INTRODUCTORY CLINICAL PHARMACOLOGY

JEANNE C. SCHERER

JEANNE C. SCHERER, R.N., M.S.

Assistant Director and
Medical-Surgical Coordinator,
Sisters of Charity Hospital
School of Nursing, Buffalo, N.Y.

Introductory Clinical Pharmacology

J. B. LIPPINCOTT COMPANY PHILADELPHIA / NEW YORK / TORONTO

Distributed in Great Britain by Blackwell Scientific Publications
Oxford, London, and Edinburgh

ISBN 0-397-54168-6

Library of Congress Catalog Card Number 75-4606

Printed in the United States of America

3 5 7 9 8 6 4

Library of Congress Cataloging in Publication Data
Scherer, Jeanne C.
Introductory clinical pharmacology.

1. Pharmacology. I. Title. DNLM: 1. Drug therapy—Nursing texts. 2. Pharmacology—Nursing texts.
QV4 S326i
RM300.S264 615'.1 75-4606
ISBN 0-397-54168-6

Introductory Clinical Pharmacology

Acknowledgments

I owe the idea for this text to the students who participated in my classes in pharmacology. Their questions led to marginal notations on lecture material, which ultimately became an outline and, finally, after several transitions, a manuscript. If a dedication of this text were to be made, it would be to the students of the Sisters of Charity Hospital School of Nursing, especially the class of 1974; and to the physicians, nurses, and other health professionals who attended my seminars and challenged me to present the principles of pharmacology in clear and relevant terms.

Behind the scenes there are many people who contribute to a textbook. Paul A. Young, Ph.D., of Canisius College, worked with me on the original draft of the manuscript. Sister Geraldine P. Coleman, B.S. in Pharmacy, M.P.H., the administrative assistant of Sisters of Charity Hospital, painstakingly read the completed manuscript and made many valuable suggestions. Antoinette DeMarco was an ever-patient typist.

My thanks also go to Mary Dennesaites Morgan and David T. Miller of the J. B. Lippincott Company, especially for their invaluable editorial assistance and encouragement. The thoughtful attention of copy editor Joyce Mkitarian is especially appreciated.

Without the help of all these individuals, those marginal notes would most probably still be in my lecture file.

Preface

This text is designed for students and practitioners who wish a concise, clear introduction to pharmacology. However, the basic explanations presented here should not lead anyone to the conclusion that pharmacology is a simple subject. Drug therapy is one of the most important treatment modalities in modern health care. Because of its importance and complexity, and the ever-increasing new knowledge in the field, it is imperative that all health professionals develop a system of study to help them cope with drug information. This book is designed to aid the student and practitioner in that study.

Each chapter is followed by a table which summarizes the clinical considerations of the specific drugs discussed in that chapter.* An attempt has been made to use charts and tables wherever possible for quick and easy reference; key points are highlighted in color, and material on patient education is discussed. An appendix, covering basic mathematics related to drug administration, has been included for review.

* The only exception is Chapter 35, Anesthetic Agents; the wide variations in uses, dosages, etc. encountered with this group of drugs would make such a summary impractical.

The drugs and dosages listed in this text have been compiled from several references. The reader should keep in mind, however, that drug therapy is constantly being revised; that new products are continuously being marketed and older ones withdrawn; and that the Food and Drug Administration (FDA) often orders changes in labeling on the basis of ongoing research in safety and effectiveness. Therefore it is advisable that current references be consulted. Periodic supplements are issued by the *Hospital Formulary* and the *Physicians' Desk Reference* (PDR); manufacturers' package inserts should also be checked for changes. Some drugs have a wide dose range, indicating that different doses are advised for specific disease conditions and/or degrees of severity.

If official references are not available or if there appears to be a discrepancy between the dose ordered and the reference consulted, the hospital pharmacist should be contacted for updated information. No health professional should administer, or permit a patient to take, a medication when there is doubt as to the correct dosage.

Chapter 1

Introduction

Throughout the ages man has used drugs to produce desired changes in the body, but the exact science of the study of drugs—**pharmacology**—is relatively recent when considered in light of the number of years drugs have been used. Yet even with the advancement of modern science the exact mechanism of action of many pharmacological agents is not well understood. Physical differences among individual patients also influence the action of any one drug; these factors must be taken into consideration when drugs are administered.

Factors Influencing Drug Action

The **age** of the patient may influence the action of drugs. Children almost always require smaller doses of a drug than adults. Elderly patients also may require smaller doses, although this may well depend on the type of drug administered. As an example, the elderly patient may be given the same amount of an antibiotic as a younger adult, but may not require the usual adult dose of a sedative or a hypnotic.

