BASIC FACTS OF

PHARMACOLOGY

BROOKS

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STEWART M. BROOKS, Ph.G., B.S., M.S.

Science Instructor, Lasell Junior College, Auburndale, Massachusetts; formerly, Science Instructor, Muhlenberg Hospital School of Nursing, Plainfield, New Jersey

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PREFACE

This text is designed to present the essential facts of pharmacology to the members of the nursing profession—especially the student nurse. Of all the many and varied branches of medical science in the nursing curriculum, pharmacology is second to none in importance. Indeed, our declining death rate is due principally to our ever increasing list of "miracle drugs." Every year, every month, every week and every day bring forth important discoveries. Even the pharmacologist cannot predict what wondrous agent will appear next. You, the reader, therefore, are about to start on a fabulous sojourn through one of the most interesting subjects known to science and man.

Like all good things, pharmacology is not easy. Pharmacology is not easy because it is an ever changing science. As indicated above, new drugs (both good and bad) appear on the market each day. This means that new names are the rule. Further, since drugs are a product of big business, we can expect the same drug to appear under several different names. Specifically, the chief obstacle to the study of pharmacology is the multiplicity of synonymous terms. It would seem, therefore, that a text on pharmacology would be an impotent attack on such a mercurial problem. The author believes that any text on pharmacology is weak which does not stress those facts which do not change. Those facts which do not change are concerned with how drugs act—and this is the nucleus of the text you are about to read. About this nucleus, the author has tried to include all the important drugs in use at the time the manuscript was sent to the publisher. Drugs of extensive use and established efficacy have naturally received more attention than those agents which have not been thoroughly investigated.

For some dubious reason, pharmacology texts for nurses make little or no mention of chemistry. When one considers that even the layman realizes that drugs are a product of the chemical laboratory, this practice is hardly pardonable. Moreover, any reference source on drugs always includes some chemical information. In this text a few structural formulas have been incorporated—in the form of illustrations—to impress upon the student the relationship between chemical constitution and pharmacologic action. These formulas require no knowledge of chemistry, and are intended merely as visual aids.

The sequence of chapters (except Chapter 1) is arbitrary. Obviously, however, the sequence presented is recommended. All medical and pharmacologic terms employed in the text are defined in the glossary. The experiments (in the appendix) are suggested as demonstrations. Each is designed to dramatically demonstrate a particular type of pharmacologic action.

Little originality is claimed for most segments of the text except the organization and literary style. Several standard and reliable works have been freely consulted. These include *The Pharmacological Basis of Therapeutics* by Goodman and Gilman (Macmillan), *A Manual of Pharmacology* by Sollmann (Saunders), *Pharmacologic Principles of Medical Practice* by Krantz and Carr (Williams and Wilkins), *Clinical Toxicology* by Thienes and Haley (Lea and Febiger), *The United States Pharmacopeia* (Mack Publishing Company), *New and Nonofficial Remedies* (Lippincott), and *The Modern Drug Encyclopedia* (Drug Publications).

The author hopes that the text will prove serviceable not only to students in the United States but also to those in Canada. In this connection an attempt has been made—when practicable—to present certain facts peculiar to practices in that country. It is further hoped that instructors will be materially aided in the teaching of the subject.

The author is proud of the opportunity of having his thoughts ventilated through the accurate and cordial agency of the W. B. Saunders Company. He also wishes to acknowledge the assistance of Marie Litterer in the preparation of many of the illustrations. Last (but not least), he offers a powerful thanks for the great part his wife played in making the book possible.

STEWART M. BROOKS

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CHAPTER 1

INTRODUCTION

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QUESTIONS

Pharmacology is the study of drugs. A drug may be defined as any substance—other than food—which is used to improve the health of the body. Thus, Vaseline, which is used to soothe irritated skin, is technically just as much a drug as morphine.

Pharmacology is an extremely broad field. This statement cannot be fully appreciated until one has had the opportunity of visiting a pharmaceutic manufacturing plant. The development of a new drug requires the skills of thousands of technicians and scientists. The chief areas of study encompassed by pharmacology are pharmacognosy (the study of medicinal plants), pharmacy (the study of the preparation of drugs), pharmacodynamics (the study of how drugs act), pharmacotherapeutics (the study of how drugs are used in disease) and toxicology (the study of poisons). Each of these branches is nurtured by the basic physical and biological sciences (viz., chemistry and physiology).

