Ann. Rev. Pharmacol. Toxicol. 1985. 25:27–31

CLINICAL PHARMACOLOGY IN THE UNITED STATES: A PERSONAL REMINISCENCE

Louis Lasagna

Sackler School of Graduate Biomedical Sciences, Tufts University Medical School, Boston, Massachusetts 02111

In 1950, I moved from New York City to Baltimore to start a fellowship in pharmacology and experimental therapeutics at the Johns Hopkins University School of Medicine after completing my residency training in internal medicine. I had opted for Hopkins in part because of the eminence of Dr. E. K. Marshall, Jr., the chairman of the pharmacology department, but also because C. Gordon Zubrod was starting a program in clinical pharmacology with a dual base in the departments of medicine and pharmacology.

When I arrived in Baltimore, I quickly saw that while some excellent trials were being conducted (e.g. studies of antibiotic dosage regimens in the treatment of pneumococcal pneumonia), Zubrod was hampered in developing a full program by the call on his time from a welfare clinic where he functioned as an outpatient physician. (He soon thereafter left for the National Cancer Institute, where for many years he was of crucial importance in the development of that institute's cancer chemotherapy program.)

In 1952, I was assigned to an army project at the Massachusetts General Hospital directed by Henry K. Beecher, Harvard professor and chairman of the hospital's anesthesia department. There I began to learn how to conduct analgesic trials, studied the interaction between psychological variables and the response to placebos and CNS drugs, performed the first modern clinical trial of hypnotics, and became convinced that clinical pharmacology would be a satisfying and exciting career.

0362-1642/85/0415-0027$02.00

At the end of that two-year tour of duty, I accepted an offer to return to Johns Hopkins, more or less in the position that Zubrod had filled, except that I had a full-time salary that was not contingent on my duties to a patient clientele. Thus started the first academic division of clinical pharmacology in the world. For the next sixteen years I toiled in the Hopkins vineyard, recruiting our share of superb postdoctoral fellows, many of whom have gone on to distinguished careers in academia, government, or industry, but with relatively modest space and a small core faculty.

In 1970, I moved once more—this time to the University of Rochester, where I assumed the chairmanship of the Department of Pharmacology and Toxicology. Now the home base for clinical pharmacology was a basic science department, although my colleagues and trainees collaborated in research with scientists in clinical departments, and we provided consultation service to all the clinical units at Strong Memorial Hospital. Recently, I have moved to Tufts University in Boston as academic dean of the medical school and dean of the Sackler School of Graduate Biomedical Sciences but with academic titles in psychiatry and pharmacology. Richard Shader and David Greenblatt have developed a division of clinical pharmacology at Tufts in which I hope to play a useful role.

Looking back at the field of clinical pharmacology over the thirty-two years of my own involvement, I see a number of high spots.

In the beginning, funding to encourage training and the creation of new programs came from a variety of sources and played a big role in getting the field off to a good start. Early in the history of our group at Hopkins, E. R. Squibb and Sons and the American Drug Manufacturers Association (later to become the Pharmaceutical Manufacturers Association) contributed fellowship stipends. Over the years, many United States drug companies, as well as the Pharmaceutical Manufacturers Association, have supported academic clinical pharmacology in a variety of ways.

In 1959, a very important support system, clinical pharmacology training grants, was established by the National Heart Institute under the far-sighted leadership of Robert Grant. Over time, a number of the National Institutes of Health have stimulated the discipline in other ways beside training grants. (The era of modern cancer chemotherapy, for example, owes much of its vigor to the cooperative clinical groups whose collaborative research was made possible by National Cancer Institute funds.)

The Burroughs-Wellcome Foundation has also served the field well, giving substantial support to faculty members pursuing careers in clinical pharmacology.

Another program, organized by the Merck Foundation, has stimulated clinical pharmacology both in the United States and abroad by giving two-year

fellowships to foreign physicians wishing to study in the United States. The graduates of the program, like those of the Wellcome program, have been of high quality. Many are now pursuing careers of great achievement and promise, either in their homelands or in other countries. While in the United States as trainees, they have often been effective collaborators of United States scientists.

A delightful chapter in the history of United States clinical pharmacology was the establishment of the Non-Society. Several of us were standing on the boardwalk in Atlantic City during the 1962 spring meetings and decided to form a club with no dues, no rules, and no officers whose only purpose was to get together for discussion, drinks, and dinner once a year. The first meeting convened on April 29, 1963. The Non-Society lasted less than a decade, as I recall, but it was fun.

