PHARMACOLOGY OF RESPIRATORY THERAPY MEDICATIONS

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Foreword

The pharmacotherapy of disorders of pulmonary and respiratory function remains one of the most vital, yet controversial, areas of medicine. There is little disagreement that the classes of drugs available to the practitioner for the management of pulmonary and respiratory diseases provide many valuable options for therapy. But with these increased options comes the awareness that a great deal of physiologic, biochemical, anatomical, physical and pharmacologic principles must be mastered in order to use these agents rationally and effectively. The usual textbooks on pharmacology and therapeutics often deal with the subject in a manner that does not allow rapid access to the key facts that permit correct and rapid assessment of indications, side effects, contraindications, dosages, drug interactions and other elements of therapeutic decision making. Particularly, there has been a glaring deficiency in material specifically directed to the needs of specialized respiratory care personnel, including intensive care nurses, cardiopulmonary technologists, coronary care and associated paramedical personnel.

In this compendium, the author sorts out a complex maze of information in a lucid, telegraphic format that affords the reader an easy and accurate picture of the medications available to respiratory therapy. The format was chosen with the knowledge that the busy practitioner seeking information often wishes to avoid excessive prose and personal interpretation of facts. Thus, as a modern compilation of accepted and controversial information, this compendium offers the reader a chance to see the facts and then judge what modality of therapy is appropriate for any given clinical setting. However, the author has detailed those areas where opinions differ and the evidence for and against any given position. The sources of information for the compilation included first-hand review of original articles in professional journals, as well as reviews and monographs. The excellent cross section of source material and diversity of references assures that the material presented represents a fair and thorough overview of the field. The author has avoided the usual traps and temptations to preach and advocate therapy based on a narrow selection of information from one specialty journal or monograph. The uniform format allows a quick and easy scan of pages for the desired information.

Moreover, the use of trade names and manufacturers facilitates identification of drugs and agents. This is in contrast to those publications where only generic names are used, and where references to availability, manufacturers or distributors are totally lacking. Modern drugs come from the pharmaceutical industry in large part, and this compendium is correct to emphasize the fact that a pharmaceutical house is often a key and vital source of information about its products. The author has utilized this source of information, yet has balanced it carefully whenever there has been evidence of deficient or biased information.

Pharmacology is a difficult subject to master because of the requirement that a solid base of other sciences be obtained first. The author has outlined many physiological and biochemical mechanisms. There may be criticism that the presentation is too simple or lacks sophistication. If the reader seeks more in-depth knowledge of such biochemical subjects, the reference lists are replete with such sources. The author has attempted to inform without overwhelming the reader with trivia. This well-written and well-conceived compendium should find an important place in every respiratory therapist's drug information library.

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Preface

There are many books that deal with pharmacology in general. This book represents one of the first attempts to provide specific information about respiratory therapy pharmacology and is intended to be a summary of "the state of the art." Previously, this information was available only from a wide variety of references. This book is designed to be a complete and compact reference of those drugs associated with respiratory therapy.

Books on pharmacology designed for the respiratory therapist are just beginning to emerge. It is hoped that this book can further improve the knowledge of our field. As respiratory therapists, we administer powerful drugs to our patients, and it is important that we understand their pharmacologic effects.

Pharmacology is a constantly changing field. Research will, at times, provide contradictory results. It is therefore the intent of this book to be as factual as possible with the current research available and to develop an understanding of the various respiratory therapy pharmacologic agents. The adrenergic medications are presently one of the most extensively studied groups of pharmacological agents, and this is not intended to be a final and conclusive review of the current literature. Where there is controversy and inconsistency, both views are presented in an effort to be as objective as possible. Some inconsistencies are due to manufacturers' reluctance to issue certain information.

Not all investigational drugs are discussed, as this would go beyond the scope of this text, but rather only those drugs found in our journals and related sources.

This book is designed primarily for respiratory therapy personnel, respiratory care unit nurses, intensive care nurses, coronary care nurses, cardiopulmonary technologists, pulmonary physicians and any medical personnel interested in the pharmacology of respiratory therapy.

The purpose of this book is to facilitate the learning process by utilizing standard sentence structure in conjunction with outline form, thereby eliminating the wordiness and length of standard textbooks. The amount of factual information is intended to be similar.

This book can be used as a textbook in the classroom, as a handbook

at the bedside and as a reference book at the nursing station or in the physician's office.

The sections on methods of administration and on dosage and strength are intended to give minimum to maximum ranges by incorporating the values given by several different texts.

Readers who can make any additions for future editions will have the gratitude of the author; in addition, they may possibly save a patient's life.

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MICHAEL J. STRAUCH

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1 / Drugs and Their Administration

Pharmacology is the science of drugs—their nature, classification, effects, administration, mechanism of action and composition. Respiratory therapists are primarily concerned with pharmacodynamics, the branch of pharmacology that deals with the effects of drugs on the human body.