The nurse obviously is not concerned with all phases of pharmacology. Like the physician, she is interested primarily in pharmacodynamics and, especially, pharmacotherapeutics. It has been observed, however, that students who have a little insight into the chemistry and pharmacy of drugs usually have a better idea of the subject as a whole.

NATURE AND SOURCE OF DRUGS

As the word "drug" is ordinarily used, it refers to an agent, or substance, administered for the purpose of improving the body's health. This fact has already been stated. Of concern here is the chemical interpretation of the term substance. Specifically, is this substance a single compound or a mixture of two or more compounds? The answer is this: A drug may be a single compound or a mixture of compounds. The student will be greatly aided in her study of pharmacology if she understands and appreciates this answer. For example, aspirin is a single chemical compound; actually the word is the common name for an organic compound called acetylsalicylic acid. On the other hand, a popular remedy by the name of Anacin contains three compounds: aspirin, acetophenetidin and caffeine. These three compounds all possess therapeutic activity. Some drug mixtures have constituents which are not all active. For example, milk of magnesia is a suspension of magnesium hydroxide in water. The magnesium hydroxide is the active constituent; the water, although a necessary constituent from the standpoint of pharmacy, is inert. Sometimes inert constituents are present because the drug manufacturer is unable to isolate the pure therapeutic principle. An antiserum which is prepared from the blood serum of a horse, for example, contains a multitude of organic compounds in addition to the desired antibodies.

Drugs are derived from either natural or synthetic sources. Natural sources include the plant, animal and mineral worlds. From the plant world man obtains such drugs as quinine, digitalis and morphine; from the animal world, certain vitamins, hormones and antiserums; from the mineral world, radium, Epsom salt and iodine.

The last decades have greatly changed the world of drugs. Most drugs used in medicine today are synthetic; that is, they are prepared in the chemical laboratory from compounds of simpler molecular constitution. The modern chemist has been able not only to duplicate the drugs which occur in nature, but also to improve them. Morphine is a good example. The chemist has produced a variety of agents which possess morphine's ability to relieve pain but not its bad qualities. Moreover, the chemist has created a large number of valuable drugs whose actions are not mimicked by natural drugs. It is evident, therefore, that advancements in chemistry have played a vital role in the development of pharmacology and medicine.

DRUG NOMENCLATURE

Unfortunately, not only for the student but also for all those engaged in any area of pharmacology, viz., physicians, pharmacists and nurses, there is little "rhyme or reason" to the way drugs are named. Moreover, the multiplicity of terms reaches the ridiculous. These facts together represent the chief difficulty encountered in studying the subject, and the student will do well to realize the problem. There seems to be no solution, for one reason: business. It must not be forgotten that medicinal agents are produced by "big business" and that business is entitled to a profit. If a company feels that its profit can be increased by calling a certain vitamin preparation by a different name from that employed by another company for the same preparation, one can hardly question the economic logic. It is best to accept the problem and not attempt to memorize the synonyms for every drug. The student should, however, attempt to learn the synonyms of the commonest and most important agents. Ether, for example, should be recognized by its other two names, ethyl ether and diethyl ether.

It is of decided advantage to know the differences among the following terms: trade name, generic name, chemical name and common name. A trade name (or brand name) is the name given by the manufacturer to his product. The generic name is usually the name which is listed in the U.S.P., N.F. or N.N.R.¹; it is the formal medical name. The chemical name is the name given to a compound by the chemist. It is usually long and means little per se to people who are not chemists. Often, however, compounds with similar chemical names are similar pharmacologically. For this reason, a chemical name may sometimes prove of value to the physician or nurse.

The drug companies have succeeded so well in pushing their products that the trade name has in most cases supplanted the generic title. No doubt there are many physicians who would not recognize the popular antiseptic Zephiran² by its generic name, benzalkonium chloride. Even so, the student should attempt to remember the generic names for important drugs. They are stated on the label beneath the trade name. Thus, if two or more companies are producing the same drug under their own trade names, it is only necessary to know the generic name in order to recognize it. Serpasil, Sandril and Reserpoid, for example, are all trade names for a drug whose generic and official name is reservine.

