LEGACY ARTICLES

Research and Pharmaceutical Progress¹

GLENN L. JENKINS

College of Pharmacy, University of Minnesota

The renaissance period of history was marked by the revival of learning, great advances in literature and in art, by the discovery of the process of printing, and by religious and political revolt. During this period, even the sciences gave evidence of an awakening. Astronomy led the way with the epoch making discovery of Copernicus in 1530 that the sun and not the earth is the center of the solar system. Pharmacy and chemistry were less fortunate since they could free themselves only with difficulty from the mysteries and superstitions of alchemy with its vain quest for the philosopher's stone, the elixir of life, and the riches and bodily vigor their discovery would insure.

The spirit of the times, especially in pharmacy and medicine, was ripe for reform. The ancient school of Galen then retained its authority and dominated the medical sciences.

¹Read before the National Conference of Pharmaceutical Research at the Minneapolis meeting August 1938.

75th 1937-2011 ANNIVERSARY || AJPE

Under suitable astronomical conditions crude drugs were collected, prepared and administered, almost exclusively for internal use. Chemical compounds were used to some extent externally. The volatile oils from a few roots and herbs had been isolated through the practice of distillation. Beyond this there had been little advance. When Paracelsus, after Valentine had paved the way, declared "Chemistry is not designed to make gold but medicines", the foundations for a renaissance in pharmacy and medicine were laid. Despite the fact that the disciples of Paracelsus failed to separate the wheat from the chaff of his doctrines, the pharmacopoeia began to improve under their influence, particularly by the introduction of inorganic chemicals and the so-called elegant preparations, tinctures and fluidextracts. What there was of science in medicine was summed up by Paracelsus in the aphorism which was accepted as an axiom by his disciples "Man is a chemical compound; his ailments are due to some alteration in his composition and can only be cured by the influence of other compounds." Thus was founded the iatrochemical school that eventually overthrew the older galenical school of thought.

Progress was made slowly by the iatrochemists. Their work established firmly the use of such chemicals as mercury, lead, iron, antimony, arsenic and various salts. A decline in the iatrochemical influence occurred when Boyle, in the middle of the 17th century, after the ground had been cleared of the remains of alchemy, pointed the true road to chemical progress; the road guarded by diligent experiment and stringent induction wherein the theorists were also the experimenters. Chemistry then became a science in fact and iatrochemistry became a division of chemistry.

The transition of iatrochemistry into pharmaceutical chemistry is not clearly marked. We think of pharmaceutical chemistry as having arisen from the works of Scheele, Serturmer, Pelletiere, Caventou, Baume, Courtois, and a host of others. The results of their work were far reaching in their effects on pharmacy, medicine and chemistry. A single illustration will make this clear. Serturmer working in his apothecary shop isolated morphine and described it in 1817 as a "new salifiable base". This announcement created a stir in chemical circles of that time because it completed the analogy between inorganic and organic chemistry. Inorganic

75th 1937-2011 ANNIVERSARY || AJPE

chemicals long had been classified as acids, salts and bases. Organic acids and salts were known but the organic bases were lacking. Sertturner's salt forming base filled the gap in organic chemical classification for a time. When the alcohols were discovered to be the true organic bases a few years hence, the interest of most chemists in Sertturner's discovery ceased. The importance of his discovery increased with time however, for (1) It marked the isolation of the first pure alkaloid from a crude drug. Thus it pointed the way and method of isolating a number of other principles such as other alkaloids and glycosides, etc, which continues in the work on hormones and vitamins in our time. (2) The isolation of active principles in pure form led to their administration in place of the crude drugs and their preparations. Through the use of pure principles, the accurate control of dosage became possible in a time before analytical methods of standardization were known. The accurate control of dosage made quantitative measurements of drug action possible so that Sertturner's discovery has been said to have laid the foundation for modern pharmacology. By separating the active principle from inert matter, Sertturner's discovery also paved the way for the hypodermic administration of medicines. Other discoveries in pharmacy have extensively influenced the allied sciences but we are more concerned with the influence of the allied sciences upon pharmacy.

The rapid increase in chemical knowledge following the establishment of analytical methods by Lavoisier and Liebig, the new concepts of the structure of organic molecules which followed Kekule's theory of the benzene ring, the discoveries of Van't Hoff and LeBel relative to stereoisomerism, the overthrow of the vitalistic doctrine after Wöhler transformed ammonium cyanate into urea, and numerous other profound researches in chemistry, especially the advance in the knowledge of atomic relationships, led to an understanding of the constitution of many naturally occurring substances that had been isolated in a pure condition after Sertturner showed the way. Studies of the nature of the reactions and of the mode of genesis of these compounds threw light on their structure, and the knowledge thus gained enabled other workers to conceive of methods by which these compounds could be prepared synthetically. Synthetic organic chemistry progressed so rapidly that by the

75th 1937-2011 ANNIVERSARY || AJPE

beginning of the 20th century it was commonly said "that whenever the constitution of an organic compound is clearly understood its formation by synthesis becomes a practical possibility." The recognition of infections as due to the invasion of the body by living organisms following the work of Pasteur, Koch and others gave a new direction to the therapeutics of infective diseases and established the bacteriological era of 1880 to 1890 which was followed by the immunological era of 1890 to 1900. Lord Lister's application of Pasteur's discoveries in the field of surgery, the rise of endocrinology following the recognition of deficiency diseases caused by the lack of substances present in the normal body, the discovery of Roentgen and X-rays in the field of physics, the recent findings in plant pathology of the virus cause of disease and innumerable other advances in science have contributed to pharmaceutical and medical progress. These contributions more than those made from pharmacy itself have brought about the trend from the use of vegetable drugs and their preparations to the use of specific synthetic agents and symptomatic remedies, serums, vaccines and antitoxins, antiseptics and diagnostic agents and an ever growing list of new products.

