Remington's Pharmaceutical Sciences

16

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16

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Remington's Pharmaceutical Sciences . . . *a treatise on the theory and practice of the pharmaceutical sciences, with essential information about pharmaceutical and medicinal agents; also a guide to the professional responsibilities of the pharmacist as the drug-information specialist of the health team . . . A textbook and reference work for pharmacists, physicians, and other practitioners of the pharmaceutical and medical sciences.*

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Preface to the Sixteenth Edition

As with every edition of this work since it was first published in 1885, "the rapid and substantial progress made in Pharmacy" has again necessitated revision of the book (see the *Preface to the First Edition*). Thus, eight of the 108 chapters in this edition are entirely new, dealing with subjects that have taken on major importance in the increasing professional diversification of pharmacy. All but a few of the 100 other chapters have been extensively revised. The subject matter of several pairs of chapters in the Fifteenth Edition has been combined into single chapters; the chapters on Quantum Chemistry and Veterinary Services have been deleted. Compared to the Fifteenth Edition, the condensed typeface used in this edition has permitted a substantial increase in overall text content with some reduction in the number of pages but not of legibility.

One of the new chapters, titled *Diseases: Manifestations and Pathophysiology* (Chapter 35), is intended to provide pharmacists a brief overview of information about certain diseases, for the purpose of facilitating communication with other members of the health professions team in discussions concerning drug therapy. Although the chapter is one of the longer ones in this book, it does not provide information about all diseases or describe fully the characteristics of any disease that is included.

New chapters on *Basic Pharmacokinetics* (Chapter 37) and *Principles of Clinical Pharmacokinetics* (Chapter 38), which complement the revised chapter on *Drug Absorption, Action, and Disposition* (Chapter 36), provide a base of theoretical and clinical knowledge essential for general understanding of the behavior of drugs, as well as an introduction to in-depth study of pharmacokinetic parameters of individual drugs with the objective of learning how drugs may be utilized optimally in the treatment of disease.

Increasing opportunities for patient-oriented services in pharmaceutical practice are described in four new chapters in Part 9, on *Pharmaceutical Practice*, namely, *Long-Term Care Facilities* (Chapter 95), *The Pharmacist and Public Health* (Chapter 96), *The Patient: Behavioral Determinants* (Chapter 97), and *Patient Compliance* (Chapter 99). The chapter on *Drug Interactions* (Chapter 101) has been expanded to include a comprehensive table of interactions.

The eighth new chapter, titled *Intravenous Admixtures* (Chapter 85), describes services that can only be provided by pharmacists in preparing and participating in the administration of large-volume parenterals specially formulated for individual patients, a mode of therapy now widely used in hospitals.

Included in two of the new chapters are discussions of age-related differences and changes in body composition and physiological functions that may require individual adjustment of drug dosage; this important information is given in Chapter 38, on *Principles of Clinical Pharmacokinetics*, and in Chapter 95, on *Long-Term Care Facilities*, in the latter chapter in the sections titled *Physiologic Variables in the Elderly, Disease Considerations*, and *Geriatric Pharmacology*.

In Chapters 39 to 84, inclusive, in Part 6, on *Pharmaceutical and Medicinal Agents*, the descriptions, actions, uses, adverse effects, and dosages of drugs have been substantially amplified to provide basic information needed by pharmacists in their role as drug information specialists. This information may serve well as a source of counseling information for patients. The sections on dosage have been expanded particularly with regard to pediatric dosage.

In Part 8, on *Pharmaceutical Preparations and Their Manufacture*, much new material has been added, in addition to the aforementioned chapter on *Intravenous Admixtures*. Chapter 79, on *Tonicity, Osmoticity, Osmolality*, and *Osmolarity*, replaces the earlier chapter on *Isotonic Solutions*; the broadened scope of the replacing chapter is indicated in the new title. In Chapter 75, on *Preformulation*, and Chapter 76, on *Bioavailability and Bioequivalency Testing*, evidence is presented that many more factors are involved in evaluating the bioavailability and equivalence of drug products than can be measured and controlled by compendial tests and standards, or decreed by legislative dictum. Collectively, the chapters of Part 8 present many new roles and opportunities for pharmacists who have adequate academic training and develop the necessary skills for formulating and compounding medicinals, whether on a large-scale manufacturing or on an individual prescription-order basis.