Drugs for children may be calculated on a weight basis; however, drugs for the adult patient may also be calculated in this manner. For example, the recommended dosage

for a drug may be stated as 20 mg./Kg./day (20 milligrams per Kilogram of body weight per day). This particular drug may also be given in equally divided doses several times per day. An example of this is shown below.

> DRUG DOSE: 20 mg./Kg./day in 3 equally divided doses
> WEIGHT OF PATIENT (child): 39 pounds or 17.7 Kilograms
> (2.2 pounds = 1 Kilogram;
> 39 ÷ 2.2 = 17.7 Kilograms)
> 20 milligrams per Kilogram equals 354 milligrams *per day* (20 × 17.7). Since this drug is to be administered in 3 equally divided doses, then *each dose* is 118 milligrams (354 ÷ 3).

Body size influences the action of some drugs. For example, a common dose of meperidine (Demerol), a synthetic narcotic agent, is 75 milligrams. This dose may produce the desired effect, relief of pain, in most adult patients, but a very large patient may require a larger dose and a slender patient may require a smaller dose to produce the desired effect.

The **sex** of the individual may also influence the action of some drugs. Women may require a smaller dose of some drugs than men. This is based on the fact that many women are smaller than men and have a different ratio of fat and body water than males. Sex is not so great a factor as age and body size.

The **presence of disease** may influence the action of some drugs and in some instances may be an indication for omitting one drug and possibly using others in its stead. The patient with liver disease for example might have an impaired ability to metabolize a specific type of drug. If the average or normal dose of the drug is given, the liver will be unable to metabolize it; consequently lower doses may be required or other drugs not metabolized or detoxified by the liver may be necessary. The package insert, the *Physicians' Desk Reference,* the *Hospital Formulary,* and other drug references should be consulted concerning cautions or contraindications of drugs, as certain diseases or conditions may warrant the withholding of a drug until the physician is consulted.

Adverse Drug Reactions

Along with factors discussed above that may influence the action of a drug, the possibility of an untoward response of the patient to a pharmacological agent is also important. An **adverse reaction** to a drug is unpredictable and sometimes unexplainable. An adverse reaction may occur the first time a drug is given or after several and even many doses.

Drug allergy appears to occur after more than 1 dose of the drug has been given. The individual becomes *sensitized* to the drug; that is, the drug has become an *antigen* which stimulates the body to produce *antibodies.* If the patient takes the drug again after the antigen/antibody response has occurred, an allergic reaction will result. This can be compared to an allergy to ragweed pollen ("hay fever"). The rag-

weed pollen is the antigen; the response of an individual allergic to ragweed pollen usually includes itching and watering of the eyes, increased nasal discharge, swollen nasal membranes, and sneezing.

Allergic reactions to drugs can be mild or extremely serious and may be manifested by a variety of symptoms and complaints. Even a mild reaction can become serious if it goes unnoticed and the drug is repeated. It is possible, then, for a mild reaction to be followed by an extremely serious reaction. This is why even the most mild reaction should be detected early and reported to the physician before the next dose is administered.

Drug allergic reactions may occur immediately, within minutes (and even seconds) after administration, or they may be delayed, occurring hours or days later. In many instances, immediate reactions are the most serious. **Anaphylactic reactions** usually occur shortly after the administration of the drug to which the individual is sensitive (or allergic) and they are extremely serious and require immediate medical intervention. Shock, bronchospasm, loss of consciousness, cyanosis, dyspnea (due to the severe bronchospasm), convulsions, and cardiac arrest are signs of an anaphylactic reaction. It is believed that this type of reaction is due to the sudden release of histamine. (See Chapter 29.)

Milder drug reactions include rashes of varying types, urticaria (hives), itching, and nasal stuffiness. *Any* patient complaint or overt symptom should be considered as a warning that a drug reaction *may* be occurring, and the drug should be stopped until the physician has been notified and a decision made as to the cause of the complaint or symptom.

Drug idiosyncrasy is a term usually used to describe any unusual or abnormal reaction to a drug, that is, any reaction that is different from the one normally expected of a specific drug and dose. For example, a patient may receive a normal dose of secobarbital (Seconal), a sedative/hypnotic barbiturate, and still be unable to sleep or show evidence of drowsiness. This is an *underresponse* and is abnormal. Another patient may receive the same drug and dose, sleep 8 hours, and find it extremely difficult to waken from sleep. This is an *overresponse* and is also abnormal. It is believed that drug idiosyncrasies occur because of a genetic deficiency wherein the patient is unable to tolerate certain chemicals.

