Profiles in Pulmonary Hypertension

Jane Morse, MD—A Physician-Investigator Whose "New Career" Gave Immeasurably to the Pulmonary Hypertension Community



In the field of observation, chance favors the prepared mind. —Louis Pasteur

Jane Morse, MD

Jane Morse, MD, possessed a prepared mind, and she used her years of preparation to serve patients and families whose lives were devastated by pulmonary arterial hypertension.

The story of her contributions is a tale of two careers, both of which were essential to her brilliant success.

Dr Morse began her career in research after she received her MD degree from Columbia University's College of Physicians and Surgeons. This was the right direction for a young physician with insight for careful observation, in-depth study, and the unique ability to identify important research questions. Dr Morse's skills were honed under the tutelage of Dr. Henry Kunkel, her mentor at the Rockefeller Institute, who, she says, was very astute at knowing how to follow up observations. With her innate abilities and Dr Kunkel's mentorship, the stage was set for an investigative career.

After her postgraduate studies at the Rockefeller Institute, she returned to the College of Physicians and Surgeons with an academic appointment in rheumatology. Her initial interests were in autoimmune phenomena. However, fortunately for the pulmonary hypertension community, she became interested in the link between autoimmune phenomena and pulmonary hypertension. She investigated relationships between unexplained pulmonary hypertension and major histocompatibility complexes; and then began to turn her attention to the immunogenetic findings in families with pulmonary hypertension. In 1992 she published her observations of autoantibodies and the major histocompatibility locus in four families with pulmonary arterial hypertension.

The known occurrence of pulmonary arterial

hypertension in families with scleroderma triggered Dr Morse's career change from autoimmune studies to genome studies of pulmonary arterial hypertension. One of her scleroderma families included a father and daughter in New Jersey. Dr Robyn Barst followed the child.

Dr Barst not only followed the child, she followed a number of pulmonary arterial hypertension families. The collaboration of Drs Morse and Barst created the foundation needed for future investigations. Their initial work examined human leukocyte antigens (HLA) in patients with pulmonary hypertension. However, they realized that they needed to examine microsatellite markers across the human genome. One of Dr Morse's technicians learned how to place microsatellite markers, which quickly suggested five possible regions of the genome where a causative gene might be found. Dr Morse had made the transition to her new career in genetic research. Soon, with the help of her colleagues, she located and reported the chromosome locus of the familial primary pulmonary hypertension gene to 2q33. This was a major breakthrough, providing independent confirmation of the location of a critical genetic determinant of inherited pulmonary arterial hypertension.

The original work at Columbia was based in part on a family shared with a group of researchers led by investigators at Vanderbilt University who were doing similar studies. The Columbia group identified another family and confirmed their work; shortly thereafter, they identified another family whose data pointed to the same locus. Dr Morse remembers how exhilarating it was to find the mutations in the families. "When we had approximately 20 people with the mutations in the two affected families, we were in business...it was really exciting."

With the recruitment of more families, she and her colleagues identified the gene associated with familial pulmonary hypertension. They reported mutations in bone morphogenetic protein receptor 2 (BMPR2) as causing familial pulmonary arterial hypertension; Dr Morse credits Dr James Knowles and especially Dr Zemin Deng (a fellow in her lab) for narrowing the search to BMPR2. His suggestion that they look first at that gene was based on his background reading on lung development, once again showing the advantage of having a prepared mind.

Dr Morse's work continues. The group is now fine mapping. "We're also doing some studies to see if different mutations cause more or less severe disease *(continued on page 57)*

Advances in Pulmonary Hypertension Author Guidelines 2006

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Profile - Jane Morse, MD

(continued from page 56)

and could affect clinical outcome." There may be more genes to be found (BMPR2 accounts for approximately 10% of idiopathic pulmonary arterial hypertension cases in the United States, although in Japan the number is reported to be as high as 40%). However, it is also possible that there are no modifying genes and the trigger is environmental. Dr Morse feels fortunate to have found a whole new career just before retirement. "I've been very lucky." She is most grateful to the patients, their families, and their doctors. The work she's done could not have been done without them and "it has enriched my life tremendously. I've always enjoyed people and have been fascinated by the differences. I'm grateful to patients and peers who have helped." ■