonary vascular disease was so severe that the risk of surgery was very high and should not be attempted. We studied the findings at cardiac catheterization and the structural abnormalities present in the lung," she recalled in speaking of her work at Great Ormond Street Hospital for Children, where she continues to work as a Consultant in Paediatric Cardiology. "We studied this relationship on the many lung biopsies we used to take in those days and, unfortunately, on the autopsy specimens."

The safe selection of children for intracardiac repair became an important research interest, particularly because the current criteria for determining which patients were candidates for surgery tended to be more suitable for adult patients. Dr Haworth also focussed on the pathobiology of idiopathic pulmonary arterial hypertension and persistent pulmonary hypertension of the newborn, but there was, in those days, frustratingly little one could do to help these children clinically. These years of experience in clinical and basic research provided a superb background that enabled Dr Haworth to exploit the new therapies trialled in the past few years with confidence.

Dr Haworth trained in the United Kingdom and then did a fellowship in fetal physiology and neonatology at Columbia College of Physicians and Surgeons, Columbia University, New York, New York, returning to London to become a consulting physician and to continue research on pulmonary hypertension in childhood.

Building the UK Network to Optimize Care

The spectrum of available therapies did not change dramatically until 1996, when epoprostenol was approved for use in adults, and 1999, when it was approved for children. "This was the signal that there were drugs available and that they worked." Following the approval of another drug in development, bosentan, in 2002, Dr Haworth began work on assembling a clinical network for the care of all children in the UK with severe pulmonary hypertension, an achievement that has more compellingly established her credentials as a preeminent thought leader in the international pulmonary hypertension medical community. As the organizer of this network she has personally overseen its evolution.

As part of standardizing such care in the UK, she has drawn upon her contribution to the development of British national guidelines promulgated by groups such as the British Cardiac Society, the British Thoracic Society, and the Society for Rheumatology. She also contributed to the World Health Organization's guidelines for pulmonary hypertension published in 2004 in the *Journal of the American College of Cardiology*. As author of more than 275 clinical and basic science papers, chapters, and reviews, she is known widely as a prolific contributor to the literature on pulmonary hypertension.

Looking toward new horizons in research in pediatric pulmonary hypertension, she suggests: "One of the areas that we need to work on is better noninvasive assessment of disease progression in the individual patient. It is not in the best interest of the child to be repeatedly catheterized. Echocardiography is sophisticated but does not give us all of the information we need; we still can't measure vascular resistance. When we assess patients we're looking at their clinical status, their exercise tolerance, the ECG, echocardiogram, CT scan, perhaps MRI, perhaps biomarkers as we put the results of all of these tests together to assess the child's status and response to therapy. Although biomarkers are helpful in describing classes of patients, they are of limited value in the individual patient," she added.

"There are still too many outliers and we need a single test or a more limited number of reliable tests to assess prognosis, to determine whether a patient can respond to therapy and, say, live another 5 years or more without transplantation. Advances in basic science will drive research into new medicines. Understanding how the disease starts and is maintained indicates how pulmonary vascular disease might be arrested and even reversed and how new medicines could be designed to modify these processes."

Considering trends in the literature, Dr Haworth added: "Investigators are rather polarized; there is a camp that suggests the principal cell at fault is the

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Scope of Manuscripts

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endothelial cell, while others say it is the smooth muscle cell. Actually, both are right and I don't think it's a polarizing issue. As we move forward, there is a great deal we can learn from other fields of biology, including immunology, oncology, genetics, and developmental biology. What we learn about the evolution of pulmonary vascular disease in children can be applied to adults. We are accustomed to translating the adult experience with new drugs to children but it's not a one-way track from the adult to the child. Perhaps one of the most encouraging aspects of our work in the past 10 years has been the incredible expansion of international collaboration, both in clinical trials of new drugs and in basic science. This bodes extremely well for the future." ■

Errata

In a previous issue of *Advances in Pulmonary Hypertension*, (Autumn 2005, Vol. 4, No. 3), the article, "Cardiac catheterization in pulmonary arterial hypertension: an updated guide to proper use," incorrectly listed information for the use of adenosine on page 22. The dose range for adenosine should have been listed as 50-500 micrograms/kg/min.
On page 20, the article also should have listed an abnormally high pulmonary artery saturation as a left-to-right shunt due to congenital heart disease.