Looking back on these last four decades, I have the strong feeling that the success stories in academic clinical pharmacology have been due to a small number of charismatic, energetic, scientific entrepreneurs who have been able to put together large, successful, well-funded programs. I refer to people like Daniel Azarnoff, Thomas Gaffney, John Oates, and Kenneth Melmon. In Europe the list includes such folks as Colin Dollery, James Crooks, Paul Turner, and Folke Sjöqvist.

The success of these people contrasts with the fate of many other physicians in the field, who toil alone or in a group that lacks both a critical mass and adequate academic support. (The developing countries are in even worse shape.) I believe that this lack of recognition is due to many factors: the heterogeneity of interests of the art's practitioners, the suspicion that academics have of so-called generalists, the failure to take continuing responsibility for a definable body of patients, and the absence of a definite spot in the curricular sun. I find that most deans and clinical chairmen still do not understand either the nature of clinical pharmacology or its potential.

Periodically, some urge that a certifying board be set up, as if somehow board qualifications would convey a respectability now lacking. I doubt this very much. The fact is that a department chairman in medicine who would not dream of doing without a gastrointestinal group or a hematology division feels that he can live comfortably without a clinical pharmacology group.

These problems are not new, nor have they been ignored in the past. In 1965, a first-rate group of clinical pharmacologists met in Basin Harbor, Vermont, to discuss their status and their future. The group bemoaned the lack of stable support of senior faculty and the inadequate space and staffing of most units. The conclusions are as valid today, by and large, as they were then (1).

There is an interesting contrast between the sad state of academic clinical pharmacology in the United States and the burgeoning importance of the

discipline in industry and the regulatory agency. The difference is easily explained, in my view: for the Food and Drug Administration and industry, the study of drugs in man is a raison d'etre. One cannot imagine the discipline dying in a given pharmaceutical firm or the FDA because of the loss of a single leader. The same cannot be said of the successful academic units referred to earlier. Indeed, some clinical research wards run by industry are the envy of scientists in academia. So are their budgets.

The failure of academic clinical pharmacology to thrive is a great pity. Such scientists have a great deal to contribute to society: better teaching of undergraduate medical students as well as physicians, improvement in the methodology of clinical trials, expert monitoring of drug usage and of post-registration experience in regard to unsuspected therapeutic benefits and adverse reactions, the providing of appropriate drug information to patients and advice to both regulatory agencies and industry, the facilitation of increased research cooperation between industry and academia, and a source of help to governments as they try to cope with media and other pressures.

What I do not foresee is any fundamental change in the image of clinical pharmacology. Nothing can convert it overnight from a young discipline to an ancient one. It will continue to fuse basic science skills with clinical ones. The field's domain will remain broad, and its practitioners will have great variability in their clinical backgrounds: internal medicine, pediatrics, anesthesiology, psychiatry, oncology, etc. Their research will be—and should be—all over the lot: developing new drugs, investigating mechanisms of action, studying biotransformation, quantifying drug benefits and risks in epidemiologic terms, etc. What must occur, therefore, is a better understanding of all this on the part of university administrators and granting agencies.

Lest this account appear unduly negative, I want to also list some of the positive developments. There are now two United States societies devoted to clinical pharmacology, the American Society for Clinical Pharmacology and Therapeutics and the American College of Clinical Pharmacology, and their membership continues to grow. *Clinical Pharmacology and Therapeutics* is a well-respected and widely read journal. Europe has spawned several other first-class journals. Substantial numbers of competent physicians are engaged in clinical trials. A lot of clinical pharmacology is subsumed under the umbrella of medical specialties: oncology, cardiology, anesthesiology, psychiatry, etc. However, these latter disciplines have constituencies that tend to think of themselves not as clinical pharmacologists but as medical specialists, and they tend to meet separately and to seek to publish for their own colleagues rather than for the clinical pharmacology fraternity.

The achievements of United States clinical pharmacology have been substantial, but they have fallen far short of what could be done. Can we improve

the present state of affairs? Will the various segments of society involved recognize the need for outstanding academic programs to train the broadly based clinical pharmacologists of the future? Is it not important for academia to contribute its share of new ideas, new insights, and general intellectual ferment to the field? Will the clinical pharmacologists of today reproduce themselves or will they gradually die out like some sect of scientific Shakers?

Literature Cited

1. Lasagna, L. 1966. Clinical pharmacology: Present status and future development. *Science* 152:388–91