The common name is the name other than the generic or chemical name which is commonly used in lay and professional circles as a

² In this text trade names are capitalized.

¹ These reference works are discussed on pages 4-6.

synonym for a medicinal agent. Sodium bicarbonate, for example, is commonly known as baking soda.

Not all drugs have a trade name or common name. Drugs which have been in use for many years are usually sold under a recognized

generic or official name.

The picture is further complicated at the practical level by the fact that there are an astronomical number of trade names for different *drug combinations*. This book could perhaps be filled with the trade names for vitamin preparations. The student, however, will usually discover that a new trade name is not a new drug but just a new combination of old agents.

PHARMACEUTICAL LITERATURE

It is essential for the student to know the best sources of information concerning drugs, especially since new drugs are constantly being added to the already vast list of medicinal agents. Also, drugs which are not new are constantly undergoing change. Sometimes new uses are discovered; sometimes a drug is deleted. Therefore, if the student is going to grow in the subject of pharmacology—or for that matter just maintain a state of equilibrium—she must constantly consult the appropriate literature. As a guide to this end, the following information sources are presented.

United States Pharmacopeia³

The *United States Pharmacopeia* (usually referred to as the U.S.P.) is a publication prepared by a pharmacopeial committee, the members of which are outstanding pharmacologists, physicians and pharmacists. The first U.S.P., U.S.P. I, appeared in 1820. Fourteen editions have since appeared; the current edition is U.S.P. XV. The present plan is to revise the U.S.P. at five-year intervals, with supplements to be published when necessary.

The U.S.P. describes the chemical and physical properties, source, method of storage and therapeutic dosage of approved medicinal agents. Because new drugs are constantly being added to the market, even the latest edition cannot be completely up-to-date. At each revision, therefore, new approved agents will be added. At the same time certain agents will be deleted, especially those which have been supplanted by more efficacious agents, or those which have proved over the years to be of questionable value or too toxic. Since the Federal Food, Drug

In Canada the *British Pharmacopoeia* (B.P.) is the counterpart of the U.S.P. Its format, scope and purpose are almost identical. The B.P. is the official reference work not only of Canada, but also Great Britain and her other colonies and dominions. The last revision was published in 1953.

and Cosmetic Act designates the U.S.P. as a "standard of purity," the drugs and drug preparations listed therein are considered official.

The U.S.P. is intended principally as a guide for the pharmaceutic manufacturer and pharmacist. However, when the nurse wishes to know the chemical or physical properties of a drug or its official dose, the U.S.P. is the information source of choice. The student will do well to thumb through the U.S.P. and get an idea of its content and organization.

National Formulary⁴

The National Formulary (usually referred to as the N.F.) is a publication similar in content and organization to the U.S.P. It is published by a committee consisting of outstanding pharmacists under the auspices of the American Pharmaceutical Association. Like the U.S.P., the N.F. has been designated an official drug standard.⁵ The current edition is N.F. X, published in 1955.

The N.F. differs from the U.S.P. chiefly in regard to the therapeutic efficacy of the drugs included. The N.F., unlike the U.S.P., includes not only drugs of proved medicinal value but others in demand. In this respect the N.F. serves a useful purpose, because it sets up certain manufacturing standards which otherwise would not exist. The N.F. is principally of value to the pharmaceutic manufacturer and pharmacist. The student should become familiar with the character of its contents and organization.

Epitome of the U.S.P. and N.F.

As indicated, the physician and nurse are not concerned with the bulk of the information set forth in the U.S.P. and N.F. For this reason a small book called the *Epitome of the United States Pharmacopeia* and the National Formulary is published under the sponsorship of the American Medical Association, to present facts which are of direct medical importance, i.e., the official name, properties, use and dose of drugs. Only those drugs which appear in the U.S.P. and N.F. are included. The "Epitome" is a valuable and inexpensive book to own.

