Pharmacology: Its Nature in Medicine

Thomas H. Maren

We have to be modest, except in our aims—OTTO LOEWI, at age 72.

In this generation a curious paradox has arisen with respect to the role of pharmacology in medical schools. In the same era that the basic interest in drugs, and their number, complexity, dangers, and therapeutic and legal significances have enormously increased, responsible medical educators have raised the question of whether pharmacology should have status as an administrative and teaching unit in our schools. It is worthwhile to inquire whether pharmacology can be defined as a unit for our medical schools, and then to assess manpower problems in this field.

What Is Pharmacology?

Research and Teaching

Superficially, pharmacology has the aspects of a derivative discipline; it uses the tools and techniques of biochemistry, physiology, and sometimes pathology, and the internist is on easy speaking terms with drugs. A closer look, however, yields the following: pharmacologists, at their best, have a special, significant, and unifying contribution to make. They are interested in interactions of drugs with living systems at all levels of complexity—from their use in research as molecular probes for the exploration of fundamental biological processes to their use in the clinic. Over this range, the pharmacologists' intimate knowledge of drugs is virtually unique in the medical school.

The relation of chemical structure and physical properties to physiological disposition and action of these agents is the particular concern of the pharmacologist. Starting with this, he may proceed to more intimate details: does the drug function as an enzyme inhibitor, as a neurohumor, as a hormone? In such investigations much is revealed of normal physiology or biochemistry, just as the study of pathology reveals much of normal structure and function. It is at this level, of course, that there is much overlap with other fields. But the pharmacologists are more especially interested in a rigorous and intimate quantitative assessment of drug actions and toxicity than are their colleagues. An important aspect of this is the correlation (or lack of correlation) between effects in vitro and in vivo and critical differences among species. Here such matters as dosage, solubility, molecular structure, protein binding, metabolism, distribution, and excretion, almost classically overlooked by colleagues in biochemistry and physiology, come strongly into focus.

In systems examined closely, with proper quantitative account taken of both the chemistry of the drug and the underlying physiology, a smooth and illuminating relation can be established between events in vitro and in vivo, or even between molecular phenomena and the control of disease. The key word, special aspect, and reason for future excitement is this *continuum*.

How may these matters of basic pharmacology be transferred to the curriculum and be made an introduction to the rational use of drugs? The student, ideally is given a "feel" for drugs as chemical entities, each with a spectrum of characters demanding knowledge and respect. The concept of *continuum* is conveyed to the student, so that he sees the profound relation between the chemistry of drugs, their physiological effect, and their power to cure the sick. The details of teaching in any program are less important than motivation of students and faculty. In the College of Medicine of the University of Florida we attempt to meet this reality by using the traditional second-year course as an introduction, and by presenting a major part of pharmacology in the third and fourth years of the medical curriculum. Extensions of these principles and activities into house-staff and postgraduate training of physicians are desirable and, given the manpower, immediately feasible. When such educational programs, in scope and quality, are achieved, the whole absurd and artificial cycle of recriminations involving "pharmaceutical house claims and profiteering," "government control of drugs," "reckless use of medicines by doctors" will disappear. For the physician is in ultimate and perfect control; no ethical drug is bought or taken that he does not prescribe.

What Is an Academic Pharmacology Department?

The pharmacology department is a group of men and women loosely unified by an interest in how chemicals affect living systems. This commitment covers a very broad range and very different levels of complexity, but within the pharmacology department there is a unity not found elsewhere in the medical school. The department is simply and ideally a center for knowledge of how drugs work.

Most internists are much concerned and vaguely uneasy about the use of drugs, but they do not regard a close and critical appraisal of drugs as part of their formal or informal teaching responsibilities. This task has fallen to the clinical pharmacologist, who acts either as an arm of the pharmacology department, or as a therapeutics unit of the department of medicine. However, in the latter case, the men involved must have had primary training in a pharmacology department. In this way the department has a vital role in the training and teaching of people who prescribe drugs every day. We find that the closest possible relations between clinical and basic pharmacologists are very satisfying on each side. The clinical pharmacologist often does his research in a basic area. Thus pharmacology departments have a large role to play in the medical school. Few have taken full advantage of their opportunities, and most have somewhat neglected their obligations as working consultants to clinicians in every aspect

The author is professor of pharmacology and therapeutics at the University of Florida College of Medicine. This article is an extension of Maren's editorial that appeared in the *Journal of Chronic Diseases* [16, 437 (1963)].

of drug treatment, from antibacterial chemotherapy to regulation of blood pressure.

It has been proposed that the teaching of pharmacology might be taken over by a committee composed of men in the various basic and clinical sciences who are interested in drugs. Even if this were sucessful as a teaching device, owing to the fortunate collection of an interested group, it would nevertheless be disastrous for the long-range training of pharmacologists in that particular area or school. The training of pharmacologists for industry and for government, as well as for medical schools, has lagged far behind the needs.