These impacts coming at a time when research was subordinated to a position of insignificance in most of our educational and industrial organizations coupled with the rise of medical education and science led to the establishment of foundations and research grants for the development of therapeutic agents. While their work has enriched pharmacy, they have encroached upon a field that had been almost exclusively pharmaceutical. Here we are witnessing a breakdown of the borderlines between the professions and sciences that is occurring in every field.

Specialization has grown with science so that while a research worker can become well versed in a number of the common fundamentals of many sciences, he can become an expert in only one branch of one science. For example, Sir Humphrey Davy when a youth at the beginning of the nineteenth century outlined a scheme for his life of study. It included theology, botany, chemistry, physics, pharmacy, anatomy, surgery, mathematics, mechanics, history, logic and seven languages. It is said that he became well versed in all of them. Schlichter expressed it well when he said—

75th 1937-2011 ANNIVERSARY || AJPE

“We not only have scientists, we have chemists, we have colloid chemists, we have inorganic colloid chemists, we have aerosol inorganic colloid chemists, and we not only have aerosol inorganic colloid chemists but we have high temperature aerosol inorganic colloid chemists.” Thus the research worker at the time of Davy may be said to have comprehended a natural order while his descendent of today comprehends only a subspecies of science.

Specialization of individual ability does not give rise to a lone Scheele or a Serturner making far reaching discoveries in the back of an apothecary's shop but it has made possible the modern research laboratories of our present day pharmaceutical manufacturers. Here many departments each having a number of individual specialists in its ranks are brought together. In one establishment there are divisions of bacteriology, botany, pharmaceutical chemistry, synthetic chemistry, biological chemistry, germicides, mycology, nutrition, pathology, pharmacy, pharmacology, physiology, veterinary medicine, and clinical medicine. Some of these divisions include several sections, the biological division as an example consists of sections on tissue extracts, chemistry of bacterial products, and serum concentration. The reintegration of pharmaceutical research in laboratories of this type with specialized scientists coordinated and, with almost unlimited facilities, deliberately organized to produce new remedial agents holds forth great promise of progress.

The maker of medicines in the time of Paracelsus as a pharmacognosist collected and cured his drugs, as a pharmaceutical chemist he prepared his compounds, and as a pharmacist he compounded and dispensed these initial products. No marked change in the pharmacist's operations occurred in this country until the war of 1861. The demand for medicines in large quantities at that time led to the conversion of a few pharmacies into manufacturing plants. In the early years the manufacturers simply prepared on a large scale products that had been originally discovered through years of pharmaceutical experience and research. As they expanded, some concerns instituted research programs but usually under the dictum—“produce or get out.” Later some of them, after learning that research pays, have adopted long range research policies where the research worker is relatively secure in his job in a coordinated lab-

75th 1937-2011 ANNIVERSARY || AJPE

oratory. We are pleased to refer to these companies as the ethical pharmaceutical companies. There are other manufacturers, not so ethical, which have contributed little or nothing to pharmaceutical research which need not be considered. It is interesting to note that the early competition between the industrial companies has resolved itself largely into competition between products with a seemingly unlimited and often unnecessary multiplicity of the latter.

There are many in our profession who continue to seek the return, in part at least, of manufacturing to the drug store. They overlook the fact that the complexity of modern business, with its facilities for distribution, the economy of mass production, the power of the trade mark and advertising, the burden of licenses and taxes, the need for standardization and control of products, and other factors but above all, the need for continued research, makes this return impracticable and unprofitable. We must resign ourselves here as in other spheres of human activity to the loss of an individual art to organized scientific production.

We have instances in pharmacy where we can designate individual workers as heroes of discovery. Our greatest claim for recognition however, is not in the discoveries of individuals but in the accomplishments through cumulative research and by the cooperation of industrial, college and other investigators in the standardization, stabilization and perfection of practically every type of product used in therapy. The result is that the people of this country have available the best pharmaceutical service of any people at any time in history. A large share of the credit for the quality of these products belongs to that small group of manufacturers that, while research lagged behind the other sciences in our educational institutions, have set well balanced teams of research workers to solving problems and developing new products without unduly subordinating the humanity service motive to the profit motive.

We need be concerned lest the future progress of pharmacy be retarded because our industrial leaders are not sufficiently concerned with laying the foundations for the industrial future by strongly supporting pure scientific work in pharmacy at the present time.

