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Arnold Stern

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Pharmacology

PreTest® Self-Assessment and Review

Tenth Edition

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Pharmacology

PreTest® Self-Assessment and Review

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

In this tenth edition of *Pharmacology: PreTest® Self-Assessment and Review,* significant changes and improvements have been made. Questions that use clinical vignettes have been added; the responses require interpretation and data synthesis. The number of items per group of matching questions has been reduced in accordance with the new format used on United States Medical Licensing Examination (USMLE) Step 1. A High-Yield Facts section containing two sample Drug Classification Tables has been added; these tables serve as simple examples for collating and comparing information about various drug classes. References have been updated, and this section is preceded by a List of Abbreviations and Acronyms used throughout the book.

The author remains indebted to his students and colleagues at New York University Medical Center for their continuing support and encouragement.

Introduction

Each *PreTest® Self-Assessment and Review* allows medical students to comprehensively and conveniently assess and review their knowledge of a particular basic science—in this instance, pharmacology. The 490 questions parallel the format and degree of difficulty of the questions found in the United States Medical Licensing Examination (USMLE) Step 1. Practicing physicians who want to hone their skills before USMLE Step 3 or recertification may find this to be a good beginning in their review process.

Each question is accompanied by an answer, a paragraph explanation, and a specific page reference to an appropriate textbook. A bibliography listing sources can be found following the last chapter.

Before each chapter, a list of key terms or classifications of drugs or both is included to aid review. In addition, suggestions for effective study and review have been added afterward.

The most effective method of using this book is to complete one chapter at a time. Prepare yourself for each chapter by reviewing from your notes and favorite text the drugs classes listed at the beginning of each section and the drugs listed in the "High-Yield Facts" section. You should concentrate especially on the prototype drugs. Then proceed to indicate your answer by each question, allowing yourself not more than one minute for each question. In this way you will be approximating the time limits imposed by the examination.

After you finish going through the questions in the section, spend as much time as you need verifying your answers and carefully reading the explanations provided. Pay special attention to the explanations for the questions you answered incorrectly—but read *every* explanation. The editors of this material have designed the explanations to reinforce and supplement the information tested by the questions. If you feel you need further information about the material covered, consult and study the references indicated.

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High-Yield Facts

SAMPLE DRUG CLASSIFICATION TABLES

TIPS FOR LEARNING PHARMACOLOGY

Pharmacology is best learned by comparing drugs within a particular class or by their specific use.

A chart highlighting the similarities and differences among the various agents can be a helpful tool. The charts included in this section are simple examples. More elaborate charts can be constructed that would include how the drug is administered, its pharmacological effects, its adverse effects, its mechanism of toxicity (if known), and significant drug-drug interactions. For infectious disease agents, the spectrum of antimicrobial activity and the basis of antibiotic resistance can be added.

Explanations for the abbreviations used in these charts are found in the List of Abbreviations and Acronyms, which appears before the Bibliography.

Drugs for Treating Bacterial Infectious Diseases

Drug Class	Prototype	Action	Spectrum
Penicillins		Inhibit bacterial cell-wall synthesis by binding to penicillin-binding proteins, inhibiting crosslinking enzymes, and activating autolytic enzymes that disrupt bacterial cell walls.	Streptococci, meningococci, pneumococci, gram-positive bacilli, gonococci, spirochetes.
Narrow spectrum			
Penicillinase-susceptible	Penicillin G		
Penicillinase-resistant	Methicillin		Staphylococci.
Wide spectrum	Ampicillin		Similar to penicillin G; also includes *E. coli*, *P. mirabilis*, and *H. influenzae*.
Penicillinase-susceptible	Carbenicillin		Gram-negative rods and especially useful for *Pseudomonas* spp.
Cephalosporins			
First-generation	Cephalothin		Gram-positive cocci, *E. coli*, and *K. pneumoniae*.
Second-generation	Cefamandole		Greater activity against gram-negative organisms than first-generation cephalosporins.
Third-generation	Cefoperazone		Broader activity against resistant gram-negative organisms; some derivatives penetrate the blood-brain barrier.
Carbapenem	Imipenem		Wide action against gram-positive cocci, gram-negative rods, and some anaerobes.
Monobactam	Aztreonam		Resistant to β-lactamases produced by gram-negative rods.