New and Nonofficial Remedies

New and Nonofficial Remedies, usually referred to as N.N.R., is a book containing a description of the action, uses and standards of the proprietary articles which have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Med-

⁴ In Canada the Canadian Formulary and Reference Companion is the counterpart of the National Formulary.

⁵ The student should remember, therefore, that the term official drug correctly used means a drug listed in either the U.S.P. or the N.F.

ical Association; of such simple nonproprietary and nonofficial substances as seem of sufficient importance to warrant their inclusion; and of simple pharmaceutic preparations the inclusion of which is believed to give information to physicians.

N.N.R. is one of the most, if not the most, authoritative sources of information on new medicinal agents. Since it is especially designed for the physician (and indirectly the nurse), the student should become thoroughly familiar with each new edition. This is probably one of the best ways to learn the pharmacology of important new drugs.

Useful Drugs

Useful Drugs is a valuable and inexpensive little book published by the Council on Pharmacy and Chemistry of the American Medical Association. It is especially valuable for the beginning student who desires a brief and practical guide to the more important drugs. Since relatively few drugs are listed, Useful Drugs probably serves better as a textbook than as a reference work.

United States Dispensatory

The United States Dispensatory, published by the American Pharmaceutical Association, is a large, scholarly, encyclopedic commentary on the pharmacognosy, chemistry, pharmacy, pharmacodynamics and therapeutics of official and nonofficial drugs. It is chiefly a reference work designed for persons who are in need of detailed information. Unless the student has an inordinate thirst for pharmacology, she will rarely, if ever, have occasion to use this work.

Hospital Formularies

Many large hospitals publish a formulary or handbook which presents the pertinent information on the drugs most frequently prescribed in the institution. This is an excellent trend because it presents the physicians and nurses of the hospital with information which would otherwise have to be obtained from the pharmacy. Moreover, since most hospitals which have a formulary require the physician to prescribe only from the drugs listed, the pharmacy is not burdened by a multitude of agents of similar or identical use. If company X and company Y manufacture the same drug under different trade names, there is no reason for stocking both.

Modern Drug Encyclopedia

The Modern Drug Encyclopedia and Therapeutic Index (published by Drug Publications) is an essential book. It is the only reference work in the field of pharmacology which lists all the drugs in current use. Drugs are arranged in alphabetical order and indexed therapeutically, generically and according to manufacturer. Each entry is briefly described in such a manner that all the pertinent practical facts are presented. All editions (the present is the 6th) of this valuable book are supplemented bimonthly by a journal called Modern Drugs. In time the supplements are incorporated into a new edition. The speediest way to find information on a new drug, then, is to look it up in the "encyclopedia." If it is not there, the monthly supplements should be searched. All persons dealing with drugs, viz., pharmacists, physicians and nurses, should have ready access to the encyclopedia and its supplements.

Textbooks

For detailed information on pharmacology the student should go to a comprehensive textbook on the subject, of which several are available. The Pharmacological Basis of Therapeutics, by Goodman and Gilman, is one of the best in the field. This textbook, although large, is a masterpiece of clear writing. It has an easy and interesting style. The Pharmacological Basis of Therapeutics will be or should be found in all medical libraries. The student is cautioned against accepting information from just any textbook. The best policy is to consult more than one. Two other reliable works in pharmacology are Sollmann's Manual of Pharmacology (W. B. Saunders Company) and Krantz and Carr's Pharmacologic Principles of Medical Practice (Williams & Wilkins Company).

Manufacturer's Literature

The drug industry in the United States and other countries has made phenomenal contributions to medicine. The research conducted in the larger companies is on a par as to type and caliber with that found in the best universities. The number of scientists and the facilities available are paralleled by only a few federal or public institutions. The majority of "miracle drugs" were discovered, developed and produced by the pharmaceutical industry. The literature disseminated by the leading companies to promote their products is reliable and informative. It presents one of the first sources of information on many medicinal agents. Brochures, pamphlets and books may be obtained at the pharmacy or by writing to the appropriate company.

LAWS REGULATING DRUGS

There are many state and federal statutes which regulate directly or indirectly the handling of drugs and drug products. The various state

⁷ 2nd Edition, New York, 1955, the Macmillan Company.

