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药理学

（第3版）

STEPHANIE T. WEISS

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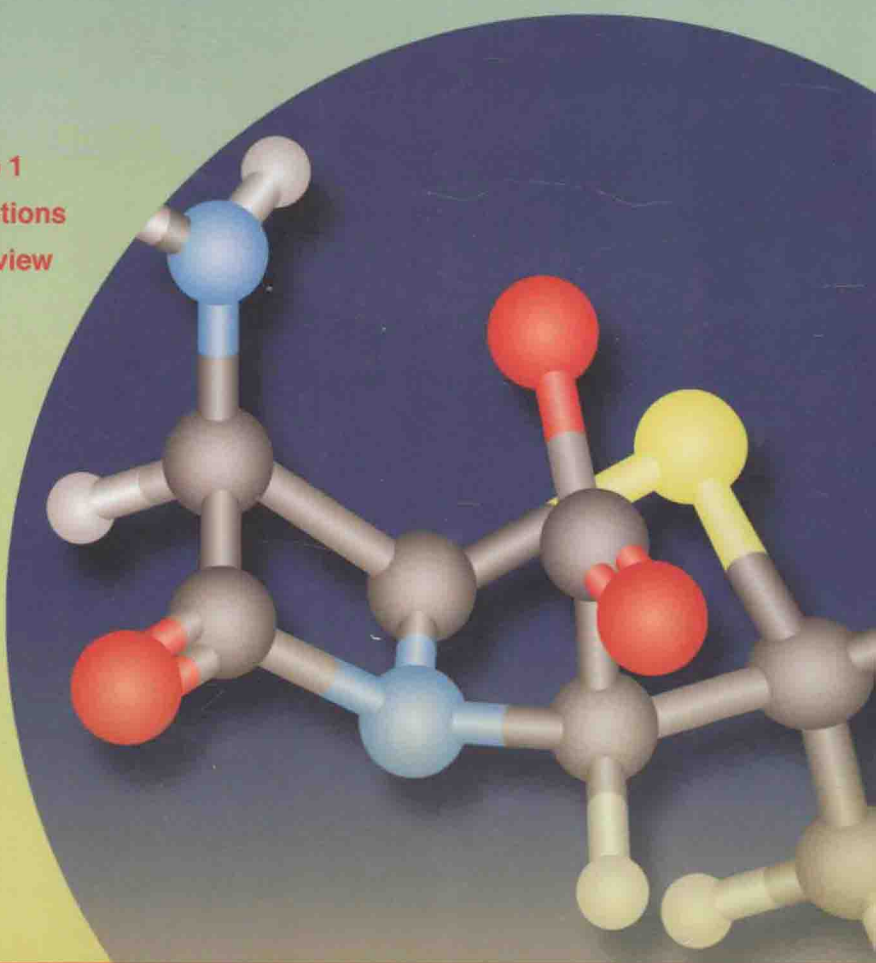

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High-Yield™ 药理学

Pharmacology

（第3版）

Stephanie T. Weiss, PhD

Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Cleveland, Ohio

First and Second Editions by

Daryl Christ, PhD

Associate Professor of Pharmacology
South Bend Center for Medical Education
Indiana University School of Medicine
Notre Dame, Indiana

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出版说明

High-Yield™ 系列丛书是针对美国医师执照考试（United States Medical Licensing Examination, USMLE）的知名品牌图书，受到世界各地读者的欢迎。该系列丛书具有以下特色：

1. 内容高度概括，重点突出，有利于读者快速掌握学科的核心知识。
2. 编排新颖，既有基础知识要点的介绍，又有以疾病为核心的综合归纳，并体现了相关学科的横向联系。
3. 语言规范、地道，既有利于读者快速掌握专业词汇，又有利于医学英语思维的培养。

本系列丛书是参加美国医师执照考试的必备辅导用书，也可作为我国医学院校从事双语教学的教材和参考用书，对教师进行英语授课，学生学习、参加考试具有重要的参考价值。

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This book is dedicated to the spirit of the Cleveland Clinic Lerner College of Medicine.

Preface

The discipline of pharmacology encompasses both how drugs affect the body (pharmacodynamics), as well as how the body affects drugs (pharmacokinetics). Because it is such an interdisciplinary field, pharmacology necessarily is built upon a foundation consisting of nearly every other basic science discipline that is part of a medical school curriculum. You must have a good grasp of physiology, pathology, biochemistry, microbiology, and molecular biology in order to study pharmacology. Even many disciplines that people have not traditionally associated with pharmacology are turning out to be essential for understanding pharmacology, such as anatomy and genetics. In fact, one of the hottest areas in pharmacology right now is pharmacogenomics, where a patient's treatment is tailored based upon his or her unique genetic makeup.