Macrolides	Erythromycin	Inhibits protein synthesis by binding to part of the 50S ribosomal . subunit	Gram-positive cocci, mycoplasma, corynebacteria, *Legionella, Ureaplasma, Bordetella.*
Vancomycin	Vancomycin	Inhibits synthesis of cell-wall mucopeptides (peptidoglycans).	Gram-positive bacteria, especially for resistant mutants.
Chloramphenicol	Chloramphenicol	Inhibits peptide bond formation by binding to the 50S ribosomal subunit, inhibiting peptidyl transferase.	*Salmonella* and *Haemophilus* infections and meningococcal and pneumococcal meningitis.
Aminoglycosides			
Systemic	Gentamicin	Inhibits protein synthesis by binding to the 30S subunit of ribosomes, which blocks formation of the initiation complex, causing misreading of the code on the mRNA template and disrupting polysomes.	*E. coli, Enterobacter, Klebsiella, Proteus, Pseudomonas,* and *Serratia* species.
Local	Neomycin		
Tetracycline	Tetracycline	Inhibits protein synthesis by binding to the 30S ribosomal subunit, which interferes with binding of aminoacyl-tRNA.	Mycoplasma, chlamydia, rickettsia, vibrio.
Sulfa drugs	Sulfonamides	Inhibit folic acid synthesis by competitive inhibition of dihydropteroate synthase.	Gram-positive and -negative organisms, including chlamydia and nocardia.
Trimethoprim	Trimethoprim	Inhibits folic acid synthesis by inhibition of dihydrofolate reductase.	Used in combination with sulfamethoxazole.
Fluoroquinolones	Norfloxacin	Inhibits topoisomerase II (DNA gyrase).	Gram-negative organisms, including gonococci, *E. coli, K. pneumoniae, C. jejuni, Enterobacter, Salmonella,* and *Shigella* species.

Drugs for Treating Hypertension

Drug Class	Prototype	Action
Sympathetic nervous system agents		
Central	Clonidine	α_2-agonist; causes decreased sympathetic outflow.
Peripheral	Guanethidine	Uptake by transmitter vesicles in nerve depletes and replaces norepinephrine in neurosecretory vesicles.
	Prazocin	α_1-antagonist.
	Propranolol	β-antagonist.
Central and peripheral	Reserpine	Binds tightly to storage vesicles, which consequently lose their ability to concentrate and store norepinephrine.
Vasodilators		
Arterial	Hydralazine	Unknown.
	Diazoxide	Opens K^+ channels and causes hyperpolarization of smooth muscle.
Arterial and venous	Nitroprusside	Releases NO, which binds to guanylyl cyclase to generate cGMP.
Ca^{++} channel-blockers	Nifedipine	Inhibits voltage-dependent "L-type" Ca^{++} channels.
ACE inhibitors	Captopril	Inhibits conversion of angiotensin I to angiotensin II.
Diuretics		
Thiazides (benzothiadiazides)	Hydrochlorothiazide	Inhibits Na^+ channels in luminal membrane in the proximal segment of the distal tubule.
Loop agents	Furosemide	Inhibits cotransporter of Na^+, K^+, Cl^- in the ascending limb of the loop of Henle.

HIGH-YIELD FACTS

General Principles

- Serum concentration vs time graphs
  - Relationship of drug elimination half-time ($t_{1/2}$)
  - Apparent volume of distribution
  - Drug clearance
- Drug distribution
  - Henderson-Hasselbalch equations
  - Diffusion
- Partition coefficients
- Bioavailability
- Log-dose response curves

Anti-Infectives

- Cell-wall synthesis inhibitors
  - Penicillins
  - Cephalosporins
  - Monobactams
  - Carbapenem
  - Vancomycin
  - Cycloserine
- β-lactamase inhibitors
- Protein synthesis inhibitors
  - Chloramphenicol
  - Tetracyclines
  - Macrolides
  - Lincosamides
  - Aminoglycosides
- Folic acid synthesis inhibitors
  - Sulfonamides
  - Trimethoprim
- DNA synthesis inhibitors
  - Fluoroquinolones
- Antimycobacterials
  - Isoniazid
  - Rifampin
  - Ethambutol
  - Pyrizinamide
  - Streptomycin
- Antileprosy agents
- Antifungals
  - Amphotericin B
  - Flucytosine
  - Azoles
  - Terbinafine
- Antivirals
  - Antiherpes agents
- Antiretrovirals
  - Nucleoside reverse transcriptase inhibitors
  - Nonnucleoside reverse transcriptase inhibitors
  - Protease inhibitors
  - Amantadine
  - Interferons
  - Ribavirin
- Antiprotozoals
- Antihelminthics