The services of editorial board members, section editors, and contributors, whose names and professional affiliations are listed on the foregoing pages, in the planning of the subject matter of the book and in writing/revising and editing its 108 chapters, are gratefully acknowledged. Special thanks are extended the following editorial colleagues, who had responsibility not only for editing the nine parts of the book but generally of writing major portions of it: Dr. C. Boyd Granberg, of Drake University, for Part 1, *Orientation;* Dr. Alfred Martin, of the University of Texas, for Part 2, *Pharmaceutics;* Dr. Alfonso R. Gennaro, of the Philadelphia College of Pharmacy and Science, for Part 3, *Pharmaceutical Chemistry*, and Part 5, *Testing and Analysis;* Dr. Grafton D. Chase, of the Philadelphia College of Pharmacy and Science, for Part 4, *Radioisotopes in Pharmacy and Medicine;* Dr. Ewart A. Swinyard and Dr. Stewart C. Harvey, of the University of Utah, for Part 6, *Pharmaceutical and Medicinal Agents*, 29 of the 37 chapters of which are principally of their individual authorship; Dr. Gilbert L. Zink, of the Philadelphia College of Pharmacy and Science, for Part 7, *Biological Products;* Dr. Robert E. King, of the Philadelphia College of Pharmacy and Science, for Part 8, *Pharmaceutical Preparations and Their Manufacture;* Dr. Melvin R. Gibson, of Washington State University, for Part 9, *Pharmaceutical Practice*. For meticulous preparation of the comprehensive index, from approximately 15,000 individual items, credit is due Mrs. Ellen P. Gilligan, Editorial Associate of the Remington Editorial Board.

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The Philadelphia College of Pharmacy and Science extends to the heirs of Professor Joseph P. Remington its thanks for their assignment of the copyright of the book to the College, which has used income from sales of the book to endow the Joseph Price Remington Memorial Chair of Pharmacy.

ARTHUR OSOL
Chairman of the Editorial Board

Preface to the First Edition

The rapid and substantial progress made in Pharmacy within the last decade has created a necessity for a work treating of the improved apparatus, the revised processes, and the recently introduced preparations of the age.

The vast advances made in theoretical and applied chemistry and physics have much to do with the development of pharmaceutical science, and these have been reflected in all the revised editions of the Pharmacopoeias which have been recently published. When the author was elected in 1874 to the chair of Theory and Practice of Pharmacy in the Philadelphia College of Pharmacy, the outlines of study which had been so carefully prepared for the classes by his eminent predecessors, Professor William Procter, Jr., and Professor Edward Parrish, were found to be not strictly in accord, either in their arrangement of the subjects or in their method of treatment. Desiring to preserve the distinctive characteristics of each, an effort was at once made to frame a system which should embody their valuable features, embrace new subjects, and still retain that harmony of plan and proper sequence which are absolutely essential to the success of any system.

The strictly alphabetical classification of subjects which is now universally adopted by pharmacopoeias and dispensatories, although admirable in works of reference, presents an effectual stumbling block to the acquistion of pharmaceutical knowledge through systematic study; the vast accumulation of facts collected under each head being arranged lexically, they necessarily have no connection with one another, and thus the saving of labor effected by considering similar groups together, and the value of the association of kindred subjects, are lost to the student. In the method of grouping the subjects which is herein adopted, the constant aim has been to arrange the latter in such a manner that the reader shall be gradually led from the consideration of elementary subjects to those which involve more advanced knowledge, whilst the groups themselves are so placed as to follow one another in a natural sequence.

The work is divided into six parts. Part I is devoted to detailed descriptions of apparatus and definitions and comments on general pharmaceutical processes.

The Official Preparations alone are considered in Part II. Due weight and prominence are thus given to the Pharmacopoeia, the National authority, which is now so thoroughly recognized.

In order to suit the convenience of pharmacists who prefer to *weigh solids* and *measure liquids*, the official formulas are expressed, in addition to parts by weight, in *avoirdupois weight* and *apothecaries' measure*. These equivalents are printed in *bold type* near the margin, and arranged so as to fit them for quick and accurate reference.

Part III treats of Inorganic Chemical Substances. Precedence is of course given to official preparations in these. The descriptions, solubilities, and tests for identity and impurities of each substance are systematically tabulated under its proper title. It is confidently believed that by this method of arrangement the valuable descriptive features of the Pharmacopoeia will be more prominently developed, ready reference facilitated, and close study of the details rendered easy. Each chemical operation is accompanied by equations, whilst the reaction is, in addition, explained in words.

