

Mosaic

Reflections on the history of pharmacology

Although experiments on the physiological effects of drugs and poisons upon animals and humans have been performed since ancient times, the birth of experimental pharmacology is generally associated with the work of the French physiologist Francois Magendie in the early nineteenth century. Magendie's researches on strychnine-containing plants clearly established the site of action of these substances as being the spinal cord and provided evidence for the view that drugs and poisons must be absorbed into the bloodstream and carried to the site of action before producing their effects.

The work of Magendie, and that of his pupil, Claude Bernard, on curare and carbon monoxide poisoning, helped to establish some of the techniques and principles of the science of pharmacology. But these men were physiologists and their pharmacological work represented only one aspect of their research interests. Bernard, for example, seemed to be largely interested in poisons as tools of physiological analysis. By studying the mechanism by which the toxic agent caused death, one might hope to learn something about the physiological role of the tissue attacked. In order for pharmacology to establish itself as an independent discipline, individuals were required who would devote their full time and efforts to the new science. It was in the German-speaking universities in the second half of the nineteenth century that pharmacology really began to emerge as a well-defined discipline.

Perhaps we might date the beginnings of this process to the appointment of Rudolf Buchheim to teach materia medica (among other subjects) at the University of Dorpat in 1847. While Dorpat was in Russian-governed Estonia, the University was essentially German. Chairs of materia medica, of course, had long existed in medical schools. But materia medica concerned itself largely with questions about the origins, constituents, preparation and traditional therapeutic uses of drugs. It was more closely allied to botany, chemistry and pharmacy than it was to physiology. Buchheim called for an independent, experimental science of pharmacology, involving the study of the physiological action of drugs. He established the first institute of pharmacology in the world.

Among the students receiving research

training in Buchheim's laboratory was Oswald Schmiedeberg, who succeeded his mentor in the chair of pharmacology at Dorpat in 1866. It was after Schmiedeberg was appointed to the chair at the University of Strassburg in 1872, however, that he had his greatest influence. It has been estimated that about 120 students from some 20 different countries worked in his pharmacological institute, and that his students later occupied approximately 40 academic chairs in pharmacology throughout the world. Schmiedeberg also founded the first *Journal of Experimental Pharmacology*. Among the students trained under Schmiedeberg were John J. Abel, who brought the new science of experimental pharmacology from Germany to the U.S.A., and Arthur Cushny, who was one of the pioneer pharmacologists of Britain.

In recent years, increasing attention has been devoted to the history of pharmacology. Professor David Cowen has just recently made an important contribution to the literature on this subject in his essay on the history of teaching of materia medica and pharmacology in American medical schools¹. A number of articles and monographs have appeared over the past two decades dealing with selected aspects of the subject, such as the influence of Dorpat on pharmacology, the development of pharmacological journals in Germany, and the state of pharmacological teaching and research in the German-speaking universities in the 1860s². The history of theories of drug action has been the subject of several studies^{3,4}. A few biographical articles on key figures such as Buchheim and Schmiedeberg have appeared^{5,6}.



Fig. 1. Rudolf Buchheim (1820-1879). (Photo courtesy of the National Library of Medicine.)

The overall impression that one receives upon surveying the literature, however, is that the science of pharmacology has received relatively limited attention from historians. Aside from the fact that there is no scholarly treatise that attempts to cover the history of the field, there are many important specific aspects of pharmacology's history which have not been investigated. We still know, for example, relatively little about the specific factors leading to the actual emergence of the discipline. No booklength biography of Schmiedeberg exists. In fact, Schmiedeberg, who is probably the single most important figure in the history of the discipline, was not even included in the *Dictionary of Scientific Biography*. On Buchheim we have only a relatively brief study (ca. 60 pages) for a medical dissertation which is useful, but certainly not definitive⁷. Buchheim, incidentally, was also excluded from the *Dictionary of Scientific Biography*.

There is thus much to be done in the history of pharmacology, and few historians who are devoting attention to the subject. Yet the history of pharmacology offers, I believe, much of interest to the scholar from the point of view of both intellectual and social history. The study of the development of ideas about the mechanism of drug action necessarily brings the historian into the realm of ideas about the nature of living processes. One can see in different time periods the relationship of theories of drug action to contemporary concepts about life and matter. In the seventeenth century, for example, efforts were made to relate drug action to the corpuscular or mechanical philosophy. One often sees quoted a statement from John Locke's *An Essay Concerning Human Understanding* that if we knew the 'mechanical affections' of the particles of drugs and of man, as a watchmaker does those of a watch, we would be able to tell in advance that rhubarb will purge and opium will produce sleep. Less well known is Robert Boyle's 1685 treatise, *On the Reconcilableness of Specifick Medicines to the Corpuscular Philosophy*. Boyle devoted his entire book to trying to show that the fact that certain drugs exert a specific action on a given disease, such as the action of Peruvian Bark on ague, can be explained in terms of the corpuscular philosophy. He offered a number of possible mechanisms, all admittedly speculative, that could account for this phenomenon. For example, he suggested that since the different parts of the body have different textures, it is not implausible that when the corpuscles of a medicine are carried by the body fluids throughout the organism they may, accord-