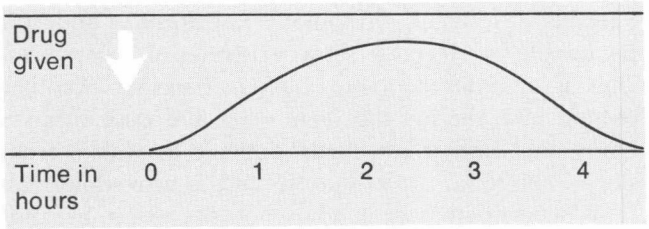
Other Responses to Drugs

Besides those factors which influence drug action and adverse drug reactions, there are other factors that must be considered regarding the administration of drugs. **Drug tolerance** is a term used to describe a *decreased* response to the dose of the drug, usually requiring an increase in dosage to elicit the desired effect. Drug tolerance may be seen in the patient taking a barbiturate every night for sleep. After a period of time, which may vary, the individual may find that 1 capsule no longer produces sleep and that 2 capsules are now required. Not all pharmacological agents are capable of creating drug tolerance.

A **cumulative effect** may be seen in some patients. This effect occurs when the body is unable to metab-

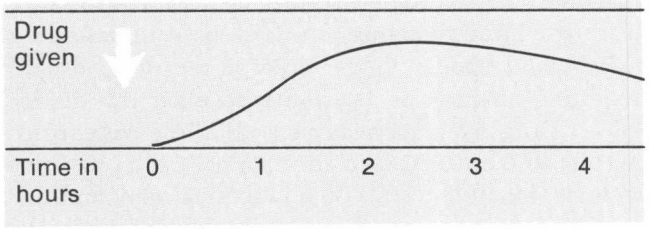
olize and excrete 1 dose of a drug before the next dose is administered. Below is a hypothetical example of the course of a narcotic dose during normal metabolic breakdown and excretion.

NORMAL METABOLISM



Note that at the end of 4 hours there is very little drug left in the body of this patient. Compare this with a patient with severe cirrhosis of the liver receiving the same drug and dose.

ABNORMAL METABOLISM



At the end of 4 hours very little of the drug has been metabolized and excreted. If a second dose of the drug were given, the patient would most likely experience toxic drug effects, namely symptoms of narcotic overdose, even though normal doses were given both times.

Drug interaction is another factor that must be considered during drug administration. Some drugs may interact with other drugs, foods, or chemicals, producing an *antagonistic* (or opposing) *effect.* In some instances an antagonistic drug effect may be extremely serious. On the other hand, drug *synergism* may occur. Drug synergism is an effect *greater than* the sum of the separate actions of two (or more) drugs. Depending on the agents involved, synergism can be serious.

An illustration of drug synergism is seen in the individual using secobarbital (Seconal) indiscriminately, taking more of the drug than is ordered by the physician. If whiskey is also taken at the same time, the action of the barbiturate may be potentiated and the individual will most likely obtain a greater response from the combination of the two agents than from either of the agents taken singly. For example, the ordinary effect of 1 ounce of whiskey is a slightly elevated feeling; that of 1 capsule of Seconal is sleep. Taken together, however, these agents may produce *deep* sleep. On occasion, the results of a combination such as this can be extremely serious and even fatal.

The **route of administration** is another consideration that may influence drug action. The intravenous route of administration almost always produces the most rapid drug effect, whereas the oral route almost always produces the slowest. Some drugs may be manufactured to be absorbed slowly or to have a delayed absorption. Examples of these products are enteric coated aspirin, procaine penicillin, and protamine zinc insulin.

It must be remembered that all drugs administered orally, parenterally, or sublingually will not produce the desired results in exactly the same time. For example, an intravenous short-acting barbiturate produces its effect in a matter of seconds, whereas an intravenously administered diuretic may require 3, 4, or even more minutes to produce diuresis. Similarly, an oral drug may work faster when the stomach is empty rather than full.

Drugs are complex chemicals producing a variety of effects on the body. No drug is absolutely safe, and all drugs appear to be capable of producing serious adverse effects, at least in some individuals.

The **autonomic nervous system** is one part of the peripheral nervous system. The autonomic nervous system has two divisions: the *sympathetic nervous system* and the *parasympathetic nervous system.*

The sympathetic nervous system tends to regulate the expenditure of energy and is operative when the organism is confronted with stressful situations such as danger or intense emotion. The parasympathetic nervous system works to help conserve body energy; it is partly responsible for such activities as slowing the heart, digestion of food, and elimination of body wastes.

There are two neurohormones of the sympathetic nervous system that are of clinical significance as adrenergic drugs: **epinephrine** (also called adrenaline) and **norepinephrine** (also called noradrenaline). Epinephrine is secreted by the medulla (central portion) of the adrenal gland. Norepinephrine is mainly found at the nerve endings of sympathetic (also called adrenergic) nerve fibers.

Types of Adrenergic Drugs

There are two types of adrenergic drugs: **catecholamines** and **noncatecholamines.** The catecholamines, organic compounds normally found in the sympathetic nervous sys-

Chapter 2

Adrenergic Drugs