The Carbon Compounds, or Organic Chemical Substances, are considered in Part IV. These are naturally grouped according to the physical and medical properties of their principal constituents, beginning with simple bodies like cellulin, gum, etc., and progressing to the most highly organized alkaloids, etc.

Part V is devoted to Extemporaneous Pharmacy. Care has been taken to treat of the practice which would be best adapted for the needs of the many pharmacists who conduct operations upon a moderate scale, rather than for those of the few who manage very large establishments. In this, as well as in other parts of the work, operations are illustrated which are conducted by manufacturing pharmacists.

Part VI contains a formulary of Pharmaceutical Preparations which have not been recognized by the Pharmacopoeia. The recipes selected are chiefly those which have been heretofore rather difficult of access to most pharmacists, yet such as are likely to be in request. Many private formulas are embraced in the collection; and such of the preparations of the old Pharmacopoeias as have not been included in the new edition, but are still in use, have been inserted.

In conclusion, the author ventures to express the hope that the work will prove an efficient help to the pharmaceutical student as well as to the pharmacist and the physician. Although the labor has been mainly performed amidst the harassing cares of active professional duties, and perfection is known to be unattainable, no pains have been spared to discover and correct errors and omissions in the text. The author's warmest acknowledgments are tendered to Mr. A. B. Taylor, Mr. Joseph McCreery, and Mr. George M. Smith for their valuable assistance in revising the proof sheets, and to the latter especially for his work on the index. The outline illustrations, by Mr. John Collins, were drawn either from the actual objects or from photographs taken by the author.

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Table of Contents

Part **1**

Orientation

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Chapter 1

Scope

pharmacy careers
pharmaceutical education
the American Foundation for Pharmaceutical Education
licensure
colleges of pharmacy

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Pharmacy has been defined[1] as that profession which is concerned with the art and science of preparing from natural and synthetic sources suitable and convenient materials for distribution and use in the treatment and prevention of disease. It embraces a knowledge of the identification, selection, pharmacologic action, preservation, combination, analysis, and standardization of drugs and medicines. It also includes their proper and safe distribution and use, whether dispensed on the prescription of a licensed physician, dentist, or veterinarian, or, in those instances where it may legally be done, dispensed or sold directly to the consumer.

The word pharmacy is derived from the Greek word *pharmakon,* meaning medicine or drug. A pharmacist, then, is the person of drugs, or, the expert on drugs. He is the *only* expert on drugs, for expertise regarding drugs requires knowledge in depth in all the facets of pharmacy as outlined in the definition of the term pharmacy above.

The physician, dentist, and veterinarian may prescribe drugs and be primarily interested in the effect of those drugs on the patient, their therapeutic value, and toxicology. The nurse may administer the drug and be concerned with dosage forms, routes of administration, and toxic manifestations. But the pharmacist *is the only expert on drugs.* It is his legally granted responsibility to handle drugs. It is his professional responsibility to know *all about* those drugs. No educational program other than that in pharmacy provides the background to understand completely all there is to understand about drugs. The pharmacist, and the pharmacist alone, is in that unique position of embracing complete drug expertise.

Pharmacy Careers

Most persons when thinking of pharmacy tend to think first of the community pharmacist. And this generalization is numerically justified. It is estimated there are 127,325 registered pharmacists now in practice. About 76% are community pharmacists, 12% are hospital pharmacists, and the rest are in other areas of the profession.[2]

The *community pharmacist* in the US is a unique hybrid of businessman and professional. Born out of the necessity for back-up income, the business aspects of some pharmacies now all but inundate and obscure the primary unit of the pharmacy—the prescription laboratory. The supermarket and cut-rate pharmacies may be important factors in forcing a future dichotomy of pharmacy practice into stores selling merchandise and professionally oriented pharmacies of the Pharmaceutical Center type. An extensive coverage of the current practice of pharmacy and its future may be found in Chapter 4.

