Bertram G. Katzung
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BASIC & CLINICAL PHARMACOLOGY

12th Edition

Mc Graw Hill LANGE™

SCHEDULE OF CONTROLLED DRUGS[1]

SCHEDULE I

(All nonresearch use illegal under federal law.)

Flunitrazepam (Rohypnol)

Narcotics:

Heroin and many nonmarketed synthetic narcotics

Hallucinogens:

LSD

MDA, STP, DMT, DET, mescaline, peyote, bufotenine, ibogaine, psilocybin, phencyclidine (PCP; veterinary drug only)

Marijuana

Methaqualone

SCHEDULE II

(No telephone prescriptions, no refills.)[2]

Opioids:

Opium

Opium alkaloids and derived phenanthrene alkaloids: codeine, morphine, (Avinza, Kadian, MSContin, Roxanol), hydromorphone (Dilaudid), oxymorphone (, Exalgo), oxycodone (dihydroxycodeinone, a component of Oxycontin, Percodan, Percocet, Roxicodone, Tylox)

Designated synthetic drugs: meperidine (Demerol), methadone, levorphanol (Levo-Dromoran), fentanyl (Duragesic, Actiq, Fentora), alfentanil (Alfenta), sufentanil (Sufenta), remifentanil (Ultiva), tapentadol (Nycynta)

Stimulants:

Coca leaves and cocaine

Amphetamine

Amphetamine complex (Biphetamine)

Amphetamine salts (Adderall)

Dextroamphetamine (Dexedrine, Procentra)

Lisdexamfetamine (Vyvanse)

Methamphetamine (Desoxyn)

Methylphenidate (Ritalin, Concerta, Methylin, Daytrana, Medadate)

Above in mixtures with other controlled or uncontrolled drugs

Cannabinoids:

Nabilone (Cesamet)

Depressants:

Amobarbital (Amytal)

Pentobarbital (Nembutal)

Secobarbital (Seconal)

SCHEDULE III

(Prescription must be rewritten after 6 months or five refills.)

Opioids:

Buprenorphine (Buprenex, Subutex)

Mixture of above Buprenorphine and Naloxone (Suboxone)

The following opioids in combination with one or more active non-opioid ingredients, provided the amount does not exceed that shown:

Codeine and dihydrocodeine: not to exceed 1800 mg/dL or 90 mg/tablet or other dosage unit

Dihydrocodeinone (hydrocodone in Hycodan, Vicodin, and Lortab): not to exceed 300 mg/dL or 15 mg/tablet

Opium: 500 mg/dL or 25 mg/5 mL or other dosage unit (paregoric)

Stimulants:

Benzphetamine (Didrex)

Phendimetrazine (Bontril)

Depressants:

Schedule II barbiturates in mixtures with noncontrolled drugs or in suppository dosage form

Butabarbital (Butisol)

Ketamine (Ketalar)

Cannabinoids:

Dronabinol (Marinol)

Anabolic Steroids:

Fluoxymesterone (Androxy)

Methyltestosterone (Android, Testred, Methitest)

Nandrolone decanoate (Deca-Durabolin) Non US

Nandrolone phenpropionate (Durabolin) Non US

Oxandrolone (Oxandrin), Oxymetholone (Androl-50)

Stanozolol (Winstrol),

Testolactone (Teslac),

Testosterone and its esters

SCHEDULE IV

(Prescription must be rewritten after 6 months or five refills; differs from Schedule III in penalties for illegal possession.)