⁶The inclusion of a drug in this work does not necessarily indicate that it possesses merit.

laws that define the duties of the physician, pharmacist, nurse, dentist and veterinarian are concerned indirectly with drugs. The student will become familiar with the laws regulating nursing in her course in jurisprudence. Of the laws which are directly concerned with drugs, the most important are the Federal Food, Drug and Cosmetic Act and the Harrison Narcotic Act.

Federal Food, Drug and Cosmetic Act8

The Federal Food Drug and Cosmetic Act became law in 1938; it replaced the original law of 1906. Its provisions are enforced by the Food and Drug Administration of the Department of Health, Education and Welfare. A rather lengthy piece of legislation, its purpose relative to drugs may be summarized as follows: It controls the standards, purity and composition of all drugs and drug mixtures and specifies the character of the label a given drug must bear. Since the law is stringently enforced, unethical practice in the pharmaceutic industry is almost a thing of the past.

Harrison Narcotic Act9

The chief law controlling the handling of narcotics in the United States is the *Harrison Narcotic Act*. This law applies to opium and its derivatives and synthetic substitutes, cocoa leaves (cocaine), and marihuana. The law requires that all physicians and pharmacists be registered with the collector of internal revenue in their district. Prescriptions for narcotics must bear the physician's registry number. The nurse is permitted to handle narcotics only under the supervision of the physician. Penalties for violation of the provisions of this law are severe. All persons who in any way handle narcotics should become thoroughly familiar with the regulations that are applicable to their respective professions.¹⁰

PHARMACEUTICAL PREPARATIONS

The term "pharmaceutical preparations" refers to the various forms in which drugs are "fashioned" for the purpose of administration. This area of pharmacology is the concern of the pharmaceutical manufac-

o In Canada the counterpart of the Harrison Narcotic Act is the Opium and

Narcotic Act, passed in 1920.

⁸ In Canada the *Food and Drug Act* (revised in 1954) is the counterpart of the Federal Food, Drug and Cosmetic Act. The provisions of this law are enforced by the Minister of National Health and Welfare.

¹⁰ Booklets on various phases of the Harrison Narcotic Act may be obtained for a few cents by writing to the U.S. Government Printing Office, Washington, D.C.

turer and pharmacist.¹¹ The student, however, should become familiar with the short descriptions presented below.

Solid Forms

For convenience let us consider the chief semisolid and solid pharmaceutical forms under the above heading. (See Fig. 1.)

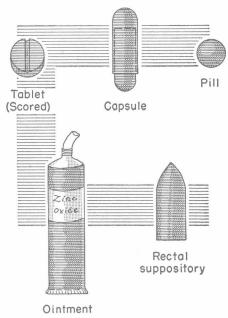


Fig. 1. The principal forms of "solid medication."

Cachets. Cachets are wafers made of starch or flour so shaped that dry drugs can be contained between them. They are intended for oral administration. They are seldom used at the present time.

Capsules. A capsule is a bullet-shaped, hollow body made of gelatin. It is composed of two parts so shaped that one fits securely into

¹¹ A great many mechanical duties which were formerly performed by the pharmacist have been taken over by industry. And this is good, because the neighborhood pharmacy does not have the equipment or time to make complicated preparations. Moreover, industry has the combined skills of all scientists, not the skill of just one. The pharmacist, however, is still the "keeper of the drugs." His services are probably even more vital than in former years because of the large number of drugs which are placed on the market. Physicians and nurses are often confused by the multiplicity of names, dosage forms, modes of administration, and so on. The pharmacist is prepared to dispense this information, usually on a minute's notice.

the other. Capsules are filled by separating the two parts, filling them with a drug and fitting them together again. There are two types of capsules, hard and soft. Hard capsules are used for dispensing powdered drugs, and soft capsules, for oils or oil solutions. Hard capsules range in sizes from 000 to 5, with the smaller number representing the larger size. The size of a capsule obviously depends upon the character of the drug or drugs to be dispensed.