President Isaiah Bowman of Johns Hopkins has said: "The trade school exists for the admirable purpose of putting prac-

75th 1937-2011 ANNIVERSARY || AJPE

tically trained men into jobs; the universities exist among other things to create and expand the sciences that provide the jobs.” The early American colleges of pharmacy existed for the purpose of putting practically trained men into jobs. They made little effort to found pharmaceutical education on the teaching of the fundamental sciences of biology, chemistry and physics. The regeneration of medical education in the decade of 1870 to 1880 with its subsequent rise and emphasis on research had no counterpart in pharmaceutical education. It is true that the establishment of the school of pharmacy at the University of Michigan in 1876 marked the beginning of a new trend in pharmaceutical education. This was without appreciable significance until the University of Wisconsin established a similar coordinated school in 1883. There under the late Dr. Power, research was encouraged. Later, under the direction of Dr. Kremers, research flourished and graduate work as it is now known in our universities was inaugurated in pharmacy. For too long a time Wisconsin stood alone in the creation and expansion of the sciences that make the jobs. Eventually, graduate students after imbibing the spirit of research that existed in Dr. Kremers laboratories went forth as disciples and established graduate work in other schools and they in turn have sent forth disciples. A number of our schools now offer a sound graduate education in pharmacy.

The question is often asked: “Can we continue to expand graduate education in pharmacy until most or all of our schools offer such work?” The answer to this question is difficult. We are afforded some insight to the answer through the observation that the continued expansion of research in biology, medicine, chemistry, and physics does not seem to have reached the saturation point. We also know that manufacturers in many cases have little or insufficient control and research staffs. Expansion of governmental regulation of drug and cosmetic products will call for more workers in manufacturing and in government laboratories. Many of our colleges have insufficient teachers. These facts added to the fact that research tends to create new jobs indicate that the danger of an oversupply of competent research workers in pharmacy is rather remote.

It may not be practicable to establish graduate education in pharmacy in all of our schools, but every school of phar-

75th 1937–2011 ANNIVERSARY || AJPE

macy worthy of the name should have one department in which the spirit of research resides. Teaching and research should be inseparable in our colleges. One who teaches without investigating the problems of his subject becomes a pedant dispensing knowledge at second hand. Association with younger investigators stimulates the more experienced researcher and keeps him alert to new points of view. It has been said "A man need not be given free time for research; he would still find time to do research if he had the spark to do it." There is some truth in this remark, but the spirit of research does not thrive where time and routine are of first importance. Too many of the teachers in our colleges of pharmacy are overburdened with teaching and routine. They often hold positions like that described by Oliver Wendell Holmes who taught anatomy and physiology at Harvard from 1847 to 1871, holding as he later remarked "not a chair but a settee."

The lack of financial support for research programs in our colleges of pharmacy has been deplored by a number of our leaders. Instances of wealth gained in pharmacy and used to encourage and make possible comprehensive studies in foreign fields are common. The remark by President Elliott of Harvard that "The first step toward obtaining an endowment is to deserve it" is true of pharmacy. Wishful thinking will not produce the desired results. It is our responsibility to do good work and then make known and interpret the results of our investigations so that others may know of our accomplishments. The National Conference on Pharmaceutical Research has made a very good beginning in this direction. But a distinction should always be made between publication and publicity.

It would appear to be self evident that the value of literature in the sciences is so well known that mention of the subject is unjustified. Nevertheless, we frequently see evidences of incomplete searches. Occasionally, we find those who feel apparently that they need have neither interest nor responsibility in maintaining the highest possible standards of scientific publication in pharmacy. Of course, the results of an investigation should always be published if they are to be of value at all. The research achievements of pharmacy should be shared with the public but only after they have been received and subjected to criticism by other work-

75th 1937-2011 ANNIVERSARY || AJPE

ers competent to judge of their merits. When a research worker directly or indirectly proclaims his work and virtues to the public press, he often unconsciously, enters the field of the mountebank, endangers the reputation of the institution with which he is associated and compromises other workers in the same line of work. Our status in the professions and in science is determined by the quality of our publications and not by the publicity we secure. Consequently, we should make every effort to elevate the scientific quality of our journal by contributing the results of our best efforts to it.

Pharmacy has had to become one of the most highly organized divisions of science to meet the varied and expanding needs of modern therapy. It now needs pastures and stables, the cooperation of abattoirs, chemical plants adapted to the difficult synthesis of complex and delicate compounds or to the separation of unstable natural principles, incubation rooms for the large scale culture of a wide variety of organisms and sterile rooms for the manipulation of products. It needs chemists, bacteriologists, pharmacologists and many other services that have little to do with the art of the individual pharmacist known to our fathers compounding their pills and potions among the bottles and jars of the prescription counter. To go forward we must submit to the guidance of progressive and continuous research and education. I mean research and education undertaken in the spirit of free inquiry often without a practical aim or product in view except the increase of fundamental knowledge.

The research of today more than anything else will determine what pharmacy will be tomorrow. We have work to do individually and within the ranks of our fellow pharmacists to impress this truth upon them. Unfortunately, we can not follow the example of the City Council, which, by motion, resolved: "That the Fourth Ward Marsh be, and it hereby is, drained."