Opioids:

Butorphanol (Stadol)

Difenoxin 1 mg + atropine 25 mcg (Motofen)

Pentazocine (Talwin)

Stimulants:

Armodafinil (Nuvigil)

Diethylpropion (Tenuate) not in US

Modafinil (Provigil)

Phentermine (Ionamin, Adipex-P)

Depressants:

Benzodiazepines

Alprazolam (Xanax)

Chlordiazepoxide (Librium)

Clonazepam (Klonopin)

Clorazepate (Tranxene)

Diazepam (Valium)

Estazolam (ProSom)

Flurazepam (Dalmane)

Halazepam (Paxipam)

Lorazepam (Ativan)

Midazolam (Versed)

Oxazepam (Serax)

Prazepam (Centrax)

Quazepam (Doral)

Temazepam (Restoril)

Triazolam (Halcion)

Chloral hydrate (Somnote)

Eszopiclone (Lunesta)

Meprobamate (Equanil, Miltown, etc)

Methobarbital (Mebaral)

Methohexital (Brevital)

Paraldehyde

Phenobarbital

Zaleplon (Sonata)

Zolpidem (Ambien)

SCHEDULE V

(As any other nonopioid prescription drug)

Codeine: 200 mg/100 mL

Difenoxin preparations: 0.5 mg + 25 mcg atropine

Dihydrocodeine preparations: 10 mg/100 mL

Diphenoxylate (not more than 2.5 mg and not less than 0.025 mg of atropine per dosage unit, as in Lomotil)

Ethylmorphine preparations: 100 mg/100 mL

Opium preparations: 100 mg/100 mL

Pregabalin (Lyrica)

Pyrovalerone (Centroton, Thymergix)

[1]See http://*www.usdoj.gov/dea/pubs/scheduling.html* for additional details.

[2]Emergency prescriptions may be telephoned if followed within 7 days by a valid written prescription annotated to indicate that it was previously placed by telephone.

a LANGE medical book

Basic & Clinical Pharmacology

Twelfth Edition

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Notice

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Preface

The twelfth edition of *Basic & Clinical Pharmacology* continues the important changes inaugurated in the eleventh edition, with extensive use of full-color illustrations and expanded coverage of transporters, pharmacogenomics, and new drugs. Case studies have been added to several chapters and answers to questions posed in the case studies now appear at the end of each chapter. As in prior editions, the book is designed to provide a comprehensive, authoritative, and readable pharmacology textbook for students in the health sciences. Frequent revision is necessary to keep pace with the rapid changes in pharmacology and therapeutics; the 2–3 year revision cycle of the printed text is among the shortest in the field and the availability of an online version provides even greater currency. In addition to the full-color illustrations, other new features have been introduced. The Case Study Answer section at the end of chapters will make the learning process even more interesting and efficient. The book also offers special features that make it a useful reference for house officers and practicing clinicians.

Information is organized according to the sequence used in many pharmacology courses and in integrated curricula: basic principles; autonomic drugs; cardiovascular-renal drugs; drugs with important actions on smooth muscle; central nervous system drugs; drugs used to treat inflammation, gout, and diseases of the blood; endocrine drugs; chemotherapeutic drugs; toxicology; and special topics. This sequence builds new information on a foundation of information already assimilated. For example, early presentation of autonomic nervous system pharmacology allows students to integrate the physiology and neuroscience they have learned elsewhere with the pharmacology they are learning and prepares them to understand the autonomic effects of other drugs. This is especially important for the cardiovascular and central nervous system drug groups. However, chapters can be used equally well in courses and curricula that present these topics in a different sequence.

Within each chapter, emphasis is placed on discussion of drug groups and prototypes rather than offering repetitive detail about individual drugs. Selection of the subject matter and the order of its presentation are based on the accumulated experience of teaching this material to thousands of medical, pharmacy, dental, podiatry, nursing, and other health science students.

Major features that make this book particularly useful in integrated curricula include sections that specifically address the clinical choice and use of drugs in patients and the monitoring of their effects—in other words, *clinical pharmacology* is an integral part of this text. Lists of the commercial preparations available, including trade and generic names and dosage formulations, are provided at the end of each chapter for easy reference by the house officer or practitioner writing a chart order or prescription.