In the guise of kings (Mithridates VI; receptor theory applied to toxicology), witches (Macbeth's basic science tutors), and old ladies of the roadside (Withering's advisers in clinical pharmacology), our race has dispensed drugs through all of its history. Results have ranged from the tragic to the miraculous. Although there is not a perfect correlation, ignorance is associated with tragedy, and knowledge with miracles. Since the greatest impact of drugs in the treatment of disease will unquestionably take place in the future, the pharmacology department has an obligation and challenge to strengthen its hand for the future.

Who Are Pharmacologists?

The impulse to discontinue pharmacology departments (no school has actually done this, although uneasy alliances or subjugations have been formed with physiology and even with medicine) seems to arise in part from dissatisfaction with available candidates for the vacant chairs. As might be expected, this is greatest in the leading schools, and here too the implications are the most serious. Some schools have attempted to solve the problem by going outside pharmacology and appointing excellent men from other disciplines—medicine, microbiology, physiology, and biochemistry—to chairs in pharmacology. But most of these men have held the jobs in pharmacology for only a few years, and then reverted to their original field of interest. Similarly, the "combined" department has always been to the detriment of teaching and research in the field. We might ask why committees formed to find new professors of pharmacology become discouraged.

The training of pharmacologists in America has left much to be desired. For a long time, a number of leading medical schools granted a very weak Ph.D. in pharmacology; other schools had programs of varying merit. Nothing more was demanded in some schools than a thesis and the first 2 years of medical school. A characteristic of these graduates is their overt weakness in chemistry, which is the heart of pharmacology. Unfortunately, this situation is continuing to some extent even now. On the other hand, there is a generation of older pharmacologists, with the M.D. degree and perhaps some clinical training, with little "hard science" background. There are also, in pharmacology, a number of excellent chemists and biochemists, who occupy a special position in pharmacology departments and are somewhat dissociated from the overall teaching program because of their lack of interest and training in biology. Conversely, there are some biologists and physiologists who have drifted into pharmacology departments, but whose chemistry is deficient.

The foregoing paragraph characterizes a fairly large segment of pharmacology; all of these models fall short of the ideal or even the practical; none is suitable for leading positions in the field. What is needed is simply stated: a thorough training in chemistry (physical, quantitative, organic, biochemistry) and a sound knowledge of cellular and organ physiology. There are many sequences to this theme, and a strong M.D. or Ph.D. can form the base. But both degrees are not held to be necessary, and too often they appear to be emasculating; a formal "combined degree" program sets a long string of academic roadblocks, at just the most creative time of life. To me, the medical training seems desirable, for a professor of pharmacology sits on administrative and curricular councils in a school of medicine, and his rapport with medical students and clinical colleagues may be easier with the common background. This more personal reaction may be countered by the fact that there are oustanding pharmacologists in this country with the Ph.D. who are sensitive and responsive to the medical environment.

With this bewildering array of types, and with the obvious rigors behind a thorough training in biology, chemistry, and medicine, it is not surprising that the selection of pharmacologists is difficult and that relatively few candidates are available for critical positions in universities, government, or industry. The heart of the matter is that pharmacology is an extremely demanding discipline. Our colleagues in physiology expect and should expect, that we be as well versed in the general aspects of their subject as they; the biochemists should demand the same; even the clinicians expect us to have a knowledge of disease, and the extension into therapeutics is logical and obvious. I can only conclude that training in pharmacology offers an important and fascinating challenge, which has not yet been met in terms of quality or quantity. Fortunately, there is still reason for optimism for the future, in part due to the training programs financed by the National Institutes of Health, Burroughs Wellcome Company, Life Insurance Medical Research Fund, and Pharmaceutical Manufacturers Association. These programs take cognizance of the importance of both medicine and chemistry; the obvious problem is manpower, both teachers and trainees. Fortunately, there are in the United States a number of excellent young pharmacologists who are making their influence felt.

A special and vulnerable aspect of pharmacology is that, unlike its sister sciences, it cannot be found or even mentioned (except in pharmacy schools —already professionalized) in the undergraduate curriculum. Seniors in chemistry and biology generally have no idea of the differences among a pharmacologist, a pharmacist, and in some regions possibly a pharmer. Here is a real challenge to the recruiter!

This may be characterized as a transitional time, in which the training programs have not yet been able to produce the number of leaders which are necessary for the future. Whether there have ever been enough great men in this field, as compared to the other basic sciences, is questionable. Now, however, to strive toward the great goals possible it is essential that the medical schools support and give fullest recognition to pharmacology departments as teaching and administrative units.