

THE ANNALS: 40-YEAR EVOLUTION

2006 marks the 40th year of publication for *The Annals*. Over that time, *The Annals* has been an important contributor to the development of clinical pharmacy. Throughout 2006, we are publishing articles reflecting on the history of clinical pharmacy through the eyes of practitioners, including those pioneering clinical pharmacy, as well as those who have more recently entered the profession and a well-established specialty. In addition, we are also presenting articles and editorials from the early history of *The Annals* that have given direction and shape to the practice of clinical pharmacy (see page 1417).

Pulmonary Clinical Pharmacy Practice

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Clinical pharmacists made their first inroads into the care of pulmonary patients through clinical pharmacokinetics following the seminal publications in the early 1970s by Mitenko and Ogilvie¹ and Masseli et al.² describing the relationship between serum concentrations of theophylline and improvement in lung function. In combination with the advent of technologies that allowed rapid measurement of drug concentrations in patients' plasma, the clinical utility of therapeutic drug monitoring and the application of pharmacokinetic principles to determine optimal doses became readily available.

Clinically trained, institutional-based pharmacists took advantage of their pharmacokinetics training to provide assistance in dosing patients with asthma and chronic obstructive pulmonary disease. Routine therapeutic monitoring of theophylline in hospitalized patients spawned awareness that recommended doses did not fit all patients; this realization provided an avenue of research for exploration by clinical pharmacists. Severely ill patients were often overdosed, which produced toxicity, as documented

in a much quoted study by Hendeles et al.³ published in *Drug Intelligence and Clinical Pharmacy*. This and other studies led to the concept of individualization of therapy. In the early 1980s, a similar phenomenon occurred with the dosing of aminoglycoside antibiotics in children with cystic fibrosis, again bringing pharmacists into contact with pulmonary patients.⁴

In the mid-1970s, publications suggested that oral administration of theophylline on a continuous basis in children resulted in the control of asthma symptoms.⁵ Thus, clinical pharmacists began consulting in ambulatory care pulmonary specialty clinics. The National Institutes of Health Maternal and Child Health funded pediatric pulmonary centers that provided funding for a multidisciplinary approach to the care, research, and education of pediatric pulmonary disease. It soon became clear that, at least in children, more noninvasive approaches were desirable for monitoring theophylline, and exploration into salivary monitoring of theophylline concentrations was initiated.^{5,6} In addition, it became obvious that patient education about the importance of adherence and instruction on the use of aerosol delivery devices was equally important to clinical pharmacokinetics. The concept of using sustained-

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release theophylline preparations to improve adherence significantly increased the manufacture of many different preparations that became the mainstay of asthma therapy in the 1980s, although these preparations still required significant dosing individualization.⁷ In the late 1980s and early 1990s, practitioners gained an increased understanding of allergic inflammation as the predominant pathophysiology of asthma, as well as an increased awareness of the potentially severe adverse effects of theophylline. As a result, the use of antiinflammatories such as cromolyn and inhaled corticosteroids became standard of care.⁸

The publication of the first National Asthma Education and Prevention Program's (NAEPP) Expert Panel Report on the Diagnosis and Management of Asthma began the integration of evidence-based practice into the treatment of asthma. *The Annals* provided support for this concept by publishing a series of evidence-based articles on the treatment of acute severe asthma that were initially part of the literature review for the NAEPP report.⁹⁻¹² The shift in the paradigm of treatment also resulted in the need for pharmacists to begin looking at other patient-centered outcomes of improvement, such as more symptom-free days, fewer exacerbations, and increased quality of life. The use of inhaled products put a premium on patient education for adherence and inhaler technique. The treatment of airway inflammation has led to the introduction of new inhaled corticosteroids and leukotriene modifiers, which has led to the ongoing development of noninvasive methods for assessing inflammation and therapeutic response, such as fraction of exhaled nitric oxide and inflammation mediator content of exhaled breath condensates.¹³ The newest field of pharmacogenetics has led to findings that response to bronchodilators, leukotriene modifiers, and inhaled corticosteroids may be genetically determined.¹⁴

We have come almost full circle and are in the beginning of a new age of technology that will allow individualization of asthma therapy based not on pharmacokinetics but on more direct noninvasive measures of airway pathology and genetic analysis of patients. Future clinical pharmacists will need an understanding of genetic principles, as well as of pharmacokinetic, pharmacodynamic, and patient-centered endpoints, to maintain the high quality of pulmonary management offered now.

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Published Online, 27 Jun 2006, www.theannals.com

DOI 10.1345/aph.1G484

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