Respiratory therapy pharmacology is that area of drug therapy that provides care for the body's airways, either through control of smooth muscle or through control of secretions. A background knowledge of pharmacology is presupposed, as is knowledge of basic chemistry, biology, anatomy and physiology. Some basic pharmacologic principles are reviewed here to aid the reader in his understanding of this specialty area of respiratory therapy pharmacology.

DRUG NOMENCLATURE

All drugs have three names:

1. *The chemical name* is a complete description of the drug's content and structural formula. Often, it is identical to the generic or official name.
2. *The generic* or *official name* is a brief description of the drug's chemical composition.
3. *The trade* or *proprietary name* is one given a drug by its manufacturer or seller. Generally, it is a simplified spelling and/or pronunciation of the drug's generic name.

ROUTES OF DRUG ADMINISTRATION

There are several routes of drug administration. The three we will concentrate on here are parenteral (including intravenous, intramuscular and subcutaneous), oral (gastrointestinal) and aerosol (inhalation).

Parenteral

Intravenous Injection

The most rapid and the most reliable mode of administration to obtain the desired blood level of a drug is by injection directly into a

vein. This route makes possible an accurate control of dosage and a rapid onset of drug action. In critically ill patients, this is the route of choice.

Intramuscular

Drugs injected intramuscularly are absorbed through the abundance of vasculature. If circulation is intact, it is generally a reliable method of attaining a prescribed drug level. Compared to the intravenous route, absorption by this method is slower. Lower blood levels of the drug are achieved and preserved over a longer period of time.

Subcutaneous

Drugs administered subcutaneously are absorbed more slowly than by intramuscular injection because of the decreased amounts of vasculature in the fatty tissues. This method is less reliable than the aforementioned methods. Irritating solutions might be painful by this route.

Oral (Gastrointestinal)

Absorption through the small intestine is extremely good. It is not as good through the stomach or large intestine but still of consequence. The oral administration of drugs (by the use of pills or liquids) is the most frequently practiced method of drug administration. It is painless, convenient and economical. Compared to intravenous or intramuscular absorption, that through the gastrointestinal route is slower and less dependable. Onset of drug action is delayed. The oral route is also the method of choice when self-administration of medication is indicated. Not only is it more conducive to patient comfort, but it is more easily learned and practiced safely by the subject. The major limitations of this route are as follows:

1. The drug may not be well absorbed from the GI tract.
2. It may be irritating and cause local side effects.
3. There may be an unpleasant taste.
4. Some agents, such as proteins, which are digested, or steroids, which are inactivated by the liver, may not reach general circulation. In such cases a sublingual (under the tongue) or rectal route of drug administration may be used.
5. It relies on the patient for compliance.

Aerosol (Inhalation)

The major advantage of drug administration by inhalation is the potential surface area available for drug absorption. The inhalation of drugs will attain desired blood levels quickly. Intravenous administration is the only route that achieves the desired result more quickly.

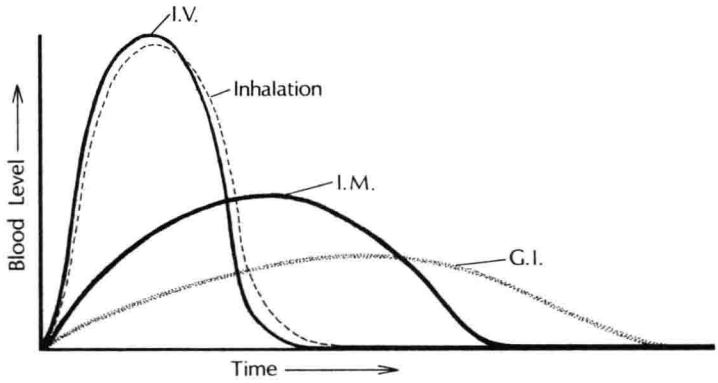

Fig 1–1.—Blood levels achieved by equal doses of a drug administered via different routes: I. V. = intravenous; I. M. = intramuscular; G. I. = gastrointestinal (pill or liquid). Only direct I. V. injection achieves a faster and higher blood level than the inhalation route. (From Shapiro, B., et al.: Pharmacology in Respiratory Therapy, in *Clinical Application of Respiratory Care* [Chicago: Year Book Medical Publishers, Inc., 1975].)

Lung parenchyma provides the large surface area for absorption. Medication must be delivered to the alveolar surfaces for exchange to occur across the alveolar-capillary membrane. The mucosa that lines the pulmonary tree is supplied by an abundance of capillary blood flow which provides rapid absorption. Medications administered by inhalation may act in three ways: (1) topically; (2) by absorption across the a-c membrane, i.e., systemically; or (3) by both of these mechanisms.