Significant revisions in this edition include:

- In addition to the Case Studies used to open many chapters, Case Study Answers at the end of these chapters provide an introduction to the clinical applications of the drugs discussed.
- A Drug Summary Table is placed at the conclusion of most chapters; these provide a concise recapitulation of the most important drugs.
- Many new illustrations in full color provide significantly more information about drug mechanisms and effects and help to clarify important concepts.
- Major revisions of the chapters on sympathomimetic, sympathoplegic, antipsychotic, antidepressant, antidiabetic, anti-inflammatory, and antiviral drugs, prostaglandins, nitric oxide, hypothalamic and pituitary hormones, and immunopharmacology.
- Continued expansion of the coverage of general concepts relating to newly discovered receptors, receptor mechanisms, and drug transporters.
- Descriptions of important new drugs released through August 2011.

An important related educational resource is *Katzung & Trevor's Pharmacology: Examination & Board Review,* ninth edition (Trevor AJ, Katzung BG, & Masters SB: McGraw-Hill, 2010). This book provides a succinct review of pharmacology with over one thousand sample examination questions and answers. It is especially helpful to students preparing for board-type examinations. A more highly condensed source of information suitable for review purposes is *USMLE Road Map: Pharmacology,* second edition (Katzung BG, Trevor AJ: McGraw-Hill, 2006).

This edition marks the 30th year of publication of *Basic & Clinical Pharmacology.* The widespread adoption of the first eleven editions indicates that this book fills an important need. We believe that the twelfth edition will satisfy this need even more successfully. Spanish, Portuguese, Italian, French, Indonesian, Japanese, Korean, and Turkish translations are available. Translations into other languages are under way; the publisher may be contacted for further information.

I wish to acknowledge the prior and continuing efforts of my contributing authors and the major contributions of the staff at Lange Medical Publications, Appleton & Lange, and McGraw-Hill,

and of our editors for this edition, Donna Frassetto and Rachel D'Annucci Henriquez. I also wish to thank my wife, Alice Camp, for her expert proofreading contributions since the first edition.

This edition is dedicated to the memory of James Ransom, PhD, the long-time Senior Editor at Lange Medical Publications, who provided major inspiration and invaluable guidance through the first eight editions of the book. Without him, this book would not exist.

Suggestions and comments about *Basic & Clinical Pharmacology* are always welcome. They may be sent to me in care of the publisher.

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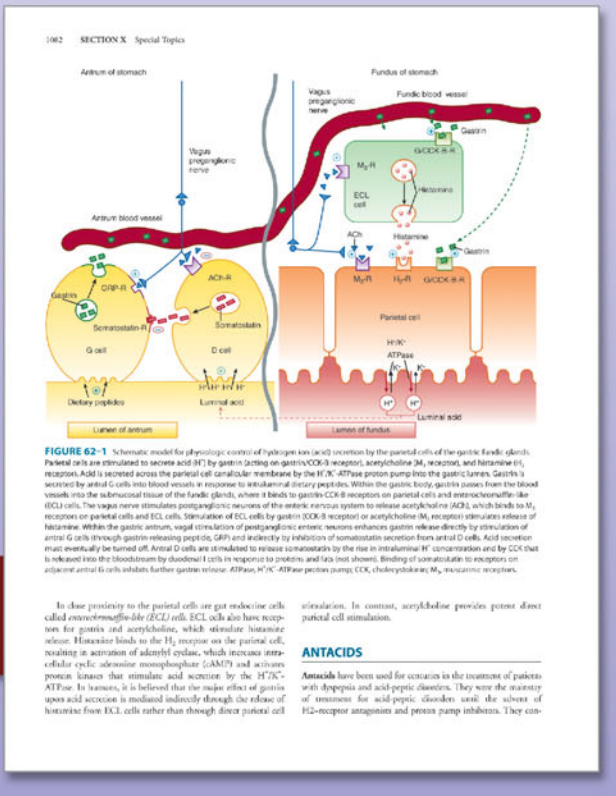
*Deceased

Key Features of *Basic & Clinical Pharmacology, 12e*

The most comprehensive, authoritative, and engaging pharmacology textbook for students in the health sciences

