

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 1651).

The Beginnings of Pharmacoepidemiology in *The Annals*

Abraham G Hartzema

Two thoughts motivated me to contact Harvey Whitney for a series on pharmacoepidemiology in *The Annals*; the first was the conviction that pharmacoepidemiology would be a natural fit for pharmacist scientists. Not having prescribing prerogatives or access to patients for conducting randomized clinical trials, pharmacoepidemiology as signified by its observational methods would be extremely suited as research methods for pharmacist scientists. Moreover, the developing clinical pharmacy needed a knowledge base to foster its practice. What was more logical than pharmacoepidemiology as a contributing science to clinical pharmacy? Second, although definitions for pharmacoepidemiology had been published, the scope and reach of the specialty was not well understood. There was a need to define that scope and the content of pharmacoepidemiology, taking a more expanded approach.

These considerations led me to send a letter to Harvey proposing to edit a series on pharmacoepidemiology. If there is any complaint about “snail mail,” this certainly was contradicted by the speed of Harvey’s response. It was almost instant! Yes, Harvey said in the telephone conversation pursuant to the letter, let us do it.

Upon Harvey’s positive response, I met with Miquel Porta, a physician from Spain with a deep interest in pharma-

coepidemiology who was enrolled in the epidemiology PhD program at the University of North Carolina at Chapel Hill. Miquel suggested to also engage Hugh Tilson in this endeavor. Hugh was, at that time, director for epidemiology at Burroughs Wellcome. The 3 of us met and outlined a series of articles and suggested authors to be invited. From there a wonderful collaboration evolved that is still standing through the years.

The series was well received and grew into *Pharmacoepidemiology: An Introduction*, a widely adopted text, with a new edition, *Pharmacoepidemiology and Therapeutic Risk Management*, forthcoming.

Expansion of the Specialty

The series did well and brought a lot of attention to pharmacoepidemiology. The number of requests for reprints we received was overwhelming. For example, the Canadian government circulated copies among its staff involved in drug safety issues. Major teaching programs used the series, and most of the established pharmacoepidemiologists today will acknowledge that their first exposure to pharmacoepidemiology was through the series. I have often been asked to speak at schools of pharmacy worldwide, often by deans who wish their faculty to incorporate pharmacoepidemiology in the curriculum and sometimes by junior faculty to bring the message to the administration. In other cases, the invitation was extended by professional organizations that envisioned a political need for pharmacoepidemiology. However, it was not until the

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Draft Revisions of American Colleges of Pharmacy Education (ACPE) standards 2000 and proposed guidelines (Draft 2.0) were approved at the June 2005 ACPE board meeting that pharmacoepidemiology became a mandated part of the PharmD curriculum in the US.

Progress Achieved

Since the appearance of the series on pharmacoepidemiology in *The Annals* in 1987, the field has evolved rapidly. Signified by a growth in infrastructure, colleges of public health and pharmacy, as well as epidemiology programs, established teaching programs in pharmacoepidemiology. In addition, most colleges of pharmacy recruited faculty with an interest in pharmacoepidemiology. Consequently, the educational capacity to provide the necessary manpower has increased significantly. However, the need for well-trained pharmacoepidemiologic researchers is scarcely met today.

The increased need for this manpower has several origins. Manpower growth resulted because pharmaceutical companies established departments in pharmacoepidemiology and the intrinsic growth of these programs to deal with increased regulatory requirements. The Food and Drug Administration (FDA) has added significantly to its staff mainly because of the Prescription Drug User Fee Act of 1992, which provided supplemental resources. More recently, contract research organizations have shown a significant increase need for manpower. The driving force for this need of highly educated pharmacoepidemiologists is the increasing complexities of the healthcare system, the strengthening of regulatory requirements because of a lower tolerance of the public for violations in drug safety, and the rising awareness of the many contributions pharmacoepidemiology can make to improve health care.

The role of pharmacoepidemiology in drug safety is well established. The quest for improved drug safety has gained urgency over the last years, and significant resources will be allocated to enhance our knowledge of drug safety. However, the current role of pharmacoepidemiology has expanded well beyond drug safety. An area that has shown rapid growth is the development of quality indicators based on drug use. For example, the Centers for Medicaid and Medicare 8th Scope of Work quality of care indicators are based on drug use indicators. Pharmacoepidemiology methods and pharmacoepidemiologists are playing an extended role in medication (variances) error prevention research. The FDA RiskMAPs offers a new paradigm for risk management for drugs that may have an

adverse drug reaction profile but may be beneficial for certain subpopulations. In the management of RiskMAPs, pharmacoepidemiology is married with behavioral interventions to reduce the risk potential of drugs. In the pharmaceutical industry, pharmacoepidemiology has found status in the assessment of the market potential of new chemical entities, risk/benefit, and Phase IV follow-up studies.

Part of the growth in pharmacoepidemiology is because new pharmacoepidemiologic techniques and methods are being developed, allowing for added scientific rigor to the investigations and a better understanding of the findings. Some of the newer methodologies include propensity scores. The use of propensity scores in cohort study analysis allows for ensuring internal validity and addressing the potential for confounding. Propensity scores can compensate for the lack of randomization in cohort designs. Newer matching strategies, such as flexible matching on exposure, have been developed for case-control studies. Non-inferiority tests are proposed that provide approaches allowing for head-to-head trials while reducing the risk that the comparators effect size is a type I error. Pharmacovigilance has grown with the development of data mining techniques. These techniques offer efficient ways to look at the potential association of drug exposures and drug effects in larger data sets of spontaneous reports.

Summary

Pharmacoepidemiology has made good on its promises; it has gained stature and credibility and has evolved as an important tool to safeguard the public's health. Recent withdrawals of marketed drugs underline the contribution that pharmacoepidemiology makes. Changes in FDA regulations, the introduction of RiskMAPs, and the institution of a patient safety board have made pharmacoepidemiology the cornerstone of the new FDA policy. *The Annals* provides the pharmacoepidemiologist an outstanding forum to reach the clinical pharmacist and have an impact on therapy. *The Annals'* rich history of 40 years of promoting innovations in pharmacy therapy is only the beginning of its continuing contribution to the public's health.

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