Hospital pharmacy, the practice of pharmacy in private and government-owned hospitals, is emerging as one of the most important areas of pharmacy practice. The number of pharmacists in the hospitals of the future will increase for three principal reasons:

1. There will be an increase in population.
2. There will be a greater utilization of hospitals by those who need hospitalization and, hence, will receive better medical care. Hospitalization insurance, both private- and government-sponsored, will foster this trend. There is little question that more adequate care of the sick by government-sponsored programs will increase greatly in the years ahead requiring more of all medical facilities.
3. The pharmacist in the hospital will be given a greater role in all aspects of the use and monitoring of the use of drugs; this is related to the health manpower shortage brought about by the two conditions mentioned above. Current trends of progressive hospitals make the need for pharmacists per hospital much greater than ever before, because of their involvement in assuring better and safer[3] use of drugs.

A very active American Society of Hospital Pharmacists with special studies, imagination, and zeal vigorously promotes this vital aspect of American pharmacy. A comprehensive study of hospital pharmacy may be found in Chapter 94.

Wholesale pharmacy offers opportunities for a limited number of pharmacists. Like most wholesalers, the pharmacy wholesaler serves as the middleman between manufacturer and community pharmacist. Because of the special nature of the products handled and their legal restrictions, all wholesale drug firms employ registered pharmacists in supervisory capacities. These wholesale firms may specialize in a broad range of products sold in a pharmacy, both prescription and nonprescription drugs as well as merchandise items, or sometimes they deal in a limited line of quick-moving items.

Whatever their scope, the wholesale drug firms play a vital role in assuring the community pharmacist of a quick and convenient source of supplies from a multiplicity of manufacturers. This makes possible better service by the pharmacist to his patients of those drugs which may be vital to the patient's welfare. It also lessens the community pharmacist's financial burden of carrying large volumes of stock and the necessity of negotiations with hundreds of manufacturers. Recently, the larger wholesalers have assumed advisory roles to pharmacists in providing them with information and consultants on store redecorating and remodeling. The Pharmaceutical Center concept described in Chapter 4 is a project of one wholesaler, McKesson-Robbins and Co.

Industrial pharmacy offers opportunities to pharmacists of all educational levels. The greatest number of pharmacists are involved in marketing and administration. The medical service representative, or detail man, who is in contact with physicians and pharmacists regarding his company's products may or may not be a pharmacist. But the most effective use is made of a pharmaceutically trained detail man because he is the only person educated as an expert on drugs. Some manufacturers employ pharmacists almost exclusively in this capacity; others do not.[4] The shortage of pharmacists is usually given as the reason why companies do not employ more pharmacists in detailing. This can be a rewarding career for persons with the right personality and inclinations.[5] It also is sometimes a stepping-stone to supervisory positions in sales and to integration into the administrative and sales structure of a pharmaceutical firm.

Pharmacists with master's degrees in business or additional bachelor's degrees in law find opportunities in the pharmaceutical industry in the marketing, sales, and legal departments. Production and quality control supervisory positions in the industrial plant are often held by pharmacists with bachelor's degrees. Research and development personnel often have advanced degrees, but not necessarily so. A more complete discussion of pharmacists in industry may be found in Chapter 5.

Government service offers opportunities to pharmacists in various capacities. They may serve as noncommissioned officers and commissioned officers in the Army, Navy, and Air Force. Also, they may serve as commissioned officers in the United States Public Health Service, which furnishes pharmacists for the Coast Guard and Bureau of Prisons. Civil Service appointments are available for pharmacists in various capacities: in the Drug Enforcement Administration of the Department of Justice, National Institutes of Health, Social Security Administration, Food and Drug Administration, Department of Labor, Department of Agriculture, and various other areas. See Chapter 6.

Pharmaceutical education offers an opportunity for pharmacists with advanced degrees in any of the professional specialties. Expanding enrollments in colleges to meet the manpower needs of the future offer opportunities for careers in college teaching. Higher salaries, more freedom for research and writing, independence of action, and cultural surroundings in pharmaceutical education make teaching attractive. A survey conducted by the American Association of Colleges of Pharmacy indicated that there were 77 unfilled positions in pharmaceutical education at the beginning of the 1977–1978 school year. It should be noted that, of the 77 unfilled positions, 33 were in clinical pharmacy. Persons interested in a future in pharmaceutical education should read *Graduate Study in the Pharmaceutical Sciences*[6] and the issues of the *American Journal of Pharmaceutical Education*.[7]

For a limited number of pharmacists with writing and editing talent, *pharmaceutical journalism* offers rewarding experiences. National, regional, state, and industrial publications require a pharmaceutical background for their effective publishing, editing, and writing.