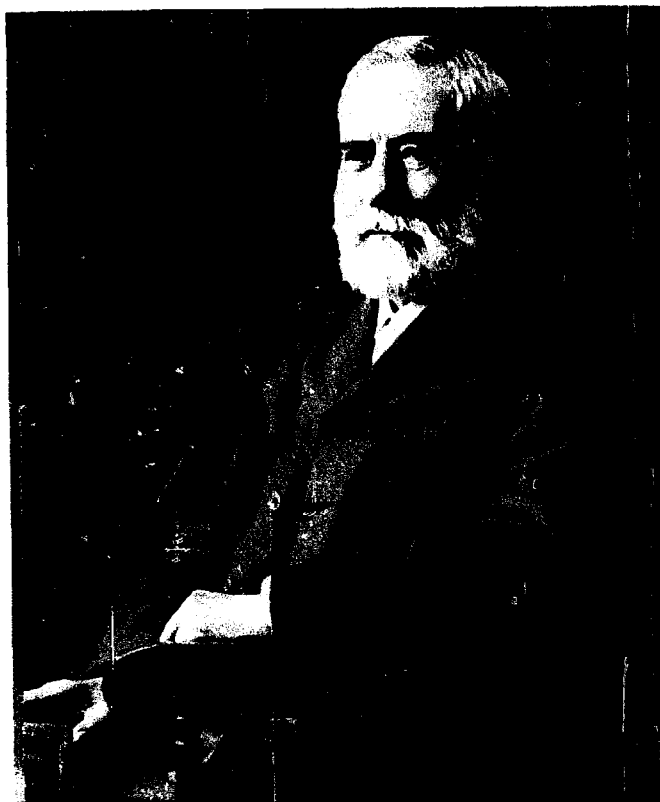


Fig. 2. Oswald Schmiedeberg (1838–1921). (Photo courtesy of the National Library of Medicine)

ing to their size, shape, motion, etc., be more fit to be detained by one organ of the body than another. Because of their mechanical properties, the corpuscles of the medicine may thus tend to lodge themselves in the pores or associate themselves with the fibers of a given organ, hence acting on it to a greater degree than on other parts of the body.

Jumping ahead to the beginning of the twentieth century, we see that Paul Ehrlich's view of the chemoreceptors for drugs was intimately connected with his view, derived from Eduard Pflüger, of the cell as a giant protoplasmic molecule. The receptors for drugs, he believed, were chemical side chains of this molecule which were ordinarily involved in the normal processes of cellular metabolism. The controversy during this period over whether the action of drugs depended upon the formation of chemical bonds with protoplasmic constituents or upon physicochemical processes was part of a broader controversy in the biomedical sciences, involving a structural organic chemistry approach v. a physical chemistry (especially colloid chemistry) approach. My point in citing these examples is to emphasize that an investigation of the understanding of drug action in a given period can tell us much

about the biology and chemistry of that period. Pharmacology is an interdisciplinary field that must draw upon chemistry, physiology, bacteriology, and other sciences for its own advance.

The relationship of pharmacology to therapeutics, and hence to medical and pharmaceutical practice, is a close one and offers interesting opportunities for historical research. The development of animal experimentation and clinical testing for the evaluation of new drugs, for example, is a fascinating subject whose history is in need of further investigation. The relationship between the laboratory pharmacologist and the clinical medical practitioner has not always been a smooth one, and this tension between laboratory and clinic in the use of drugs merits attention from the historian.

Pharmacology and its subdiscipline of toxicology have necessarily become involved with areas of social concern, such as forensic medicine, industrial toxicology, environmental toxicology, food and drug control, and drug abuse. These subjects pose for the historian many significant questions relevant to the social history of science. The role of pharmacology and pharmacologists in the Food and Drug Administration, for example, would make an interesting study. As just one example of

this involvement, one may cite the role of pharmacologists and toxicologists in the FDA's effort in the 1920s and 1930s to set tolerances for lead and arsenic residues on fruits, resulting from the use of lead arsenate as a pesticide. Academic pharmacologists provided the FDA with advice on toxicity, testified in court cases on behalf of the FDA, and constituted the majority of the members of an *ad. hoc* advisory committee established by the agency, the Hunt Committee (chaired by Harvard pharmacologist Reid Hunt). The FDA's own Division of Pharmacology also played an active part in this effort¹⁰. Another possible area for historical research involving social issues would be a study of the development of knowledge concerning the pharmacology of alcohol and other abused drugs and the influence of this knowledge on public attitudes and policy. The history of pharmacology thus offers the historian ample opportunity to explore interesting questions related to the development of the science itself or to its social impact.

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Reading list

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