It is being postulated that two mechanisms for bronchodilation exist: one is at the smooth muscle vasculature of the tracheobronchial tree and the other at the mast cell. These two sites are sources of bronchospasm. It is possible that systemic sympathomimetics may reach the mast cell in ineffective amounts, whereas via inhalation both sites are reached in therapeutic amounts. This would give them a double effectiveness. Most medications delivered by inhalation may also be effectively delivered by another route, except for mucolytics or decongestants. The delivery of drugs by an aerosol is a safe and convenient form of self-administration. Inhaled medications are usually considered to be active topically, when in actuality they are being absorbed rapidly into the circulatory system through the mucosa of the tracheobronchial tree.

It should be kept in mind that our present knowledge of drug dosage, metabolism, absorption and side effects is still incomplete.

Figure 1-1 demonstrates the relationship of the four routes of administration with reference to how quickly and how well drugs are systemically absorbed.

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2 / The Nervous System

It will be helpful for the reader to have a basic understanding of the structure and function of the human nervous system, since many drugs commonly used in respiratory therapy affect the body through changes within this system.

The nervous system is composed of the central nervous system (which consists of the brain and the spinal cord; Fig 2–1) and the peripheral nervous system, which we will concentrate on here.

PERIPHERAL NERVOUS SYSTEM

The peripheral nervous system consists of the autonomic nervous system, the cranial nerves (Table 2–1) and the paired spinal nerves. The cranial nerves and spinal nerves are collectively known as soma-

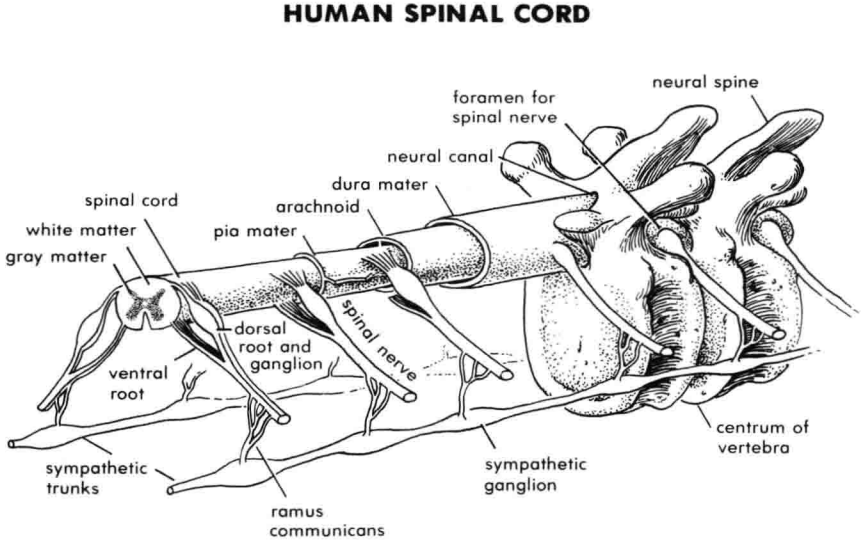

Fig 2–1.—The human spinal cord, spinal nerves and sympathetic nervous system in relation to the vertebrae and the membranes (meninges) about the cord. (From Storer, T., and Usinger, R.: *General Zoology* [New York: McGraw-Hill Book Co., 1965]. Used by permission.)

TABLE 2-1.—THE PAIRED CRANIAL NERVES OF VERTEBRATES

NUMBER AND NAME OF NERVE	ORIGIN (IN BRAIN)	DISTRIBUTION (EXTERNAL CONNECTIONS)	FUNCTION (CHIEFLY AS IN MAN)
I Olfactory	Olfactory lobe (or bulb)	Olfactory epithelium in nasal cavity	*Sensory:* smell
II Optic	Optic lobe on midbrain	Retina of eye	*Sensory:* sight
III Oculomotor	Floor of midbrain	Eye: 4 muscles of eyeball; also iris, lens, upper lid	*Motor:* movements of eyeball, iris, lens, and eyelid
IV Trochlear	Floor of midbrain (emerges dorsally)	Eye: superior oblique muscle of eyeball	*Motor:* rotation of eyeball
V Trigeminal	Side of medulla	Top and sides of head, face, jaws and teeth	*Sensory:* forehead, scalp, upper eyelid, side of nose, teeth *Motor:* movement of tongue and of muscles used in chewing
VI Abducens	Side of medulla	Eye: external rectus muscle of eyeball	*Motor:* rotation of eyeball
VII Facial	Side and floor of medulla	Tongue (anterior ⅔); muscles of face, of mastication, and of neck	*Sensory:* taste *Motor:* facial expression, chewing, movement of neck
VIII Auditory (acoustic)	Side of medulla	Inner ear: (1) organ of Corti in cochlea (2) semicircular canals	*Sensory:* (1) hearing (2) equilibrium
IX Glossopharyngeal	Side of medulla	Tongue (posterior ⅓); mucous membrane and muscles of pharynx	*Sensory:* taste *Motor:* movements in pharynx
X Vagus (pneumogastric)	Side and floor of medulla	Pharynx, vocal cords, lungs, heart esophagus, stomach, and intestine	*Sensory:* taste and touch *Motor:* pharynx, vocal cords, lungs, esophagus, stomach, heart; inhibits heartbeat
XI° Spinal accessory	Floor of medulla	Muscles of palate, larynx, vocal cords, and neck	*Motor:* muscles of pharynx, larynx, and neck
XII° Hypoglossal	Floor of medulla	Muscles of tongue (and neck)	*Motor:* movements of tongue