Key Features

- More than 300 full-color illustrations
- Emphasis is placed on discussion of drug groups and prototypes within each chapter
- NEW case studies open several chapters, adding clinical relevance to the material
- NEW case study answers at the end of the chapters provide an introduction to the clinical application of the drugs discussed
- NEW drug summary tables conclude most chapters, providing a concise summary of the most important drugs
- Expanded coverage of general concepts relating to newly discovered receptors, receptor mechanisms, and drug transporters
- Lists of the commercial preparations available, including trade and generic names and dosage formulations, are provided at the end of each chapter
- Selection of the material and order of presentation is based on the author's years of experience in teaching this material to thousands of students
- Material is organized according to the sequence used in most pharmacology courses


1002 SECTION X Special Topics

Antrum of stomach

Fundus of stomach

Vagus preganglionic nerve

Fundic blood vessel

Gastrin

G/CCK-B-R

M_3-R

ECL cell

Histamine

Antrum blood vessel

ACh

Histamine

Gastrin

ACh-R

GRP-R

Gastrin

Somatostatin-R

Somatostatin

M_3-R

H_2-R

G/CCK-B-R

Parietal cell

G cell

D cell

H^+/K^+ ATPase

K^+

K^+

H^+

H^+

Dietary peptides

Luminal acid

Luminal acid

Lumen of antrum

Lumen of fundus

FIGURE 62–1 Schematic model for physiologic control of hydrogen ion (acid) secretion by the parietal cells of the gastric fundic glands. Parietal cells are stimulated to secrete acid (H^+) by gastrin (acting on gastrin/CCK-B receptor), acetylcholine (M_3 receptor), and histamine (H_2 receptors). Acid is secreted across the parietal cell canalicular membrane by the H^+/K^+-ATPase proton pump into the gastric lumen. Gastrin is secreted by antral G cells into blood vessels in response to intraluminal dietary peptides. Within the gastric body, gastrin passes from the blood vessels into the submucosal tissue of the fundic glands, where it binds to gastrin-CCK-B receptors on parietal cells and enterochromaffin-like (ECL) cells. The vagus nerve stimulates postganglionic neurons of the enteric nervous system to release acetylcholine (ACh), which binds to M_3 receptors on parietal cells and ECL cells. Stimulation of ECL cells by gastrin (CCK-B receptor) or acetylcholine (M_3 receptor) stimulates release of histamine. Within the gastric antrum, vagal stimulation of postganglionic enteric neurons enhances gastrin release directly by stimulation of antral G cells (through gastrin-releasing peptide, GRP) and indirectly by inhibition of somatostatin secretion from antral D cells. Acid secretion must eventually be turned off. Antral D cells are stimulated to release somatostatin by the rise in intraluminal H^+ concentration and by CCK that is released into the bloodstream by duodenal I cells in response to proteins and fats (not shown). Binding of somatostatin to receptors on adjacent antral G cells inhibits further gastrin release. ATPase, H^+/K^+-ATPase proton pump; CCK, cholecystokinin; M_3, muscarinic receptors.

In close proximity to the parietal cells are gut endocrine cells called *enterochromaffin-like (ECL) cells*. ECL cells also have receptors for gastrin and acetylcholine, which stimulate histamine release. Histamine binds to the H_2 receptor on the parietal cell, resulting in activation of adenylyl cyclase, which increases intracellular cyclic adenosine monophosphate (cAMP) and activates protein kinases that stimulate acid secretion by the H^+/K^+-ATPase. In humans, it is believed that the major effect of gastrin upon acid secretion is mediated indirectly through the release of histamine from ECL cells rather than through direct parietal cell stimulation. In contrast, acetylcholine provides potent direct parietal cell stimulation.

ANTACIDS

Antacids have been used for centuries in the treatment of patients with dyspepsia and acid-peptic disorders. They were the mainstay of treatment for acid-peptic disorders until the advent of H_2-receptor antagonists and proton pump inhibitors. They con-

Hundreds of full-color illustrations enrich the text