This edition of *High-Yield Pharmacology* has been substantially updated and revised. Specifically, new sections on biologics have been added in the appropriate chapters, as well as several new figures and tables. In addition, the cardiovascular pharmacology chapter has been expanded and split in half, reflecting the rapid growth in the pharmacology of this area. Readers who desire a very brief review can read the bolded printed text, which highlights the most important concepts in each chapter. In addition, the index can be used to help you review the class of every drug in the book.

It is unfortunate that many medical students approach pharmacology as just a list of drug names and side effects that must be memorized for the United States Medical Licensing Examination. You may be using this book to review pharmacology for Step 1 of the USMLE, and I hope you will find it helpful as you prepare. But I also hope that it will give you at least an inkling of how interesting and dynamic the field of pharmacology is. Please feel free to contact me at weisss@ccf.org if you have any comments or suggestions about the book.

Stephanie T. Weiss

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Contents

Chapter 1

General Principles

I Pharmacokinetics: General Principles

A. PHARMACOKINETICS is the study of the movement of drugs into and out of the body, including **absorption (bioavailability), distribution, metabolism (biotransformation),** and **elimination (ADME).**

B. Clinical pharmacokinetics, which involves the **mathematical description** of the **processes of ADME,** is useful to predict the serum drug concentrations under various conditions.

C. PHARMACOKINETICS can be thought of as **what the body does to the drug.**

II Pharmacokinetics: Administration and Absorption of Drugs

A. Many routes of drug administration can be used.

1. The oral route (PO) is usually preferred.

a. **Advantages** include:

i. **Convenience**

ii. A **large surface area** for absorption

iii. Fewer **abrupt changes of serum drug concentrations** than with parenteral administration

b. **Disadvantages** include:

i. **First-pass metabolism** by the liver

(a) All the blood flow from the intestinal tract goes initially to the liver through the portal vein; therefore the **drug may be metabolized before being distributed** to the other tissues in the body

(b) First-pass metabolism of a drug can be **avoided by parenteral administration of the drug** and partially avoided by rectal administration.

ii. **Systemic exposure to the drug**

2. The parenteral routes of administration are technically more difficult and usually must be performed by a health care professional. Common methods are **inhalation, sublingual, intravenous (IV), intramuscular (IM), and subcutaneous (SQ) administration.**

a. **Advantages** include:

i. A **faster onset** (usually)

ii. **More reliable** absorption

iii. **No first-pass metabolism**

b. **Disadvantages** include:

i. **More difficult** administration

ii. **Pain or necrosis** at the site of infection
iii. Possibility of **infection**
iv. **Toxicity from a bolus intravenous (IV) injection**
v. **Necessity of dissolving the drug if given intravenously**

B. Some drugs are actively or passively transported by carrier proteins, but the movement of drugs across cell membranes usually occurs passively by **diffusion.**

C. THE RATE OF DIFFUSION IS HIGH IF:

1. The unionized form of a drug has a high lipid solubility.

a. Lipid solubility is related to the oil-water partition coefficient.
b. Cell membranes are basically lipoidal in nature, and only lipid soluble substances will diffuse through them.

2. A large proportion of the drug is present in the unionized form.

a. **Only the unionized form can cross cell membranes,** because the ionized form will have a very low solubility in lipids.
b. The equilibrium between the ionized (A^-) and unionized (HA) forms of a weak acid is:

$$\mathbf{HA \leftrightarrow H^+ + A^-}$$

c. The equilibrium constant (K_a) for the dissociation of an acid is defined as:

$$\mathbf{K_a = \frac{[A^-][H^+]}{[HA]}}$$

d. By taking the negative log (–log) of both sides of the K_a expression and rearranging, we can get the Henderson–Hasselbalch equation for a weak acid:

$$\mathbf{pH = pK_a + \log \frac{[A^-]}{[HA]}}$$

e. The proportion of unionized drug will depend on the pH and can be determined with the Henderson–Hasselbalch equation.
f. Weak bases also dissociate, and the equation for dissociation of the conjugate acid of a weak base is:

$$\mathbf{HB^+ \leftrightarrow H^+ + B}$$

g. The equilibrium constant (K_a) for the dissociation of the conjugate acid of a weak base is defined as:

$$\mathbf{K_a = \frac{[B][H^+]}{[HB^+]}}$$

h. By taking the negative log (–log) of both sides of the K_a expression and rearranging, we can get the Henderson–Hasselbalch equation for a weak base:

$$\mathbf{pH = pK_a + \log \frac{[B]}{[HB^+]}}$$

i. Note that the conjugate base should always go in the numerator, while the conjugate acid belongs in the denominator.
j. When the pH equals the pK_a, 50% of a drug will be ionized and 50% will be unionized.
k. The most dramatic changes in the amounts of ionized and unionized drug occur with pH changes near the pK_a.