°Nos. XI, XII are lacking in amphibians, fishes, and cyclostomes.

From Storer, T., and Usinger, R.: *General Zoology* (New York: McGraw-Hill Book Co., 1965). Used by permission.

THE MYELIN SHEATH

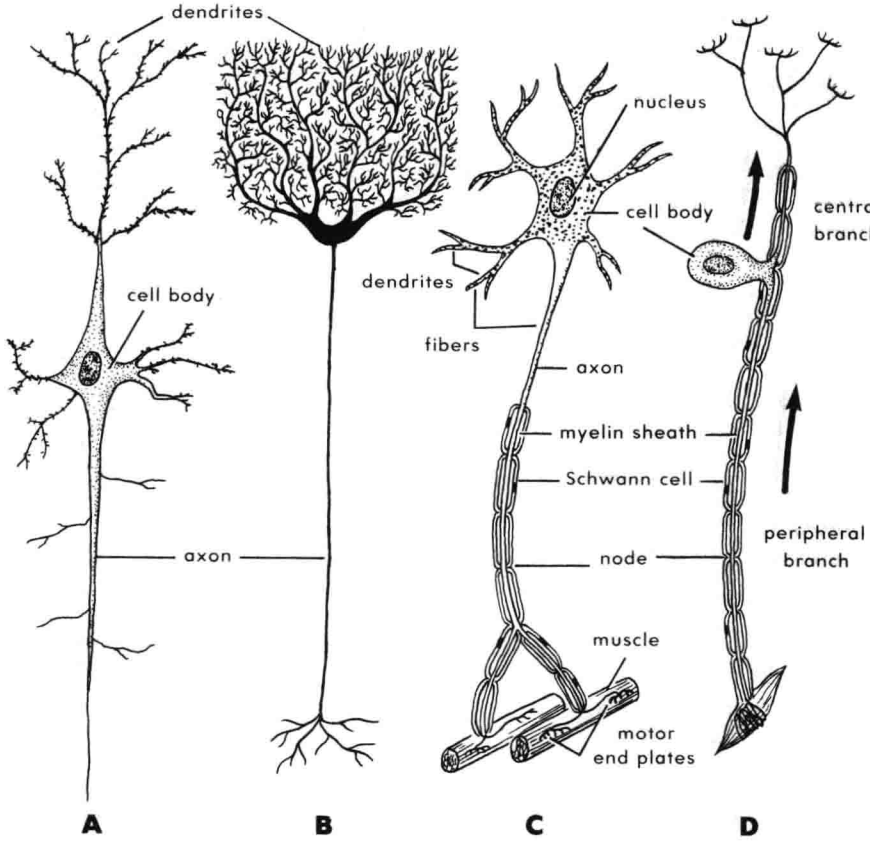

Fig 2–2.—A variety of neuron types in human beings. **A,** the dendrites, unlike the axon, often have a spiny look. **B,** the dendrites of certain brain cells branch profusely, giving the cell a tree-like appearance. **C,** motor neurons have long axons that run from the central nervous system to the effector (in this case muscle); these axons are frequently, but not always, myelinated. Note the presence of many dark granules in the cell body and dendrites. **D,** a sensory neuron. There is only one fiber, which branches a short distance from the cell body, one branch (peripheral) running between the receptor site and the dorsal-root ganglion in which the cell body is located, and the other branch (central) running from the ganglion into the spinal cord or brain. Except for its terminal portions, the entire fiber is structurally and functionally of the axon type, even though the peripheral branch conducts impulses toward the cell body. A sensory neuron thus has no true dendrites, although the peripheral branch is often called a dendrite because of the direction in which it conducts impulses. (Modified from many sources, including Ranson and Clark, 1959, Gardner, 1963, Peele, 1961 and others. Reproduced from Keeton, W. T.: Nervous Control, in *Biological Science* [New York: W. W. Norton and Co., Inc., 1967]. Used by permission.)