The capsule is one of the most important and popular oral dosage forms. It affords a convenient way to administer a given dose of a drug in a disguised form. Since gelatin readily dissolves in the secretions of the stomach and intestine, the capsule can be relied upon to deliver its charge to the body. Sometimes, when it is desirable for a drug to bypass the stomach (viz., when a drug would prove irritating or be destroyed by high acidity) capsules are equipped with a so-called *enteric coating* so that they will pass through the stomach intact.

Cerates. Cerates are ointments which contain wax or paraffin. They differ from regular ointments in having a higher melting point. It would seem that cerates are of value only in climates where conventional ointments would melt. They are not popular in current medicine.

Disks. Disks are so named because of their shape. They are made of *gelatin* containing some active principle for application to the conjunctiva of the eye.

Extracts. Extracts are solid or semisolid preparations made by the evaporation of a *fluidextract*. A fluidextract is a liquid preparation made by percolating a crude plant drug (usually the roots or leaves) with water and/or alcohol. In this manner all of the active constituents of the plant are removed. Fluidextracts are so prepared that 1 cc. is equivalent to the potency of 1 Gm. of crude drug.

The present practice of prescribing drugs in the pure chemical state has almost completely supplanted the use of so-called *galenical*¹² forms, that is, *extracts*, *fluidextracts* and similar preparations. Since a few drugs are still employed in extract form, however, extracts must be considered. They are administered *orally* (usually in pills and capsules) and *topically* (usually as an ointment).

Jellies. Pharmaceutically, a jelly is a soft, more or less translucent colloidal mass made by the incorporation of a medicinal agent into some mucilaginous substance such as glycerin or tragacanth. In general, they are considerably softer than ointments and easily liquefy in an aqueous environment. Jellies enjoy a fair amount of popularity for topical application to sores and mucous membranes.

Ointments. An ointment is a soft, semisolid preparation (with the consistency of petrolatum) intended for topical application to the skin or mucous membranes. Ointments are prepared by incorporating one

¹³ After Galen (born 130 A.D.), a famous Greek physician and writer.

or more active constituents into a so-called base. There are many types of ointment bases. The more popular ones include solid petrolatum (Vaseline), lanolin (wool fat), certain vegetable fats and polyethylene glycol. Polyethylene glycol (also called Carbowax) has the important advantages of being inert and water-soluble. It probably is the most useful base.

Ointments continue to be an efficacious and popular means of local application. Almost any agent which is capable of exerting a local effect can be dispensed in the form of an ointment.

Pastes. Pastes are ointment-like preparations generally made from one or more powders and some adhesive substance, usually starch and water. They are more protective and absorbent than ointments and

are especially valuable for application to oozing surfaces.

Pills. A pill is a spherical or globular medicinal form intended for oral use. It is usually about the size of a pearl. Smaller ones are called granules and larger ones boluses. Pills are manufactured by mixing the active constituent or constituents with an adhesive (called an excipient), moistening, shaping and allowing them to dry and harden. A coating (chocolate, for example) is then applied to disguise the taste; some pills are enteric coated. Pills should be reasonably fresh in order to ensure their complete disintegration in the gastrointestinal tract.

Plasters. A plaster is an adhesive solid preparation intended for topical application to the skin. Plasters are named after the principal ingredient employed; *mustard plaster*, for example, is a mixture of powdered black mustard and an adhesive spread on cotton cloth or other fabric. Plasters represent a type of home remedy sometimes of value for enhancing local circulation. Care must be exercised so as not to burn the skin.

Powders. Powdered drugs were at one time popularly dispensed in folded papers and called "powders." The contents of a paper were placed on the tongue and swallowed with water or were stirred into water before being swallowed. Powders are seldom prescribed at present.

Poultices. Poultices are hot, soft, solid preparations which are placed on the skin for the purpose of applying heat and moisture. The heat is believed to influence the circulation of the deeper layers. A poultice may be a warm soft mass of an inert substance (such as a bread poultice) or a warm mass of an agent which per se causes hyperemia by its irritant action. Poultices sometimes are fairly effective home remedies. Care should be exercised, however, so as not to burn the skin.

Suppositories. A suppository is a medicated mass which slowly melts at body temperature, releasing the active agent or agents to the surrounding area. Suppositories are intended for instillation into the