Organizational management also offers an opportunity for those pharmaceutically educated persons who wish to be officers of national and state associations and boards of pharmacy. With the increase in number of pharmacists, the responsibilities of associations and boards will increase and be complicated by the greater involvement of state and federal governments in health care. The demand for such personnel will be limited, but persons with organizational interests and talents will be in great demand and will play important roles in the *future of pharmacy* in this country.

Pharmaceutical Education

The first school in the US to include pharmacy in the title of one of its professors was the Medical School of the College of Philadelphia in 1789. Pharmacy at this institution was taught by physicians for physicians. Prior to the founding of the Philadelphia College of Pharmacy in 1821, only a few attempts to provide instruction in pharmacy for pharmacists had been made.[8]

The education in medicine and law as in pharmacy evolved from entirely apprenticeship training to the current extensive collegiate education. At the beginning of the century, minimal standards for colleges of pharmacy which were members of the AACP (known as the American Conference of Pharmaceutical Faculties prior to 1925) were unspecified until 1904 when grade school plus a 40-week course was the requirement. This was increased to grade school plus 50 weeks to be done in two years in 1907. In 1908 the one year of high school plus a two-year course was the requirement which was changed to two years of high school prerequisite in 1918. The entrance to pharmacy curricula prerequisite was raised to high school graduation in 1923. In 1925 the pharmacy curriculum was increased to three years and the PhG degree given, four years in 1932 with the BS (or BS in Pharmacy) degree, and five years in 1960 giving the BS in Pharmacy (or BPhar) degree.

Most colleges of pharmacy today offer the five-year program which is often so formulated that either the first year or the first two years may be taken at junior colleges or liberal arts colleges. Three years is the minimal requirement for registration in a college of pharmacy as prescribed by the AACP. The state of California requires four years of registration in a college of pharmacy for those applying for registration in that state. If all five years are not to be taken at an institution where pharmacy is taught, students are strongly advised to communicate with the college of pharmacy they are to enter to insure that their prepharmacy curriculum meets the prerequisite requirements for entrance into the formal pharmacy instruction years.

Two schools in California (University of California, University of Southern California), and the University of Nebraska require a total of six years of education for the lowest degree offered (PharmD). Twenty-two other colleges in the US offer six-year programs on an optional basis.

The undergraduate curriculum in pharmacy is intended to prepare men and women for the profession of pharmacy. *The Pharmaceutical Curriculum*[9] defines this:

> Undergraduate education in pharmacy is intended to prepare men and women for the profession of pharmacy. Stated in another way, it trains students to think and act like pharmacists. These general objectives need to be comprehended in light of the activities which are required (1) to recognize, identify, select, procure, create, process, standardize, stabilize, fabricate, test, evaluate, and preserve all substances of whatever kind and combinations used in preventive, palliative, and curative medicine, and (2) to distribute them to other members of the health professions and to the public. No single individual today engages in all of these activities, but every pharmacist has to do with one or more of them. Out of these specific activities arise a number of others, such as (1) acting as the informed and readily accessible adviser to health-service personnel and the health-seeking public; (2) contributing to the continuing improvement in professional service and sharing his contributions freely with other professionals; (3) assisting in training the manpower for the profession of pharmacy; and (4) evaluating the numerous proposals for social and political improvement and actively supporting those which his informed judgment can approve.

The curriculum is divided into a number of areas to provide the future pharmacist with the background to achieve the goals quoted above.

General Education—One of the principal objectives of the extension of the curriculum to five years in 1960 was to provide the pharmacy student with more general education so that he could, as a practicing pharmacist, more easily take his place in society as a more well-rounded individual whose formal education was not so completely monolithic. As the pressures for more pharmacists in the future become more apparent, there well may be arguments presented to reverse the upward historical trend in the length of time required to educate a pharmacist. History has shown that more educational requirements have consistently attracted more students, not less. There are no ways to test the increased caliber of the students attracted by a longer, more well-rounded education, but those who have seen the progress of pharmaceutical education over the years have expressed subjective judgment that the general caliber of pharmacy students has increased along with increased educational requirements.

The pharmacist of the future will need in his ever-increasing responsibilities to evince ever-increasing intellectual powers to meet the demand of moral, political, and social problems. Only a broad general education can provide the background for that responsibility.