Organism	Drug
Pneumococcus	Penicillin G, ampicillin
Pneumococcus (penicillin-resistant)	Fluoroquinolones
Streptococcus	Penicillin G, macrolides (allergic patients)
Staphylococcus (penicillinase-resistant)	Penicillinase-resistant penicillin
Staphylococcus (methicillin-resistant)	Vancomycin
Enterococcus	Penicillin G and gentamycin
Enterococcus (vancomycin-resistant)	Linezolid
Gonococcus	Ceftriaxone, fluoroquinolones
Menigicoccus	Penicillin G, ampicillin, cephtriaxone
Escherichia coli, Proteus, Klebsiella	Second- and third-generation cephalosporin, trimethoprim-sulfamethoxazole, ampicillin, fluoroquinolones
Shigella	Fluoroquinolones
Enterobacter, Serratia	Imipenem, trimethoprim-sulfamethoxazole, fluoroquinolones, pipericillin/tazobactam
Hemophilus	Second- or third-generation cephalosporins, trimethoprim-sulfamethoxazole, fluoroquinolones
Pseudomonas	Cephtazidime, cefepime, imipenem, aztreonam, ciprofloxacin, aminoglycoside, and extended-spectrum penicillin
Bacteroides	Metronidazole, clindamycin
Mycoplasma	Macrolide, tetracycline
Treponema	Penicillin G

Drug	Adverse Drug Reaction
Penicillins	Cross-allergenicity
Cephalosporins	Cross-allergenicity
	Contraindicated in patients with history of anaphylaxis to penicillins
	Disulfiram-like reaction with ethanol
Vancomycin	"Red person" syndrome
Chloramphenicol	"Gray baby syndrome," aplastic anemia
Macrolides	Arrhythmias with coadministration of astemizole

Drug	Adverse Drug Reaction
Clindamycin	Clostridium difficile colitis
Aminoglycosides	Ototoxicity and nephrotoxicity
Tetracycline	Discolored teeth, enamel dysplasia, and bone growth disturbances in children
Sulfa drugs	Cross-allergenicity with other sulfa drugs and with certain diuretics and hypoglycemics
Fluoroquinolones	Tendonitis, Achilles tendon rupture, contraindicated in patients less than 18 years old because of effects on cartilage development
Amphotericin B	Shocklike reaction
Azole antifungals	Arrhythmias with astemizole
Isoniazid	Hepatotoxicity prevented by coadministration of pyridoxine
Ethambutol	Visual disturbances
Pyrazinamide	Nongouty polyarthralgias
Dapsone	Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency

Antiviral Agent	Adverse Drug Reaction
Zidovudine (AZT)	Anemia
Didanosine (ddI)	Neuropathy, pancreatitis
Stavudine (d4T)	Neuropathy
Abacavir	Hypersensitivity reaction
Efavirenz	Central nervous system toxicity
Protease inhibitors	Hepatotoxicity, hyperlipidemia, nephrolithiasis, lipodystrophy
Acyclovir	Nephropathy
Ganciclovir	Neutropenia
Foscarnet	Renal toxicity
Ribavirin	Anemia
Interferons	Flulike symptoms
Lamivudine	Lactic acidosis
Rimantadine, amantadine	Central nervous system toxicity
Zanamavir	Bronchospasm

Cancer Chemotherapy and Immunology

Cell cycle kinetics

Antimetabolites
- Cell cycle sensitive (CCS)—primarily in the S phase

Plant alkaloids
- Vinblastine and vincristine—CCS—primarily in the M phase
- Ectoposide—CCS—S and early G2 phase
- Paclitaxel—spindle poison

Antibiotics
- Bleomycin—CCS—primarily in G2 phase
- Doxyrubicin, dactinomycin, and mitomycin—cell cycle non-sensitive

Alkylating agents and hormones—cell cycle nonspecific (CCNS)

Cardiovascular and Pulmonary Systems

Drugs used in congestive heart failure
- Positive inotropes
- Diuretics
- ACE inhibitors
- PDE inhibitors
- Vasodilators

Antianginals
- Calcium channel blockers
- Nitrates
- β-adrenergic blockers

Antiarrhythmics
- Sodium channel blockers
- β-adrenergic blockers
- Potassium channel blockers
- Calcium channel blockers
- Adenosine
- Digoxin

Antihypertensives
- Diuretics
- Adrenergic receptor blockers
- Vasodilators
- Angiotensin antagonists

Antihyperlipidemics
- Resins
- HMG-CoA reductase inhibitors
- Niacin
- Gemfibrozil

Drugs used in clotting disorders
- Clot reducers
  - Anticoagulants
  - Antiplatelet agents
  - Thrombolytics
- Clot facilitators
  - Replacement factors
  - Plasminogen inhibitors

Antiasthmatics
- Bronchodilators
- Anti-inflammatories
- Leukotriene antagonists